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ABSTRACT BOOK

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on Lung Health of the
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Tuberculosis and Lung Disease (The Union)**

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The International Journal of Tuberculosis and Lung Disease

The Official Journal of the International Union Against Tuberculosis and Lung Disease

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SYMPOSIA: THURSDAY 25 OCTOBER 2018

SP01 Children exposed to tuberculosis have rights too! Improving child contact identification

Very low yield of child TB contacts to adult TB cases in Lesotho

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Identification of children exposed to TB in the household is essential to eliminating pediatric TB. Review of data on the number of child contacts for all TB patients listed in the TB Register was done for the period 01/2017 through 06/2018 at five clinics in Berea District, Lesotho. Of 512 new adult TB patients in the TB register, 468 patient TB cards were located with 146 child contacts recorded, for a ratio of 0.29 child contacts to TB patients. This very low ratio was noted despite training of nurses about the importance of contact tracing and the rollout of a contact management register in November 2015. Effective identification of children at risk for TB may require a broadening of household definition and a detailed risk assessment beyond household exposure. Our findings indicate that healthcare providers would benefit from specific tools to aid in defining household and assessing exposure risk of potential child contacts. The PREVENT Study for Yael Hirsch-Moverman's presentation.

Child contact identification: a comparison between urban and rural populations in Kenya

A Masese¹ ¹Center for Health Solution, Nairobi, Kenya.
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WHO recommends that high TB burden countries conduct child contact management to identify and care for children exposed to TB in the household. Through a TB Reach funded project, we implemented an active child contact management strategy in nine counties across Kenya in both urban and rural health facility settings. The strategy includes healthcare worker training, child contact management registers, and transport reimbursement. Previous data from our setting demonstrated that 1 child contact would be identified for every 2 index cases. In urban settings, 52/289 (18%) bacteriologically-positive index cases had contacts documented compared to 58/183 (32%) in rural settings. Our findings indicate that contact identification in urban settings is lower than rural settings at 1 contact for every 6 bacteriologically-positive index cases compared to 1 for every 3 bacteriologically-positive index cases in rural settings. It is important to consider potential reasons for this discrepancy and explore possible solutions. TB REACH Fikia Project for Ann Masese's presentation.

TB contact management experience from Pakistan: a household with a child TB patient can have more children with TB

H Hussain¹ ¹IRD Global, Singapore, Singapore.
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A child contracting TB is a sentinel event. Systematic household contact tracing is often not performed in a household where an index case is a child as the focus is to find children exposed to bacteriologically-positive adults.

In an ongoing contact management intervention in Karachi, between 10/16-03/18 we verbally screened and investigated 5,053(53%) adults and 4,461(47%) children (1,909 (43%).

Child contact screening and management in high TB setting in Papua province, Indonesia

T Lestari¹ ¹Center for Tropical Medicine, Universitas Gadjah Mada, Yogyakarta city, Indonesia.
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We report initial findings from research to improve tuberculosis contact management using a multi-component intervention at three primary healthcare centres (PHC) and two hospitals in Papua, Indonesia.

The intervention comprises training, staff support using social media, guideline dissemination and quality-improvement workshops. During the baseline period, from January to December 2016, only 11/1213 (0,9%) tuberculosis cases had contact tracing undertaken. This increased to 111/213 (52%) at PHCs in the first six months after study commencement in mid-September 2017, but only to 18/511 (3,5%) in the hospitals. Since study commencement, 59/93 (63%) children.

Reduced losses in the latent tuberculosis care cascade in Regional Prospective Observational Research in Tuberculosis (RePORT-) Brazil

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The Brazilian Ministry of Health estimated that in 2015, only 37% of TB contacts in the country were investigated for latent tuberculosis infection (LTBI). Most losses in the cascade occurred in the first two steps: 57% of contacts were identified, and of these, only 9% were tested for LTBI.

We examined the LTBI cascade of care in RePORT-Brazil, an ongoing prospective cohort study that enrolls and follows close contacts (children and adults) of culture-confirmed pulmonary TB patients. Since 09/15, 718 index TB cases and 1334 contacts have been identified at study sites in Rio de Janeiro, Salvador, and Manaus. Of contacts, 899 (67%) were evaluated for LTBI.

Preliminary results indicate a lower proportion of losses in the LTBI cascade of care in RePORT-Brazil sites than reported in Brazil. The groups at highest risk of progression to active TB, i.e., children aged <5 years and PLHIV, had high cascade completion rates.

SP02 Social and programmatic solutions to engage marginalised populations – the case of indigenous communities

Tuberculosis in indigenous communities: global and Peruvian evidence

C Evans¹ ¹Universidad Peruana Cayetano Heredia, Lima, Peru. e-mail: carlton.evans@ifhad.org

Indigenous communities worldwide experience an elevated burden of TB and TB-associated morbidity, mortality, stigma, social and economic impoverishment. These issues are confounded by limited access to healthcare and to socioeconomic support. Global evidence concerning the scale of these challenges will be reviewed, taking into account that the marginalized nature of many indigenous populations limits available information.

Published evidence will be critically reviewed concerning the acceptability, impact and sustainability of interventions focused on TB in indigenous communities, including TB prevention, case finding, cure and strategies towards elimination. Evidence concerning interventions that empower people to tackle TB in their own communities will be emphasised.

These global themes will also be considered for the example of Peru, including the Amazonian rain forest and Andean mountain communities in their indigenous setting, and after displacement to desert periurban and urban shantytown slum communities.

Integrating novel approaches to enhance tuberculosis elimination efforts in indigenous communities

V Cook¹ ¹University of British Columbia, Vancouver, Canada. e-mail: victoria.cook@bccdc.ca

Some Indigenous communities in Canada have ongoing challenges with tuberculosis (TB). This talk will briefly review novel strategies to enhance TB contact investigations in community including social network analysis (SNA), geographic information systems (GIS), genotyping and genomics.

Using data to describe TB transmission and support the prioritization of contacts for LTBI treatment will be emphasized.

TB in indigenous peoples: achieving meaningful results through culturally appropriate interventions

P Orr¹ ¹University of Manitoba - Faculty of Medicine, Manitoba, Canada. e-mail: porr@hsc.mb.ca

This talk will address TB prevention and care through a culturally appropriate lens. Using the Canadian aboriginal population as an example, lessons learned in working with indigenous populations for TB care and control, will be shared. The talk will also draw comparisons with work in other cultural contexts and recommend how best practices can be shared between countries.

A holistic approach to tuberculosis control by incorporating traditional perspectives of indigenous people

P Basta¹ ¹Oswaldo Cruz Foundation, Rio de Janeiro, Brazil. e-mail: paulobasta@gmail.com

This presentation will provide unique perspectives of the Brazilian indigenous peoples about tuberculosis. Their explanations and reasoning provide insight into their thought process and deserve the attention of people responsible for developing public health policies. The talk will describe work done in Brazil and compare with work done elsewhere. To conclude, the talk will summarize recommendations for health systems to integrate traditional medicine with bio medicine for the effective control of TB among indigenous populations.

SP03 Monitoring the tobacco industry: a vital factor in tobacco control

Step up in the monitoring the tobacco industry: models in monitoring tobacco industry and the way forward in working together

B Ritthiphakdee¹ ¹Global Centre for Good Governance in Tobacco Control (GGTC), Thammasart University, Patumthani, Thailand. e-mail: bungon@ggtc.world

WHO Framework Convention on Tobacco Control (WHO FCTC) is the first international treaty negotiated under the auspices of WHO. In the Preamble, Parties recognise the need “to be alert to any efforts by the tobacco industry to undermine or subvert tobacco control efforts and the need to be informed of activities of the tobacco industry that have a negative impact on tobacco control efforts”. In an effort to strengthen Parties’ monitoring of the tobacco industry activities in accordance with Article 5.3 guidelines, in 2016 the Convention Secretariat started a pilot project aimed at establishing

tobacco industry observatories in selected institutions of Parties to the Convention. Currently the observatories are operational in three Parties (Brazil, South Africa and Sri Lanka).

This presentation will highlight the need to strengthen tobacco industry monitoring globally and way forward to work together to scale up and strengthen the implementation of Article 5.3 and its Guidelines.

Observatory on the tobacco industry: strategies in Brazil two years after launching

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The tobacco industry is the vector in tobacco-related diseases epidemic. Their main aim is to increase profits, which is an antagonist principle to public health objective of reducing tobacco consumption. By ratifying the WHO FCTC in 2005, Brazilian government has committed, among other things, to monitor tobacco industry activities in order to comply with Article 5.3 of the Convention. In this regard, the Fiocruz/Ministry of Health launched the ‘Observatory on Tobacco Industry Strategies’ in March 2016. It is the first Observatory in the American continent and the first in a public health institution. After two years we have now gathered more than 850 documents that show us how the industry have been acting over the years. The Observatory has been very useful in complying with the ‘Monitoring’ part of the MPOWER, the WHO initiative in tobacco control.

Capacity building in tobacco industry monitoring by the Africa Observatory: infrastructure for sustainable tobacco industry monitoring

L Ayo-Yusuf¹ ¹Sefako Makgatho Health Sciences University, Pretoria, South Africa. e-mail: lekan.ayo-yusuf@smu.ac.za

Effective monitoring of tobacco industry interference (TII) in Africa requires the development of an effective network of tobacco control stakeholders with the necessary skills and capacity to monitor and further develop tobacco control in Africa. The African TIM Observatory - African Centre for Tobacco Industry Monitoring and Policy Research (ATIM), has been supporting the development of this capacity through short courses, drawing on global expertise on both tobacco industry monitoring (TIM) and, tobacco control research and advocacy. The training also provide the basis for development of policy analysis capabilities, which is further enhanced through post-attendance mentorship.

The project was conceived out of need to further develop current initiatives on TIM in Africa, and crucially to develop capacity to utilise this information effectively

and timeously in countering TII. These efforts will culminate in the formation of effective networks at country and regional levels to spearhead TIM and accountability and, policy research.

Industry monitoring in South Asia and the role of the Sri Lankan observatory in advocacy and action

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South Asia (SA), hosting 1.5 Billion people, contributes to 23.3% of the world population. Tobacco is a major causal factor for the increasing noncommunicable disease burden and related premature mortality in the region, hindering its progress on sustainable development. Controlling tobacco and its adverse effects in the region has a major impact at global level as SA hosts nearly one fourth of the world population. SA countries share many similarities in socio-economic contexts. They also share another major factor, British American Tobacco, the transnational tobacco giant that influences tobacco use and its control in the region. Sri Lanka hosts the first and only FCTC endorsed tobacco observatory in the region, Centre for Combating Tobacco (CCT) (www.cct.lk). CCT, functioning for its third year, is engaged in more than monitoring tobacco industry interference. The successfully tried-out advocacy model can be easily adopted, especially in countries with similar socio-cultural and economic contexts.

SP04 Building a competent workforce for decentralised, quality and patient-centred DR-TB care

How training and mentoring have accelerated the decentralisation of quality DR-TB care in Tanzania

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In 2014, the National TB Program (NTP) of Tanzania started decentralizing DR-TB care from Kibong'oto Infectious Disease Hospital (KIDH) to DR-TB initiation and ambulatory sites. The NTP with technical support from KNCV, built the capacity of DR-TB teams at DR-TB initiation sites and ambulatory sites through competency based training and hands-on clinical training at KIDH. Intensive supportive supervision and mentoring are being conducted quarterly. Staff from initiating sites train staff from the ambulatory sites and conduct clinical

mentoring. Currently, 56 DR-TB treatment initiation sites and 135 ambulatory sites are providing decentralized DR-TB treatment in the country supported by the KIDH as center of excellence. The number of DR TB patients notified increased from 124 in 2015 to 158 per year in 2017. The patient centered care, decrease of patient costs, and less costs for the health system are important benefits of this decentralized care model.

Successful decentralisation of DR-TB care through capacity building of DR-TB teams in Nigeria

S Useni¹ ¹KNCV TB Foundation Nigeria, Abuja, Nigeria. e-mail: useni.sani@kncvtbc.org

The National Tuberculosis Programme of Nigeria and main partners made important progress to decentralize DR-TB care and implement the shorter regimen and new drugs countrywide.

Since 2014 the DR-TB community care was expanded from 10 outpatient department (OPD) clinics to 148 clinics, increasing the number of patients enrolled on treatment from 423 in 2014 to 1,367 in 2017. Since September 2017, all DR-TB patients start either shorter treatment regimens or individualized treatment regimen containing new drugs.

This rapid scale up was possible through an initial training of trainers followed by a cascade of intensive, structured, task oriented trainings for health care workers of DR-TB teams (clinicians, nurses, laboratory technicians and pharmacists) at all levels of health service delivery. State DR-TB teams subsequently provided monthly hands on supportive mentoring and supervision visits to the OPD clinics and conducted home visits with the facility directly observed treatment officers.

The role of advisory bodies to build capacity of DR-TB staff in Ukraine

O Pavlova¹ ¹PATH, Kyiv, Ukraine. e-mail: opavlova@path.org

In 2017 the National Institute of TB and Lung Disease started a pilot to introduce Bedaquiline, through the USAID funded Challenge TB donation project.

The Oblast Advisory Councils and the newly established International Advisory Council are responsible for patient triage and design of an effective new drugs & (shorter) drug-resistant TB treatment regimen (ND&STR). Each patient who is potentially eligible for a new drug regimen is first vetted by an Oblast Advisory Council.

If found eligible, the International Advisory Council reviews the patient case and provides recommendations on the treatment plan. These advisory bodies have proven to be highly efficient and effective mechanisms to ensure proper patient management and good treatment success results, as well as to build capacity of health providers.

This presentation aims to share experiences on how the advisory bodies built staff competence and improved the quality of care in the introduction of ND&STR.

Implementation of the programmatic management of DR-TB benchmarking tool to improve quality of DR-TB care in Indonesia

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In early 2017 Challenge TB (CTB) and the National TB Program (NTP) of Indonesia developed and introduced a self-assessment “PMDT Benchmarking Tool”. It was used at treatment initiation centers, initially in 6 CTB supported provinces. PMDT benchmarking aims to assess current PMDT practice, improve and standardize quality of care for DR-TB patients in every site across the country. Self-assessment using the proposed benchmarks has been done by 32 PMDT hospitals in 15 provinces. Clinicians who used the tool found it very useful as it provides opportunities to discuss PMDT policies and procedures, and helped to develop action plans for quality improvement. The “PMDT benchmarking tool” is adopted by the NTP as the national supervision tool in DR-TB hospitals. This presentation aims to share experiences and lessons learned on the introduction of the “PMDT benchmarking tool.”

Access to quality DR-TB care for children with tuberculosis in Kyrgyzstan

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Children with TB are often neglected in national TB programs and international projects because they are considered “less infectious” and without significant epidemiological impact. Since January 2017 the USAID Challenge TB project led by the KNCV team in Kyrgyzstan is introducing shorter regimen and new drugs for treatment of DR-TB children and adolescents. The presentation will highlight how the children’s needs are addressed, and staff competence has increased through countrywide capacity building activities. This included conventional classroom trainings, supportive supervision visits accompanied by on-job training via clinical mentoring for clinically sound decision making. Digital health technologies were applied to ensure continuity of those activities starting from 2018.

Key results so far: 98 clinical team members were trained on diagnosis and treatment of DR-TB in children and – 25 children and adolescents were enrolled on treatment with new drugs and regimens.

SP05 Optimisation of standard drugs in the treatment of tuberculosis, finally?

What is the right dose of rifampicin?

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Rifampicin is a key drug that, when combined with pyrazinamide, reduced treatment to 6 months. The standard dose of 10 mg/kg was chosen in the 1960s because of cost. Several studies in mice and human showed that higher doses may accelerate cure and increase killing of active TB and likely also persisting bacilli.

Higher doses may lead to shorter treatment, prevention of emergence of drug resistance and decrease morbidity and mortality in severe TB such as TB meningitis. In this talk we will review the evidence and discuss the way forward.

What is the right dose of pyrazinamide?

K Dooley¹ ¹Johns Hopkins School of Medicine, Baltimore, United States of America. e-mail: kdooley1@jhmi.edu

Pyrazinamide is a sterilizing drug with unique activity against the semi-dormant “persister” and intracellular organisms that cause relapse. It also demonstrates impressive synergy with key first-line and new TB drugs. However, there is mounting evidence in mice and humans that pyrazinamide is not given at the dose and duration that optimizes its activity. Current doses do not reach concentration targets associated with maximum effect and do not approach doses associated with higher risk of hepatotoxicity in past trials.

In this talk, Dr. Dooley will review the evidence on efficacy and toxicity of pyrazinamide and explore strategies for optimizing its use.

What is the right dose of isoniazid?

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Isoniazid (INH) has been used for >60 years as a first-line agent protecting companion drugs from resistance. However, doubts remain as to the optimum dose to use in tuberculosis management. INH is metabolised by N-acetyl transferase and individuals are homozygous, heterozygous rapid or homozygous slow INH acetylators. Despite considerable differences in INH exposure resulting from these genotypic differences, it is usually stated that these differences are insignificant with use of multidrug therapy.

Personalization of dosing for each acetylator group might improve outcomes for rapid acetylators and reduce the danger of hepatotoxicity in slow acetylators.

Pro/con rifampicin against optimally dosed rifapentine, which, when and how?

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Rifampicin and rifapentine are the most promising rifamycins to shorten and optimize treatment of drug sensitive tuberculosis. Currently, there are several phase II and phase III trials ongoing to evaluate this potential effect.

In this debate we will discuss and speculate on the potential implementation of these drugs at optimized doses: what dose, how will they be included in TB programs, how can they be used in fixed dosage combinations, what effect this will have on the cost of treatment, will they be used in special populations such as TB meningitis, TB and HIV, TB in children and in pregnancy.

Pro/con rifampicin against optimally dosed rifapentine, which, when and how?

M Boeree¹ ¹The Radboud university medical center, Nijmegen, Netherlands.
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Rifampicin and rifapentine are the most promising rifamycins to shorten and optimize treatment of drug sensitive tuberculosis. Currently, there are several phase II and phase III trials ongoing to evaluate this potential effect. In this debate we will discuss and speculate on the potential implementation of these drugs at optimized doses: what dose, how will they be included in TB programs, how can they be used in fixed dosage combinations, what effect this will have on the cost of treatment, will they be used in special populations such as TB meningitis, TB and HIV, TB in children and in pregnancy.

SP06 Pharmacokinetics and pharmacodynamics of drugs used in the treatment of non-tuberculous mycobacterial infections

Buruli ulcer

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Buruli ulcer (BU) is a necrotizing cutaneous infection caused by *Mycobacterium* (*M.*) *ulcerans*, is one of the WHO's neglected tropical diseases (NTDs). The large majority of cases come from West Africa, where it affects mostly children. The characteristic feature of the disease is deep skin ulceration with undermining. Mycolactone, a lipid toxin secreted by *M. ulcerans*, is identified to be

the main underlying cause for this unique feature, but its pathogenesis remains incompletely understood. The current therapeutic modalities include antimycobacterial drugs, surgery and wound care. However, optimal management is still under investigation. Finally, its transmission route(s) also remain unknown, preventing from development of effective preventative measures. This session will provide a brief overview of this very unique mycobacterial disease from basic to clinical science, and public health implications.

Novel combination treatment for the treatment of *Mycobacterium kansasii*

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Mycobacterium kansasii is the second most common cause on non-tuberculous mycobacterial lung disease in the USA. Treatment is copied from that of tuberculosis; a combination of rifampin, isoniazid, and ethambutol administered for 12 months after negative sputum. One possible reason for the need for such a prolonged treatment duration could be that the drug doses currently recommended for *M. kansasii* have been obtained from tuberculosis drug trials, and not optimized for *M. kansasii* nor rigorously studied in combination with other drugs of potential activity in pre-clinical models. We tested several combinations of high dose moxifloxacin and standard dose tedizolid by adding/replacing the drugs in the standard treatment regimen to create a novel treatment regimen using the intracellular hollow fiber model of *M. kansasii* (HFS-*Mkn*).

Clinical and preclinical development of new treatments for non-tuberculous mycobacteria: it takes two to tango

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There is a big mismatch in current clinical trials and studies and the preclinical studies (including pk/pd). This mismatch delays progression of new regimens based on pk/pd data into clinical studies. Trials are very conservative and focus on minor deviations from current practice.

On the other hand, the preclinical studies often look at single new drugs and stop prior to developing truly novel regimens. Truly novel regimens can't make it into trials because the risks for stakeholders (e.g. pharmaceutical companies) are too high or they are unwilling to invest in NTM.

This presentation will highlight new findings in clinical and preclinical studies to point out this mismatch and discuss potential new treatment regimens for NTM diseases.

SP07 Quality of tuberculosis care - moving from evidence to action

What high-quality care means—a patient perspective

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Ms. Chavan began treatment for TB in 1999 and eventually completed treatment in 2005 after being told her disease was resistant to most medicines. She went through two major surgeries to remove affected areas of lung and was told she had a 1% chance of survival. She will describe her care experience, highlighting gaps in the quality of care she received and their impact on her life. Now as a drug-resistant TB survivor and patient advocate, she will discuss what high quality care means to patients.

Recommendations from Lancet Global Health's Commission on high-quality health systems in the SDG era and The Lancet TB Commission

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Two Lancet Commissions (on TB, and on High Quality Health Systems) will publish reports in 2018 that include specific recommendations on quality of TB care, as well as quality improvement interventions. Dr. Pai has contributed to both Commissions, and will review key Commission recommendations and discuss their implications for TB programs and TB care.

Lessons learned from the implementation of quality management in HIV/AIDS programmes across 15 PEPFAR-funded countries: the HEALTHQUAL experience

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Dr. Agins will describe the paradigm of quality management and its components, and then discuss experience and lessons learned from implementing HIV-specific quality management programs in >10 PEPFAR-supported countries through HEALTHQUAL. Challenges will be discussed related to both implementation of quality management programs and integration of disease-specific quality management into national quality systems.

Using the International Standards of Tuberculosis Care to define quality of care indicators

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Dr. Cattamanchi will use examples from completed and ongoing projects in high TB burden countries to show how quality-indicators derived from the International Standards for TB Care (ISTC) can be measured at the facility-level using routine programmatic data and then be used to drive quality improvement. He will also discuss the planned update of the ISTC, which will propose quality indicators for key standards across the continuum of TB care.

Integrating quality management into the South African National TB Programme

L Mvusi¹ ¹National Department of Health, Johannesburg, South Africa. e-mail: mvusil@health.gov.za

The South Africa NTP is among the first to embrace quality management. Dr. Mvusi will describe how the NTP is integrating quality management. She will describe progress, successes and lessons learned. The talk will be followed by a panel/audience discussion moderated by Paul Nunn (Head, TB Section, IUATLD).

SP08 Pharmacovigilance and active drug safety monitoring and management in the context of new drugs: lessons from the field

Safety monitoring in new drugs and shorter regimens in patients with multidrug-resistant tuberculosis in Swaziland

S Haumba¹ ¹University Research Co., LLC (URC), Mbabane, Swaziland. e-mail: samsonh@urc-sa.com

This session will discuss the Swaziland pharmacovigilance unit, including its registration with the World Health Organization, Uppsala Monitoring Centre, reporting practices, and experiences in revising the routine ADR form to add specific information on adverse effects (AE) for new drugs including Bedaquiline and Delamanid. Experiences with the introduction of a Client Management Information system (CMIS) at health facilities and how the system has enabled incorporation of the ADR module will also be discussed. Finally, some preliminary data on AE frequency will be discussed and next steps defined.

Building health systems capacity for active drug safety monitoring for effective DR-TB treatment in Georgia

T Gabunia¹ ¹University Research Co. LLC Branch in Georgia, Tbilisi, Georgia. e-mail: tgabunia@urc-chs.com

One of the major challenges that National TB Program (NTP) in Georgia faced in 2015 – at the time of programmatic roll out of Bedaquiline – was lack of a highly functional pharmacovigilance system.

The presentation focuses on interventions that were implemented by the NTP with USAID and Global Fund support for strengthening capacity of the system for active monitoring and management of adverse events among patients receiving M/XDR TB treatment. It describes mechanisms utilized by the Ministry of Labor, Health and Social Affairs (MoLHSA) to improve access to laboratory and clinical investigation services for adequate monitoring of adverse effects of anti-DR TB drugs including bedaquiline and delamanid.

The characteristics of a functional aDSM model are presented and roles of various actors (including civil society and people with TB experience, health facilities, tertiary TB treatment centers, drug agency and Ministry of health) are highlighted.

South Africa: DR-TB care package pilot experience

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The DR-TB Care Package supports DR-TB patients during treatment to ensure they can access the care and treatment they need to complete treatment. South Africa will share their experiences monitoring and managing side effects and drug reactions during the pilot of the care package.

Indonesia: shifting from cohort event monitoring (CEM) to aDSM to monitor bedaquiline patients

P Daru¹ ¹Bangladesh. e-mail: pdaru@urc-chs.com

Indonesia monitors and manages patients on bedaquiline (BDQ) through cohort event monitoring (CEM).

As access to BDQ expands and more patients will be monitored, Indonesia is shifting from CEM to aDSM for BDQ patients. In 2017, Indonesia planned to start integrating e-TB manager and e-meso reporting and recording systems into their reporting structure.

This session will provide an update on how the transition is going and discuss any challenges and lessons learned.

SP09 Towards optimisation of Xpert networks: sharing tools, approaches and experiences

Xpert MTB/RIF as the primary test for all presumptive TB patients: improved service utilisation and case finding in four regions of Ethiopia

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Despite concerted efforts to improve case finding, Ethiopia continued to miss about a third of people with TB. As part of the strategy to identify more missed people, the country implemented “Xpert for all” policy for patients visiting testing centers since January 2017.

We assessed whether this policy contributed to improved service utilization and case finding in 4 regions supported by CTB/MSH project. The rate of utilization improved from 41.8% in January 2017 to 70.8% by December 2017. Moreover, drug sensitive TB case finding increased by up to 30% and drug resistant TB case finding showed 25.2% improvement in assessed sites.

However, there was regional variation with regard to the rate of utilization as well as improvements in case finding. Nevertheless, the data suggest use of Xpert MTB/RIF as the primary test for all presumptive TB patients would lead to significant improvements in finding missing people with TB.

Mapping and analysis of a country laboratory network to strengthen the national TB control programme

S Van Beers¹ ¹Royal Tropical Institute, Amsterdam, Netherlands. e-mail: s.v.beers@kit.nl

The goal of the End TB Strategy is that “Everyone with TB should have access to the innovative tools and services they need for rapid diagnosis, treatment and care. This is a matter of social justice, fundamental to our goal of universal health coverage. A country network of TB laboratories plays a pivotal role in achieving this goal, but how to know to what extent the country network is fulfilling this role adequately?

This presentation will show how gaps and challenges can be identified in the TB program and how laboratory network effectiveness can be evaluated through examination of its critical parameters and the country’s diagnostic and treatment monitoring algorithms.

The presentation will show the power of simple visualization- and map-tools using open software and demonstrate that additional disaggregated data-analysis from the individual network-laboratories can provide invaluable information to improve the TB control program in the country.

Data-driven approaches to optimising the Xpert network in Uganda

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Data-informed decision-making is critical for innovative public health interventions and creative use and analysis of data is critical to increase the positive impact of programs. Uganda's recent TB prevalence survey indicates a large TB case-finding deficit; approximately 41,000 or ~50% of prevalent cases go undetected and untreated each year. Optimization and expansion of access to Xpert MTB/RIF will be critical.

This presentation will highlight Uganda's experience using geospatial mapping of facilities, disease burden, and current Xpert MTB/RIF utilization as a data-driven approach to optimize allocative efficiency and ensure patient access to diagnostics.

Xpert expansion in Nigeria: a lesson in strategic partnerships

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KNCV supported the Nigeria NTBLCP with early implementation of GeneXpert with over 2/3 of GeneXpert placements in the country of the current 396 instruments. One major stride to adopt GeneXpert as the primary initial diagnostic was the installation of 185 GeneXpert machines across 36 states which was achieved through tripartite strategic partnerships between KNCV, the AIDS Control Agency and the Global Funds.

Standardized suitability assessment for placement at 261 sites was performed using a national tool. Nearly 2,000 laboratorians & clinicians have been trained and mentored using 55 master trainers. KNCV has been engaged since July 2014 as an authorized national service provider (CEPHEID) to ensure machine maintenance. Major challenges encountered include infrastructural disrepair, unstable power supply, HR shortages and adverse ambient temperatures.

The look ahead entails optimization of existing capacity through sample referral networks, tracking machine functionality with GXAlert Systems and a National Integrated Sample Transport system.

Evolution of South Africa's Xpert MTB/RIF programme: Xpert Ultra and the multi-disease diagnostic landscape

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South Africa has provided Xpert MTB/RIF testing services for 6 years across 9 provinces, with 203 testing sites, 325 platforms, and 4212 modules. To optimise the existing GeneXpert footprint, instrument utilisation, and spare capacity, tests other than MTB/RIF, to sup-

port the multi-disease diagnostic landscape (particularly for HIV), have been incorporated. In 2018, Xpert Ultra (Ultra) was implemented into the national TB diagnostic algorithm due to its improved sensitivity, specifically amongst patients living with HIV. However, Ultra's reduced specificity is dependent on interpretation of 'MTB trace detected' (trace) in the clinical context.

One aspect of the presentation addresses the complexities of South Africa's initial and subsequent modified programmatic approaches to the clinical management of cases reporting trace by specimen type (pulmonary/non-pulmonary) and subsequent diagnostic testing. Integration of additional diagnostic modalities such as line probe assays, urine-lipoarabinomannan, and drug susceptibility testing to support the national TB laboratory testing algorithm will be explored.

SP10 Pharmacokinetics and pharmacodynamics (PK/PD) based dosing for children with tuberculosis

Pharmacokinetics and pharmacodynamics in designing clinical trials in children

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The pathophysiology and natural history of tuberculosis in children differs substantially from adults.

Additionally, children differ in how drugs are handled due to both developmental changes related to age and to differences in size. These differences have traditionally been underappreciated, but have important implications for how TB should be optimally treated in children.

This talk will explore how these concepts translate into the way that tuberculosis medications and regimens are investigated in children to maximise efficacy while minimising toxicity.

Pharmacokinetics of first-line anti-tuberculosis drugs in children from rural Tanzania

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Revised dosing strategies for drug-susceptible TB among children, set forth by the World Health Organization, have increasingly been associated with insufficient drug exposures within pediatric pharmacokinetic studies.

However, correlations between drug exposures and treatment outcomes are understudied. To improve our understanding of TB drug pharmacokinetics as they relate to treatment response, a prospective cohort of pa-

tients initiating first-line TB treatment in rural Tanzania commenced in 2016. We enrolled 50 pediatric patients (3 months-15 years of age) and performed pharmacokinetic testing at 2 weeks, 8 weeks, and 24 weeks after treatment initiation.

Pharmacokinetics of the first-line drugs will be presented. Treatment response will be correlated with cumulative drug exposures and predictors of pharmacokinetic variability will be presented.

Ensuring children benefit from scientific progress: the paediatric tuberculosis pipeline report

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This section will focus on the relationship between human rights and the appropriate inclusion of children in TB research. It will highlight advocacy to date to push for pediatric PK/PD work and the filling of other research gaps necessary to ensure equity and other aspects central to the fulfillment of the right to health and the right to the benefits of scientific progress. It will include an overview of funding for child-focused TB R&D in comparison to estimated need, and an analysis of current TB treatment and prevention pipeline advances and gaps in relation to childhood TB, and how these analyses are central to informing evidence-based advocacy. This talk will also summarize how recent advocacy towards and commitments from the UN High Level Meeting on TB can influence the pediatric TB research movement.

Safe and repurposed drugs for the treatment of drug-resistant tuberculosis in children

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Current therapy for M/XDR-TB is prolonged over 9-24 months and is associated with serious adverse events in 39-42% of children. The rates of ototoxicity with aminoglycosides used in the treatment of drug-resistant TB in children are extremely high and can be particularly devastating at the language acquisition stage in children. The current process for drug discovery and development takes up to a decade to bring a new drug to clinical use. We have instituted a program on screening of multiple antimicrobial agents already on the market for other bacterial infections for efficacy against *Mycobacterium tuberculosis*.

Those that demonstrate bactericidal effect are then studied in the hollow-fiber model of intracellular tuberculosis (HFS-TB) and doses for optimal microbial kill identified. Ceftazidime-avibactam and benzylpenicillin are two such examples of repurposed agents; several

other classes are in publication. Given the low toxicity profiles of these known agents, they are available for immediate clinical use.

SP11 Global Laboratory Initiative (GLI) tuberculosis diagnostic connectivity symposium

Global perspectives on the implementation of diagnostic connectivity solutions: best practices and learning experiences from the field

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Rapid and accurate diagnosis of TB is essential to start treatment on time, and ultimately, control of the TB epidemic by limiting transmission. Faster laboratory feedback (to clinician, TB program and patient) can be achieved by implementation of diagnostic connectivity, which also supports building better linkages between diagnosis and treatment initiation.

Over the last years, several countries implemented TB diagnostic connectivity solutions. Different country-settings and contexts require tailored pathways for appropriate selection and implementation which contributes to the extent countries are currently utilizing these solutions.

In this presentation an overview of the global adoption of TB diagnostic connectivity solutions will be provided. Also, country-specific insights, learnings and experiences will be shared to support defining best practices for successful selection, implementation and utilization of diagnostic connectivity solutions.

Linking diagnostic data to patient care, a success story from Kenya

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Many countries struggle to manage and optimize use of diagnostic connectivity, limiting patient impact. Using diagnostic data for, among others, clinical decision making, forecasting of inventory or drugs, quality control, capacity building and surveillance can be challenging. The Kenya National Tuberculosis Leprosy and Lung Disease Program (NTLP) implemented a diagnostic connectivity solution for their GeneXpert devices in 2014. Jeremiah Ogoro will present experiences from Kenya on setting up linkages between diagnostic data and patient care and how this contributed to programmatic impact.

Building capacity for practical and applicable use of connectivity

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Where data are collected electronically and automatically, the vast amounts sometimes make it difficult to interpret their meaning or determine necessary action requirements. The adoption of diagnostic connectivity solutions should therefore be accompanied by a program of capacity building and process change to better utilize data to improve decision making within health systems. In 2017, FIND and CHAI worked with the Myanmar NTP to perform a comprehensive survey of data collection and review of diagnostic data usage by stakeholder groups.

The project identified blockers to data use, examined why data did not translate to better management, and identified interventions to address these challenges. Kaartikeya Chauhan will present field experiences of this approach and the capacity building activities that followed.

Interpreting the meaning of diagnostic data: the TB Data Fellowship Programme

A Umubyeyi Nyaruhirira¹ ¹Management Sciences for Health (MSH), Pretoria, South Africa.
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In 2018, the TB Data Fellowship program was established by the Tableau Foundation, MSH and SystemOne to initiate a first-of-its-kind program to build sustainable TB analytics programs. TB Data Fellows, selected from within Ministries of Health, National TB Programs, National TB Reference Labs, or Implementing Partners, are professionally trained to acquire the skills and expertise to become TB data analysts capable of supporting the MoH, NTP and NTRL with data-driven insights and recommendations using diagnostic data.

Alaine Nyaruhirira will share experiences and challenges in launching this program, highlight the first participating countries and share the future vision of the TB Data Fellowship program.

SP12 Pathways to ensure impact of innovations

Innovation for tuberculosis elimination: pathways from introduction to nationwide access—a multi-country analysis

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An analysis of innovations helped identify different types of innovations with common pathways from introduction to scale-up, ranging from policy innovation to methodological, technological or pharmaceutical innovations. Drivers and barriers to programmatic introduction of innovations are identified and suggestions are made to shorten introduction pathways in the future. The analysis draws on information from different countries and settings and relates to different funding sources.

Innovation for tuberculosis elimination: getting started through non-governmental organisations and flexible funders

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Based on his experience of leading the development and piloting of interventions in TB control, the presenter will discuss the role and requirements for donors and technical agencies willing to fund and support the introduction (studying or piloting) of innovations. The role of “seed” money and flexible funding arrangements will be explored.

Modelling and mainstreaming of innovations

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Lined with examples from the practice in Vietnam, professor Nhung argues that well documented studies or pilots provide the data for decision making on policy innovation and scale-up of new interventions. Modeling is used to prioritize interventions for mainstreaming. Well justified choices, expressed in strong strategic plans are used to mobilize the large investments needed for nationwide scale-up of major innovations, to realize maximum impact.

Funding for innovation scale-up: daring donors and pre-loading scale-up and risk management

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While other donors are funding research and pilot projects, often the Global Fund is asked by countries to fund the scale-up of the piloted and successful innovations. This presentation discusses the considerations and risk calculation from the perspective of a large donor, balancing the need to achieve significant impact (by scale-up) with the need to create healthy and sustainable budgeting practices in recipient countries, necessary to sustain the resulting achievements. Examples from different countries illustrate the presentation.

SP13 EU—collaborative TB-HIV activities in the WHO European Region

The current situation of TB-HIV in the WHO European Region

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The European Region is the only WHO region with an increasing rate of new HIV infections, and TB/HIV incidence continues to rise by an annual average of 13%. People with TB/HIV co-infection in the Region are seven times more likely to fail treatment and three times more likely to die than HIV-negative TB patients. In 2016, 12% of incident TB cases were estimated to be people co-infected with HIV.

The five countries with the highest number of TB/HIV co-infections are the Russian Federation (18,000) and Ukraine (8,100), followed by Uzbekistan (1,200), France (670), Kazakhstan (580) and the United Kingdom of Great Britain and Northern Ireland.

Results from two surveys on TB-HIV collaborative activities in the WHO European Region

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A survey was done among national TB and HIV Focal Points of countries in the European Region. In 2017, the TB Focal Points were contacted: 43 responded (73%). 63% of responding countries had specific national TB/HIV guidelines, while others used WHO or other guidelines. In 82% of countries TB/HIV patients are hospitalized initially and continue treatment ambulatory, while in 18% of the countries patients are hospi-

talized throughout treatment. In 63% of the countries, HIV specialists treat HIV and TB specialists treat TB patients. In 32% of the countries, HIV specialists treat both both diseases, while in 5% of the countries TB specialists treat both diseases. In 33% of countries patients will need to go to two different facilities for their medication. The same questionnaire is forwarded to the HIV Focal Points in 2018. Final response is awaiting and will be presented during the conference.

The social support for tuberculosis patients is key to treatment adherence

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Kazakhstan is one of the countries with a high TB burden in Eastern Europe and Central Asia. According to the Comprehensive Plan to Combat Tuberculosis in the Republic of Kazakhstan for 2014-2020, the state policy aims reforming the anti-tuberculosis service.

One of the measures to implement this plan is to involve civil society in TB control: to provide psychosocial support to patients in order to increase their adherence to treatment, especially to the patients with HIV co-infection. The Public Foundation "Sanat Alemi" was created by people who have recovered from TB and who want to help people affected by TB. A Project 'Improved TB/HIV Prevention & Care - Building Models for the Future' Project is now running in its fourth year.

One of the unique achievements of the Public Foundation is its location, inside the TB-clinic, where it provides treatment adherence support and social-psychological consultations, and organize self-support groups.

Use of bedaquiline to treat drug-resistant TB-HIV co-infected individuals in Ukraine

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Ukraine has the second largest HIV epidemic in Eastern Europe and Central Asia and second highest TB burden in the European region. Current global recommendations propose delamanid for treatment of DR-TB in HIV-positive people on antiretroviral therapy, to avoid negative drug interactions. In Ukraine delamanid is not available, so alternative treatment approaches for TB/HIV co-infected people are required. Pilot implementation of bedaquiline started in Ukraine in July 2017 and developed recommendations regarding how and when to use bedaquiline in co-infected patients. Medical providers from both services closely collaborate to quickly assess patients' eligibility for treatment initiation and monitoring.

Assessing the feasibility, acceptability and outcomes of implementing routine LTBI testing for patients with HIV: insights from the UK

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People living with HIV (PLHIV) are at an increased risk of acquiring latent tuberculosis infection (LTBI) and progressing to active TB disease. Although testing PLHIV for LTBI is strongly recommended by a number of international organisations, testing policies are highly heterogeneous and implementation of routine LTBI testing is limited.

This presentation will provide some background to what is known about LTBI testing for PLHIV in the United Kingdom before moving on to share the insights gained, and lessons learned, on the feasibility, acceptability (to patients and healthcare professionals) and outcomes when a novel routine LTBI testing programme is implemented as part of HIV clinical care.

SP14 National TB prevalence surveys: digital innovations and their applicability in routine TB control efforts

Namibia TB Prevalence Survey—digital innovations: CAD4TB and tracking participants (monitoring of field flows and household members)

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The Namibian National TB DPS is the first national TB prevalence survey in the world to use CAD4TB software to assist in the field interpretation of digital chest x-ray images.

The digital innovation was to include the CAD4TB score directly into the field database allowing automated decision making for sputum eligibility. Image reading was also conducted by trained Medical Officers (MO), who were blinded to the CAD4TB score and CAD4TB reading. With a CAD4TB threshold of 60 overall, concordance between MO and CAD4TB reading was 88%.

The second innovation in this survey was monitoring of the field flow of participants fully digitally using guiding dashboards.

The third digital innovation was the use of a digital overview provided by the digital solution to monitor whether other invited household members participated or not. In addition, using GIS the missing invited household members were mapped to aid participation.

Mozambique TB Prevalence Survey—digital innovations: GXAlert, digital online applications for re-reading chest X-rays and Medical Panel Discussion

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In this presentation the innovative first fully digital Data Management Solution (DMS) named 'Nsinya', which was developed for the Mozambique TB prevalence survey (TBPS) will be presented. This innovative system was later adapted for the TBPS in Swaziland.

The presentation will focus on the following aspects: Overview of the DMS: A brief introduction of how the developed DMS covered the requirements for Mozambique TB PS data collection process and flow and show case real-time events and errors that were evaded thanks to this system. Digital innovations: Show case of the digital innovations for Mozambique 'Nsinya': GxAlert integration at field level, CAD4TB and Chest X-ray Reading (Field).

The system includes fully new developed online applications for CXR re-reading (Central Level) and for medical panel decision making. Important IT lessons learned are that digital innovations from recently conducted national TB prevalence surveys, can be implemented in routine settings.

Swaziland TB Prevalence Survey—digital innovations: integrated laboratory (Digital imaging South Africa) system

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Data collection for studies and surveys which involve laboratory testing is usually done using a dedicated survey software running parallel to the routine testing system, however, for the TB Prevalence Survey (TBPS) in Swaziland a new innovative approach was taken.

The TBPS was integrated with the routine Laboratory Information System (LIS) (DISA). In the developed system, patient demographic data is electronically imported in LIS and results exported to the TBPS seamlessly. This innovative approach improves data quality by minimizing data entry mistakes. A key advantage was that the routine laboratory data processing system was maintained. At the same time the routine system benefited from the digital data processing improvements made for the survey.

Besides the innovations in the central lab, one of the outstanding innovations was sharing GeneXpert results real-time between different field sites. This facilitated early treatment initiation.

Application of digital innovations in routine surveillance: the example of the District Health Information System 2 case-based system introduced in Tanzania

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In Tanzania the NTLTP evaluated the existing routine TB notification system and decided to explore utilizing the existing DHIS2 platform for case-based data collection, processing and data monitoring at district level including TB/DR-TB and Leprosy notification.

This resulted in the design and subsequent development of an innovative case-based surveillance system using the DHIS2 platform. The nationwide roll out of this new innovation was completed at the end of 2017. From the first of January 2018 onwards the system captures at national level all notifications case-based.

In the 'blue print' of the design it was decided to develop the system stepwise and to include lab results of presumptive TB cases once the implementation of the first step was successfully completed. Data utilization has been customized to the needs of users of the system at different levels.

How digital innovations from TB prevalence surveys can assist routine TB control

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This concluding presentation will summarize how the new digital innovations presented by the different countries in this symposium, can play a role in routine TB control settings. It will be outlined how surveys can stimulate digital innovations in routine TB control. For example, the fully digital processing of results from GeneXpert using GxAlert. This was designed and implemented in survey settings in Mozambique and Swaziland. It creates the possibility for routine programs to benefit from the same technique. For example having test results automatically feed into the electronic case-based surveillance systems allowing real-time result notifications and more timely follow up action.

The presented new innovations for patient tracking/GIS technology can aid tracing of patients and finding of missing cases.

SP15 High-impact interventions for tuberculosis case finding: global updates and successful country examples

Targeting urban slums for finding missing people with tuberculosis in Kabul, Afghanistan

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Afghanistan has faced the challenge of low TB case notification. Thus, USAID funded TB projects, assisted national TB program (NTP) to implement urban DOTS strategy in five cities. NTP established coordination/partnership with health sectors, trained health staffs, distributed anti-TB drugs, laboratory consumable and DOTS packages. In 2017, NTP covered 106 (58%) health facilities, 49 (32%) (2015).

The case notification (CN) reached 8,147, from 6,492 (2015). Also, in 2017, NTP notified 2,715 bacteriologically confirmed (BC), from 1,748 (2015). In Kabul, CN improved, from 1,900 (2009) to 6,700 (2017) with treatment success rate (TSR) reaching 85% from 47% (2008). Private sector contribution in CN increased by 16%, from 7% (2015) to 23% (2017) for all forms and 11%, from 7% (2015) to 18% (2017) for BC TB cases.

Urban DOTS approach and private sector involvement in DOTS assisted NTP in TB CN in Afghanistan and improved TSR significantly. We recommend urban DOTS approach scale-up in Afghanistan.

What is the place of new technologies in finding missing people with tuberculosis?

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Missing TB cases and drug-resistant TB are major challenges in fighting the disease, and pose a serious threat to reach global targets. Therefore, urgent action is needed to break the transmission cycle of TB and drug-resistant TB to save millions of lives and achieve the global goal of ending TB as an epidemic by 2030. Active case finding (ACF) for TB has been recognized as an important complementary strategy to PCF, in order to diagnose and treat patients earlier, reducing the period of infectiousness and therefore transmission.

This means systematic and routine screening during health visits, as well as early diagnosis of TB and drug-resistant TB through the use of more sensitive screening, and more specific diagnostic tools such as X-rays and GeneXpert MTB/RIF, ULTRA technology and engagement of private/public sector providers to accelerate TB case finding and treatment.

SP16 The Strategic Initiative to Find the Missing People with TB: unprecedented efforts to detect and notify additional 1.5 million people with TB in 13 countries

Implementing the Strategic Initiative: how Stop TB Partnership and the WHO provide technical support to countries in finding their missing people with TB

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Under the Strategic Initiative to find the missing people with TB (SI), the goal is to find 1.5 million additional people with TB by end of 2019 (compared to 2015) in 13 priority countries – an unprecedented ambition level for the TB community.

Stop TB and WHO are providing targeted support to these countries (including India, Pakistan, Kenya and South Africa), monitoring progress and pushing for change of interventions, as needed. The SI is built on principles of people-focused, community driven, rights-based, and gender-transformative approaches to diagnose and treat more people with TB.

This presentation showcases partners' support to countries and how this informs strengthened case detection efforts. Reaching an additional 1.5 million people with TB can only be achieved if interventions target populations with large numbers of TB, involve the private sector, engage vulnerable and under served populations as well as remove barriers to accessing TB care.

'Know your epidemic, key populations and hotspots': ensuring a people-centred approach to improve TB case detection and notification in South Africa

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WHO estimates that South Africa missed almost half of the 438,000 people estimated to have developed TB in 2016. Ensuring a people-centered approach for improved TB case detection, the country stresses the importance of 'know your epidemic, key populations and hotspots', as presented at this panel.

The country is putting mechanisms in place to find the missing people with TB, prioritizing key populations at elevated risk of TB infection, including PLHIV, informal settlements dwellers (especially neighboring mines), diabetics, pregnant women, inmates and miners. The country set a target of minimum 80,000 missing persons infected with TB to be found within 12 months. South Africa is providing a package of TB services including systematic screening of health facilities attendees and inmates (during admission, incarceration and release).

In addition, contact tracing, especially of close family members, is strengthened. The country is exploring routine testing of selected key populations for enhanced case finding.

Successfully engaging private general practitioners, private hospitals and clinics for improved TB case detection and reporting: how International Relief and Development Global contributes to Pakistan's impressive gains

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Of Pakistan's 518,000 people estimated to have developed TB in 2016, routine health services missed more than 30%. Approximately 70% of its people seek health care through private providers. To ensure that all patients treated in the private sector get notified, Pakistan is implementing mandatory TB notification and focuses on engaging more private general practitioners, private hospitals and clinics.

Pakistan's patient-centered approach is also realized through bringing more TB services into the community, including mobile outreach via chest camps and mobile clinics for marginalized, hard-to-reach populations. The country has made impressive case detection gains partnering with non-governmental partners like IRD who will present results from a year of implementation of the Zero TB Karachi initiative.

This initiative has resulted in large increases at city level in the number of people screened, tested and treated for TB, as well as through uptake of drug susceptible and drug resistant TB prevention efforts.

Finding the missing people with TB in Kenya: innovative interventions from civil society organisations as local solutions for underserved and key population groups

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Of Kenya's 169,000 people estimated to have developed TB in 2016, routine health services missed more than 92,000 people according to the National TB prevalence survey. With Global Fund's Catalytic Investments, the country has prioritized finding the people missed with TB cases, through more people-centered, human rights based and social protection approaches in TB service delivery and an emphasis on key populations.

This presentation will showcase how the National TB Programme (NTLD), through NGO Amref Health Africa, is implementing its first-ever County Innovation Challenge Fund (CIC-F) for TB. This seeks to generate demand and provides two-year financial support to county-specific, innovative interventions from civil society organizations as local solutions for underserved and

key population groups. The CIC-F complements the NTLD's national TB response with empowering community-based organizations to set up tailored responses through active involvement of communities in identifying and addressing barriers towards reducing their local TB case detection gaps.

SP17 Preclinical models for tuberculosis drug development and testing—what can be predicted?

New concepts and tools in the research of tuberculosis drug development research

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The diagnosis and treatment of tuberculosis is compromised by the lowered metabolic state that the organism adopts (dormancy). This affects the description of the minimum inhibitory concentration for drugs and pharmacokinetic assessment. The use of innovative molecular viable count methods and techniques to study dormancy in isolated organisms and in infected tissues will be described. The impact of these methodologies on our understanding of pathogenesis and the drug development pathway will be emphasised.

New techniques to increase through-put in screening

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The discovery and development of novel drugs against *Mycobacterium tuberculosis* is a major priority. However, development of new intervention strategies is not easy; *M. tuberculosis* is a slow-growing persistent bacterium with an unusual and highly impermeable cell envelope that protects the bacterium from antibiotics. To accelerate research on this topic we need new techniques for high-throughput screening. Using *Mycobacterium marinum* as initial target is the first step, as this pathogen can be used at BSL2 level and grows faster. Furthermore, rapid testing of compounds that work in vivo, i.e. in zebrafish larvae, further accelerates drug screening significantly.

We have used these improvements to screen for compounds that inhibit the secretion of proteins through type VII secretion systems. Interestingly, these compounds also reduced the bacterial burden in macrophages infected with *M. tuberculosis*.

The current landscape and new applications of mouse efficacy models for tuberculosis

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Animal infection models are essential to vaccine and drug development by generating data that are a prerequisite for clinical trials. Therefore, animal models aim to be highly reflective of human disease.

The standard laboratory mouse models have provided critical information on the efficacy of novel compounds and regimens in TB drug development, as well as on safety and pharmacokinetics. A drawback of the standard mouse infection models for tuberculosis is their lack of advanced lung lesion types with caseous necrosis and non-replicating bacteria. The heterogeneous lung pathology in C3HeB/FeJ mice has proven useful in studying the impact on drug efficacy of both drug partitioning across the diverse lesion types and the micro-environmental conditions within granulomas.

Other mouse models are being explored to identify novel sterilizing drugs against non-growing persisting bacteria to potentially shorten the length of treatment.

Pharmacometric models to assist decision-making in tuberculosis drug development

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The evidence for the current treatment paradigms (drugs and doses) used in treatment of tuberculosis (TB) is weak and not based on pharmacokinetic-pharmacodynamic (PKPD) principles.

A key challenge during drug development of anti-TB drugs is to predict the efficacy of drug combinations due to potential of pharmacodynamic interactions. A translational model needs to correctly capture the effects on persistent bacteria and to be able to predict different biomarkers such as CFU and MGIT.

A novel pharmacometric model-based framework for translational predictions of clinical efficacy of anti-TB drugs allows support for dose selection of Phase IIa TB trials without the need of prior studies in TB patients. As the approach also includes a framework for studying PD interactions it could inform the selection of combination regimens for Phase IIb TB trials.

The pharmacometric approach is closing the translational gap between preclinical and clinical development in TB drug development.

Doing drug development differently

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Drug development in tuberculosis is lengthy and expensive. Effective progression of novel drugs into Phase III trials is hampered by limited understanding of the biology of the disease and the complex pharmacology of combination therapy.

While many preclinical models have been developed to select and triage drugs and regimens, their predictive value remains unclear. Recent failures in Phase III trials have focussed attention on improving the effectiveness of the drug development pathway and reducing the time to arrival of novel treatment regimens in the clinic. The PreDICT-TB consortium supported a comprehensive collaborative scientific effort to generate and compare preclinical and clinical data using different quantitative pharmacology approaches.

The presentation will summarise the major findings of this six-year programme and how they may impact on future drug development efforts.

SP18 Eliminating catastrophic costs due to TB: policy translation of findings from TB patient cost surveys

TB patient cost surveys: translating findings into policy and actions to eliminate catastrophic TB patient costs

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The outcomes of a TB patient cost survey have the potential to significantly inform policy discussion in two distinct areas.

First, costs can be mitigated by changing health service delivery towards patient-centred care, including alterations to health financing schemes, fee structures, and service delivery policies and practices such as decentralization, ambulatory care or community-based care, complementing efforts to move towards UHC.

Second, any costs that remain after optimization of health financing and delivery policies, can be mitigated by improved social protection measures in collaboration with stakeholders across the social sector.

The opportunities arising from a TB patient cost survey should be fully utilized to facilitate policy discussion in both areas and stimulate the engagement of multisectoral partners

Multi-sector actions to address catastrophic patient costs due to tuberculosis in Kenya

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Following the TB prevalence survey findings that showed that more than half of TB incident cases are undetected and untreated, the Ministry of Health has identified finding all people with disease and successfully treating them as an important priority for the country.

Since addressing costs and affordability is a key issue in improving access to care for any disease, Kenya undertook a nationwide survey to assess the economic burden incurred by TB patients and their households. The survey found that 28.8% of all TB affected households and 65.6% of DR-TB affected households' experienced catastrophic. To address these costs, the country is undertaking policy changes and multi-sectoral actions to address cost and affordability related to TB care.

These actions include linking TB-affected vulnerable households to existing social protection programs; alignment of food support with patients' needs; inclusion of TB care in the National Hospital Insurance Fund benefit package.

Ghana's first national TB patient cost survey: national stakeholder consultation for the dissemination of survey findings, policy dialogue and action planning

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Ghana is a lower-middle income country with a moderate TB burden (TB incidence 156/100,000 people per year) and existing country-level social protection schemes. This presentation will highlight findings from the TB patient cost survey in Ghana which was conducted in 2016. In addition, it will describe how these findings have been disseminated among key stakeholders and how they have helped identify policy and practice implications and priority actions to mitigate/eliminate TB patient costs through enhancing social protection and improving TB service delivery and financing.

SP19 Reaching all of those in need by extending active tuberculosis case finding in the community

Active case finding approaches supported by TB REACH: the good, the bad and the ugly

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TB REACH supports partners to implement innovative approaches to improve TB case detection by providing financial and technical support with a strong monitoring and evaluation emphasis. Key populations for TB are often those that are missed by the routine health services and active case finding may offer a better chance to reach them. Some interventions have had huge success, more than doubling the numbers of people put on treatment while others have had little or no impact.

This presentation will highlight a number of the lessons learned and key results from more than 220 past and present TB REACH projects that have sought to improve TB case detection. Both positive and negative recommendations will be discussed. The ways national TB programs and their partners can approach the design, planning, implementation and evaluation of interventions will be presented.

Cluster randomised controlled trials (RCTs) of active case finding for TB in Viet Nam

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The tuberculosis prevalence survey conducted in Vietnam in 2006-07 revealed that many patients with prevalent TB had not been diagnosed by the health care system and many patients with TB do not have symptoms that would allow them to be considered “presumptive TB”. Active case finding is the most direct way to increase case detection among these previously undiagnosed cases.

We have conducted two cluster-randomised controlled trials of active case finding in Vietnam: one, using a traditional screening algorithm starting with chest x-ray, in a high risk cohort, that is, people who are household contacts of patients with known smear positive pulmonary TB; and the other, using a novel algorithm based on screening sputum using Xpert MTB/RIF, in the general population.

These two studies have the potential to inform active case finding strategies in other moderate to high burden countries, as well as in Vietnam itself.

TREATS: evaluating the impact of universal testing and treatment for HIV and TB together

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The “Tuberculosis Reduction through expanded ART and TB screening” (TREATS) study has been designed to measure the impact of a universal test and treat (UTT) intervention for HIV, including universal TB screening and treatment (the HPTN071 PopART intervention), on TB at community level. Utilizing the platform of a UTT intervention for HIV, we took the opportunity to actively screen every member of the population for TB at the same time, on a repeated basis over 4 years.

We will describe our experiences with implementing universal case finding for TB and the approaches to measure its impact at community level.

IMPACT-TB: building sustainable strategies for active tuberculosis case finding in Asia

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IMPACT TB (www.impacttbproject.org) is implementing active case finding in four districts of the Nepal Terai and in Ho Chi Minh City, Vietnam. Around this implementation we are testing different models of active case finding and evaluating the costs from the patient and health system perspective of different approaches. This data will be used to model the short and long term impacts of different intensities and designs of active case finding. While Vietnam is now a middle income country with increasing resources for health, Nepal remains one of the world’s least developed countries.

We will discuss the relative experiences, challenges and knowledge gaps for implementing ACF in these two settings. The IMPACT TB project is funded by the EU horizon 2020 programme.

From evidence to action for elimination—understanding the context when developing and implementing active TB case-finding policies

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Making policies “fit” complex and dynamic contexts in health is critical for successful implementation. This is particularly true in a complex policy area such as active case finding for TB.

As momentum for active case finding builds and evidence accumulates, there is a need for stakeholder engagement (incl. ministries of health and national TB programmes) and understanding of local contexts to facilitate knowledge translation in the area of ACF.

We will present early findings from the knowledge translation work package of IMPACT TB with results of elite interviews and a scoping review. These results include an analysis of contextual factors at the levels of the health system, the community and the individual that have influenced global and national active case finding policy development and implementation.

SP20 Key operational and clinical issues in scaling up new drugs and a shorter treatment regimen for drug-resistant tuberculosis

The Right Diagnosis-Right Treatment Initiative: emerging challenges and successes in implementation

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KNCV has developed the Right Diagnosis, Right Treatment approach and implemented it in several countries through Challenge TB (CTB) project. The end-point is to offer early and correct 'clinical triaging' of patients to the least toxic, shortest regimen according to either genotypic DR-TB test results or country-specific DR-TB patterns.

The objective of the presentation is to highlight challenges and successes, as the approach gains traction and scale-up is accelerating. Despite initial hesitation on patient enrollment in several countries, the initial treatment outcomes are very promising for both shorter treatment regimen (STR) and individualized treatment regimen (ITR) containing new and repurposed drugs. The presentation will include CTB country experiences in using a patient triage approach in settings with and without access to gSL-DST, clinical decision making process, regimen design and regimen deviations, enrollment progress, final and interim treatment outcomes of shorter and individualized DR-TB treatment regimens.

Diagnostic challenges in managing patients on ND&STR—progress and lessons from Africa and Central Asia

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Most countries have limited capacity, both in coverage and quality of diagnostic services preventing the achievement of Universal DST. A country network of TB laboratories plays a pivotal role in achieving this goal. It is important to understand the extent at which the country laboratory network is fulfilling this role adequately. Expanding essential diagnostic services (eg.

Xpert MTB/RIF, 2nd Line Probe Assay (SL LPA) and 2nd line drug susceptibility test (DST)) entails much more than procurement of diagnostic equipment and supplies. It requires reliable systems for specimen transportation, laboratory supply management, and maintenance of equipment. The testing of full drug resistance still relies on complex culture technologies. This results in delays before the most appropriate regimen is applied - based on reliable laboratory results.

Implementation of sequencing technologies to assess DNA mutations leading to resistance will be important in the near future.

Use of STR for DR-TB patients with resistance to medicines included in the regimen: practical and innovative approaches

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The recommendations of WHO on the use of STR for DR-TB indicate that "shorter DR-TB regimen should not be used in patients who have documented or likely resistance to medicines in the regimen", leading to the concept that DR-TB patients with additional resistance not only to fluoroquinolones (FQs) or second line injectables (SLIs), but also ethambutol (E), prothionamide (Pto) and pyrazinamide (Z) would not be eligible for the STR. This conservative approach will deprive many DR-TB patients in high DR-TB burden countries of a short and highly effective regimen.

The main issues are fluoroquinolone resistance and whether moxifloxacin and levofloxacin are as effective as gatifloxacin.

Monitoring and management of adverse events of the new drugs and shorter treatment regimen for MDR-TB

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Many second line drugs are associated with high rates of unacceptable adverse drug reactions, needing frequent interruption and change of regimen. The STR avoids the use of the most toxic and poorly tolerated drugs such as cycloserin (Cs) and para amino salicylic acid (PAS), and uses prothionamide (Pto) only during the intensive phase. Active drug-safety monitoring and management (aDSM) during several observational studies on STR conducted in Africa revealed that severe adverse reactions were very limited and that treatment could be managed without removing more than one drug.

The presentation shares practical approaches to monitoring and management of the most common adverse reactions of the STR based on studies in Africa, and addresses the management of adverse reactions to new drugs for patients non eligible for STR.

Increased access to DR-TB diagnosis and treatment in Indonesia: on the introduction and roll out of ND&STR

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The roll-out of STR alongside active TB drug-safety monitoring and management (aDSM) started in September 2017. The Challenge TB (CTB) project developed implementation tools (e.g. PMDT hospital benchmarking tool, clinical audit tool, and monthly internal cohort analysis).

By March 2018, a total of 622 MDR patients were enrolled in STR. BDQ access expanded to 10 hospitals in 5 CTB provinces (231 DR-TB patients total). Patients not eligible for the STR are considered for treatment with new drugs (BDQ or DLM) through patient triaging. The NTP approved the use of DLM (3 hospitals at present), with revised guidelines in March 2018. A rapid expansion of treatment of DR-TB patients is expected.

Currently 530 GeneXpert machines are operational. Another 455 machines will be distributed in 2018. The number of hospitals where treatment for DR-TB is initiated will increase from 107 at present to 514 in 2020; one per district of Indonesia.

SP21 Latent tuberculosis infection screening and management in low tuberculosis incidence countries: what to do, how to do it and how to monitor

Programmatic management of latent tuberculosis control in the European Union and candidate countries—a guidance

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To support European Union countries in implementation of evidence based interventions for management of latent TB infection the European Centre for Disease Prevention and Control (ECDC) initiated and comprehensive assessment of the components that should be considered, collected the evidence base, performed mathematical modelling and cost effectiveness studies, and convened an ad-hoc expert panel to assess the evidence. As a result of this process, ECDC has issued a Public Health Guidance.

This presentation will summarise the suggested measures for prevention, identification and treatment of LTBI, including a brief overview of the underlying scientific evidence.

Modelling the effect of latent TB infection control on TB transmission and elimination in Europe

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We estimated the potential impact of LTBI control strategies in key populations of European countries for reducing transmission, in particular to assess their contribution in moving towards elimination and their cost-effectiveness.

A deterministic TB transmission model was developed that accounts for transmission within and between the general population and key population groups. LTBI control included LTBI screening and preventive therapy. The effectiveness of the screening included averted TB disease and life years lost. The model was used for the Netherlands, Czech Republic, Portugal, and Spain. LTBI screening was cost-effective for migrants at entry, people who inject drugs/homeless, and contacts. LTBI screening for healthcare workers and travellers was not cost-effective, except in extremely high transmission risk situations. LTBI screening for immunocompromised patients only seems cost-effective for migrant patients. None of the modelled LTBI control strategies will result in reaching the elimination target of less than 1 per million within 20 years.

Programmatic screening for latent tuberculosis infection in England—is there any impact?

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The national TB strategy for England (2015-2020) is now in its fourth year. Programmatic LTBI screening for new migrants is one of the key interventions of the strategy. There is good evidence that significant reductions in TB incidence in England over the last few years are to a large extent related to better TB control, including LTBI screening.

This presentation will review the national roll out of LTBI screening and explore initial outcomes, results and experiences and explore the early evidence of its impact on case prevention and TB epidemiology in England until now.

Barriers and enhancers for latent tuberculosis infection screening and treatment among migrants in the Netherlands

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Screening and treatment of latent tuberculosis infection (LTBI) among migrants from high endemic countries will be crucial to reach pre-elimination. However, the feasibility of this intervention is unknown.

We used a mixed-method design to study the implementation of LTBI screening and preventive treatment (PT) in three migrant groups. PT acceptance rates were low among immigrants, mainly because of anticipated return to country of origin. Asylum seekers had higher PT acceptance but required intensive treatment support from TB nurses.

Outreach activities through churches were most successful to motivate the Eritrean community to participate in LTBI screening. Thorough explanation of LTBI in a language understandable for the client is important for acceptance of screening and PT in all migrant groups. In general, TB staff perceived the LTBI screening as feasible intervention.

However, they stress the importance of further discussing the specification of eligibility of the different migrant groups for future LTBI screening.

SP22 Tuberculosis in the digital age: leveraging technology as a social intervention to empower the affected

Digital agenda for action toward the End TB Strategy

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The End TB Strategy of the World Health Organization (WHO) aims to bring the TB epidemic in the world to an end by 2035. Digital technologies present innovative and improved strategies for patient care, surveillance, programme management and eLearning at large scale.

In September 2015, WHO and the European Respiratory Society (ERS) jointly released a digital health “agenda for action” for the End TB Strategy. Since then, there has been continued implementation and evolution of digital technologies aligned to target product profiles (TTPs) developed since 2015, to work towards optimized solutions as well as case studies in countries applying some of these technologies.

The presentation will also update the audience on important WHO documents produced in the last two years to facilitate the study and implementation of digital technologies in TB control.

Mobile technology interventions to engage and enable patients in their own care

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The rapid uptake of mobile phones globally has provided public health programs with unprecedented access to patients. Although mHealth as the mode of intervention delivery for TB management has been evaluated, a limited number of mobile phone applications have been developed to support TB patients’ involvement in their own care or to improve interaction with their healthcare providers.

This talk will also address SureAdhere Mobile Technology, which provides VDOT service to increase treatment adherence and will discuss the impact of VDOT among TB patients and providers in both high and low-resource settings.

Social media initiatives for tuberculosis advocacy and empowering the affected

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Individuals and communities affected by TB often lack sufficient information on basic aspects of TB such as treatment side-effects, proper nutrition, or stigma.

Social media as a platform of communication allows the sharing of survivor experiences, which can be useful for increasing patient adherence through peer support and overcoming isolation. As a survivor of MDR-TB, the speaker will share personal experiences that shaped her work as a patient advocate and enabler.

Her group - Survivors Against TB - recently launched a number of social media efforts, including a Talking TB app, to provide TB affected individuals and families with relevant information on various aspects of TB in an easy to understand and accessible format for the Indian public.

Patients and their families can become empowered through information exchange and discussion.

Connecting the dots: enabling integrated tuberculosis control using innovative technology

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Technology has the ability to improve the accessibility, availability, and the exchange of information to empower patients, health providers, and policy makers.

This presentation will explore the use of digital technologies like diagnostic connectivity among GeneXpert devices, using adherence technologies to support differ-

entiated care, and linking information systems to inform policy and programmatic activities within a variety of country contexts.

The utility of technology-enabled surrogate endpoints: matching expectations to outcomes

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With the recognition that new tools are urgently needed to achieve global TB control targets, one area that is extremely promising is technology-based interventions. However, there is an unrealistic expectation of what technology can really do.

Although they enable achievement of intermediate endpoints, the question needs to be asked about how much they can impact patient outcomes and programmatic endpoints. Critical review based on published studies in this area using real world examples, will be presented. The talk will make recommendations on matching realistic expectations of technology-based interventions with feasible patient outcomes and program impact.

SP23 Ending tuberculosis deaths among people living with HIV—what will it take to change the status quo?

Global perspective on scaling up effective TB prevention, early diagnosis and early treatment of HIV-associated TB: how can we move forward?

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At the first “WHO Ministerial Conference on ending TB in the SDG era: A multisectoral response” in November 2017 ministers signed up to rapidly scaling up access to patient-centred, integrated TB and HIV services and collaborative activities to end preventable deaths due to TB among PLHIV. This was in line with the target of reducing TB-related deaths among PLHIV by 75% by 2020, adopted by the UN General Assembly in the Political Declaration on HIV and AIDS in 2016. However, TB deaths among people living with HIV have reduced by less than 30% from 2010 to 2016.

This presentation will set the stage for the symposium and provide an overview of the essential package of interventions to end TB deaths among people living with HIV, review global progress on effective prevention, early diagnosis and early treatment of HIV-associated TB, and identify barriers and opportunities for optimization and rapid scale-up.

Ensuring effective TB prevention, early diagnosis and treatment of TB among PLHIV in a Concentrated HIV Epidemic setting – Experience from India

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With the second highest burden of HIV-associated TB in 2016 in the world after South Africa, within a concentrated HIV-epidemic setting, and 14% of notified HIV-positive patients dying during TB treatment in 2015, India faces enormous challenges in increasing access to TB/HIV services.

However, more recently great strides have been made to decentralize and integrate HIV services to the level of TB services, and to roll out WHO-recommended Xpert MTB/RIF and TB preventive treatment to people living with HIV.

This presentation will provide an overview of India's strategies, past and present, to overcome the barriers and scale-up access to the essential package of interventions to prevent, find and treat HIV-associated TB.

Reducing tuberculosis deaths among PLHIV: perspectives from the civil society

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As people living with HIV are 16-27 times at higher risk of acquiring TB and 3 times at higher risk of dying of TB, impacting livelihoods and quality of life, People Living with HIV groups have increasingly highlighted TB as an area of focus, from general advocacy, to strengthening patient literacy about TB prevention, early diagnosis and effective treatment, to providing peer support for adherence and retention.

The presenter from the International Community of Women living with HIV (ICW) Global based in Kenya will share her community perspective on reducing TB deaths among People Living with HIV.

SP24 Health for all—front-line systems to close gaps in paediatric tuberculosis

Decentralising child tuberculosis services increases case finding and uptake of preventive therapy

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A lack of capacity to diagnose tuberculosis (TB) in children at peripheral health facilities and limited contact screening and management contribute to low case-

finding in TB endemic settings. DETECT Child TB, a project implemented by The Union-Uganda from June 2015 to December 2016, strengthened diagnosis, treatment and prevention of child TB at peripheral health facilities in two districts in Uganda. The project trained healthcare workers at 46 peripheral health facilities to diagnose and treat child TB and community healthcare workers to undertake screening and management of household contacts of index TB cases.

The presentation will present the impact of the interventions on case finding and prevention of child TB, and steps towards scale-up and sustainability.

Contact investigation for paediatric tuberculosis in Viet Nam

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This presentation will discuss the paediatric outcomes of the ACT2 trial, a cluster randomised trial of household-contact investigation in Vietnam. In contrast to other settings, the case notification and mortality rates among child contacts were low compared to older populations. These findings suggest differences in the epidemiology of childhood TB in Vietnam, in contrast to other settings.

We will draw upon findings from the ACT2 study, and other studies, to explore possible explanations for the low rates of TB in children, discuss their implications for age-related screening policies in Vietnam and comparable settings.

If we did it right—the impact of scaling up household contact management for tuberculosis on children

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Tuberculosis is now recognised as a major cause of morbidity and mortality in children, but household contact management (HHCM) - screening, treatment, and preventive therapy - has low coverage in many settings.

We consider the global impact on health outcomes in children of moving from no HHCM to HHCM with full coverage. We find that on average, preventing one child death from tuberculosis requires around 50 household visits, screening 80 children, and an extra 50 preventive therapy and 2 anti-tuberculosis courses.

HHCM could substantially reduce childhood disease and death tuberculosis globally. Funding and research to optimize its implementation should be prioritized.

SP25 Towards zero hearing loss: access to new TB drugs and the right to enjoy the benefits of scientific progress

Deaf or dead: where is the choice here?

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Science has made tremendous advances globally. In the context of TB, while deaths due to this infectious disease have declined, drug resistant TB—which is more difficult to treat—is rearing its ugly head. One area where science has consistently failed TB patients is ototoxicity. I had an 8-year long battle with TB and became deaf at the prime of my life due to the pernicious drug kanamycin, which shattered my self-esteem and slammed the brakes on my ambitions.

The ototoxic drugs are given with the justification to “save your life.” What life is being talked about? A soundless & lifeless life, robbed of independence? It is here that I will make the case for making audiometry a baseline test for every TB patient on second-line drugs. It is important that patients are educated about side effects by their doctors, and given the right to choose between various treatment options.

The human right to science and new treatments for drug-resistant tuberculosis

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This presentation will frame treatment-induced hearing loss as a human right issue, focusing on the right to enjoy the benefits of scientific progress and its applications (the right to science) and the interrelated rights to health, information, and nondiscrimination.

The right to science is enshrined in Article 27 of the Universal Declaration of Human Rights, Article 15 of the International Covenant on Economic, Social, and Cultural Rights, and many regional human rights treaties. It is an underexplored but increasingly relevant human right at the center of debates concerning innovation and access to health technologies. Under the right, states must support the development and diffusion of scientific advances, with particular attention to equity, non-discrimination, and the needs of vulnerable groups. The right provides a useful framework for analyzing the rights and responsibilities of different actors with respect to access to newer TB drugs, treatment monitoring (e.g., audiometry), and patient empowerment.

Clinical considerations and consequences of DR-TB treatment, hearing loss and access to new TB drugs

J Stillo¹ ¹Wayne State University, Detroit, United States of America. e-mail: jstillo@gmail.com

While second-line injectable antibiotics remain part of the standard approach to treating drug-resistant TB (DR-TB), a growing body of evidence questions whether the clinical benefit of these drugs is worth the permanent hearing loss and other adverse reactions they cause. Injectable-related adverse reactions are known to interfere with treatment completion. Hearing loss can limit people's ability to return to work and even communicate with their family. Despite this, informed consent, counseling, and audiometry—all recommended for DR-TB regimens—are oftentimes limited or entirely absent. This presentation will focus on current DR-TB guidelines including challenges associated with the use of injectable agents from an ethics and human rights perspective. The possibility of updated guidelines offering an injectable-free treatment option using new and repurposed drugs for people with DR-TB will also be considered.

Strategies for changing clinical practice

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For the first time in almost 50 years there are two new drugs available for the treatment of drug-resistant TB. In spite of high rates of toxicity—most notably ototoxicity—and poor outcomes with current regimens, only 15% of people who need new drugs are able to access them.

Front-line providers should be able to prescribe these medications for individual patients in need, but they describe multiple barriers to doing so, including lack of availability, lack of guidelines to support their use, and concerns that they could lose their ability to practice medicine if they use these agents outside of formal national and international approval. Yet many describe a desire to use the new agents and would themselves want to receive them if they became sick.

This session will explore barriers to use of new drugs among clinical providers and discuss strategies for changing clinical practice on the front lines.

Linking advocacy to end TB treatment-induced hearing loss to global advocacy for the health and human rights of people with disabilities

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Persons with and affected by TB offer unique expertise in developing services to meet the needs of others seeking TB treatment. This presentation will connect advocacy to end DR-TB treatment-induced hearing loss to global advocacy for the health and human rights of people with disabilities (PWDs) through the example of the Masaka Association of Persons with Disabilities Living with HIV&AIDS (MADIPHA). MADIPHA works through a human rights approach focusing on right to health principles (Availability, Accessibility, Acceptability, Quality), non-discrimination, informed decision-making, privacy and confidentiality, participation, and accountability. This experience has shown investing in PWDs to respond to HIV offers a more inclusive approach to meeting patient needs, relieves overburdened health systems, improves knowledge and behavior, and increases use of health services. Grassroots advocacy that partners with affected communities and health systems can ensure the delivery of high quality and comprehensive services while respecting the dignity of people with disabilities.

SP26 Post-tuberculosis chronic lung disorders

Non-communicable lung disease in LMICs—where does post tuberculosis lung disease care fit in?

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Non-communicable diseases are now recognised to be the leading causes of ill health and death globally. In LMICs they hold back the development of individuals, communities and countries economically and socially and the World Health Organization has identified the prevention and control of these conditions as an urgent development issue.

Non-communicable lung diseases like asthma, chronic obstructive pulmonary disease (COPD) and bronchiectasis are common, affecting about 1 in 10 people around the world. In LMICs where vertical and communicable disease-focused health systems often dominate, diagnostic and treatment services for these conditions can be limited.

This is especially so for bronchiectasis and post TB lung disease. In this presentation recent studies about bronchiectasis and post TB lung disease from LMICs will be reviewed in the context of other non-communicable lung diseases and pulmonary tuberculosis.

Post-TB chronic symptoms and chest x-ray abnormalities in Uganda

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People with pulmonary TB are at higher risk of developing chronic respiratory disorders due to lung damage. However, the scope of the problem in high burden TB countries is relatively unknown.

Using data from the latest national TB prevalence survey, we compared chronic respiratory symptoms (cough and phlegm >2 weeks) and radiological lung abnormalities between adults with and without a history of TB in 70 villages of Uganda. Estimates were adjusted for age, gender, smoking, education, setting, region and village clustering.

The results showed that a history of TB was a very strong predictor of chronic respiratory problems in Uganda, even before older age and smoking. The results will be presented as well as implications for policy, practice and future research.

Pulmonary rehabilitation for post-tuberculosis lung disorders in Uganda, Greece, Kyrgyzstan and Viet Nam

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How do you help people with post TB lung disease? The damage is permanent and medication has little to offer for most.

Pulmonary rehab is an important new option and addresses a range of issues including: the symptoms such as breathlessness and fatigue; anxiety and depression; stigma, productivity and relationships issues. Pulmonary rehab uses local resources and is sustainable and scalable. Results of implementation studies in the FRESH AIR Horizon2020 project in Uganda, Greece, Kyrgyzstan and Vietnam will be presented.

Plans will be presented for an international rehabilitation database to gather existing data and, in future, data from India, Bangladesh and Sri Lanka where deployment is planned.

Post-tuberculosis lung damage and the link with recurrent risk of tuberculosis

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An important health threat among people who previously recovered from pulmonary tuberculosis is the risk to develop tuberculosis again. Severity of pulmonary TB disease, i.e. the (radiographic) extent of lung tissue involved, pre-treatment cavitation, and residual cavitation at the end of TB treatment have been frequently reported as independent risk factors for recurrent TB.

This talk reviews evidence that lung damage incurred during an initial tuberculosis episode may increase the risk of recurrent TB and discusses potential mechanisms that might underlie this increased risk. Finally, the challenges to distinguish between post TB lung disease and recurrent TB are being discussed.

Tuberculosis morbidity in paediatric populations

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This presentation will provide an overview of the long-term complications of tuberculosis (TB) disease and treatment in children and adolescents—a topic on which few studies have been published. The focus will be on cognitive delays, which are well documented complications of TB meningitis and which have been associated with hearing loss from second-line injectable agents.

Additionally, the presenter will highlight ways in which TB disease and treatment may lead to other types of developmental delays. For instance, hospitalization for the long duration of multidrug-resistant TB treatment can cause educational delays and compromise social development. The presentation will conclude with a discussion of research and programmatic needs in this area.

SYMPOSIA: FRIDAY, 26 OCTOBER 2018

SP27 Preventive therapy for DS- and DR-TB in household contacts: programmatic implementation

Scaling up DS- and DR-TB preventive therapy in Karachi: adverse events and keeping patients on treatment

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The Karachi TB program commenced scale up of preventive therapy for drug sensitive and drug resistant TB within household contacts in 2016 as part of operational research. Preventive therapy has used isoniazid for 6 months and switched to 3HP as it became available for DS-TB and levofloxacin for fluoroquinolone sensitive DR-TB and moxifloxacin-ethambutol for fluoroquinolone resistant DR-TB. To date more than 6000 DS-TB contacts and 300 DR-TB contacts have been traced and offered preventive therapy. Overall rates of adherence have been high. Adverse events have generally been low and well managed and mainly include reduced appetite, joint and muscle pain and generalised weakness. Lessons learnt during the scale up will be discussed.

Family-based preventive therapy in an urban setting: lessons from Dushanbe, Tajikistan

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MSF and the Ministry of Health and Social Protection of Tajikistan commenced household contact tracing for drug resistant TB in Dushanbe within a family based DR-TB program. Households were identified through both the paediatric and adult TB services. Standardised assessments of household contacts were developed that could be performed by nurses or doctors. Challenges to preventive therapy included high workloads for key staff, linkage to diagnostic services and ensuring appropriate adherence support.

Preventive therapy monitoring and evaluation using a best practice framework of programme indicators

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The updated WHO guidelines on treating latent TB infection pave the way for expanded use of preventive therapy in high-burden countries thanks to expanded eligibility recommendations and endorsement of shorter regimens. However, in many high-burden settings, major gaps exist in the use of preventive therapy for household contacts, even for young children and people with HIV. To improve existing programs and expand use of preventive therapy, it will be necessary to start programmatically monitoring household contact management. A best-practice framework of indicators for monitoring contact management can help identify gaps in existing programs and guide program improvement. An indicator framework will be presented, with examples of how it has been used to guide planning in Lima, Peru.

People-centred preventive therapy

J Stillo¹ ¹Wayne State University, Detroit, United States of America. e-mail: jstillo@gmail.com

Implementation of contact tracing and preventive treatment can raise a number of ethical challenges. Teams must understand informed consent, risks of stigmatisation, how to communicate the risks and benefits for treatment of latent TB infection in a person who does not feel ill.

Case finding and preventive treatment programs have the potential to empower people who are often vulnerable and marginalised. However, this can easily get overlooked in the high burden, high workload settings of many programs.

This talk will focus on the human rights and ethical perspectives of implementing and scaling up preventive therapy programs providing guidance on a people centred approach.

SP28 Leave no one behind—ethical and human rights considerations in TB prevention and care among mobile populations

The right to complete anti-tuberculosis treatment—best practiced by the Netherlands

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Since 1996 the Netherlands Immigration Act allows undocumented migrants with tuberculosis (TB) to complete TB treatment in the Netherlands - the now called Article 64 arrangement. A temporary postponement of eviction is arranged until TB-treatment is completed.

During this period costs for living, housing and (health)-insurance are also covered. The application for Article 64 arrangement is initiated by Public Health TB nurses in consultation with the patient and enables TB patients to complete TB treatment. The arrangement is only used for 2 thirds of the undocumented migrants with TB.

Since the absolute number of undocumented migrants is low individual TB nurses may not be aware of the possibilities and inexperienced with the complicated administrative procedure of the application.

KNCV Tuberculosis Foundation offers support to TB nurses with a roadmap and helpdesk and intends to maintain awareness among TB nurses to make use of the Article 64 arrangement through professional training.

Tuberculosis control in migrant populations: guiding principles and proposed actions

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World Health Organization (WHO)'s End TB Strategy places greater emphasis on ensuring universal access to quality TB care for all people with particular focus on vulnerable populations including migrants.

Recognizing that addressing TB in migrant populations will require improvements in TB surveillance, policy, health service delivery, and cross-country collaboration and coordination, WHO Regional Officer for the Western Pacific developed the guidance document Tuberculosis Control in Migrant Populations: Guiding Principles and Proposed Actions through extensive consultation with Member States and key stakeholders.

The document adapted the four pillars of the global migrant health framework recommended in Madrid in 2010, which consisted of the four pillars:

- 1) monitoring migrant health;
- 2) policy and legal frameworks;
- 3) migrant-sensitive health systems; and
- 4) partnerships, networks and multi-country frameworks.

This session will provide an overview of the framework together with some other WHO policies and documents related to the issue.

Tuberculosis among nomadic pastoralists in Nigeria: results of two years of active case finding in Adamawa State

S John¹

TB remains a serious public health problem among the estimated 450,000 Nomadic Pastoralists in Adamawa State of Nigeria largely due to poor access to health services, poor housing and overcrowding, high rates of bovine TB infection and consumption of unpasteurized milk among other factors.

With support from Stop TB Partnership through its Wave 2 TB REACH grant in 2011, TB control services were launched within Nomadic Communities of Adamawa State. This intervention added 1,294 Bac+ and 1,777 All Forms of TB cases which represents 49.5% and 24.5% increase in B+ and AF TB case notifications in Adamawa State.

This pilot led to the adoption of the Adamawa strategy for TB control among Nomads in Nigeria's current TB strategic plan (2015 – 2020). The vision is to leave no Nomad behind as we work towards Ending TB.

Where have all the patients gone? Safeguarding patient care and treatment in sudden-onset and complex emergencies

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The 'UNHCR Global Trends Forced displacement in 2016' report states that by the end of 2016 an estimated 65.6 million people worldwide were deemed forcibly displaced due to persecution, conflict, generalized violence, or human rights violations. Of these 10.3 million were newly displaced in 2016. This estimate does not include displacement due to other reasons (e.g. natural disasters, etc.). Safeguarding TB treatment and care for these extremely vulnerable and traumatised populations has posed a continuous challenge and the moral and ethical obligation of the international community to respond to this crisis remains often ignored.

This presentation explores potential approaches to address these issues and advocates for better policies and commitments for TB care in this vulnerable group.

Ethical challenges arising in the context of providing tuberculosis care to non-refugee migrants in high-income countries

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While attention to the ethical issues that migrants face in accessing tuberculosis care has increased in the last few years, most of the attention has focused on challenges that refugees face when emigrating. Less attention has been given to the ethical challenges that arise in the context of providing tuberculosis care to non-refugee migrants in high-income countries, particularly those that do not face immediate danger.

In this presentation, I analyze some of the ethical challenges associated with treating migrants with tuberculosis in the Canadian context, particularly in the province of British Columbia. I will discuss:

- (a) inter- and intra-jurisdictional issues that challenge quotidian public health governance structures, and;
- (b) the ethical imperative for the Canadian government and its provinces to clearly differentiate access to health-care from a person's immigration status in order to help overcome power imbalances that may exist between public health workers and their clients.

SP30 Novel strategies to accelerate tuberculosis treatment trials in children

The current landscape of paediatric trials for the prevention and treatment of DS- and DR-TB: feeding the pipeline

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This presentation will provide an overview of current and planned trials for the prevention and treatment of tuberculosis in children affected by both drug resistant and drug susceptible TB. The gaps in current research landscape will be highlighted and opportunities for accelerating the TB trials pipeline in children will be discussed.

Accelerating information from tuberculosis pharmacokinetic studies using innovative modelling methods

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This presentation will focus on the use of pharmacometric modeling methods to inform the design and analysis of paediatric pharmacokinetic studies. Recent

and concrete examples of optimized study designs will be presented and the benefits and drawbacks of model-based analysis will be reviewed. Furthermore, the possibilities for exposure-response (PK/PD) evaluation in children will be discussed.

Statistical trial design considerations and innovative approaches to paediatric Phase III trials

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This presentation will focus on biostatistical methods for clinical trial design for phase 2b and 3 trials in children with tuberculosis. Specific aspects including entry points and outcomes, disentangling efficacy and safety (and tolerability and acceptability) will be discussed.

Justification for use of the non-inferiority approach to evaluating efficacy by demonstrating superiority of safety will also be addressed, especially in the context of MDR-TB trials. Barriers to using doing a superiority trial using a DOOR or scored composite outcome in the context of decreasing risks associated with the proposed regimen will also be addressed.

Use of existing tools for entry points and end points in paediatric TB trials: how can we better use the chest radiograph?

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This presentation will focus on the current use and potential future methodological approaches to using chest radiography (CXR) in children in TB treatment trials. Consideration will be given to the role of CXR in the classification of paediatric pulmonary TB using clinical case definitions, and to trial entry and end-points. Current standard practice for CXR reading methods will be reviewed, and the robustness of these methods discussed.

High-quality social science to inform the design and interpretation of paediatric tuberculosis treatment trials

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There are multiple practical challenges to implementing TB research with child participants. Many of these challenges would be easier to manage if we better understood the perspectives, experiences and values of child participants, their caregivers, and health workers and the context in which these studies are developed and implemented. Social science offers a range of ways to improve our understandings.

We present field examples, lessons learnt, and points of discussion for social sciences priorities in paediatric TB research.

SP31 Towards tackling tuberculosis in vulnerable groups in the European Union. Results from the European Commission funded E-DETECT TB Project

Vulnerable populations for tuberculosis in the European Union/European Economic Area countries

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TB is more frequent in individuals with certain risk factors. Information on these risk factors and TB is needed to target TB control. The European Centre for Disease Prevention and Control collects surveillance information from all 31 European Union (EU) and European Economic Area countries. The EU level database contains case-based information of >1.5 million TB cases. In this presentation an analysis of EU level surveillance data will be presented with a focus on TB in migrants. In 2016, 33% of all TB cases diagnosed in the EU were of foreign origin. This percentage is increasing over the years. To achieve TB elimination in the EU specific interventions are needed targeting migrants and other risk groups.

Outreach programme of tuberculosis screening and strengthening care integration in Romania

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Romania has the highest TB burden in the EU/EEA with almost one quarter (13,617) of the reported patients, and with the highest rate of 69 per 100,000 population. The number of patients decreased sharply since 2005 when almost 30,000 patients were notified. The decline, however, is not observed among vulnerable populations. The outreach programme, using a mobile truck equipped with a digital x-ray, computer aided detection for TB and Xpert MTB/RIF, aims to screen 12,500 persons per year. The target populations are prisoners, homeless persons, illicit drug users and Roma population. The project also aims to strengthen care integration using an outreach strategy with a one-stop shop which brings together social support to vulnerable groups, peer support, and close links to the national TB programme to ensure treatment completion.

In the presentation the results of the first 6-months screening are presented, including challenges to start such a screening project.

Implementation of active and latent tuberculosis screening strategies in migrant reception facilities in Italy

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The current migrant crisis affecting several EU Member States and its increasing political and social impact provides an imperative for interventions targeting the immediate health and needs of migrants.

In the year 2017, a total of 178,500 refugees and migrants reached European shores. 119,369 of them reached the south Italian shores, making Italy the main point of entrance in Europe through the Mediterranean routes. Several determinants of health interplay to increase the vulnerability of migrants to TB infection, TB disease and poor treatment outcome, making them a key population for TB elimination.

In this presentation we will present the results of the active TB screening performed in first-line reception facilities in South of Italy. Screening was performed by questionnaire and on-spot sputum collection for Xpert MTB/RIF ULTRA analysis. Data were collected using a smartphone application created to support and facilitate latent and active tuberculosis screening practice outside healthcare facilities.

Implementation of national strategic plans in European Union/European Economic Area countries

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The development and implementation of national TB strategies is widely regarded as key to successful TB control policy. Yet, only about 55% of EU/EEA countries currently have a strategic plan for TB.

We completed a pan-European survey amongst national TB control leads and two systematic reviews on the topic and this presentation will review this evidence, which is being used to inform a stakeholder meeting and develop a toolkit to aid the development and implementation of national plans later this year.

SP32 Strengthening TB care and treatment among the underserved: implementing the ECHO tele-mentoring model around the world

The experience of developing and implementing an MDR-TB and a paediatric MDR-TB ECHO programme in Kenya, the first in Africa

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This presentation will provide an overview of the experience of developing an MDR TB ECHO program in Kenya, as well as a Pediatric MDR-TB ECHO, the first in Africa.

The presentation will review both the challenges and successes to date. The teleECHO sessions include a didactic presentation by an expert followed by case discussions from clinicians facing a challenging situation and needing guidance from experts. The goal of tele-ECHO sessions are to address the complex issues of MDRTB, sharing best practices and suggesting the best treatment/solution. The eventual aim is to develop the capacity of county level medical officers in the treatment of MDR-TB. The ECHO program is currently attended by participants from >50 centers with approximately 70+ participants joining the sessions every week.

The experience of developing and implementing a TB ECHO programme in New Mexico, a low-burden context

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The New Mexico (NM) Department of Health (DOH) launched the NMDOH TB ECHO program in 2015 to ensure effective nurse case management for New Mexicans diagnosed with active TB. Since 1996, NM has seen a decrease of 66% in persons with active TB; with fewer than 40 cases per year.

As rates decline, TB Elimination strategies are the goal. In June 2018, the NMDOH launches the 4th TB ECHO clinic in NM, the TB Infection ECHO, geared to meet the needs and develop the expertise in community providers to effectively diagnose and treat TB infection. It is essential to treat persons prior to developing active TB to break the chain of infection.

During each TB Infection ECHO clinic, an expert presents a 10-minute didactic on relevant clinical topics, community providers present their cases of persons with TB infection. CMEs are awarded each month after completion of the clinic evaluation.

The experience of integrating medical students from public and private universities into a TB certification programme conducted through the TB TeleECHO programme in Guatemala

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The CDC Central America Regional (CAR) Office supports a PEPFAR funded HIV/TB program. Within CAR, Guatemala has the highest TB burden, and a low TB case detection rate (30%).

Some of the challenges faced to obtain TB epidemic control in the rural areas are: lack of resources, poor referral of patients for care and treatment and lack of specialized trained physicians to treat TB. Nurses and medical students serve as health care providers in many rural areas but lack the proper training to detect and refer TB patients for proper care and treatment.

In order to strengthen the knowledge of health care workers, an introductory TB certificate program was developed by the Guatemalan Ministry of Health, and is being conducted through the TB Tele-ECHO program in CAR.

Improving access to high quality treatment for drug-resistant tuberculosis in Viet Nam using ECHO

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TB is a major Vietnamese public health problem with an estimated 5500 DR TB cases per year among approximately 100,000 active TB cases notified annually (WHO, 2017). The Viet Nam NTP launched the first global TB ECHO program in February 2015 and has been implementing the ECHO education and training model as a tool for maintaining and improving the quality of DR TB treatment during scale up of PMDT throughout the country.

During weekly ECHO sessions a team of multidisciplinary experts at the NTP office review cases presented over the video network by PMDT sites, then provide verbal and written consultations. Each teleECHO session includes several standardized case presentations, questions and discussion, and a brief 15-20 minute didactic presentation.

In addition, updated policies and other guidance from the NTP is shared with participants in different ECHO sessions. NTP aims to decentralize the use of ECHO to regional and provincial levels, also, expand the use of ECHO in various fields in addition to DR TB management, for example, TB in children, chronic lung diseases (COPD, asthma ...), lung cancer.

Expanding TB ECHO to include HIV-TB: National Initiative to Strengthen Collaboration between HIV-TB through e-learning (e-NISCHIT)

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National Institute of TB & Respiratory Diseases is implementing MDR TB ECHO program since 2015. Addressing HIV-TB has been the priority for the national HIV and TB programs in India. Rolling out single window services for management of HIV-TB co-infections at all ART centres attempts to ensure the HIV-TB care continuum. With the new expanded role of ART staff to diagnose and treat TB, capacity building on the clinical and operational aspects is needed. ECHO platform provides case-based learning opportunities to effectively identify, treat, and manage cases of HIV-TB, bringing expertise for TB and HIV together. This initiative also aims at building capacity for TB prophylaxis treatment provision. We started with 115 ART Centres from Uttar Pradesh, Delhi, Andhra Pradesh and Tamil Nadu. This presentation will provide an overview of the experience of implementing the HIV-TB ECHO.

SP33 TB and TB-HIV in vulnerable populations

Identifying TB-HIV among Mozambican miners—novel approaches to increasing care

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The International Organization for Migration (IOM)-Mozambique has implemented activities in the Mozambican health sector since 2007.

IOM-Mozambique currently works on several projects with cross-border mine workers that include facilitating community mobilization for accessing TB treatment in health facilities; working with the Ministry of Health to screen miners for TB during holidays, periods of massive migration, and when Mozambican miners return home from South Africa; and working with traditional healers to increase referrals of suspect cases.

Scientific literature from the region supports the implementation of targeted interventions that emphasize early diagnosis and cross-border continuity of care as miners travel across borders.

TB case finding and TB-HIV integration among prison populations in Southern Africa

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Aurum is an internationally respected organization rooted in Africa that improves health in communities living in poverty. It accomplishes this through innovation in global research, systems and delivery, with over 19 years' experience in leading the response, treatment and research efforts to eradicate TB and HIV. Their research has found that undiagnosed TB and HIV prevalence was high in prisons, justifying routine screening for tuberculosis at entry, and intensified case finding among existing prisoners.

The presentation will describe experience of TB case finding in prisons in South Africa, using Xpert and chest x-ray. In addition, the presentation will describe TB HIV integration within a Test and Treat programme in the South Africa.

Burden of tuberculosis among refugees, need for new guidance

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Refugees are vulnerable to tuberculosis (TB) partly due to overcrowded living conditions, often poor nutrition status and delays in diagnosis. The United Nations Refugee Agency (UNHCR), which has the primary responsibility for providing international protection and assistance to refugees, has worked with Ministries of Health, WHO and partners for decades on policies, guidelines and strategies for integrated TB prevention and care for refugee populations, in countries in Africa, the Middle East, Europe and elsewhere. UNHCR has also worked with Ministries of Health, among others, to enhance case detection and treatment such as in Jordan refugee program and to provide access to multi-drug resistant TB programs, such as Dadaab refugee camps.

In light of new diagnostics, treatment and guidance, call to early TB treatment initiation/continuation in humanitarian situations and a comprehensive assessment of TB control programs, a revised inter-agency field manual is needed. The process and steps will be discussed.

Estimating tuberculosis burden among newly displaced populations

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Tuberculosis is not a priority in emergency response. However, little is known about the TB burden among acutely displaced populations (IDPs) during humanitarian emergencies.

Quantification of this burden is an important opportunity to guide prevention and control efforts in reducing

TB-associated morbidity and mortality among these vulnerable persons.

This presentation will review a recent analysis of the estimated TB burden among IPDs from 2009-2016, and discuss potential strategies for TB prevention and control efforts.

Finding missing cases among children

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Most strategies aimed to increase TB case finding are suboptimal to reach children, who are among the most vulnerable for TB disease, severe disease and death.

The presentation will provide an overview of efforts to reach children affected by TB through household and community-based interventions, integrated service delivery models and new partnerships with the broader maternal and child health and nutritional service community. It will also explore novel methods to improve bacterial confirmation of TB among children.

SP34 Critical reflections on the role of technology and innovations in tuberculosis care

Who's the expert? Physician perspectives on implementing Xpert in India, the last mile

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Access to XpertMTB/RIF machines and cartridges has expanded across sub-Saharan Africa and South Asia but the predicted reduction in diagnostic delay has not occurred.

This talk presents data from interviews and clinical observations of public and private sector pulmonologists, general physicians, and paediatricians in five Indian cities conducted from 2014 to 2016 to examine:

- 1) Xpert prescription practices,
- 2) Xpert's effects on clinical knowledge and practice, and;
- 3) barriers to its clinical use.

It triangulates physician narratives with patient pathways from these cities to show how physician appraisals of Xpert's cost benefit ratio and role as a TB or MDR-TB diagnostic effects test prescription and patient access. Physicians are the last mile in the pipeline from product inception to patient care and epidemiological shifts. Examining this crucial threshold helps predict what diagnostic technology might be easily integrated in clinics and how new technologies will interface with existing clinical practices.

Developing a good POC diagnostic: global norms and local practices of aligning with the POC

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Point-of-care (POC) diagnostics have caused much enthusiasm in the TB community in recent years. Developers and global health actors stress values and norms such as simplicity, rapidity and connectivity for realizing diagnostic innovations that are aligned to the requirements of POC settings.

This talk examines how such norms are operating in practice. Fieldwork among global health actors involved in diagnostic development for TB including manufacturers, donors, industry consultants, international organisations, policymakers, regulators and researchers is combined with fieldwork among users of diagnostics in India, including decision-makers, NGOs, program officers, laboratory technicians and nurses.

The particular practices and politics of developing POC diagnostics have consequences for design and utilization of these technologies and who is able to access these. Making a diagnostic work locally is turning ideas of simplicity, rapidity and connectivity on their head and challenging global norms and valuation practices of what is considered a good diagnostic.

Protecting drugs and wasting drugs: provider perceptions on access to novel treatments for persons living with DR-TB

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The treatment of drug-resistant tuberculosis (DR-TB) is a long and painful journey with multiple toxic agents given for 9-24 months that result in cure for only about half of those treated. Recently, two new drugs--bedaquiline and delamanid--have been recommended for people living with DR-TB, but roll out has not kept pace with need.

This talk will discuss barriers in access to these medications with a focus on provider perceptions that their role is to 'protect' the new drugs for future use and that administering these medications to persons who currently have DR-TB is 'wasting' these life-saving medications. This finding will be explored within a human rights and TB elimination framework.

Digital technologies in adherence: challenges and opportunities

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Mobile health technologies such as text-messages, automated phone calls, and electronic medication monitoring are increasingly being used to educate and support

individuals on TB treatment, and monitor research participants without direct investigator contact. This urges renewed attention to the mechanisms by which providers and researchers consider issues of patient (and participant) consent, privacy, and engagement in TB care.

While digital innovations may empower patients, improve health communication, and promote adherence to treatment, they may also alter how patients interact with their medical and social environments, and unveil extant inequities tied to gender, income and literacy.

This talk will illustrate how adherence technologies were used in TB/HIV implementation science studies in sub-Saharan Africa, to identify mechanisms by which pragmatic gains can be feasibly maximized and social harms mitigated.

SP35 Measuring the magnitude and impact of multidrug-resistant tuberculosis stigma on patients and healthcare workers

High levels of perceived tuberculosis stigma among DOTS service providers in Lagos, Nigeria

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We report TB stigma levels among 266 public and private DOTS providers using a modified Van Rie stigma scale. TB stigma in public and private DOTs facilities was high and both clients and staff were thought to actively avoid TB patients. TB stigma perceptions did not differ by level or facility type. TB stigma scores were not significantly different by providers' age, gender or years of practice. A third of HCWs believed that having TB was permanently discrediting at the community level. Stigma reduction efforts are needed in DOTS facilities to improve the climate for TB patients.

Tuberculosis-related stigma among adults presenting for human immunodeficiency virus testing in South Africa

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We estimated the prevalence of tuberculosis-related stigma and associated factors among adults presenting for outpatient HIV testing in KwaZulu-Natal, South Africa. Among 1,159 adults, mean age was 32 years (standard deviation 10), 615 (53%) adults were men, and 613 (53%) were HIV positive. Mean tuberculosis stigma score was 19 out of 36 (standard deviation 7).

In multivariable logistic regression, greater income was associated with higher perceived tuberculosis stigma (adjusted odds ratio 2.63, 95% confidence interval 1.39 - 4.98) comparing those in the highest tertile of stigma scores to those in the lowest tertile.

In conclusion, tuberculosis-related stigma was common among adults presenting for HIV screening in KwaZulu-Natal. The implications of stigma after one year of longitudinal follow-up are discussed.

The role of awareness raising activities on stigma and discrimination: a case study from Afghanistan

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Tuberculosis (TB) is still one of public health problem in Afghanistan. Tuberculosis was seen as a shameful, dirty and poverty disease due to its prevalence in the lower income families. National Tuberculosis program with assistance from CTB and GF addressed TB stigma through via advocacy, communication, and social mobilization activities. During 2017, NTP conducted 1800 community events, broadcasted TB messages, conducted 1200 cured TB patients *shora* meetings, and celebrated world TB day in 750 health facilities.

During the 2015- 2017, TB messages reached 18,500,000 people. Attendances for TB increased and TB case notification increased from 37,001 in 2015 to 47,406 in 2017. A comprehensive package of interventions, adapted to the local context, may have decreased TB stigma and improved in TB case notification.

SP36 Individualised versus standardised second-line treatment for multidrug-resistant tuberculosis

Strengthening the health system to address the individualised vs. standardised treatment dichotomy in MDR-TB management

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WHO recommends countries implement universal drug susceptibility testing to inform the management of treatment of people affected with TB. A progressive-realization approach means that, while countries build capacity to implement this practice, reasonable alternatives should be offered to patients and health providers. The options for strengthening the health system towards universal DST while providing DR-TB treatment that cures will be discussed in this presentation.

Standardised short treatment regimen for multidrug-resistant tuberculosis: the details (how standard is it?)

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As applied now, the short regimen is not standardized. Many exclusions and adaptations were imposed, not because of available evidence but based on lack of trust, besides a vision shift from public health to individualised care. Originally the short regimen was devised for easy application by field staff under low-income conditions with minimal resources. Control of MDR-TB had become urgent to prevent patients from acquiring fluoroquinolone resistance in private, as for decennia they had not been taken care of by WHO, The Union or TB programmes. Exclusions were limited to patients previously treated with second-line drugs to avoid failures and amplification of resistance. Regimen changes for initial resistance were never made, replacement of toxic drugs very rarely by limiting their use. The only protocol individualizations were weight-based gatifloxacin dosing and intensive phase extension till complete smear conversion, both to minimise the risk of acquired fluoroquinolone resistance, failure and relapse.

Individualised MDR-TB treatment is highly effective and prevents additional drug resistance

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The global number of patients identified with multidrug-resistant tuberculosis (MDR-TB) has dramatically increased in recent years. In some countries of Eastern Europe, more than 40% of all patients with TB are currently infected with a MDR strain of *Mycobacterium tuberculosis*. The two dominant drivers of evolution are variation and selection. For many years and in different geographic settings standardized treatment regimens have been recommended for the therapy of patients with MDR-TB, leading over time to a selection of drug-resistant bacillary strains and fueling the global MDR-TB epidemic. Tailor-made treatment regimens, guided by comprehensive genotypic and phenotypic drug-resistance testing is highly effective and prevents the further selection of drug-resistant strains of *Mycobacterium tuberculosis* on therapy. Under optimal management conditions, cure rates in MDR-TB can be achieved with individualized therapies that are comparable to those observed in pan drug-susceptible TB.

Will new drugs lead to a single regimen for everyone?

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There are several new drugs in the pipeline that are potentially safer, more tolerable and more efficient than the existing drugs. Bedaquiline and delamanid are already widely used in MDR TB. Will these new drugs lead to a single pan TB regimen or will there be several regimens with a combination of old optimized drugs such as rifampicin and these new drugs. A review and an opinion.

SP37 Children included: a human rights-based approach to the inclusion of children in advances in drug-resistant TB

Patient perspectives—success stories of children affected by tuberculosis

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For children, TB is too often a death sentence. Misdiagnosed, they quickly develop M/XDR-TB and are put on treatments that last sometimes longer than they have even lived and scar their young and fragile bodies. In Kyrgyzstan, shorter treatment regimen (STR) is saving children from one extra year of strong pills and months of painful injections, bringing them home earlier to their parents. An individualized regimen with Delamanid finally put a 3-year-old, unable to walk for one year, back on his feet and running. Heart-breaking stories and successes of the smallest people torn by TB create empathy in donors, authorities, doctors and community and increase commitment to defending patients' human rights and chance to life.

The need for and success in using new drugs and short DR-TB regimen in children—experiences from Kyrgyzstan and Nigeria

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KNCV has developed the Right Diagnosis, Right Treatment approach and implemented it in several countries through the Challenge TB (CTB) project. The endpoint is to offer early and correct 'initial clinical triaging' of patients, including children to the least toxic, shortest regimen according to either genotypic DR-TB

test results, TB treatment history and DST pattern of the source of infection. The objective of the presentation is to highlight challenges and successes during field implementation.

The presentation will include CTB country experiences in using new drugs and shorter treatment regimen in children and adolescents with M/XDR-TB. This will include data on enrolment progress, regimen selection, regimen design, final and interim treatment outcomes and treatment tolerability among children and adolescents.

Second-line drug formulations for children

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After years of advocacy and public private collaboration, for this first time ever, child-friendly formulations are available for many of the second-line drugs used to treat MDR-TB. They are desperately needed since the current practice of cutting, crushing and mixing adult tablets violates Good Clinical and Pharmacy Practice.

So few children, however, are diagnosed and treated for MDR-TB annually that there is insufficient 'demand' to even justify a single batch of these products being made. This presentation will discuss the yawning gap between estimated numbers of children who become sick with MDR-TB (25-33,000) and the actual number of children started on treatment for MDR-TB (fewer than 1000 annually), barriers to diagnosing and treating children with MDR-TB, and a failure of uptake of innovation for this vulnerable population.

The session will conclude by suggesting ways forward including active case finding among children exposed to MDR-TB in their households and pooled procurement.

Trauma of treatment and frequency of adverse effects—why we need injectable-free regimens

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Less than 5 % of children showing symptoms of drug-resistant TB are ever diagnosed and treated. There is a great reluctance to start children on DR-TB treatment due to diagnostic challenges coupled with fear of treatment toxicities and pain related to injectables.

In general, children tolerate treatment well, with fewer adverse drug reactions than adults. Though ototoxicity could affect up to 25% of children[1]. Monitoring hearing loss is a challenge in children below 4yrs and the required age-specific tests are not available in the field. The injectable drugs cause permanent irreversible damage (sensory-neural hearing loss), that impact the speech, language, social-emotional-cognitive development and academic achievement. What is the evidence base around the injectable? Is it better deaf than dead?

Do we have other better options? With the new TB drugs and paediatric formulations, it should become easier to cure children while avoiding unnecessary trauma, pain and risk of disability.

Research update on the clinical management of drug-resistant tuberculosis in children

J Seddon¹

The landscape for drug-resistant tuberculosis treatment is changing rapidly, with two new drugs recently licenced, and a shorted regimen now endorsed by the World Health Organization. However, children have been left behind in these drug developments and new recommendations. Paediatric formulations for bedaquiline and delamanid are not widely available and essential pharmacokinetic work has yet to be completed to inform dosage. Although there is acknowledgement that children may not need the same regimens used to treat extensive disease in adults, it is currently unclear how to approach paediatric drug-resistant tuberculosis treatment. Studies are being undertaken, however, and clinical trials are in advanced stages of planning.

This talk will describe the current landscape of paediatric drug-resistant tuberculosis research and outline strategies for treating children with the data we have currently available.

SP38 Importance of zoonotic TB surveillance using whole genome sequencing to trace TB outbreaks at the human-animal interface

Whole genome sequencing of *Mycobacterium orygis* for in-depth molecular analysis of isolates

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Mycobacterium bovis and *M. caprae* are causative agents of animal tuberculosis (TB) with zoonotic importance. Previous work characterized isolates from tuberculous dairy cattle and rhesus monkeys in Bangladesh as *Mycobacterium orygis*. While all isolates had the same spoligotype pattern, there were three different Multiple-locus variable-number tandem repeat patterns with the monkeys and most cattle (15) in one group and the other 2 groups containing 2 and 1 isolates respectively. To better understand the evolutionary relationships, whole genome sequencing (WGS) was performed.

Method: Eighteen isolates of *M. orygis* were sequenced on a MiSeq (Illumina). Analysis was performed using

variable Single Nucleotide Polymorphism (SNP), The National Veterinary Services Laboratories's in-house pipeline (<https://github.com/usda-vs>).

The prevalence of gross lesions of bovine TB in slaughtered cattle and assessment of the pastoralists' knowledge of the disease in Hoima District, Uganda

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Introduction: Bovine tuberculosis (bTB) is more prevalent in animal species leading to social, economic and public health disruptions. The objective of the study was to establish the prevalence of gross lesions compatible with bovine tuberculosis in slaughtered cattle and pastoralists' knowledge in Hoima district, Uganda.

Methods: Daily postmortem inspections were carried out in designated slaughter places and surveys conducted among pastoralist using structured questionnaires, The collected data was analyzed using PASW statistics 18 and WINPEPI portal version 11.30.

Results: Of the 1815 cattle slaughtered at the four (4) key slaughter places, 2.6% cattle had gross lesions compatible with bovine tuberculosis. Among the 220 respondents interviewed, 86.4% had heard about bovine tuberculosis and 68.2% had good overall knowledge on bovine tuberculosis.

The study revealed significant associations ($p < 0.05$) between sex, breed, level of education and good overall knowledge and occurrence of gross lesions suggestive of bovine tuberculosis.

Molecular and phylogenetic profiling of Mycobacterium bovis circulating among slaughtered cattle in Nigeria

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Due to dearth of surveillance on bovine tuberculosis, it continues to be a Public Health concern in Nigeria. Using genus and deletion typing, 30 *M. bovis* isolates were characterised from cultures of suspected tuberculous lesions obtained from slaughtered cattle in three abattoirs in Nigeria.

Thereafter, 25 were whole genome sequenced (WGS), results were analysed using NVSL bioinformatics pipeline (<https://github.com/USDA-VS>). Eight unique spoligotypes were identified; SB0944, SB0951, SB1025, SB1027, SB1421 SB1433 and two orphans, with SB0944 predominating. In-silico spoligotyping matched the conventional genotyping methods.

A global strain of phylogenetic comparison reveals all isolates cluster with other African 1 clonal complex isolates, although there is a great deal of diversity between isolates.

The findings demonstrate the unique utility of WGS in tracking evolution, emergence/introduction of strains of *M. bovis* in cattle population in Nigeria, thus, making WGS, a cornerstone for public health interventions in the country and other Sub-saharan African regions.

SP39 Capitalising on the complementarity of analytical tools and frameworks in support of the TB prioritisation agenda

Combining the patient pathway analysis and MATCH to better understand the supply and demand of TB services

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The Patient Pathway Analysis presents an assessment of the alignment between the TB patient care seeking behavior and the availability of tuberculosis diagnostic and treatment services at the national level and subnational level in Kenya. Also at the subnational level, the Mapping and Analysis for Tailored Disease Control and Health System Strengthening (MATCH) framework analyzes spatial trends in the TB epidemic which may help to validate hypotheses made by the PPA regarding the degree of misalignment between TB patients care-seeking and the services available to them.

Together, the PPA tool and MATCH framework provide an improved understanding of patient care seeking while revealing the subnationally differentiated health system barriers to finding the missed TB cases.

Sharpening the case detection rate using sub-national incidence estimates and inventory studies

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The LSHTM tool estimates subnational incidence rates based on a number of demographic, geographic and socio-economic variables, including population-based surveys and census data. This tool has recently been used to model district level incidence rates in Indonesia.

TB inventory / capture-recapture studies estimates the number of TB cases which were detected in a given annual reporting period, by analyzing the amount of overlap between multiple TB-related registers. The total number of detected cases can then be disaggregated by those regions or districts included in the study. Combining the outputs of these two approaches, we can potentially ob-

tain more accurate district level case detection rates: the inventory study's number of detected cases make up the numerator, and the LSHTM incidence data are in the denominator. It should be possible to identify districts of notification for each TB case in the TB registers consulted for the IS/CRC study.

SP40 Paediatric lung function measurements in low-middle-income countries with high burden of TB-HIV, malnutrition and environmental exposures

Early-life determinants of lung function in African infants

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Low lung function in early life is associated with later respiratory illness. There is limited data on lung function in African infants despite a high prevalence of respiratory disease and risk factors for respiratory disease. Our study has identified several factors including infant size at birth, sex, maternal smoking, maternal alcohol, maternal HIV, household benzene exposure and early life lower respiratory tract infections associated with altered lung function in infancy. Many of these factors may be amenable to public health interventions.

Lung function in children presenting with symptoms suggestive of pulmonary TB

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Advances in molecular diagnostics have strengthened the ability to identify potential respiratory pathogens, but the clinical relevance is questioned. In addition, there is limited data on respiratory pathogen co-infection in children with (suspected) pulmonary tuberculosis (TB), including the extent to which they may contribute to disease and severity of disease. Respiratory illnesses during early childhood, a critical period of lung growth, may have serious impact on lung function. Emerging data indicate that there is an association between lung function in childhood and in adulthood ("lung function tracking"). Infectious diseases and environmental exposures can result in "detracking" of lung function.

Given the burden of TB, HIV and respiratory infections in African children, there is a significant unmet need to study the combined effects of these acute and chronic infections on lung function in children.

The long-term effects of severe acute malnutrition on lung function

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Based on evidence from low birth weight infants, it is thought that adult lung health is influenced by early-life nutritional insults. Severe acute malnutrition (SAM) affects more than 17 million children under 5 years worldwide, and stunting affects 155 million; both could be contributing to the growing burden of non-communicable diseases, including lung disease, in low and middle income countries.

We followed up a cohort of survivors of SAM 7-years after treatment in Malawi and assessed their lung function, among other health indicators, compared to a sibling control and an age-sex-matched community control. We found remarkable preservation of spirometric and oximetry outcomes between SAM survivors and controls. We did find negative associations between spirometry and HIV infection, stunting and sex.

This study also informed us about the applicability of the GLI-Black spirometry references to sub-Saharan African children.

The long-term effects of severe acute malnutrition on lung function

N Lelijveld¹ ¹University of Malawi college of Medicine, Blantyre, Malawi.
e-mail: natasha.lelijveld.11@alumni.ucl.ac.uk

This talk will be together with Dr Jane Kirkby. Based on evidence from low birth weight infants, it is thought that adult lung health is influenced by early-life nutritional insults. Severe acute malnutrition (SAM) affects more than 17 million children under 5 years worldwide, and stunting affects 155 million; both could be contributing to the growing burden of non-communicable diseases, including lung disease, in low and middle income countries.

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SP41 Boats, drones and motorcycles—optimising specimen referral networks to meet the needs of TB diagnostic networks

Landscape of specimen referrals: what's new and what's next

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During last year's Union Conference, the GLI Guide to TB Specimen Referral Systems and Integrated Networks was launched. Since then, an accompanying toolkit has also been developed, tested and released to the general public. We have also seen countries starting to shift the focus on system implementation to improvements, seeking efficiencies and introducing innovations.

This presentation will give an overview of the landscape of specimen referrals, in TB and beyond, over the past year and what is possibly to come in the next.

Towards an integrated specimen referral network in Burkina Faso using the national post

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To strengthen laboratory systems, networks, quality, Global Health Security Agenda (GHSA) readiness, and capacities for antimicrobial resistance (AMR), the African Society for Laboratory Medicine (ASLM) is working to develop and strengthen the Sample Referral Networks in GHSA priority countries, including Burkina Faso. This strengthening of Sample Referral Networks is being conducted through a regional consultancy, which began with a situational analysis across eight countries. The objective is to see how current referral networks can be developed and strengthened in light of global health security threats. This work has been furthest developed in Burkina Faso, where a pilot specimen referral system was set up with the national postal service and has been running for over one year.

Past performance of the specimen referral system was reviewed and currently scale-up and full integration (including all specimen- and disease-types, including TB) of the system is being considered.

Malawi's specimen transport network model and the potential for introducing drones

J Kandulu¹ ¹Malawi Ministry of Health, Lilongwe, Malawi. e-mail: jrkandulu@gmail.com

Malawi's TB and HIV diagnostic networks have gone through changes over the recent years. With the expansion of laboratories and introduction of point-of-care (POC) and near POC devices, there was a need to map out and design the changing diagnostic networks, as well as the specimen referral network that would support it. To support the specimen referral network design, an exercise was conducted to optimize the transportation network across two districts, including potentially using unmanned aerial vehicles (UAVs). To achieve efficiencies, other cargo such as vaccines and safe blood for transfusions were considered for inclusion. Software modeling was used to optimize routes based on various scenarios for the transport network and the Ministry of Health (MoH), along with stakeholders, chose the scenario to be implemented. This presentation will focus on the steps taken and the MoH leadership across diagnostics, HIV and TB programs required to complete this process successfully.

Implementation of a sample referral system for DR-TB diagnosis and treatment follow-up: the Bangladesh experience

S Hossain¹ ¹Management Sciences for Health, Dhaka, Bangladesh. e-mail: shossain@msh.org

Due to limited geographical coverage of GeneXpert and uneven distribution of TB reference laboratories, many presumptive TB and DR-TB patients do not have timely access to testing. Follow-up culture tests of DR-TB patients are thus delayed or missed due to distance barriers. The CTB Bangladesh Project implemented a sample referral system to overcome the challenges.

Orientation on sputum transportation standard operating procedures (SOPs) and kits were provided to 500 field staff in three city corporations and 22 districts. A total of 7,660 samples from 2,314 presumptive DR-TB patients and 1,700 DR-TB patients on treatment were transported by courier. Estimated cost per courier is less than \$1 compared to travel costs per patient of \$40-\$55. Considering low comparative costs and replicability of system, the NTP should consider sustaining this system beyond project support. Testing of a specimen referral tools kit has been planned in Bangladesh to help in nationwide scale up.

SP42 Ensuring tuberculosis free prisons: achievements and challenges

Azerbaijan's experience in the introduction of new TB drugs for treatment XDR-TB in prisons

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Background: The lowest cure among our cohort of 444 patients with rifampicin-resistant (RR) tuberculosis (TB) with the overall 78.4% cure rate, was achieved among those with extensive drug resistance (XDR) and RR-TB with additional resistance to fluoroquinolones, but susceptible to 2nd-line injectables (SLI) (20% and 63%, respectively). In 2017, Azerbaijan prisons introduced new/repurposed bedaquiline, linezolid and clofazimine to treat RR-TB.

Results: A total of 29 and 11 patients treated without and with the new/re-purposed TB drugs were identified with 59% and 100% of culture conversion by the 6th month of treatment, respectively. Increasing number of effective drugs at the treatment regimens significantly contributed to the culture conversion rate by the 6th month of treatment OR 2.30, 95% CI 1.01-5.25, $p=0.048$. The HCV co-infection had a negative impact to the culture conversion rate by the 6th month of treatment (OR 0.14, 95% CI 0.02-0.79, $p=0.026$).

Bacteriological positivity from the 2nd month of treatment onwards significantly decreased the chance for culture conversion by the 6th month ($p<0.05$).

Improving tuberculosis case finding in Malawian prisons: implementation of systematic screening

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Since 2014 MSF has included symptomatic screening followed by MTB/RIF GeneXpert and/or smearing for presumptive TB in Malawian prisons. In 2017 MSF in collaboration with Challenge TB, accomplished a mass campaign using digital X-rays.

A change in TB case finding was assessed, and factors contributing to TB disease development in prisons determined.

A retrospective analysis of 2014-2017 data was performed and multivariate logistic regression to evaluate factors associated with TB development was applied.

TB case notification ($/10^5$) increased in average 6,5 times. The risk to develop TB was associated with HIV+ (aOR=3.8, 95% CI; 2.9-5.2, p 1 year (aOR=7.1, 95% CI; 4.7-10.6, p .

X-rays inclusion into systematic screenings led to case finding increase in Malawian prisons in 2014-2017.

Country-wide TB screenings were suggested for prisons; and identified TB disease determinants recommended for preventive measures.

Key achievements of the tuberculosis control activities in the penitentiary system of Kazakhstan

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Aim of this presentation is to present a comprehensive analysis of TB including drug resistant TB epidemiological situation in Kazakhstan prisons during the last ten years. The country will share the examples of impact of legislation liberalization, political solutions and donor support to TB notification, mortality, treatment coverage and treatment outcomes.

Ensured early case detection, how can we ensure treatment completion? Example from India

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Globally as in India, the policy is to screen all inmates for communicable disease including TB. The screening is done at the time of entry and at regular intervals.

Through GF supported TB grant to India, (Project Axshya) we reached to 210 prisons and analysed data across 157 prisons in India which showed entry/regular screening was practised in 50%/60% of prisons and diagnostic services were available in 18% and treatment services in 54% prisons. Advocacy efforts over three year period in these prisons led to regular screening of inmates for TB.

Secondly, the National TB programme also revised its data recording and reporting format to include "inmates of prisons" as one of the Key-affected Population.

Project Axshya efforts have been towards early case detection to ensure all diagnosed are initiated on treatment. However, there are gaps which needs attention of policy makers which will be also discussed during the presentation.

Tuberculosis care among prison inmates in the Netherlands, best practices and barriers

N Jansen¹ ¹KNCV Tuberculosis Foundation, Den Haag, Netherlands. e-mail: niesje.jansen@kncvtbc.org

TB screening of prisoners on entry has been routine practice in the Netherlands since the early 1990's. The presentation will highlight briefly the way the screening was performed and adapted in the past 25 years, based on monitoring and evaluation of the screening performance indicators.

In addition it will be presented how quality diagnosis and care and case holding for prisoners with TB is safeguarded through intensive collaboration of the prison medical services and public TB control services. But despite this efforts treatment results are lagging behind the national success rates.

Case studies will be presented describing best practices as well as remaining barriers for case holding, and the important role of cross border TB control in this group.

SP43 Techniques and approaches to address the right to knowledge of the sub-national TB burden data among local TB programmers

Sub-national estimation of tuberculosis burden

P Glaziou¹ ¹WHO Global TB Programme, Geneva, Switzerland. e-mail: glazioup@who.int

There is increasing global demand for estimates of TB incidence at the subnational or subpopulation level in low and middle-income countries, to improve TB programme planning, forecasting and budgeting.

This talk will present options to derive such estimates, including small area estimation approaches applied to prevalence survey results, the use of infection surveys and data on subpopulation risk levels.

Generation, interpretation and dissemination of sub-national tuberculosis burden estimates in a high burden setting—a model for Indonesia

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In many high TB burden countries there is substantial geographical heterogeneity in TB burden. In addition, decisions on TB funding and policy are highly decentralised. While this offers opportunities to tailor activities to the needs of the local burden and current health system performance, subnational estimates of burden are usually unavailable for advocacy or target setting.

We aimed to estimate TB burden and current health system utilisation to the relevant subnational level in Indonesia, where 510 district health offices have complete autonomy on TB policy and resource allocation.

We developed a simple model to distribute regional TB incidence that included population size, level of urbanisation, and socio-economic indicators (living floor space and high school completion). The facility-based case detection rate varied between 0 and 249% with high

variation between neighbouring districts, highlighting both low-performing districts, and cross-district health utilisation. Methods and results were successfully disseminated to district-level policy makers.

Estimating local level tuberculosis burden—warts and all

J Levy¹ ¹KNCV Tuberculosis Foundation, The Hague, Netherlands. e-mail: jens.levy@kncvtbc.org

The burden of TB is only ever directly measured using sample surveys designed to arrive at national prevalence estimates and therefore not powered to estimate prevalence at sub-national levels. However, estimates at lower administrative levels could allow for limited resources being prioritized, appropriate case detection target setting, and improved accountability.

Local level prevalence estimates may be estimated using the distribution of TB related risk factors across census statistical units (CSUs). A recently developed tool allows for this by dividing the overall WHO national incidence estimate among regions based on the distribution of cases in the prevalence survey.

The region specific burden is further distributed among the CSUs according to weights based on region specific risk factors estimated from an analysis of the prevalence survey. KNCV looks forward to using this tool in Nigeria to meet a need and explore ways to produce more stable and valid estimates e.g. geospatial smoothing.

Development and validation of a statistical model to estimate tuberculosis under-notification

E Rood¹ ¹Health Unit, KIT Royal Tropical Institute, Amsterdam, Netherlands. e-mail: e.rood@kit.nl

Nationally representative tuberculosis (TB) prevalence surveys provide invaluable empirical measurements of TB burden and a valuable source of data to estimate the rate at which TB programs detect, diagnose and treat people with TB. However as surveys are resource demanding undertakings, they are scarcely available, limiting its use for routine monitoring of TB treatment coverage (formerly case detection).

In this session the application of a new analytical framework: Mapping and Analysis for Tailored disease Control and Health system strengthening (MATCH), and its use to estimate subnational levels of TB under detection, is presented. Using the MATCH framework, the effect of TB risk factors, program efforts and factors affecting access to TB services on subnational rates of TB notifications are analysed and quantified.

TB prevalence data obtained from cluster level TB prevalence surveys are then used to validate the use of MATCH to monitor TB treatment coverage.

Sub-national tuberculosis burden estimate in India using TB notification data and TB drug sales data

K Rade¹ ¹RNTCP, New Delhi, India. e-mail: radek@rntcp.org

India with largest TB burden in the world has a diverse TB epidemiology. Subnational TB prevalence surveys, ARTI surveys and notification data show the wide variation in the TB burden. The TB notification data with a good case based electronic system shows a wide range of annual TB notification from 10 per 100,000 to more than 600 per 100,000 population at sub district level.

In order to focus attention to missing people with TB and provide targets at subnational level, state level TB burden estimation was done using innovative modelling using sub national TB notification data and its trend to estimates TB cases in public health system. Patients getting treatment from private hospitals were assessed using sub national data on sale of anti TB drugs.

Model was refined with additional data from district family health survey. The methodology and its use for defining targets at subnational level will be presented.

SP44 Meeting patients where they are: a patient-centred approach to tuberculosis

Differentiated models of care for multidrug-resistant tuberculosis: experience and lessons learnt from South Africa

N Ndjeka¹ ¹Director: Drug-Resistant TB, TB & HIV, National Tuberculosis Control Programme, South Africa, Johannesburg, South Africa.
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This presentation will provide an overview of the scaling up of universal access to MDR/XDR TB care in South Africa, with a special emphasis on finding the missing cases of DR-TB and improving patient retention using close-to-patient solutions.

The presentation with cover:

- Challenges to managing M(X) DR-TB in South Africa
- Policy development and implementation
- Scaling up access to diagnosis and care through differentiated models of care
- Improving patient retention
- Improving data management

The presentation will discuss the main challenges towards increasing universal access to care for presumptive and confirmed M(X) DR TB patients and the different approaches used to improve the diagnosis, treatment and care of M(X) DR TB patients.

By discussing these aspects, participants will contribute to the identification of the realities of the various differ-

entiated models of care for drug-resistant TB, and what challenges can be expected when implementing these various approaches.

Front-line tuberculosis diagnostics: how close are we to point-of-care diagnostic tests in the most rural of places?

J Robinson¹ ¹FHI 360, Durham, United States of America.
e-mail: jrobinson@fhi360.org

This presentation will provide an overview of some of the latest development in TB diagnostics. It will review the following with a special emphasis on point-of-care and close-to-patient solutions:

- The technology and how to perform the test
- Performance data including published studies
- Ease of use
- Cost data
- Limitations on use
- Criteria when considering deployment

The presentation will discuss what are the ideal characteristics of a new TB diagnostic test. We will review what is currently in the diagnostic pipeline globally and what new technologies we can hope to see to improve TB diagnosis in point-of-care settings. By considering this, we can conclude how close we might be to the 'ideal' TB diagnostic test and what challenges we might expect to face when deploying these new diagnostics.

Meeting patients where they are: experience and lessons learnt from Kyrgyzstan

T Toichkina¹ ¹FHI 360, Bishkek, Kyrgyz Republic.
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This presentation will consider patient-centered TB case management system, focusing on the primary health-care level:

- Clinical case management, taking into account the category, sensitivity and choice of treatment regimen
- Assessment of the psychological state for further psychological support
- Assessment of adherence and identification of reasons for suboptimal adherence to treatment
- The impact of social support on successful treatment
- Reorganization of DOTs involving public assistants and others from the patient's immediate surroundings
- Involvement of social workers, volunteers, NGOs, religious representatives to increase commitment and complete treatment

The presentation will discuss new approaches to managing each TB case at primary health care level, increasing the capacity and motivation of family doctors and nurses for the successful completion of TB treatment. Based on experience in Kyrgyzstan we will discuss how this approach is suitable for scale up as the country transitions to outpatient TB treatment.

Patient-centred care for multidrug-resistant tuberculosis: experience and lessons learnt from China

L Li¹ ¹FHI 360, Kunming, China. e-mail: lli@fhi360.org

Treatment for multidrug-resistant tuberculosis (MDR-TB) patients is long and expensive, with treatment delay, default, and/or failure all too common. The USAID Control and Prevention of Tuberculosis (CAP-TB) Project developed a patient-centered care model in Yunnan in 2012, and refined it under the National Action Plan (NAP) 2017-18 pilot study on a supportive care package.

The comprehensive approach, including individualized care plans developed with and for patients; face-to-face and online education and counseling for patients and their families provided by nurses and peer counselors; a robust case management platform; and community-based care reveal great improvements. In March 2018, the Chinese National Center for Tuberculosis Control and Prevention ranked Yunnan's MDR-TB treatment success rate the highest in China.

Loss-to-follow-up (LFTU) rates have improved dramatically under the CAP-TB/NAP pilot program (e.g. no LFTU among 43 patients in Yichang; LFTU reduced from ~75% to ~20% in Xinjiang), despite high MDR-TB drug costs for patients.

Strengthening the public-private mix for tuberculosis: experience and lessons learned from Kenya

J Chakaya¹ ¹Kenya. e-mail: chakaya.jm@gmail.com

This presentation will provide an overview of the pioneering work done in Kenya in strengthening the public-private mix (PPM) on TB diagnosis, treatment and surveillance. It will review the following, with a special emphasis on PPM approaches to finding the missing cases:

- Establishment of partnerships between the public and private sectors on TB management
- Improving case detection and reducing diagnostic delays
- Referrals between public and private sector health care providers
- Enrollment on appropriate treatment
- Monitoring of treatment under program guidelines

The presentation will discuss lessons learnt from the work done through the collaboration of the Kenya Association for the Prevention of Tuberculosis and Lung Disease (KAPTLD) and the Government of Kenya at various levels of the healthcare system.

SP45 Confronting the commercial drivers of disease—how and what needs to be done to protect health gains at global and local levels

The rise of the tobacco industry and what it means for tobacco control

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Tobacco industry foundations and funded front groups are increasing along with tobacco industry interference in health and economic policies. What this means for tobacco control, health policies and SDGs will be explored along with key challenges, risks and way forward.

Putting ethics to work: how UNDP has evolved exclusion criteria to achieve the Sustainable Development Goals

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The United Nations Development Programme (UNDP) will share how they were guided by ethics in identifying exclusionary criteria for their partnerships that would help achieve the Sustainable Development Goals.

The influence of tobacco and alcohol industry interests often impede pursuit of the multisectoral approach necessary for effective action on non-communicable diseases.

To ensure this in its organizational guidance, UNDP revised its due diligence criteria to exclude any partnerships with the tobacco or alcohol industries. The starting point of this policy is the recognition that the interests of the tobacco and alcohol industries are fundamentally incompatible with sustainable development.

SP46 Reaching the unreached to find the missing millions

Reaching key tuberculosis populations through case detection activities: an overview of TB REACH work

J Creswell¹ ¹Stop TB Partnership, Geneva, Switzerland. e-mail: jacobc@stoptb.org

The Stop TB Partnership's TB REACH initiative funds and supports a variety of TB case detection activities aimed at finding, treating, and supporting individuals that are most affected by TB with a strong monitoring

and evaluation emphasis. In many countries, those people who are missed by the routine health services often belong to key populations that have special needs and require different approaches to successfully reach them. This presentation will provide an overview of successful, tools, and innovative approaches to reach these groups.

Active TB case finding among transgender and male sex workers in Pakistan

S Shah¹ ¹Dadabhoy Institute of Higher Education, Karachi, Pakistan. e-mail: drsharafshah@yahoo.com

In Pakistan, transgender women and Male Sex Workers (MSWs) are highly socially marginalized groups and at increased risk of TB due to poverty, malnutrition, overcrowded living conditions and high prevalence of HIV. They have limited access to health care services due to stigma and discrimination.

We present the results of a Wave 5 TB REACH project that used active case finding among these key populations to enhanced access to TB diagnostic and treatment services. The results of the intervention showed that through community outreach we were able to verbally screen 42525 people, test sputum on Xpert of 7472 individuals, and diagnose 625 (of which 438 were bacteriologically confirmed) transgender women and MSW with TB and registered 97.3% of them on treatment through April 30th 2018. Total 1451 individuals were tested for HIV and 19.2% among transgender women and 15.3% among MSW were found HIV +ve.

Reaching the unreached to find the missing millions: community-based approaches in India's tribal pockets

A Vyas¹ ¹Asha Kalp, Gwalior, India. e-mail: ashvini.vyas@ashakalp.org

The Sahariya tribal communities have a documented TB burden that is 10 times higher than India's national average. These communities historically have had limited access to government-run health services due to stigma, language, and geographic barriers. To address this problem, Asha Kalp, a local NGO, has implemented active case finding activities. To date, Asha Kalp's activities have resulted in 146,929 persons screened for TB and 2,027 people started on treatment.

This presentation will discuss the successes and challenges of trying to improve care in this often neglected community.

Integrated provider initiated TB and HIV services among internally displaced persons in North-Eastern Nigeria

S Abdulkarim¹ ¹Gombe State Agency for the Control of AIDS, Gombe, Nigeria. e-mail: surajkwami@yahoo.co.uk

This project promotes TB and HIV awareness, increase detection, and improves linkages/referrals among Internally Displaced Persons (IDPs) in camps and host communities through active involvement of community volunteers and community based organizations.

Working in sometimes challenging environments in Gombe state, the project delivers crucial interventions to IDPs affected by HIV and TB and has significantly scaled up case finding in the region.

Community rising to address tuberculosis: working in peri-mining communities

V Muzuka Kabwebwe¹ ¹Service Health and Development for People Living Positively with HIV/AIDS, Kahama, Tanzania, United Republic of. e-mail: venancez@yahoo.co.uk

In Shinyanga region, Tanzania, people with TB face numerous challenges. The general population often seeks care from traditional healers and lacks knowledge about TB. Key populations such as gold miners and female sex workers (FSW) face additional challenges that include high rates of HIV, stigma and occupational risks. The Kahama Community TB Outreach program succeeds in increasing case detection among these key populations through community education, house-to-house and other forms of community screening, sputum transportation and follow up.

SP47 Overcoming gender inequity in TB by understanding factors that drive excess male burden of disease

Gender gap in tuberculosis burden

C Sismanidis¹ ¹WHO, Geneva, Switzerland. e-mail: sismanidisc@who.int

National tuberculosis (TB) surveillance and survey data, when disaggregated and analysed by gender, provide important evidence for understanding which gender is most affected by the disease. These results can then be used to inform response efforts for the strategic allocation of resources and greatest impact. Case notification rates are higher among men than women in the majority of countries. Globally 60% of TB cases and 65% of TB deaths occur among men. Prevalence surveys show an even more pronounced male disadvantage for undiag-

nosed TB disease, suggesting lower case-detection rates and a disproportionate role in transmission.

Together these data suggest substantial gender disparity in TB with the burden of disease among men greater than among women.

Gender differences in smoking behaviour among TB patients: is there a need for programme collaboration?

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Smoking substantially increases the risk of tuberculosis, delay in diagnosis, failure of treatment and death from tuberculosis. Globally, the prevalence of tobacco smoking is nearly six times higher among men than women, although in some regions gender differences are even more extreme.

The Union Working Group assessed smoking behaviour and smoking cessation among TB patients in Indonesia and other countries. It was found that smoking prevalence was 75.1% in males and 2.5% in females. We found that smoking prevalence in TB patients was 30.5% in China (all males). In India, among the current tobacco users, 89.6% were males and 10.3% were females. In Bangladesh, smoking prevalence among TB patients was 20%, predominately males.

The findings suggest that smoking might be one of the significant drivers of TB especially among males. Smoking interventions are one of the best ways to prevent unwanted tuberculosis outcomes.

Masculinity and men's decisions about tuberculosis care

J Chikovore¹ ¹Human Sciences Research Council, Durban, South Africa. e-mail: jchikovore@hsrc.ac.za

Both men and women face long periods of untreated TB disease, but prevalence-to-notification ratios and modelling work show that delays are much longer for men. Focus group discussions and individual interviews were conducted in Blantyre, Malawi, to investigate the role of masculinity in care-seeking delay for men with TB-suggestive symptoms. An expectation to provide for and lead their families and to control various aspects of their lives, while facing limited employment opportunities and small incomes, leaves men feeling inadequate, devoid of control and anxious about being marginalised as men. Men's struggles to achieve ideal images seem to influence their engagement with their health, and important barriers to utilising TB services come from opportunity costs of care-seeking and perceptions of vulnerability.

Targeted approaches to improve utilisation of diagnostic and treatment services are needed and must address men's concerns, for example, by affording them privacy, a sense of control and flexibility.

Modelling gender disparities in tuberculosis in Viet Nam

K Horton¹ ¹London School of Hygiene and Tropical Medicine, London, United Kingdom.
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Men's higher burden of tuberculosis disease may be explained by a number of biological and socio-cultural factors that increase risk of infection and disease. We developed a gender-stratified dynamic transmission model that incorporates gendered risk factors to describe gender disparities in Viet Nam, where the male-to-female ratio in smear-positive tuberculosis prevalence is one of the highest in the world at 5.1:1. Our model allows us to examine the contribution of specific factors including HIV infection, tobacco smoking and access to care, as well as social contact patterns and other risks, and to explore the impact of interventions in any of these areas on gender disparities in tuberculosis burden.

Following presentation of these results, the session chairs will lead a panel discussion to discuss concrete solutions to overcoming gender inequity in TB.

SP48 Scaling up childhood tuberculosis care: lessons learnt, challenges faced, solutions proposed

Catalysing the use of innovative tools and programmatic models to improve paediatric TB care: an overview of the Catalysing Paediatric TB Project in Kenya

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Paediatric TB is a priority area in the current strategic plan for the Kenya National Tuberculosis, Leprosy and Lung Disease Program (NTLD-P). NTLD-P, in collaboration with partners, has made important strides in the prevention, care, and treatment of paediatric TB.

Despite these successes, key challenges remain to be addressed. Current limited capacity for TB diagnosis, inconsistent screening for TB among child contacts and children living with HIV, insufficient integration of TB into other services, leads to missed opportunities for improved case finding and timely management. EGPAF will partner with NTLD-P to implement the UNITAID funded Catalysing Paediatric TB Innovations Project (CaP TB).

CaP TB aims at improving management of childhood TB by developing integrated and innovative models for delivery of TB care in child health services in both the public and private sectors as well as by facilitating transition to the latest tools for paediatric TB diagnosis and treatment.

Scaling up childhood tuberculosis programmes: experiences from Uganda

M Sekadde¹ National TB and Leprosy Control Programme Uganda, Kampala, Uganda.
e-mail: moorine.sekadde@gmail.com

This talk will highlight child TB management challenges from a resource limited perspective. Dr Sekadde will share the programmatic steps taken to scale up child TB care in Uganda and provide lessons learned from implementing a cascade training approach to improve child TB case finding and management. In addition, she will share Uganda's experience in integrating child TB into routine child health programs.

Child's play: the failure of the global community to scale up treatment and prevention for children with DR-TB

J Furin¹ Harvard Medical School, Boston, United States of America. e-mail: jenniferfurin@gmail.com

Each year it is estimated that there are between 25-33,000 children who become newly sick with DR-TB. Data show, however, that fewer than 5% of them ever receive a diagnosis and treatment for their disease. There are multiple barriers to diagnosing children with DR-TB and to starting them on effective treatment, and this session will explore these barriers and possible solutions. Special focus will be given to the lack of new drug use in pediatric populations and to the dire need for an injectable-free regimen for this vulnerable population.

Turning points for children with tuberculosis

L Mckenna¹ Treatment Action Group, New York, United States of America.
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This talk will describe progress and remaining challenges in raising political will and resources to address childhood TB, both in research and in programmatic implementation. It will provide an overview of annual investments in pediatric-focused TB R&D compared to estimated need, and the resultant state of the research pipeline and remaining knowledge and development gaps. Regulatory and other barriers that hinder access to pediatric TB medicines will also be discussed.

The presentation will highlight advocacy campaigns and efforts to build political will (including efforts made in the lead up to the UN High Level Meeting on TB), and identify concrete next steps to be taken to end childhood TB.

SP49 Laboratory human resources: abating attrition, closing the gap and finding solutions

Building capacity for sustainable training and credential maintenance systems for laboratory professionals to address HR concerns in TB laboratory programmes

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The workforce in TB laboratories is impaired by insufficient supply, unfair distribution, compromised safety containment, and limited motivating opportunities. These factors contribute to high rate of attrition and professionals prefer other fields where there are good opportunities.

Additionally, basic pre-service trainings, professional registration, level of qualification, and certification requirements vary in different countries which hinders the free movement of professionals. The African Society for Laboratory Medicine provided two rounds of Laboratory Quality Management System training to TB laboratory professionals from 18 African countries in order to build a cadre of professionals to support network diagnostic services. From this experience the ASLM advocates for the development of strategic plans that can address the integration of laboratory practices, standardizing training and certification programs across countries.

In addition, the ASLM encourages African countries to establish mutual recognition of laboratory specialists in order to allow for free movement of professionals across countries.

Assessment of the status of laboratory professionals in East Africa and government actions to strengthen the profession as a key pillar of quality health care

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The labor market for laboratory workers in many developing countries has been characterized by constrained supply (especially well qualified staff), sluggish public-sector demand, and relatively low wages. This leads to a high turnover of staff with highly skilled staff finding work in the private sector. The East Africa Public Health Laboratory Networking (EAPHLN) Project conducted an assessment to review the status of laboratory workers in East Africa focusing on their roles in health care and the current status (production and employment, remuneration, career progression and representation).

The report highlighted a number of action points:

- (i) improve and expand pre-service training to match with the labor market, laboratory professionals career growth and HR development;
- (ii) advocate for investment in laboratory services and support of laboratory professionals;
- (iii) advocate for representation in decision making levels within the ministries.

Progress has been made in implementing some recommendations and will highlight with this presentation.

Human resources development plan as the ultimate tool to address challenges with TB laboratory staff management

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Although human resources are the backbone of diagnostic services, national TB programs are constantly challenged by a lack of qualified staff. Over the past ten years, SRL Gauting continuously assisted TB laboratory networks in Central Asia with human resource planning and development. The commissioning of new BSL-3 laboratories adjusted to the TB diagnostic needs and accompanied with the long-term on-site training programs. Such programs included a step-wise assistance with the implementation of ISO 15189-conform quality management systems.

These programs have been evaluated through monitoring of laboratory quality indicators, workloads and output per staff, successful proficiency testing, as well as decreases in staff turnover and occupational TB cases. The efficiency of this integrative approach and its impact will be presented.

Addressing HR challenges to improve laboratory systems performance: approaches, experiences and lessons learnt from SRL Milan

R Alagna¹ ¹WHO Supranational Reference Laboratory, Milan, Italy. e-mail: alagna.riccardo@hsr.it

Building capacity and facilitating more equitable access to comprehensive and appropriate TB diagnostic is essential to substantially progress toward TB elimination. However, the numbers, distribution, knowledge, skills and motivation of the workforce represent an important asset for strengthening laboratory services. In low-income countries, human resources constraints continue to be a challenge severely impacting on quality, timeliness, uptake of new technologies and universal access to services.

This presentation will briefly describe the experience, challenges and lessons learnt from SRL Milan in building capacity to strengthen quality of service and accelerate the introduction and expansion of new molecular

diagnostic technologies in LIC where HR data quality, lack of comprehensive national HR plan/strategy and little attention to continuing education programmes still remains a hurdle.

Investing in sustainable solutions for strengthening the diagnostic workforce

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Panel discussion designed to engage participants to identify practical and logical solutions to build local training in academic programs and curriculum for new lab scientists in LMICs. Building curriculum for advanced sciences such as microbiology and molecular biology are needed as technologies become more sophisticated. Building a cadre lab scientists which are able to handle new technologies as well as empower skills development in critical thinking, troubleshooting, and instrument maintenance are essential to ensure routine lab operations. Involving local colleges and universities to design local solutions by engaging Ministries of Health and Education are needed. Budgeting funds to support these developments and pay sufficient wages to ensure a strong and competent workforce is essential.

The presenter will pose several questions to stimulate discussion. Members of the audience may be recruited to the panel from NRLs, MoHs, and academia that attend.

SYMPOSIA: SATURDAY, 27 OCTOBER 2018

SP50 Implementation of the revised WHO tuberculosis infection control guidelines: what's new?

An introduction to the new WHO guidelines on tuberculosis infection control: what is new?

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The presentation will provide the background information on the updated WHO TB infection prevention and control guidelines and provide an update on the recommendations of the new guidelines. Unlike previous TB IPC guidelines, this guideline is not written in such a way that it could be adopted directly into a national policy. The discussion will include how the guidelines can be incorporated into a comprehensive infection prevention program at the national level as well as the local level. Other presentations will include discussions of how the new recommendation might influence the incorporation of changes and the implementation of the evidence-based measures in local TB IPC plans.

Research gaps in infection prevention and control (IPC): what we know and what we don't

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Due to complexity of airborne infection transmission factors the evidence base for recommended preventive interventions is quite limited.

This presentation will focus on current knowledge gaps, on what is currently known and what is not about effective tuberculosis infection prevention and control measures. A roadmap for future TB IPC research will be discussed.

How to implement the WHO infection control guidelines: experience from India

S Baveja¹ ¹Lokmanya Tilak Municipal Medical College, Mumbai, Mumbai, India. e-mail: smbaveja@yahoo.com

Most health care facilities in India are overcrowded, and hospital administrations generally have difficulty in committing to all aspects of infection control. In addition, there are many challenges in working with large vulnerable populations in a high-TB burden setting.

There are many opportunities to improve infection control in India, including the strengthening of the health care infrastructure and practices which is now under consideration.

The presentation will focus on implementation of airborne infection control practices in Mumbai.

Measuring impact of infection control measures

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Monitoring and evaluation of TB IC interventions have been challenging for health staff implementing these interventions as there seem to be no grossly obvious indicators to measure TB IC activities. This has led to unsustained interventions have been limited.

This presentation would present list of practical and measurable indicators and measures for TB IC implementation.

Implementing the new WHO guidelines: procurement of equipment and supplies by the Global Drug Facility

W van Gemert¹ ¹World Health Organization, Geneva, Switzerland. e-mail: vangemertw@who.int

The Global Drug Facility (GDF) is the procurement arm of the Stop TB Partnership and provides a one-stop shop for national TB programmes, as well as technical assistance for procurement and supply management.

Aside from its catalogue of medicines, GDF maintains a catalogue of over 500 items to equip and maintain TB laboratories and also to provide needed equipment, consumables and personal protective equipment for infection control. GDF is revising its portfolio and scope of work to respond to the latest WHO guidelines.

SP51 Clinical trial capacity building to address multidrug-resistant tuberculosis: challenges and the way forward

Multidrug-resistant tuberculosis clinical trial landscape overview

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The growing epidemic of MDR- and XDR-TB affects over a half a million people worldwide. Those affected will have varying ability to tolerate effective drugs and varying patterns of resistance to these drugs. Therefore, it will be important to identify a number of effective and

well-tolerated treatment regimens. This will require a robust network of clinical trial sites, investigators, laboratories and data management teams.

This presentation will describe current and proposed MDR/XDR clinical trials, review current global trial capacity and project future needs.

Ethics and regulatory capacity building

A Aseffa¹ ¹Armauer Hansen Research Institute (AHRI), Addis Ababa, Ethiopia. e-mail: aseffaa@gmail.com

Clinical trials must adhere to the highest standards of ethics and good practices to ensure human subject protection and deliver credible data irrespective of where they are conducted. TB high burden countries are often plagued with a multitude of health system challenges including absence of a vibrant research network and a conducive environment. Communities are often unaware of the difference between research and practice. Along with building institutional core competence for MDR-TB trials, researchers are thus obliged to contribute to strengthening their national regulatory capacity and to developing national ethical review systems without which trials would be at risk of losing credibility. The Ethiopian experience will be discussed to illustrate challenges faced in setting up a regulatory agency, experience in reviewing in-country and international clinical trials and efforts to build capacity.

Challenges, efforts in strengthening site pharmacies and pharmacists in the STREAM Trial

J Komrska¹ ¹Vital Strategies, New York, United States of America. e-mail: jkomrska@vitalstrategies.org

Uninterrupted availability of investigational medicinal products (IMPs) is crucial for successful implementation of a clinical trial. However associated challenges such as regulatory requirements, extensive supplier's lead-times, substantial costs, batch management and limited shelf life create complexities in supply chains.

Therefore, designing and establishing responsive supply chain for IMPs is a priority for STREAM pharmacy team. Clinical trials must comply with Good Clinical Practice (GCP) guidelines that emphasize on safety and well-being of patients as a priority. Analyzing potential risks and establishing preventive measures was another critical step in supply chain management of IMPs. These included introduction of temperature monitoring of storage conditions throughout the supply chain (from manufacturer to patients) and developing electronic IMP accountability system.

Special attention is paid to the pharmacy staff development. An online GCP course and Continuous Professional Development was created for the benefit of all pharmacy staff from the hospitals involved in the trial.

Mycobacteriology laboratory capacity building for tuberculosis clinical trials

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Microbiology laboratory strengthening is mandatory in the context of TB clinical trials given the crucial role they play in:

- (i) determining patient eligibility for enrolling in trials and
 - (ii) generating data (culture results, drug sensitivity profiling) that are key outcomes for most TB clinical trials.
- This presentation from the National Institute for Research in Tuberculosis (Chennai, India) will present some of the main challenges faced by site laboratories in strengthening their physical and human resource capacity to make them trial-ready. Importantly, it will focus on quality management issues that are central to reliability of data generated from laboratories and that determine their suitability to conduct trials during pre-trial assessment visits and subsequently in inspections by regulatory authorities, other relevant bodies.

The speaker will draw on the site's experience functioning as a National/Supranational Referral Laboratory as well as a site laboratory for TB clinical trials for over 50 years.

Community engagement in multidrug-resistant tuberculosis clinical trials

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Community engagement (CE) is an ethical requirement for tuberculosis (TB) trials. It enables communities to participate during all stages of research, shaping the research agenda and advocating for evidence-based policy change. It also improves trial implementation, providing community feedback about feasibility and acceptability of research. Vital Strategies/The Union partnered with REDE-TB to incorporate CE into the STREAM clinical trial, which is evaluating shorter, more tolerable regimens for MDR-TB.

This session will describe the process of, and challenges related to, integrating CE into a multi-site clinical trial and will explore:

- initial development of a community engagement plan following a pilot at the STREAM site in Mongolia;
- establishing CE mechanisms at STREAM sites with a wide range of exposure to and cultural affinity for CE;
- scope of CE activities supported by the STREAM trial, and;
- monitoring and evaluating the impact of CE.

SP52 How prices could affect universal access to anti-tuberculosis treatment of the future? Options for solutions

What would the tuberculosis regimens of the future look like?

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The aim for TB is not just to develop a new compound but to combine new and existing compounds earlier in the clinical development process to develop new regimens to treat TB. The WHO Target Regimen Profiles outlines target indicators for three different types of regimens, including a pan-TB regimen. How the TRP's can be interpreted for novel regimens for the future will be discussed.

Trends in multidrug-resistant tuberculosis treatment prices and scale-up

C Perrin¹ ¹MSF, Paris, France. e-mail: christophe.perrin@paris.msf.org

MSF has been tracking the prices of MDR-TB drugs in the Under the Microscope report since 2011 and the latest results of the cost and access barriers to existing MDR-TB drugs will be presented as well as the pricing/scale up trends since 2011 and what can be learned from this data for future TB treatments.

Trends in the tuberculosis drug market

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Despite the fact that TB is the leading infectious disease killer globally, incentivizing investment in the field of TB innovation has been challenging, due in large part to perceptions of low potential for return on commercial investment. Segmentation across public and private sector buyers obscures the size and value of the aggregate market. Non-standardization of treatment due to formulation variation and diversity across drug-sensitive and drug-resistant regimens further fragments the market. This presentation will look at the aggregate public and private sector TB markets in 10 countries. Improved visibility into the TB market can help drive further investment in TB, while at the same time informing strategies to ensure affordability, appropriate stewardship, and access.

Modelling costs of new tuberculosis regimens

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Higher costs of novel TB treatment regimens are likely to be offset to some degree by associated reductions in other expenditures (e.g. on treatment safety monitoring). Additional drug spending may also be justified by the value of health gains (e.g. improved treatment outcomes) that novel regimens achieve. Different decision-makers will give different weight to budgetary impact versus cost effectiveness considerations, and both perspectives will vary between settings with differing TB epidemiology and health care costs.

This presentation will explore what increased drug expenditures on novel tuberculosis regimens are likely to be considered acceptable, from affordability and cost-effectiveness perspectives and in a variety of settings.

SP53 Chronic lung disease in older children with human immunodeficiency virus infection

Chronic lung disease in young adults living with human immunodeficiency virus—not just bronchiectasis

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Worldwide, chronic lung diseases are an increasingly recognized complication of HIV among older children and adolescents, especially those living with perinatally-acquired HIV. The term chronic lung diseases is broad and encompasses pathophysiologic processes such as bronchiectasis, obliterative bronchiolitis, asthma, post-tuberculous sequelae and lymphocytic interstitial pneumonitis.

The symptomatic presentation of these heterogeneous diseases can be non-specific, highlighting the importance of lung function testing and imaging to characterize these disease processes and target clinical management.

Lung function in human immunodeficiency virus infected children and adolescents

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Chronic lung disease is common in HIV-infected adolescents despite increased access to antiretroviral therapy (ART). Lung function measurements may help to delineate the spectrum, pathophysiology and guide therapy.

There is limited information on the spectrum, determinants and progression of lung function in HIV-infected adolescents on ART. Lung function abnormalities reported in HIV-infected children and adolescents include irreversible lower airway obstruction and reduced functional aerobic impairment on exercise with more severe spectrum in the ART-naive. Previous pulmonary tuberculosis or lower respiratory tract infection and chronic cough were associated with low lung function.

The radiological morphology of chronic lung disease in human immunodeficiency virus-infected adolescents

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The outlook for people living with HIV has improved with the global scale-up in ART. In children the incidence of perinatally-acquired infections has declined and survival improved. However, chronic respiratory symptoms are common. Imaging tests have a role in the investigation of chronic symptoms but plain chest radiography (CXR) is insensitive and terminology used to define abnormalities often inconsistent. More recently, high-resolution computed tomography has been used to explore the morphological basis of chronic lung disease. This has provided new insights into the pathophysiology of chronic lung disease in HIV-infected older children.

Cytomegalovirus virus in perinatally acquired HIV-infected children and its association with chronic lung disease

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Cytomegalovirus (CMV) is a common herpes virus that infects most African children in infancy: therefore children with perinatally-acquired HIV infection (PHIV) very probably acquired CMV infection at a time of uncontrolled HIV infection. The long-term consequences of CMV co-infection in African children with PHIV are not known. We found a high prevalence of CMV DNA-aemia in both ART-treated and untreated older children and adolescents with PHIV in Harare, Zimbabwe. Significant correlations were observed between CMV DNA-aemia with stunting and abnormal lung function (defined as FVC or FEV1/FVC ratio z scores less than <-1.64 (below the 10thcentile).

Distinct lung microbiota associated with chronic lung disease in children with HIV on antiretroviral therapy

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The lung microbiota is thought to play a role in HIV-related lung pathology. We hypothesized that compositionally distinct lung microbiota exist, and are differentially related to the risk of HIV-related chronic lung disease (CLD).

We analysed the microbiota of 151 HIV-infected adolescents. Principal coordinate analysis (PCoA) using weighted Unifrac distance matrices demonstrated that sputum dominated by Haemophilus, Moraxella or Neisseria (HMN) were compositionally distinct from sputum dominated by Streptococcus or Prevotella (SP) ($p < 0.001$, $R^2 = 0.492$). The HMN group ($n = 35$) had a 1.5 times higher risk of having CLD compared to the SP group ($n = 116$) ($p = 0.024$). Cluster sampling using Dirichlet multinomial mixtures (DMM) identified four compositionally distinct groups and iterated that the HMN group (DMM Cluster 3/4) had a significantly higher risk of CLD than the SP group (DMM Cluster 1/2) ($RR = 1.48$, $p = 0.035$).

Our data suggests that HIV-infected older children have two compositionally distinct sputum microbiota with HMN being associated with CLD.

SP54 Building models for the future—innovative partnerships addressing legal issues, and systems and human rights-related barriers to TB-HIV care

“Improved TB-HIV prevention and care-building models for the future” project—innovative partnerships

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Four “unlikely” organisations have joint forces in the “Building Models for the Future” project with the aim to improve TB and HIV prevention and care in line with the Global End TB Strategy, the Sustainable Development Goals and the Fast-Track Strategy to End AIDS.

The focus is on system related barriers to quality of care in the non-governmental and private health care delivery sectors, and removing human rights and gender related access barriers to TB/ HIV care and prevention. And the goal is to ensure access to affordable, adequate, quality care for vulnerable and marginalized key affected populations so that no one is left behind in the fight against TB/HIV.

The presentation introduces the partnership, philosophy and overarching strategy.

Establishing and strengthening NGO networks providing a full range (legal, psycho-social, anti-discrimination, etc.) of supportive patient-centred activities for vulnerable and key affected populations

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In the frame of 'Improved TB/HIV Prevention & Care - Building Models for the Future' Project, we created a NGO network in Almaty city, providing psychological-social and legal consultations to key populations (PLHIV, TB patients, drug users, internal migrants). The NGO network screens clients for TB and refers presumptive patients for further examination. It is involved in intensified case finding, patient follow-up and support provision for those from risk groups on ambulatory treatment. NGOs are providing consultations for clients on patients' rights and advice on selection of PHCs such as cases of discrimination in PHCs that are being discussed during TB/HIV TWG meetings with the management of public and private clinics.

The NGO network augmented the effectiveness of patient-centred services, and improved treatment outcomes by increasing the number of clients on comprehensive treatment adherence support, by giving counselling, peer support, self-help groups and legal advice.

Supporting the mechanisms and legal framework of collaboration between public and non-public/private sector—changing perspectives

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In Kazakhstan, TB care was traditionally a responsibility of the public healthcare sector (TB service and primary healthcare). Private clinics were not allowed to provide TB care. Since 2014 the Ministry of health has been expanding health care provision through the Guaranteed Volume of Free Medical Care (GVFMC) system entitling public and private clinics to provide a package of free care, including ambulatory primary health care, for which they would be reimbursed by the government. In 2017, 16 private clinics were entitled to provide the ambulatory package in Almaty city.

Although the ambulatory care package included TB care, private clinics were not aware of regulations and organisational requirements to provide TB care. They all assumed that they needed to refer any presumptive TB patient to the public sector for diagnosis and treatment, and that their clinic conditions would not meet the specific requirements.

Improving the quality of TB-HIV services in the non-public sector through the internationally accredited SafeCare standards and International Standards for Tuberculosis Care

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The integrated quality improvement tools (ISTC; SafeCare Standards) used by the BMF Nigeria project stimulates progressive and sustainable achievements in improving the quality of holistic health service delivery and TB/HIV services. Following an assessment, the standards are able to identify critical gaps in patient care quality and patient safety. A quality improvement plan is developed to address these gaps, facility staff are trained and regular M&E visits are conducted to assist the facilities achieve these activities in good timing. Beyond the use of these tools in the BMF project, the SafeCare Standards have been used to support the Lagos State Government in developing the empanelment guidelines for the upcoming State-wide Health Insurance Scheme. The ISTC was also used to develop a simple checklist that is being used by the Health Facility Accreditation and Monitoring Agency (HEFAMAA) to check the quality of TB/HIV services during monitoring visits to private healthcare providers.

Non-public sector one-stop shop TB-HIV service provision prototypes tailored to vulnerable and at-risk populations—seen from a human rights perspective

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Care seeking behaviour and provider choice are determined by individual needs and priorities, socio-economic factors, (perceived) stigma and discrimination, and a sense of safety. Most vulnerable and at-risk populations in the Philippines seek care in the non-public sector. The project seeks to provide tailored (patient-centred) and yet standardised (quality and scope) integrated TB/HIV service through one-stop-shop prototypes.

The project further ensures the financial resilience and long-term sustainability of community-led HIV and TB service provision, by supporting both capacity development of their operations, and also their official accreditation under the Philippine Health Insurance Corporation (PhilHealth).

The project focuses on local Key Populations, such as: young people, people leaving in urban poor settings, men who have sex with men, transgender people, sex workers, and people who use drugs.

SP55 Multi-disease: testing the next paradigm

Integrated TB-HIV diagnostic platforms—potential for synergy and efficiency

C Gilpin¹

New laboratory technologies are currently available or are being developed to allow for testing of different conditions using disease-specific tests on the same platform. For example, a single platform may be able to test for the presence of tuberculosis (TB), drug-resistant TB and HIV. Separate assays quantitatively measure HIV viral load or can be used for early infant diagnosis of HIV. Some of these technologies are being developed as high throughput platforms for use at centralized reference laboratories while others may be positioned at lower levels of the health system where patients may access both TB and HIV services in the same facility. The introduction of multi-disease testing devices such as the GeneXpert (Cepheid, Sunnyvale USA) brings new opportunities for collaboration and integration, which can provide significant system efficiencies and cost savings, increase patient access, and ultimately improve quality of care in decentralized healthcare settings.

A systems approach to maximise multi-disease testing

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The continued provision of vertical HIV/TB prevention and treatment services, and the slow implementation of WHO recommendations to establish and scale up collaborative TB/HIV activities at the country level have resulted in significant missed opportunities to realize optimal health outcomes for populations affected by both diseases. Establishing links between TB and HIV programs in settings with a high prevalence of both diseases is essential to maximize the effectiveness, efficiency, quality and sustainability of the health sector response. The potential for technologies such as GeneXpert (Cepheid), m2000 (Abbott), Cobas (Roche) and others to drive the integration of TB/HIV diagnostic services as part of a coordinated response to expand access to comprehensive integrated and quality assured services within the TB/HIV care continuum is being recognized.

Multi-instrument/multi-disease connected diagnostics, is this the next frontier?

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In Malawi, the same “connected diagnostics” infrastructure used for the Abbott m2000 HIV VL testing platform across clinical sites is being leveraged as a connectivity solution for GeneXpert Tuberculosis testing. In Mozambique, the GeneXpert MTB/RIF, MGIT culture, and Line Probe Assay are being connected to the same platform to allow real-time viewing of TB and drug susceptibility results across diagnostics. New multi-plexing platforms promise lab-in-a-box but each disease is still managed in separate silos. In the absence of a strong unique Patient ID for most nations, how can data be matched or tracked across instruments, patients, or diseases to ensure maximum health impact? How much of the connectivity infrastructure and cost can be shared when an instrument produces results across several diseases, but the funding for each disease remains silo'd and uncoordinated? What are the lessons learned from 2017-2018?

What's missing to improve efficiency across the laboratory value chain? The Zambian e-LABS experience

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After assessing 653 laboratories in Zambia, it was recognized that a connected solution to remotely monitor the entire laboratory value chain would be of value. eLABS is an mHealth/eHealth solution aimed at strengthening the clinical-laboratory-patient interface within the HIV VL value chain. It is a mobile workflow solution comprising of a monitoring and data management system tracking a range of activities focusing largely on pre-analytic and post-analytic systems. In October 2017, eLABS began its demonstration within the Copperbelt (15 facilities and 2 laboratories). Roll-out of eLABS within three additional provinces commences in April 2018, connecting further 144 facilities and 3 laboratories. Using the Zambian eLABS experience, what lessons can be learnt from: stakeholder engagement, field evaluation, system design, and implementation and user-experience evaluations). How can this experience be applied to improved efficiencies of the laboratory value chain, albeit in HIV/TB?

Leveraging Xpert's expanded assay menu for the integrated management of HIV/HCV/TB co-infections: a MSF field experience

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MSF has been using the GeneXpert platform for TB testing since its WHO endorsement in 2010. Because HIV Viral Load (VL), HIV Early Infant Diagnosis (EID), and HCV VL remain restricted to centralized laboratories, the recent expanded menu of GeneXpert holds the potential to further decentralize testing and increase access in a variety of contexts.

Since their release in 2015, MSF began introducing HIV VL and EID testing in a number of programmes and, more recently, HCV VL testing. Notwithstanding the easiness to bring in new tests in already existing GeneXpert platforms, additional programmatic considerations were necessary to successfully integrate testing under routine practice.

Although the deployment of the GeneXpert polyvalent platform in more remote healthcare settings demanded substantial planning and resources, this was counterbalanced by increased patient access to testing and timely diagnosis in areas where complicated logistics is commonplace.

SP56 Final STREAM Stage 1 results with implications for implementation

Final results of the Standardised Treatment Regimen of Anti-TB Drugs for Patients with MDR-TB (STREAM) Stage 1 trial

A Nunn¹ ¹UCL, London, United Kingdom. e-mail: andrew.nunn@ucl.ac.uk

The STREAM Stage 1 trial compared the short 9-11 month MDR-TB regimen with the standard of care 20+ month regimen in a randomized controlled trial. 424 patients from seven sites in four countries were enrolled. In this talk, the final efficacy and safety results of the STREAM Stage 1 will be presented.

Preliminary results were presented at the Union conference in 2017, but a number of patients were still in follow-up and only a sub-set of results were available. Full and final results from all patients will be presented.

Understanding the potential toxicity of the short regimen

S Meredith¹ ¹MRC Clinical Trials Unit at UCL, London, United Kingdom. e-mail: s.meredith@ucl.ac.uk

To evaluate the toxicity of the short MDR-TB regimen compared to the 20+ month standard of care, regular ECG monitoring as well as liver and renal function testing were undertaken for all patients in the trial.

In this talk, results of this monitoring will be presented together with other safety data from the trial, and the approach taken to management of patients experiencing QT prolongation while on treatment will be discussed.

The presentation will consider the implications of the STREAM Stage 1 experience for monitoring and managing patients on the short regimen in programmatic settings.

What do we learn about giving this regimen to patients co-infected with human immunodeficiency virus?

F Conradie¹ ¹University of Witwatersrand, Houghton, South Africa. e-mail: fconradie@witshealth.co.za

A large number of patients with MDR-TB across the globe are also co-infected with HIV, particularly in Sub-Saharan Africa. One third of the patients in the STREAM Stage 1 trial were HIV positive, and this talk will cover the available data on the efficacy and safety of the short regimen in patients co-infected with HIV. The speaker will draw on her experience as investigator treating TB/HIV patients in the trial and put the results in the context of available treatment options for MDR-TB/HIV co-infection.

The presentation will also include suggestions for patient management for MDR-TB/HIV co-infection for the short regimen in programmatic settings.

What are the real benefits for the patient and the health system?

B Squire¹ ¹Liverpool School of Tropical Medicine, Liverpool, United Kingdom. e-mail: bertie.squire@lstm.ac.uk

An important secondary objective of the STREAM Stage 1 trial was to compare the economic costs incurred by patients and by the health system during treatment on the short MDR-TB regimen as compared to the long MDR-TB regimen.

This presentation will cover results addressing this objective, using the Impact Assessment Framework as a basis for presenting the impact of the short MDR-TB regimen.

Disseminating Stage 1 results to the community: successes and challenges

B Tsogt¹ ¹Mongolian TB Coalition, Ulaanbaatar, Mongolia. e-mail: bazra.ts@outlook.com

Guidelines for the treatment of MDR-TB have seen a number of changes since 2016, prior to and subsequent to the release of the preliminary results from STREAM Stage 1.

This talk will showcase the experience from the dissemination of STREAM Stage 1 results in the Mongolian STREAM site, including both successes and challenges.

SP57 Harm reduction, e-cigarettes and new tobacco products

From banning to regulating: attempts at e-cigarette and new tobacco product regulation in Mexico and Brazil

J Laucirica¹ ¹The Union, Mexico City, Mexico. e-mail: jlaucirica@theunion.org

This presentation provides an overview on new tobacco product regulation in Latin America, with a focus on Mexico and Brazil, the two largest regional battlegrounds. Mounting pressure from user groups and the tobacco industry is sparking a shift from banning to regulated commercialization. The outcome will hinge on the political will to uphold and strengthen the overall tobacco control framework. In Brazil, a regional leader in tobacco control, the government has taken the initiative through an inclusive consultation process.

The experience in Mexico, where tobacco control laws are much weaker, is quite different: concerted government and civil society action temporarily blocked two bills of law favoring lax regulation of new tobacco products. The outcome of these processes may have a lasting impact across the region.

The Union perspectives on harm reduction, e-cigarettes and heated tobacco products

M Wisotzky¹ ¹International Union Against Tuberculosis and Lung Disease (The Union), Seattle, United States of America. e-mail: myra.wisotzky@gmail.com

Marketing, awareness and use of e-cigarettes and heated tobacco products has dramatically increased over the past few years. The Union has developed position statements regarding e-cigarettes and heated tobacco products.

This presentation will highlight The Union's perspectives on these products and on tobacco harm reduction. Debate exists in the public health community about

the, as yet unproven, role of these products in tobacco control. However proven harm reduction interventions, such as the policies embodied in the WHO MPOWER policy package, exist and need to be strengthened and increased.

SP58 Learning from patients to design an improved tuberculosis care delivery system

Tuberculosis patients are the solution, not the problem!

E Fekadu¹ ¹Volunteer Health Services, Addis Ababa, Ethiopia. e-mail: enda.pharm@gmail.com

In this presentation Person-centric TB care system, based on his experience in DR-TB care in Ethiopia.

DR-TB patients have complex medical and social needs, as well as personal preferences, that all members of the health care system need to understand and respect in order to truly provide patient-centered care. The system has to be flexible, responsive, exhaustive and innovative enough to accommodate the needs of people.

More precisely, patient care patient & family preference, values, culture & socio economic conditions has to be respected, Care has to be collaborative, coordinated and accessible at right time and right place, Tools, system had to couple up with the needs and rapidly changing factors and Compressive clinical as well the socio-economic needs of patients has to be addressed. Any health care system and strategies can never be a solution or sustain itself by neglecting the patients' needs and priorities.

Strengthening the tuberculosis system using survivors

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In this presentation, Dr. Saurabh Rane who is a Drug resistant TB survivor from India, will offer concrete suggestions on how TB survivors can, and should be engaged in order to strengthen national TB programs and improve healthcare delivery systems in low and middle income as well as high burden countries.

SP59 Innovations in private provider engagement

Doubling the number of notifications in Mumbai using a private provider interface agency

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The Private Provider Interface Agency (PPIA) in Mumbai engaged private providers, diagnostic facilities, and pharmacies into a referral network; extended TB support services; and monitored patients' cascade of care at diagnosis, notification, treatment initiation, and treatment adherence. To optimize patient coverage, the program mapped and targeted high-value providers. Notifying providers were given access to free diagnostics (chest x-ray, Xpert MTB/RIF with sputum transportation services) and free anti-TB drugs through e- vouchers. TB patients on treatment were tracked through daily SMS reminders, supported by a call center and dedicated health workers.

This model resulted in notification of 61,000 TB patients (2014 to 2017) from the private sector, representing a 2-fold increase in total patients notified in Mumbai, and improved microbiological diagnosis of private notified patients from 23% to 40%. Subsequent to evaluation by NTP and WHO, this and related models are now being scaled up across India.

Driving private sector notifications in Indonesia using the district public-private mix (DPPM)

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A recent inventory study in Indonesia confirms that one third of identified TB patients were treated in the private sector, two thirds of whom were unnotified to the National TB Program (NTP). The NTP with support of the USAID-funded, KNCV-led Challenge TB project developed several measures, including improved electronic registration and the District Public Private Mix (DPPM) approach to increase notification and engage all providers in TB elimination. While respecting patients' preferences for diagnosis and treatment in private or public sector, DPPM aims to limit the costs of TB care through health insurance incentives, promoting down-referral of uncomplicated TB to (private and public) primary care providers, with access to modern tools for diagnosis and treatment and patient support if needed.

This symposium shares results and effects on notification and discusses essentials of DPPM: Mandatory Notification, tailored primary care and hospital approaches, ownership by health offices, professional societies and communities.

Regulation as an essential tool for successful tuberculosis public-private mix in Ethiopia

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Since 2006, Ethiopia has enrolled an increasing number of private facilities in PPM-TB. This engagement is regulated by the National TB Program (NTP) and the Food, Medicine and Health Administration Agency (FMHCA). Private health facilities operate at different, defined levels based on the standards set by the Ethiopia Standards Agency. FMHCA licenses and re-licenses health facilities using the health facility standards, and for NTP-engaged facilities has waived its restriction not to hold and dispense government procured medicines in private health facilities, and not dispensing drugs by non-pharmacy personnel. The NTP has set regulatory requirements for PPM-TB including signing an MoU, staffing and training, recording and reporting, and adhering to national pharmaceutical standards. This enabling regulatory environment has allowed the progressive increase in the PPM-TB contribution to the national TB case notification from less than 11.4% in 2014/15 to more than 14% in 2016/17.

Digital technologies for the notification of tuberculosis by private providers

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Collection of information from patients evaluated and treated for TB in the private sector presents a challenge to national public health authorities in different settings worldwide. Notification of TB cases and information about the quality of care received and treatment outcomes achieved are thus often incomplete.

For this reason, the elaboration of a target product profile (TPP) for the electronic notification of TB was prioritised by a technical consultation held on the subject by the World Health Organization and the European Respiratory Society since February 2015. An application to help collect information about latent TB infection treatment was later developed through the same effort. This presentation will describe how different digital technologies can help improve data collection for TB patients at different junctures, not only by facilitating the transmission of information electronically from the private sector but also by linking notification to patient and/or caregiver incentives delivered digitally.

Open source and design considerations for private notification apps for tuberculosis

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Electronic tools are an important way to link public and private sector TB control efforts and in particular to collect and aggregate data from different sources. Given the near ubiquity of cellular connectivity in most countries, mobile applications have emerged as a way to quickly and efficiently collect and share data, whether this is in the form of case notification tools like WiFi TB in Indonesia or more powerful applications like those used in Pakistan's ZeroTB Karachi Initiative to collect and analyze data from across the TB care cascade. The use of open source solutions can help reduce duplication of effort in building and deploying such applications. However, it is important to design from the perspective of reuse; adaptability; and scale; and to understand what it takes to develop and then support these systems once they are in place.

SP60 Country approaches to finding missing persons with tuberculosis

WHO perspective: finding missing cases in the context of universal coverage/strategic initiative to find missing people with TB

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The underlying causes of the poor access to quality TB care are multi-factorial ranging from physical and financial barriers, insensitive diagnostic networks, unengaged care providers and vulnerabilities of key populations among other causes.

A range of strategies and interventions are available to address these causes such as the engagement of all care providers, mandatory notification, diagnostic retooling and decentralization, TB screening among high-risk populations, and improving TB service delivery and financing in line with national efforts towards universal health coverage. In order to identify the most effective strategies in each setting, a systematic assessment of epidemiological and health system information is critical. WHO continues to support countries to identify the bottlenecks in each country setting and identify policy interventions to ensure the access to quality TB care for all. In this context, the Global Fund Strategic Initiative acts as a catalyzer for strengthening the national response.

Strategic approaches to addressing the gap

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In response to the global call for action to close the gap for persons with TB who are 'missing' from either the national registers or have not been found and diagnosed, KNCV Tuberculosis Foundation has developed a strategy and related Operational Guide, Find and Treat all Missing Persons with TB (FTMP).

This Guide aims to support district-level FTMP planning and implementation. Based on country experiences, it provides practical approaches and tools to develop, implement, monitor implementation and assess the impact of the FTMP interventions. The guide focuses on implementation at district level, in collaboration with the national and sub-national levels for strategic guidance, data collection and implementation support.

In this presentation, the KNCV approach to FTMP will be presented and discussed, including the rationale for the selected implementation areas as part of a learning cycle that includes assess/prioritize and building evidence.

Intensive contact investigation approach in Swaziland

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Since 2010 Swaziland experienced progressive decline of TB case notifications. Case detection was 59% in 2015 signifying 41% missing TB patients. In 2016 Swaziland introduced active case finding strategy to trace contacts of index patients complementing passive case finding.

The aim was to increase TB case detection. 369 Active Case Finders visit homesteads to educate, screen for TB, collect sputum samples and link TB patients for treatment. Presumptive patients who cannot produce sputum samples are referred to health facilities. 418,655 people were screened and 1,510 TB patients were identified. Case detection increased from 59% to 84%. Contact investigation contributed to case finding by 2.4 above national average. This intensive contact investigation approach shows to be successful in identifying more TB-patients and treating them early.

The community involvement leads to successful implementation of activities, however planning of these interventions was time consuming. Engaging community leaders as advocates increased meaningful participation.

District health planning: experiences from Indonesia

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Indonesia has decentralized government authority to district level, where funding for all programs, including health, largely originates from local funds. The de-

velopment of District Action Plans was supported by Challenge TB and KNCV TB Foundation. The budget for TB in Jember District has significantly increased from USD 44,800 (2017) to USD 117,400 (2018). More than half is allocated for case finding/treatment and PPM activities, each contributing substantially to Find and Treat all missing Persons with TB (FTMP).

The Jember District Health Office has allocated operational funds to conduct contact investigation, patient support and communication - education activities. In a 3-month pilot of contact investigation, 13,567 contacts of 421 index patients were investigated. This covered 10 health centers reaching 25% of the total Jember population, yielding 21 patients put onto treatment and 92 children eligible for isoniazid preventive therapy (IPT), of which 52 received it.

Finding males with tuberculosis: experiences from the Wings Over Wetlands Project in Nigeria

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In Nigeria, the persistently low TB detection rate underscores the necessity of moving beyond the patient-initiated pathway to identify TB patients. Wellness on Wheels (WoW) is a program aiming to find people with TB that are not found by the current health system, specifically people in slums, hard to reach areas and focusing on males who are heavily under-notified in Nigeria. Two trucks equipped with GeneXpert machines and digital X-ray with CAD4TB software go into selected communities in Ogun and Nasarawa states engaging the community for TB awareness raising and systematic screening.

Early results show that among 9,030 people screened, 64% were men, 11.9% were presumptive and 1.3% were positive for TB. Men testing positive (1.7%) at more than three times the rate of women (0.5%). In addition to finding patients that elude facility-based strategies, the program offers opportunities to learn more about TB hot spots.

SP61 Implementation of TB infection control: approaches to monitoring and measuring programmatic success and impact

Assessing the sustainability of tuberculosis infection control interventions/programmes, Nigeria

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Nigeria is ranked 7th among the 30 high TB burden countries globally, and the TB burden in the country is further compounded by a high national HIV prevalence. To address the global burden of TB and HIV, the World Health Organization (WHO) recommends implementation of TB infection control (TBIC) measures as part of the collaborative TB/HIV activities. The national TB program has worked with partners to pilot and scale up some novel TBIC models using the TB BASICS approach and the FAST strategy. The quality of TBIC implementation and continuing implementation after these pilot projects varied across sites depending on the implementation approach, existing partners support, facility ownership and commitment of the facility management. Knowledge of the determinants of sustainability of TBIC implementation will be key in any TBIC program design and implementation for a maximal and lasting impact on the TB program in Nigeria.

Monitoring healthcare workers for tuberculosis using routine screening, Ethiopia

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Healthcare workers (HCWs) have higher risk of developing active tuberculosis (TB) due to workplace exposures. In 2015, rapid assessment of facilities in Dire Dawa Ethiopia showed that TB notification rate among HCWs was 1.4 times that of the general population. However, there is no strong national system for TB surveillance among HCWs in Ethiopia.

As part of a pilot TB Infection Control (TBIC) initiative (Building and Strengthening TBIC Strategies), we implemented HCW TB screening to help monitor the impact of TBIC activities.

SP62 Second annual symposium: Preventing a public good from becoming a market failure—introduction and scale-up of innovations in the era of decentralised financing and procurement

Effects of sustainability financing on procurement: a view from programmes

G Dravniece¹ ¹Challenge TB (CTB), KNCV Tuberculosis Foundation, Den Haag, Netherlands. e-mail: gunta.dravniece@kncvtbc.org

This presentation will provide high-level observations and trends on the effects of sustainability financing on procurement of TB commodities. These observations will include what products are procured with national funds, the quality standards that are used and what barriers programmes face procuring TB products. The effect of the chosen procurement approach on country programmes will be discussed with particular focus on new tool introduction and scale-up.

Risks of sustainability financing to fragile TB markets: evidence from recent innovations, and projections of future impact

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This presentation will provide an overview of shifting procurement trends for TB medicines and diagnostics in relation to changes in donor financing. The impacts of decentralized procurement on new tool introduction and scale-up, including market fragmentation, will be assessed. How this procurement approach will affect the introduction and scale-up of new tools in the pipeline will be explored.

Human rights implications of Venezuela's transition from donor funding

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This section will analyze the impact of donors' transition policies and self-financed procurement in Venezuela on human rights. It will illustrate implications of these policies on the availability of essential health products and quality of care, with a particular focus on HIV and TB products. The section will articulate how the intersection of donor and national policies and politics can impact on affected communities and their human rights. It will include an exploration of what alternative courses or policies would have been needed to be established to prevent the impacts seen on procurement systems and health.

SP63 Tuberculosis contact investigation in high tuberculosis burden settings

Global updates on tuberculosis contact investigation

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Operational experience as well as a number of modeling exercises have indicated that active case-finding will likely be necessary to reach the goals established by the WHO for ending TB. Investigation of the contacts of persons with newly-identified infectious TB is a form of active case-finding that falls within the purview of TB control programs and, thus could be implemented relatively easily. Global recommendations have been developed by WHO but implementation is still limited mostly by staffing and financial constraints. However, to reach the WHO goals for 2035 scale-up of this and other approaches of active case-finding will be necessary.

Ethiopia's experience in scaling up tuberculosis contact investigation

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Ethiopia is a high TB burden country with a third of TB patients reported to be missing each year. As part of the country's comprehensive strategy to improve case finding and treat latent TB among young children, Ethiopia started pilot implementation of household-contact investigation in 2013 in two regions of Ethiopia. Based on the results of the pilot implementation, the strategy was scaled up to all regions of the country. National TB recording and reporting tools were updated to include indicators of contact investigation. Moreover, the country introduced a new contact investigation approach known as "retrospective" contact screening, which was found to have higher yield than the routine approach.

By December 2017, of cumulative number of 182,632 patients screened for TB, 1,711 were diagnosed with TB; and 8,053(46.5%) of TB-free under-five children received IPT. The cumulative yield was 936 per 100,000 which is over four times the average national prevalence.

TB stigma and its impact on enrolling household contacts in clinical trials and cohort studies: an Indian perspective

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Stigma is a major barrier to enrolling household contacts (HHC) in HHC studies. Due to stigma, index cases sometimes refuse to contact their HHCs, and HHCs refuse to enroll in studies due to fear of neighbors questioning them. Enrollment of female adolescents is challenging as they worry about marriage prospects. Misconceptions, beliefs, and lack of TB knowledge increase refusal rates.

Additionally, job loss of the index case due to TB poses an economic burden and can result in migration leading to loss to follow up of the whole household. Strategies to address stigma include: addressing knowledge gaps, community engagement to explain benefits of HHC enrollment, flexibility in operational hours, and coordination with local health care system, taking time to examine family members for other medical conditions, and using motivational behavioral interventions.

This talk will describe experiences from two HHC studies in India: the “Phoenix” study and the “RePORT” study.

Tuberculosis among household contacts in Afghanistan

M Rashidi¹ ¹Management Sciences for Health, Kabul, Afghanistan. e-mail: mrashidi@msh.org

National TB Programs (NTP) agreed to conduct active household contact screening of all bacteriologically confirmed TB cases in Afghanistan. The CTB project assisted NTP to update SOPs and guideline and promote active contact screening in five cities. In 2014, 6200 houses visited and 53,189 households screened, 9403 (17%) were presumptive TB and 770 (1.4%) diagnosed as all form of TB cases identified and 8792 children put on IPT. However, in 2017: 19364 index TB cases evaluated, 129,738 household screened for TB among them 129738 (16%) were presumptive TB cases and 3071(2.4%) all form TB cases identified (15% of presumptive TB). 30821 children put on IPT. The yield of TB among households was 2,367 per 100,000 household contacts. Household contact screening promoted increased access to quality TB services and the yield of TB was significantly higher than passive case finding.

Determining transmission of tuberculosis outside of the household setting

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The standard approach to tuberculosis control today relies on detection and treatment of tuberculosis disease. However, by the time a case is diagnosed and treated, the next generation of cases has already been newly infected. To make progress in curbing the epidemic of tuberculosis, new cases must be prevented, either by reducing transmission or preventing disease once infected.

We already have effective ways to prevent tuberculosis once infected but reducing transmission in the community remains a challenge. For over two decades, many household contact studies have shown that household transmission accounts for only a small proportion of all tuberculosis transmission in a community.

This observation leads to two important questions: how do we locate transmission of *M. tuberculosis* in a community? And what interventions are effective in curbing transmission or mitigating the impact of transmission? Answers to these questions will help define the research agenda for the next decade.

SP64 Asthma, an international development issue: how to go further?

The Global Asthma Report 2018

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The Global Asthma Report (GAR) 2018 is the third report published by the Global Asthma Network (GAN). GAN was established in 2012 to improve asthma care globally, with a focus on low- and middle-income countries, through enhanced surveillance, research collaboration, capacity building and access to quality-assured, affordable, essential asthma medicines. GAN was formed by scientists from the International Study of Asthma and Allergies in childhood (ISAAC) and from the International Union Against Tuberculosis and Lung Disease (The Union). The first GAR was launched in New York in 2011 at the time of the United Nations High-Level meeting on non-communicable diseases. A second GAR produced by GAN in 2014 was launched in October at the 45th Union World Conference on Lung Health, Barcelona, Spain.

The GAR 2018 provides updates on the global burden of asthma and evidence-based recommendations for cost-effective management of asthma, especially in low- and middle-income countries.

The Union multi-countries experience on asthma management

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Asthma has become an issue of international development; it is now recognized as one of the most important NCD in all regions of the world, affecting people in non-affluent as well as affluent countries.

The Union's approach to asthma management is adapted from international asthma guidelines and uses a framework based on The Union's model for tuberculosis services. This framework advocates for standard case management, use of simple tools for the diagnosis, classification of asthma severity, provision of essential medicines, careful monitoring and evaluation of asthma care. The Management of Asthma: a Union guide to the essentials of good clinical practice provides, a detailed description of this approach. It is based on 12 years of experience and field-testing to ensure that the recommendations are feasible and sustainable in low- and middle-income countries.

This presentation reflects The Union Multi Countries experience on asthma management.

Capacity building for chronic respiratory disease: lessons from the TB Union model

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Health personal capacity building is one of the main gaps identified for chronic respiratory diseases (CRD) management. Based on The Union experience for TB management health personal capacity building will be linked to international and national commitment for CRD to:

- Identify a responsible manager for CRD in the Ministry of health department;
- Provide national guidelines based on WHO Package of Essential Non-communicable Disease Interventions;
- Ensure effective drug supply
- Support capacity building for managers and health personal based on The Union experience: International Development Management Course and Operational Research course;
- And organize monitoring and evaluation at national level.

During this presentation the objectives and lessons learnt from the several courses organized by The Union for TB and asthma and by WHO for practical approach to Lung Health will be discussed.

Actions needed to improve access to medicines for asthma and other respiratory diseases

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The major goal of improving access to medicines for patients with respiratory disease is to reduce mortality and serious morbidity due to these conditions. Achieving this goal requires an interconnected series of strategies to improve:

- a) prescribing and dispensing by providing feasible, evidence based guidance, and associated tools, to clinicians in primary care and in hospitals;
- b) supply of quality-assured, affordable medicines; and
- c) access to care by universal health coverage.

This talk will review the barriers and facilitators to each of the components of the strategy and point out directions for research and for advocacy.

SP65 Time to change tuberculosis treatment outcome definitions?

The multidrug-resistant tuberculosis epidemic: measuring burden and treatment outcomes

M Zignol¹ ¹World Health Organization, Geneva, Switzerland. e-mail: zignolm@who.int

This presentation will set the scene for the symposium by providing the latest insight into the burden of MDR-TB. It will highlight how the extent of the epidemic is measured and reported. It places a special emphasis on how the estimates of treatment outcome are collected, and which difficulties are encountered for doing so.

Rationale for a revision of the multidrug-resistant tuberculosis outcome definitions

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Application of current WHO definitions for treatment outcomes in non-MDR-TB and MDR-TB is complicated in clinical practice. WHO definitions for cure from non-MDR-TB or MDR-TB are rarely applied outside of clinical trials. TB cure rates based on WHO-definitions are unrealistically low. In contrast, treatment failure on MDR-TB regimens is underestimated by current WHO treatment outcome definitions.

This presentation highlights the rationale for rethinking current WHO TB treatment outcome definitions. It discusses new "simplified" definitions, and shares results

from studies that underline the usefulness and feasibility of these new outcome definitions.

The presentation will argue that the frequency of relapse-free cure from MDR-TB is much higher than previously anticipated. Under optimal management conditions the frequency of relapse-free cure rates in patients with MDR-TB does not differ from those with drug-susceptible TB.

Feasibility of applying the new treatment outcome definitions in a high prevalence setting: experience from Latvia

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The newly proposed TB outcome definitions include a period of follow-up after finalizing treatment. Which operational implications does this have in a setting overburdened with TB patients?

The presentation reports from Latvia where physicians were able to contribute valuable data for the new definitions in TB net's European clinical cohort.

What implications do the new treatment outcome definitions have for the designing of future clinical trials?

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The choice of treatment outcome definition to be used in clinical trials that compare treatment efficacy is crucial. They need to be a valid representation of the underlying disease process, measureable, and align with clinical management. This is often at odds with the wish to have rapid answers to pertinent research questions. This presentation highlights the potential impact that the proposed new treatment outcomes have on the design of future clinical trials.

Is it time to change tuberculosis treatment outcome definitions? A roundtable discussion

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This component of the symposium will be a roundtable discussion aimed at synthesising the perspectives expressed during the symposium and facilitating active participation by the audience. Key attributes of proposed definitions will be explored as will sources of dissent. Special consideration will be made of attributes that facilitate interpretation of treatment outcome results across populations, treatments and over time.



ABSTRACT PRESENTATIONS THURSDAY 25 OCTOBER 2018

ORAL ABSTRACT SESSIONS

OA01 Will we get there? Challenges to ending tuberculosis

OA01-200-25 Impact assessment of a social protection policy on tuberculosis treatment outcomes: a prospective cohort study

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Background: Tuberculosis (TB) still represents a major health problem in Latin America. From 1998 to 2016, success and default rates ranged from 53-74% and 15-20% respectively in high burden areas. Poor adherence represents a major threat for TB control and promotes emergence of drug resistant tuberculosis. The global model for TB prevention, management and research has been mainly focused on biomedical rather than socioeconomic approaches. Expanding social protection programs could have a substantial effect on the global burden of TB accelerating progress towards the End TB targets, however, there is little operational evidence to evaluate the impact of TB-related socioeconomic support interventions. This study used causal inference analysis to evaluate the impact of a conditional cash transfer (CCT) provincial policy on TB treatment outcomes in a prospective cohort of socioeconomically disadvantaged patients.

Methods: Patients with first diagnosis of pulmonary TB seen in 47 public health care facilities from high TB burden departments in Buenos Aires. Since the CCT was not randomly assigned among the participants, we used hierarchical models, propensity score matching and inverse probability weighting (IPW) to estimate treatment effects adjusting for potential confounders.

Results: Of 963 people enrolled, patients registered for the program showed significantly higher success rates (82% vs. 69%), and lower default rates (11% vs. 20%). After controlling for age, educational and income level, employment and marital status, source of care and modality of treatment received, OR for treatment success was 2.9 [95% CI 2, 4.3] and default was 0.36 [95% CI 0.23, 0.57]).

The protective effect was especially marked in high risk subgroups.

Conclusions: The CCT policy significantly improved TB treatment outcomes. This may represent a cost-effective investment and support a much wider implementation of this policy which may have a considerable impact on the control of TB in similar high burden areas.

OA01-201-25 Tuberculosis-entry screening for asylum seekers aged <18 years: an evaluation of more than 34 000 cases

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Background and challenges to implementation: Unlike in many other countries, as soon as they can sit, all minor asylumseekers arriving in the Netherlands from high tuberculosis (TB) incidence countries (> 50 TB cases/100,000 population), will have a mandatory radiographic screening for intrathoracic TB performed on the days after arrival. TB screening is performed seven days per week by the TB Department of the Regional Public Health Service of Groningen and chest X-rays are read within 24 hours through teleradiology by a team of Public Health TB physicians and two pulmonologists. Apart from making chest X-rays, upon request of the TB-physician, the team on location can take standardised questionnaires with telephone translators, collect sputum for bacteriology, or perform tuberculin skin testing. In the current study the justification of this programme was evaluated.

Intervention or response: The results of radiographic TB entry screening in 2 national reception centres for all minor asylum seekers aged 0-4, 5-11 and 12-17 years of age were collected from the local and national tuberculosis database from 2013-2017, as was the country of origin.

Results and lessons learnt: During 2013 - 2017 34,157 asylum seekers < 18 years were screened for intrathoracic TB. None of the 7,402 children younger than 5 years were diagnosed with TB at entrance. Two (0,01%) of the 14,192 children aged 5 -11 years were diagnosed with TB and 21 (0,17%) of the 12,563 children aged 12-17 were diagnosed with TB at the first entrance screening.

Conclusions and key recommendations: Between 2013-2017 during radiographic entry screening of minor asylum seekers, 23 children were diagnosed with intrathoracic TB, excluding those who were diagnosed and started treatment prior to their entry in the Netherlands,

from a total of 34,157 screened. It seems justified only to perform radiographic screening of children older than 12 years from countries with a TB incidence >200/100,000 at entrance and examine these under-twelves for latent TB infection.

Age category	Number screened	Number of Questionnaires	Positive/total tuberculin skin tests (%positive)	Positive/total IGRA tests (% positive)	Positive/total Sputum examination (% positive)	Number of intrathoracic TB cases	Country of origin
0-4 years	7402	81/7402 (1,1%)	4/41 (9,8%)	0/1 (0%)	0/0 (0%)	0	
5-11 years	14192	132/14192 (0,9%)	4/28 (14,3%)	2/2 (100%)	0/19 (0%)	2	Somalia (2)
12-17 years	12563	471/12563 (3,7%)	13/15 (86,6%)	4/6 (66,7%)	15/62 (24,2%)	21	Eritrea (11), Somalia (9), Kazakhstan (1), Sudan (1), Chad (1)
Total 0-17 years	34157	684/34157 (2,0%)	21/84 (25%)	6/9 (66,7%)	15/81 (18,5%)	23	

[Results of first screening minor asylum seekers for intrathoracic TB 2013-2017]

OA01-202-25 The TB care cascade for rifampicin-resistant TB: adherence to the South African Department of Health algorithm for the management of MDR-TB patients

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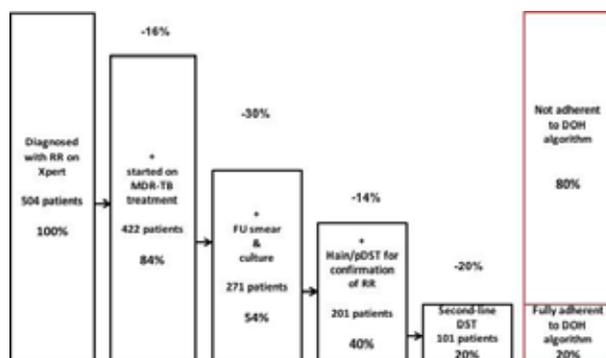
Background: Xpert MTB/RIF (Xpert) allows rapid diagnosis of rifampicin resistant (RR) tuberculosis (TB). The benefit of this test for patient management is likely dependent on the correct implementation of testing and treatment algorithms.

Methods: Observational cohort study ('EXIT-RIF') of patients diagnosed with RR-TB by Xpert in 3 South African provinces (Gauteng, Free State and Eastern Cape) between Feb-2012 and Dec-2013. We evaluated adherence to the Department of Health (DOH) algorithm for patients with RIF-resistance on Xpert, which recommends MDR-TB treatment for all, collection of a specimen for smear and culture, confirmation of RR, and drug susceptibility assay for isoniazid, fluoroquinolones (FQ) and aminoglycosides (AG).

Results: Of the 504 patients diagnosed with RR-TB by Xpert, 83.7% ever initiated MDR-TB treatment after a

median of 10 days (IQR 6-20), 7.7% only received first-line treatment, and 8.1% never initiated any treatment because of death (2.2%) or lost to follow-up prior to treatment initiation (3.0%), or another reason (2.9%). Among those starting 2nd line treatment, 23.5% first started first-line treatment before 2nd line. Only three quarters of patients (72.2%) had a follow-up sample taken within 30 days of diagnosis, which was processed by smear microscopy only (7.7%), culture only (6.7%) or smear and culture (57.7%). Altogether, less than half (48.6%) had any test done for the confirmation of RR (42.5% Hain only, 2.4% phenotypic DST only, 3.8% both Hain and pDST). Among these, Hain confirmed RR in 80.2% and pDST in 61.3%. Less than one in four (23.4%) of all patients had a drug susceptibility test result for second-line drugs (FQ and AG). Median number of cultures for follow-up was 4 (IQR 1-7).

Conclusions: Overall adherence to the algorithm was poor, with substantial losses at each step and full adherence to the DOH algorithm in only 20% of patients diagnosed with RR-TB by Xpert.



[Proportion of patients for which each sequential step in the MDR-TB care cascade was adhered to]

OA01-203-25 Implementation of a revised screening and diagnostic algorithm following a tuberculosis prevalence survey leads to improved tuberculosis case notification in Uganda

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Background and challenges to implementation: Uganda conducted her first national population based Tuberculosis (TB) prevalence survey between 2014 and 2016. The survey determined Uganda's TB burden. TB prevalence was 253/100,000 and incidence 234/100,000 translating to about 87,000 prevalence and 82,000 incident TB cases. In 2016, Uganda notified 46,000 TB cases, resulting in over 36,000 missed cases. Majority of missed TB cases were among clinically diagnosed forms of TB. Survey findings compelled the National TB and Leprosy Program (NTLP) to come up with new strategies to tackle

the epidemic which included changing screening and diagnostic approaches. An revised integrated TB screening, diagnostic and management tool was one of them.

Intervention or response: A five-day meeting of key TB stakeholders was held to review the algorithms for existing screening and diagnostic tools including microscopy, Xpert MTB/RIF, chest X-rays as well as new ones such as the TB LAM. A revised integrated TB screening, diagnostic and treatment algorithm (guide) responsive to finding missed TB cases was developed, printed and disseminated at various fora in late 2016. Intensified capacity building for health workers about the guide through mentorships and enhanced performance reviews were conducted.

Results and lessons learnt: By December 2017, Uganda registered a 4.5% increase in overall TB case notification from 44,939 cases in 2016 to 46,976. The largest increase was in the number of clinically diagnosed TB cases from 12773 in 2016 to 15,602 (22% increase). Among bacteriologically confirmed and extra pulmonary TB cases, there from 28,427 in 2016 to 27970 (1.6%) and from 3739 in 2016 to 3,404 (9.0%) in 2017.

Conclusions and key recommendations: Implementation of a revised integrated screening and diagnostic algorithm was followed by an increase in TB case notification, especially among clinically diagnosed forms of TB. Countries should priorities revision, dissemination and aggressive implementation of integrated TB screening and diagnostic algorithm in line with results of their TB prevalence surveys.

OA01-204-25 Improving government funding to end tuberculosis through sustainable financing methods and reforms: what is the cost?

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Background: Nigeria is highly dependent on donor funding for its TB control with low government financing (9% government, 27% donor and 64% of required efforts unfunded); a great cause of concern considering increasing global donor fatigue. Mechanisms identified for increased sustainable government funding for TB include the State Health Insurance Schemes (SHIS). The actuarially determined premium for the Lagos SHIS is 9700 Naira (NGN) (approx. \$26.9) per person/year. A major concern of stakeholders for provision of TB services through the SHIS is the anticipated high cost of TB service provision and its impact on affordability of the SHIS premium.

Methods: To convince policy/decision makers of the financially feasibility of TB service provision through SHIS; an actuarial analysis to determine the additional risk premium(ARP) and financial impact of providing

TB services through the Lagos SHIS was conducted. Modular pricing over a 3 year period for priority TB services including testing, and treatment costs for; Drug Susceptible (DS)-pediatrics and adults, and Drug Resistant (DR) adopting historical data on population, TB incidence, service utilization rates, and projected costs from the National TB Program data was used to determine the ARP for TB with sensitivity analysis to compare input assumptions with probable situations.

Results: The ARP of TB service provision at a modest estimate of 10% SHIS enrolment rate is NGN488.79 (\$1.36@360NGN/1dollar) per year; a 5% increase in premium cost which is a much lower cost than expected. Sensitivity analysis considering 20% enrolment caused a 50% drop (NGN244-68cents) and a 50% enrolment rate further reduced the ARP (NGN97.88-27cents) as shown below.

Conclusions: Provision of TB services through SHIS is an affordable and financially feasible mechanism for the government to increase its financial responsibility towards ending TB while weaning off dependence on donor funding. TB actors can utilize similar evidence in advocating for increased government funding of TB efforts.

TB Priority Services	Additional Risk Premium assuming 10% of Lagos State populace is enrolled (Projected amount in Naira)	Additional Risk Premium assuming 20% of Lagos State populace is enrolled (Projected amount in Naira)	Additional Risk Premium assuming 50% of Lagos State populace is enrolled (Projected amount in Naira)
TB Testing (GeneXpert Test/Sputum Test x 3)	122.55	61.31	24.51
DSTB (Pediatrics + Others/Adults)	89.51	44.78	17.91
DRTB for All	276.74	138.43	55.39
Total Cost for additional TB Cover	488.79 (approx. 1.36 dollars)	244.51 (approx. 68 cents)	97.83 (approx. 27 cents)

[Additional Risk Premium for TB Cover]

OA01-205-25 India's commitment to end TB by 2025: advances and way forward

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Background and challenges to implementation: Specific targets set in the End TB Strategy include 90% reduction in TB mortality, 80% reduction in TB incidence, and 0% catastrophic expenditure due to TB by 2030. India is amongst the top five countries with largest number of incident TB cases in 2016, accounting 56% of global burden (Global TB Report 2017). In 2017, Government of India (GOI) announced its commitment to eliminate TB by 2025; 5 years ahead of the Global milestone.

Intervention or response: While launching the TB-Free India Campaign, Indian Prime Minister announced a funding of over 12,000 crore Indian Rupees for next 3 years to ensure access to quality diagnosis, treatment and support for every TB patient. A multi-pronged approach has been adopted to detect all TB patients with an emphasis on reaching all TB patients, including those seeking care from private providers, undiagnosed TB in high-risk population, as well as adopting a patient-centric approach. GOI announced several schemes, including nutritional support to TB patients through financial incentives, expanding public-private partnership models and aligning our strategies to achieve success. In addition, the entire programme implementation and progress is being reviewed by Prime Minister through PRA-GATI platform.

Results and lessons learnt: Financial incentives are supporting TB patients in preventing catastrophic expenditure. Active Case Finding (ACF) in vulnerable population has been adopted in a phased manner since January-2017, which has resulted in increased TB-notification. During December-2017, 378 districts were covered, wherein 5.5 crore population was screened and 26781 TB patients were diagnosed. A reduction in TB mortality is reported over the years, which has remained constant at 4% since last 5 years.

Conclusions and key recommendations: A strong political and administrative commitment providing fresh impetus to TB combat efforts; coupled with efforts towards innovations to set aspirational goals and targets, and availability of new drugs/regimens, diagnostic approaches and strategies to end TB are the strengths making a progress towards TB elimination in India.

OA02 Tuberculosis infection: from latent to eliminated

OA02-206-25 Toward safe and reachable preventive therapy for latent tuberculosis infection: a multicentre randomised controlled trial in Taiwan

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Background: Treatment of latent tuberculosis (TB) infection (LTBI) effectively prevents its progression to active TB. However, long treatment duration and drug-related hepatotoxicity limit effectiveness of the 9-month daily isoniazid (9H). Data on the 3-month weekly rifampine plus isoniazid (3HP) in Asian populations are currently unavailable.

Methods: We prospectively randomized the LTBI contacts aged ≥ 12 years with positive tuberculin skin test into 9H and 3HP groups in four hospitals between January 2014 and May 2016 in Taiwan. The primary and secondary outcomes were treatment completion rate and adverse drug reactions (ADRs), respectively.

Results: Overall, 263 participants with LTBI were randomised into the 3HP (n=132) and 9H groups (n=131); 14 (10.6%) and 29 (22.1%) participants in the 3HP and 9H groups, respectively, discontinued therapy (p=0.011). Discontinuation rates owing to ADRs were 9.1% (3HP) and 5.3% (9H) (p=0.241). Clinically overt hepatotoxicity was more common in the 9H than in the 3HP group (5.3% vs. 1.5%; p=0.103), whereas systemic drug reaction was more common in the 3HP than in the 9H group (3.8% vs. 0%; p=0.060).

Conclusions: Compared with the 9H regimen, the 3HP regimen had a higher completion rate and similar ADR risks. Its ADRs were generally well-tolerated, mild, and transient.

OA02-207-25 BRIEF TB treatment of latent TB infection with one month of isoniazid and rifampine in HIV-infected people: interaction of treatment and CD4 count

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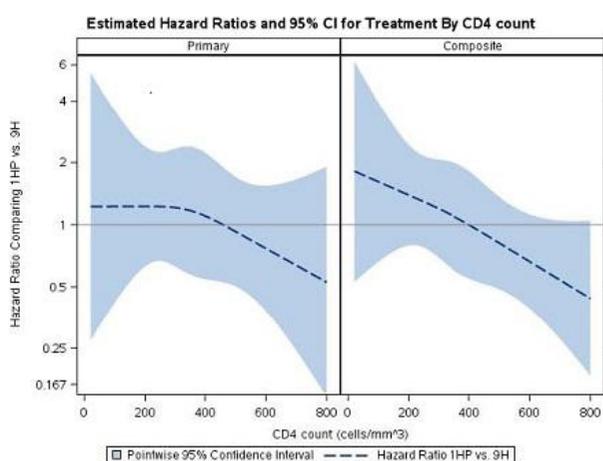
Background: Preliminary results of the BRIEF-TB study demonstrated that one month of rifampine with isoniazid (1HP) was non-inferior to nine months of INH (9H) in preventing TB, had fewer adverse events, and was more likely to be completed in HIV-infected adults and adolescents. We observed higher rates of study endpoints in participants with CD4 count ≤ 250 on 1HP.

Methods: The primary study endpoint was TB diagnosis, or death from TB or unknown cause. In a secondary analysis, we used time-dependent Cox models to examine the interaction of study treatment and CD4 count on the primary endpoint, and on the composite endpoint of TB diagnosis or death from any cause. The effect of CD4 was flexibly modeled as a time-dependent covariate using restricted cubic splines, and models were adjusted for time-dependent ART status, and baseline variables age, sex, TST/IGRA status, and country.

Results: 3000 HIV-infected adults & adolescents were randomized to 1HP or 9H at 45 sites in 10 countries. 399 participants had a CD4 count ≤ 250 and 2601 had >250

cells/mm³ at entry, balanced between the arms. 33 in the 9H arm and 32 in the 1HP arm experienced a primary endpoint. For each outcome, estimated hazard ratios for 1HP vs. 9H decreased from higher risk to lower risk with increasing CD4 count (Figure). The test of interaction between CD4 and treatment was not statistically significant for the primary outcome ($p=0.55$) or the composite outcome ($p=0.099$).

Conclusions: While a deeper examination of treatment effects by CD4 count failed to show a statistically significant interaction, the data suggest a possible trend of increased risk at lower CD4 counts and decreased risk at higher CD4 counts on the 1HP arm for the TB or all-cause mortality endpoint. Further study on the treatment effects in these subgroups is warranted.



[Estimated Hazard Ratios and 95% CI for Treatment by CD4 Count]

OA02-208-25 Impact of maternal isoniazid preventive therapy timing on acquisition of infant TB infection in the IMPAACT P1078/TB APPRISE trial

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Background: We hypothesized that IPT during pregnancy results in less infant TBI compared to IPT initiated in postpartum.

Methods: A Phase IV randomized, double-blind, placebo-controlled trial (IMPAACT P1078/TB APPRISE) compared initiation of 28 weeks of IPT during pregnancy versus at 12 weeks postpartum in women living with HIV (WLWH). 956 pregnant WLWH from 13 sites (10 in Africa, 1 in Haiti, 1 in India, 1 in Thailand) were enrolled and mother-infants followed until 1 year post-delivery. Infant TBI was assessed at 1 year of life using tuberculin skin test (TST) and QuantiFERON gold-in-tube interferon gamma release assay (IGRA) in a secondary analysis. Infant TBI was compared by maternal IPT arm, infant HIV status, reported BCG, TB exposure status, and weight-for-age z-score using Fisher's exact or t test.

Results: Of 751 infants assessed, 731 (97%) had IGRA and 730 (97%) had TST performed. Seven were HIV-infected, 489 had BCG, 20 had reported TB exposure, and 9 received IPT. At 1 year, 41/731 (6%) were IGRA+ and 55/730 (8%) were TST+. There was no difference by timing of maternal IPT initiation in infant TBI by either IGRA ($p=0.87$) or TST ($p=0.67$). Nearly half of infant TBI cases (22/41 IGRA+, 27/55 TST+) came from Uganda, which had 19% IGRA+ (24% TST+) compared to < 8% IGRA+ at other sites (< 15% TST+, except for India with 37%). TBI did not differ by infant HIV status or weight-for-age z-score. TST+ and IGRA+ were higher among infants who received BCG ($p=0.008$ and 0.017). TST+ was higher with TB exposure ($p=0.040$). Agreement between IGRA and TST was poor; only 8 infants positive by both measures and 78 with discordance (Kappa [95% CI] = 0.113 [0.006, 0.220]).

Conclusions: Timing of maternal IPT did not affect infant TBI acquisition. Infant TBI differed across sites. Agreement between infant TST and IGRA was poor.

OA02-209-25 The yield of active tuberculosis from screening migrant populations for latent tuberculosis infection: a systematic review and meta-analysis

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Background: The identification and treatment of both LTBI and active TB are key components of the End TB Strategy. Programmatic screening of migrants for LTBI now occurs in many high income, low TB incidence countries. We sought to quantify the yield of prevalent TB from LTBI screening in this group.

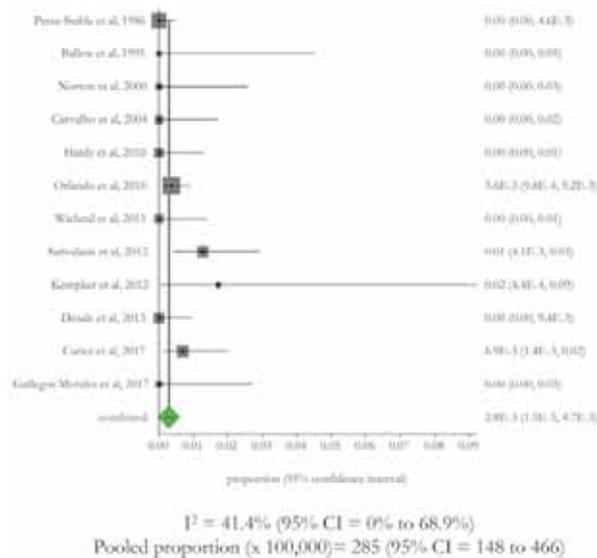
Methods: A systematic review of all articles in the Cochrane Library, Embase, and MEDLINE until December 2017. Papers reporting the number tested for LTBI, the number with a positive result (IGRA, TST) and the number of prevalent active TB cases were included. Data was extracted separately for adults and children. Analysis was performed using Stata version 15 and Statsdirect. **Results:** 7,931 unique manuscripts were identified, 385 full papers were reviewed, and 41 in English were included for data extraction.

These reported screening in North America (United States=22, Canada=2), Europe (Italy=5, UK=3, Spain=2, Sweden=2, Germany=1, Switzerland=1), and Australasia (Australia=2, New Zealand=1). There were 13 papers reporting screening in both adults and children, 12 papers with data for adults only, and 17 with data for children only.

The pooled proportion for a positive LTBI test across all studies was 0.30 (95% CI = 0.25 to 0.36, $I^2 = 99.6\%$), in children (including teenagers) was 0.15 (95% CI = 0.12 to 0.18, $I^2 = 97.9\%$), and in adults was 0.37 (95% CI = 0.27 to 0.48, $I^2 = 98.1\%$).

The pooled proportion for yield of active TB across all studies was 322 (95% CI = 172-520, $I^2 = 93.6\%$) per 100,000, in children (including teenagers) was 223 (95% CI = 92-410, $I^2 = 86.3\%$) per 100,000, and in adults was 285 (95% CI = 148-466, $I^2 = 41.4\%$).

Conclusions: The identification of prevalent active TB cases is an important secondary benefit of LTBI screening in migrants. Heterogeneity was high, pooled national data may provide stronger evidence.



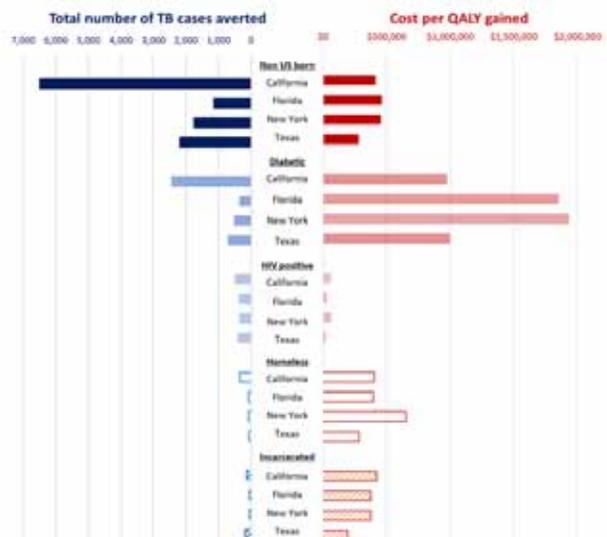
[Figure: the yield of prevalent active TB cases identified from LTBI screening in adult migrants]

OA02-210-25 Model-based cost-effectiveness of state-level tuberculosis interventions in California, Florida, New York and Texas

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Background: Targeted testing and treatment (TTT) for latent tuberculosis infection (LTBI) is a priority to eliminate tuberculosis in the United States (US), but the impact and cost-effectiveness of TTT may vary between states, and by population tested. We estimated health outcomes, costs, and cost effectiveness of TTT for LTBI in California, Florida, New York, and Texas where half of US TB cases occur.

Methods: Using previously developed TB transmission models, we estimated the numbers of individuals tested by interferon- release assay and completing 3 months of directly observed LTBI treatment with rifapentine and isoniazid from rapidly scaling up (over one year) TTT of non US-born (50% of the non-US-born resident population in each state), diabetic (80%), HIV-positive (100%), homeless (100%) and incarcerated (100%) populations. We projected costs (in 2016 dollars) of efforts and reductions in TB incidence beginning in 2016 over 10 years with each TTT strategy. Using the healthcare system perspective, we assessed TTT costs and incremental cost effectiveness (cost per quality-adjusted-life-year [QALY] gained) for TTT of each key population by state.



[Total number of TB cases averted and cost per QALY gained of the risk populations (2016-2025)]

Results: The projected impact and cost effectiveness of TTT differed substantially by state and population. The number of TB cases averted was greatest for TTT among non-US-born persons, followed by people with

diabetes and those living with HIV (Figure). TTT was most cost-effective among people living with HIV (cost ranging from \$18,504/QALY gained in Texas to \$64,305/QALY gained in New York), and least cost-effective among people with diabetes (ranging from \$975,844/QALY gained in California to \$1,900,000/QALY gained in New York). Cost-effectiveness varied substantially across states.

Conclusions: TTT is highly cost-effective among people living with HIV in the United States, but TTT of non-US-born populations can avert more TB cases. These estimates of cost-effectiveness can help inform strategies toward TB elimination in the US.

OA02-211-25 Evaluation of a long-acting bedaquiline formulation in a mouse model of latent tuberculosis infection

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Background: The potent anti-tuberculosis activity and long half-life of bedaquiline make it an attractive candidate for long-acting/extended release (LA) formulations for treatment of latent tuberculosis infection (LTBI). Our objective was to evaluate the anti-TB activity of an injectable bedaquiline LA (B_{LA}) formulation in a validated paucibacillary mouse model of LTBI treatment.

Methods: Six weeks after immunization with *Mycobacterium bovis* rBCG30, BALB/c mice were challenged by low-dose aerosol infection with *M. tuberculosis* H37Rv. Treatment began 13 weeks after challenge infection with one of the following regimens: untreated negative control; positive controls of daily rifampin, once-weekly rifapentine and isoniazid, or daily bedaquiline at 25 mg/kg; test regimens of one, two, or three monthly doses of the B_{LA} formulation at 160 mg/dose (B_{LA-160}); and test regimens of daily bedaquiline at 2.67 ($B_{2.67}$), 5.33 ($B_{5.33}$), and 8 (B_8) mg/kg to deliver the same total bedaquiline as one, two, or three doses of B_{LA-160} , respectively. All drugs were administered orally, except for B_{LA-160} (administered by intramuscular injection). The primary outcome was the decline in *M. tuberculosis* lung colony forming unit (CFU) counts during 12 weeks of treatment.

Results: Stable, low-level *M. tuberculosis* infection of around 4.75 log₁₀ CFU/lung was established. and positive control regimens performed as expected. One, two, and three doses of B_{LA-160} resulted in decreases of 2.9, 3.2, and 3.5 log₁₀ CFU/lung, respectively by week 12. Daily dosing with $B_{2.67}$, $B_{5.33}$, and B_8 decreased lung CFU counts by 1.6, 2.8, and 4.1 log₁₀, respectively. A single dose of B_{LA-160} exhibited activity for at least 12 weeks post-dose.

Conclusions: Over 12 weeks, once-monthly dosing with B_{LA-160} demonstrated superior or equivalent activity compared to daily oral administration of rifampin or the same total bedaquiline dose in this LTBI mouse model. The sustained activity of B_{LA-160} indicates promise as a short-course LTBI treatment.

OA02-212-25 Defining adequate contact for transmission of Mycobacterium tuberculosis in an urban African environment

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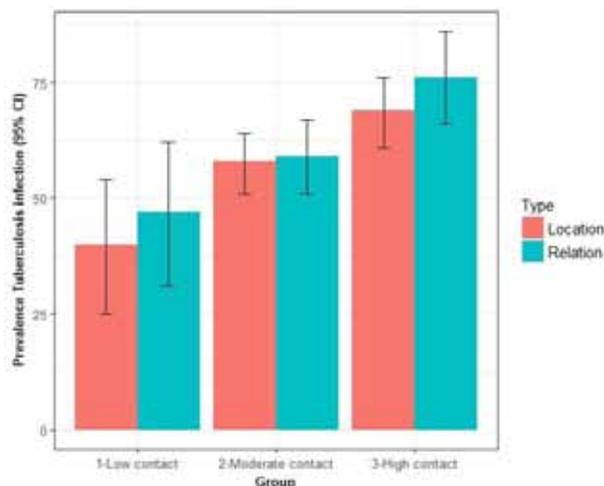
Background: Exposure to an individual with tuberculosis is necessary for transmission to occur. However, quantifying adequate contact between a tuberculosis case and their social network has been rarely performed in African settings.

Methods: This was a cross-sectional study conducted in Lugaba, Uganda. We developed two scores to quantify 'closeness' between individuals in social networks. These scores were built using exploratory factor analysis and were based on responses provided by 120 index cases about the nature of their interactions with contacts. We defined low, moderate and high-contact groups according to these scores. A modified Poisson regression model was used to assess congruence between these scores and tuberculosis infection, among 349 household contacts.

Results: Two scores were identified to characterize closeness, named 'Location' and 'Relation'. The Location score comprised six variables related to the nature of the usual place of meeting, sleeping location, shared meals and frequency of contact. The Relation score included variables associated with trust, shared tuberculosis diagnosis, providing healthcare, relationship duration, knowledge of each other and transportation used together. The prevalence of tuberculosis infection in the low location-contact, moderate location-contact and high location-contact groups were respectively 40%, 59% and 69% ($P=0.0017$). By the Relation score, the prevalence of tuberculosis infection in the low-contact, moderate-contact and high-contact groups were respectively 47%, 58% and 76% ($P=0.0026$) (Figure). In a multivariable model, only the Location factor was associated with tuberculosis infection. A high location-contact score was associated with a higher prevalence of tu-

berculosis infection in household contacts as compared to the low-contact score, especially those 5-14 years old (Prevalence Ratio= 3.3, 95% CI, 1.16-9.36).

Conclusions: In this large cross-sectional study from an urban African setting, a score quantifying “closeness” between individuals was derived from location- and relationship-level characteristics and identified contacts at higher risk for tuberculosis infection.



[Prevalence TB infection in household contacts, by level of Location and Relation contact.]

OA03 Clinical investigation for tuberculosis

OA03-213-25 Sustained high rate of successful treatment outcomes: interim results of 75 patients in the Nix-TB clinical study of pretomanid, bedaquiline and linezolid

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Background: Nix-TB is an ongoing open label study at three South African sites of bedaquiline (400 mg daily for two weeks followed by 200 mg three times a week), pretomanid (200 mg per day) and linezolid (1200 mg per day) given orally for six months for Extensively Drug Resistant (XDR) tuberculosis (TB) or Multidrug Resistant (MDR-TB) intolerant or failure.

Methods: Clinical, laboratory and sputum liquid culture evaluations are performed at baseline and weeks 1, 2, 4,

6, 8 and then every 4-6 weeks through the end of treatment. Participants who complete treatment are followed for 24 months after treatment end with repeat clinical and sputum assessments. This interim ITT analysis assigns outcomes to all 75 patients followed to the primary endpoint of bacteriologic failure, relapse or clinical failure at six months after treatment end.

Results: 109 participants (62% XDR-TB, 38% MDR-TB treatment intolerant or failures, 51% who are HIV+) have been enrolled from April 2015 to November 15, 2017. Of the first 75 patients, all enrolled at two sites, six died during the early stages of treatment, one in follow-up and one after withdrawal due to relapse. All remaining patients completed six months of therapy with no extensions. Two patients (3%) relapsed. Durable cure at six months was found in 66 patients (88%). The expected linezolid toxicities of peripheral neuropathy and myelosuppression were common and manageable at site level, usually requiring protocol mandated reductions of dose and/or interruptions in linezolid dosing in the majority of patients. There were no withdrawals for reasons other than death or relapse.

Conclusions: Interim results of this simplified, shortened all oral regimen for drug-resistant TB continue to be encouraging in terms of both efficacy and safety. A follow-on protocol, ZeNix, has started to investigate the optimal dose and duration of linezolid in this regimen.

OA03-214-25 Double-blinded randomized controlled trial of double or triple dose oral rifampicin for tuberculous meningitis

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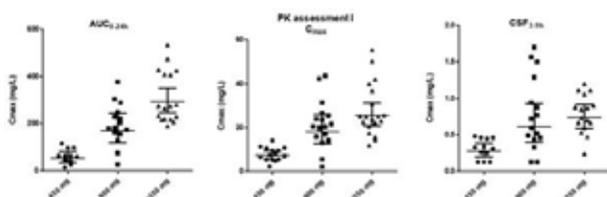
Background: High doses of rifampicin may help Tuberculous Meningitis (TBM) patients to survive. Twenty mg/kg doses of oral rifampicin for TBM patients were previously found to be safe, but pharmacokinetic-pharmacodynamic evaluations suggested that higher doses may be warranted to optimize treatment response.

Methods: In a double-blinded, randomised, placebo-controlled phase II trial (ClinicalTrials.gov NCT02169882) we assigned 60 adult TBM patients in Bandung, Indonesia, to standard 450 mg (10 mg/kg), 900 mg (20 mg/kg) or 1350 mg (30 mg/kg) oral rifampicin with other

standard TB drugs and adjunctive dexamethasone. After 30 days the patients received standard TB treatment. Endpoints included pharmacokinetic measures, adverse events and survival.

Results: A double and triple dose of rifampicin led to three- and five-fold higher geometric mean total plasma exposures in the critical early days (2 ± 1) of treatment (AUC_{0-24h} ; 53.5 mg.h/L [95% CI 45.3-61.6] vs. 170.6 mg.h/L [95% CI 147.7-193.4] vs. 293.5 mg.h/L [95% CI 265.1-321.8], $p < 0.001$), with proportional increases in peak plasma concentrations and single CSF concentrations at 3-9 h after the dose, without an increase in the incidence of grade 3 and 4 adverse events. Tripling the dose resulted in 100% plasma $AUC_{0-24h} > 116$ mg.h/L and 74% $C_{max} > 22$ mg/L, as previously assessed target attainment measures for better survival. Mortality after six months was 7/20 (35%), 9/20 (45%) and 3/20 (15%), $p=0.12$, in all patients and 5/14 (36%), 6/14 (43%) and 1/15 (7%), $p=0.07$ in culture-confirmed TBM patients after the standard, double and triple rifampicin doses.

Conclusions: Tripling the standard dose caused a more than proportional increase in rifampicin exposure, with no increase in grade 3 and 4 adverse event. The rifampicin 30 mg/kg dose resulted in an increase in pharmacokinetics' target attainment. This dose should now be evaluated in a larger phase III clinical trial.



[Distributions of pharmacokinetics parameters in TB meningitis patients]

OA03-215-25 Meta-analysis of rifampicin exposure and mortality in three Phase II tuberculosis meningitis trials

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Background: The mortality of tuberculosis meningitis (TBM) is frightfully high (often $>40\%$). Increased rifampicin doses during the first critical days of treatment may improve outcomes. Our objective was to characterize the population pharmacokinetics of high-dose

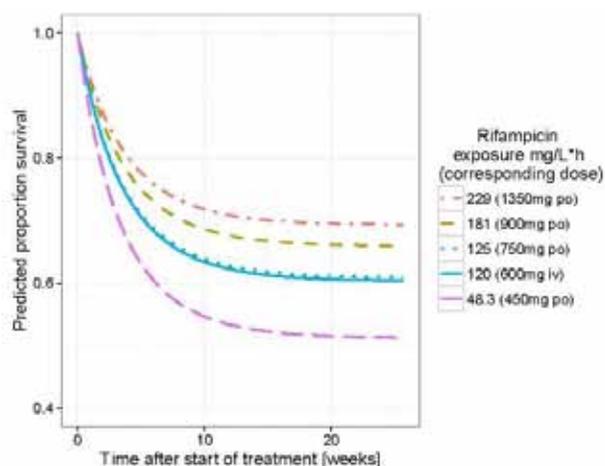
rifampicin in plasma and cerebrospinal fluid (CSF) and evaluate the relationship between individual exposures and mortality.

Methods: Data originated from three randomized controlled phase II trials (Bandung, Indonesia) comparing oral rifampicin 450mg to intensified 14 or 30-days regimens including 750, 900 or 1350mg orally, or a 600mg intravenous infusion (1.5h). Intensive pharmacokinetic sampling was performed at day 2 ± 1 ; for two of the studies also at day 12 ± 3 , and single CSF samples were taken 3-9h after dose. The 6-month survival was described with parametric time-to-event models. Analyses were performed in NONMEM.

Results: The pharmacokinetic analysis included 133 individuals and 1150 rifampicin concentrations (170 from CSF). The final model featured two disposition compartments, a well-stirred liver model, saturable clearance and autoinduction. The oral bioavailability was estimated at 78% (95% CI 71-84); volume of distribution was 19% (12-26) lower at late time points.

Rifampicin CSF concentrations were described by a partition coefficient (5.0% [4.5-6.4]) and half-life for the distribution between plasma and CSF. Higher CSF protein concentration increased the partition coefficient.

The survival analysis included 148 individuals of whom 58 died and 15 dropped out. An exponentially declining hazard described the survival well. Lower age, higher baseline Glasgow Coma Scale score and higher individual rifampicin plasma AUC_{0-24h} reduced the hazard. The figure shows simulations of expected mortality over rifampicin exposures with up to 20% reduction in mortality achieved.



[6-month survival for median age (30 years), GCS score (13) and varying rifampicin day 2 ± 1 exposure.]

Conclusions: Higher rifampicin exposure early during treatment substantially decreases the risk of death. Maximal effect was not reached within the studied range of exposures. The optimal dose of rifampicin in treatment of TBM should be further investigated in phase III type trials.

OA03-216-25 Prevalence of baseline versus acquired pyrazinamide resistance during MDR treatment

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Background: Pyrazinamide (Z) is a crucial companion drug for treatment of both rifampicin sensitive and -resistant (RR) tuberculosis, due to its sterilizing activity. High prevalence of Z resistance was previously reported among RR-TB patients; regardless, the standard shortened 9 months regimen includes Z during both intensive and continuation phases. We determined the prevalence of baseline Z resistance and the rate and timing of its acquisition (during treatment) amongst MDR-TB patients enrolled in the multi-country randomized STREAM clinical trial.

Methods: Genotypic Z resistance was determined with the Genoscholar PZA-TB II, (NIPRO Cooperation, Japan) line probe assay on baseline isolates from patients enrolled in the STREAM stage 1 clinical trial, and all the follow-up isolates from the recurrent (relapse/failure) cases with baseline susceptible Z pattern.

Results: Overall 59.4% (199/335) of baseline isolates harboured pncA mutations, and 2 out of 11 (18.2%) recurrent (relapse/failure) patients acquired resistance during treatment. Stratified by country, Ethiopian patients had a baseline Z resistance rate of 66.4%, South Africa 56% and Vietnam 55.3% (differences not statistically significant). The acquisition of Z resistance was detected at 12 weeks in one South African patient and at 48 weeks in one Vietnamese patient.

Conclusions: The high rates of Z resistance we observed in this setting confirm previous reports. Few patients acquired Z resistance, suggesting that the regimens used in the trial do not increase the selection for Z resistance. The time of acquisition of Z resistance observed in one case was as early as in the intensive phase of the treatment.

OA03-217-25 A randomized controlled clinical trial of Diammonium Glycyrrhizinate Enteric-coated Capsule for the prevention of antituberculosis drug-induced liver injury

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Background: Hepatitis is a common adverse effect of antituberculosis drugs. Diammonium Glycyrrhizinate Enteric-coated Capsules (DGEC) is a hepatoprotector widely used in China. We aimed to explore the effectiveness of preventive usage of DGEC in patients with tuberculosis (TB) receiving anti-TB treatment (ATT).

Methods: A multicenter, open, randomized, parallel controlled clinical study was conducted in 14 tuberculosis specialized hospitals in China. 1085 pulmonary tuberculosis patients were enrolled, of which 547 were divided into experimental group and 538 into control group. The experimental group received DGEC during ATT, while the control group received no hepatoprotective drugs but ATT. The incidence of liver injury, occurrence time, level of severity and the proportion of regimen change associated with liver injury were compared between the two groups.

Results: The total ratio of liver injury in the experimental group was lower than control (27.7% vs. 36.8%, $P < 0.05$), however, the subgroup analysis showed that there was no significant difference in the incidence of moderate liver injury between the two groups, and there was a statistically significant difference in the incidence of mild and severe liver injury. Proportion of regimen change associated with liver injury in the experimental group were lower than control (2.4% vs. 5.0%, $P < 0.05$). The incidence of other adverse reactions (abnormal liver function excluded) in the experimental group and the control group was 25.4% vs 30.7%, $P = 0.053$.

Conclusions: In this study Diammonium Glycyrrhizinate Enteric-coated Capsules showed some effect of reducing liver enzymes in mild liver injury, but it had little effect on the prevention of moderate liver injury, the anti-tuberculosis and liver protection regimens had changed when severe liver injury occurred, so its liver protective effect could not be evaluated in severe liver injury patients. It showed effect to keep regimen consistency and didn't increase the adverse reaction of patients with anti-tuberculosis chemotherapy.

OA03-218-25 Risk of relapse after 9-month regimen for multidrug-resistant tuberculosis in francophone Africa

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Background: The Union-coordinated observational study on short treatment regimen (STR) for MDR-TB in 9 African countries reported 82% treatment success with 4KmMfxPtoHhCfzEZ / 5MfxCfzEZ regimen. We report on the risk of relapse after treatment completion.

Methods: Adult patients with rifampicin resistance and without history of 2nd line treatment (1,006) were included from 2013 to 2015 in Benin, Burkina Faso, Burundi, Cameroon, Cote d'Ivoire, Niger, Central African Republic, Democratic Republic of Congo and Rwanda. Patients who completed 9 to 11 months of treatment and had a "success" outcome underwent clinical examination, sputum smear and culture every 6 months until

24 months after treatment completion. The proportion of relapse, defined as a positive culture at any post-treatment visit, was determined and analyzed according to patient characteristics and initial drug resistance.

Results: Among 823 successfully treated patients, respectively 52.2%, 52.4%, 29.2% and 22.1% attended their 6, 12, 18 and 24-month scheduled post-treatment visit, and 558 (67.8%) had ≥ 1 culture result available during follow-up. Main reasons for no culture were death (17%), unreachable patient (41%), declining screening (27%) or other reason (15%). A total of 15 relapses were reported among the 558 patients with follow-up information (2.7%): 9 (60%) 6 months, 4 (27%) 12 months and 2 (13%) 18 months after treatment completion. No relapse was reported among HIV-infected patients. The risk of relapse did not differ by patients characteristics, but was significantly higher in patients with initial fluoroquinolone resistance (11% versus 2% for sensitive). Failure plus relapses were respectively 7.2%, 22.2% and 55.6% for sensitive, low and high resistant bacilli to fluoroquinolones.

Conclusions: Results of the 9-month regimen are excellent in the absence of resistance to fluoroquinolones. They could be even better if a double dose of moxifloxacin was used instead of a single dose.

OA03-219-25 Bedaquiline for multi-drug resistant TB, including extensively or pre-extensively drug-resistant pulmonary *Mycobacterium tuberculosis*, in adolescent patients

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Background: Paediatric MDR-TB is an increasing public health concern, accounting for ~15% of global MDR-TB cases, with an unmet medical need for new treatments and often inadequate dosing recommendations for existing therapies. TMC207-C211 (NCT02354014) will evaluate the pharmacokinetics, safety/tolerability and antimycobacterial activity of BDQ in children and adolescents (birth- ≤ 18 years) with MDR-TB, and provide guidance on BDQ dose selection for Cohorts 1 (≥ 12 - ≤ 18 years), 2: (≥ 5 - < 12 years), 3 (≥ 2 - < 5 years) and 4 (birth- < 2 years).

Methods: This Phase 2, open-label, multicentre, single-arm dose de-escalation study will include ≥ 60 children (planned). Patients receive BDQ for 24 weeks with an anti-MDR-TB background regimen (BR) selected accord-

ing to WHO/NTP guidelines/current SOC, and then BR only for up to 96 weeks under supervision. We present the primary analysis of Cohort 1, when all adolescents had completed 24-weeks of BDQ (400mg qd for 2 weeks, 200mg tiw for 22 weeks) or discontinued earlier.

Results: 15 patients were enrolled in Cohort 1 and received BDQ+BR (South Africa, n=8; Russia, n=5; Philippines, n=2); 80% were female, 53% Black/African American, median age 16 years, with confirmed/probable pulmonary MDR-TB resistant to isoniazid+rifampin (53%), rifampin-mono-resistant-TB (27%), pre-XDR-TB (13%) or XDR-TB (7%). Through Week 24, BR drugs used most frequently were levofloxacin (100%), pyrazinamide (87%) and kanamycin (80%). 14 patients completed Week 24 (93%). Steady-state BDQ plasma concentrations were comparable to those previously observed in adults (Table 1).

Disposition	All patients (N=15)		
Completed	14 (93%)		
Discontinued	1 (7%)		
Failure to convert	1 (7%)		
PK parameter (mean \pm SD; T _{max} : median)	Week 2 (N=8)	Week 12 (N=15)	Week 24 (N=12)
AUC _{0-24h} , ng·h/mL	39,100 \pm 32,600	26,300 \pm 10,300	ND
C _{min} , ng/mL	1,220 \pm 1,010	544 \pm 263	774 \pm 420
C _{max} , ng/mL	2,310 \pm 1,770	1,800 \pm 736	ND
T _{max} , h (range)	2 (2-8.25)	4 (2-8)	ND
Safety analysis	All patients (N=15)		
Any AE (regardless of cause or severity)	14 (93%)		
Most common AEs			
Arthralgia	6 (40%)		
Acne	4 (27%)		
Prothrombin time prolonged	3 (20%)		
Blurred vision, eye pain, eye pruritus, hypoacusis, nausea, rash, tinnitus, URTI, vulvovaginal candidiasis	Each occurring in 2 participants (13%)		
AEs at least possibly related to BDQ			
Nausea	1 (6.7%)		
Vomiting	1 (6.7%)		
Any serious AE ^a	2 ^b (13%)		
Any Grade 3 or 4 AE ^a	4 ^c (27%)		

^aNone were considered at least possibly related to BDQ by the investigator

^bNumber of participants with 1 or more events: overdose, increased alanine aminotransferase, increased aspartate aminotransferase and increased blood bilirubin

^cNumber of participants with 1 or more events: increased alanine aminotransferase, increased aspartate aminotransferase, increased blood bilirubin, increased blood creatine phosphokinase, prothrombin time prolonged
 SD = standard deviation; ND = not determined; AE = adverse event; URTI = upper respiratory tract infection

[Table 1. Patient disposition, pharmacokinetic and safety analyses outcomes during 24 weeks]

No QTcF > 500 ms, AE-related discontinuations or deaths and few serious AEs or grade 3/4 AEs occurred (Table 1). 6/8 MGIT evaluable patients (75%) had culture conversion at Week 24.

Conclusions: In TMC207-C211 in adolescents with MDR-TB, including pre-XDR-TB and XDR-TB, 24-weeks of BDQ (adult dose and regimen) gave a comparable PK profile to that which is effective in adults, and was generally well tolerated, with no new safety findings.

OA03-220-25 Sub-therapeutic rifampicin concentration is associated with unfavourable treatment outcomes in pulmonary tuberculosis patients on thrice weekly regimens in India

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Background: In the Revised National Tuberculosis (TB) Control Programme (RNTCP) in India, patients were treated for TB with thrice-weekly regimens. Understanding anti-TB drug concentrations is critical to inform drug dosing. We assessed plasma concentrations of rifampicin (RMP), isoniazid (INH) and pyrazinamide (PZA) and its relationship to treatment outcomes in adult pulmonary TB patients.

Methods: A cohort of newly diagnosed pulmonary TB patients (>14 years) (n = 394), receiving thrice-weekly anti-TB treatment (ATT) in the RNTCP were studied. At months 1 and 5, 2-hour post-dose concentrations of RMP, INH and PZA were determined by high performance liquid chromatography, after directly observed drug administration. The effect of drug concentrations on unfavourable TB treatment outcomes (death, failure, recurrence) was assessed using random effects logistic regression.

Results: Sub-therapeutic RMP, INH and PZA were observed in 86% & 74%, 29% & 22% and 12% of patients at months 1 and 5 respectively (sub-therapeutic cut-offs: RMP < 8µg/ml; INH < 3µg/ml; PZA < 20µg/ml). Females had higher INH and PZA than males (p = 0.013 and 0.008 for INH and PZA respectively), and those with diabetes mellitus had lower PZA levels than those without diabetes (p = 0.012). RMP levels were significantly lower in HIV co-infected than HIV uninfected (1.6 vs. 4.6µg/ml; p = 0.015). Favourable outcome was observed in 85% patients, RMP being significantly lower in unfavourable than favourable responders (2.5 vs. 4.7µg/ml; p = 0.037). RMP concentration was associated with unfavourable treatment outcome (aOR, 1.12; 95% CI 1.02 - 1.25)

Conclusions: Sub-therapeutic RMP was observed in a high proportion of patients on intermittent ATT and was associated with unfavourable outcome. A study on drug levels in patients on daily ATT and treatment outcome is in progress.

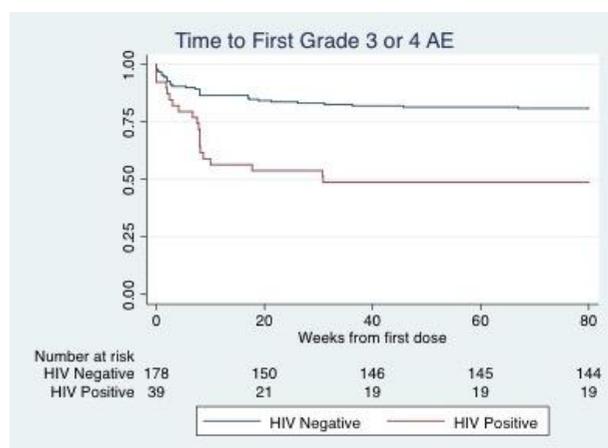
OA04 Anti-tuberculosis treatment in patients with comorbidities

OA04-221-25 Toxicity of TB treatment in HIV-positive patients and treatment outcome: a case-control study

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Background: The phase III REMoxTB study prospectively enrolled HIV-positive (with CD4 >250 cells, not on anti-retroviral therapy) and HIV-negative patients. Those on the control arm received standard TB therapy. We investigated the incidence of adverse events and cure rates according to HIV status.

Methods: HIV-positive cases were matched to HIV-negative subjects by age, gender, ethnicity, and trial site using coarsened exact matching. Grade 3 and 4 adverse events (AEs) were summarised by MedDRA System Organ Class. Kaplan-Meier curves for time to first grade 3 or 4 AE were constructed according to HIV status with hazard ratios calculated. Patients were considered cured if they were culture negative 18 months after randomisation with ≥2 consecutive negative culture results.



[Kaplan-Meier curves demonstrating the time to first grade 3 or 4 adverse event by HIV status]

Results: Forty-two HIV-positive cases were matched to 220 HIV-negative controls. A total of 20 of 42 (47.6%) HIV-positive patients experienced ≥1 grade 3 or 4 AE, and 34 of 220 (15.5%) HIV-negative patients. Hepatobiliary disorders accounted for the majority of grade 3 or 4 AEs: 12 of 40 events (30.0%; 6 of 42 patients [14.3%]) among HIV-positive patients, and 15 of 60 events (25.0%; 9 of 220 patients [4.1%]) among HIV-negative

patients. The median time to first grade 3 or 4 AE was 54 days (IQR 15.5 - 59.0) for HIV-positive patients and 29.5 days (IQR 9.0 - 119.0) for HIV-negative (see Figure). The hazard ratio for experiencing a grade 3 or 4 AE among HIV-positive patients was 3.25 (95% CI 1.87 - 5.66, $p < 0.01$). Cure rates were similar, with 38 of 42 (90.5%) HIV-positive and 195 of 220 (88.6%) HIV-negative patients ($p = 0.73$) cured at 18 months.

Conclusions: HIV-positive patients receiving standard TB therapy in the REMoxTB study were at greater risk of adverse events during treatment but cure rates were similar when compared to a matched sample of HIV-negative patients.

OA04-222-25 Effects of rifampicin dose increase and co-administration of efavirenz-based antiretroviral therapy on rifampicin pharmacokinetics in HIV-tuberculosis co-infected patients: ANRS 12292 Rifavirenz trial

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Background: There is increasing interest towards a potential reduction of tuberculosis (TB) treatment duration using high-dose rifampicin (R). Little is known among HIV-positive patients on antiretroviral therapy (ART). The Rifavirenz trial in HIV-TB co-infected patients showed moderate effect of doubling the R dose on the efavirenz (EFV) pharmacokinetics (PK). From the same trial, we present results of the rifampicin PKs with and without ART, and their relation to hepatotoxicity.

Methods: Confirmed pulmonary TB, ART-naïve adults were randomized to 2 high-dose (R-20) and one standard dose (R-10) rifampicin-based regimens. EFV-based ART was initiated after 2-4 weeks at 600mg or 800mg daily. At 8 weeks of follow-up, all patients were switched to standard R and EFV doses. Liver toxicity was monitored after 2, 4 and 8 weeks. Samplings for PK were performed 2 weeks after starting R (off ART) and 4 weeks after starting ART. Plasma concentrations were assayed by validated High Performance Liquid Chromatography assay. PK parameters were determined by non-compartmental analysis and compared by geometric mean ratio (GMR).

Results: We enrolled 98 patients (R20EFV600: 32; R20EFV800: 33; R10EFV600: 33): median age 33.6 years, 26.5% females, median BMI 19.5kg/m², median CD4 count 142 cells/μL. At week 2, doubling the dose of R increased the median AUC₀₋₂₄ and C_{max} by more than twice compared to standard dose. EFV co-administration reduced R AUC₀₋₂₄ and C_{max} (Table). At week 8,

15/65 (23.1%) patients experienced an increase in transaminases or bilirubin ≥ grade 2 in the R-20 group vs 6/33 (18.2%) in the R-10 group ($p=0.577$). C_{max} > 8 μg/mL at weeks 2 and 8 were not associated with hepatotoxicity.

Conclusions: Doubling the dose of rifampicin resulted in a more than dose-proportional increase of rifampicin AUC₀₋₂₄ and C_{max}, without increase in hepatotoxicity in HIV-TB co-infected patients. The effect of EFV on rifampicin PK requires further investigation.

	Rifampicin alone			Rifampicin with ART			GMR (90%CI)		
	R10 EFV600 N=33	R20 EFV600 N=32	R20 EFV800 N=31	R10 EFV600 N=31	R20 EFV600 N=29	R20 EFV800 N=31	R10 EFV600 N=30	R20 EFV600 N=29	R20 EFV800 N=30
AUC ₀₋₂₄ - μg.h/mL, median (IQR)	40.6 (28.9, 47.0)	99.5 (63.5, 135.1)	101.3 (79.5, 126.0)	27.7 (19.7, 38.0)	76.8 (53.0, 110.0)	61.1 (44.3, 80.0)	0.77 (0.65, 0.90)	0.80 (0.66, 0.96)	0.63 (0.55, 0.72)
C _{max} - μg/mL, median (IQR)	5.3 (3.5, 6.9)	16.0 (10.7, 20.0)	15.6 (12.2, 19.0)	4.0 (2.6, 5.3)	11.5 (7.2, 14.5)	8.7 (6.4, 13.4)	0.70 (0.59, 0.83)	0.67 (0.56, 0.81)	0.60 (0.51, 0.71)
C _{max} >8μg/ mL, n(%)	4 (12.1)	30 (93.8)	29 (93.6)	2 (6.5)	20 (69.0)	17 (54.8)			

[Rifampicin pharmacokinetic parameters]

OA04-223-25 Linezolid pharmacokinetics in South African patients with drug-resistant tuberculosis and high rates of HIV co-infection

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Background: There are limited data on the pharmacokinetics (PK) of linezolid in patients with TB, particularly in African populations and in those with HIV co-infection. We aimed to describe the PK of linezolid and explore the effect of covariates on linezolid exposure in South African patients with drug-resistant TB.

Methods: Consecutive adult patients on linezolid-based regimens for drug-resistant TB were recruited from a public-sector TB hospital in Cape Town. Plasma was collected at steady-state after a standardized meal and observed linezolid dosing. Linezolid concentrations were measured using liquid chromatography-tandem mass spectrometry, and non-compartmental analysis was performed to determine PK parameters.

Results: 14 participants underwent intensive PK sampling. Median age was 36 years (IQR 22-45); 9 participants (64%) were male, 7 (50%) were HIV-infected, and the median weight was 59.9 kg (IQR 49.9-71.2). Median duration on linezolid was 60 days (range 20-78); 12 (86%) participants were on the initial dose of 600

mg daily at the time of sampling, and 2 participants were on 300 mg daily after dose reduction for toxicity. On univariate analysis, there was a trend towards higher linezolid trough concentrations with increasing age (1.34-fold increase (95% CI, 0.99-1.81) per 10 years) and HIV infection (1.98-fold increase; 95% CI, 0.99-3.9). Both doses achieved an efficacy target of free drug area under the concentration-time curve ($fAUC$)/MIC > 100 at MICs ≤ 0.5 µg/mL, but the probability of target attainment was 58% for the 600 mg dose at the critical concentration of 1 µg/mL.

Conclusions: This first PK study of linezolid in an African population suggests that the standard 600 mg daily dose achieves the efficacy target for wild type *M tuberculosis*, but may be suboptimal at elevated MICs. Linezolid exposure may be associated with age and HIV status, but this needs confirmation with a larger sample size.

Variable	600 mg (n = 12)	300 mg (n = 2)	Overall (n = 14)
AUC ₀₋₂₄ , mg·h/L	199.2 (131.4 – 247.6)	150.6 (129.1 – 172.1)	177.3 (130.7 – 244.4)
$fAUC_{0-24}$, mg·h/L*	139.4 (91.9 – 173.3)	105.4 (90.4 – 120.5)	124.1 (91.5 – 171.1)
k_{el} , h ⁻¹	0.1 (0.07 – 0.13)	0.06 (0.06 – 0.06)	0.08 (0.07 – 0.13)
T _{1/2} , h	6.9 (5.2 – 9.7)	11.2 (11.1 – 11.2)	8.3 (5.5 – 10.3)
C _{min} , mg/L	14.2 (12.9 – 16.5)	9.8 (8.6 – 11)	14 (12 – 14.9)
T _{max} , h	3 (2 – 4)	2 (2 – 2)	3 (2 – 4)
C _{max} , mg/L	1.7 (0.9 – 3.2)	2.4 (2.2 – 2.6)	2.03 (0.97 – 3.21)
Cl/F, L/h*	3.0 (2.4 – 4.6)	2.0 (1.7 – 2.3)	2.7 (2.3 – 4.5)
V _d /F, L*	32.9 (23.1 – 47.8)	32.7 (27.9 – 37.5)	32.9 (24.4 – 38.8)

Data are median(IQR)
*Assuming 30% protein binding. *Dose/AUC, ^aCl/F, ^bV_d/F.

[Pharmacokinetic measurements in 14 participants receiving linezolid for drug-resistant TB]

OA04-224-25 Hepatitis C and drug-resistant tuberculosis co-morbidities: no longer an untreatable combination

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Background: Hepatotoxicity is common during drug resistant tuberculosis (DR-TB) treatment. Active hepatitis C (HCV), which increases hepatotoxicity, has been documented amongst 19.2% of DRTB patients in Armenia. Until recently, treatment of HCV was not possible in patients with active tuberculosis. Despite no contra-indications to the treatment of HCV with direct acting antivirals (DAAs) and DRTB with second line TB drugs, no data currently exists and DR-TB patients have little access.

Methods: Patients with DRTB in Armenia with active HCV were offered treatment based on prioritisation criteria. A DAA regimen of either 12 weeks of sofos-

buvir (SOF), daclatasvir (DCV) or ledipasvir (LDV) or 24 weeks of sofosbuvir, daclatasvir and ribavirin (RBV) was provided.

Results: During 2017, 26 DRTB patients started DAA treatments: majority males (24/26, 92.3%), with a median age of 47.5 years (range 28-71), most with genotype 3 (18/26, 69.2%) and fibroscan F0-1 (15/26, 57.6%). Other co-morbidities included diabetes (5/26, 19.2%), HIV (4/26, 15.4%) and hepatitis B (1/26, 3.8%). The DAA regimens given were: 65.4% (17/26) SOF/DCV, 19.2% (5/26) SOF/LDV and 15.4% (4/26) SOF/DCV/RBV. Concomitant DR-TB treatment and DAA was given in 57.6% (15/26) of patients including 10 (10/15, 66.7%) on delamanid or bedaquiline. All patients completed full DAA treatment without interruption. The results of viral PCR testing at the end of DAA treatment were: 76.9% (20/26) negative, 15.4% (4/26) positive and 8.7% (2/26) not performed due to technical problems. The results of the sustained viral response test at 12 weeks post DAA treatment amongst 21 eligible patients were: 80.9% (17/21) negative, 9.5% (2/21) positive and 9.5% (2/21) not performed as patients had left the country. No deaths or major intolerance were reported during DAA treatment.

Conclusions: Treatment with DAAs is possible in DRTB patients and should be considered as a priority in patients experiencing hepatotoxicity or at high risk of disease progression.

OA04-225-25 Rifampicin alters metformin plasma exposure but not blood glucose levels in diabetic tuberculosis patients

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Background: The pharmacokinetic and clinical implications of combining metformin with rifampicin are relevant to increasing numbers of tuberculosis (TB) patients with type 2 diabetes mellitus (DM) worldwide. Nonetheless, pharmacokinetic interaction studies in patients are lacking. Therefore, we assessed the impact of rifampicin, a prototypical inducer of drug-metabolizing enzymes and transporters, on steady-state metformin pharmacokinetics and on its glucose-lowering effect in type 2 diabetic TB patients.

Methods: In a within-subject, 2-period (during and after TB treatment), fixed-order pharmacokinetic-pharmacodynamic interaction study (Bandung, Indonesia),

the effect of rifampicin on metformin pharmacokinetics was assessed with two 8-hour plasma curves and urine collections during the dosing interval. The glucose-lowering effect of metformin was evaluated with two 3-hour blood glucose curves following ingestion of 75 grams of glucose on an empty stomach. A bioequivalence approach and paired samples t-tests were used to evaluate the rifampicin-metformin interaction.

Results: Rifampicin increased metformin exposure: area under the plasma concentration-time curve ($AUC_{0-\tau}$) and peak exposure (C_{max}) geometric mean ratios for metformin during TB treatment vs. metformin alone (after TB treatment) were 1.28 (90% CI 1.13-1.44) and 1.19 (90% CI 1.02-1.38) ($n=22$). Tubular secretion ($CL_{0-\tau}$) of metformin was unaffected by rifampicin ($\Delta CL_{0-\tau}$ $p=0.777$, $n=16$). Also metformin glucose-lowering efficacy did not change significantly after stopping rifampicin (Δ glucose- AUC_{0-3h} $p=0.441$ ($n=18$)). 57% of patients combining metformin with TB treatment and 38% of patients on metformin without concurrent TB treatment experienced gastrointestinal adverse effects, despite preventive measures.

Conclusions: Co-administration of rifampicin resulted in increased metformin plasma concentrations, but not in significantly altered blood glucose concentrations, rendering additional monitoring of glycemic control unnecessary. Considering the high incidence of gastrointestinal adverse effects, especially when patients were taking rifampicin and metformin simultaneously, without food or an antiemetic, we suggest TB-DM patients to take metformin and rifampicin together with food and metoclopramide, and preferably separated in time.

OA04-226-25 The impact of glycaemic control on tuberculosis treatment outcomes

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Background: Many studies have demonstrated that individuals with diabetes (DM) have poorer tuberculosis (TB) treatment outcomes, however there has been very little research on how hyperglycaemia impacts on this association. This is important to understand to better target patients who would benefit from enhanced monitoring and management.

Methods: Newly diagnosed pulmonary TB patients aged 18 years and over enrolled onto the TANDEM study with a laboratory HbA1c result available. HbA1c

was categorised based on the following cut-points less than 5.7, 5.7 to 6.4, 6.5 to 8.9 and 9 and over. Treatment outcomes included mortality, treatment failure and relapse according to standard WHO definitions and were combined as "any poor outcome". Statistical analysis was completed using mixed effect logistic regression, controlling for key potential confounders (age, sex, HIV status, smoking status and SES), and adjusting for site differences as a random effect with robust standard errors.

Results: 2280 patients had at least one baseline laboratory HbA1c value. The risk of a poor outcome was increased (OR 1.98 95% CI 1.10-3.58) for those with HbA1c 6.5% to 8.9% and for those 9% and over (OR 1.62 95% CI 1.20-2.19). Treatment failure was also seen to increase for those with HbA1c 5.7% to 6.4% (OR 1.41 95% CI 1.05-1.89), 6.5% to 8.9% (OR 2.13 (95% CI 1.63-2.78) and for those 9% and over (OR 1.67 95% CI 1.15-2.42). Death was increased amongst those with an HbA1c 9% and over (OR 2.41 95% CI 2.37-2.45). No increased risk of relapse was seen in relation to baseline HbA1c.

Conclusions: Associations were seen between rising HbA1c with treatment failure and death. Poor outcomes increased for those with a baseline HbA1c > 6.5%, and modestly increased even for those with lower levels (5.7-6.4%). Mortality was substantially increased only for those with HbA1c >9%; resources could also be targeted at this group.

OA04-227-25 The effect of intensified clinical monitoring on glycaemic control in patients with combined diabetes and tuberculosis in Indonesia: a randomized trial

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Background: Diabetes mellitus (DM) increases the risk of tuberculosis (TB) treatment failure. Glycemic control during TB treatment is challenging as TB-associated inflammation increases hyperglycemia and rifampicin decreases the activity of most anti-diabetic drugs. We assessed the effect of frequent blood glucose monitoring with DM treatment adjustment during the course of TB treatment on clinical outcomes.

Methods: In an urban setting in Indonesia we randomized patients with DM and newly diagnosed TB to:

(1) routine DM management in primary health clinics (*control arm*) or

(2) regular scheduled counselling, glucose monitoring, and adjustment of anti-diabetes medication using standardized algorithms in a research clinic (*intervention arm*).

HbA1c were measured at baseline, months 3 and 6. Physicians were blinded to the primary endpoint: month 3 HbA1c results. Mean HbA1c were compared between arms using repeated measures ANOVA test. Secondary endpoints included DM medication and hypoglycemia.

Results: Of 150 patients recruited (76 intervention and 74 control) there were no significant baseline characteristic differences. At baseline mean HbA1c was 11.0% in the intervention arm and 11.6% in the control arm. At 3 months mean HbA1c was 8.3% in the intervention arm compared to 9.7% in the control arm, and at 6 months mean HbA1c was 7.6% and 9.8% in the intervention and control arm respectively ($P < 0.0001$). In the intervention arm 35 (48.6%) received insulin compared to 6 (8.6%) in the control arm and metformin was prescribed to 37 (51.4%) patients in the intervention arm versus 53 (75.7%) patients in the control arm. One patient in the intervention arm on insulin had a grade 3 hypoglycemic episode at month 3 that resolved after taking a sugary drink.

Conclusions: Patients with combined TB and DM can attain adequate glycemic control in TB clinics through regular glucose monitoring and algorithmic adjustment of DM treatment.

OA05 Epidemiology of tobacco use and effects and some quick facts behind tobacco farming

OA05-228-25 Impact of environmental tobacco smoke on wheezing disorders and early childhood caries among children aged 30-60 months

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Background: Children are exposed to Environmental Tobacco Smoke (ETS) not only in homes but also in child-care settings, restaurants, vehicles and other public places. ETS exposure in utero and early childhood has been found to increase risk of respiratory disease and dental caries. These findings, however, have not been evaluated in the same cohort. This study assessed impact of ETS on wheezing disorders and Early Childhood Caries (ECC) among children aged 30-60 months.

Methods: A descriptive study was conducted in Mangaluru, South India, among children visiting the Paediatric departments of two tertiary care hospitals. After obtaining ethical clearance and parental consent, data on

parental tobacco use, exposure to ETS in utero, and past and current exposure at home were obtained by parental interviews. Medical history was accessed from hospital records and ECC was assessed by oral examination. The ² test was used to find the association between study variables.

Results: Among 147 children diagnosed with wheezing disorders, 63.3% parents reported presence of one or multiple smokers within their homes, a majority of whom smoked indoors. None of the mothers smoked and 61.9% parents knew about the ill-effects of tobacco use. Among children exposed to ETS at home, 70% presented with a history of wheezing disorders in contrast to 22.8% without history of exposure ($p < 0.001$). Among those exposed to ETS in utero, 57.4% reported with history of wheezing disorders in contrast to 46% without history of exposure. ECC was present among 72.6% children with history of exposure to ETS and in 27.4% without exposure history ($p = 0.001$).

Conclusions: ETS exposure was found to significantly impact occurrence of both wheezing disorders and ECC. With little headway on minimising ETS exposure in domestic settings, it constitutes a significant public health problem in young children who have no control over their environment.

OA05-229-25 Use of smokeless tobacco by low socio-economic populations and risk factors associated with it

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Background: Smokeless Tobacco (SLT) is neglected in the policy area in South Asian countries including Bangladesh and the products are inexpensive, as well as easily available. This study investigated the use of SLT and risk factors associated with it.

Methods: This cross-sectional study using both quantitative and qualitative approaches was used. Four hundred sixty participants were interviewed after being selected through systematic random sampling technique, and four focus group discussions (FGDs) were conducted. Descriptive and inferential analyses were done including binary logistic regression to find out the factors associated smokeless tobacco use.

Results: Almost half of the respondents initiated SLT usage at a very young age (15-24 years), and another 22 percent respondents were smoking and using SLT concurrently. Majority of the women respondents used SLT during their pregnancy. Nearly one-fourth of the respondents tried to quit SLT use and one-quarter had a plan to quit SLT in future. More than one-fifth of the respondents were suffering from dental decay. Significant association was found by gender ($p < 0.01$), sufferings from SLT related disease ($p < 0.05$). The logistic regression analysis suggested that, males were 2.7 times more

knowledgeable than females ($p < 0.01$) about the adverse health effects of SLT usage. The respondents suffering from SLT related diseases were 3.7 times more knowledgeable than the respondents without diseases ($p < 0.01$). Regarding the knowledge on health effects of SLT use, one participant in the FGD session commented that “*although mouth is the gateway to health, we infected our mouth by using Zarda and Gul*”. Again, informants opined that peer, family, curiosity and hospitality culture are influencing factors for SLT initiation.

Conclusions: Counseling on tobacco, including SLT, health hazards have to be emphasized through mass media and there is a need for development of relevant policies and communication messages to make people aware.

OA05-230-25 Prevalence of precancerous lesions and conditions amongst Indian tobacco users: systematic review and meta-analysis

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Background: Prevalence of smokeless tobacco use among South East Asian Region is higher than smoking and this is where 80% of the burden lie. According to GATS-2 in India, 28.6% of all the adults currently either smoke tobacco and /or use smokeless tobacco. Since, literature was limited regarding the prevalence of precancerous lesions and conditions caused due to use of tobacco, a systematic review and meta-analysis was planned among Indian studies.

Methods: A systematic search was conducted in PubMed, Google scholar and Ind med for the observational cross-sectional studies on prevalence of lesions and conditions between 08 / 2016-12 / 2017. Grey literature, bibliographies of retrieved articles and hand searching was done according to the relevance of this review. 2 authors independently reviewed the studies which had no restriction on age, extracted the data and assessed for methodological quality with the help of predetermined criteria which categorized the studies. Random effects model was used for performing meta-analysis as the estimates arose from dissimilar population. Comprehensive Meta-Analysis software was used.

Results: Search strategy yielded 490 records. 128 estimates from 99 studies, yielded 67 high, 57 medium and 4 low quality studies from amongst 10,95,169 participants. Pooled prevalence for leukoplakia (CI- 0.03-0.04) and oral submucous fibrosis (CI- 0.02-0.04) was 3%, for palatal lesions in reverse smokers and nicotina palatine it was 2% (CI -0.01-0.06) and for erythroplakia it was 1% (CI-0.003-0.03). Subgroup estimates for hospital and community based studies are very close to the overall pooled estimates. Heterogeneity varied from 97-99%.

Conclusions: According to GATS-2, 92-96% of the adults believe that smoking and or use of smokeless tobacco causes serious illness. Through the meta analysis, it is indicated that the prevalence of lesions and conditions range from 1-3% in India. This should help the government to step up tobacco advocacy.

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OA05-231-25 Preventing cancers through mobile phones - a potential medium for delivering tobacco cessation intervention for college students: a randomized control trail

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Background: Tobacco smoking remains the most established cause of lung carcinogenesis and its incidence was predicated to be more among smokers than non-smokers with more than 4 in 5 cases developing into cancer. Thus, it is essential to provide an effective cessation intervention for all tobacco users at earliest. As most of the college students around the globe own a mobile phone, it can be utilized to provide an inexpensive tobacco cessation intervention. Thus we aimed to find the feasibility of mobile phone text messaging for a smoking cessation programme among college students aged 20 - 30 years of Bangalore city, India.

Methods: A two-arm randomized controlled trial with sixty college students, who were intended to quit smoking in the next 30 days were randomized to intervention or control group. Text messages tailored to smoking related variables were sent to the participants of the intervention and health related messages not tailored to smoking were sent control group at 2 times per day over a period of 3 months. Abstinence from smoking was identified through Fagerstrom test for nicotine dependence and urinary cotinine level in the base line, 4th week and 12th week. A descriptive statistics along with the ² test was used to test the difference between the two groups.

Results: Twelve weeks after program initiation, the intervention group had a significant reduction in Fagerstrom dependence score when compared to control group from baseline ($P = 0.002^*$). Similarly, participants in the intervention group showed negative urinary cotinine results 13(43.3%) compared to control group 03(10%) and the results were statistically significant.

Conclusions: This cessation intervention significantly reduced smoking rates at end of program, thus providing a potentially efficacious and easily disseminated method to quit smoking.

OA05-232-25 Why do farmers cultivate tobacco? A case study from Sri Lanka

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Background: Tobacco is known to negatively impact health of farmers and farming lands. In 2016, government of Sri Lanka announced an intention to eliminate tobacco cultivation by year 2020. Ceylon Tobacco Company (CTC), the British American Tobacco subsidiary holding the monopoly of manufacturing and sales of cigarettes in Sri Lanka, protested stating it disrupts farmers' livelihoods. This study aimed to explore the factors supporting tobacco cultivation in Sri Lanka.

Methods: A qualitative study was implemented using a desk review on documented research, industry reports and media articles (N=93; analysed by content analysis); and in-depth interviews (N=36) and focus group discussions (N=2) among tobacco farmers; non-tobacco-growing farmers; government officers; society officials and other leaders of farming communities (analysed by thematic analysis).

Results: The main observation was that CTC plays a major role in initiating and sustaining tobacco cultivation in Sri Lanka. CTC engages farmers and farming communities via barn owners and farmer agents who coordinate their activities at the field level. Those two categories are portrayed as representatives of tobacco farmers in policy related issues and to showcase benefits in tobacco cultivation, which is inaccurate and misleading. CTC's material-on-credit approach engages farmers in a vicious cycle of credit and their forward-buying approach deflects a false-sense of security. Farmers not being empowered to assess their return of investment gauge their economic gain by the amount of money they receive after a harvest, leading to inaccurate belief that tobacco cultivation generates high profits. CTC exploits this phenomenon by timing the payments with the Sri Lankan New Year celebrations. CTC also distributes gifts to farmers and farmer officials and conduct small community projects with high propaganda, portraying themselves as a 'friend' of the farming communities.

Conclusions: Tobacco farmers in Sri Lanka are trapped in a vicious cycle of tobacco cultivation due to strategies employed by the tobacco industry.

OA05-233-25 Health and environmental impacts of tobacco farming in selected districts of Bangladesh

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Background: Bangladesh is one of the countries where both production and consumption of tobacco are high. There are many health and environmental impacts associated with tobacco farming. Health problems related to tobacco use and their impact on the environment need to be explored further in the Bangladeshi context. The objective of this research was to assess the impacts of tobacco farming on health and the environment in seven selected districts of Bangladesh.

Methods: This is a cross-sectional study design using both quantitative and qualitative techniques including tobacco farmers and non-tobacco farmers in seven districts of Bangladesh. In-person interviews were conducted with a representative sample of 818 respondents using a semi-structured questionnaire including 10 key informant interviews. Comparative analyses of data were done between the tobacco farmers and the non-tobacco farmers with respect to perceived knowledge, practices, and proportion of Green Tobacco Sickness (GTS). For chemical analyses, collected water and soil samples of each district were tested in the laboratory according to Bangladesh standard.

Results: The main factors influencing farmers to grow tobacco were that cultivating tobacco was more profitable than others crops and the seeds were usually provided by the tobacco companies. Almost all farmers had some idea about the adverse health effects of tobacco farming, irrespective of farmer type. Tobacco farmers had less knowledge of the harmful environmental effects resulting from tobacco harvesting than non-tobacco farmers. The laboratory results revealed that tobacco cultivation created adverse impacts on the environment.

Conclusions: The study concluded that earning more profit and receiving incentives provided by tobacco companies were the main factors influencing tobacco farmers. The study recommends developing local evidence to support tobacco control policy development for alternative crops. Recognizing the current state of the tobacco epidemic, there is a need for active participation by stakeholders in the country's tobacco control movement.

OA05-234-25 Factors influencing farmers turning into tobacco cultivation in the Khulna division of Bangladesh

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Background: Despite health and social costs, tobacco, along with traditional crops has been cultivating in the Khulna division of Bangladesh for few decades. The study attempted to identify factors responsible for turning farmers into tobacco cultivation.

Methods: Primary data was collected from 285 tobacco farmers and 174 traditional crop growers (TCGs) from Khulna division in 2015. A number of 157, 160 and 142 farmers were interviewed individually from Kushtia, Chuadanga and Jhenaidah districts respectively. Random sampling technique was followed. Logistic regression (with marginal effect) was used in quantitative data analysis.

Results: Limitations of traditional crops in both input and output market, prudent role of tobacco processing companies (TPCs), and distinctive features of tobacco itself were responsible for continuing tobacco cultivation. Insufficient input support, nonguaranteed sale, and price instability were reported with traditional crops. TPCs' counter-incentives in inputs and guaranteed sale encouraged farmers to cultivate tobacco. Result showed that 76 percent tobacco growers and only 22 percent TCGs received input subsidy. Moreover, 100 percent contractual tobacco farmers enjoyed sales guarantee even before production, where no TCG enjoyed such. Non-contractual tobacco farmers also enjoyed full-sale. TPCs provided full payment immediately after sale, where 83 percent TCGs experienced credit-sale even through middleman. One-time yield and zero in-house consumption supported tobacco's 98 percent sale. Despite higher production cost, tobacco had higher profit than TCGs. Tobacco farmers were also motivated by house-neighbors and land-neighbors. Statistically significant variables increasing probability of tobacco production over traditional crops were sales guarantee, price stability, input incentives, profit, sales-production ratio, and land neighbors' choice of cultivation. Annual average health cost of tobacco growing households was BDT 4,540 (1 USD = 82 BDT) higher than that of TCGs. **Conclusions:** The main challenges of traditional crops including unstable price, volatility in sales guarantee and insufficient input incentive should be taken care by the authority.

OA05-235-25 Using green supply chain management to overshadow environmental and health costs of tobacco farming by the tobacco industry: a case study of Sri Lanka

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Background: The Ceylon Tobacco Company (CTC) is the monopoly tobacco company in Sri Lanka which 84% shares owned by British American Tobacco. CTC is being criticized by many professionals and general public for its unethical practices affect to health and environment degradation in tobacco farming and its supply chain. Tobacco farming has highly contributed in soil degradation, deforestation and causing respiratory and skin diseases for members in the tobacco farm families while hindering rural development of Sri Lanka.

Methods: A systematic literature review was conducted using journal articles, newspapers, web-pages, books, industry reports, statements from government and non-government officials, related to tobacco farming and green supply chain strategies used by the tobacco industry in Sri Lanka. The strategies used by the industry and counter strategies are discussed using a model.

Results: CTC has established and modifying its supply chain to increase profits by increasing effectiveness and efficiency in production, marketing and access to market by green supply chain concepts. The more robustly green the supply chain becomes, more the company become a public relations and marketing boon. To offset the social, environment, economic and health costs by the tobacco industry, the green supply chain management is used as defense mechanism and to improve their image to imply outcomes of tobacco farming as environmentally friendly. Exposing green investments, lobbying politicians and making policy reforms are suggested to counter the revealed strategies.

Conclusions: CTC uses green supply chain concepts to resemble tobacco farming in Sri Lanka, a sustainable agriculture option while overshadowing the negative impacts it causes to health and environment. Counter strategies should be taken into action to minimize the tobacco industry interventions in agri-supply chains.

OA06 Multidrug-resistant tuberculosis: pearls and wisdom

OA06-236-25 Treatment outcomes of delamanid-containing regimens for multidrug-resistant tuberculosis in Japan

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Background: Delamanid is a promising new drug for the treatment of multidrug-resistant tuberculosis (MDR-TB). However, little is known about the efficacy of the use of delamanid in Japan. The aim of this study was to assess treatment outcomes of MDR-TB receiving delamanid-containing regimens in Japan.

Methods: We conducted a nationwide survey among MDR-pulmonary TB patients registered during 2014-2016 in Japan. We evaluated clinical characteristics, treatment modalities and treatment outcomes in patients with MDR-TB who were treated with or without delamanid-containing regimens.

Results: A total of 140 MDR-TB cases were analyzed: mean age was 48.6 years, 63.6% were male. Eighty four (60.0%) patients were new cases and 57 (40.7%) patients were foreign-born, most coming from high TB burden Asian countries. HIV was positive in one (0.7%) patient. The frequencies of resistance to LVFX, to KM, and to both drugs were 26.4%, 23.6%, and 14.0%, respectively. Overall, 87 (62.1%) patients achieved favourable treatment outcomes. Fifty three (37.9%) patients were classified as having unfavourable treatment outcomes: 20 died, 6 failed, 9 lost to follow-up, 18 transferred to home country. Delamanid was used in 58 (41.4%) of the 140 patients with MDR-TB. Among 17 XDR-TB patients, 11 (64.7%) patients were treated with delamanid-containing regimens. Favourable treatment outcomes were more frequent in patients receiving delamanid-containing regimens (40/58: 69.0%) than in those not receiving delamanid-containing regimens (47/82: 57.3%), although the difference was not statistically significant ($p=0.11$). Two patients discontinued delamanid due to QTcF prolongation.

Conclusions: These results suggest that the use of delamanid can improve treatment outcomes in patients with MDR-TB.

OA06-237-25 Comparing early treatment outcomes in patients on bedaquiline-based regimens vs. conventional multidrug-resistant tuberculosis regimens at primary health care facilities in Cape Town, South Africa

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Background: Less than 5% of patients globally have access to bedaquiline. A WHO review of bedaquiline use in South Africa showed a survival benefit in patients with Rifampicin-resistant TB.

Bedaquiline was first introduced in two inpatient units in the Cape Metro, in January 2015, with progressive rollout to 122 primary health care facilities in September 2015.

Methods: This is a retrospective cohort study of adults treated at PHC for pulmonary MDR-TB between September 2015 and December 2016. All cases were selected from facilities across 6 subdistricts using the electronic drug resistant TB register (EDRweb). Variables included demographics, HIV status, antiretroviral therapy (ART), time to sputum culture conversion, severity of disease on chest x-ray, adverse effects, reason for bedaquiline initiation and change in corrected QT interval (QTcF).

Results: Seventy-eight patients were included, 39 in each group. 16/39 (41%) in bedaquiline arm were HIV co-infected, and 11/39 (28%) in the conventional arm. 22/39 (56%) of patients started bedaquiline due to ototoxicity. Median time to culture-conversion in the conventional arm was 56 days (IQR 28-64), and 56 days (IQR 41-83) in the bedaquiline arm both arms was 56 days. 11/39 (28%) patients were lost to follow-up in the conventional arm versus 4/39 (10%) in the bedaquiline arm. 2 deaths occurred in the bedaquiline-arm. Mean QTcF at baseline was 416ms, and mean increase was 14ms. 1/39(2.5%) discontinued bedaquiline due to increase in QTcF>500ms.

Conclusions: Successful programmatic implementation of bedaquiline at PHC can be done with existing health resources. Bedaquiline-based treatment at PHC has a manageable side-effect profile, and comparable rates of sputum culture conversion at 6 months compared to conventional MDR TB treatment.

OA06-238-25 Extension of bedaquiline and delamanid combination beyond 24 weeks for MDR-TB treatment

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Background: There is limited evidence on using bedaquiline (BDQ) and delamanid (DLM) in combination for drug-resistant tuberculosis treatment beyond 24 weeks. Médecins Sans Frontières (MSF) in Mumbai has been using these two drugs in combination on compassionate basis for patients with limited treatment options since 2016. For patients who would not have 4 working drugs, the combination is extended beyond 24 weeks. The objective of this study is to describe the safety and microbiological efficacy of using BDQ and DLM in combination beyond 24 weeks.

Methods: This is a retrospective cohort analysis of patients who were initiated on treatment regimens containing BDQ and DLM in combination from January 2016 till September 2017 and have received the combination beyond 24 weeks. We report culture at 6 months and 12 months after treatment initiation, QTcF interval and serious adverse events during first 12 months on BDQ and DLM combination.

Results: Thirty-seven patients were initiated on the combination and among them, 24 (65%) were female with a median age of 25 years (IQR: 21-30). Nineteen (51%) had PreXDR-TB while 18 (49%) had XDR-TB. Two patients experienced transient QTcF increase of >500ms while 2 other had >60ms increase. Seven patients had serious adverse events during the study period. None of these led to permanent discontinuation of treatment. One patient died during the study period due to disease progression.

At treatment initiation 30 were culture positive. At 6 months, 27 were culture negative. The 3 culture positive patients had converted by 12 months. Nineteen patients completed 12 months on treatment and 17 (89%) were culture negative. The two culture negative patients had reconverted at 12 months.

Conclusions: Early results of efficacy and safety of extension of BDQ and DLM combination beyond 24 weeks for treatment of drug resistant tuberculosis from programmatic setting are encouraging.

OA06-239-25 Exploring the barriers to and facilitators of enrollment for free DR-TB treatment in Nigeria using the access concept

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Background: In response to the growing threat of drug resistant tuberculosis (DR-TB), the National TB programme in Nigeria and implementing partners provide free treatment and economic support to DR-TB patients. Despite these, some confirmed DR-TB cases fail to enroll for treatment and remain a source of infection. This study examined the constraints and enablers to patients' enrollment for free DR-TB treatment.

Methods: A qualitative case study approach was used to generate data on patients' experiences in enrolling for DR-TB treatment. In-depth interviews were conducted with 28 purposively selected DR-TB patients who initially declined treatment enrollment and 30 patients who willingly enrolled. This was triangulated with the views of 20 TB service providers and 20 TB program managers via key informant interviews. Interviews were audio-taped and transcribed verbatim. Thematic content analysis was guided by Thomas and Penchasky Access framework: availability, acceptability, affordability and accessibility.

Results: Enablers included availability of free treatment and treatment options, provision of economic support for the duration of treatment, in depth counseling of patients and patient's family, reassurance from other patients undergoing treatment. Constraints were mainly acceptability factors - patients living in denial of diagnosis of DR-TB, cultural belief that TB is not amenable to medical treatment, religious convictions of the ultimate power of faith in overcoming diseases, patient's family making the final decision on patient's treatment pathway, stigma, preference for alternative medicine, regimen with daily injections, pill burden and drug side effects. Affordability factors- fear of loss of means of livelihood and accessibility factors- separation from family for facility based DR-TB treatment, long duration of treatment. These factors were non-mutually exclusive.

Conclusions: The study highlighted the complexities that influence the uptake of free DR-TB treatment. It is imperative to design context specific interventions to address these barriers in order to achieve effective TB control in Nigeria.

OA06-240-25 Community-based approach to reduce initial loss to follow-up for DR TB in Nelson Mandela Bay Metro, Eastern Cape Province

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Background and challenges to implementation: Rapid identification of TB clients and treatment initiation is a key cornerstone in tuberculosis control. South Africa diagnosed 19073 Drug Resistant TB cases but only 11192 of these cases were initiated on treatment, representing 7,881 Initial Loss to Follow-up (ILTFU). Data from published studies suggests that ILTFU is a significant global problem and its management is key to the attainment of the End TB strategy.

Intervention or response: Nelson Mandela Metro Bay, with highest ILTFU rates was identified as a pilot site for USAID TB South Africa Project to address the ILTFU problem. In partnership with the National Institute of Communicable Disease (NICD), a list of patients with resistance to the drug *Rifampicin*, referred to as 'Rif alerts' were shared with the project. The project cross referenced if all the patients were initiated on treatment as evidenced by records in the electronic drug-resistance register (EDR.web). Clients that were found not 'initiated' on treatment were referred to community health institutions for tracking and eventual linkage to care.

Results and lessons learnt: A total of 501 Rif. alerts were received between January and September 2017 of which 292 (58%) were found registered in the EDR.web and an additional 97 (19%) were found in other facility registers, thus 112 (22%) were ILTFU cases. Through the projects interventions 76 of the 112 ILTFU cases were tracked, referred and linked to care through community based institutions. Thus, of the 501 Rif alerts received from NICD, a total of 465 (93%) were initiated on treatment and registered on the EDR.web.

Conclusions and key recommendations: Through community-based interventions, two-thirds of the ILTFU clients were found and initiated on treatment, which increased Rif cases initiated on treatment by 15% and increased the overall Rif cases linked to treatment to 93%. It is feasible to use community resources to reduce ILTFU and improve linkage to TB care.

OA06-241-25 Contribution of the spectinamide 1810 to the standard and new drug regimens in a murine relapse model of tuberculosis

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Background: The spectinamides are narrow-spectrum semisynthetic analogs of spectinomycin that have increased potency as protein synthesis inhibitors against *Mycobacterium tuberculosis*. Spectinamides, including lead 1810, have been previously shown to exhibit a promising therapeutic profile in mice as single agents. Here we explore the bactericidal activity and relapse potential of 1810 when used in combination with the first-line regimen (HRZE) or as part of a novel regimen with bedaquilline and pretomanid (BPa).

Methods: Mice were infected with a lethal high-dose aerosol of *Mycobacterium tuberculosis* Erdman. Treatment was initiated 11 days after infection and administered once daily, 5 days per week, for up to 16 weeks. Spectinamide 1810 was administered by subcutaneous injection at 200 mg/kg. All other drugs were administered by oral gavage. Efficacy was assessed on the basis of lung CFU counts and on the proportion of mice with culture-positive relapse 12 weeks following treatment completion.

Results: Addition of 1810 to the standard regimen of HRZE significantly improved bactericidal activity by about 1.7 log₁₀ CFU at 4 weeks compared to HRZE alone. Paired with BPa, 1810 was equipotent to a highly effective regimen of BPa plus linezolid after 4 weeks of treatment, and by reducing bacterial burdens to the limit of detection with 8 weeks of treatment. The comparative abilities of all four drug regimens to shorten treatment duration in relapse studies, which shows their ability to sterilize, will be presented.

Conclusions: Spectinamides including the lead 1810 are safe, effective partner drugs with potential to shorten treatment duration of drug-resistant tuberculosis.

OA06-242-25 Adverse events during treatment of multidrug-resistant tuberculosis in Viet Nam: a cohort event monitoring study

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Background: The safety data during multidrug-resistant tuberculosis (MDR-TB) treatment still varied not only among Vietnamese patients but also among patients in other areas of the world. The aim of this study was to determine the incidence of adverse events (AEs) that occurred during the 20-month standard MDR-TB treatment in Vietnam.

Methods: AEs were collected from MDR-TB patients treated with standardized MDR-TB regimens in 9 sentinel sites in Vietnam through a cohort event monitoring (CEM) program. The enrolment period was from April to December 2013 and patients were monitored with a follow-up of approximately 20 months. AEs were detected and defined based on clinical assessment and laboratory tests. Serious AEs (SAEs) and were classified according to WHO definition and clinical significant AE were identified if patients had SAEs, AEs required anti-TB regimen modification or any other clinical intervention. Cox's proportional hazard regression models were used to explore factors associated with the reported AEs.

Results: The enrolled cohort included 658 MDR-TB patient, among whom 16.3% experience at least one SAEs, 56.7% has clinical significant AEs. The most common SAEs and AEs required anti-TB regimen modification were ototoxicity, ophthalmic disorders, hepatotoxicity, vomiting and nephrotoxicity. For clinical significant AEs, arthralgia, hyperuricemia, vomiting and hepatotoxicity appeared to be the most common reported conditions. Serious nephrotoxicity occurred in the first six month of treatment and associated with higher body-weight based dose of the injectable drug. Alcoholic and baseline alanine aminotransferase (ALT) level were predictors for clinical significant hepatotoxicity.

Conclusions: AEs were common during MDR-TB treatment in Vietnam, including SAEs and AEs that required proper interventions. Predictors for hepatotoxicity observed in this study underscore the importance of patient history investigation, baseline laboratory examination, and monitoring during standardized MDR-TB treatment. The dose of injectable drug deserved more attention to prevent nephrotoxicity on low body weight patient.

	SAE	Serious AE and AE required anti-TB regimen modification	Serious AE and AE required clinical intervention		SAE	Serious AE and AE required anti-TB regimen modification	Serious ADE and AE required clinical intervention
Ototoxicity	24 (3.6%)	33 (5.0%)	54 (8.2%)	Nephrotoxicity	10 (1.5%)	14 (2.1%)	37 (5.6%)
Ophthalmic disorders	21 (3.1%)	23 (3.5%)	24 (3.6%)	Hyperuricemia	4 (0.6%)	12 (1.8%)	120 (18.2%)
Hepatotoxicity	19 (2.9%)	25 (3.8%)	89 (13.5%)	Number of patient experienced AE	107 (16.3%)	143 (21.7%)	373 (56.7%)
Vomiting	10 (1.5%)	24 (3.6%)	118 (17.9%)	Total number of AE	165	234	1215

[Adverse events occurred during MDR-TB treatment (n=658)]

OA06-243-25 Shorter regimen for multidrug-resistant tuberculosis patients in Mozambique

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Background: Recently, the shorter MDR-TB regimen has been recommended by WHO for MDR-TB patients under certain conditions. Recent results from the STREAM trial confirms the effectiveness of the regimen however more evidence is needed in patients co-infected with HIV.

Methods: A prospective cohort study was conducted in Maputo, Mozambique, including patients with active pulmonary TB diagnosed as rifampicin resistant and no previous treatment with second-line drugs received. We described 6-month culture conversion and treatment outcomes in HIV-positive and HIV-negative patients.

Results: As of January 31st 2018, 150 patients started the short MDR-TB regimen: 57.3% were males, median age was 32 [IQR 25-40] and median BMI was 17.9kg/m² [IQR 16.4-19.8]. Among them, 95 (63.3%) were HIV-positive. Baseline resistance was: 53.8% resistant to pyrazinamide, 47.9% to ethionamide, 1.3% to kanamycin and 9.5% to fluoroquinolones. Culture conversion at 6 months was achieved among 49/63 (77.8%) patients and was similar according to HIV status (p=0.335). Treatment outcomes were assessed among 63 patients: 29 cured (46.0%), 16 (25.4%) completed treatment, 6 (9.5%) died, 7 (11.1%) failed treatment and 5 (7.9%) lost to follow-up. Success rate was higher among HIV-negative (18/22, 81.8%) compared to HIV-positive patients (27/41, 65.8%) although not statistically sig-

nificant ($p=0.091$). All deaths occurred among HIV-positive. Treatment failure was slightly higher among HIV-positive and was experienced in 3/4 (75.0%) fluoroquinolones-resistant patients.

Conclusions: Among the first patients receiving short MDR-TB regimen in Mozambique, a high rate of culture conversion and a higher success rate than the conventional treatment are reported. However, HIV-positive patients seem to have a lower success rate mainly due to higher death rate. High proportion of treatment failure among fluoroquinolone-resistant patients stresses the need to use rapid molecular testing in order to adapt their treatment and exclude them from the 9 months regimen.

OA07 Highlights from the laboratory

OA07-244-25 Routine performance and clinical significance of Xpert MTB/RIF in tuberculous meningitis: a prospective cohort study from Indonesia

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Background: Xpert MTB/RIF is recommended by WHO as an initial diagnostic test for TB meningitis (TBM). However, there are still relatively few published data comparing Xpert MTB/RIF with microscopy and culture, or evaluating the effect of sample pretreatment (centrifugation) prior to Xpert testing.

Methods: This study was embedded in a longstanding prospective cohort study of TB meningitis in Bandung, Indonesia. Cerebrospinal fluid (CSF) samples of meningitis suspects enrolled between July 2014 and June 2017 were included and examined with Xpert MTB/RIF, ZN-microscopy, and *M. tuberculosis* culture. For microscopy and culture, sediment of centrifugated CSF samples was used; for Xpert MTB/RIF, CSF samples were used without centrifugation prior to December 2014, and subjected to centrifugation afterwards. Sensitivity of different methods was compared and results were stratified for HIV status. For Xpert MTB/RIF, results with and without centrifugation were compared. Finally, Xpert MTB/RIF were examined in relation to disease severity.

Results: Among 312 TBM suspects, Xpert MTB/RIF, microscopy and culture were positive in 108 (34.6%), 63 (20.2%), and 125 (40.1%) patient samples. Four positive Xpert results showed rifampicin resistance. Using culture as reference, sensitivity of Xpert MTB/RIF was 75.2% compared to 45.2% for ZN-microscopy. Using clinically diagnosed TBM as a reference, sensitivity of Xpert, ZN-microscopy, and culture was 45.8%, 26.6%, and 52.1% respectively. With culture as a reference, sensitivity of Xpert was 75.0% using centrifugated samples and 76.9% using direct samples ($p>0.05$). All methods gave higher yields in HIV-negative patients. Xpert-positive patients had severe (grade II/III) disease (99.1% vs. 61.0% in Xpert-negative, $p<0.05$) and lower CSF:blood glucose ratio.

Conclusions: This is one of the largest study evaluating Xpert MTB/RIF for diagnosis of TB meningitis. Xpert MTB/RIF is more sensitive compared to microscopy and may contribute to early detection and treatment of TBM. Centrifugation of samples prior to Xpert-testing does not seem to increase sensitivity.

OA07-245-25 Diagnostic yields of the urine LF-LAM and sputum Xpert MTB/RIF assays for the detection of TB among adult out-patients newly diagnosed with HIV in Cameroon

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Background: The WHO recommends the use of the urine LF-LAM assay to improve TB detection among people living with HIV who are severely ill or with CD4 < 100 cells/ μ L. In practice, it is often difficult to know the CD4 count of someone newly diagnosed with HIV, especially in the era of 'Test and Treat.' On the other hand, people newly diagnosed with HIV are routinely screened for TB symptoms, and this may provide a more useful means to determine who to recommend for urine LF-LAM testing.

Methods: Consecutive adult outpatients newly diagnosed with HIV at the Care and Treatment Center of the Bamenda Regional Hospital were administered the WHO symptom questionnaire (cough, fever, night sweats, weight loss), sampled for blood for CD4 count testing, and requested to provide sputum and urine specimens. Anyone with sputum Xpert, sputum culture, and/or urine LAM positive for TB was defined as having bacteriologically-confirmed TB. The diagnostic yield of the urine LAM and the sputum Xpert were determined as compared to the total number of bacteriologically-confirmed TB cases.

Results: From September 2013 to September 2014, 803 outpatients newly diagnosed with HIV were enrolled, 754 (94%) submitted specimens for testing, and 95 of these (13%) had bacteriologically-confirmed TB. Among the 90 symptomatic people with TB, the diagnostic yield of sputum Xpert was 46% (N=41/90), of urine LF-LAM was 32% (N=29/90), and of combined sputum Xpert and urine LAM was 69% (N=62/90). As shown in the Table, the diagnostic yields varied depending on the symptoms reported, and the greatest incremental yield of urine LAM compared to sputum Xpert was +31% among people reporting fever.

Symptoms	Diagnostic yield: urine LF-LAM % (95% CI)	Diagnostic yield: sputum Xpert % (95% CI)	Diagnostic yield: sputum Xpert and urine LF-LAM % (95% CI)	Incremental yield of urine LF-LAM over sputum Xpert %
Any fever (n=29)	41 (26-59)	41 (26-59)	72 (54-85)	31
Cough, no fever (n=48)	27 (17-41)	52 (38-66)	71 (57-82)	19
No cough, no fever (n=13)	31 (13-58)	31 (13-58)	54 (29-77)	23
Total (n=90)	32 (24-42)	46 (36-56)	69 (59-78)	23

[Diagnostic yield and incremental yield of urine LF-LAM assay compared to sputum Xpert MTB/RIF assay among 90 people with BAC+ TB, by symptoms reported]

Conclusions: Urine LF-LAM testing may add important value for the detection of TB among symptomatic outpatients newly diagnosed with HIV as compared to sputum Xpert testing alone, especially among those who report having fever.

OA07-246-25 Molecular characterization of mutations associated with resistance to second-line tuberculosis drugs among rifampicin-resistant tuberculosis patients in Mongolia, 2016

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Background: Extensively drug-resistant tuberculosis (XDR-TB) represents an emerging public health problem worldwide. National anti-TB drug resistance survey was conducted 1999 and 2007 in Mongolia. In purpose to determine the current prevalence of drug resistance, a third survey was conducted in 2016. The objective of this study was to determine the prevalence and gene mutations of drug resistance to second-line TB drugs among rifampicin-resistant cases.

Methods: A new and previously treated 1664 smear positive TB cases had been reported from February 2016 to January 2017 in 21 provinces, 9 districts, 1 prison, which provide TB services nationwide. A total of 1560 (93.8%) cases participated in the survey and collected sputum specimen. Smear, culture and conventional and molecular drug susceptibility testing were performed at the National Reference TB laboratory, NCCD of Mongolia. Mutations associated with second-line anti-tuberculosis drug resistances were determined by using GenoType MTBDRsl assay among 110 rifampicin-resistance isolates.

Results: Resistance to second-line anti-TB drugs was determined for 110 rifampicin-resistance isolates using both phenotypic and genotypic DST, 90% (99/110) were susceptible to fluoroquinolone and injectable SLD and 10% (11/110) resistant, which are 2.7% (3/110) was XDR-TB, 7.3% (8/110) was pre-XDR.

GenoType MTBDRsl assay results: Among any fluoroquinolone resistance isolates A90V (MUT1), D94A (MUT3A), D94N-D94Y (MUT3B) and D94G (MUT3C) mutations of the *gyrA* gene detected as 42.8% (3/7), 28.6% (2/7), 14.3% (1/7) and 14.3% (1/7), respectively. Among any second-line injectable resistance strains, 85.7% (6/7) had *rrs* gene mutations at A1401G (MUT1) and 14.3% (1/7) had *eis* gene mutations at C-14T (MUT1).

Conclusions: Prevalence of the second-line anti-TB drugs resistance was 10% and XDR was 2.7% among rifampicin-resistant cases. The most frequent gene mutations associated with the resistance fluoroquinolones and second-line injectables were observed in the codon A90V of *gyrA* gene and codon A1401G of the *rrs* gene, respectively.

OA07-247-25 Redefining MDR-TB: comparison of *M. tuberculosis* clinical isolates from Russia and Taiwan

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Background: Tuberculosis with multidrug resistance (MDR) and extensively drug-resistance (XDR) is a global challenge due to limited number of effective drugs for treatment. Use of less than 4-5 effective drugs for treatment leads to further emergence of drug resistance. For better prediction of treatment outcomes, we compared drug resistance profiles of sequential MDR *Mycobacterium tuberculosis* isolates from high and low-burden settings.

Methods: This was a retrospective cohort study. We respectively analyzed 225 and 229 MDR strains from Moscow and Taiwan between 2014 and 2015. Drug susceptibility testing for 14 drugs was performed by the Bactec MGIT 960 automated system and/or the agar proportion method. Detection of resistance associated mutations in *M. tuberculosis* genome was performed by hybridization analysis on microarrays and Sanger sequencing of selected loci.

Results: We found the principal difference between resistance profiles of MDR clinical isolates in two settings: the percentage of pre-XDR (40.9% vs. 14.8%) and XDR (34.7% vs. 1.7%) stains were significantly higher from Moscow. Consequentially, the median number of effective anti-tuberculosis drugs was lower (3 vs. 7). A notable percentage (6%) of isolates resistant to kanamycin harbored mutations in the *whiB7* locus was not detected by WHO-recommended molecular tests targeting common mutations in the *rrs* and *eis* genes. Furthermore, 99.6% and 45.9% of MDR strains were resistant to streptomycin from Moscow and Taiwan, respectively.

Conclusions: Molecular tests for detecting drugs other than MDR and XDR drugs are needed for individualized therapy. Some MDR stains resistant to nearly all available anti-TB drugs, but not to fluoroquinolones or second-line injection drugs, were not defined as XDR-TB. The conventional MDR treatment schemes might probably fail in these cases due to the limited number of effective drugs.

OA07-248-25 Diagnostic performance of a five-marker predictive model for differential diagnosis between intestinal tuberculosis and Crohn's disease

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Background: The differentiation between intestinal tuberculosis (ITB) and Crohn's disease (CD) is a challenge. The aim of this study was to investigate a predictive model for differential diagnosis between ITB and CD.

Methods: A total of 268 patients who were suspected to have ITB or CD were prospectively recruited between January 2013 and September 2016. The clinical, laboratory, radiological, endoscopic, and histological features were investigated and subjected to univariate and multivariate analyses. The final predictive model was developed based on the regression coefficients of the multivariate logistic regression. To validate the model, the same regression equation was tested on the other group.

Results: 239 patients had a final diagnosis, including 86 ITB and 153 CD. Five variables (perianal disease, pulmonary involvement, longitudinal ulcer, left colon, and TBAg/PHA ratio (ratio of tuberculosis specific antigen

to phytohaemagglutinin)) were selected for the predictive model to discriminate between ITB and CD. In the predictive model of the training data set, the area under the receiver operating characteristic (ROC) curve, sensitivity, specificity, and accuracy with a cutoff level of 0.29 were 0.975 (95% confidence interval (CI) 0.939-0.993), 96.7%, 90.7%, and 92.8%, respectively. Application of the predictive model to the validation data set showed similar performance in distinguishing ITB from CD. The area under ROC, sensitivity, specificity, and accuracy were 0.950 (95% CI 0.871-0.987), 88.5%, 93.5%, and 91.7%, respectively.

Conclusions: This five-marker predictive model could be conveniently used by clinicians to draw a reliable differential diagnosis between ITB and CD in clinical practice.

OA07-249-25 Experience of new algorithm for TB diagnosis in BRAC implementing area: screening by X-ray and confirmed by GeneXpert

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Background and challenges to implementation: BRAC, a development organization initiated community based tuberculosis control program in 1984 in one sub-district and since 1994 it works in collaboration with NTP currently covering two third of the country. In 2017, NTP adopted a new strategy to implement an updated algorithm for diagnosing missing cases. As part of this initiative, BRAC established 23 X-ray centres along with 23 GeneXpert machines in cities and district towns in an effort to improve early case detection.

Intervention or response: Since 2017, NTP changed the definition of presumptive from three weeks to two weeks of persistent cough and laid out a new framework of diagnosis algorithms (based on availability of diagnosis tools). To align with the algorithm, BRAC has already established 23 TB diagnostic centers in combination of X-ray and GeneXpert machines that are fully functioning from January 2018. Through this algorithm all TB presumptive screened by X-ray, following those who have abnormal X-ray finding are confirmed by GeneXpert test. Additionally, all DR TB presumptive are directly sent for X-pert test if they meet 10 criteria.

Results and lessons learnt: From January to March 2018, in 23 TB diagnosis sites, a total of 31,123 TB presumptive were screened by X-ray and 8,033 (26%) were found abnormal. Subsequently, among 6,490 TB presumptive with abnormal X-ray findings 1,311 (20%) TB patient were detected by GeneXpert. In January-March quarter 2018 case notification of bacteriologically confirmed TB

(Pulmonary) was observed 105% increase in intervention areas compare to January-March quarter 2017.

Conclusions and key recommendations: X-ray is found to be an effective screening tool prior to rapid detection of drug sensitive and drug resistant TB cases by GeneXpert. Using this effective algorithm, more TB cases could be detected and treated earlier that will prevent the transmission of disease and reduce the TB burden in the country.

OA07-250-25 A study of variability in minimum inhibitory concentrations of *Mycobacterium tuberculosis* isolates against first-line anti-tuberculosis drugs in global settings with differing rates of drug-resistant tuberculosis

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Background: Although antibiotic dosing guidelines for treatment of drug susceptible tuberculosis (DS-TB) are internationally standardised, the degree of global variation in Minimum Inhibitory Concentrations (MICs) of non-genotypically resistant *Mycobacterium tuberculosis* (*Mtb*) isolates against first-line drugs is not well described. Relationships between antibiotic exposure and treatment response are also poorly understood.

Methods: Clinical isolates of *Mtb* previously categorised as fully drug susceptible were obtained from countries where the incidence of multi-drug resistant (MDR-TB) was low (Malawi [73 isolates]), medium (Nigeria [49 isolates] and Vietnam [48 isolates]) or high (Moldova [51 isolates]). Customised sensititre MYCOTB plates were used to compare finely graded MICs to rifampicin and isoniazid. Available pharmacokinetic data describing the area under the concentration time curve (AUC_{0-24h}) for rifampicin (dosed at 10mg/kg) from the Malawian patients were used to relate AUC_{0-24h}/MIC to treatment response in that cohort.

Results: Differences were observed in the MIC distributions of genotypically drug susceptible *Mtb* isolates between low/medium and high MDR-TB incidence countries. Median rifampicin MICs were 0.015 (0.01-0.06), 0.06 (0.015-0.25) and 0.015 (0.015-0.06) mg/L in Malawi, Nigeria and Vietnam compared to 0.25 (0.06-0.50) mg/L in Moldova (p< 0.001). Median isoniazid MICs were 0.015 (0.01-0.06), 0.03 (0.015-1.00) and

0.015 (0.015-0.06) mg/L in Malawi, Nigeria and Vietnam compared to 0.06 (0.03-0.12) mg/L in Moldova (p< 0.001). The median AUC_{0-24h} for rifampicin in Malawi was 27.6 (IQR: 23.6-32.7) mg/ml.hr, which is lower than described elsewhere. No association between AUC_{0-24h}/MIC and treatment response was detected in Malawi.

Conclusions: We have demonstrated raised MIC to key first-line TB drugs in circulating *Mtb* strains currently categorised as drug susceptible in areas with a high burden of MDR TB. The influence of raised (>15-fold higher) MIC on treatment outcomes for DS-TB patients on standard regimens should be characterised, particularly for countries in Eastern Europe with extremely high MDR TB rates.

OA07-251-25 miRNAs as molecular tool for diagnosis of pulmonary tuberculosis and to predict treatment response

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Background: There is an unmet need to identify biomarkers that can predict *Mycobacterium tuberculosis* (MTB) infection, which can be used for TB diagnosis. The objective of the study is to identify circulating miRNA as molecular tool for TB diagnosis as well as to differentiate treatment response.

Methods: Confirmed cases of pulmonary tuberculosis patients (120) were recruited for the study before treatment initiation. In addition, 22 uninfected controls were also recruited in the study. At enrollment, baseline resistance to Rifampicin was ascertained by GeneXpert MTB/Rif. The serum and sputum samples were collected from all healthy controls and TB affected patients. Total small RNAs isolated from serum samples were used for preparation of small RNAs libraries and sequenced by Illumina HiSeq, while sputum samples were used for bacterial culture and drug-sensitivity assays. The study was performed as per Institutional Ethics Approvals, and Informed consent of study participants were obtained.

Results: Bioinformatics analysis of small RNA sequence data identified >600 circulating miRNAs in serum samples. Quantitative analysis of miRNAs by DE-Seq method identified several miRNAs which showed differential levels between patient cohort and healthy controls.

Conclusions: Our study showed that specific circulating miRNA patterns are associated in individuals with pulmonary-TB as compared to healthy controls. These miRNA patterns in serum are potential molecular tools for diagnosis of TB and to predict response to anti-TB drugs.

OA08 Has MPOWER empowered nations to tackle tobacco epidemic?

OA08-252-25 The evaluation of 7 years of local smoke-free legislation implementation in Bali province, Indonesia, and the next steps to improve compliance

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Background: The government of Bali Province implement a local legislation no. 10/2011 regarding smoke-free area or local smoke-free legislation (LSFL) since 2011. The legislation is very important to educate the community and reduce the harm of smoking. An evaluation is needed to describe recent compliance, progress and planning the next steps policy.

Methods: This was a cross-sectional study that conducted from January to February 2018 in Bali Province, Indonesia. The population is all area that ruled in the legislation including education, health facilities, worship places, children's playground, work places and public places. Samples were selected by proportional probability to size (PPS). The compliance defined by 8 criteria that established in the legislation. Observation and data collection is done using a mobile-based application called Open Data Kit (ODK) Collect. We adopt the standard check list from the Guidelines of Assessing Compliance with Smoke-Free Laws.

Results: The study succeeded to observe 1,263 smoke-free areas. The compliance to LSFL was 930(73.6%). The 3 most violation were found cigarette butts indoor 250(19.8%), providing ashtray indoor 219(17.3%) and found people smoking indoor 124(9.8%). The worst area complies to LSFL were public places, such as bus terminal (21.4%), pub/bar (30.0%), traditional markets (46.9%), restaurant (45.5%) and hotel (54.8%). The LSFL compliance was associated with the knowledge of managers regarding principal, penalty and their responsibility on LSFL implementation. Moreover, the support of managers and internal monitoring team in each smoke-free area were important factors to improve the compliance.

Conclusions: The LSFL compliance after 7 years' implementation was not yet reached target 80%. Prioritisation program such as supervision and law enforcement are needed at the public places. We recommend the forming an effective tobacco control team in each district, disseminating and mentoring the implementation of smoke-free policy at each area to improve the compliance.

OA08-253-25 Examining tobacco control policy interventions in Brazil, Mexico, China, and Indonesia: a landscape assessment from 1990 to 2016

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Background: Country progress in tobacco control has been variable, particularly among lower and middle-income countries (LMIC), since adoption of the WHO's framework convention. The objective of this study is to assess the landscape of tobacco control policies and programs in four populous LMIC at various stages of the tobacco epidemic to better identify effective strategies and remaining challenges.

Methods: We completed a landscape assessment of tobacco use and tobacco control policies and programs in four countries: Brazil, Mexico, China, and Indonesia, at the national and subnational level, working in-country with relevant partners. Using the MPOWER framework, we collated data on prevalence of primary smoking and associated secondhand smoke exposure and identified all existing data on prices, programs, policies, enforcement, and compliance from 1990 to 2016.

Results: Levels and trends in smoking prevalence vary greatly between and within the four countries, and also by age and sex (Table 1). Across all locations, policy interventions were not guided by socioeconomic or other demographic considerations, and tended to focus on smoke free and TAPS (tobacco advertising, promotion, and sponsorship). Lastly, we found little data on compliance and enforcement of policies, with comparable data across subnational locations particularly lacking.

Conclusions: The broad lack of information on enforcement and compliance of tobacco control across all focus countries is a critical void which complicates any effort to understand the effectiveness of contemporary tobacco control measures globally. Further, the impact of major tobacco control interventions across various population subgroups needs to be studied, so as to better tailor tobacco control to the demographic groups that comprise the majority of the smokers in each location.

OA08-254-25 An analysis of tobacco industry interference strategies during COP-7 India

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Background: The Conference of Parties (COP) is the governing body of WHO FCTC and provides guidelines and policy options for implementation of FCTC. Seventh Session of Conference of Parties (COP7) of WHO Framework Convention on Tobacco Control was held in India from 7th to 12th November 2016. A media analysis was done in order to understand the interference strategies adopted by tobacco industry to influence the policy decisions taken during the COP7.

Methods: Thematic content analysis of the news published in print media was done during one month period from 15th October to 15th November. A total of 200 news items, press releases etc. were analyzed. The overall analysis was done on the basis of guidelines of article 5.3 of FCTC.

Results: Tobacco farmers appealed to Prime Minister and Health Minister to boycott COP7. Industry demanded a softer stand on FCTC. Industry Farmer groups approached High Court to compel government to allow farmers to attend the COP7. Farmer association protested at WHO office and conference venue demanding transparency in decision making. Tobacco Institute of India and farmer group written letter to agriculture ministry to represent their views.

6000 page petition signed by 1 lakh farmer seeking protection from FCTC rules sent to agriculture ministry. Group of Indian cigarette makers urged Prime Minister to ensure that health ministry does not make any anti tobacco commitments. Industry bodies requested government to allow farming association and trade bodies in COP7. Industry highlighted that FCTC ratification is not a legal obligation on government and decision in COP7 will be against cigarette industry and chewing tobacco, bidi, zarda etc might not be considered.

Conclusions: Tobacco industry try to influence the government & COP7 decision making body to protect their interest. In order to protect government policies and treaties like FCTC special interventions are required to stop industry interference.

OA08-255-25 Written consent by tobacco shopkeepers and regular monitoring by law enforcers sustained city free from tobacco advertisements at POS

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Background and challenges to implementation: Under section 5 of Indian Tobacco Act - COTPA 2003, direct and indirect advertisements are prohibited. Unfortunately tobacco companies use display boards and posters to advertise their products through shopkeepers. GATS-II says in Madhya Pradesh 34.2% people use tobacco in one or other forms. 10.2% adult smoke and 28.1% use smokeless tobacco. The city Indore of Madhya Pradesh was full of advertisement, youths and children were attracted by the advertisements, enforcers were not well informed and skilled to handle POS advertisements. Violation under section 5 is non-compoundable, therefore, enforcers did not want to appear in court frequently for too many cases.

Intervention or response: District Collector-cum-Chairperson, Tobacco Control Committee was briefed about the violation through photographs and number of places as evidence. Meeting was organized, directives issued, law enforcers oriented, monitoring done. Large number

of shopkeepers removed their boards. After few months again it cropped up. Administration was informed, warning announcement made, strict monitoring started, all display boards removed with written consent from shopkeepers that they will not repeat in future.

Results and lessons learnt: Around 900 big hoardings and posters were there in the city. Out of which 800 removed by the shopkeepers. 500 shopkeepers gave written declaration not to advertise or sponsor any program in future. In addition a group of 350 shopkeepers jointly decided that violation of section 4 & 5 will not be allowed in their marketing complex.

Awareness, monitoring and enforcement should go together. Written consent by shopkeepers to the administration has helped in self sustaining the process. Officers do not have to appear frequently in the court.

Conclusions and key recommendations: Planned, systematic evidence based advocacy and written consent by the violators helped keeping city free from advertisement and the number of litigations in court.

OA08-256-25 Change of smoking trends with the policy interventions in Sri Lanka and industry tactics to lower the impact

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Background: Sri Lanka (SL), has an annual death toll of 20,000 due to tobacco. Governments have been increasing the control over tobacco during the past few decades. In 2006, SL implemented National Authority on Tobacco and Alcohol (NATA) act, a comprehensive legislation package incorporating MPOWER strategies. In 2015, pictorial warnings were introduced on cigarette packs. In November 2016, the price of cigarettes was increased by 43% via tax increase. This study aimed to compare the tobacco smoking trend with the aforementioned policy changes and to explore the industry interference to reduce the impact.

Methods: The smoking trends were compiled based on the SPOT survey conducted by Alcohol and Drug Information Centre, a bi-annual survey among 2500 males. The details on industry interference were collected through a desk review and expert interviews.

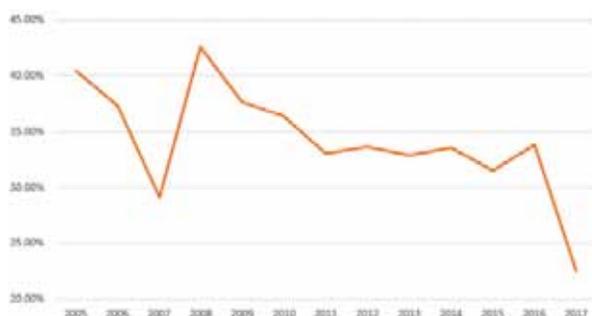
Results: Proportion of current users reduced to 29.1% from 37.3% after the enactment of NATA. However, in the following year (2008), it rose to 42.6%. According to the experts, tobacco industry carried out significant activities to overcome the negative impact for sales using the loopholes of the act.

The variation of smoking trend was lower with the pictorial warnings: 33.6% (2014) to 31.5% (2015) to 33.8%.

Not banning sale of single sticks the preferred mode of buying cigarettes, was a major contributing factor.

The highest decrease was observed with the cigarette price increase in 2016: 33.8% to 22.5%. However, many strategies are in place by the tobacco company to overcome this, including expanding the dealer network to increase availability.

Conclusions: The policy changes seem to have an impact on the smoking trend in Sri Lanka and tobacco company have executed many counter strategies to reduce the impact. Therefore the government needs to be vigilant to sustain the significant reduction of consumption achieved on 2017.



[Smoking Trends from 2005 - 2017 (Source: SPOT Surveys, ADIC Sri Lanka)]

OA08-257-25 Effect of tobacco taxation on smoking prevalence and smoking attributable deaths in India

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Background: Tobacco smoking is a major cause of many preventable diseases and premature deaths globally. Taxation on tobacco products is a major component of WHO MPOWER policy to curb tobacco use. The present study aims to estimate the effect of raising tax of smoked tobacco products (cigarette and bidi) on the prevalence of smoking and smoking attributable deaths in India.

Methods: A mathematical model was developed in the study which used the data on estimated population size, overall tax, smoking rates and price elasticity of demand. Four scenarios, involving increased taxes, were evaluated. The outcomes are smoking prevalence and the number of smoking-attributable deaths by age and gender from 2017 to 2025.

Results: The model projected that with an increase in taxation rates, the smoking prevalence can be reduced to 9.3%, 9.1%, 9% and 8.7% respectively against each assumption, taking smoking prevalence in 2017 as baseline prevalence.

Further, the smoking attributable deaths can be decreased by 1.39%, 2.87% and 6.04% in scenario 2, scenario 3 and scenario 4 as compared to scenario 1.

Around 12,162 extra deaths can be averted in scenario 4 by the end of 2025.

Conclusions: Higher taxes on smoked tobacco could have substantial health and economic gains for India. The model will assist the governments in fixing the taxation rates on smoked tobacco products.

OA08-258-25 Tobacco control in Nepal: collaborative effort of government officials, member of Parliaments, civil society and media

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Background and challenges to implementation: Tobacco is one of the major public health challenges in Nepal. It kills more than 25000 people yearly. To combat this epidemic, Nepal has adopted a comprehensive Tobacco Control and Regulatory Act 2010 with the provision of 100% smokefree laws, TAPS Ban and mandates government to implement 75% pictorial health warning (PHW). The successful enforcement of 75% PHW in 2014 prompted the MoH to increase the size requirement to 90% with an enforcement date of 15th May 2015. However, the enforcement of 90% PHW across the variety of tobacco products is still a challenge.

Intervention or response: To disclose tobacco industry interference and building policy pressure in implementation of 90% PHW we carried out different interventions such as;

1. Monthly market monitoring.
2. Diagnose, Document and disclosing tobacco industry interference with policy makers through media intervention.
3. One to one policy meeting and interaction with govt. officials, MP's, policy makers to gain their commitment for enforcement, monitoring and policy making.
4. Series of Press release, Media mobilization to build policy pressure on policy makers and enforcement agencies.
5. Registering the case in Supreme Court against the government for immediate enforcement of 90% PHW.

Results and lessons learnt: TI lobbying with political leaders and government officials were disclosed and diluted through media and their arguments were countered through round table talks inviting Policy makers, experts and media. Conducting the series of interaction programs, one to one policy meeting, group interviews of policy makers, and MPs gain their commitment and build the significant pressure to implement the PHW as per the law. Almost all products complied the 90% PHW except one domestic product.

Conclusions and key recommendations: A political commitment, collaborative effort and inter sectoral coordination among government officials, NGO's, civil society and media played crucial role in policy development and implementation of 90%. These collaborative efforts need to be sustained.

OA08-259-25 Knowledge of harms of tobacco and awareness of text warnings among tobacco users in Kenya: findings from the ITC Kenya Wave 1 Survey

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Background: Tobacco use kills about 9,000 Kenyans annually and is a major risk factor for many diseases. The Kenya Tobacco Control Act (TCA) of 2007 and 2015 provide a legal framework for the implementation of WHO FCTC policies including health warnings. This study assessed the knowledge of harms of tobacco use and effectiveness of text warnings on cigarette packs.

Methods: Data from the International Tobacco Control (ITC) Kenya Wave 1 (2012) Survey was used to make this assessment. This survey had a nationally representative sample of 1,427 tobacco users and 571 non-users aged ≥ 15 years. Key variables analyzed were knowledge of specific harms of tobacco use and noticing of text warnings on cigarette packs.

Results: Although 67% of Kenyan smokers were aware that smoking causes heart disease, only 47% were aware that smoking causes stroke. 70% were aware that secondhand smoke causes lung cancer in non-smokers. Smokeless users were less aware of the harms of smokeless tobacco on causing heart disease (31%), throat cancer (36%) and mouth cancer (38%). 64% of Kenyan male smokers noticed the text-only warnings "often" or "very often", the highest among ITC countries with text-only warnings. 32% of smokers who were aware of the warnings stated that they were "a lot" more likely to think about the health risks of smoking and 28% reported that the warnings made them "a lot" more likely to quit. 85% of tobacco users want the government to do more about the harms of tobacco use.

Conclusions: Knowledge of harms of tobacco use was low among smokers in Kenya compared to smokers from other ITC countries, although noticing of warnings was relatively high. This study supports the recent implementation of pictorial health warnings and highlights the need for sustained public education campaigns to raise awareness of harms of tobacco use among Kenyans.

OA09 Diagnosis, screening, prediction of disease in people living with human immunodeficiency virus and for diabetes

OA09-260-25 A rapid TB diagnosis algorithm including TB-LAM and gastric lavage among severely ill hospitalised HIV patients in Conakry, Guinea

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Background: In 2016 Doctors Without Borders opened an inpatient HIV unit in Conakry, Guinea. Mortality was 40% during the first 6 months of 2017 and 71% of patients were treated for TB.

We describe the diagnostic yield of the different elements of a TB screening algorithm that included TB-LAM, Gene-Xpert on sputum, and unprocessed gastric aspirates.

All newly admitted patients underwent TB-LAM on urine and provided a sample for Gene-Xpert. Patients who were too incapacitated to give quality sputum routinely underwent gastric lavage (GL).

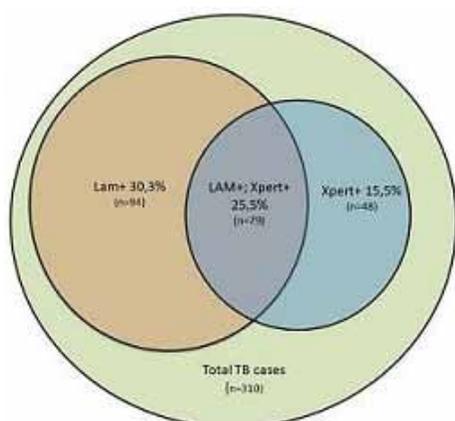
Methods: Data was collected in the laboratory and IPD databases as part of routine activities between Nov-2016 and Nov-2017. Statistics were calculated using STATA Ver14.2.

Results: Of 495 patients admitted, 395 (80%) had at least one Gene-Xpert done on sputum or gastric aspirate during their hospitalisation; 355 (72%) underwent a TB LAM at admission. A total of 565 Gene-Xpert results could be retrieved, averaging 1.4 per patient.

Overall, 310/495 (63%) patients were diagnosed with a new episode of tuberculosis. Of the TB cases, 79/310 (25%) had a positive result for both GeneXpert and LAM, 48 (15%) had a positive Gene-Xpert only, 94 (31%) had a positive TB-LAM only and 89 (29%) were diagnosed on clinical grounds. Of the 9 patients diagnosed with Rifampicin resistance, 4 (44%) had a negative TB-LAM.

The per-patient positivity rate from GeneXpert and TB-LAM was 35% and 56%, respectively. 85% of all positive Xpert tests were on the first sample (n=376). Among first samples, the positivity rate was 40% for patients recorded as providing GL, 25% for patients recorded as providing sputum, and 20% for the patients whose sample type was missing.

Conclusions: The use of TB-LAM and gastric lavage as part of a TB screening algorithm for severely ill hospitalised HIV patients showed promising yields in this difficult to diagnose population.



[Venn diagram showing the proportions of TB diagnoses by Gene Xpert and TB-LAM]

OA09-261-25 Estimating the impact of a combined C-reactive protein and LAM-based diagnostic algorithm for TB disease in HIV clinics in South Africa: a mathematical modeling-based analysis

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Background: Better tools are needed for screening and diagnosing active HIV-associated TB in clinical settings. A diagnostic algorithm that includes non-sputum tests and can be administered rapidly at the point-of-care could potentially reduce population level TB incidence and TB-related mortality.

Methods: We used the EMOD-TB epidemiological and health care model of TB in South Africa to estimate the impact of a C-reactive protein (CRP) screening followed by urinary lipoarabinomannan (LAM) confirmatory testing on TB incidence and mortality. The model accounts for the natural history of TB and HIV and the co-dynamics of disease progression, as well as the TB care cascade and potential impacts of new diagnostics on timely TB treatment. The model explored offering the CRP-LAM diagnostic algorithm to PLHIV at both ART initiation and then annually during ART continuation, a schedule synchronized with laboratory testing during HIV treatment. CRP was assumed to have a sensitivity and specificity of 90% and 60%, based on published data.

We explored a range of LAM sensitivities from 60% to 90%. Those negative for LAM were assumed to be referred for sputum-based testing per the standard of care. **Results:** Implementation of the CRP-LAM diagnostic algorithm into HIV care in South Africa, in conjunction with existing passive case finding, was estimated to result in 18% (13-20%) reduction in TB incidence and 30% (26-31%) reduction in TB-related mortality by 2025, as compared to 2015 levels. The CRP test was found to reduce the number of LAM tests by more than 50% while maintaining the same impact at the population level.

Conclusions: A diagnostic algorithm combining CRP screening with LAM confirmation for PLHIV may substantially reduce TB mortality in South Africa, and would have a moderate reduction in onward TB transmission.

OA09-262-25 Screening tuberculosis in HIV infected patients: which algorithms work best? A multicountry survey in Benin, Guinea and Senegal (RAFAscreen project)

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Background: The aim of this study was to determine the most effective algorithms to diagnose tuberculosis (TB) in HIV infected patients.

Methods: A cross-sectional study was conducted in three HIV clinics in Benin, Guinea and Senegal. Two sub-groups were considered: patients naive of antiretroviral treatment (ART) but about to start ART and those already on ART. All patients had clinical examination, chest X-Ray (CXR) and provided two sputa for microscopy, Xpert MTB/RIF, and culture. Patients without TB at enrolment, were seen after 6 months for clinical examination, microscopy and culture. The gold standard used to define TB was positive culture and/or positive Xpert MTB/RIF or clinical diagnostic confirmed by a panel of experts.

Different algorithms were compared using Sensitivity (Se), Specificity (Sp), Positive Predictive Value (PPV), Negative Predictive Value (NPV) and the Area under Curve (AUC).

Results: A total of 2,820 HIV infected patients were enrolled; of which, 1000 were naive of ART. The estimated prevalence of TB was 10,256 cases per 100,000 (95 % CI: 8,400-12,470) in patients naive of ART and 3,125 cases per 100,000 (95% CI: 2,400-4,060) in patients on ART. In patients naive of ART, the three most effective algorithms were: Xpert systematically (Se =80.68%, Sp=100%, PPV=100%, NPV=97.84% and AUC=0.91), Xpert if TB symptoms or abnormal CXR findings (Se=70.45, Sp=100%, PPV=100%, NPV=96.73%, AUC=0.86) and Xpert if TB symptoms, and CXR if Xpert negative (Se=70.45%, Sp=97.14%, PPV=73.81%, NPV=96.64%, AUC=0.84). In patients on ART, the three most effective algorithms were : Xpert systematically (Se =74.07%, Sp=100%, PPV=100%, NPV=99.17% and AUC=0.89), Xpert if TB symptoms or abnormal CXR findings (Se=55.56, Sp=100%, PPV=100%, NPV=98.59%, AUC=0.79) and CXR systematically (Se=68.52%, Sp=76.82%, PPV=8.70%, NPV=98.7%, AUC=0.74).

Conclusions: The role of Xpert is key for TB screening in HIV infected patients. Cost- effectiveness analyses are currently conducted to guide National TB Programmes for choosing the best algorithm.

OA09-263-25 Host inflammation markers IFN- γ , IL-6 and IL-15 strongly associated with risk of incident TB in advanced HIV

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Background: In high TB burden countries, the majority of HIV-infected persons are likely to be latently co-infected with TB. In advanced HIV (<200 cells/ μ L), TB reactivation potential is high, yet not uniform. The REMEMBER randomized clinical trial enrolled HIV-infected participants (CD4 <50 cells/ μ L) at antiretroviral therapy (ART) start; we analyzed cytokine responses at baseline in participants who developed TB or died compared to those who did not.

Methods: A case-cohort study stratified by country and treatment arm was performed. Cases were defined as incident TB or death by 48 weeks after ART initiation. Serum from participants who developed incident TB or died during the 1 year follow-up to a control group of participants who did not were assayed for 25 cytokines (meso-scale discovery, ELISA). Biomarker associations with TB or death were assessed using Wilcoxon rank

sum and adjusted weighted Cox regression models.

Results: We analyzed serum from 55 TB cases, 47 deaths and 222 controls; 50% were male, median age 36 (IQR 31-43), median CD4 20 (IQR 10-36) cells/ μ L. 35% (19/55) of participants developed TB within 10 weeks of ART. 14 had both incident TB and died. Both median IFN- and IL-6 levels (IU/ml) were elevated in those who developed incident TB compared to controls [55.8 (18.7 - 209.8) vs. 20.5 (10.9 - 44.5), and 3.26 (1.80 - 7.15) vs. 1.48 (0.91 - 2.91), respectively, P< 0.001] with significant time to event (both P< 0.001 log rank). Using a weighted Cox model, having a value in the highest quartile was associated with an adjusted HR of 3.30 (1.55-7.04) P=0.02 for IFN- , 6.85 (2.72-17.24) P< 0.001 for IL-15, and 2.23 (1.11-4.52) P=0.03 for IL-6.

Conclusions: Among very advanced HIV infection, having a pro-inflammatory cytokine profile at baseline predicted incident TB after ART initiation and were non-overlapping with those predicting death.

Cytokine	GM-CSF >Q3	IFN- γ >Q3	IL1- β <LLD	IL-10	IL-15	IL-6	IP-10	TNF- α	VEGFA
Incident TB aHR (95% CI)	>Q3: 4.94 (2.16 - 11.28)	>Q3: 3.30 (1.55 - 7.04)	<LLD: 0.47 (0.22 - 0.97)		>Q3: 6.85 (2.72 - 17.24)	>Q3: 2.23 (1.11 - 4.52)	Linear (log): 0.34 (0.12 - 0.98)	Linear: 0.96 (0.86 - 1.06)	Linear: 1.00 (0.99 - 1.002)
Incident TB P-value	< 0.001	0.002	0.04		<0.001	0.03	0.047	0.41	0.82
Death aHR (95% CI)				Linear: 4.22 (1.55 - 11.49)	Linear: 1.08 (1.04 - 1.13)	Linear: 0.89 (0.82 - 0.97)	Linear: 1.11 (0.99 - 1.22)	>Q3: 2.45 (1.11 - 5.41)	
Death P-value			0.005	<0.001		0.009	0.051	0.03	

[Adjusted weighted Cox proportional hazards model for incident TB and for death by 48 weeks]

OA09-264-25 The association of diabetes status and pre-treatment bacillary load among pulmonary TB patients in Indonesia

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Background: Tuberculosis (TB) is one of the major infectious diseases in Indonesia. Its burden becomes more prominent as the number of diabetes cases increases. However, little is known on the association of baseline status and pre-treatment sputum smear results.

Methods: A national multiyears observational cohort study on drug resistance pulmonary TB in Indonesia (TRIPOD) is ongoing at 7 hospitals. Persons with TB symptoms, suggestive pulmonary TB chest X-ray, aged ≥ 18 , without liver and kidney diseases were enrolled to the study. Demographic data, sputum and blood specimens were collected before TB treatment. Diabetes status was categorized into: normal (HbA1c $< 6\%$); pre-diabetic (HbA1c 6-6,4%); and diabetic (HbA1c $\geq 6,5\%$). Bacillary load was measured by sputum smears examination for AFB using Ziehl-Neelsen staining and graded as negative, scanty, 1+, 2+, and 3+. Data until March 2018 were analyzed.

Results: 191 pulmonary TB patients participated in TRIPOD study. Most participants were in the 25-44 year-old group (39%), male (60%), and treated as drug sensitive TB (67%). 54% of participants were categorized as normal, 16% as pre-diabetes and 30% as diabetes.

The AFB in 41% of subjects within the normal group was negative, whereas in the pre-diabetes and diabetes were 32% and 26%, respectively. In contrast, the proportion of AFB 3+ in the three groups were 12%, 26% and 30%.

The association between diabetes status and baseline bacillary load was significant ($p,0.02$) so as the proportion of AFB 3+ in pre-diabetes and diabetes compared to normal group ($p,0.01$).

Conclusions: The prevalence of diabetes in pulmonary TB patients in Indonesia was high. Baseline diabetic status was associated with pre-treatment sputum smear results. Pulmonary TB patients who has diabetes has higher baseline bacillary load, suggesting that they are more infectious. Therefore screening for diabetes in TB patients could be a mean of controlling TB infection.

OA09-265-25 Tuberculosis case detection in diabetic patients in three west African countries: which screening algorithms work best? The RAFAscreen project

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Background: The aim of this study was to determine the most effective screening algorithms to diagnose tuberculosis (TB) in diabetic patients.

Methods: A cross-sectional study was conducted in three diabetic care centers in Benin, Guinea and Senegal. Diabetic patients were consecutively enrolled and underwent a clinical examination and a chest X-Ray (CXR). In case of presence of one of the TB symptoms or abnormal CXR findings, two sputa were taken for microscopy, Xpert MTB/RIF and culture. A clinical and bacteriological check was performed 6 months later for patients without TB at enrolment to detect TB patients missed at baseline. The gold standard used to define TB was positive culture and/or positive Xpert MTB/RIF or clinical diagnostic confirmed by a panel of experts. Different algorithms were compared using Sensitivity (Se), Specificity (Sp), Positive Predictive Value (PPV), Negative Predictive Value (NPV) parameters and the Area under Curve (AUC).

Results: A total of 5,910 diabetic patients were recruited. The estimated prevalence of TB in diabetic patients was 2,699 cases per 100,000 (IC95%: 2,260 - 3,220). The most effective screening algorithms were : Xpert systematically (Se=84.8%, Sp=100%, PPV=100%, NPV=99.6%, AUC=0.98), Xpert if TB symptoms or abnormal CXR findings (Se=84.8%, Sp=100%, PPV=100%, NPV=99.6%, AUC=0.96), Xpert if TB symptoms (Se=82.2, Sp=100%, PPV=100, NPV=99.5%, AUC=0.96) and Microscopy if TB symptoms and Xpert if microscopy negative (Se=83.1%, Sp=99.2%, PPV=74.8, NPV=99.5%, AUC=0.96).

Conclusions: Taking into consideration the increased prevalence of diabetes mellitus in low and middle income countries and the prevalence of TB in this population, implementing systematic TB screening for diabetic patients is worth to be done. All the four algorithms have good performance parameters but cost implications may be important for National TB programmes. A cost effectiveness analysis is currently conducted for better informing Programmes in their policy decision.

OA09-266-25 Comparison of point of care HbA1c with laboratory HbA1c for real world screening for diabetes among tuberculosis patients

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Background: Diabetes (DM) is common among tuberculosis (TB) patients and affects TB treatment outcomes. DM is often undiagnosed and many TB clinics are using point of care tests (POC) to screen TB patients for DM. We compared POC and laboratory glycated haemoglobin (HbA1c) levels among newly diagnosed, untreated TB patients to assess their accuracy and safety for use in screening TB patients in settings where immediate access to DM diagnostic facilities may be difficult.

Methods: We obtained POC (Haemocue) and accredited laboratory HbA1c (HPLC method) for nearly 2000 patients with bacteriologically confirmed, untreated pulmonary. Patients were over 18 and recruited from field sites in Peru, Romania, Indonesia and South Africa (TANDEM study; <http://www.tandem-fp7.eu/>). POC and laboratory HbA1c were compared by calculating overall agreement; stratified by country, age, sex, HbA1c level and comorbidities (anaemia, HIV).

Results: 1942 patients had both a POC and laboratory HbA1c test result available (89%). POC HbA1c was modestly greater than laboratory HbA1c by 0.15% (95% CI 0.11 to 0.19). Agreement at an individual level was quite variable though, with a 95% range (mean \pm 2 standard deviations) up to 1.88% higher or 1.58% lower for POC versus laboratory HbA1c. Overall disagreement appeared greater for patients with anaemia (Table), but lower for those with HbA1c >9% (mean 11.8 vs. 11.9, $p = 0.53$). Over 80% of individuals had both POC and lab HbA1c < 6.5%.

Conclusions: Although agreement is less than ideal, POC and laboratory tests were consistent for most patients and POC HbA1c is a pragmatic approach to screen for risk of DM amongst TB patients in real-world settings.

All tests should be followed up during or after treatment and elevated POC values should be scrutinised or referred and not solely used to guide DM management. Interpretation is also challenging for those with severe anaemia and more moderate rises in HbA1c.

	All patients (n=1942)	Moderate anaemia (n=352)	Severe anaemia (n=27)	HIV- (n=1652)	HIV+ (n=72)
Mean POC HbA1c (95%CI)	6.00 (5.94, 6.06)	6.03 (5.91 - 6.14)	6.39 (6.02 - 6.76)	6.03 (5.96 - 6.09)	5.95 (5.74 - 6.16)
Mean Lab HbA1c (95%CI)	5.85 (5.79, 5.91)	5.82 (5.72 - 5.93)	5.32 (5.11 - 5.54)	5.87 (5.81 - 5.94)	5.66 (5.49 - 5.82)
Mean Difference (95% CI)	0.15 (0.11, 0.19)	0.20 (0.12, 0.29)	1.07 (0.67, 1.46)	0.15 (0.12, 0.19)	0.30 (0.10, 0.49)
Individual variations (mean \pm 2SD POC - Lab HbA1c)	+ 1.88 to -1.58	+1.85 to -1.45	+3.06 to -0.93	+ 1.90 to -1.47	+1.86 to 1.65

[Table. Mean difference and individual variation for HbA1c from POC and laboratory tests, stratified by anaemia and HIV status]

SHORT ORAL ABSTRACT SESSIONS

SOA01 Multidrug-resistant tuberculosis: patients and programmes

SOA01-1000-25 Suitability of the shorter duration multidrug-resistant tuberculosis regimen for patients receiving treatment in settings with limited rapid susceptibility testing

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Background: A shorter duration regimen for multidrug-resistant tuberculosis (MDR-TB) is composed of three MDR-specific drugs (kanamycin, moxifloxacin and clofazimine) and three (isoniazid, ethambutol and pyrazinamide) that are part of the first-line TB regimens. In addition, prothionamide is included yet has cross-resistance with isoniazid. Thus patients may still be treated with drugs that their *Mycobacterium tuberculosis* (MTB) is not fully susceptible.

Methods: We examined the susceptibility profile of pretreatment MTB from patients initiating MDR-TB regimens embedded within a prospective cohort study of MDR pharmacokinetics and outcomes that would otherwise be deemed eligible for shorter MDR-TB regimens. We predicted the composition of active drugs based on minimum inhibitory concentration (MIC) testing (customized Sensititre MYCOTB plate) and vetted with molecular tests of resistance determining regions by Taqman array card (TAC) format when available. Accordingly, patients with MTB susceptible to both a fluoroquinolone and injectable agent by conventional methods were considered eligible for shorter MDR-TB regimen thus included for analysis.

Results: Of 57 eligible patients enrolled from April 2016 through April 2018, the mean age was 41 ± 12 years and 40 (70%) had history of previous TB treatment. Resistance to ethambutol, isoniazid and prothionamide was 31 (54%), 48 (84%) and 8 (14%) correspondingly. MTB of 6 (11%) patients had combined resistance to ethionamide, isoniazid and ethambutol while only 5 (9%) were entirely susceptible to all three agents. Clofazimine was full susceptible in 92%. Pyrazinamide MIC results were not available nevertheless among completed TAC as-

says, 53% had mutations on the *pncA* region connoting potential pyrazinamide resistance. Despite high-dose isoniazid in the regimen, 100% of TAC results had mutations in *katG* while none in the *inhA* locus.

Conclusions: These findings raise concern for treatment failure without additional drug-susceptibility testing. A combination of molecular diagnostic triage and quantitative MIC testing may elucidate the earliest and most effective combination.

SOA01-1001-25 A patient-centered psychosocial support intervention for DR-TB patients: challenge TB Project's experience in Bangladesh

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Background and challenges to implementation: Depression is commonly comorbid with chronic illnesses and associated with adverse clinical and psychosocial outcomes. To improve adherence to the long-term treatment and psychosocial wellbeing of drug resistant tuberculosis (DR-TB) patients, the Challenge TB (CTB) project provided psychosocial support for DR-TB patients at the National Institute of Diseases of the Chest and Hospital (NIDCH). This study examined the psychosocial wellbeing of patients with DR-TB in Bangladesh, as well as the impact of psychosocial interventions on them.

Intervention or response: This pilot used several evidence-based psychosocial interventions and evaluated psychosocial and structural aspects of health, as well as the wellbeing of 141 DR-TB patients at NIDCH. The interventions consisted of bi-weekly support groups, expressive art therapy sessions, edutainment and symbolic celebrations, and workshops on income generation activities (such as preparing handicrafts, clay art, glass paints). Baseline and post-intervention assessments were carried out. Depressive symptoms were measured using a validated Bengali version of the Patient Health Questionnaire-9 (PHQ-9). Data were analyzed using SPSS and associations between depression and patient characteristics were explored using regression analysis.

Results and lessons learnt: The prevalence of probable depressive symptoms (PHQ-9 score ≥ 5) was significantly higher at baseline than post-intervention (39% vs. 21%, $p < 0.001$). Depressive symptoms were more common among patients with low income (OR 2.43, $p < 0.01$), poor social support (OR 4.65, $p < 0.001$), adverse drug reactions (OR 2.17, $p < 0.05$), and poor adherence (OR 1.86, $p < 0.05$) at baseline. Depression was less common among patient aged ≥ 65 years (OR 0.39, $p < 0.05$) both at baseline and follow-up. Only 1.8% of pilot patients defaulted from treatment, compared to 7.3% of all patients in 2017.

Conclusions and key recommendations: CTB's interventions significantly improved the psychosocial wellbeing of DR-TB patients and their treatment adherence. Data indicates that psychosocial support should be a crucial component alongside DR-TB treatment in order to improve adherence and enable psychosocial rehabilitation after treatment.

SOA01-1002-25 The palliative care needs of patients with drug-resistant tuberculosis in the southern sub-district of Cape Town

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Background: The palliative care needs of DR-TB patients are little known and under-researched globally, yet pertinent in their holistic management. A reliable, validated means of palliative care needs assessment for these patients - particularly in a low- to middle-income setting is unavailable. The aim of this recent study was to determine the palliative care needs of patients infected with DR-TB living in the southern sub-district of Cape Town with the objectives of determining their quality of life, functional status and symptom burden.

Methods: In this cross-sectional study, 28 participants were posed a culturally-sensitive questionnaire that comprised: Likert-type question for the African Palliative Care Association- Palliative Outcome Score (APCA-POS) tool, Eastern Co-operative Oncology Group (ECOG) score, a symptom checklist and open patient dignity questions pertaining to the preceding week. Quantitative and qualitative data was collected. Pre-determined numerical scores in the Likert-type questions were deemed indicative of palliative care need.

Results: Quantitative and qualitative analysis showed that each participant had a palliative care need: be it either (or a combination of) unmet clinical, psychological, social and/or spiritual needs - despite being at differing stages of the DR-TB disease trajectory. Predominant physical complaints were tiredness (79%), joint pains (64%), confusion (61%) and shortness of breath (51%). Respondents also experienced a loss of autonomy, poor self-value and financial insecurity. Fifty percent of patients interviewed required urgent further management and referral to the local clinic.

Conclusions: Despite the small cohort of patients and possible recruitment bias, this research concurred with suggestions of a palliative care approach being implemented from the point of DR-TB diagnosis and recommended palliative care assessment throughout the treatment period - regardless of treatment outcome. DR-TB patients had significant unmet palliative care needs that affected their quality of life, functional status and dignity - regardless of whether pain was present.

SOA01-1003-25 Managing drug resistant tuberculosis in refugees and migrants: partnership in Jordan, 2012-2018

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Background and challenges to implementation: The influx of refugees and migrants from Syria and other neighboring conflict affected countries (e.g., Yemen, Iraq, Sudan, Somalia, Palestine) into Jordan impacts tuberculosis case finding and management including drug resistant tuberculosis (DRTB). Jordan hosts a large number of refugees and one-third (2.9 million) of the total population (9.5 million) are either refugees or migrants. IOM - The UN Migration Agency with funding support of various donors has strengthened the Jordanian National Tuberculosis Programme (NTP) and its designated collaborating DRTB treatment facility—Annoor Sanatorium's capacity in addressing the challenges of the unique regional context.

Intervention or response: IOM's support included: Introduction of liquid culture (MGIT 960) and Line Probe Assays, supply of lab consumables and additional lab staff and training.

Access to DRTB drugs including new(Bedaquiline and Delamanid) and re-purposed molecules (Clofazimine and Linezolid).

Active case finding using mobile X-ray and Xpert for refugees and migrants, support to other diagnostic investigations (culture & DST), referral and hospitalization at Annoor Sanatorium.

DOT and supplementary nutritional support.

Training for doctors on standard and shorter MDRTB and use of new drugs to treat XDRTB.

Results and lessons learnt: From January 2012 - March 2018, 38 DRTB cases diagnosed that includes 1 XDRTB, 1 pediatric, and 27 (71%) male and 11 (29%) female MDRTB cases. 26 (69%) cases were either refugee or migrant.

79% patients had favorable treatment outcome out of standard MDRTB treatment.

DRTB Patients by Nationality			Treatment Outcome				
Jordanian	Migrant or refugee **	Total	Treatment completed/ cured	Died	Treatment failure	Lost to follow-up	On-treatment
12 (32%)	26 (68%)	38 (100%)	27 (79%)	4 (12%)	2 (6%)	1 (3%)	4

[DRTB Patients in Jordan during January 2012—March 2018]

**Yemeni (11), Iraqi (5), Syrian(4), Saudis(2), Palestinian(1), Sudanese(1) Indonesian(1) and Indian(1)

Conclusions and key recommendations: Extensive collaboration, close partnership and sound technical support across implementing partners ensures successful DRTB control and treatment outcomes in a unique regional setting. Joint approaches are essential for DRTB case management, reducing morbidity and mortality among displaced vulnerable refugee and migrant populations.

SOA01-1004-25 Programmatic introduction of new TB drugs in Ethiopia: lessons in the stepwise approach for national scale-up

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Background and challenges to implementation: The World Health Organization (WHO) recommended two new TB drugs, bedaquiline (Bdq) and delamanid (Dlm), in 2013 and 2014, respectively and a Policy Implementation Package (PIP) has been issued in 2014. Ethiopia is one of the countries that introduced new TB drugs under programmatic conditions in 2016. We describe the steps followed and the practical application of the WHO PIP guidance in the introduction of new TB drugs in Ethiopia.

Intervention or response: Ethiopia followed a stepwise approach in the programmatic introduction of new TB drugs.

Step 1 Defining a national framework: this was focused on setting up the coordination framework and defining the phases of implementation.

Step 2 Development of a national plan: the national plan was developed following the WHO PIP and the steps in the WHO Bedaquiline Implementation plan.

Step 3 Meeting the minimum requirements for new TB drugs introduction: step-by-step actions to meet the minimum requirements for new TB drugs introduction were taken as per the plan.

Step 4 Phased Implementation and monitoring for scale-up: Based on the lessons learnt during the first six-months of implementation at the initial site, NTP expanded services to more DR-TB Centers.

Results and lessons learnt: New TB drugs were successfully introduced and scaled up in Ethiopia under programmatic conditions following WHO's guidance. Nine referral MDR-TB centers provide treatment ser-

vices with new drugs. Active drug safety monitoring, functional multidisciplinary Clinical Review Committee, updated clinical guides for proper case management were put in place. Existence of pre-registration and pre-import waiver system helped faster importation of the new drugs.

Conclusions and key recommendations: The WHO PIP was successfully applied in Ethiopia. Stepwise approach on meeting the minimum conditions, country leadership in defining the framework and having a national plan were very critical for rapid scale-up. We recommend for programs planning to introduce new TB drugs to follow stepwise approach for rapid scale-up.

SOA01-1005-25 Implementation of community-based drug resistant TB treatment in Southern Swaziland and national implications

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Background: The WHO recommends community-based drug-resistant TB (DRTB) treatment (CBT) to improve access to care. However, the feasibility of implementing CBT models in resource-poor settings has not been described comprehensively. Thus, many countries face obstacles to translate this recommendation into policy and practice. We describe the outcomes of CBT programme evaluation, its policy and funding implications in Swaziland.

Methods: We evaluated the CBT programme in the predominantly rural Shiselweni region (Swaziland) from 2009 to 2013. The programme built on trained community volunteers providing injectable drugs during intensive phase under nurse supervision and the provision of a comprehensive adherence support package including monthly transport allowances, food voucher for patients, and stipend for community volunteers. Lastly, we describe utilization of results and its impact at national level.

Results: Of 467 patients initiated on DRTB treatment, CBT increased from 17% in 2009 to 55% in 2013 and the nurse to patient ratio increased from 1:8 to 1:21 respectively. Of 188 patient files reviewed, no gluteal abscess and 6 transient paraesthesia were reported. Treatment success was higher in CBT (76%) compared to clinic-based care (68%, $p=0.07$). The risk of death was non-significantly reduced by 34% (adjusted sub hazard ratio: 0.66, 95% CI 0.35-1.25; $p=0.21$). Costs per completed DRTB regimen were comparable between CBT (USD 13361) and clinic-based care (USD 13006), with the adherence support package only contributing 11% of costs. Findings of the evaluation were presented in consultative meetings with national decision makers in

June 2016, Thereafter in November 2016, the patient support package was adapted nationally by the MoH and funded by the Global Fund, and widely rolled out nationally in June 2017.

Conclusions: Decentralized CBT was feasible in one region of Swaziland and informed national policy. It resulted in adoption of patient support package at national level supported by the Global Fund.

SOA01-1006-25 Implementation of biomedical and social support for people affected by multidrug-resistant tuberculosis in Guinea

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Background: In 2016, Guinea had an estimated notification rate of 177 new tuberculosis (TB) cases per 100.000 population, with 360 estimated-number of rifampicin-resistant (RR) TB cases. In 2014, Damien Foundation and the National Tuberculosis Programme (NTP) of Guinea started a biomedical-social-support to people treated by multidrug-resistant TB (MDR-TB) in one-pilot health-facility. The aim of this study is to analysis the effectiveness of biomedical-social-support on MDR-TB-care.

Methods: All MDR-TB-cases treated during 2016 to 2017 were analysed. Treatment-outcomes of in one pilot-health-facility were compared to two-health-facilities according to the provision of biomedical-social-support or not. In biomedical-social-support, all biological-tests, ancillary drugs were provided free of charge and a nutritional-kit and transport-refunds were monthly provided during the whole treatment. Treatment duration was 20-month with a regimen composed of Kanamycin (Km), Levofloxacin (Lfx), Cycloserine (Cs), Pyrazinamide (Z) and Prothionamide (Pto) during 6-month in the intensive-phase, followed by 12-18-month of same drugs but Km.

Results: We included 75 MDR-TB cases, 7(9%) HIV-positive. Mean-age was 26 years (interquartile range-IQR 15-49). All cases were pulmonary-TB, from which 10(13%) were new-cases. There were 27 MDR-TB cases with biomedical-social support and 48 without it. Mean delay of treatment-start in days was 20(IQR 9-110) in the pilot health-facility compared to 34(IQR 9-111). Treatment outcomes in the group with biomedical-social support were: cured 22(82%), treatment-completion 0(0%), death 2(7%), failure 1(4%) and 2(7%) lost-to-follow-up compared to those without biomedical-social support 23(48%), 2(4%), 9(19%), 2(4%) and 12(25%)

respectively. Treatment success compared to unfavourable-outcomes (failure, death and lost-to-follow-up) in the pilot health-facility was 82% and 18% respectively compared to 52% and 48% respectively in those health-facilities without biomedical-social support ($p < 0.01$).

Conclusions: The introduction of biomedical-social support to people affected by MDR-TB was successful in Guinea. People who benefited from this strategy had more favourable treatment-outcomes. The biomedical-social support could improve treatment-success if extended to all MDR-TB people under treatment.

SOA01-1007-25 Impact of strong support in improving drug supply management of TB and related supplies in Tigray, Ethiopia

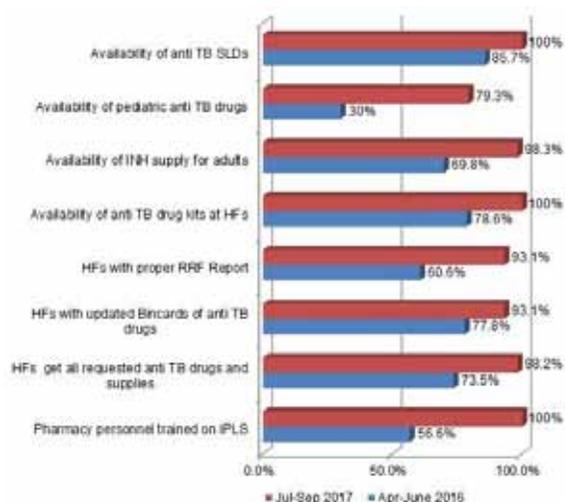
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Background and challenges to implementation: Ensuring an adequate supply of anti-TB drugs is a prerequisite for well-functioning TB programs, but this has always been a challenging area of support. At the launch of the 18-month USAID/Challenge TB project in Tigray Region in June 2016, a baseline assessment revealed critical gaps in the supply of anti-TB commodities. Here we report how joint actions led to significant improvements in the supply of anti-TB commodities in the region.

Intervention or response: In June 2016, we conducted a baseline assessment that revealed critical gaps, including a shortage of trained personnel, stock-outs, and poor inventory management. Based on the identified gaps, we trained 431 health professionals and program managers on Integrated Pharmaceutical and Logistics Supply (IPLS), Second Line Drug (SLD) supply management, and TB patient kit use. This was followed by the development of an improvement plan and regular monitoring. Further, we supported the integration of SLDs and other MDR-TB supplies into the main IPLS. We conducted a follow-up assessment of progress in September 2017 and compared the findings with the baseline values

Results and lessons learnt: By July 2017, the proportion of health facilities receiving all requested anti-TB drugs increased from 73.5% (36/49) to 98.2% (55/56). There was an adequate supply of SLDs, and no emergency requests were made. The average stock-out rate of adult anti-TB drugs fell to zero, and the availability of pediatric anti-TB drugs increased from 30% to 79.3%. The availability of INH supplies for both adult and pediatric groups reached 98.3%, and bin card updating for all anti-TB commodities improved from 77.8% to 93.1%.

Conclusions and key recommendations: Continuous and evidence-guided technical support at all supply chain levels contributed to improving drug supply management and increased the availability of anti-TB health commodities. Therefore, such focused and result-driven support needs to be continued and scaled up.



[DSM findings at baseline (Apr-June 2016) and at assessment (Jul-Sep 2017), Tigray Region, Ethiopia]

SOA01-1008-25 Effectiveness of thematic TB health education on outcomes for 125 pulmonary MDR-TB patients

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Background and challenges to implementation: An estimated 63,000 multi-drug-resistant tuberculosis (MDR-TB) cases arise every year in China, approximately one third of the global MDR-TB burden. To improve treatment adherence and outcomes, the USAID Control and Prevention of Tuberculosis Project supports Yunnan TB Clinical Center (TCC), the provincial designated hospital for MDR-TB diagnosis and treatment in Yunnan, to deliver an essential supportive care package for MDR-TB patients. Thematic TB health education (TTHE) is one key essential supportive care service in the package.

Intervention or response: Beginning in May 2012, TCC conducted TTHE group activities twice a month to ambulatory MDR-TB inpatients and family members. The patient-centered and participatory group activities are designed and coordinated by nurses, peer educators and MDR-TB patients. Main topics include social-psychological counselling, infection control, MDR-TB treatment course and adherence, regular re-examination, adverse reaction, diet and nutrition. Facilitators use multiple tools, such as flipcharts, pictures, videos, and

demonstrations. MDR-TB patients share their illness status and treatment experience, and engage in discussion on motivations for and barriers to treatment adherence. After approximately 90 minutes, participants receive a small gift to reinforce motivation.

Results and lessons learnt: From May 2012 to August 2015, 125 MDR-TB inpatients joined the group activities at TCC. As of August 2017, 83 of 125 reached treatment success (66.4%), and 42 (33.6%) resulted in treatment failure or default. Multivariate analysis showed that a patient's age ($P<0.01$, $OR=0.53$), participation in TTHE activities on treatment adherence ($P<0.05$, $OR=2.49$), and participation in TTHE activities on psychological support ($P<0.01$, $OR=4.55$) are the significant predictors of MDR-TB treatment outcomes. Logistical regression analysis also found that the patients who participated in a greater number of group activities were more likely to reach treatment success ($P<0.001$, $OR=2.58$).

Conclusions and key recommendations: TTHE group activities improved MDR-TB patients' treatment adherence and outcomes and should be replicated elsewhere.

SOA01-1009-25 Half of rifampicin-resistant tuberculosis patients received new tuberculosis drugs in a decentralized setting, South Africa

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Background and challenges to implementation: Access to the new anti-tuberculosis drugs bedaquiline and delamanid for the management of rifampicin resistant tuberculosis (RR-TB) remains poor. Globally, only approximately 5% of patients with RR-TB have access to these new drugs. Approximately 200 RR-TB patients are managed annually within a decentralized model of care in South Africa.

Intervention or response: Collaboration between national and provincial departments of health, City of Cape Town and Médecins Sans Frontières enabled the implementation of the bedaquiline clinical access program in 2012. Bedaquiline was registered in 2014; since then access has been scaled up by application through a drug advisory committee. Qualifying patients are those with RR-TB who are at risk of, or develop, intolerance to the injectable agents, or who have limited therapeutic options including those with second-line resistance.

Although not yet registered in South Africa, delamanid was first available through compassionate use, and now through the delamanid clinical access program. It is expected that it will be scaled up in a similar manner than bedaquiline.

Results and lessons learnt: Among 187 individuals initiated on RR-TB treatment in Khayelitsha in 2017, 98 (52%) received bedaquiline and/or delamanid. Overall, 30 (16%) had additional second-line resistance; of those 22 (73%) received bedaquiline and/or delamanid. Of the 157 patients with RR-TB with second-line susceptibility (72% HIV positive), 76 (48%) received BDQ or DLM; in most cases as replacement for the injectable drug. Overall, 71% (70/98) received bedaquiline and/or delamanid in a revised regimen, after a median of 33 (interquartile range 22-44) days on second-line treatment.

Conclusions and key recommendations: With strong commitment and collaboration between various stakeholders, wider access to new drugs is possible at a decentralized primary health care level. Efforts to reduce access delays and incorporate new drugs from the start of RR-TB treatment regimens are underway. Similar efforts are urgently needed to increase access to new drugs in other high burden RR-TB settings.

SOA01-1010-25 'Missing million': a pilot study to assess the potential of offering upfront chest X-ray for sputum smear-negative TB cases to reduce the gap

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Background and challenges to implementation: The WHO has found that India tops the list of the world's missed tuberculosis (TB) cases. The objective of this pilot study is to assess impact of offering chest X-Ray (CXR) to all sputum smear negative (SN) cases in preventing new smear negative (NSN) cases getting missed otherwise. In Bhiwani district of Haryana on a pilot basis, we offered CXR upfront to all SN presumptive TB Patients (PTBP) during April - June 2017.

Intervention or response: Project Axshya in collaboration with district TB cell offered CXR to all sputum smear negative patients symptomatic of TB by linking them with free CXR facility made available at a place near their residence. During intervention period, in the 4 Tuberculosis Units (TUs), where Axshya is working, sputum of 600 PTBP was tested. If sputum was found negative, the person was advised to get CXR done. Thereafter a comparative analysis was done with state and national level to assess utility of upfront CXR for all SN cases in an easily accessible manner.

Results and lessons learnt: Positivity rate of new sputum positive (NSP) is found close to 9% (55 out of 600 cases) among selected group. All SN cases (545 cases) offered for CXR. Positivity rate in these SN patients was found to 10% (57 out of 545 cases). In our study group, the

NSP:NSN ratio of TB patients has been found to be reversed (1:1.04*) as compared to state (1.94:1**) and national (2.12:1**) data. Offer of CXR to all SN patients helped in identifying 9% more TB cases.

Conclusions and key recommendations: The study founds offer of CXR facility to all smear negative cases can prevent sizeable number of NSN TB cases getting missed. We recommend replicating this on a larger scale to significantly reduce the existing gap of 'missing million' in India.

* Projected figure

** TB India Report, 2016

SOA02 Xpert optimisation and sustainability towards universal testing

SOA02-1011-25 Implementation of Xpert MTB/RIF in a tertiary referral hospital: a retrospective evaluation of successful and unsuccessful outcome from Lagos, Nigeria

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Background and challenges to implementation: Despite the roll-out of the genexpert at national level, there is paucity of data on performance and outcomes. The objective of the current study is to evaluate the performance of genexpert machine under operational condition at the reference laboratory of Lagos State University Teaching Hospital, Nigeria.

Intervention or response: We reviewed National Tuberculosis and Leprosy Control Program Laboratory register for all the Genexpert/MTB RIF tests conducted between January 2016- December 2017. Data were collected on total samples processed disaggregated into successful results and unsuccessful results (invalid and errors). Data were also abstracted for age, sex and HIV status

Results and lessons learnt: Between January 2017 and December 2017, a total of 1198 samples were processed with Genexpert. The mean age of subjects was 37.6 yrs (2-90). 54.4% (178/327) were females and 45.6% (149/327) were males. 64.8% (212/327) were HIV negative and 35.2% (115/327) were HIV positive. 72.7% (871/1198) were successful results and 27.3% (327/1198) were unsuccessful results. Of the 361 unsuccessful results, 59.9% (196/327) were categorized as errors and 40.1% (131/327) were categorized as invalid. Majority (79/194; 40.7%) of the error codes documented were related with sample processing (code 2008, 5006 and 5007) followed by other Genexpert reasons (codes 2034, 2035) like ultrasonic horn failure (72/194; 37%); cartridge/

module related (2032 and 5011) causes (32/194;16.5%) and temperature related (1001,1002,2014) was the least common reason (11/194; 5.7%). Age, sex and HIV status were not significantly associated with unsuccessful outcome

Conclusions and key recommendations: 40% of the errors were human related (operator competence, insufficient sample volume) while only 5% were temperature related. There is a need to integrate on-the-job mentorship for genexpert operators to be able to process sputum samples following standard operating procedures. Minimizing the unsuccessful results is the roadmap to early diagnosis and prompt initiation of TB treatment.

SOA02-1012-25 Test and treat TB: using Xpert MTB/RIF as primary test by health extension workers in Ethiopia

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Background and challenges to implementation: The utility of smear microscopy for TB case finding in the era of ensuring universal access to DST for presumptive tuberculosis cases has increased the rapid decentralization of using Xpert MTB/RIF. In Ethiopia, Xpert testing is scaled up to limited facilities. However, the access to such care is limited in communities due to the need of transporting samples to few centres and inadequate linking mechanism. We employed community Health Extension Workers to collect samples for presumptive in the community for testing by Xpert to test and treat in the community. We report the findings of the implementation of the project in rural districts of Ethiopia.

Intervention or response: This is an innovative community-based collaborative project with the Ministry of Health of Ethiopia implemented in southern Ethiopia. The key interventions are familiarization, capacity strengthening for health workers and Health Extension Workers (HEWs), awareness raising and community mobilization, house to house visit by HEWs and health development army, collecting sputum and transporting it to diagnostic facilities for testing and treating in the community.

Results and lessons learnt: Health Extension Workers and Health Development Army screened 9,266 people, identified 1,096 presumptive cases (646, 59% women), collected and tested 1,065 sputum samples (647, 61% women). Seventy MTB+ cases (37, 53% women) were diagnosed and started on treatment. Compared to baseline and control, there is an increment of 30% while the control has increased 3%. The intervention has increased the 27% case finding for bacteriologically confirmed cases.

Conclusions and key recommendations: Utilization of Xpert MTB/RIF is feasible using HEWs and HDAs in rural communities. Increasing access to community improves access to women and improve their case finding. This increased the case finding in communities and access to universal DST in line with end TB strategy.

SOA02-1013-25 Xpert MTB/RIF Ultra: early implementation in high TB and Low HIV prevalent country - Pakistan Experience

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Background and challenges to implementation: Pakistan is high TB and MDR TB and low HIV burdened country. Xpert MTB/RIF was introduced in 2011 and its use was mostly limited to testing of patient at risk of drug resistance and presumptive TB cases among vulnerable groups. Because of its limited use no visible role of Xpert testing is yet seen in improving bacteriological diagnosis of tuberculosis among notified cases.

Intervention or response: Before roll out of Xpert ultra, it was first introduced in National TB Reference Laboratory (NRL). Impact of introduction of Xpert Ultra on TB and RR diagnosis was analyzed by comparing four months Pre(Xpert MTB/RIF) and post (Xpert ultra) intervention performance data.

Results and lessons learnt: A total of 3690 samples were tested with Xpert MTB/RIF before and 4075 after switching to Xpert Ultra. Proportion of presumptive TB cases with no history of previous treatment and smear positive among specimen tested was same in both groups. but test performed on processed specimen was higher in Xpert Ultra group.

Higher proportion of valid results were obtained with Xpert MTB/RIF for MTB (99.4 vs. 96.9) as well as for Rifampicin resistance (95.9 vs. 69.6). MTB detected excluding trace was significantly lower (15.1 vs. 18.5%) but with trace calls was significantly higher (21.5 vs. 18.5%) in post intervention with Xpert Ultra.

	Before (Xpert MTB/RIF Assay V4.0)		After (Xpert MTB/Rif Ultra V2.0)		p-Value
	N	% (95%CI)	N	% (95%CI)	
Test Performed	3690		4075		
Valid MTB results	3669	99.4 (99.1-99.6)	3947	96.9 (96.2-97.3)	<0.005
MTB+ve (Exc. Trace)	677	18.5 (17.2-19.7)	597	15.1 (14.0-16.2)	<0.005
MTB+ve (inc. Trace)	677	18.5 (17.2-19.7)	850	21.5 (20.2-22.9)	0.001
MTB+ve with Rif results	649	95.9 (94.1-97.2)	592	69.6 (66.4-72.7)	<0.005
# Rif resistant	49	07.6 (05.6-09.9)	41	06.2 (05.0-09.3)	0.635

[Performance Xpert Ultra versus Xpert MTB/RIF assay]

Conclusions and key recommendations: Pakistan is low HIV prevalent country, proportion of MTB detected in trace (29.7%) is much higher than reported in earlier studies and such Rifampicin results were not reported in

large number of MTB positive with trace call. Further investigation are in progress to understand reason for lower number of valid results and MTB detected (excluding trace) and higher proportion of MTB detected with trace call. Countries need to evaluate Xpert ultra at one or few sites before roll out.

SOA02-1014-25 Optimizing TB diagnosis and GeneXpert utilization using a courier for specimen transport in Akwa Ibom State, Nigeria: a two-year review

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Background and challenges to implementation: The scale up of GeneXpert in Nigeria has been faced with challenges of poor utilization and long turn-around-time for results. To compliment other interventions initiated by the National TB program, a courier service was engaged by Challenge TB in 2016 as a pilot for specimen transport to GeneXpert sites to address challenges and improve outcomes.

Intervention or response: In 2016, four motorbike courier riders were recruited to transport sputum-specimen and ensure results retrieval from GeneXpert sites in Akwa Ibom State, following a hub and spoke matching of GeneXpert sites (hubs) to DOTS facilities (spokes). The couriers were trained on specimen handling, bio-safety procedures and completion of recording and reporting tools. A review of the state's GeneXpert data was conducted for 2015 - 2017; delivery registers were reviewed of the couriers for 2016 - 2017.

Results and lessons learnt: Between 2015 and 2017, the number of GeneXpert tests performed increased exponentially with incremental introduction of sample transport (See table 1). The average turn-around-time for test results being sent back to facilities was reduced with introduction of courier services from 6 days to 3-4 days. A high yield of MTB positives was achieved from samples transported. For Akwa Ibom state, the courier intervention was attributed to 10% of all TB cases in 2016 which increased to 20% of all TB cases in 2017.

Time Period (Year)	# (%) GeneXpert tests performed in the state	# (%) of samples transported by courier	Average turn-around-time for results	# (%) of MTB+ couriered samples
2015 (Baseline)	1,469	0 (0%)	6 days	0 (0%)
2016 (Intervention)	7,899	2,222 (28%)	3 days	288 (12.9%)
2017 (Intervention)	16,571	5,223 (32%)	4 days	595 (11.4%)

[Table 1: Courier intervention results (2016-17) compared to baseline (2015)]

Conclusions and key recommendations: The courier service in Akwa Ibom contributed significantly to the optimization of GeneXpert machines for TB diagnosis. This intervention can be scaled up in similar settings.

SOA02-1015-25 Implementation of sample referral for drug resistant TB diagnosis and treatment follow up: Bangladesh experience

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Background and challenges to implementation: Presumptive DR TB and TB patients don't have timely access to TB reference laboratories because of limited geographical coverage of GeneXpert and uneven distribution of those laboratories. As a result, follow up culture tests of DR-TB patients are often delayed or missed entirely. Challenge TB) Bangladesh Project implemented a sample transportation intervention to overcome the challenges. The objective of this study was to determine the number of TB and DR-TB cases diagnosed and follow-up solid cultures performed using this system between January 2015-December 2017.

Intervention or response: Sputum transportation SOP orientation was provided to 500 field staff in three city corporations and 22 districts. CTB project provided sample transportation kits to local health facilities to collect and send samples by courier (without requiring a cold-chain) to the nearest reference laboratories. Courier bills were reimbursed.

Results and lessons learnt: A total of 7,660 samples from 2,314 presumptive DR-TB patients and 1,700 DR-TB patients on treatment were collected and transported by courier; 95 follow-up samples were discarded from lack of necessary information. Of these, 5,251 samples from 1,700 DR-TB patients on treatment were inoculated for culture at NTRL Dhaka and RTRL Chittagong. Of these, 188 (4%) were positive. Among the 2,314 samples, 889 (38%) TB and 54 (2%) DR-TB cases were diagnosed by GeneXpert. Estimated cost per courier is less than \$1 compared to travel costs of per patient (\$40-55). Average time for sample transportation was 2.5 days. Coverage gaps and challenges in courier system were managed through the use of implementing partners staff to transport samples to the district/ sub-district level.

Conclusions and key recommendations: The sputum sample referral reduces the burden and barriers to patients' access to timely DS-TB and DR-TB diagnosis and

ensured follow-up cultures of DR-TB patients. Considering cost effectiveness and countrywide replicability of system, NTP should consider sustaining this system in absence of project support.

SOA02-1016-25 Lessons learned and surveillance of GeneXpert repair service provision and maintenance at the country level, 2016-2017

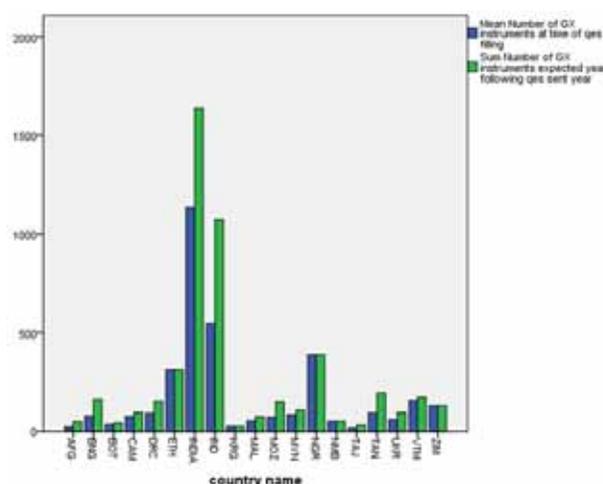
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Background: Over the last 4 years, KNCV has acted as the authorized service provider for Nigeria and Vietnam on behalf of Cepheid. In 2016, we conducted an assessment of 9 KNCV-supported countries in 2016 which suggested sub-optimal service provision in many of these countries. In 2017, we expanded our assessment to all countries under its flagship Challenge TB project to further understand how we might influence optimization of the TB diagnostic network with GeneXpert as the current primary initial diagnostic.

Methods: In December 2017, KNCV repeated a survey to 21 Challenge TB countries on experiences with GeneXpert repair and maintenance. We administered a standardized questionnaire as in 2016. Responses were compiled, data entered and analyzed in SPSS (version 21).

Results: 19 Asian and African country representatives (90.5%) responded. As in the 1st survey, the 2nd survey suggests that countries are largely expanding GeneXpert services; 10 countries reported that they have a designated service provider. Less than half of countries are able to track time from report of a problem to repair. Those able to track indicated the mean time to repair was 105 days. Module failure was reported as the most common problem. Mean downtime was higher for instruments not under warranty compared to under warranty.

Conclusions: While countries continue to expand GeneXpert coverage to replace smear-microscopy as the initial diagnostic for TB, service provision remains sub-optimal in countries KNCV supports including countries directly supported by other coalition partners under the Challenge TB project. KNCV will continue to actively engage with national TB programs and reference laboratories, donors, technical partners and Cepheid to optimize a functional TB diagnostic network that includes planning and facilitating for the newer, rapid technologies to guide diagnostic results with treatment regimens, optimizing our strategy to ensure the right diagnosis and the right treatment.



[Figure 1: Number of GeneXpert instruments reported in December 2017 vs. expected in 2018]

SOA02-1017-25 South Africa's experience in national implementation of Xpert MTB/RIF Ultra

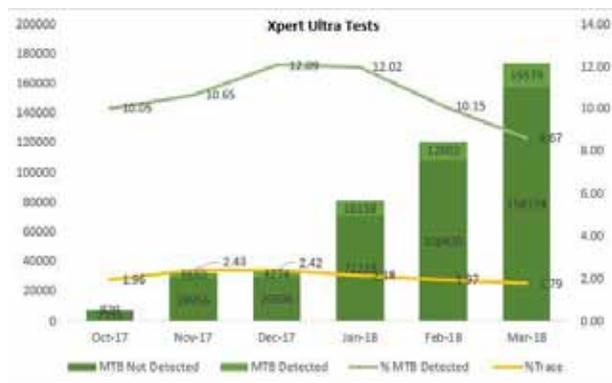
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Background: South Africa's National TB Program has provided Xpert MTB/RIF testing since 2011. In October 2017, based on the WHO recommendations and in-country evaluation, the program adopted the Xpert MTB/RIF Ultra due to its increased sensitivity among HIV and TB co-infected individuals. The national implementation scale-up challenges are described.

Methods: The implementation plan required the following key components: stakeholder engagement, site selection, training (clinical and laboratory), verification and EQA, connectivity, forecasting, clinical laboratory algorithm integration and on-going monitoring.

Results: A phased approach was adopted for implementation to be completed within 5 months, and moving from small to large provinces. This involved a total 203 GeneXpert testing sites comprising 325 platforms and 4212 modules. A communication protocol was developed to align the technical and LIS rollout as each GeneXpert instrument required manual software upgrade (4.7b), ADF upload and result transmission testing. Laboratory training was conducted for all GeneXpert sites and 547 operators were trained in 70 sessions. Each GeneXpert system was verified "fit for purpose" using Smartspot quality panels (consisting of 4 result types, including trace). The most complex was the adoption of the clinical algorithm for the interpretation of the additional semi-quantification category of "trace".

The testing profile since implementation is summarized in Figure 1, with 467 977 specimens processed using Ultra, of which MTB detected in 46 798 (10%), and an additional 2% (9 389) reported with Trace, and an overall test-failure rate of 1.64%.



[Figure 1: South Africa's Xpert Ultra implementation profile]

Conclusions: In spite of a national program being experienced in >8 years with GeneXpert technology, several challenges were met during implementation. The use of Ultra, however, has led to 2% additional specimens reporting trace.

SOA02-1018-25 GeneXpert Omni falls short when compared to target product profiles for a diagnostic tool to be placed in remote healthcare facilities

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Background: In 2014, Target Product Profiles (TPPs) were designed to guide development of TB diagnostic tools. TPPs outlined criteria for accuracy, placement, and operational performance within specific settings. This study evaluated the upcoming single-module GeneXpert Omni platform against relevant TPP criteria for placement and testing in remote peripheral healthcare settings.

Methods: Since the platform is being promoted for use in remote clinics or healthcare facilities below the district level laboratories, two TPPs (*Rapid Biomarker* and *Sputum Smear Replacement*) were aligned with information gathered from promotional releases, presentations, and discussions with company representatives. The Omni was graded 'compliant', 'questionable' or 'non-compliant' for each TPP criterion.

Results: When compared to the *Rapid Biomarker* TPP for test placed in remote peripheral health centers, the Omni was 62% compliant, 12% questionable and 26% noncompliant. When compared to the *Sputum Smear Replacement* TPP, the Omni was 76% compliant, 6%

questionable and 18% non-compliant. Areas considered 'questionable' related to ease of use in the proposed settings as this data remains unknown (studies pending). Questionable issues relate to; establishing sustainable user competency, providing remote training, operability-suitability for context (i.e. temperature, humidity, and dust), cartridge storage and distribution, power access for recharging, and use beyond MTB/RIF Assay (multi-disease) as Omni specific cartridges require an NFC chip for operation. Criteria considered non-compliant included; cost/test, cost/instrument, time to result, waste management, and daily throughput. In addition, the Omni will require sophisticated calibration and maintenance, as well as connectivity to update software and transmit data.

Conclusions: As it currently stands, the Omni platform does not fully comply with criteria outlined for testing below district level laboratories. This evaluation suggests that the affordability, suitability and utility of this device, particularly for use in remote healthcare facilities will be sub-optimal.

SOA02-1019-25 Xpert/RIF utilization rate improved through strong monitoring and innovative interventions in Tigray Region, Northern Ethiopia

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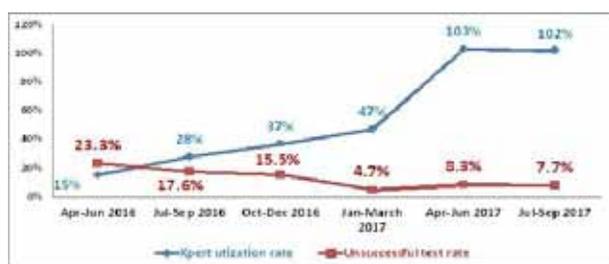
Background and challenges to implementation: The low utilization rate of Xpert/RIF tests for TB diagnosis was a key challenge for the national TB program. The situation in Tigray was even worse, with a utilization rate of 15% by the end of June 2016.

Here we report the improvement in the Xpert/RIF utilization rate following the assessment of the process and outcomes of multicomponent innovative strategies implemented by the regional team.

Intervention or response: Following a baseline assessment in July 2016, the Tigray Regional Health Bureau, in partnership with the USAID/Challenge TB project, implemented quick fix and medium-term action plans. The initial action included sensitizing 325 health professionals, training 83 lab technologists, assigning focal persons, and ensuring an adequate supply of lab consumables. The regional team then instituted a weekly monitoring system using Excel; information was collected by telephone. Further, the regional team quickly adopted the national guidance of "Xpert for all in testing sites" starting in April 2017. We analyzed routinely collected quarterly data for the period April 2016-Sept 2017.

Results and lessons learnt: The regional Xpert MTB/RIF utilization rate increased from 15% at baseline to 102% between Jul-Sept 2017, becoming the highest rate in the country. Of 13,708 successful tests conducted, 1,188 DS-TB and 46 RR-TB patients were identified and treated. The Xpert MTB/RIF detected cases comprised 64.3% (1,188/1,819) of all bacteriologically confirmed PTB cases notified in the region over the aforementioned period.

Conclusions and key recommendations: Good planning, staff orientation/training, adequate supply of consumables, and technical support led to dramatic improvements in the Xpert/RIF utilization rate in the Tigray Region. The approach can be replicated in similar settings to ensure maximum utilization of the services.



Note: The utilization rate exceeded 100% because of tests conducted outside working hours.

[Figure: GeneXpert service utilization quarter trend, April 2016 to Sep 2017, Tigray Region, Northern Ethiopia]

SOA02-1020-25 Xpert MTB-RIF guided diagnosis and treatment of drug-resistant tuberculosis patients in West-Java, Indonesia

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Background: Most drug-resistant tuberculosis (DR-TB) remains undetected in Indonesia. Xpert MTB/RIF assay (Xpert) has recently been introduced in Indonesia. Patients with risk factors for DR-TB are prioritized for Xpert-testing, followed by phenotypic drug-susceptibility (DST) for those with rifampicin-resistant tuberculosis (RR-TB).

This study aimed to evaluate the Xpert-based management of presumptive DR-TB cases in relation to diagnosis and uptake of second-line treatment under routine practice in West-Java, Indonesia.

Methods: We examined all records of patients tested with Xpert in the referral hospital for West-Java in 2015-2016. We measured time to Xpert diagnosis and the commencement of initial second-line treatment, and identified factors associated with diagnostic and treatment delay. We analyzed the appropriateness of revised treatment according to DST results and conducted an overall cascade of care summary assessment.

Results: From 3415 patients fulfilling criteria for presumptive DR-TB, 94% were tested by Xpert. Out of 339 Xpert RR-TB patients, 85% started initial MDR-TB second-line treatment. The biggest loss occurred from the time of diagnosis to pre-treatment assessment (48 of 339 cases). MDR treatment was started a minimum median of 41 days (IQR 29-70) after TB diagnosis by sputum microscopy. Rural residence was associated with delay in Xpert DR-TB diagnosis (aOR 2.73; 95% CI 1.5-5.2) and initiation of second-line treatment (aOR 1.9; 1.1-3.2). Out of 152 Xpert RR-TB patients with DST results, appropriate second-line treatment had been started in 122 (80%). 133 cases had MDR/XDR-TB confirmed by phenotypic DST (46%), drug-sensitive (6.6%), or culture not done (25%), negative (19.4%) or contaminated (3%). Overall, we estimated that 70% of attending DR-TB cases were ultimately on an appropriate treatment regimen.

Conclusions: Under programmatic conditions, Xpert MTB/RIF guided management of drug-resistant tuberculosis in Indonesia is associated with significant loss and delay with respect to diagnosis and treatment, compromising efforts to control MDR-TB and its spread in Indonesia.

SOA02-1021-25 Impact of Xpert MTB/RIF implementation on time to treatment initiation among people with multi-drug resistant tuberculosis in Karachi, Pakistan

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Background: Xpert MTB/RIF® assay (Xpert) has been cited as a landmark development in the diagnosis of TB, particularly for its drug-resistant form, by simultaneously detecting *Mycobacterium tuberculosis* and rifampicin resistance-conferring mutations in less than two hours, within basic laboratory facilities. The conventionally used TB culture takes up to eight weeks for results. Increased speed of results using Xpert may decrease the time to treatment initiation of second line drugs and improve treatment outcomes, however, this has not been evaluated in a programmatic setting.

Methods: Data of individuals registered for MDR-TB treatment at three Programmatic Management of Drug-resistant TB (PMDT) sites in Karachi was retrospectively analyzed, from June 2009 to February 2017. Individuals were categorized on the basis of baseline diagnostic test used (Xpert vs. Culture) and time to treatment initiation was compared.

Results: A total of 1,659 and 893 individuals with MDR-TB were diagnosed using Xpert and culture as the baseline diagnostic test, respectively. The mean time to treatment initiation in the Xpert group was 37 (SD \pm 123.1) days relative to 121 (SD \pm 126.3) days for culture and this difference was statistically significant (P value $<$ 0.01). The time to treatment initiation for majority (81%) of people with MDR-TB diagnosed using Xpert was less than 30 days, whereas only 5% of those diagnosed on culture started treatment before 30 days of diagnosis. Only 9% of all the study participants diagnosed using Xpert had a time to treatment initiation more than 90 days whereas this number was larger (47%) for the culture group.

Conclusions: Xpert significantly reduced the time to second-line treatment initiation in our study population. Further studies are needed to investigate the association between time to treatment initiation and treatment outcomes in various MDR-TB treatment programs.

Time to treatment initiation (days)	Xpert N (%)	Culture N (%)	P-value
<30 days	1345 (81%)	41 (5%)	<0.001
31-90 days	175 (11%)	430 (48%)	<0.001
91-180 days	59 (4%)	281 (31%)	<0.001
>180 days	80 (5%)	139 (16%)	<0.001

[Time to treatment initiation for people diagnosed with MDR-TB, by frontline diagnostic test (Xpert vs culture)]

SOA02-1022-25 Xpert networks: understanding barriers to optimization and sustainability toward universal testing

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Background: Eight years after WHO endorsement of Xpert MTB/RIF, countries still struggle to optimize networks. This is critical considering scale-up is key to achieve universal testing for all. To identify barriers to achieving expected testing goals, a multi-country survey was conducted.

Methods: A standardized questionnaire was distributed to country-level representatives of 22 TB high-burden countries. Questions focused on issues regarding testing capacity, procurement, service and maintenance (S&M), and programmatic experiences with scaling-up.

Results: Survey participation was 77% (17/22). Data revealed that 59% have Xpert as the initial test in current guidelines with only 32% widely implementing. From 2015-2017, nearly 70% have doubled testing capacity by procuring instruments. Others slowed instrument procurement to focus on: optimizing utilization, improving maintenance, expanding uptake of new diagnostic algorithms, improving access to testing, and systems strengthening.

Overall, utilization rates remain low with the primary reasons reported as: low clinical sensitization, poor instrument placement, and insufficient specimen transportation. Instrument S&M continues to be challenging even though 81% have in country authorized service providers, with only 46% of these countries being satisfied with current service provision.

Warranties covered 65% of reported modules with annual module failure rates ranging from 2% to 21%. Turnaround times for module replacements ranged from 7 days to as long as one year. Mean replacement rates range from 2 to 4 months, regardless of warranty status. Only three countries reported procurement of extended warranties, while most countries considered them unaffordable. Finally, 94% of countries rely on Global Fund to support network development and expansion activities.

Conclusions: Network assessments are needed to pinpoint obstacles to utilization and ensure placement according to epidemiological and geographical need as countries scale-up technology. Countries must provide domestic resources for sustainability. And while the manufacturer should improve pricing and conditions for S&M, countries are encouraged to build local solutions to ensure network operations.

SOA03 Hospital-based infection control and prevention; reports from the field

SOA03-1023-25 Hospital-based cough officer and 24-hour TB laboratory reduce delays in diagnosis, treatment and TB mortality in Beira, Mozambique: quasi-experimental study

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Background: In Beira Central Hospital (HCB), patients are not adequately screened for tuberculosis (TB) when they are admitted and often experience a delay in getting

tested and diagnosed with TB. We assessed the contribution of hospital-based cough officer (HBCO) and 24 hours working of TB laboratory (lab) on delays in TB diagnosis, treatment (TBDT) and TB mortality.

Methods: Quasi-experimental pre-post-test time series non-equivalent control group design methods were used. Auxiliary workers were trained to act as HBCO and 24 hours working of the TB lab was ensured. HCB was the intervention site and compared to Nampula Central Hospital (HCN). Baseline data regarding the time from hospital admission to TBDT and medical outcome of the TB patients were collected retrospectively from medical records for the 6-month period preceding implementation and compared to the 6-month period post implementation in both hospitals.

Results: Of 522 TB patients, 52% were in the intervention group, the characteristics in both groups before and after intervention were similar ($p > 0.050$): 71.6% were HIV+, 58.2% were males and median age (IQR) was 34 (16) years. After the intervention phase, the median (IQR) time delays for diagnostic [5 (3) days] and treatment [10 (4) days] in the control group were statistically different to the intervention group [1 (1) day] for TBDT ($p = 0.001$). Patients in the control group were eight times more likely to die from TB (aOR=8.0; 95% CI: 4.5-13.2) when compared to the intervention group, adjusting for sociodemographic and clinical factors.

Conclusions: Hospital delays in TBDT are common in the HCB and HCN and is one of the main factors associated with TB mortality. Availability of HBCO and 24 hours working of the TB lab are potential approaches to ensure early TBDT and reduction of the hospital TB mortality in resource limited settings.

SOA03-1024-25 Healthcare worker interactions with TB patients during clinical care: findings from two high burden countries, 2014

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Background: Healthcare workers (HCWs) have an increased risk for exposure to, and acquisition of, TB in the workplace. We sought to better characterize the

frequency, duration and timing of HCWs' interactions with TB patients during clinical care and the use of protective measures.

Methods: Trained assessors conducted structured, anonymous observations of HCWs' interactions with TB patients (presumptive and confirmed) at 22 hospitals in Vietnam and Thailand over 4 days per site. An interaction was defined as entry of a HCW into the room of a TB patient in an inpatient or outpatient department. For each interaction, assessors documented the ward/clinic, HCW's cadre, shift and time in room, number of patients in the room, and use of respirators and masks. Adherence was defined as combined use of respirators (HCWs) and masks (patients) during interactions. Logistic regression was done to identify predictors of non-adherence.

Results: A total of 3377 HCW-TB patient interactions, representing 250 contact hours, were documented. Physicians (47%) and nurses (31.5%) accounted for most interactions; cleaners had the third most frequent (8.3%) room entries. Interactions lasted a median of 3 minutes (Interquartile Range [IQR], 1-5); cumulative exposure times by cadre ranged from 13 minutes (clerks) to 8055 minutes (nurses). There was a median of 3 (IQR, 1-8) patients/ room. HCW respirator use in combination with patient mask use occurred in only 5% of interactions. Non-adherence was independently associated with being a nurse ($p=.01$), working the evening shift ($p=.04$), working on a medicine (vs chest or infectious diseases) ward ($p< .001$), and fewer patients/room ($p=.001$).

Conclusions: HCWs had frequent, unprotected exposures to TB patients. Adherence to protective measures was associated with cadre and possible work conditions. Effective interventions are urgently needed to improve use of protective measures by patients and staff (clinical and non-clinical) in order to minimize HCWs' TB exposures.

SOA03-1025-25 Use of N95 respirators amongst health workers in Akwa Ibom and Kano State

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Background: According to the 2017 Global TB Report, TB infection control has been credited for saving lives of healthcare workers (HCWs). The use of N95 respirator plays a significant role in infection control in the programmatic management of drug-resistant tuberculosis (PMDT) in Nigeria and is popularly used amongst HCWs providing care for drug resistant TB (DR-TB)

patients. Poor adherence to standard TB infection control measures contributes to the risk of transmission among healthcare workers. This study aims to describe the knowledge, attitude and practices of HCWs regarding the use of N95.

Methods: A random sampling of HCWs providing care for DR-TB patients attending monthly community clinics in two Challenge TB supported states in Nigeria: Akwa-Ibom and Kano was conducted. . In March 2018, de-identified semi-structured questionnaires were administered (with consent) at the clinics. Data collected were analyzed to show HCWs perception and use of the N95, using SPSS version 21.

Results: The mean working experience for the 136 participants is 3.82 years (SD 11.723). We found 96 (70.6%) to be male and 65 (47.8%) between the ages of 30-41 years. Majority of the respondents (75.9%) think surgical masks offers protection against TB infection. Consistent N95 use demonstrated by 93% of respondents with 97.7% especially during the community clinics. Only 38.7% had fit test done and 47.9% sometimes or never conduct seal check. Respondents indicating use of one N95 for upwards of a month before replacement was 51.2%.

Conclusions: This assessment has shown that the knowledge of HCWs concerning the proper use of N95 respirator is poor. Also the usage adherence is sub-standard as fit test and seal check is not routinely done. Factors responsible for these lapses have to be identified and addressed. Strengthening the standardization of best practices to avert occupational transmission of tuberculosis among HCWs in Akwa Ibom and Kano state is recommended.

SOA03-1026-25 Health promotion through surgical mask use among TB patients and visitors at Xinjiang Chest Hospital, China

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Background and challenges to implementation: Xinjiang Uyghur Autonomous Region has China's highest TB case notification rate. Xinjiang Chest Hospital (XCH) is the provincial designated TB diagnosis and treatment hospital, where 30% of TB patients are bacteriologically-confirmed. China's national guidelines on TB infection control recommend that TB patients wear surgical masks at hospitals to prevent TB transmission. As many patients do not wear masks or wear masks incorrectly, XCH introduced measures to promote wider and correct surgical mask use with support from the USAID Control and Prevention of Tuberculosis Project.

Intervention or response: For TB patients and families, XCH conducted small group activities and one-on-one counselling on infection control, choosing correct masks

and using masks correctly in both Chinese and Uyghur languages from 2016. XCH also disseminated bilingual communication materials and posters to increase mask use awareness.

TB Division 4 of XCH piloted and placed a mask vending machine next to an inpatient ward in October 2017, enabling rapid access to surgical masks for TB patients, family members and hospital visitors. Users paid 2 Yuan (~\$0.3) in cash or by mobile electronic payment, or selected a free mask.

Results and lessons learnt: Surgical mask distribution totaled 708 over five months, increasing from 82 in October 2017 to 191 in February 2018, and paid distribution varied from 43% to 79% over this period. Nurses also recorded the number and rates of mask users twice per week. Mask use among TB inpatients increased from 14% (37/260) to 32% (113/351), and use among TB patients' family members and visitors increased from 40% (55/137) to 51% (55/107).

Conclusions and key recommendations: Health promotion activities increased TB patients' and their close contacts' awareness of surgical mask use, improved mask accessibility, increased the willingness to pay, and improved surgical mask use significantly over five months. The activities should be continued and scaled up to other sites in Xinjiang, China.

SOA03-1027-25 Efficiency of the FAST strategy for tuberculosis diagnosis and treatment in a resource-limited hospital in Viet Nam

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Background: Hospitals in a high Tuberculosis (TB) burden country with limited resource can act as TB transmission hotspots. FAST - a strategy to Find cases Actively, Separate temporarily and Treat effectively - was introduced at Quang Nam Provincial Hospital of TB and Lung Diseases (QNH) in Vietnam with support from the USAID TB CARE II Project in collaboration with the National TB Program. This study analyzed the data of pulmonary TB patients diagnosed and initiated on treatment at QNH in the two consecutive project years of 2015 and 2016 to demonstrate efficiency of FAST for TB diagnosis and treatment.

Methods: QNH implemented key FAST activities including improved patient screening to quickly detect presumptive cases, order appropriate diagnostic tests, and initiate treatment early with routine performance indicator monitoring for improvement. FAST expanded Xpert MTB/RIF (Xpert) testing to outpatients and pro-

moted Xpert testing as initial or simultaneous tests with smear for both outpatient and inpatient to make earlier bacteriological-confirmation diagnosis. Prior to FAST, smear was the initial sputum testing and Xpert was restricted to inpatient.

Results: For patients having the initial sputum test as outpatient, 34 (26.0%) with drug-susceptible pulmonary TB (DS-TB) and 8 (72.7%) with drug-resistant TB (DR-TB) had outpatient Xpert results. Eighty-five percent of 34 DS-TB patients initiated treatment within one day while 75.0% of 8 DR-TB patients initiated treatment within three days from admission. For patients having the initial sputum test as inpatient, 181 (22.2%) DS-TB and 12 (48.0%) DR-TB patients had Xpert testing as initial or simultaneous diagnostic tests with smear. Seventy-seven percent of 181 DS-TB patients (median time: 2.0 days) and 41.7% of 12 DR-TB patients (median time: 4.0 days) initiated treatment within three days of admission.

Conclusions: FAST strategy successfully changed practices of physicians to shorten time to diagnosis and treatment initiation with quicker Xpert utilization at the selected resource-limited setting.

SOA03-1028-25 Implementation, scale-up and impact of FAST strategy in South African hospitals: what lessons have we learnt?

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Background and challenges to implementation: Tuberculosis infection prevention and control (IPC) is sub-optimally implemented in the health facilities in resource limited settings due to a variety of factors, including lack of infrastructure. To address these challenges the National Department of Health has adopted FAST (Find cases Actively, Separate temporarily, and Treat effectively) Strategy to strengthen TB services in the country. We present screening and case-detection data to highlight the current experience in piloting FAST in South Africa.

Intervention or response: The FAST Strategy has been adopted and implemented in all provinces to improve early diagnosis by ensuring TB cases are tested quickly and treated sooner. There was no additional staff recruited for the implementation. Data were collected on indicators along the TB cascade of care from 15 hospitals across 5 provinces (Limpopo, Gauteng, Eastern Cape and Free State) during the pilot phase, from April 2017 to Feb 2018. Implementation plans, data collection and monitoring tools were developed and discussed with staff.

Results and lessons learnt: More than 373,809 clients were screened (1961 HCWs) the 5 provinces since April 2017, and detection of TB cases has increased from 13% to 34%. The pilot has fuelled interest in monitoring IPC routinely, intensified screening of inpatients, reducing time to commencement of treatment, screening of healthcare workers for TB and effective linkage to care of diagnosed patients and contacts. However, the pilot has also highlighted gaps such as unavailability of occupational health & safety programs, lack of commitment from management, lack of dedicated personnel for screening & data capturing, poor data recording and reporting, and inadequate maintenance of equipment.

Conclusions and key recommendations: FAST implementation is feasible in the South African setting. Increased commitment by management stakeholders to provide sustainable resources for TB (and HIV) prevention, and implementation of CQI can strengthen the capacity of FAST implementation teams.

SOA03-1029-25 Results of a 2-year pilot project on health care worker tuberculosis surveillance in Nigeria; April 2016 - March 2018

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Background and challenges to implementation: Nigeria has the second highest burden of Tuberculosis (TB) in Africa and TB constitutes a major public health problem. The burden of TB among Health Care Workers (HCWs), an at risk group for TB, is unknown as TB surveillance among HCWs is not currently implemented within the TB program. We implemented a 2-year pilot project of TB surveillance among HCWs in 13 health facilities located in three states of Nigeria. We integrated HCW TB surveillance into the facility based Occupational Health (OH) program to reduce TB-associated stigma, increase uptake of TB screening and ensure sustainability. Lessons learnt are to inform a national level scale up.

Intervention or response: A base line assessment of TB infection control (TBIC) and OH services was conducted across the pilot facilities. TBIC practices were strengthened using the TB BASICS (Building and Strengthening TB Infection Control Strategies) model. OH clinics were established and equipped. We instituted routine health assessments in the OH clinics for Diabetes, Hyperten-

sion, Obesity, TB and HIV and provided staff log books for the assessment as well as referral booklets. Staff sensitizations were carried out to mobilize staff for health assessment. HCWs with presumptive TB were referred for diagnostic evaluation using smear microscopy and GeneXpert MTB/RIF, and persons with TB were linked to DOTS.

Results and lessons learnt: A summary result of the HCW TB screening cascade for year 1 and 2 of the project is shown in (Table 1).

Year	TB screening cascade						TB Rate per 100,000	General Population	Rate ratio
	No of HCWs screened for TB	% of HCWs screened for TB	No of Presumptive TB	% of Presumptive TB among HCWs screened	No confirmed TB	No HIV/TB co-infection			
1	10068	20	75	3.7	4	1	198	50	4.0
2	11030	23	49	1.9	3	0	118	54	2.2

[Table 1: A summary result of HCW TB screening]

Overall, uptake of TB screening among the HCWs was low. However, in both years, the rate of TB among the HCWs screened was higher than that of the general population.

Conclusions and key recommendations: The project helped to integrate routine TB surveillance among HCWs into OH services, but participation was low. Further work is needed to identify barriers to participation of HCWs in OH services before pursuing national level scale up of the project.

SOA03-1030-25 Perception of the risk of tuberculosis transmission for health care workers at a public hospital in Lima, Peru

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Background: Hospitals in tuberculosis (TB)-endemic countries like Peru are hotspots for TB transmission. Healthcare workers (HCWs) are particularly vulnerable to infection. Implementation of transmission controls, including administrative and environmental controls as well as the use of personal protective equipment (PPE), depends on support from the hospital. We conducted a qualitative study of hospital stakeholders about their perception of tuberculosis transmission risk for HCWs at Hospital Nacional Hipolito Unanue in Lima, Peru.

Methods: We performed nine in-depth interviews with nurses and physician stakeholders as part of a clinical trial evaluating the implementation of an administrative TB transmission control intervention. Open cod-

ing was used to identify emergent themes. Axial coding organized themes into a codebook and selective coding was used to identify relevant text citations. Finally, summaries of coded data were compiled in a narrative form using grounded theory technique.

Results: Overall, stakeholders regarded HCWs at the hospital to be at high risk for TB transmission due to four emergent themes (Table 1): 1) high TB incidence among patients at the hospital, 2) variable implementation of environmental controls in the emergency room, including obstructed natural ventilation and crowded treatment areas, 3) low usage of PPE, particularly in moderate or low TB transmission risk areas as a result of limited PPE supplies and 4) low awareness of TB transmission control procedures despite HCW concerns about TB transmission risk. There was limited mention of implementation of administrative transmission controls in relation to transmission risk.

Conclusions: Stakeholders held accurate perceptions of high TB transmission risk faced by HCWs at the hospital. They recognized that risk could be mitigated by improvement in implementation of environmental TB transmission control measures and use of PPE. Strengthening knowledge and practices around administrative TB transmission controls may help to further reduce risk of TB transmission among HCWs at the hospital.

Theme	Quotations
High tuberculosis prevalence	"The risk at Hipolito is high because we are in East Lima... [referring to East Lima having a high burden of TB]" (Physician) "...we have seen colleagues of whom we share emergency duty who have been infected with this disease [tuberculosis]..." (Physician)
Environmental controls	"...the ambulatory rooms are not well ventilated, with very short, very narrow rooms or corridors that cannot accommodate the number of patients safely" (Nurse) "...we design emergency room with skylights, wide windows to assure good air flows, but... many times health workers don't understand... they close the windows... and the skylight have been covered with glass, so we are losing [proper ventilation]." (Physician)
Use of personal protection equipment	"... Almost monthly we do not have the personal protection barriers, the hospital is in crisis right now, they do not give us the [respirators]... it is not as it should be..." (Nurse) "... sometimes they [healthcare workers] trust too much and they stop using the biosecurity measures." (Physician)
Knowledge of TB transmission controls	"... you have to be there [on the wards] reminding them [health care workers] of the measures they must take to be able to decrease tuberculosis transmission..." (Nurse) "... in the other areas, apart from the pulmonology and infectious diseases wards, despite having all the same information to prevent tuberculosis, the HCWs fail to comply." (Physician)

[Reasons for TB transmission risk as reported by hospital stakeholders]

SOA03-1031-25 Infection control in MDR decentralised sites in South Africa

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Background: Prior to 2011, national policy mandated that all DR TB patients be initiated on treatment in specialised TB hospitals. New cases outstripped the bed capacity and South -Africa moved to the decentralized MDRTB. Infection Control (IC) is one of the requirements for decentralised MDR TB care. After a baseline study was done at 75 facilities and interventions implemented a follow-up assessment was done.

Methods: The objective of the study was to determine if infection control can improve after recommendations made to facilities following baseline assessments.

A cross-sectional descriptive study of 75 decentralized MDR TB facilities (10 Community Health Centres, 34 hospitals and 31 Primary Health Care clinics) was conducted with assessment and with the follow-up assessment, using a standard assessment instrument comprising of the following: availability of IC guidelines, IC committee, safe sputum collection area, infection control plan, risk assessments done, patients screening, fit testing and availability of N95 respirators. Key informants were interviewed and hospital walkabout conducted. Following the initial assessments, infection control plans were developed to help them attain the minimum requirements to support decentralization.

Results: Infection control practises improves. Access to IC policies increased from 92% to 100%; screening practices from 50% to 70%; implementation of IC committees from 15% to 40%, IC plans from 20% to 45%, IC officers appointed from 20% to 40%; safe sputum collection points from 30% to 50%. 80% of facilities had N95 respirators available with the baseline assessment and 90% with the follow-up assessment, although it was not visible at all facilities.

Conclusions: These findings demonstrate that recommendations after baseline assessments on IC practices can improve IC practices.

SOA03-1032-25 Implementation of a health care worker tuberculosis screening program: experience from a regional initiative in Dire Dawa, Ethiopia

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Background and challenges to implementation: Health-care workers (HCWs) have higher risk of developing active tuberculosis (TB) due to frequent exposure in their work place. In 2015, rapid assessment of facilities in Dire Dawa (DD) showed that TB notification rate among HCWs was 1.4 times that of the general population. However, there is no strong national system for TB surveillance among HCWs in Ethiopia. As part of a pilot TB Infection Control (TBIC) initiative (Building and Strengthening TBIC Strategies), we implemented HCW TB screening to help monitor the impact of TBIC activities and improve occupational health and safety.

Intervention or response: Pre-implementation site visits were done to assess opinions and concerns of HCWs about the screening program. Facility TB-BASICS team were trained on confidential screening procedures and standardized screening tools distributed. A health screening package, including quarterly TB symptom screening and anthropometric measurements, and annual HIV, blood sugar and blood pressure tests were initiated at 10 public health facilities in DD.

Results and lessons learnt: From March 2016 - March, 2017, four quarterly screening programs have been conducted. Overall, 1240 (98%) out of the total 1261 HCWs were ever screened at least in one round. Average participation was 70% (n=870), 90% (n=1132), 91% (n=1148), and 91% (n=1139) for the first, second, third and fourth rounds respectively. Nearly 60% have participated in all the four and 95% at least in two rounds of quarterly screening programs. Participation for at least 2 rounds was 100% for physicians, 99% for nurses and 93% for other staff. HIV test acceptance was 94%.

Conclusions and key recommendations: In this region, HCWs acceptance of the comprehensive workplace health screening including TB and HIV was very high. These findings showed that confidential HCW TB screening program is feasible and can be successfully implemented as part of facilities' TBIC programmatic activities and in a comprehensive health screening approach.

SOA04 Tuberculosis in migrants in Europe**SOA04-1033-25 Missed opportunities for TB control: a population-based cohort study of primary care access and TB among migrants in the UK**

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Background: England is implementing a systematic primary care based latent TB infection (LTBI) screening programme for new entrant migrants. Good access to primary care is associated with improved health outcomes but migrants can be affected by barriers to access. We followed a cohort of migrants and tracked their journey within the National Health Service and TB control programme from initial UK entry to first contact with primary care and development of active TB after arrival to the UK to estimate the number of preventable cases through primary care based LTBI screening and treatment.

Methods: Retrospective population based cohort study of all visa-applicants aged 16 to 35 years screened for active TB before entry to UK in 72 high-burden countries between 2011 and 2014. We used data record linkage of the pre-entry screening, the NHS Personal Demographic Service (PDS), the Enhanced TB Surveillance system and LTBI service utilization databases.

Results: 224,234 migrants eligible for LTBI screening entered the UK between 2011 and 2014. A low proportion 103,990(46.3%) registered in primary-care in the year of arrival. We estimated the number of delayed registrations of the same age group; 118,740 immigrants from the 72 high-burden countries registered between 2011 and 2014, of whom 84,257 (70.9%) arrived before 2011. There were 1598 incident TB cases, estimated incidence 288 per 100000 person years (95%CI 273-304), and TB cases had a longer time between arrival to UK and GP registration ($p < 0.0001$). Accordingly, the incidence rate was higher in the cohort of delayed registrants (IRR 216, 95%CI 191-244; $p < 0.0001$). (86.5%) of TB cases were potentially preventable through primary care based LTBI screening and treatment.

Conclusions: Most TB cases could be prevented in primary care. The programme may be limited by low and delayed primary-care registration, but could be improved by promoting GP registration and community-based screening to reach unregistered migrants.

SOA04-1034-25 Seeking help in a hostile environment: experiences of health care access amongst UK migrants with TB

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Background: 'Health for all' is a founding principle of both the WHO and the UK's National Health Service which celebrates its 70th anniversary this year. Recently, healthcare access for migrants has been restricted as part of the UK Department of Health's Visitor and Migrant Cost Recovery Plan, and in association with a wider 'hostile environment' strategy targeted at undocumented. This research explores the experiences of healthcare access for recent migrants with TB.

Methods: This is a mixed methods study. 100 recent migrants with active TB were sequentially recruited from a large NHS Trust in London. All 100 were administered a questionnaire which collected demographic information and healthcare access experiences. A maximum diversity sample of 16 participants were interviewed in-depth using the Biographic Narrative Interpretive Method to elicit migratory and health-seeking stories. Quantitative data is reported using descriptive statistics. Qualitative data was analysed thematically using both inductive and deductive reasoning through a situated, intersectional lens.

Results: 100 participants migrated from 32 different countries to the UK between 2011 and 2017. Mean age was 31 years, 58 % were male. Median time from symptom onset to starting TB treatment was 119.5 days (IQR = 55.5-215). 72% did not know that TB care was free. Preliminary qualitative analysis indicates the theoretical construct of 'candidacy' as a useful tool to understand healthcare access experiences. Routes to diagnosis were often circuitous involving many actors. Fear, the role of documents, social capital, and transnational ties were all important. Final analysis will be presented at the conference.

Conclusions: These data reveal the micro, meso and macro level influences on healthcare access for migrants with TB in the UK. This research highlights the ways in which anti-immigrant policies undermine the national TB strategies and an international vision of health as a right, not a privilege.

SOA04-1035-25 Is it worth screening for comorbidities when screening for tuberculosis? Lessons from the UK's refugee resettlement programme

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Background: Since 2004, the UK has been resettling refugees from all over the world through the Gateway Programme. People resettled include those fleeing well know conflicts such as those in Somalia, Sudan and Democratic Republic of Congo. In January 2014, the UK government set up a scheme to resettle Syrian refugees. This was further augmented in 2016 to include "children" at risk living in the Middle East. Refugees are known to be at high risk of diseases such as tuberculosis because of high prevalence in their countries of origin and are therefore screened for diseases of public health significance e.g. tuberculosis (TB).

Methods: Our study cohort consisted of refugees from 24 countries screened for disease pre-entry by the International Organisation for Migration (IOM) between March 2013 and August 2017. Odds ratios (ORs) were estimated to identify factors associated screening positive for TB. Multivariate analysis was to adjust for confounding.

Results: The cohort consisted of 9,828 refugees screened for TB, hepatitis B, HIV infection and diabetes. Univariate analysis demonstrated some association with TB infection and diabetes (OR 2.29; 95% CI 1.53-3.43) and HIV infection (OR 2.94; 95% CI 0.90-9.63, $p=0.075$) but these were lost in multivariate analysis. After adjusting for age and sex, factors associated with screening positive for TB infection included hepatitis B (Odds ratio (OR) 1.81; 95% CI 1.01-3.25), region (OR 2.22; 1.67-2.94, Middle East versus Africa) and history of TB (OR 31.01; 95% CI 12.83-74.98).

Conclusions: Our results show screening positive for TB infection was associated with screening positive for hepatitis B, region of origin and a history of previous active TB disease. This would suggest that screening for hepatitis B when screening for TB could benefit the refugees coming from the 24 countries in study cohort. This would allow refugees to receive better medical care upon settling.

SOA04-1036-25 Tuberculosis screening of new migrants to the Netherlands: asylum seekers have a higher risk of tuberculosis

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Background: Migrants from tuberculosis (TB) endemic (>50 per 100,000) countries undergo mandatory post-entry radiological screening in the Netherlands. Migrants from high incidence (>200 per 100,000) countries are also offered bi-annual TB screening during two years after entry. Screening effectiveness is evaluated periodically to guide policy decisions.

Methods: Data on asylum seeker and immigrant screenings in 2011-2015 were collected from the nation-wide TB client registration system of the Municipal Health Services implementing the screenings. Data included demographics, chest X-ray results, laboratory diagnostics, TB diagnosis and treatment outcome.

Results: 116,301 immigrants and 99,506 asylum seekers were screened for TB. TB was diagnosed in 97 immigrants and 126 asylum seekers through entry screening and in 24 immigrants and 52 asylum seekers through follow-up screening. Respectively 96% and 80% of immigrants and asylum seekers diagnosed with pulmonary TB within 6 months after entry were detected through screening. Of patients with pulmonary TB diagnosed 6-29 months after entry, 60% and 41% were detected through follow-up screening, respectively.

The yield of entry screening was considerably higher among asylum seekers than among immigrants, especially for those from countries with an incidence of 51-100 per 100,000 (32 versus 189 per 100,000). Yield during follow-up screening was very high among both asylum seekers and immigrants with chest X-ray abnormalities at entry (>4000 per 100,000 screenings).

Incidence in country of origin per 100,000	Number immigrants screened	Yield per 100,000 (immigrants)	% immigrants with TB detected through screening	Number asylum seekers screened	Yield per 100,000 asylum seekers screened	% asylum seekers with TB detected through screening
≤50	26,101	31	100%	49,142	31	89%
51 t/m 100	37,787	32	100%	5,833	189	85%
101 t/m 200	36,548	134	97%	10,385	299	92%
>200	13,028	322	92%	23,966	204	60%

[Yield of pulmonary tuberculosis in entry screening by TB incidence in country of origin 2011-2015]

Conclusions: Radiological post-entry screening is effective to detect TB in migrants from TB endemic countries and to identify migrants with a high likelihood to develop TB. Follow-up screening is less effective given the low proportion of patients detected through screening and the low coverage. Post-entry screening for latent

TB infection and preventive treatment may be a more cost-effective intervention for migrant populations and is currently being piloted and evaluated in the Netherlands.

SOA04-1037-25 Epidemiology of lymph node tuberculosis in Denmark from 2007 through 2016: a review of 489 cases

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Background: Lymph node tuberculosis (LNTB) is among the most common extrapulmonary manifestations of tuberculosis (TB). The diagnosis may be challenging and patients are often diagnosed and treated with a delay. Most studies include a very limited number of patients, and in Denmark, the characteristics of the disease has never been examined.

Methods: We conducted a retrospective register-based study of all LNTB patients in Denmark from 2007 through 2016 to clarify the current epidemiology and microbiological features.

Patients were identified using national surveillance registers at Statens Serum Institut, Copenhagen. Diagnosis was either microbiologically verified by culture, direct microscopy, nucleic acid amplification, or based on a clinical examination suggestive of TB.

Results: During the study period, 489 were notified with LNTB corresponding to 13.5% of all TB patients. Annual incidence rates ranged from 0.95 to 1.49 patients per 100,000 citizens.

A majority of patients were migrants ($n = 444$) between the age of 25 and 34 years. Danes were generally older and had a significant higher proportion of risk factors notified compared with migrants. Additionally, Danes had a mean delay from symptom onset to treatment initiation of 30 days more.

Isolated disease was common (86.3%) while the most frequent concomitant site of TB infection was pulmonary (10.8%). However, for more than half of the patients, sputum or similar material was not sent for any bacteriological examination, and for one-fifth, lymph node material was not sent for culture.

Conclusions: Of great importance is that TB patients are diagnosed promptly to identify infected individuals and to maintain an effective control programme. Relevant samples must be examined to verify the diagnosis, discover drug resistance, and contagiousness. In our ongoing study, we have demonstrated that LNTB patients have a considerable delay from symptom onset to treatment initiation, and often, appropriate material is not sent for diagnostics.

SOA04-1038-25 Systematic screening for active tuberculosis in asylum seekers in Italy: a three-year results evaluation

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Background and challenges to implementation: Global migration has increased over the past years. From 2014 to 2017, a total of 624,747 people arrived to Italy through the Mediterranean sea on unseaworthy boats. Asylum seekers represent a subgroup of migrants at particularly high risk for tuberculosis (TB): targeted interventions are recommended in this population to address its special needs. We report three-year data of active TB-screening in asylum seekers performed in a regional reception center (hub) located in Bologna, Emilia Romagna Region, Northern Italy.

Intervention or response: A voluntary and free active TB screening was offered to all asylum seekers arriving to the hub in Bologna. The screening strategy was based on systematic chest X-ray (CXR), regardless the presence of TB suggestive symptoms, through a mobile CXR facility installed inside the center. An individual questionnaire about the presence of TB suggestive symptoms was filled with the aid of cultural mediators. In case of abnormal CXR, individual patient's management was agreed upon by the hub's medical doctors and the infectious diseases and pneumology specialists.

Results and lessons learnt: From July 2014 to December 2017, 17,053 individuals were screened for active TB with systematic CXR. Overall, 56 individuals were diagnosed with active TB: 52/56 (93%) were males, mean age was 21 year (range 16-45); 41/56 (73%) were from West Africa, 10/56 (18%) from North Africa, while the others from Indian subcontinent. 53/56 (95%) of patients presented pulmonary TB, while 3/56 had extra-pulmonary TB. Overall, 38 patients (68%) were completely asymptomatic at diagnosis, and 5 of them had smear positive respiratory samples.

Conclusions and key recommendations: These findings reveal a post-entry screening prevalence rate of 328/100,000 (95% CI 247-426) individuals screened and a number of needed to screen (NNS) equal to 304. The high proportion of asymptomatic cases (68%) detected by CXR shows the higher sensitivity of this tool compared to symptoms screening alone.

Years	N° of CXR done	N° of identified TB cases	Prevalence (N° of cases/100.000 individuals screened, 95% CI)	NNS (Number Needed to Screen)
2014	1.331	7	526/100.000 (211-1.080)	190
2015	4.165	11	264/100.000 (131-472)	378
2016	5.536	16	289/100.000 (165-469)	346
2017	6.021	25	415/100.000 (268-612)	240

[Active TB screening in asylum seekers results between 2014 and 2017]

SOA04-1039-25 New algorithm for screening immigrants for latent tuberculosis infection (LTBI) in Norway - testing only with intention to treat

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Background and challenges to implementation: Until 2015, screening for TB upon arrival in Norway also included testing for LTBI. Only those with positive IGRA and known risk factors for progression to active TB were offered preventive treatment. As individual pre-test risk assessment was not feasible, considerable resources were spent on testing without an intention to treat if positive. In 2015, with increased arrivals of asylum seekers, the need for a more targeted algorithm for testing immigrants for LTBI became evident.

Intervention or response: The challenge was to establish a new algorithm for LTBI screening targeting those with the highest risk of developing disease without having access to information about medical risk factors.

Country of birth was considered a potential risk factor. TB rates among asylum seekers was analyzed in order to support the decision. Based on these data and estimated incidence data from WHO (> 200/100 000), a list of countries with very high TB incidence was established. Among asylum seekers coming from these countries, we found that almost one percent were notified with TB within one year upon arrival (table 1).

Country of birth or nationality	Somalia	Etiopia	Sudan	Eritrea	Afghanistan	Total
TB cases notified within one year of arrival to Norway 2006-2015 (MSIS)	213	35	20	116	57	457
Asylum seekers in Norway 2006-2015 (UDI)	12899	3774	3082	18808	16928	55727
TB rate per 100 000	1651	927	649	617	337	820

[Cases of tuberculosis notified 2006- 2015 in asylum seekers within one year of arrival in Norway, according to country of birth or nationality.]

Results and lessons learnt: The high TB rate observed in this group was interpreted as partly due to a high proportion being recently infected or re-infected, mean-

ing IGRA positive in this group are at increased risk of developing TB and would benefit from preventive treatment.

A new algorithm including only those originating from countries with very high incidence was developed. As a result, fewer IGRA tests are performed, but all who test positive should be offered treatment or follow-up.

Conclusions and key recommendations: Targeted screening of LTBI among immigrants with high risk of developing TB disease is possible without having access to individual medical data. The cost-efficiency of screening immigrants for LTBI, even after targeting those with highest risk, remains to be established.

SOA04-1040-25 Clustering of Mycobacterium tuberculosis analyzed by WGS in the metropolitan area of Rome, Italy

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Background: Characterization of *Mycobacterium tuberculosis* transmission dynamics is needed to design control strategies aimed at progressing toward tuberculosis (TB) elimination in low incidence countries.

The aim of our work was to characterize by whole-genome sequencing (WGS) the TB strains circulating in the metropolitan area of Rome, which has a TB incidence twice as high compared to the national Italian average and an ethnically diverse patient population.

Methods: All TB strains isolated from patients consecutively admitted at the National Institute for Infectious Diseases in Rome between January 2016 and March 2017 were subjected to WGS. Sequences were uploaded on SeqSphere+ (Ridom© GmbH) in order to generate a cgMLST-based minimum spanning tree and to identify clusters and on PhyResSE 1.0 for lineage attribution.

Results: Two-hundred-nine (209) *M. tuberculosis* isolates were analyzed during the study. Of these, 153 (73.2%) were from foreign born (FB) patients, mostly (51%) from Romania.

Twenty-nine clusters were identified, involving 81 patients (39%). The majority (17/29) of clusters belonged to the Haarlem sub-lineage. The proportion of patients in clusters was similar for Italian born (IB, 26/56;46%) and FB (55/153, 36%) patients. 11 clusters included patients born in a single country (1 cluster with IB patients only). Of the remaining 18 clusters, 16 included IB and FB patients.

Conclusions: This study, conducted in a metropolitan area in Italy using WGS, shows that approximately one fourth of TB cases may be attributable to recent infection both in IB and FB patients: this is a minimum esti-

mate given the short duration of the study and the fact that it was conducted in a single center. We also documented a significant mixing between autochthonous and migrant patients, most of whom were long term residents in Italy.

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SOA04-1041-25 TB case finding and treatment in cooperation with charities and volunteer organizations: experience from Tyumen Region, Russia

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Background and challenges to implementation: TB incidence in Tyumen fell by 7.1% from 2016 to 2017 and TB mortality decreased by 8.6%. However, despite the declining TB rates the TB situation among socially disadvantaged populations such as homeless populations remains dangerous. Homeless patients account for 3% of newly diagnosed TB patients and this group contributes to TB transmission.

Intervention or response: In 2016 a special service for TB case-finding and treatment of the homeless population was organized at the local TB dispensary in cooperation with local social care services (labor and employment, migration, shelters, police, medical and other state and civic organizations). The service works on a contractual basis and cooperates with volunteer organizations that refer homeless people for free x-ray and bacteriological examinations. If an active TB case is diagnosed, the homeless patient is immediately hospitalized for the duration of treatment.

Results and lessons learnt: 147 homeless people were examined for TB; 14 were diagnosed with active TB. When homeless persons enter the service, they are seen by a psychologist and a social worker who map a plan for social services, subsidies, allowances and other measures to help the patient. Between 2016 and 2017, 52 people had identity cards and insurance policies re-issued, seven had pensions paid, 11 received allowances for buying food, clothes, shoes and hygiene products, and 26 received free legal assistance. Eight homeless people who successfully completed TB treatment received help to apply for social housing. TB patients on treatment receive regular psychological care: an appointed psychologist assists with treatment adherence issues, encourages patients to attend follow-up appointments and prevents treatment interruption.

Conclusions and key recommendations: The comprehensive package of care from a team of specialists contributes to better social adaptation of patients and helps them feel accepted by society. Early detection of TB among the homeless population positively influences TB incidence rates in Tyumen and helps decrease transmission in the population.

SOA05 Integrating support across the tuberculosis care cascade

SOA05-1042-25 Understanding reasons for delays in treatment start in Papua New Guinea through qualitative research

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Background: Delays in treatment start are frequent in Papua New Guinea (PNG), a high burden TB country. Qualitative research was used to explore why and contribute to finding patient adapted solutions in the National Capital District (NCD) and Gulf Province.

Methods: We contacted key actors in the diagnostic and treatment cascade in NCD and Gulf Province including: TB patients and their family members, health workers, traditional healers and community members and used in-depth interviews and focus groups discussions to identify reasons for delays in diagnosis and treatment start. All participants provided written informed consent including permission for audio-recording.

Results: Diagnostic delays were often linked to lack of bio-medical knowledge of TB symptoms leading to misinterpretation of the illness at its onset. Stigma was a strong deterrent to seeking TB screening, further compounded by confusion with HIV/AIDS. Traditional interpretations of illness and healing practices resulted in delays, especially when services were hard to reach or had initially failed to diagnose TB. Health service delays were common in patients' experiences, including long waiting times, non-functioning diagnostic tools and multiple unsuccessful attempts to receive the correct diagnosis over extended periods of time. In Gulf province, geographical, linguistic and socio-cultural barriers were important deterrents to an early diagnosis and treatment start, especially for some of the most isolated communities.

Conclusions: Multiple and inter-related social, economic and health systems challenges undermine timely treatment start in PNG. Investment in community awareness to increase general knowledge of TB and reduce stigma is needed. Integration of TB and HIV/AIDS activities might contribute to prevent additional stigma. Provision of transport for persons to be evaluated for TB in geographically challenging settings can facilitate access to health services, together with forms of linguistic and socio-cultural mediation. Capacity building of health workers in general services is needed to reduce diagnostic delays.

SOA05-1043-25 Institutionalization of community-based treatment supporters in Kyrgyzstan improves TB treatment adherence and provides more patient-centred care

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Background and challenges to implementation: Kyrgyzstan is one of the 30 high multidrug-resistant tuberculosis (MDR-TB) burdened countries. The toll of daily visits to a health clinic to receive treatment causes some TB patients to interrupt or stop their treatment, which can lead to the development of MDR-TB.

Intervention or response: To improve TB treatment adherence, the USAID Defeat TB (DTB) Project in Kyrgyzstan introduced and institutionalized a Community-based Treatment Supporter (CBTS) approach in Chui region, where the treatment default rate was as high as 15.4% in 2016. A CBTS is a community member who voluntarily administers and oversees the patient's daily TB treatment. DTB assisted the National TB Program with the development and endorsement of a CBTS policy which describes CBTS selection procedures, training, and monitoring and institutionalizes the CBTS position within the National TB Program by integrating CBTS into case management and detailing the roles, responsibilities, and communication between the CBTS and health workers. To roll out the CBTS approach, DTB trained 47 community members to perform CBTS duties, including picking up pills at the clinic, administering the daily treatment, completing a treatment administration form, recording the patient's side effects, and implementing simple infection control measures. DTB also trained 14 health workers at clinics to supervise the CBTS to ensure correct administration of treatment.

Results and lessons learnt: Since June 2017, a total of 76 TB patients have received their treatment through CBTS and none of these patients have stopped or interrupted their treatment.

Conclusions and key recommendations: The CBTS approach is easier on both patients and the health system. Patients can take their drugs at a time and place that is most convenient to them and health workers can see their TB patients once a month instead of every day. Most importantly, the CBTS approach is leading to better treatment adherence, which will contribute to better treatment outcomes and decreases in MDR-TB.

SOA05-1044-25 Evaluating therapeutic food support and tuberculosis treatment outcomes in Kenya: a historical cohort study

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Background: Nutritional depletion is often seen in people with tuberculosis (TB) at diagnosis. Lack of weight gain during treatment is associated with unfavourable treatment outcomes. In Kenya, therapeutic caloric food support provided by the national TB programme to people with TB might improve weight-gain and thus the likelihood of TB treatment success.

Methods: The study was a historical cohort study using data obtained from the Kenyan national TB data surveillance system: TIBU. The study population was everybody notified with pulmonary TB in Kenya between 2015 and 2016, older than 16 years, with a BMI at diagnosis < 18.5. We excluded anyone without an evaluated treatment outcome. The study exposure was receipt of therapeutic caloric food support during treatment. The outcome was TB treatment success (cure or treatment completion). The association between food support and TB treatment success was evaluated via uni- and multivariable logistic regression. Multivariate adjusted estimates for food support were tested for effect modification by region, BMI, and HIV coinfection.

Results: In the study period, 56,768 people were notified with TB; 20,428 (36%) received food support. The rate of treatment success was 84% amongst people with TB that received food support and 85% amongst those that didn't. In multivariable analysis, food support was not significantly associated with increased odds of treatment success in people with TB ($P=0.46$). Being HIV positive, and having a BMI < 16 were associated with adverse treatment outcomes ($p<0.001$). The association between food support and TB treatment success was modified by region of treatment ($p=0.002$), and HIV coinfection ($p=0.03$).

Conclusions: Therapeutic caloric food support is associated with increased likelihood of TB treatment success in some regions of Kenya. Pragmatic evaluation of national social protection measures for people with TB should complement experimental randomised evaluations.

SOA05-1045-25 Application of nursing assessment and management job aid on patients' side effects in MDR-TB treatment in China

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Background: Patients on treatment for drug-resistant tuberculosis face many challenges, mostly notably difficult side effects may impact the patient's quality of life. Nurses are often the first to hear of a patient's complaint of side effects during MDR-TB treatment. A job aid was developed, by nurses with clinical experience, in response to requests from nurses for additional resources to address side effects to MDR-TB medications.

Methods: This job aid was designed to help nurses identify symptoms of side effects, assess for severity and intervene appropriately to minimize patient discomfort. The job aid was translated into Chinese. Fifty-six nurses from six TB hospitals in China used the tool while providing care to MDR-TB patients in their clinical practice. They completed an online evaluation questionnaire on the job aid.

Results: Thirty-three (57.1%) nurses worked with MDR-TB patients for more than five years. Most of them 33 (58.9%) care for more than five MDR-TB patients per week on average. Fifty-two nurses reported on patient side effects. The most common side effects reported were nausea/vomiting 28 (53.8%), allergy/rash nine (17.3%), abdominal pain seven (13.5%), insomnia six (11.5%) and fatigue five (9.6%). Patients symptoms were relieved after receiving nursing interventions based on the job aid. Fifty (87.7%) nurses reported that the amount of information of the job aid was enough. It was convenient and easy to use in a clinical setting. Percentage of nurses who were confident or very confident to help MDR-TB patients with side effects increased from 29 (47.6%) to 51 (89.4%) after using the job aid.

Conclusions: The nursing assessment and management job aid on patients' side effects in MDR-TB treatment is suitable for clinical settings. It is recommended to expand the implementation of the job aid in other settings to diminish patient discomfort and improve treatment adherence.

SOA05-1046-25 Beyond routine treatment: person-centric home-based care and support for people with drug-resistant TB

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Background and challenges to implementation: Long duration treatment for DR-TB is fraught with treatment adherence challenges resulting in high loss-to-follow-up and low success rate, as low as a mere 50%. At least in part, this could be attributed to inability of health system to go beyond delivery of treatment and address the larger social determinants of disease.

Intervention or response: With support from Else Kröner-Fresenius-Stiftung (EKFS), German Leprosy and TB Relief Association (GLRA India) initiated treatment adherence project starting January 2017, for people with DR-TB belonging to slums in the catchment areas of four chest hospitals of Delhi. Trained counsellors undertake regular outreach to counsel patients and their families on treatment adherence, infection control practices and identification of adverse drug reactions providing timely, appropriate referral. Home visits also provide opportunity for needs assessment with regards nutrition, socio-economic and home renovation support under the project.

Results and lessons learnt: Currently, 308 people affected with DR-TB have been enrolled in the project; 193 underweight patients are being provided with monthly macro-nutrition support. All families are counselled about importance of natural ventilation; 34 families provided exhaust with ducting and pedestal fans for improved ventilation. 15 families have been provided income generation support and 22 families have been enrolled in vocational training. Monthly patient-provider and peer group meetings are held at chest clinics to discuss issues and challenges for better treatment outcomes. The project has reported 8 persons loss-to-follow-up and 18 deaths; while the rest are adherent to treatment as of March 2018.

Conclusions and key recommendations: Poorly ventilated living environments, undernutrition and opportunities for income-generation constitute important factors that may influence treatment outcomes favourably. Initial results of this holistic approach through home-based care have been encouraging, leading to better response to treatment and reduced loss-to-follow up rates. Addressing social determinants of health provides an opportunity to expand the current paradigm of TB care and support by entailing multi-sectoral coordination.

SOA05-1047-25 Comprehensive patient support as part of the programmatic implementation of new drugs and regimens in Kyrgyz Republic

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Background and challenges to implementation: One of the main reasons of poor outcomes of drug resistant tuberculosis (DR-TB) treatment is the high number of patients who are lost to follow up (LTFU). Socio-economic challenges, low patient education and awareness of TB, history of unsuccessful treatment of TB in the past, adverse drug reactions, stigma and discrimination are factors which significantly reduce adherence to treatment of DR-TB patients.

Intervention or response: The USAID Challenge TB Project (CTB) implemented by KNCV introduced a novel patient-friendly support model as part of the programmatic implementation of new drugs and regimens (ND&R) for DR-TB. It starts with patients' needs assessment, evaluation of risk factors for poor adherence, counselling and education backed up with TB information files, peer support, patient friendly treatment delivery by treatment supporters and video observed treatment when needed. To ensure sustainability of the model, the capacity of health care workers is developed through on-job trainings and joint active case finding activities, local non-governmental organizations are involved in routine care.

Results and lessons learnt: From January to June 2017, 156 DR-TB patients were enrolled on ND&Rs. The preliminary results show a decrease in LTFU from 14% (41/286) in six months of 2016 (standard regimen) to 7% (11/156) in six months of 2017 (ND&R). Four out of 11 patients LTFU in this period restarted DR-TB treatment as a result of counselling by case managers.

Conclusions and key recommendations: The patient-centered approach was appreciated by patients and professionals and helped to reduce LTFU in pilot sites, and therefore, it began to be applied throughout the country for patients on ND&R. The patient-friendly support model will be recommended for implementation for all TB patients by the national TB program.

SOA05-1048-25 Implementing a comprehensive patient support system for drug-resistant TB patients diagnosed in the private sector in Mumbai, India

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Background and challenges to implementation: Poor outcomes among drug-resistant tuberculosis (DR-TB) patients can be attributed to long duration of treatment, side effects, poor nutrition, lack of knowledge and treatment costs among many others. PATH is collaborating with the Mumbai Municipal Corporation to link privately diagnosed DR-TB patients to the public sector, in addition to supporting their treatment adherence.

Intervention or response: DR-TB patients from the private sector are linked to the public sector to initiate treatment and are supported by a comprehensive system encompassing:

- *Patient/family counseling.* Treatment coordinators counsel patients on treatment initiation, adherence, and adverse drug reactions. Patients are regularly followed up and encouraged to contact their treatment coordinator in the case of emergency.
- *Self-monitoring tool.* Patients are urged to complete a daily adherence chart to ensure self-monitoring and improve compliance.
- *Peer group support.* Upon culture conversion, patients are invited to peer group meetings to share their experiences and motivate others.
- *Reminder messages.* Daily text messages are sent to patients to motivate them to take their medicines.
- *Nutritional support.* Protein powder and multigrain flour are provided throughout treatment.
- *Socio economic support.* Eligible patients are enrolled in the social support systems of both government social schemes and private organizations.

Results and lessons learnt: In the first year, 1,071 patients were enrolled in the comprehensive patient support system model; 888 (83%) are continuing with their treatment and receiving support through regular follow ups and text messages, 86 (8%) migrated out of the project area, 64 (6%) died, and 32 (3%) interrupted treatment. Among total 888 patients continuing on treatment, 497 (56%) have received nutritional support and 257 (29%) have been linked to socio economic support.

Conclusions and key recommendations: The comprehensive patient support system is essential for DR-TB treatment retention and needs to be scaled up to improve the patient adherence to treatment.



[Comprehensive model for DRTB patient support system]

SOA05-1049-25 Strengthening the patient-centred care of economically stricken patients through financial support in-order to accelerate all TB case finding: a BRAC experience

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Background and challenges to implementation: Bangladesh is one of the world's most densely populated countries, with a majority of its population in the poor socio economic status and diagnosis of smear negative pulmonary (NSN) and extra pulmonary (EP) TB is expensive. BRAC in collaboration with National Tuberculosis Control Programme (NTP) has been implementing the TB control programme in Bangladesh for over two decades. Since its inception, the programme has been evolving and identifying implementation gaps and adapting the most feasible solution for case detection and treatment by reducing the financial burden of poor patients.

Intervention or response: Since 2013, BRAC began to provide financial support to economically strained presumptive cases with special attention to child and MDR cases. The financial support covered cost of transportation and diagnostic investigations. From 2013 to 2017, the number of financial support disbursed and its beneficiaries were recorded to analyze if this intervention had any significant impact on case notification.

Results and lessons learnt: In 2017, 91,740 individuals received support for diagnosis (excluding MDR TB presumptive) and 22,394 were diagnosed as confirmed. In 2011 and 2012, the numbers of NSN were 10,608 and 13,481, and the numbers of new EP TB were 13,011 and 15,209, respectively. The amount of both NSN and EP

nearly doubled in 2017, and stood at 31,453 for NSN and 24,220 for EP. A significant increase in case notification was observed in BRAC administered areas since the introduction of financial support in 2013. Notification rates leaped from 111 per 100,000 populations in 2012 to 173 per 100,000 populations in 2017.

Conclusions and key recommendations: In low income and high TB burdened countries like Bangladesh, planned and effective utilization of resources, especially allocated for presumptive TB who are financially stricken can improve the identification of missing cases, contribute to successful treatment rates and ultimately minimize transmission.

SOA05-1050-25 Building and protecting mutual trust between TB patients and their providers to promote adherence and retention in care: a qualitative study

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Background: Despite gradual improvements in treatment for tuberculosis (TB), patient losses to follow-up and poor retention-in-care are a growing concern amidst increasing rates of drug-resistance in Cape Town, South Africa. This study, guided by a constructivist grounded theory methodology, explores the role of patient-provider trust in TB treatment, and its relationship with often lengthy treatment journeys, and patient outcomes.

Methods: Between Dec. 2015 and May 2017, in-depth and focus group interviews were conducted with 31 adult (drug-susceptible or drug-resistant) TB patients and 36 health care providers, including TB nurses and doctors, private doctors, and traditional healers.

Results: Three main processes emerged that seem to influence patient-provider trust and patient outcomes. First, there was a marked absence of a baseline level of trust. Thus, an initial stage of building and establishing reciprocal trust was crucial, particularly during the first few patient-provider encounters. This involved patients adhering to provider recommendations and treatment protocols, and providers demonstrating empathy and compassion for patients' individual circumstances. Providers could achieve this through simple gestures such as positive greetings on patient arrival, and more concretely by actively listening, and addressing patients' questions and concerns in an honest, sincere fashion. Second, the manner by which patients and their providers dealt with emergent adherence barriers could quickly encourage or erode mutual trust. This was contingent on a baseline level of trust, without which patients were less forthcoming about their problems, and conversely, providers

were less available to support patients in overcoming those problems. Third, the reconstruction of trust following its erosion due to any patient, or provider, error, proved to be difficult, especially after a patient lost the trust of a provider, which could limit the patient's access to treatment options and social protection.

Conclusions: Future strategies to improve patient retention-in-care and patient outcomes should focus on establishing trust early-on in treatment.

SOA05-1051-25 A supportive care package for drug-resistant tuberculosis reduces loss to follow-up in Yichang City, China

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Background and challenges to implementation: Treatment for multidrug-resistant tuberculosis (MDR-TB) requires 18-23 months of ambulatory care. In China, many MDR-TB patients are loss-to-follow-up (LTFU) during this period. Supportive services to address patients' educational, physical, psychosocial and financial needs may improve treatment completion. As part of a National Action Plan pilot study, the USAID Control and Prevention of Tuberculosis (CAP-TB) Project, in collaboration with the local TB hospital, the Center for Disease Control (CDC) of China, and communities, piloted a comprehensive supportive care package for MDR-TB patients in Yichang City.

Intervention or response: Through a rapid system assessment, CAP-TB identified priority pilot interventions for the package: an individualized care plan developed with and for patients; face-to-face and online education and counseling for patients and their families provided by nurses and peer counselors; comprehensive case management software; and community-based care. The project established working groups to define roles for providers and routinely solve problems that arose. CAP-TB also provided intensive training on care and counseling and ongoing support to implementing staff.

Results and lessons learnt: During an eight-month pilot, 43 patients who had been on MDR-TB treatment for at least six months received the care package. Following the pilot, 41 (95%) patients were still on treatment, one failed treatment, and one died. Among those still on treatment, 20 had completed the six-month intensive phase and 21 had completed half of the 24-month treatment.

This low LTFU rate was achieved despite patients needing to pay more for their medical care compared to a 2015 cohort of 28 patients that had 90% of their treatment costs covered by a previous project and medical insurance, yet had a LTFU rate of 21% at six months.

Conclusions and key recommendations: A supportive care package to MDR-TB patients can retain patients in care and reduce LTFU. Working groups are instrumental to strengthen multi-sectoral collaboration for continuity of care.

SOA05-1052-25 Interventions to improve retention in care among patients with drug-resistant tuberculosis: a systematic review

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Background: Lost to follow-up (LTFU) rates during treatment for drug-resistant TB (DR-TB) remains high at 15% globally. In order to inform strategies to improve retention-in-care, we conducted a systematic review to investigate the effectiveness of different interventions to reduce LTFU during DR-TB treatment.

Methods: We searched MEDLINE, EMBASE, ISI-Web of Science, Scopus, PsychInfo, Global Health, Social Work abstracts, and Cochrane CENTRAL, for studies published between Jan. 2000 and Dec. 2017, which evaluated health services interventions targeting patients with DR-TB that included *at least* a psychosocial, educational, nutritional or economic component. We estimated point estimates and 95% confidence intervals (CI) of the proportion LTFU. We assessed study quality, investigated study heterogeneity (I^2) using subgroup analyses, and pooled estimates using an exact binomial likelihood approach including a random effect, to compare the effectiveness of different patient support strategies.

Results: Of 5911 identified studies, we included 23 observational and 2 quasi-experimental studies, which included 31 DR-TB patient cohorts. Cohorts that received any form of psychosocial or materials support had lower LTFU rates than those that received standard care. Restricting analyses to cohorts that received daily directly observed therapy (DOT) throughout treatment ($n=24$), we found access to psychosocial support *throughout* treatment - via counselling sessions or home visits - was associated with lower LTFU rates compared to when support was provided through a limited number of visits, with pooled proportions LTFU of 8.4% (4.0-16.7%) and 20.5% (15.2 - 27.0%), respectively.

Conclusions: Our review suggests psychosocial support should be provided throughout DR-TB treatment, rather than only during the intensive phase. Future studies should explore the potential of removing the burden of DOT on patients and health care systems, particularly during the continuation phase of DR-TB treatment, by

comparing retention rates under DOT or no DOT, while providing psychosocial support throughout treatment through counselling and home visits.

SOA05-1053-25 Finding the missing cases of TB in Kenya: translating knowledge to action

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Background: Kenya has recorded a decline in TB case-notification since 2007. Kenya's Prevalence survey (2016) however showed that approximately 40% of TB cases are missed, while three quarters of people with TB symptoms seek care in health facilities, but are not diagnosed. TB patients visit a facility up to five times before a TB diagnosis is made. Facility-based case finding is underpinned in the first pillar of the End TB strategy, on integrated, patient centered care that ensures early TB screening becomes a routine activity conducted in all service delivery points (SDPs).

Methods: ACF was implemented from September 2016 to December 2017 in 13 county referral hospitals. Key approaches included baseline assessments, sensitizing county Health Management Teams on leadership for TB case finding, building capacity of health care workers on symptomatic screening, strengthening lab capacity to handle increased workload and turnaround time, and availing monitoring tools. HCWs symptomatically screened all patients visiting facility SDPs regardless of presenting symptoms.

Results: The 13 county hospitals recorded an increase in case finding by 108% (26% - 422%, median 95%) compared to 2016. This was despite industrial action by health care workers at different times in 2017. Out-patient and inpatient departments recorded the highest yield in case finding. Additionally, success in these 13 facilities, resulted in a knock on effect resulting in a national increase in TB case finding of 12% in 2017 compared to 2016. This is the first year Kenya has reported an increase in case notification since 2007.

Conclusions: Facility based- case finding is a low lying key intervention in TB case detection by mopping out the missed cases within facilities. Loopholes between diagnosis and linkage to care require sealing for enhanced early diagnosis. Integration and patient-centered services remain necessary in accelerating and sustaining the gains in TB control.

SOA06 Tuberculosis infection: critical advances

SOA06-1054-25 Isoniazid preventive treatment is effective in children and adolescents aged 5-19 years in impoverished Peruvian desert shantytowns

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Background: Tuberculosis is a leading cause of death in children and most cases occur after missed opportunities for prevention. Although guidelines state that preventive treatment (PT) may be given to children and adolescents aged 5-19 years who are contacts of people with tuberculosis, evidence is lacking and uptake is poor. We assessed the programmatic effectiveness of PT among contacts of people with tuberculosis living in desert shantytowns in Callao, Peru.

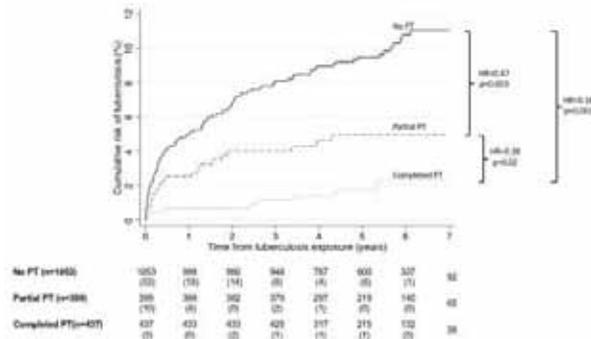
Methods: Between 2007 and 2014 we recruited 1,633 patients with laboratory confirmed, rifampicin-sensitive, pulmonary tuberculosis and identified their 2,646 contacts aged 5-19 years. Contacts were managed by the Peruvian National Tuberculosis Program, which recommended clinical and/or radiological evaluation for tuberculosis; and testing for latent tuberculosis infection with tuberculin prior to initiation of PT. Treatment registers were monitored to collect data on PT and contacts were defined as having completed PT if they took it for at least 20 weeks. Contacts were followed for tuberculosis using treatment registers until July 2016. Hazard ratios (HR) and 95% confidence intervals (95% CI) were calculated to examine the effectiveness of PT for preventing tuberculosis.

Results: Data on PT were available for 1,889/2,646 (71%) contacts. 131/1,889 (6.9%) contacts developed tuberculosis during 9,496 person-years follow up, equating to an incidence of 1,379/100,000 person-years. 836/1,889 (44%) contacts initiated PT and 437/1,889 (23%) completed PT.

Compared to contacts who didn't initiate PT, those who initiated but did not complete treatment had a significantly lower tuberculosis risk (HR=0.47, 95% CI: 0.29-0.77, p=0.003); and those who completed treatment were at further lower risk (HR=0.18, 95% CI: 0.09-0.37, p< 0.001) (Figure).

Excluding cases diagnosed during the first six months following exposure strengthened these findings.

Conclusions: These programmatic data from a middle-income country with a medium tuberculosis incidence and low HIV prevalence support the use and scale-up of PT in children and adolescents aged 5-19 years in similar settings.



[Figure. Cumulative risk of tuberculosis among 1,889 contacts aged 5-19 years of patients with tuberculosis]

SOA06-1055-25 Prevalence of latent tuberculosis infection among household and non-household social contacts of tuberculosis cases and their matched controls in an urban African setting

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Background: In settings with high tuberculosis burden, control programs typically define high-risk contacts as those sharing a household with a person with active disease. The current contact tracing approach focuses on household contacts yet non-household contacts are also at risk of infection and may be important in community transmission of tuberculosis.

Methods: We performed a cross-sectional study of social contacts of tuberculosis patients and their matched controls from Lubaga division of Kampala Capital City Uganda between 2012 and 2016. Diagnosis of latent tuberculosis infection was by tuberculin skin test. We estimated prevalence risk for latent tuberculosis infection by household status among contacts of TB cases and contacts of controls.

Results: Two hundred forty-six index participants (123 Tuberculosis cases and 123 controls) enlisted 2085 social contacts. Of these, 1050 were contacts of TB cases of whom, 410 (39%) were household contacts while 640 (61%) were non-household contacts. One thousand thirty-five of the 2085 were contacts of controls

of whom 225 (22%) were household contacts while 810 (78%) were non-household contacts. Prevalence of latent tuberculosis infection was 56% (95% CI 51.5,61.1) among household contacts and 42.5% (95% CI 38.7, 46.4) among non-household contacts of cases. Among contacts of controls, prevalence of infection was 31.1% (95% CI 25.4,37.4) among household contacts and 40.7% (95% CI 37.4, 44.2) among non-household contacts. The difference in infection between household case and control contacts represents the additional risk associated with being a household member of a TB case. **Conclusions:** Latent tuberculosis infection among non-household contacts of cases was comparable to that of non-household contacts of controls. This could suggest that being a non-household contact of a tuberculosis case does not appear to confer much additional risk beyond the background risk of infection encountered in the community.

SOA06-1056-25 Does movement between treatment centres impact on treatment completion rates for asylum seekers with latent TB infection?

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Background: Cardiff is a pre-dispersal, arrival centre for asylum seekers (AS) to the United Kingdom (UK). Following UK guidelines, the Cardiff Tuberculosis (TB) team screens and treats AS for latent TB infection (LTBI). Over half of AS diagnosed with LTBI do not remain in Cardiff for the treatment duration and are dispersed by UK Visa and Immigration (UKVI), often abruptly. We aimed to investigate whether treatment completion is affected by dispersal away from Cardiff, either before starting or during treatment.

Methods: We completed a retrospective case note analysis of AS offered treatment for LTBI in Cardiff between 1/1/2014 and 31/12/2016. Data were collected on patient demographics, dispersal destination, confirmation of treatment completion and reasons for non-completion. TB teams in the areas to which AS had reportedly been dispersed were contacted by mail and subsequently telephone for details on treatment outcomes.

Results: 264 AS were diagnosed with LTBI over the 3 years. 122 (46%) remained in Cardiff for the duration of treatment, of whom 92% completed. Completion was significantly lower in AS dispersed both prior to starting treatment (69%) and during treatment (71%). Information about 30 dispersed AS was not available from the TB teams: when these missing AS were excluded from the analysis the differences in completion between those

AS remaining in Cardiff and those dispersed either before or during treatment were no longer statistically significant.

Conclusions: Our data highlight difficulties that TB teams face in following-up AS dispersed around England and Wales. There is insufficient evidence that treatment should be delayed in case an AS is subsequently dispersed. Accurately recording the movement of AS is key to confirming completion rates. A more cohesive relationship between the UKVI service and TB teams and a centralised database of AS on treatment for LTBI are two suggestions to improve retention and follow-up.

SOA06-1057-25 Adverse events in adults treated for LTBI with daily rifampin or isoniazid: combined results of phase 2 and phase 3 randomized controlled trials

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Background: The standard latent tuberculosis infection (LTBI) treatment regimen in many settings is nine-months of daily isoniazid (9H). This regimen carries a high-risk of adverse events (AEs), particularly hepatotoxicity, which cause treatment cessation. Four-months of rifampin (4R) is an alternate regimen that is better tolerated. The objective was to identify baseline risk factors for 9H and 4R increasing risk of hepatotoxicity or other AE leading to treatment cessation using the results of two randomized controlled trials.

Methods: Patients receiving at least one dose of therapy were included. AEs were adjudicated by a blinded three-person panel. AEs included were possibly or probably related to the study drug and grade 3-5 in severity. Risk-factors evaluated were baseline age, sex, immune-deficiency, and alanine aminotransferase (ALT) level. Generalized logistic regression adjusted for these risk-factors evaluated the outcome of hepatotoxicity or an AE other than hepatotoxicity in each regimen.

Results: In total, 3417 patients received 9H and 3443 received 4R. Patients receiving 9H (2.2%; 75/3417) compared to 4R (0.9%; 31/3443) were more likely to have any AE causing therapy cessation ($p < 0.001$). Hepatotoxicity in 9H (86.6%; 65/75) and 4R (35.5%; 11/31) was the most common AE. No evaluated risk-factor significantly increased odds of hepatotoxicity, but age ≥ 65 (aOR 6.7; 95% CI 1.7-21.6) increased odds of other AE in patients receiving 4R. In patients receiving 9H, age ≥ 65 (aOR 4.5; 95% CI 1.8-9.7), age 45-64 (aOR 1.8; 95% CI 1.0-3.0), and elevated ALT (aOR 2.9; 95% CI 1.4-5.5) significantly increased odds of hepatotoxicity, while no evaluated risk-factor significantly increased odds of other AE (Table 1).

Covariate	N	Daily Isoniazid		Daily Rifampin	
		aOR Hepato- toxicity (95% CI)	aOR AE Other Than Hepatotox- icity (95% CI)	aOR Hepato- toxicity (95% CI)	aOR AE Other Than Hepatotoxic- ity (95% CI)
Age 45-64 years	1930	1.8 (1.0-3.0)	0.4 (0.1-1.6)	1.4 (0.4-4.5)	2.2 (0.9-5.6)
Age ≥ 65 years	268	4.5 (1.8-9.7)	0.9 (0.1-7.3)	1.2 (0.1-9.6)	6.7 (1.7-21.6)
Immunocom- promised	471	-	0.8 (0.1-6.5)	-	0.8 (0.1-3.4)
Sex: Male	2906	1.3 (0.8-2.1)	0.4 (0.7-1.3)	2.5 (0.2-2.6)	0.8 (0.3-1.9)
Baseline ALT: Elevated	417	2.9 (1.4-5.5)	-	0.8 (0.3-11.2)	-

[Table 1. Results of logistic regression for outcome of hepatotoxicity or other AE]

Conclusions: Hepatotoxicity was the most common AE causing treatment cessation with either treatment, but 4R was much better tolerated. For patients treated with 9H, baseline ALT, in addition to patient age, should be considered when determining AE risk.

SOA06-1058-25 TST results and confirmation by IGRA are highly dependent on the purified protein derivative used

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Background: In low-incidence settings, screening for latent tuberculosis infection (LTBI) is most cost-effective using a tuberculin skin test (TST), and if positive, followed by an interferon gamma release assay (IGRA). Due to stock-outs of purified protein derivative (PPD) from the Statens Serum Institut (SSI), PPD-Tubersol and PPD-Bulbio have been used alternatively since 2015 in the Netherlands.

The study objective was to confirm the user observation that PPD-Bulbio results in more frequent positive inductions with lower IGRA confirmation rates compared to the other PPDs.

Methods: The national TB Information System provided LTBI testing data during 2013-2016. Multivariable logistic regression analyses were used to determine if IGRA-confirmation of a TST-positive result was dependent of the PPD being used controlling for sex, age, incidence of country of origin, and BCG status. The analyses were stratified for contacts, health care workers, and BCG-vaccinated and unvaccinated immigrants.

Results: 49,990 individuals were tested for LTBI, of whom 20,956 by PPD-SSI, 10,382 by PPD-Tubersol and 18,562 by PPD-Bulbio. Of those tested with PPD-Bulbio, 21% had a TST-result of ≥ 5 mm compared to 12% among those tested by PPD-SSI and PPD-Tubersol.

PPD-Bulbio positive TST indurations were statistically significantly less often confirmed with IGRA compared to the other positive PPD results among contacts (PPD-SSI aOR=1.3 [95% CI: 1.1-1.6] and PPD-Tubersol aOR=1.3 [95% CI: 1.1-1.7], $p=0.01$) and BCG-vaccinated immigrants (PPD-SSI aOR=2.4 [95% CI 1.4-4.1], $p=0.007$). Numbers needed to test to detect a positive IGRA among those with a TST < 10mm were high among vaccinated immigrants and health care workers, irrespective of PPD used.

Conclusions: TST-testing with PPD-Bulbio leads to higher TST indurations which are less likely to be confirmed by IGRA among BCG-vaccinated individuals and those with a higher likelihood of infection compared to other PPDs. Cut-off values for the TST-reaction prior to IGRA should be reconsidered for specific target groups.

SOA06-1059-25 Prevalence of latent TB infection in five year old children in Ca Mau, Vietnam

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Background: We have recently shown that the prevalence of the latent TB infection (LTBI) among adults in the general population in Ca Mau, Vietnam is 37% (1). However, the prevalence of LTBI in children is not known. We sought to estimate the prevalence of LTBI in five year old children and, at the same time, to assess the impact of annual population screening for TB among adults on the prevalence of LTBI in children.

1. Marks GB et al. *IJTL*. 2018; 22:246-51.

Methods: We conducted a cluster RCT in Ca Mau. Clusters were randomly selected sub-communes. All adults (aged ≥ 15 years) in the active intervention clusters were screened for TB annually for three years. There was no intervention in control clusters. During the following year (2017), we sought to collect blood for QuantiFERON®-TB Gold Plus (QFT, Qiagen) testing from all children born in 2012 who were living in the study clusters.

Results: There were 1168 eligible children in 60 control clusters, of whom 843 (72.2%) had QFT performed and there were 1329 eligible children in 60 active intervention clusters of whom 821 (61.8%) had a QFT. The median (IQR) number of eligible children per cluster was 21 (13 to 26). There were three "indeterminate" QFT results. The prevalence of positive QFT was 27 (3.3%, 95% CI 2.0% to 4.6%) in the active intervention group and 18 (2.1%, 95% CI 1.3% to 3.0%) in the control group [RR 1.54, 95% CI 0.85 to 2.77, $P = 0.2$].

Conclusions: Despite the high prevalence of LTBI in adults, the prevalence of LTBI is very low in five year old children. It did not differ between those who lived in clusters that had been screened annually for active TB and those that did not.

Funding: Australian National Health and Medical Research Council.

SOA06-1060-25 Latent tuberculosis infection: animated into action. Developing novel health promotion tools with migrant communities for a national screening programme

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Background and challenges to implementation: The systematic screening of migrants for LTBI is a key component of the national TB strategy for England. Early results from a pilot for the national LTBI screening programme found that the uptake of testing was low. We identified the need to improve awareness about LTBI to improve uptake.

Intervention or response: Our collaborative approach brought together clinicians with interests in LTBI screening and the experience of healthcare access amongst migrants, two charities, specialising in health promotion and TB awareness, and Public Health England. The goal was to work with the communities eligible for testing to create health promotion tools about LTBI. We wanted tools that could be found on social media platforms using any device and were accessible to those with limited English. Animation is ideally suited to these objectives.

Through voluntary sector organisations, we ran 5 focus groups with migrants to explore knowledge about LTBI and getting tested (total: 46 participants). The sessions identified themes that formed the basis of a script and storyboard. The production was an interactive process: further interviews with migrants were held to review draft material that informed further development. For example, perceived lack of contact with active TB was identified as a potential barrier and the script was updated to engage with this.

Results and lessons learnt: The outcome is a short animated film (< 3 mins), also available as 3 "bite-size" versions, in 7 languages, formatted for use on smartphones, tablets, computers and televisions and hosted on YouTube. Links can be provided in any communication: SMS, email or letters. It will be broadcast in primary

and secondary care settings with a range of accompanying materials alongside a social media campaign aimed at reaching those eligible for testing.

Conclusions and key recommendations: The impact of the film will be assessed using local and national screening data and viewing figures.



[Figure: still from animated film]

SOA06-1061-25 Contact management of drug-susceptible TB patients in Landhi and Korangi towns in Karachi, Pakistan

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Background: Contacts of TB patient can contract TB infection 65-70% of the time with 5-10% lifetime risk of developing TB. These infected individuals are the seedbeds of future TB.

Methods: A prospective study of systematic contact screening and TB preventive treatment for household contacts of TB patients was conducted from October 2016 to March 2018. TB patients registered at 3 sites that were residents of two towns in Karachi were included in the study. All the patients enrolled for TB treatment were counselled to bring their families screening. Contacts were approached through phone calls and home visits. All contacts were evaluated by doctor clinically and by TB tests (compulsory X-ray, GeneXpert, AFB Smear etc.). Contacts that were diagnosed with TB were linked to TB treatment programs. Contacts in whom TB disease was ruled out were offered TB preventive treatment. A cascade approach with conditional probability calculations was used for evaluation.

Results: Total 2253 index patients with 8,516 household contacts consented to participate and were screened verbally for TB symptoms. 3,736 (44%) contacts were evaluated for TB disease of which 1,725 (46%) contacts were females and 606 (16%) were < 5years. 76 (2%) con-

tacts were diagnosed with TB disease and 2,685 out of 3,657 (73%) were started on TB preventive treatment. Of those started, 1,445 (46%) were females and 388 (14%) were < 5years. Outcomes are available for 1,572 contacts till date of whom 1,101 (70%) completed preventive treatment, 471 (30%) did not complete treatment. Cumulative probability of completing each step of the cascade was 22%.

Indicators	Contacts Eligible for Study N (%)	Contacts Verbally Screened for TB Symptoms N (%)	Contacts Evaluated for TB Disease N (%)	Contacts diagnosed with TB Disease N (%)	Contacts Eligible for TB Preventive Treatment N (%)	Contacts Started on TB Preventive Treatment N (%)	Contacts Completed Preventive Treatment N (%)	Contacts Didn't Complete Preventive Treatment N (%)	Contacts Still on Preventive Treatment N (%)
<5 years	1,472 (14)	1,158 (14)	606 (16)	13 (17)	593 (16)	388 (14)	133 (12)	146 (31)	109 (28)
5-14 years	2,593 (25)	2,187 (26)	1,084 (29)	41 (54)	1,043 (29)	963 (36)	418 (38)	86 (19)	459 (48)
≥15 years	6,396 (61)	5,171 (60)	2,046 (55)	22 (29)	2,021 (55)	1,334 (50)	550 (50)	232 (50)	552 (41)
Total	10,461 (81)	8,516 (81)	3,736 (44)	75 (2)	3,657 (98)	2,685 (74)	1,101 (41)	464 (17)	1,120 (42)

[Table showing the prevention cascade for the household contacts of Drug Susceptible TB patients]

Conclusions: This was the first time where TB preventive treatment for the whole household in Pakistan in a program setting. Results are encouraging for other low-income settings for implementation.

SOA06-1062-25 Yield of repeated tuberculosis screening among HIV patients: implications for tuberculosis preventive therapy

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Background: Botswana is a high TB-HIV burden country with estimated annual incidence of tuberculosis (TB, 326/100,000 and TB-HIV co-infection rate, 60%). In 2012, at 22 HIV clinics, Botswana implemented the

Xpert MTB/RIF intervention to intensify TB case-finding. Routine TB symptom screening followed by a molecular test with high specificity could be used to rapidly identify active cases and those eligible for TB preventive therapy (TPT) among people living with HIV (PLHIV).

Methods: From 08/2012 to 03/2015, PLHIV at antiretroviral therapy (ART) initiation and follow-up visits underwent systematic TB screening using a four-symptom TB screen (any duration of cough, fever, night-sweat, weight-loss) per national HIV care and treatment guidelines. We calculated the yield of baseline and repeated TB symptom screening, assessed associated factors with TB disease and the implications for scale-up of TPT.

Results: A total of 6,041 patients presenting for ART initiation were enrolled and completed 20,463 visits equating to 5,495 person-years of follow-up. Among these, 31% (1864/6041), 7% (407/5815), 5% (280/5514), 4% (210/5079) and 3% (130/4055) were classified as presumptive TB at baseline and each subsequent follow-up visit 1, 2, 3 and 4, respectively. A total of 234 TB cases were diagnosed within four follow-up periods. The proportion of persons with TB disease among presumptive TB cases was 11% (203/1864) at baseline and 2% (9/407), 3% (8/280), 3% (6/210) and 6% (8/130) at subsequent follow-up visits. At baseline, the rate of TB was 3360/100,000 patients and those with CD4 < 200 (aOR 1.5, p=0.019), BMI < 18.5 (aOR=1.5, p=0.040), cough (aOR=4.2, p=< 0.001) or fever (aOR=2.0, < 0.001) had a higher odds of TB.

Conclusions: Most cases of presumptive and confirmed TB were identified at ART initiation. A high proportion of PLHIV were asymptomatic for TB, especially at follow-up visits. Missed opportunities for TPT further compromises TB prevention efforts among PLHIV.

scribe access, administration, and adverse events of IPT in HHCC in three Colombian cities.

Methods: Prospective cohort study of HHCC (under 5 years) of confirmed pulmonary TB patients from Medellín, Bello, and Itagüí, who underwent a clinical, radiological, immunological and microbiological evaluation to rule out active TB. A TST ≥ 5 mm and/or Quantiferon-TB Gold positive defined a HHCC Mtb-infected. HHCC were referred to the Health System for active TB treatment or IPT as indicated.

Results: From March 2015 to June 2016, 292 HHCC were assessed. Eleven had active TB and 259 were eligible for IPT, of which 214 (82.6%) started IPT. Reasons for not starting IPT included primary care physician (PCP) decision (46.7%), parents/guardian decision (11.1%), loss of follow-up (11.1%), second TST interpreted as negative (8.9%), Health System barriers, moved out of the city, or being a contact of a MDR-TB case (20.0%). PCP ordered IPT in 130 cases (60%), a pediatrician in 38 (17.5%), and ID specialist in 17 (7.8%). IPT was stopped (≥ 3 months) in 89 children (41.6%), reasons included wrong instruction from health care providers (23.6%), parents/guardian decision (22.5%), a second TST interpreted as negative (12.4%), adverse events (10.1%). Twenty-four (11.1%) children had at least one adverse event, being gastrointestinal symptoms the most common (9%). There was no evidence of hepatic toxicity in 126 children that had an aspartate-aminotransferase result.

Conclusions: There is a gap between HHCC eligible for IPT and the actual number who access and complete it. Main reasons are Health System barriers, PCP decision and parents/guardian decision. Adverse events are not the main cause for treatment discontinuation. A more comprehensive approach for IPT is needed to achieve better outcomes.

SOA06-1063-25 Access to isoniazid preventive treatment of tuberculosis household contact children in three Colombian cities

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Background: Isoniazid Preventive Treatment (IPT) decreases the risk of tuberculosis (TB) in Mtb-infected household contact children (HHCC), but it has been a challenging strategy worldwide. This study aims to de-

SOA07 From local to global in tuberculosis care and prevention

SOA07-1064-25 *Mycobacterium tuberculosis* lineages in Ethiopia

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Background: There are seven lineages of *Mycobacterium tuberculosis* complex in the world and each circulates in certain geographical areas. The purpose of our study was to assess strain diversity and lineages among patients with smear positive pulmonary TB in Ethiopia.

Methods: *M. tuberculosis* isolates were collected at 32 sites in Ethiopia as part of an anti-TB drug-resistance country survey conducted between December 2011 and June 2013. Spoligotyping was performed for all isolates. The SpolDB4 database was used to generate the octal number. SITVIT WEB was used to assign international shared type (SIT) number and clades.

Results: Spoligotyping was performed on 1579 *M. tuberculosis* isolates; 284 spoligotypes patterns were identified. In 83% (1317/1579) of the isolates, the spoligotype pattern matched with existing SIT data. The overall diversity of the strains was 18%. Nearly half (47%) of the TB cases were reported from 7 sites, and strain diversity at these sites ranged from 35% to 51%. The three most frequent strains were SIT149 (15.6%), SIT53 (10.2%) and SIT25 (6.7%). The frequent strains in each sites varied and SIT149, SIT53 and SIT25 were the frequent strains in 25, 21 and 15 sites respectively. A total of 32 clades were identified. The five most frequent clades were CAS1-Delhi (23%), T3-ETH (19%), T1 (14%), H3 (8%) and T3 (8%). Clade and SIT information indicated the presence of lineages 1, 2, 3, 4 and 7. There were 19 *M. tuberculosis* isolates that were in lineage 7; these had shared type number 910 and 1729.

Conclusions: Our findings demonstrate at least 5 of 7 lineages are circulating in Ethiopia. A wide range of strain diversity was seen among sites that report large number of TB cases suggestion transmission of TB varied from site to site.

SOA07-1065-25 Geographic variation in strains of the *Mycobacterium tuberculosis* complex and implications for tuberculosis epidemiology

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Background: The host, microbial, and environmental factors that contribute to variation in tuberculosis (TB) disease are incompletely understood. Recent evidence suggests that one driver of geographic variation in TB disease is the local ecology of mycobacterial genotypes or strains. The aim of this project was to (1) map the global distribution and virulence of mycobacterial strains that cause TB disease, and (2) explore whether geographic strain variation can be used to improve global models of TB burden.

Methods: We performed a systematic review of literature indexed in PubMed and Scopus to identify human TB molecular epidemiology that used population-based sampling methods or tested all culture-positive TB cases in a given location and time period. We identified 238 human TB molecular epidemiology studies for inclusion in the study, as well as two unpublished studies from Mexico and Panama, representing over 200,000 bacterial isolates collected over 27 years in 85 countries. Of these studies, 31 also reported transmission chains or genetic clustering associated with genotypes.

Results: A map of genotypes extracted from these studies highlighted the global spread of Euro-American and East-Asian strains and geographic isolation of West African strains. These data also suggested that Euro-American and East-Asian strains may be increasing in prevalence, while Indo-Oceanic strains may be decreasing in prevalence, relative to other strains globally. A meta-analysis of the 31 studies that reported transmission chains revealed that East Asian strains may be associated with increased risk of transmission, while West African strains may be associated with reduced risk of transmission, compared with Euro-American strains.

Conclusions: We propose that a better understanding of transmission and other clinical characteristics could provide epidemiologists with tools to improve estimates of geographic variation in TB, and we conclude by providing an example of how this information could be incorporated into models of TB incidence, prevalence, and mortality.

SOA07-1066-25 Epidemiologic considerations in age-structured models of TB transmission

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Background: Mathematical models of TB transmission often categorise the population as either “children” aged 0-14 years or “adults” aged ≥ 15 years. In reality, values for key parameters including contact rates, risks of exposure, risk of progression, and risk of developing infectious TB change markedly throughout the life course. For models attempting to estimate the impact of age-targeted interventions, especially novel vaccines, this oversimplification may introduce bias.

Methods: This talk will review what is known about age-related changes in key parameters in different epidemic scenarios relevant to TB models, and compare the output of an appropriately parameterised compartmental model with seven age groups (0-4, 5-9, 10-14, 15-19, 20-24, 25-49 and 50+) to a model treating age as dichotomous (< 15 vs. ≥ 15 years). The models were used to assess the impact of a vaccination program targeted 10-14 year olds, 15-19 year olds or 20-24 year olds in a hypothetical high-transmission setting.

Results: By accounting for age-related changes in key parameters, it can be shown that a) high intra-group contact rates combined with moderate risks of progression after infection result in adolescents making a disproportionate contribution to TB transmission compared to children or adults and b) modelling age dichotomously over-estimates the number needed to vaccinate in adolescent age groups. In the scenario modelled, the most efficient age-group for vaccination is the 15-19 year old age group.

Conclusions: Age-related changes in key parameters are a major considerations for mathematical models attempting to estimate the impact of novel vaccines. If adolescents are to be considered as a target group for any vaccines which eventually reach the market, TB modellers will need to account for the unique epidemiology of TB in this age group.

SOA07-1067-25 Differential risk of progression to tuberculosis disease in men and women: findings from 9 cohort studies involving 21033 individuals with tuberculosis infection

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Background: Tuberculosis is substantially more common among men than women in all regions of the world; however, reasons for this are poorly understood. Evidence from prevalence surveys indicates that health-care-seeking or notification biases do not explain these disparities. We sought to understand whether men have higher rates of progression to tuberculosis disease conditional upon infection.

Methods: We used individual-level data from cohort studies of individuals with either a positive interferon gamma release assay or tuberculin skin test. We evaluated the risk of progressive disease among men and women with tuberculosis infection over the period of follow-up in each study and calculated relative risks through Poisson regression models. We then pooled estimates using fixed effects and assessed between-study heterogeneity.

Results: Nine cohort studies from seven countries involving 21033 participants with tuberculosis infection were included. In total, 412 (2.0%) progressed from tuberculosis infection to disease. Men had increased risk of disease progression in all studies except one study from The Gambia [Relative Risk (RR), 1.0, 95% Confidence Interval (CI), 0.3-32.9]. Three studies found a statistically significantly higher risk among men compared with women. There was no between-study heterogeneity ($I^2=0\%$). We found a fixed-effects relative risk of progressive disease of 1.68 (95% CI, 1.38-2.05; $P < 0.0001$). The risk remained elevated after stratifying cohorts by study design, the use of a Quantiferon or tuberculin skin test, or the setting. A leave-one-out sensitivity analysis found that the influence of any one study had little effect on pooled estimates (relative risk ranging from 1.6 to 1.8, all $P < 0.0001$).

Conclusions: Men may have more tuberculosis because they are more likely than women to progress to disease once infected. Further work is necessary to investigate whether this elevated risk is due to immunological differences or differences in levels of smoking, alcohol use, repeated exposure, HIV, or diabetes.

SOA07-1068-25 Early clearance of *Mycobacterium tuberculosis*: the INFECT case contact cohort study in Indonesia

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Background: Early clearance of *M. tuberculosis* is the eradication of infection before an adaptive immune response develops. We used a tuberculosis case contact study to identify host factors associated with early clearance.

Methods: Indonesian household contacts of sputum smear positive TB cases were recruited. An Interferon Gamma Release Assay (IGRA) test was performed at baseline and 14 weeks. Early clearance was defined as a persistently negative IGRA. Contacts were characterised with respect to clinical characteristics, index case exposure and disease phenotype. These were modelled for association with a positive IGRA test at each time point.

Characteristic	Persistently IGRA negative N (%) n=317	IGRA converter N (%) n=116	RR	95% CI	P	ARR	95% CI	P
BCG vaccination (Yes vs No)	276 (87)	86 (74)	0.56	0.40 - 0.79	0.001	0.55	0.40 - 0.76	<0.001
Smoking (Current vs Non smoker)	76 (24)	37 (32)	1.34	0.97 - 1.85	0.074	1.66	1.10 - 2.49	0.015
Pre-diabetes vs No diabetes	14 (4)	7 (6)	1.28	0.67 - 2.42	0.451	1.27	0.59 - 2.76	0.542
Diabetes vs No diabetes	11 (3)	6 (5)	1.35	0.69 - 2.65	0.378	1.90	1.02 - 3.51	0.042

[Assessment of risk factors for IGRA conversion in household contacts (n=433)]

Results: From 462 TB patients, 1347 household contacts (median age 27.9 years) were recruited. At baseline, 780 (57.9%) had a positive IGRA, 490 (36.3%) were IGRA negative. After 14 weeks 116/445 (26.1%) of initially IGRA negative contacts were IGRA converters and 317 (71.2%; 25.0% of all contacts) remained persistently IGRA negative. After taking into account measures of exposure, and other possible confounders, BCG vac-

ination was associated with a reduced risk (relative risk [RR]=0.90; 95% CI: 0.83 - 0.99; P=0.029) of a positive IGRA at baseline and a strongly reduced risk of IGRA conversion (RR=0.55; 95% CI: 0.40 - 0.76; P< 0.001). IGRA conversion was associated with diabetes mellitus (RR=1.90; 95% CI: 1.02 - 3.51; P=0.042) and smoking (RR=1.66; 95% CI 1.10-2.49; P=0.015).

Conclusions: Early clearance, found in a quarter of heavily exposed TB case contacts, is strongly associated with BCG vaccination. Further studies of the underlying innate immune mechanisms will inform strategies for enhanced protection against *M. tuberculosis* infection.

SOA07-1069-25 Finding gaps in TB notifications: spatial analysis of geographical patterns of TB notifications, associations with TB program efforts and social determinants of TB risk

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Background: TB case detection persistently remains too low globally to effectively curb the epidemic. In order to improve case detection a better countries should tailor their intervention to local need rather than imposing a one size fits all policy. In order to inform local interventions, a better understanding of the geographical variation of TB notification rates is required. Therefore, this study aims to assess the spatial variation of subnational TB case notification rates (CNR) and to identify factors underlying the spatial variation in Bangladesh, Nepal and Pakistan.

Methods: Aggregated subnational TB notification and programmatic data were provided by the TB programs of Bangladesh, Nepal and Pakistan. These data were combined with publicly available data on known TB risk factors and key population. A spatial cluster analysis was performed to identify subnational patterns of TB CNRs. A multivariable linear regression model was fitted for each country using case notification rate as the dependent variable. The residuals of the multivariate models were tested for unexplained spatial autocorrelation and adjusted for by fitting a simultaneous autoregressive model (SAR).

Results: Spatial clustering of TB CNRs was observed in all countries. Most of the geographical variation in TB notification rates was explained by programmatic indicators and access to healthcare such as proportion of bacteriologically confirmed cases, test positivity rate, testing rate and vaccination coverage and to a lesser extent by indicators of TB burden such as migrant distribution and sex ratio.

Conclusions: Subnational TB CNRs are more likely reflective of TB program efforts and access to healthcare than TB burden. NTP's cannot rely on CNR to assess burden without considering key factors as shown in this study. The use of spatial statistics in TB epidemiology could contribute to identifying areas with low case detection.

SOA07-1070-25 Pre-treatment lost to follow up tuberculosis patients at four health facilities, Chongwe district, Zambia, 2017: a retrospective cohort study

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Background: Tuberculosis (TB) has remained one of the leading causes of death in Zambia with about 40,000 cases being diagnosed annually. However, over 22,000 cases are estimated to be missed. Many of those missed will continue infecting others in communities. Some TB patients may be diagnosed but may not be linked to treatment services (pre-treatment lost to follow up). The magnitude of pre-treatment lost to follow up TB patients has not been explored in Zambia. We conducted a review of pre-treatment lost to follow up TB patients at four diagnostic facilities in Chongwe district, Zambia.

Methods: All bacteriologically confirmed TB patients either by sputum AFB microscopy or molecular method (Xpert MTB/RIF, Cepheid Inc., CA, USA) between 1st January and 31st December 2017 were enrolled. We extracted data from the four TB laboratory registers and cross-matched the names to the TB diagnostic registers where all confirmed TB patients are routinely registered. We further examined linkage to TB treatment units by cross-matching confirmed TB patients in the TB laboratory registers and the TB treatment registers.

Results: Two hundred and seventeen (217) bacteriologically confirmed TB patients were found in the TB laboratory registers of which 145(67%) were males and 7(3 %) were Children. Some 177 (81%) patients were diagnosed using the Xpert MTB/RIF while the rest were with sputum microscopy. A total of 35(16 %) had not been notified to NTP while 71(33 %) were not linked to treatment.

Conclusions: About one third of TB patients were not linked to treatment and 16% were not notified to NTP, who could potentially transmit TB to others thereby hindering efforts to eliminate TB as a public health challenge. World Health Organization and NTP should consider including pre-treatment lost to follow up patients in routine monitoring and evaluation.

SOA07-1071-25 Combining active case finding approaches results in better yields in finding missing TB patients in Zimbabwe

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Background and challenges to implementation: Zimbabwe is still missing about 30 percent of its TB patients. Two main outreach approaches are being implemented. to find the missing patients in the country. These are mainly the active case finding using fully equipped trucks and the door to door approach targeted at high risk groups and settings.

Intervention or response: Data from Mutasa and Chimanimani districts in Manicaland province for the period between January and June 2017 were analysed. Data from January to March included the two approached and data from April to June was for the door to door approach.

Results and lessons learnt: In Mutasa District the combined approach screened 9456 people and obtained 4599 presumptive patients of which 48 TB patients (18 bacteriologically confirmed) were diagnosed and initiated on treatment. The door to door approach screened 7 734 people and identified 2323 presumptive cases of which 16 (16 bacteriologically confirmed) TB patients were diagnosed and initiated on treatment.

In Chimanimani District the combined approach screened 9690 people and obtained 1953 presumptive patients of which 49 TB patients (12 bacteriologically confirmed) were diagnosed and initiated on treatment. The door to door approach screened 5263 people and identified 875 presumptive patients of which 8 (7 bacteriologically confirmed) TB patients were diagnosed and initiated on treatment.

Conclusions and key recommendations: There is much better yields in terms of the number of people screened, presumed patients and the identified TB patients when the two approaches to active case finding are implemented concurrently compared to using a single approach. Recommendations have been made to ensure that these two approaches are implemented together in each district at a given time for effective active case finding for the missing TB patients in Zimbabwe.

SOA07-1072-25 Active case-finding for tuberculosis through community-based contact screening in Pakistan: yield and additionality

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Background: Pakistan is among the high burden country for drug susceptible and drug resistance TB and contributes 43% of the disease towards the eastern-Mediterranean region of World Health Organization. There is a need to enhance TB case finding to meet SDG targets.

Methods: Study carried out within household and a diameter of 100m around each index case using GIS Technology. Household contacts, i.e. those normally resident or sharing the same airspace, were verbally screened initially, following by a widening circle screening of close community contacts. The coordinates of the household were entered into a GIS database via a mobile phone link. There were 50 field officers trained for this project. All the TB presumptive found from the screening were subjected to smear microscopy; those found positive are registered. However, those found negative are subject to Gene Xpert. Gene Xpert positive cases with or without rifampicin resistance were also registered for treatment at the respective sites. TB presumptive aged less than 15 years identified were referred to child TB managing sites for diagnosis and treatment and had followed up.

Results: A total of 783 043 contacts were screened for tuberculosis: 23741(3.0%) presumptive TB patients were identified of whom, 4710 (19.8%) all forms and 4084(17.2%) bacteriologically confirmed TB patients were detected. The contribution of Xpert MTB/RIF to bacteriologically confirmed TB patients was 7.6%. The yield among investigated presumptive child TB patients was 5.1%. The overall yield of all forms TB patients among investigated was 22.3% among household and 19.1% in close community. The intervention contributed an increase of case detection of bacteriologically confirmed tuberculosis by 6.8% and all forms TB patients by 7.9%.

Conclusions: Contact investigation in closed community not only detected additional TB patients but also increased TB case detection. However, further long term assessments and cost effectiveness studies are required before national scale-up.

SOA07-1073-25 Time to culture conversion, identifying independent modifiable risk factors in Indian patients

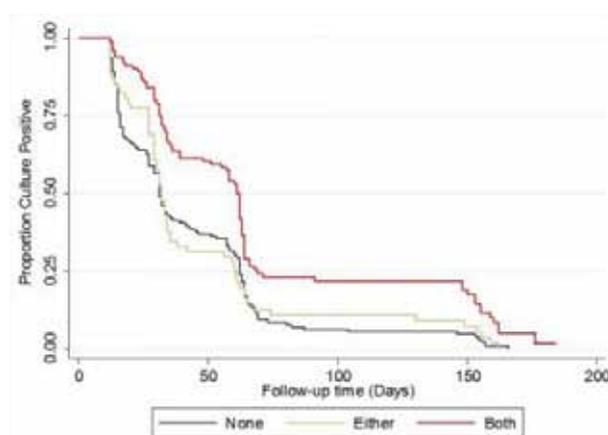
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Background: Time to culture conversion (TCC) may be associated with adverse TB treatment outcomes. We sought to assess factors associated with delayed time to culture conversion in pulmonary tuberculosis (PTB) cases on standard multi-drug therapy.

Methods: We enrolled adults (>18 years) with new culture-confirmed drug-sensitive PTB within 7 days of treatment initiation in Pune and Chennai, India. Serial cultures on Lowenstein-Jensen medium were performed at pre-specified visits during treatment. Differences in the median days to culture conversion were compared by participant characteristics at enrolment using log-rank test. Multivariable Cox-regression was used to measure hazard ratios of association between baseline and selected overlapping characteristics, and TCC during treatment.

Results: Of the 330 participants enrolled, 222 (67%) were males, 104 (34%) had ever smoked and consumed alcohol on a regular basis, 50 (16%) consumed only alcohol, 110 (38%) had diabetes and 11 (3%) were HIV co-infected. Median (IQR) age and BMI was 39 (27-50) years and 17.4 (15.7-20.1) kg/m² respectively. Median days to culture conversion was significantly shorter among females compared to males (31 v/s 39; p < 0.001), longer among ever-smokers with alcohol consumption compared to never-smokers and no alcohol use (61 v/s 31; p < 0.001, Figure).



[Kaplan-Meier estimate of Time to Lowenstein-Jensen culture by Smoking and Alcohol consumption]

Age, males, rural residence, smoking and/or alcohol consumption, diabetes, smear positivity, and anemia were associated with longer TCC in an univariable analysis. Since none of the enrolled women reported smoking

and alcohol consumption, in an adjusted model without gender, ever-smoking with alcohol consumption was independently associated with longer TCC [aHR=0.56, 95% CI 0.36-0.87, $p=0.01$]. In addition, middle age (25-40 years $v/s < 25$ years) [aHR=0.60, 95% CI 0.36-0.99, $p=0.04$] was independently associated with TCC.

Conclusions: Men who consume alcohol and smoke had longer TTC, thus may be infectious for a longer duration and have poor response to therapy. Tailored interventions to address smoking and alcohol use are needed.

SOA07-1074-25 Is distance associated with tuberculosis treatment outcomes? A retrospective study in the Kisugu and Wabigalo neighborhoods of Kampala, Uganda

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Background: Lack of geographic access to health facilities has previously been identified as a barrier to initiating and completing TB treatment. We aimed to understand if the distance from home residence to health care facility was a barrier to favorable treatment outcomes in an urban Ugandan population.

Methods: We conducted a retrospective cohort study of all patients initiating TB treatment in 5 health facilities providing TB treatment near Kisugu, Kampala, Uganda, between 2014 and 2016. We abstracted demographic and clinical data from standardized TB treatment registers. Unfavorable treatment outcomes were defined by death during TB treatment, loss to follow up or default, or treatment failure. Multivariable Poisson regression adjusted for age, sex, HIV status, site of disease, diagnostic tests, year of treatment, and facility.

Results: Clinical data was abstracted for 1,922 patients, of whom 377 (19.6%) had unfavorable treatment outcomes. The median distance from residence to facility did not differ among those with favorable (2.50 km) and unfavorable treatment outcomes (2.33 km, $p=0.26$). Relative to those living within 1km of the treating facility, we found no evidence of increased risk of unfavorable treatment outcome among those who lived further away (1-1.9km: relative risk [RR] 1.32, 95% confidence interval [CI] 0.91, 1.93; 2-2.9km: RR 1.00, 95% CI 0.68, 1.47; 3-4.9km: RR 1.13, 95% CI 0.77, 1.67; 5km or more: RR 1.11, 95% CI 0.75, 1.65). Factors associated with unfavorable outcomes included HIV-positive status (RR 1.65, 95% CI 1.27, 2.14), lack of bacteriological confirmation (sputum smear or Xpert MTB/RIF) (RR 1.31, 95% CI 1.01, 1.70), and age 65 or older (RR 2.15, 95% CI 1.19, 3.88).

Conclusions: Distance from home residence to TB treatment facility does not appear to be a barrier to TB treatment completion in this urban sub-Saharan African population. The risk of unfavorable treatment outcome was high and associated with HIV status, lack of bacteriological confirmation, and older age.

SOA07-1075-25 Modeling the role of social distance in TB transmission: implications for interrupting transmission in communities

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Background: TB transmission is determined by an individual's infectiousness throughout the course of disease, combined with the exposure of other susceptible individuals. Most mathematical models of TB transmission assume equal exposure of all susceptible individuals in a community, neglecting the potentially powerful effects of social structures. Close contacts, such as household members, may be exposed so intensely that transmission occurs early in TB disease, while exposure of distant contacts may be more sensitive to the level of infectiousness throughout TB disease. We hypothesized that incorporation of social distance in a mathematical model would increase the importance of incipient and early TB relative to late TB disease, and thus reduce the impact of late-disease interventions such as shorter and more effective treatment regimens.

Methods: We extended an individual-based TB transmission model to incorporate social distance, with differential exposure rates representing social structures (e.g., peers or familial relationships) or physical distances (e.g., household members, neighbors, community members). Under multiple hypothesized social structures and patterns of individual infectiousness, the model was re-calibrated to produce the same TB prevalence trends.

Results: In order for differently structured models to produce the same TB prevalence trends, compensating changes needed to be made in TB transmission parameters. A model with social distance required 30-50% higher rates of TB transmission per person-time of exposure as compared with models without social structure. The impact of treatment on community TB incidence was lower when social structure was accounted for, supporting the hypothesis that social structure increases the proportion of TB transmissions that occur prior to treatment.

Conclusions: Social distance and individual infectiousness interact to shape TB transmission patterns and the impact of interventions at different points in TB disease and treatment. Mathematical modeling results should be tested for robustness to assumptions about individual infectiousness and non-homogeneous exposure of susceptible individuals.

E-POSTER SESSIONS

EP01 Diagnosis, prevalence and molecular epidemiology of bovine and zoonotic tuberculosis

EP01-100-25 Rapid differentiation of *Mycobacterium bovis* by loop mediated isothermal amplification assay

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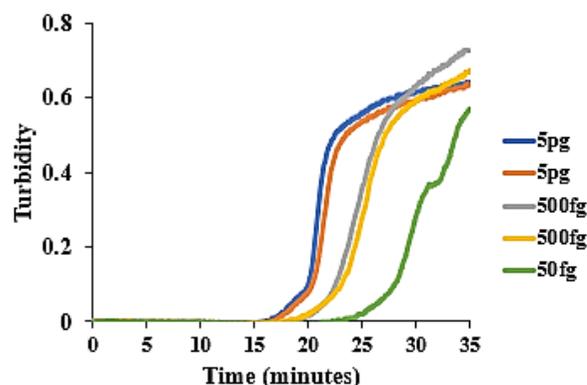
Background: Rapid and accurate differentiation of *Mycobacterium tuberculosis* species is crucial to initiate appropriate antimicrobial therapy and control of tuberculosis (TB). *M. bovis* the causative agent of zoonotic TB in humans poses special challenges for patient treatment and recovery owing to its natural resistance to pyrazinamide, one of the standard first-line anti TB drugs. Furthermore, zoonotic TB is clinically, radiographically and microscopically indistinguishable from TB caused by *M. tuberculosis* hence may result into misdiagnoses and inappropriate treatment of TB patients.

Current differentiation methods are time consuming, expensive and complicated, hence are not easily adopted for use in resource limited areas. Therefore, we are developing a rapid, simple and low-cost differentiation method using loop mediated isothermal amplification (LAMP) that can easily be integrated in resource-limited areas with high TB burden.

Methods: We designed, examined and evaluated more than 50 LAMP primer sets for specific recognition of distinct regions overlaying the deleted 12.7kb fragment region of difference (RD) 4 in all *M. bovis* strains. LAMP reactions were carried out at temperatures between 60 - 66°C for 120 minutes in triplicate to determine the optimum temperature and reproducibility of results. The resulting amplicons were detected by real-time turbidity using a turbidimeter and visual colour change inspection.

Results: The optimum temperature was 66°C for 120 minutes and reaction time could be shortened to 35 minutes. Our LAMP assay had a detection limit of 10 copies of target genomic DNA using a turbidimeter and visual colour change. The assay showed specificity against 54 other bacteria including MTBC.

Conclusions: Our developed LAMP assay successfully differentiated *M. bovis* from *M. tuberculosis*. LAMP is simple, rapid and low-cost hence suitable for use in resource-limited areas. This assay will be evaluated on clinical human sputum samples.



[LAMP assay limit of detection using Loopamp turbidimeter]

EP01-101-25 Prevalence of zoonotic tuberculosis among livestock rearing farmers in rural India

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Background: Livestock such as cattle and buffaloes are reared within household premises particularly in rural India. The absence of regular Tuberculosis (TB) screening among animals hence increases the risk of acquiring zoonotic TB among livestock farmers. The present study assesses the occurrence of active pulmonary TB due to *M. bovis* in livestock rearing farmers and documents their knowledge regarding bovine tuberculosis.

Methods: We conducted a cross-sectional survey of livestock farmers in the year 2015-2016. Farmers from 240 villages in 8 districts of Punjab and Haryana were selected through multi-stage sampling. Information on socio-demographics, knowledge, and practices regarding zoonotic TB was obtained using semi-structured questionnaires. Sputum samples were collected from respondents having a cough lasting >2 weeks. Two sample sputum smear microscopy and polymerase chain reaction (PCR) tests were used to confirm active TB due to *M. bovis*. ² test and logistic regression were used for statistical analysis.

Results: A total of 789 milk producers were surveyed (57% female and 43% male). Nearly two-thirds of the respondents (65%) had primary level education, one-fourth (25%) were illiterate and few (10%) were graduates. Seventy-six livestock farmers (9.6%) were found suffering from active TB due to *M. bovis*. Duration of work as a livestock farmer was significantly associated ($p=0.001$) with the prevalence of zoonotic TB. All diagnosed TB cases were further referred to nearby public health facilities for treatment under revised national TB control programme.

Respondents considered anthrax (44%), rabies (34%), tuberculosis (12%), and ringworm infections (7%) as zoonotic diseases. The knowledge and awareness scores for the animal to human TB transmission were significantly associated with education ($p=0.002$), a recent visit to the veterinarian ($p=0.000$) and animal house hygiene ($p=0.000$).

Conclusions: Zoonotic TB is a significant public health problem among livestock farmers in rural India. Active community engagement and mass education campaigns on zoonotic tuberculosis are needed urgently.

EP01-102-25 Mycobacterial infections in sedentary and trade cattle in Ogun State, Southwestern Nigeria

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Background: Mycobacteria remain a major cause of diseases including bovine and human tuberculosis. Cattle in particular are an important reservoir of *Mycobacterium bovis* causing bovine tuberculosis, a disease of global zoonotic importance.

Methods: Sedentary and trade cattle in Ogun State, southwestern Nigeria were investigated for mycobacterial infections through cultural isolation and molecular techniques.

Results: Mycobacteria were isolated from four (3.5%) of 114 milk samples and 30 (34.9%) of 86 lesions suggestive of TB, respectively collected from nine sedentary cattle herds and 574 trade cattle. Genus typing of the isolates revealed *Mycobacterium tuberculosis* complex, MTC (milk: 0, lesions: 11) and non-tuberculous mycobacteria, NTM (milk: 4, lesion: 19). Further characterization of the MTC using deletion typing showed two *M. tuberculosis* and nine *M. bovis*. Spoligotyping classified the MTC into Latin American Mediterranean (LAM, SIT 61) and a new strain for *M. tuberculosis* as well as SB0944 (3 isolates), one isolate each of SB0300, SB1026, SB1027 and SB1439 and two new strains for *M. bovis*.

Conclusions: The study revealed the presence of *M. tuberculosis*, *M. bovis* and NTM in cattle in Ogun State, southwestern Nigeria. These findings portend serious public health implications considering prevailing risk factors for inter-transmission between cattle and humans such as cohabitation with cattle and consumption of unpasteurized milk in the setting. The need to step up routine surveillance for mycobacterial infections amongst sedentary and trade cattle in Nigeria and other sub-Saharan African countries is advocated.

EP01-103-25 Molecular epidemiology of camel tuberculosis in camels in Northeast Nigeria

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Background: Although, camels serve as sources of food, transportation, work and income in Northern Nigeria, they are also a potential source of zoonotic diseases such as tuberculosis (TB). Camel TB is an important emerging public health problem in sub-Saharan Africa. However, there exist limited epidemiological data on the disease in Nigeria.

Methods: We conducted a cross-sectional study among camels in Maiduguri, Northeast Nigeria. Lesions suggestive of TB were collected from camels slaughtered at Maiduguri Abattoir following post-mortem examination. The lesions were subjected to acid fast microscopy (AFB), histopathology and culture. Furthermore, isolates were tested for *Mycobacterium tuberculosis* complex (MTBC) using SD Bioline and confirmed by spoligotyping.

Results: Twenty (16.26%) out of 123 camels inspected had gross TB lesions; 50% of which were positive for AFB with 60% identified by culture. Animals with poor body conditions had higher TB lesions detection rate ($P < 0.05$). There was no significant difference in the occurrence of TB lesions between male and female camels. Histologically, granulomatous inflammation characterized by multifocal areas of caseation surrounded by inflammatory cells were common in affected organs. Tubular degeneration and eosinophilic deposits in the Bowman's space were observed in affected kidneys. Thickening of inter-alveolar septa, interstitial fibrosis, fluid accumulation in bronchial lumen and hemorrhage were seen in affected lungs. SD Bioline identified four of the 12 isolates as MTBC which were further confirmed by spoligotyping to be *M. bovis*, belonging to the clonal complex SB0944 and lack spacer 30, that is dominant in West Africa.

Conclusions: The isolation and confirmation of the unique dominant *M. bovis* strain from camels underscore the importance of molecular epidemiology of tuberculosis in camels. We strongly recommend implementation of Public Health measures and policies towards addressing threat posed by tuberculosis in camels in Nigeria.

EP01-104-25 Human tuberculosis caused by *Mycobacterium bovis* in the South of Tunisia

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Background: *Mycobacterium bovis* (*M. bovis*) causing tuberculosis (TB) in humans is listed among the seven endemic neglected zoonoses around the world and especially in developing countries. Therefore, it is necessary to carry out in-depth studies about this pathogen in our region.

Methods: It is a prospective study during 2013 and 2014. All patients with *M. bovis* tuberculosis coming from the south of Tunisia were included in the study. Microbiological study included direct examination and culture on both solid and liquid media. All strains was confirmed by a molecular method (Genotype MTBC Hain Life-science®). The epidemiologic, clinical and anatomopathological data have been analyzed.

Results: Globally, 102 samples were positive to *M. bovis*. The percentage of these patients relative to all cases of TB was 12.2%. Mean age was 30.7 years old. Sex ratio was 0.34. The consumption of raw milk was recorded in 61.8% of cases. Contact with animals has been reported by 29,4% of patients. Family and history of TB was noted for only 1% of patients in both cases.

For direct examination, Lowenstein Jensen, Coletsos and MGIT cultures, we found percentages of positivity about 15.7%, 75.5%, 85.9% and 100%, respectively. Also, 77.5% of the strains were resistant to pyrazinamide. All the sensitive strains to this antituberculous were *M. bovis* spp *caprae*. In our study, all TB cases due to *M. bovis* were extrapulmonary and 94.1% were lymph node TB.

Conclusions: There is a high burden and an upward trend of *M. bovis* in our region. We noted a predominance of female gender and extrapulmonary forms. The consumption of raw milk is high in our study. Yet, an establishment of a policy against TB due to *M. bovis* is necessary to provide adapted solutions to this increasing problem.

EP01-105-25 Prevalence of bovine tuberculosis in Iraqi cattle using tuberculin skin test on live cattle and lesion on slaughtered cattle

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Background: Bovine tuberculosis in Iraq was common more than 50 years ago among low socio-economic strata. People were infected by contaminated milk. The aim of this study was to estimate the prevalence of bovine TB in cattle in Iraqi governorates. A national survey was conducted to detected bovine tuberculosis (BTB) by the comparative intradermal tuberculin test (CIDT) in live-stock and detection the causative *Mycobacterium bovis* in lesion of slaughtered cattle and water buffaloes.

Methods: In 2014, the Veterinary Directorate carried out the first comprehensive survey of the disease in cattle and buffaloes in the governorates of Iraq (11 governorates) . A total of 9197 cows and 3574 buffalos were examined to determine the prevalence and morbidity rates . Determining the prevalence of bovine tuberculosis in slaughtered hoses, based on post mortem meat inspection. A Prospective study was conducted on (120) cattle and buffaloes had suspected BTB slaughtered in the local slaughtered hose in Baghdad. Ziehl-Neelsen staining, cultivation and molecular methods was used.

Results: The results revealed among total 9197 cow, 31 (0.331%) and from 3574 buffalos, 50 (2.044%) were positive by comparative tuberculosis test (CIDT), detection of BTB in one of largest and most important Cattle station farm was surveyed used skin test, Animals in this herd (1931) showed higher prevalence 725 (37.54%) with 519 (26.87%) suspected to BTB and the test was repeated after 3 month. Then all positive and suspected animals were killed. cultivation confirmed positive for *M. bovis* by molecular detection showed 6 (5%) in all sample, water buffaloes showed high prevalence in five carcasses and only one sample of cattle was positive.

Conclusions: The conclusion is that bovine TB is prevalent in live animal and meat production abattoirs that need further study on molecular epidemiology and risk assessment of BTB in public health.

EP01-106-25 Prevalence and risk factors of bovine tuberculosis in buffaloes in the Rawalpindi, Pakistan

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Background: Bovine tuberculosis (bTB), caused by *Mycobacterium bovis*, is an infectious disease of cattle that also affects other domestic animals, free-ranging and farmed wildlife, and humans. Due to direct economic repercussions on livestock and indirect consequences for human health and wildlife, knowing the prevalence rates of the disease is essential to define an effective control strategy.

Methods: The present study was executed to determine the magnitude of bovine tuberculosis in buffaloes in native type of husbandry practices and impact of certain factors in the prevalence of bovine tuberculosis in buffaloes in the Rawalpindi, Pakistan. One year cross sectional study was carried out on female population of Nili Ravi buffaloes (n = 878) in peri urban areas of the Rawalpindi city. These animals were screened with comparative intradermal tuberculin test (CIDT). The data were analyzed by ² test and Pearson correlation. Relative risk and other associated factors were calculated to describe the association with prevalence of tuberculosis in buffaloes.

Results: The prevalence of bovine tuberculosis on the basis of CIDT was 16.32%. The bTB among different livestock farms varied significantly (7 years old age, body weight >500 kg, 3-5 parity, pregnant animals, and animals with >7 liters milk yield). The husbandry factors which greatly influence the prevalence was poor feeding (RR=2.338), high fly density (RR= 2.311), poor management (RR=1.721), contact with wildlife (RR=1.532), poor farm conditions (RR=1.423), quarantine measures (RR=1.321) and poor sanitation of farm (RR= 1.311).

Conclusions: From this it can be concluded that bTB is present in the buffalo population in endemic proportions in native type husbandry practices, due to lack of poor feeding, poor sanitation, high fly density in the farm premises, wildlife interaction and other farm management factors greatly influence the prevalence of bTB in buffaloes. The prevalence can be reduced by improving these practices at farms.

EP02 Highlights across the tuberculosis section

EP02-107-25 A systematic review and meta-analysis of clinical manifestations of tuberculosis among the elderly and the non-elderly patients - an update

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Background: There have been numerous studies comparing the clinical manifestations between the elderly and the non-elderly tuberculous patients, however, results have often been discordant. The last systematic review was published in 1999, therefore, we aimed to update the review on studies examining the differences in symptoms and comorbidities among elderly and non-elderly tuberculous patients.

Methods: Following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines and methods for systematic reviews and meta-analyses of observational studies, we performed a comprehensive search of the following databases; PubMed, EMBASE, Cochrane Library, and Ichushi, for relevant citations in English and Japanese, which were published from July 1987 to September 2016. Random-effects meta-analyses were performed for symptoms and comorbidities among the elderly and the non-elderly patients.

Results: 38 studies were included, covering 65,356 elderly and 200,273 non-elderly participants. Definition of the elderly ranged from over 55 years to over 75 years. The table indicates the pooled odds ratios and 95% confidence intervals. A significantly higher prevalence of dyspnea, anorexia, hepatotoxicity and comorbidities such as Diabetes Mellitus, COPD, and psychiatric disorders were observed among the elderly patients. Psychiatric disorders indicated high frequency among the elderly (7.1%, 60/840) compared with the non-elderly (1.1%, 9/796), and was mainly reported countries facing rapidly aging population, such as Japan, Hong Kong and Belgium.

The elderly had a significantly lower prevalence of cough, sputum, hemoptysis, fever, night sweats, and HIV comorbidity, however, the prevalence of respiratory symptoms was only significantly different in studies which included only pulmonary tuberculosis.

Conclusions: Prevalence of respiratory symptoms was significantly lower among the elderly patients, especially pulmonary tuberculosis, which is consistent with previous reports of atypical presentation of the disease among the elderly. Psychiatric disorders were found in 7% of the elderly patients and may become an important issue from the perspective of patient care.

Symptom	OR (95%CI)	Symptom	OR (95%CI)	Symptom	OR (95%CI)	Symptom	OR (95%CI)	Comorbidity	OR (95%CI)
Anorexia	1.83 (1.31-2.56)	Sputum	0.71 (0.58-0.88)	Chest pain	0.85 (0.62-1.15)	General weakness	1.62 (0.72-3.65)	Diabetes Mellitus	1.41 (1.13-1.78)
Dyspnoea	2.42 (1.76-3.33)	Hemoptysis	0.62 (0.48-0.80)	Weight loss	1.11 (0.87-1.42)	No symptom	1.14 (0.80-1.62)	COPD	4.74 (3.72-6.04)
Hepatotoxicity	1.68 (1.14-2.48)	Fever	0.65 (0.51-0.82)	Fatigue	1.15 (0.82-1.62)			HIV	0.10 (0.09-0.11)
Cough	0.76 (0.62-0.93)	Night sweats	0.52 (0.38-0.72)	Malaise	1.69 (0.84-3.38)			Psychiatric disorders	6.36 (1.33-30.42)

[Pooled odds ratios of symptom, comorbidity and adverse drug reaction between the elderly and the non-elderly tuberculous patients]

EP02-108-25 A structural and epidemiological approach to delay resistance acquisition in bedaquiline: last line resort to treat MDR-TB

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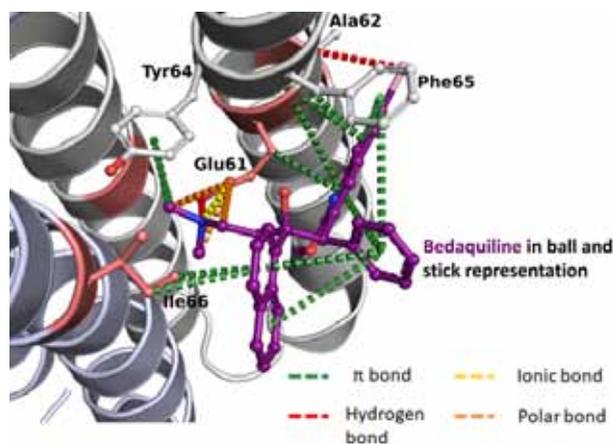
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Background: Bedaquiline is the first new anti-tuberculosis compound with a novel mechanism of action in over 40 years. While it is currently reserved as an antibiotic for use against multi- and extensively-drug resistant tuberculosis, mutations potentially conferring drug resistance have already been documented. As a new drug, however, there is currently insufficient clinical data to facilitate reliable and timely identification of genomic determinants of resistance.

Methods: We have used a structural approach to characterize how variants in the drug target, atpE, lead to resistance to guide the effective use of bedaquiline, and help minimize the development of clinical resistance. We analyzed the structural and functional consequences of 9 known resistant variants in the drug target atpE, and 49 susceptible variants identified through comparisons of bedaquiline's efficacy against 32 different mycobacterial species.

Results: Our approach identified key predictive properties of bedaquiline resistant mutations, including the effects of the mutations on protein stability and interactions with the drug. Combined with structural changes associated with the mutation, a neural network predictive tool was built that could accurately identify likely resistance mutations (95% accuracy). The model was also used to evaluate circulating variants present in the Asia-Pacific region, highlighting their susceptibility to bedaquiline in the absence of drug exposure.

Conclusions: This highlights how structural information can be used to identify and characterize resistance variants, especially significant to guide the use of newly developed therapies. A similar in-silico approach is also being applied for determining novel variants in non-target-based bedaquiline resistance like Rv0678 and pepQ. Epidemiological models of tuberculosis transmission will be further employed to consider emerging public health implications related to likelihood of resistance spreading.



[A dense network of molecular interactions between the protomers of AtpE and Bedaquiline]

EP02-109-25 Risk of tuberculosis in patients prescribed medical immunosuppressive therapy in British Columbia, Canada: retrospective cohort study

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Background: Immunosuppressive (IS) therapy to treat medical conditions comes with the risks of diminished defense against new and emerging infection, thus these therapies are potential risk factors for relapse and reinfection of *Mycobacterium tuberculosis*. We examined the relationship between IS therapies and tuberculosis (TB) in a large cohort of people who immigrated to British Columbia, Canada over an 18-year period.

Methods: We identified a population-based retrospective cohort of all foreign-born individuals who landed in Canada between 1996 and 2012, and became residents of BC at any time up to 2013. We linked multiple administrative databases and provincial disease registries together, and extracted data on demographics, immigration history, TB outcomes, and co-morbidities. We used multivariable Cox extended proportional hazards re-

gression models to determine the association of the use of IS therapy (i.e. TNF- inhibitors, high-risk DMARDs and high-dose steroids) with active TB.

Results: Of a total of 730,363 people entering the cohort, 10147 people (1.4%) were dispensed IS therapies, including TNF-alpha inhibitors (n=458 people); high-dose steroids (n=9275), and high-risk DMARDs (n=1281) in BC over the study follow-up period. There were 108 active TB cases among people dispensed IS therapy. The hazard ratio (HR) was highest for TNF-alpha inhibitors (adjHR=23.4, 95% CI:9.7,56.5), followed by DMARDs (adjHR=7.6, 95% CI:4.5,12.6) and steroids (adjHR=2.9, 95% CI:2.3,3.6), after adjustment for age at time of immigration, gender, TB incidence in birth country, immigration type, contact status, HIV, chronic kidney disease, and diabetes.

Conclusions: Active TB risk was increased following treatment with TNF-alpha inhibitors, high-risk DMARDs and steroids. This data supports the use of LTBI screening in patients starting therapy with TNF-inhibitors and high-risk DMARDs. Given the high prevalence of steroid use in the population, and the low rate of TB, further study is needed to refine thresholds and populations at risk of TB before initiating mass screening.

EP02-110-25 Impact of sputum smear results after two months of treatment on the treatment outcome of pulmonary tuberculosis

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Background: Sputum smear conversion at the end of the intensive phase of pulmonary tuberculosis (PTB) treatment is an indicator of patients' response to treatment and anti-tuberculosis program performance.

This study aimed at identifying how much treatment outcome is influenced by the result of "sputum smear on direct smear microscopy of PTB after two months of intensive treatment on anti-tuberculosis drugs" (SS-DSM2).

Methods: This cross-sectional study reviewed the national data available at central tuberculosis control program in Iraq for people had sputum smear positive PTB (SS-PTB) during the period 2009-2014. ² test used to test the significance of observed associations and univariate binary logistic regression analysis used to estimate Odds Ratio (OR).

Results: Sample size was 14,025. Age group 15-45 year constituted 61.3% of the sample, Males constituted 56.3%. The proportion of new PTB was 89.5%. Conversion rate of SS-DSM2 was 91.2% and non-conversion

rate was 8.8%. Rates of treatment outcome for studied sample were 82.0% for treatment success, 2.9% for failure and 15.1% for other outcomes.

Characteristics of people had non-conversion of SS-DSM2 (n=703): age group of 15-45 y (56.8%, P=0.004), Male sex (60.2%, P=0.003), new PTB (93.0%, P=0.001), with high treatment failure rate (18.5%) compared to 1.6% in those had converted SS-DSM2 (P<0.001).

Treatment failure is 14 times likely to be associated with delay in conversion of SS-DSM2 [OR= 14.2 (95% CI 10.9-18.5)].

Conclusions: Non-conversion of SS-DSM2 is a significant predictor for treatment failure in PTB.

EP02-111-25 Tuberculosis incidence among health care workers undergoing routine screening, Dire Dawa, Ethiopia

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Background: Healthcare workers (HCWs) are at increased risk for of developing tuberculosis (TB), but routine HCW TB screening is limited in many high-burden countries. We implemented routine HCW TB screening at 10 public sector health facilities to better define the rates and epidemiology of TB among HCWs in one region of Ethiopia.

Methods: From March 2016 -March 2017, all HCWs at the participating sites were offered quarterly TB symptom screening, using the WHO screening algorithm. Symptomatic HCWs were referred for diagnostic evaluation. Additionally, demographic and occupational information were collected and HIV testing was offered. Incidence rates and incidence rate ratios (IRRs) were calculated and multivariate analyses were done to examine factors associated with incident TB.

Results: Of 1453 HCWs at the 10 sites, 1240 (85%) were screened at least once for TB; 60% completed all four screening cycles. Participating HCWs had a median age of 29 years (IQR=10), 60.5% were female and 29.3% were nurses. 81 (6.5%) HCWs had presumptive TB; 10 were diagnosed with active TB for an overall incidence of 806 (95% Confidence Intervals [CI]: 310, 1300) per 100,000 HCWs. Factors associated with incident TB were HIV-positivity (IRR=13.3, 95% CI: 1.97, 89.3) and working on an inpatient ward (IRR=8.5, 95% CI: 1.5, 50). TB incidence among HCWs who were HIV-positive or who worked on an inpatient ward were 3,125 and 3,704 per 100K, respectively.

Conclusions: Active case finding among HCWs is warranted in high burden settings to help identify cases among this high risk group and to decrease the risk of TB transmission in the healthcare setting.

EP02-112-25 Lifting TB out of the shadows through an active case finding strategy in Swaziland: a community participatory approach

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Background: Tuberculosis remains problematic in Swaziland, exacerbated by the 27% HIV prevalence, highest worldwide, with co-infection rate of 70%. Recently, the country showed commitment to addressing the TB burden, recording increasing treatment success rates of 68% in 2009, 79% in 2016 and 84% in 2017. However, a progressive TB case notifications decline was experienced from 2010. A shift from passive case finding to community-based active case finding (ACF) to ensure cases are not missed was necessary. Door-to-door screening for active TB targeting high risk populations with limited access to services is in-progress since June 2016. Presumptive cases who expectorate, sputum samples are collected for bacteriological confirmation. TB cases are linked to care and treatment. The study aims to share experiences and lessons learnt during the planning phase for implementing the ACF strategy in Swaziland.

Methods: A community-based strategic document as framework was developed. Top to bottom sensitization process was implemented with different stakeholders indicating the purpose of the strategy. In-depth interviews were held with Regional Administrators and Regional Health Administrators to get inputs. Regional Health Management Teams sensitized facility nurses. Focus group discussions were conducted with chiefs eliciting views on implementing the ACF strategy. The chiefs continued community awareness campaigns and identified candidates who would visit homesteads screening for Tuberculosis. NGOs, politicians and civil society played various roles in pursuit of a successful ACF strategy.

Results: 1492 TB cases were bacteriologically confirmed and initiated on anti-tuberculous medications. The ACF strategy contribution in case detection was 2.4 times above the national average. Case detection improved from 59% in 2016 to 84% in 2017.

Conclusions: Implementation of case finding strategy increased case detection from 59% to 84% in a year. Community members with active TB were identified, diagnosed and treated early thus reducing the infectious pool in the communities.

EP02-113-25 A comparative assessment of treatment outcomes by intervention in tribal population and NTP data

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Background: The Indian RNTCP aims achieving 85% or higher treatment success rate in newly diagnosed B+ cases. 'Hard-to-reach' tribal populations have poor access to DOTS and face severe adherence barriers. In 2017, Asha Kalp launched a project to identify and improve TSR among new B+ patients in the Sahariya tribal pockets of central India.

Methods: Patients were identified through active household screening and transportation of sputum specimens of presumptive cases to a government laboratory. Project treated identified patients at the doorstep and recorded their treatment outcomes using a rigorous electronic platform, and compared with outcomes declared of the patients enrolled in the same quarters previous year by the RNTCP.

Results: Between May and December 2017, the project treated 502 new and 59 retreatment cases. The project achieved 74% TSR compared to 88% of the program among new B+ patients for the same duration last year. Lost-to-follow-up (LTFU) and death rates were 11% each as compared with 5% and 4%, respectively by program. Among retreatment cases, the TSR was only 8% with very high mortality rate under project interventions.

Conclusions: The ACF identified patients with a higher LTFU (11%) and death rate (11%) than the program. ACF interventions likely identified a large number of patients who were severely sick and had reached advanced stages of TB resulting deaths. There is an urgent need to start focused interventions leading to early detection & promoting adherence, while also attempting to strengthen data quality in program reported outcome data.

Treatment Outcomes	New (Implementation, 2017)	Retreatment (Implementation, 2017)	New (NTP, 2016)	Retreatment (NTP, 2016)
IC + Cured	378	5	793	188
Lost To Follow Up	67	11	49	28
Dead	56	27	31	17
Not Evaluated + Default + Treatment Regimen Changed	11	11	19	11
Total	502	59	903	244

[A comparative analysis of treatment outcome data between Intervention and NTP data]

EP02-114-25 Do cough monitors in high load district hospitals help to reduce delays in identifying presumptive TB patients? Experience from India

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Background and challenges to implementation: In India, tuberculosis remains a major public health challenge with an incident of 2.8 million TB cases and 0.42 million deaths annually. According to Global TB report, over 1 million TB cases are 'missed' annually. Low case detection and notification are two of the major challenges facing the National TB Program. Half of the TB patients seek treatment from public sector but all patients reaching Govt. hospitals for other services do not get adequately screened for TB due lack of awareness and overcrowding at the health facilities which leads to delay in diagnosis. To address this gap of delay in diagnosis, a cough monitor was deployed in the waiting area of outpatient health facility of the district hospital to identify the presumptive TB cases and fast track them for early diagnosis. This study aims to assess the impact of this intervention in identifying the missing TB patients.

Intervention or response: To improve early case detection, a trained cough monitor was placed in the waiting area of the OPD. The cough monitor screened all the clients visited the public health facility for symptoms of TB and identified presumptive TB patients were fast tracked to the diagnostic centre. The data on the number of presumptive TB patients examined and diagnosed as TB during the period October 2017 was extracted from the TB laboratory register and was compared with that of the period October 2016.

Results and lessons learnt: The results of the relative change in the number of presumptive TB patients examined and the number of pulmonary TB cases diagnosed in the five intervention districts is shown below. It is found that in each of the intervention districts, there is a significant increase in the examination and detection rates.

State	Name of the district	Number of presumptive TB patients examined			Number of pulmonary TB cases diagnosed		
		Oct-16	Oct-17	Relative change	Oct-16	Oct-17	Relative change
UK	Dehradun	39	71	97%	4	5	25%
Bihar	Vaishali	219	317	45%	21	38	81%
Haryana	Mahendragarh	164	186	13%	19	13	30%
Karnataka	Hasan	458	616	34%	28	53	125%
Rajasthan	Jhunjhunu	265	395	49%	44	52	18%

[Details of Fast-tracking intervention]

Conclusions and key recommendations: Cough monitors play an important role in early identification of PT-BPs and helps in identifying missing TB patients.

EP02-115-25 Latent tuberculosis infection and dyslipidemia: prevalence estimates from the US NHANES, 2011-2012

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Background: Recent data suggest latent tuberculosis infection (LTBI) may increase the risk of acute myocardial infarction. However, the mechanisms underlying this risk are unclear, and whether LTBI is associated with intermediates to cardiovascular diseases, such as dyslipidemia, is unknown. We sought to determine the association between LTBI and dyslipidemia using data representative of the adult US population.

Methods: We performed cross-sectional analyses using data from the US National Health and Nutrition Examination Survey (NHANES), 2011-2012. Eligible participants included adults (≥ 20 years) with valid QuantiFERON-TB Gold In-Tube and serum lipid measures. Dyslipidemia was defined by abnormal serum lipid profile (total cholesterol ≥ 240 mg/dL, triglycerides ≥ 200 mg/dL, high-density lipoprotein < 40 mg/dL, or low-density lipoprotein ≥ 160 mg/dL) or prior diagnosis of high cholesterol. Analyses were weighted to account for the stratified probability sample of NHANES, including logistic regression to estimate the adjusted odds ratio and 95% confidence intervals (CI) for the association between LTBI and dyslipidemia.

Results: Among 9,756 participants surveyed, 4,858 met inclusion criteria. The prevalence of LTBI was 5.9% (95% CI 4.9-6.9%) and dyslipidemia was 50.8% (95% CI 47.2-54.4%). Among participants with dyslipidemia, 30.0% reported statin use. Dyslipidemia was more prevalent among participants with LTBI (60.9%) compared to those without (50.2%, $p < 0.01$). Controlling for age, gender, country of birth, diabetes, body mass index (BMI), hypertension, smoking status, alcohol abuse, and statin use, the adjusted odds of dyslipidemia among those with LTBI was 1.2 (95% CI 0.9-1.7) times the odds among those without LTBI. We did not detect statistical interaction in the effect of LTBI on dyslipidemia by age, BMI, or diabetes status (all P values > 0.05).

Conclusions: Despite evidence that LTBI increases the risk of heart disease, LTBI was not associated with increased odds of dyslipidemia among US adults. Further studies are needed to determine how LTBI may increase the risk of metabolic disorders and cardiovascular diseases.

EP02-116-25 Improving TB patient support: designing digital health solutions for case managers in Kyrgyzstan

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Background and challenges to implementation: In Kyrgyzstan, case managers (CMs) have an essential role in ensuring treatment completion of DR-TB patients through direct, knowledgeable and responsive patient support. Previously, CMs used several paper forms to report information on patient registration, risk factors, contact investigation and during follow-up visits. As the number of patients and CMs and workload increased, the need for a flexible, efficient digital tool emerged.

Intervention or response: Starting January 2018, stakeholders launched efforts to develop a mobile application to support the CMs in their work, aiming to streamline data collection/reporting, facilitate contact investigations, provide case-based reminders, and enhance visit planning through patient/facility mapping.

Employing a participatory user-centered-design approach, the team began by co-creating process maps, workflows and user personas to analyze current work processes and identify key points for improvement. This ensured that the resulting Case Management Application (CMA) fit the local context and user needs. The team selected a configurable platform (CommCare) as the core system, and within two weeks of intensive development, iterations and user demonstrations, the CMA was ready for field testing.

Results and lessons learnt: Initial roll-out of the CMA in Bishkek city and Chui region has already shown 208 patients and 450 contacts registered, and 124 home visits recorded. Using an iterative design process, CMs suggest improvements and issues to technical staff, and resulting updates are automatically deployed to mobile devices. New data and learnings gathered from April- September 2018 will be included in the final abstract.



[Case Management Application]

Conclusions and key recommendations: Based on initial field observations, the CMA is proving a helpful tool for CMs—it streamlines patient data collection and sharing, enables continuous data process improvement, and provides a flexible visit planning tool on user-friendly mobile devices. Further expansion and testing of the CMA intervention will bring additional insights into process optimization, new features desired, patient data analysis, and overall impact.

EP02-117-25 Pharmacists as gatekeepers into TB care: implications for the diagnostic cascade

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Background: Retail pharmacies are the first point of care for TB symptomatic individuals in many countries. By referring patients for TB diagnostic services, pharmacists can facilitate early case-detection. We report on the determinants of pharmacists' engagement in this referral pathway in Patna city, India.

Methods: A qualitative study was nested into an operational research intervention that engaged 105 pharmacists in a TB screening and referral program. Eight focus groups and interviews (n=85) were conducted with purposive samples of consenting intervention pharmacists, physicians/physician-assistants, laboratory staff, and pharmacy-referred patients. Data were analysed using network thematic analysis and actor-network theory.

Results: Pharmacist focus groups, and interviews with 3 pharmacists, 18 physicians, 17 physician-assistants, 4 laboratory staff, and 43 patients allowed us to explore multiple viewpoints and identify contextual influences on pharmacists' referral practices. First, pharmacists play a critical gatekeeping role as patient counsellor, advisor, and liaison between the community and health system. Second, equilibrium in the patient-pharmacist-physician triad is crucial to the success of any referral pathway. While patient-pharmacist trust facilitates referral, physician-pharmacist distrust can negate the outcomes of such referral. A marked interdependence between the actors of an established triad may inhibit any one of them from disrupting equilibrium, notwithstanding traditional hierarchies that also underlie their individual practices. Third, local systematic factors including limitations of TB diagnostic tools, physician consultation fees, and poor quality of care within public health facilities may catalyse or curb pharmacists' engagement in referral programs.

Conclusions: Barriers and facilitators to engaging pharmacists in TB screening and referral intersect with pre-existing roles, relationships and norms of the social and healthcare systems in which they operate. Pharmacists may be patient gatekeepers into TB care, but their behaviour is governed by systematic factors and gatekeeping practices of other key actors. Interventions that respect these norms are more likely to be sustained.

EP03 Preventive therapy and intensified case finding among people living with HIV/AIDS (PLWH)

EP03-118-25 Assessing the tuberculosis preventive therapy cascade for people living with HIV in Namibia and identifying challenges associated with its implementation

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Background: In 2016, Namibia had ~230,000 people living with HIV (PLHIV) and 9,154 new TB cases, including 3,410 (38%) co-infected cases. PLHIV with latent TB infection have a 5-10% annual reactivation risk, and TB preventative therapy (TPT) is critical to reducing TB disease and overall mortality in PLHIV.

Methods: From April-June 2013, data was abstracted from enrolled PLHIV charts using selective sampling from 55 facilities based on size, type and location. Primary outcome was to estimate a baseline of TPT using nationally weighted proportions. Qualitative interviews were conducted with health care workers (HCW) to evaluate TPT practices and challenges.

Results: Among 861 enrolled PLHIV sampled, 825 were eligible for TPT and 85.6% were screened for TB at least once. In PLHIV eligible for TPT (77.8%), only 45.4% initiated therapy, of which 45.7% completed therapy. Overall, the proportion of eligible PLHIV completing the TPT cascade (negative TB screening, initiate preventative therapy, complete preventative therapy) was 20.7%. Qualitative interviews with 271 HCW identified barriers to implementing TPT: *lack of training* - 59.9%

reported training on TB screening, while 40.7% reported preventative therapy training; *timing of TPT initiation* - 46.7% reported TPT should be started with ART, 29.3% after ART, and 19.3% didn't know; *TB symptom screening practices* - 66.5% screened for TB at every encounter and understanding responsibilities for TPT provision and documentation varied widely; and *HCW misperceptions* - 72.2% described their clinical performance as very good, often placing responsibility of difficulties on patients and downplaying challenges like staff shortages, stock outs, etc.

Conclusions: Only 1 in 5 eligible PLHIV completed TPT in Namibia. Lack of training, irregularities with TB screening and timing of TPT, unclear prescribing and recording responsibilities, and a clinical misperception contribute to poor programmatic implementation. Addressing these challenges will be critical with TPT scale-up.

EP03-119-25 Gaps in the intensified case finding and isoniazid preventive therapy cascade among PLHIV in Lesotho

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Background: Routine screening for tuberculosis (TB), followed by prompt diagnostic testing and treatment or isoniazid preventive therapy (IPT), are essential to mitigate TB-related mortality among people living with HIV (PLHIV). We evaluated the intensified case finding (ICF)-IPT cascade among PLHIV in Lesotho.

Methods: We retrospectively reviewed routinely collected data from a sample of patients seen for HIV care at 25 purposively selected health facilities in five districts, between January-March 2016. We conducted descriptive and bivariate analyses using generalized linear mixed models to account for clustering by health facility, to assess TB screening, evaluation for TB disease, treatment initiation, and IPT initiation and completion.

Results: Among 8,098 PLHIV, 61% were female, median age was 36 years (IQR 28-45), 97% were on antiretroviral therapy, and among 4,672 with available data, median CD4 count was 472 (IQR 304-665). Overall 7,987 (99%) were screened for TB symptoms at their last clinical visit; 87 (1%) screened positive; and 56 (64%) were evaluated, with smear microscopy (66%), chest x-ray (45%), Xpert MTB/RIF (8%) and/or culture (3%). 53 (95%) were diagnosed with TB; all started treatment. Among 7,903 patients eligible for IPT (negative screen or evaluation), 1,983 (25%) initiated IPT. Median time from screening to IPT initiation was 83 days (IQR

0-206). IPT initiation was lower among PLHIV aged <15 vs. ≥ 15 ($p=0.01$); those with CD4 50-199 were most likely to initiate IPT ($p < 0.0001$) (Table). Overall, 1,605 (81%) completed IPT.

Conclusions: Although TB screening was high, yield was low. Few PLHIV with presumptive TB underwent Xpert MTB/RIF testing and over a third were not evaluated. Only a quarter of eligible PLHIV initiated IPT, however completion was comparatively high. Interventions aimed at addressing gaps in the ICF-IPT cascade, particularly expanding Xpert testing and providing IPT at higher CD4 counts, are urgently needed to mitigate TB-related mortality among PLHIV in Lesotho.

	Eligible for IPT n=7,903	Initiated IPT n=1,983 (25%)	Completed IPT n=1,605 (81%)
Age, n (%)			
<15 y	746	161 (22)	124 (77)
≥ 15 y	7,069	1,799 (25)	1,460 (81)
Missing	88	23 (26)	21 (91)
CD4 count, n (%)			
<50	36	15 (42)	9 (60)
50-199	478	206 (43)	156 (76)
200-349	939	367 (39)	298 (81)
350-499	1,002	326 (33)	270 (83)
≥ 500	2,125	641 (30)	532 (83)
Missing	3,323	428 (13)	340 (79)

[Table. IPT Cascade by Age and CD4 Count]

EP03-120-25 Intensified case finding for TB and isoniazid preventive therapy uptake among HIV patients in Kilifi, Kenya

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Background: The World Health Organization Three I's Strategy for TB-HIV recommends intensified case finding (ICF) for TB, isoniazid preventive therapy (IPT) and infection control (IC) at all clinical encounters. The objective of the study was to determine the extent of ICF for TB and IPT uptake among adults and children with HIV accessing care in sampled health facilities in Kilifi, Kenya.

Methods: Convenience sampling was used to select 373 adult and 107 pediatric patient files in the 25 health facilities with the highest numbers of HIV patients. This retrospective cohort study was done in October 2016. The purpose of the study was to evaluate the cascade of intervention for prevention of TB in HIV patients namely: the presence of the TB screening tool in patient files, screening of patients for TB, exclusion of active TB using the ICF criteria and treatment of latent TB infection using isoniazid.

Results: Out of the 373 adult files which were sampled, 88.7% ($n=331$) had ICF cards, 71.8% ($n=268$) of the patients were screened for TB, 75% ($n=280$) were eligible for IPT and 77.5% of those eligible ($n=217$) were put on IPT. Out of the 107 paediatric patient files which were

sampled, 83.2% ($n=89$) had ICF cards, 62.6% ($n=67$) of the patients were screened for TB, 66% ($n=71$) were eligible for IPT and 70.4% of those eligible ($n=50$) were given IPT. ICF and IPT uptake was lower in children than in adults.

Conclusions: This study revealed the gaps in TB screening and IPT uptake among HIV patients in Kilifi, Kenya. As a result of this study, a number of interventions were put in place to increase TB screening and IPT uptake among HIV patients in Kilifi, Kenya.

EP03-121-25 High uptake of IPT with integration of TB-HIV services in RMNCH settings in Manzini region, Swaziland

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Background: Tuberculosis (TB) is an important cause of morbidity and mortality among women of reproductive age and their children. We assessed the feasibility of enhancing integration of TB-HIV services in reproductive, maternal, newborn and child health (RMNCH) settings at four health facilities in Manzini region, Swaziland following healthcare worker training and introduction of a longitudinal register and TB contact tracing tool, to improve TB case finding and provision of isoniazid preventive therapy (IPT) among women and children.

Methods: We retrospectively reviewed the longitudinal registers including all women attending RMNCH services between April and December 2017. Descriptive statistics were conducted to assess TB screening, diagnosis of TB disease, TB treatment initiation, IPT initiation and completion, and contact tracing.

Results: A total of 3126/4199 (74%) women attending antenatal (ANC) ($n=2150$) or postnatal care (PNC) ($n=976$), and 2580 women attending family planning (FP) visits were screened for TB symptoms; 0.9% (50/5706) screened positive and 10% (5/50) of women with a positive screen were diagnosed with TB (3/5 HIV-positive); all 5 initiated TB treatment. Of 1933 HIV-positive women with a negative screen, 885 (46%) initiated IPT, including 226 (35%) from ANC, 66 (22%) from PNC, and 593 (60%) from FP (Table). Of 386 women initiating IPT during April-June 2017, 278 (72%) completed IPT. A total of 16 child contacts of the 5 TB cases were identified and screened for TB; none were diagnosed with TB, and 5/7 (71%) eligible child contacts initiated IPT.

Conclusions: Integration of TB-HIV services in RMNCH settings is feasible and ensures high TB screening coverage among women of reproductive age. Few women and

child contacts with presumptive or active TB were identified. Less than half of eligible HIV-positive women initiated IPT, although IPT initiation was comparatively high among women seeking FP services. Interventions aimed at improving IPT initiation and completion rates should be prioritized.

Point of Service	HIV-positive women screened for TB	HIV-positive women with negative screen	HIV-positive women initiated on IPT
ANC	668	652	226 (35%)
PNC	301	298	66 (22%)
FP	989	983	593 (60%)
Total	1958	1933	885 (46%)

[Table. IPT Cascade by Point of Service]

EP03-122-25 National TB prevalence rate among people living with HIV in Nigeria in 2016

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Background: Nigeria is among high burden countries for TB and TB-HIV. National routine reporting have been able to determine the prevalence of HIV among TB patients, however, the country has not been able to determine the prevalence of TB among PLHIV. This study was therefore conducted to determine the national prevalence of TB among PLHIV.

Methods: A cross-sectional, retrospective study involving data abstraction from the records of PLHIV in ART facilities. Two-stage stratified, cluster, systematic random sampling technique was used to select the sample size of 78,048 PLHIV from 50 ART facilities in 22 states. Ethical clearance obtained before the study. CSPro software used for data entry, validation, and cleaning. Data subsequently imported into SPSS for analysis.

Results: Information abstracted from 71,810 PLHIV (92% response rate) records. 72.5% (52,604) of PLHIV were screened for TB at enrolment, the prevalence of TB among PLHIV screened for TB at enrolment of 11.2% (with a 95% confidence interval of 10.9% - 11.5%) doubled the prevalence of TB among PLHIV as at the last visit to the health facilities in 2016 of 4.5% with a 95% CI given as (4.3% - 4.7%). number of HIV-TB co-infected who discontinued ART (2.3%) was higher than observed among all PLHIV irrespective of TB status (1.4%). Mortality rate among PLHIV co-infected with TB (11 per 1000 PLHIV population) higher than general population of PLHIV (4 per 1000 PLHIV population).

Conclusions: A more sensitive screening tool combining Xray and symptomatic-screening with subsequent XpertMTB/RIF assay as appropriate is needed to

enhance TB case detection among PLHIV especially at enrolment where the TB prevalence is higher. TB and HIV programme must collaborate to optimize TB screening among PLHIV to find missed cases among this group and achieve zero TB-HIV death.

EP03-123-25 Finding and treating missing persons with TB disease through systematic screening and staff empowerment in two high burden districts in Malawi

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Background and challenges to implementation: Malawi continues to register a decrease in the incidence of Tuberculosis estimated by WHO at 159 (85-256) per 100,000 population in 2016. The country has however detected just over 50% of the estimated TB burden. The USAID-funded Challenge TB (CTB) project provides support to the National TB Control Program to find and treat missing persons with TB in two districts of Lilongwe and Blantyre, with 24% and 16% respectively of total cases notified in 2016.

Intervention or response: Facility assessments were conducted by CTB staff members in 12 facilities (six in 2016 and six in 2017) to understand the readiness and quality of TB and HIV services provided and to identify the gaps in finding TB patients. The staff included a clinician, nurse, laboratory, x-ray and community mobilizer. Targeted facility staff training in TB-HIV management, coaching and mentorship visits were constituted. Implementation review meetings were also held. There was procurement of additional four (4-module) Xpert MTB/RIF platforms and three laboratories were renovated.

Results and lessons learnt: Quarterly data analyzed after one-year implementation showed an increase of 11% in TB notifications in the initial three facilities in Lilongwe and 17% increase in the initial three facilities in Blantyre. The range in increase of notified new and relapse TB cases among the six facilities was 2-70%. By December 2016, the project sites contributed to 43% and 65% of total TB notifications for Lilongwe and Blantyre district respectively. There was systematic review of contributing and inhibiting factors to case detection that included patient preferences, health seeking behavior and matching demand and supply of diagnostic and treatment services.

Conclusions and key recommendations: Finding and treating missing persons with TB disease requires a systematic step-wise approach with direct service delivery and targeted site-level assistance.

EP03-124-25 Contribution of systematic screening for symptoms of TB among a population newly accessing health care services

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Background and challenges to implementation: Elimination of TB and HIV requires early detection and treatment. Lesotho has the highest TB incidence and second highest HIV prevalence globally, 788 per 100,000 and at 25%, respectively. Men access services less frequently than women.

Intervention or response: In June 2016, Jhpiego, Lesotho Ministry of Health and Scott Hospital established 'Khotla bophelong bo botle', meaning a gathering place where men discuss health issues. The primary objective of Khotla is provision of comprehensive, integrated care for men to increase uptake and quality of primary healthcare services, particularly HIV and TB diagnosis and treatment. We conducted a retrospective record review of all clients accessing services at Khotla over the 18 month period between July 2016 and December 2017. HIV status, TB symptom screening results and TB diagnosis by microscopy, Gene Xpert and/or chest x-ray were documented for all clients.

Results and lessons learnt: Nearly 1% of all visits resulted in a TB diagnosis: 150 men were diagnosed with TB over the 18 months, where more than 16,000 clinic visits were made (multiple visits for each person given the chronic nature of care). An average of 4.9% reported at least one symptom of TB (cough, weight loss, night sweats, fever), and 21.5%, 16.3% and 22.1% of HIV-positive, HIV-negative, and men with unknown HIV status with symptoms were diagnosed with TB (Figure 1).

Conclusions and key recommendations: The implementation of a clinic focused on men's needs has led to an increase in number of visits, including increase in diagnosis of TB. Even though symptom screening is not ideal to find TB along the cascade of TB diagnosis, when applied systematically and consistently in a setting where clients who had not previously accessed health care services are, it can contribute to TB elimination efforts; however, stock-outs of Xpert cartridges at site level is proving to hinder progress gained.

Period	All client visits	TB symptoms			Total	TB Diagnosis			Total
		HIV positive	HIV negative	Unknown HIV status		HIV Positive	HIV Negative	Unknown HIV Status	
Jul 16 - Mar 17	7602	272	166	20	458	43	25	5	73
Apr 17 - Dec 17	9115	215	103	35	353	53	19	5	77
Total	16717	487	269	55	811	96	44	10	150

[TB symptoms and diagnosis by HIV status]

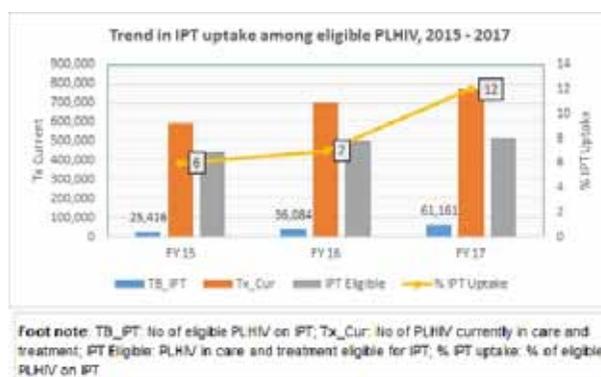
EP03-125-25 Taking TB preventive therapy implementation to a national scale: the Nigeria PEPFAR program experience

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Background and challenges to implementation: Tuberculosis (TB) is the leading cause of death for people living with HIV (PLHIV). Tuberculosis Preventive Therapy (TPT) significantly reduces mortality among PLHIV independent of Anti-retroviral therapy (ART). The scale up of Isoniazid Preventive Therapy (IPT), the form of TPT in use in Nigeria has remained slow for the past years. TPT is implemented within the HIV program but the drug procurement and logistic support has over the years been the responsibility of the TB program. This arrangement impacted on program ownership, accountability and remained an impediment to TPT scale up in the country.

Intervention or response: PEPFAR-Nigeria reviewed the key bottlenecks to TPT implementation in 2016 and worked with the government to integrate the INH logistics with Anti-retroviral (ARV) Logistics management and information system (LMIS). The drug order and requisition forms at the facility level were revised to include INH and logistics staff at sites trained on appropriate quantification and requisition of INH with the ARV. Support was provided for last mile delivery of INH directly to every implementing site alongside the ARV.

Results and lessons learnt:



[Fig 1: Trend in IPT uptake among eligible PLHIV, 2015 - 2017]

The change in the LMIS for INH in 2016 led to 41% increase in TPT achievement by the end of 2017 compared to 2016 (Fig.1). In 2017, 12% of eligible PLHIV were commenced on IPT compared to 7% and 6% in year 2016 and 2015 respectively. With the new logistics sys-

tems in place, the program has targeted 70% IPT uptake by the end of 2018 reporting period and the trend is to be sustained in the following years.

Conclusions and key recommendations: A strategic change in the INH logistic system led to a significant increase in IPT uptake among eligible PLHIV. Though INH is mainly procured by the TB program, it is recommended that TPT implementation should be driven by the HIV program for the entire logistics system for an improved program performance.

EP03-126-25 Patient's choice improves confidence and intention to complete TB prevention therapy in a routine HIV program setting in Uganda

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Background: Tuberculosis (TB) accounts for one-quarter of all deaths among people living with HIV (PLHIV). Preventive therapy can significantly reduce TB incidence. A new 12-dose, once-weekly regimen of isoniazid and rifapentine (3HP) has been shown to have similar efficacy, higher completion rates, and better tolerability relative to nine months of daily isoniazid. However, the best approach to delivering 3HP remains uncertain.

Methods: We surveyed consecutive PLHIV presenting for routine care at the Mulago HIV/AIDS clinic (Kampala, Uganda) to elicit self-efficacy and intention - both strong predictors of actual behavior - to complete 3HP. We randomized participants to respond to either a hypothetical survey-based scenario describing delivery via directly observed therapy (DOT, current standard-of-care) or one describing patient choice between DOT and self-administered therapy (SAT). Participants were read a standardized script describing their assigned scenario and asked to rate their level of confidence in, and intention to complete, 3HP on a 10-point Likert scale.

Results: Of 251 PLHIV who participated in the survey, 158 (63%) were women, median age was 39.5 years (IQR 33.6-47.5) and median CD4 count was 502 cells/ μ L (IQR 359-657). Patients assigned to the patient choice scenario expressed higher confidence (median score 9 [IQR 9-9] vs. 7 [IQR 3-9], $p < 0.001$) and greater intention (median

score 9 [IQR 9-9] vs. 8 [IQR 7-9]), $p < 0.001$) to complete 3HP. Among patients assigned to the DOT scenario, 25% expressed low confidence (score 0-3) and 10% low intention to complete 3HP. In contrast, all patients assigned to the patient choice scenario expressed high confidence and intention (score 7-10) to complete 3HP.

Conclusions: Patients offered an informed choice between 3HP delivery strategies expressed higher confidence and greater intention to complete TB preventive therapy. These data support a randomized evaluation of whether patient choice of delivery strategy actually results in higher levels of 3HP completion.

POSTER DISCUSSION SESSIONS

PS01 Drugs, bugs, biomes and biomarkers

PS01-400-25 Mycobacterial growth inhibition is associated with trained innate immunity

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Background: The lack of defined correlates of protection hampers development of vaccines against tuberculosis (TB). In vitro mycobacterial outgrowth assays are thought to better capture the complexity of the human host/ *Mycobacterium tuberculosis* (Mtb) interaction.

Methods: Here, we used a PBMC-based “mycobacterial-growth-inhibition-assay” (MGIA) to investigate the capacity to control outgrowth of Bacille Calmette-Guérin (BCG).

Results: Interestingly, strong control of BCG outgrowth was observed almost exclusively in individuals with recent exposure to Mtb, but not in (long-term) latent TB infection, and only modestly in BCG vaccinees. Mechanistically, control of mycobacterial outgrowth strongly correlated with the presence of a CD14^{dim} monocyte population, but also required the presence of T-cells. The non-classical monocytes produced CXCL10, and CXCR3-receptor blockade inhibited the capacity to control BCG outgrowth. Expression of CXCR3 splice variants was altered in recently Mtb exposed individuals. Since we observed strong MGIA control recently after Mtb exposure and we found a strong association with monocytic cells we hypothesized that trained innate immunity was responsible for the observed MGIA control. Indeed, cytokines previously associated with trained immunity were detected in MGIA supernatants, and CXCL9, CXCL10 and CXCL11 represent new markers of trained immunity. These data indicate that CXCR3-ligands are associated with trained immunity and critical factors in controlling mycobacterial outgrowth.

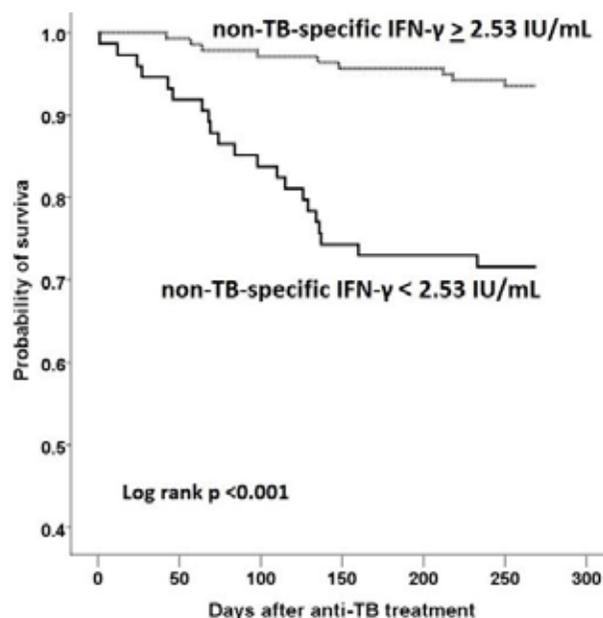
Conclusions: In conclusion, control of mycobacterial outgrowth early after exposure to Mtb is the result of trained immunity mediated by a CXCL10-producing non-classical CD14^{dim} monocyte subset.

PS01-401-25 Predictive value of interferon- γ responses in treatment outcomes of tuberculosis patients: a prospective cohort study in a TB-endemic area

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Background: Individuals with impaired immunity are susceptible to *Mycobacterium tuberculosis* (MTB) infection. Immunosuppression induced by MTB is an important component in the pathogenesis of active tuberculosis (TB). However, the impact of TB-specific and non-TB-specific IFN- response on the clinical presentations and treatment outcomes of TB patients remains uncertain.

Methods: Culture or pathology-proven active TB patients were prospectively enrolled in a tertiary medical center in Taiwan. QuantiFERON-TB GOLD In-Tube (QFT-GIT) assays were performed before the initiation of anti-TB treatment. TB-specific IFN- responses (TB antigen tube subtracted from the nil tube) and non-TB-specific IFN- responses (mitogen tube subtracted from the nil tube) were measured and associated with treatment outcomes, including two-month culture conversion and on-treatment mortality. Clinical characteristics of TB patients with depressed IFN- responses were also investigated.



[Kaplan-Meier analysis of on-treatment mortality in TB patients]

Results: A total of 212 active TB patients were included in the analysis. Lower lymphocyte counts and presence of concomitant bacterial/fungal infection were clinical characteristics associated with depressed non-TB-specific IFN- responses, and patients with higher TB-specific IFN- responses were more likely to be sputum

smear positive. Regarding treatment outcomes, patient with lower non-TB-specific IFN- responses had lower two-month culture conversion rate (71.1% vs. 84.7%, $p=0.033$) and higher on-treatment mortality (22.6% vs. 5.7%, $p=0.001$) than those with higher non-TB-specific IFN- responses. In multivariate analysis, non-TB-specific IFN- responses were an independent factor associated with two-month sputum culture non-conversion (OR 2.49, 95% CI 1.05-5.90) and on-treatment mortality (HR 2.76, 95% CI 1.15-6.62). The impact of TB-specific IFN- responses on sputum culture conversion and on-treatment mortality of TB patients was limited.

Conclusions: Depressed non-TB-specific responses, but not TB-specific IFN- responses, measured by QFT-GIT before the initiation of anti-TB treatment were significantly associated with worse treatment outcomes in TB patients.

PS01-402-25 Complement component C1q as serum biomarker to detect active tuberculosis

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Background: Tuberculosis (TB) remains a major threat to global health. Currently, diagnosis of active TB is hampered by the lack of specific biomarkers that discriminate active TB disease from other (lung) diseases or latent TB infection (LTBI). Human gene expression analysis revealed that genes encoding complement components, in particular C1q, are expressed at higher levels in active TB compared to LTBI.

Methods: C1q protein levels were determined using ELISA in sera from patients, from geographically distinct populations, with active TB, LTBI as well as disease controls.

Results: Serum levels of C1q were increased in active TB compared to LTBI in four independent cohorts and discriminated with an AUC of 0.77 [0.70 ; 0.83]. After six months of TB treatment, levels of C1q had normalized to those of endemic controls, indicating an association with disease rather than individual genetic predisposition. Importantly, C1q levels in sera of TB patients were significantly higher as compared to patients with sarcoidosis or pneumonia, clinically important differential diagnoses. Moreover, exposure to other mycobacteria such as *M. leprae* (leprosy patients) or BCG (vaccin-

ees) did not present with elevated levels of serum C1q. In agreement with the human data, in non-human primates challenged with *Mycobacterium tuberculosis*, increased serum C1q levels were detected in animals that developed progressive disease.

Conclusions: Circulating C1q is a novel TB biomarker, which discriminates active TB from most other conditions, including other lung diseases, and could have added value in diagnosing TB.

PS01-403-25 HIV and TB perturb the immune regulatory and cytotoxic subpopulations of NKT cells

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Background: In the pre-antibiotic era, ~20% of Tuberculosis (TB) patients overcame the disease without therapy; implying host immunity can sometimes control disease. The risk of disease progression is higher among HIV-infected individuals, and therefore we evaluate how HIV alters the balance of cytotoxic versus immune regulatory NKT immune phenotype in individuals with TB and latent *Mycobacterium tuberculosis* infection (LTBI). **Methods:** We evaluated the NKT immune response from 19 individuals with TB (11 HIV-infected) and 25 with asymptomatic LTBI (10 HIV-infected). Using flow cytometry based multi-dimensional immune profiling, we analyzed the expression level of previously described determinants of NKT cytotoxicity (CD3^{dim} and perforin^{hi}) and immune regulatory (CD3^{bright}) phenotype and function.

Results: Participants with TB had increased CD3^{bright}NKT cells ($p = 0.014$), while LTBI participants had increased CD3^{dim}NKT cells. TB participants had an increased frequency of the immune regulatory CD3^{bright}NKT subpopulation ($p = 0.048$), which interestingly had an increase in the cytotoxic perforin^{hi} population ($p = 0.021$). In contrast the cytotoxic CD3^{dim}NKT population was increased in LTBI, compared to TB participants ($p = 0.078$). HIV did not effect the ratio of CD3^{bright} versus dim in either TB or LTBI participants, however it did decrease the percentage of the cytotoxic perforin^{hi} sub-populations compared to HIV-uninfected participants in both TB and LTBI strata ($p = 0.005$).

Conclusions: CD3^{bright} and perforin^{hi} NKT sub-populations influence regulatory versus cytotoxic function, respectively. We demonstrate that participants with TB and HIV have perturbed NKT functionality characterized by an increased regulatory and decreased cytotoxic function. Among HIV-infected participants, the cytotoxic perforin NKT subset are predominantly altered.

In contrast, TB and HIV-TB co-infection perturb both the perforin^{hi} and CD3^{bright} populations. The resultant decrease in the cytotoxic perforin^{high} population may be a mechanism through which HIV promotes TB disease progression.

PS01-404-25 Complementary bio-informatics approaches to analyze TB-specific immune function

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Background: The immune response to *Mycobacterium tuberculosis* (*Mtb*) is critical towards distinguishing clinical outcomes, yet there are multiple, complementary approaches to analyze immune function. In this study, we compared the functional profile of the *Mtb*-induced response of Non-lymphocytes, CD4⁺T cells, and CD8⁺T cells between individuals with asymptomatic *Mtb* infections and individuals with Tuberculosis (TB).

Methods: Peripheral blood mononuclear cells (PBMCs) from 22 individuals with TB and 23 asymptomatic, infected controls were stimulated with BCG sonicate and TB-specific peptides (ESAT6/CFP10). Immune function was analyzed using median fluorescent intensity (MFI), SPICE (Simplistic Presentation of Incredibly Complex Evaluations) and CITRUS (Cluster Identification, characterization and regression).

Results: The evaluation approaches (MFI, SPICE and CITRUS) yielded complementary results. MFI demonstrated increased BCG and TB-specific CD4⁺ T cell production of TNF in participants with TB compared to infected controls. Individuals with TB had CD8⁺ T cells with elevated BCG and TB-specific perforin MFIs. Non-lymphocytes (mostly monocytes and dendritic cells) had an increase in Ki-67 MFI in diseased compared to infected participants. In comparison, by SPICE, TB participants CD4⁺ T cells demonstrated an increase in proliferating (Ki-67⁺) cells simultaneously producing IFN- and TNF and an increase in TB-specific cells expressing PD-1. CD8⁺ T cells from TB patients demonstrated decreased T-bet⁺ up-regulation of perforin. However, NK cells from TB diseased individuals had increased perforin upregulation and decreased GATA3⁺-T-bet⁺ population.

The predominance of IL-10 production occurred in non-lymphocytes and was associated with IL-4 and Ki67⁺ in TB diseased compared to infected participants. CITRUS analysis identified TB diseased participants to have increased clusters of IL-13 from non-lymphocytes, increased perforin from NK cells and elevated CD107a in CD8 cells.

Conclusions: When used in complement, multiple bioinformatic approaches provide comprehensive functional differences in immune cells of participants with TB disease compared to infected participants.

PS01-405-25 Interleukin-6, interleukin-13 and interferon-γ as potential biomarkers for treatment failure in pulmonary tuberculosis

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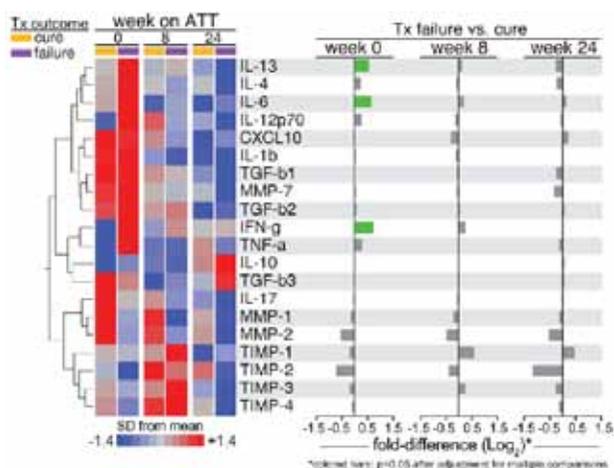
Background: Biomarkers are needed for the early identification of tuberculosis cases at risk of treatment failure.

Methods: New adult (≥18 years) drug-sensitive pulmonary tuberculosis cases were enrolled at or within one week of treatment initiation and, prospectively evaluated at 8 weeks and 24 weeks for plasma concentrations of 20 cytokines linked to the host immune response in tuberculosis through the ongoing CTRIUMPH study in Pune and Chennai, India. Cytokine concentrations were evaluated, in duplicates, using multiplex ELISA according to manufacturer protocols. Markers associated with treatment failure, defined as *Mycobacterium tuberculosis* growth on liquid or solid culture at 24 weeks of treatment, were identified using non-parametric tests. Cytokine concentrations were log₂ transformed and z-score normalized for analysis. *P* values were adjusted for multiple comparisons using the Benjamini-Hochberg procedure.

Results: Of the 30 participants enrolled, 20 (74%) were male, 7 (26%) had diabetes (defined as HbA1c≥6.5%) and 2 (7%) had HIV-coinfection. The median (IQR) age and BMI at enrollment was 36 (28-50) years and 18 (16-20) kg/m², respectively. Four (13%) participants failed treatment; none had diabetes or HIV-coinfection. While plasma cytokine concentrations significantly declined with treatment, TIMP-4 and TNF- were overexpressed at 8 weeks and 24 weeks of treatment relative to their baseline levels, respectively. Participants who failed treatment had significantly higher plasma concentrations of IL-6 (*p*< 0.001), IL-13 (*p*< 0.001) and IFN- (*p*<0.001) at treatment initiation compared to those who were cured, however this difference was not statistically significant at 8 and 24 weeks of treatment.

Conclusions: Our interim analysis suggests a possible association between overexpression of circulating IL-6, IL-13 and IFN- at treatment initiation and treatment failure among drug-sensitive pulmonary tuberculosis cases. Well powered validation studies should be under-

taken to evaluate the performance of these biomarkers, individually or in combination, for predicting unfavorable tuberculosis treatment outcomes.



[Differential cytokine expression by treatment outcomes.]

PS01-406-25 Pre-treatment patients with active tuberculosis have a perturbed oral, airway and gut microbiome

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Background: Tuberculosis (TB) is the leading infectious cause of death globally and, in South Africa, kills more people than any other condition however, its association with the microbiome is poorly understood.

Methods: To characterize the microbiome, oral washes, induced sputum and stool were collected from 105 pre-treatment patients with presumptive TB. Cases were classified based on a positive *Mycobacterium tuberculosis* culture, Xpert or Ultra result (n=58) and symptomatic controls classified based on negative culture- or Ultra result (n=47).

Up to two healthy household contacts (culture- or Ultra-negative; n=155) per patient had the same specimens collected. Microbial DNA was extracted and sequencing of the V4 16S rRNA gene region done using the Illumina MiSeq. Data was analysed using QIIME and phyloseq in R. Linear discriminant analysis effect size (LEfSe) was used for biomarker discovery. Phylogenetic Investigation of Communities by Reconstruction of Unobserved States (PICRUSt) was used to infer microbial functional content in clinical specimens.

Results: Although alpha- and beta diversity was similar between cases and controls, cases were enriched with anaerobes, *Paludibacter* and *Prevotella*, in oral washes and induced sputum, respectively. In stool, cases had higher microbial diversity than healthy controls (Shannon's diversity; $p=0.025$) and clustered separately from both symptomatic and healthy controls during Principal Coordinates Analysis ($p < 0.01$). Healthy gut commensal, *Bifidobacterium*, was significantly depleted in cases, who were instead enriched with *Erysipelotrichaceae* - members of which are highly immunogenic and positively correlate with tumor necrosis factor alpha levels. Top-ranking functions predicted by PICRUSt in cases included pyruvate, butanoate and propanoate metabolism.

Conclusions: Distinct microbiota and functional pathways were associated with active TB, most notably in stool. The gut microbiome may thus regulate lung immunity via the gut-lung axis and should be investigated as a potential marker for TB. Future analyses will explore the association of microbial metabolites and immune markers with active TB.

PS01-407-25 Aerosol spectinamide-1599 therapy against tuberculosis

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Background: The lengthy treatment for tuberculosis (TB) is the primary cause of the emergence of multidrug resistant tuberculosis (MDR-TB), as it frequently results in non-compliance. One approach to improve TB therapy is to develop an inhalational TB therapy that when administered with oral TB drugs eases and shortens treatment. Spectinamides are new semisynthetic analogs of spectinomycin with excellent activity against *Mycobacterium tuberculosis* (Mtb) including MDR and XDR Mtb strains. The lead compound spectinamide-1599 demonstrated strong efficacy against pulmonary TB when administered directly to the lungs of mice via intrapulmonary aerosol (IPA) delivery.

Methods: Using the murine TB model and IPA delivery of spectinamides-1599 we determined 1.- concentrations of spectinamide-1599 in plasma, bronchoalveolar

liquid fluid (BALF) and tissue via LC-MS/MS analysis and 2.- Efficacy in Balb/c or C3HeB/FeJ mice infected with Mtb Erdman strain followed by treatment with spectinamide-1599 via IPA during 4 and 8 weeks. At end of treatment mice were euthanized and lung samples were prepared for bacterial enumeration and histology.

Results: The plasma, BALF and tissue exposure of spectinamide-1599 over a wide range of dose levels demonstrated that plasma exposure exhibited dose-dependent increases. The lung and BALF exposure and accumulation of drug was substantially higher than plasma. Exposure in liver and spleen remained limited after multiple dose IPA administration. The efficacy results showed that there is a dose dependent efficacy where 100 mg/Kg provides highest efficacy ($> 1\log_{10}$ CFU reduction after 4 weeks of treatment). However, treatment of Mtb infected mice with lower doses (10mg/Kg) during 8 weeks achieves similar efficacy as the higher dose.

Conclusions: Spectinamide-1599 after intrapulmonary aerosol delivery accumulates in the lungs for extended periods of time. The efficacy studies indicate that low doses of spectinamide-1599 when administered for extended period of time achieves the same efficacy as higher doses.

PS01-408-25 Metformin as host-directed therapy for tuberculosis treatment

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Background: Tuberculosis (TB) is one of the top 10 causes of death worldwide, where multidrug-resistant TB remains a public health crisis. The standard drug regimen is effective with respect to cure. However increasing prevalence of drug-resistant strains has led to a paradigm shift in the search for new drugs. Therefore, rather than targeting the bacterium; augmenting the host response could optimize TB treatment by focusing on repurpose drugs and host directed therapy (HDT). FDA-approved drug metformin, which is currently used to treat type 2 diabetes has been proposed to improve the immune response to mycobacterium TB (Mtb) infection. However there remains a gap in the mechanism of action and limitations on the use of metformin. We applied live cell imaging to track Mtb infection outcomes to investigate a testing pathway for HDT using metformin as a model. We firstly assessed whether metformin affects the ability of macrophages to control intracellular Mtb.

Methods: Monocyte derived macrophages (MDM) were cultured from a healthy individual, infected with the AY360 strain, and treated with metformin (25mM), isoniazid(20mM) and a combination dose. We then used time-lapse microscopy to track the cell and Mtb interaction for a five day period. The experiment was performed in triplicate.

Results: We observed isoniazid to act as previously known, by targeting the bacterial cell wall. For the first time we observed metformin targeting live macrophages and suppressing bacterial growth, however when the cell dies Mtb growth continues. Most importantly, metformin in combination with isoniazid has a greater effect as opposed to isoniazid and metformin independently.

Conclusions: This set of data has prompted us to validate and complete the mechanism of action of metformin, by assessing the effect of metformin on phagosome acidification by flow cytometry based on the use of bi-fluorescent particles, and RNA-sequencing to elucidate alterations in gene expression under the same conditions.

PS01-409-25 Anti-mycobacterial activity of methanolic extract of *Penicillium* sp. against multidrug-resistant *Mycobacterium tuberculosis*

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Background: Tuberculosis (TB) has reemerged as one of the leading causes of death in the world, reaching a million deaths annually. The emergence of multidrug-resistant strains of *Mycobacterium tuberculosis* and co-infections with HIV has aggravated this serious situation. There is a fundamental need to explore alternative anti-TB agents. Microorganisms are important sources of bioactive natural products with enormous potential for the discovery of new molecules for drug discovery; more than 70% of the antimicrobial drugs currently in clinical use are natural products or natural product derivatives.

The aim of the study was to evaluate anti-mycobacterial activity of methanolic extract of a soil isolate, *Penicillium* sp. against MDR isolates of *M. tuberculosis*.

Methods: An endophytic fungi *Penicillium* sp. was isolated from the soil samples. Molecular identification of the fungal strain was carried out by amplification of ITS (Internally Transcribed Spacer region) rDNA sequence by making use of ITS1 as forward and ITS4 as reverse primer. Fungus was cultured on Potato Dextrose Agar (PDA) plates at 25 °C for 15 days. The secondary metabolites were extracted from solid culture medium by extraction with methanol and then dried on rotary evaporator at 45 °C, yielding 4 g/l of brown colour extract.

Results: Minimum inhibitory concentration (MIC) was performed by using 7H9 middle brook broth dilution technique. Crude extract showed a good inhibitory effect against MDR *M. tuberculosis* isolates with MIC less than 1mg/ml.

Dried extract of fungus was further subjected to column chromatography (C8, Sephadex) in order to separate out different polarity metabolites in different fractions.

ESI-MS (Electron Spray Ionization Mass Spectrophotometry) GC-MS (Gas Chromatography Mass Spectrophotometry) and APCI-MS (Atmospheric Pressure Chemical Ionization) were carried out for fractions showing higher activity against the *M. tuberculosis* in disc diffusion assay.

Conclusions: methanolic extract of penicillium sp. exhibits a strong anti-mycobacterial activity against multi-drug resistant *Mycobacterium tuberculosis*.

PS01-410-25 Tuberculous lymphadenitis is associated with changes in the microbiome at the site of disease

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Background: Tuberculous lymphadenitis (TBL) is the most common presentation of extrapulmonary tuberculosis (EPTB). The microbiome in EPTB is largely undefined and may reveal new targets for understanding host-pathogen interactions and diagnostic or therapeutic targets. The study aimed to characterize the site-of-disease microbiome and inferred metagenome in patients with lymphadenopathy undergoing investigation for active TB in Cape Town, South Africa.

Methods: Fine needle aspirates (FNAs) were collected from the necks of 23 pre-treatment TB cases (Xpert- or culture-positive) and 19 controls (Xpert- and culture-negative) with suspected TB lymphadenitis. Background specimen sampling controls (skin swab, saline needle flush) were collected. 16S rRNA gene sequencing was done using Illumina MiSeq. Taxonomy was assigned to 16S sequences using Greengenes.

Results: Overall, skin had the highest microbial diversity (alpha diversity), and FNA microbial composition was more similar to skin than saline (PERMANOVA, $p=0.001$), indicating that contamination from saline was not in FNAs. Cases had a different microbial composition compared to symptomatic controls (PERMANOVA, $p=0.009$). Furthermore, cases with HIV co-infection had a distinct microbial composition compared to HIV-negative cases (PERMANOVA, $p=0.006$). In addition to *Mycobacterium spp.*, several other members of the Actinobacteria phylum (e.g., *Dermacoccus*, *Atopobium*) were enriched in cases, while gram-negative *Bacteroidetes* phylum were abundant in symptomatic controls. While HIV-positive cases only had the *Enterobacteriaceae* family enriched, HIV-negative cases enriched several taxa, including gut (*Bifidobacterium*, *Veillonella*)

and oral (*Streptococcus*) commensals. Functional analysis using PICRUSt revealed metabolic functions involving fatty acid metabolism and amino-acid metabolism enriched in cases compared to symptomatic controls, whilst transporters, ribosome and ABC transporters functions were enriched in symptomatic controls.

Conclusions: These findings show for the first time that patients with TBL have a distinct site-of-disease microbiome, comprised of *Mycobacteria* (most abundant), as well as many non-*Mycobacteria* taxa, compared to symptomatic controls, and demonstrate a shifted functionality compared to controls known to be associated with inflammation.

PS01-411-25 MIC of sitafloxacin, a new fluoroquinolone, against multidrug-resistant M. tuberculosis

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Background: Sitafloxacin is a new fluoroquinolone which was marketed only in Japan and Thailand. Objective is to study MIC distribution of Sitafloxacin, Moxifloxacin, Levofloxacin and Ofloxacin against clinical isolates of MDR *M.tuberculosis*.

Methods: Subculture of proven MDR *M.tuberculosis* was prepared as suspension and inoculated in 96 wells microtiter plate containing 100 µl. of 2X 7H9 + OADC with serial dilution of Sitafloxacin, Moxifloxacin, Levofloxacin, and Ofloxacin at 4.0 - 0.008 µg/ml. Inoculated plates were incubated at 37 Celsius. Reading was done every day after one week of incubation to determine growth in negative control and drug containing media.

Results: 50 strains of MDR *M.tuberculosis* were included in this study from January 2016 to July 2016. Number of strains which had MIC in following drug concentration of 8.0, 4.0, 2.0, 1.0, 0.50, 0.25, 0.125, 0.06, 0.03, 0.015, 0.008 and < 0.008 µg/ml. were as follow: Sitafloxacin was 0, 0, 0, 1, 1, 2, 6, 7, 5, 7, 0, 21 strains. Moxifloxacin was 1, 3, 4, 5, 5, 2, 16, 0, 14, 0, 0, 0 strains. Levofloxacin was 2, 7, 7, 4, 1, 21, 0, 8, 0, 0, 0, 0 strains. Ofloxacin was 9, 9, 2, 2, 18, 10, 0, 0, 0, 0, 0, 0 strains. MIC50 and MIC90 of Ofloxacin, Levofloxacin, Moxifloxacin and Sitafloxacin were 0.5, 0.25, 0.125, 0.015 µ/ml. and 8.0, 4.0, 2.0, 0.125 µg/ml. respectively. 16 strains had MIC of Levofloxacin more than 1.0 µg/ml. which were extensively drug resistant tuberculosis (XDR-TB). These strains had MIC50 and MIC90 of Sitafloxacin of 0.06 and < 0.008 µg/ml. which much lower than serum maximum concentration of Sitafloxacin.

Conclusions: Sitafloxacin was the fluoroquinolone which has the lowest MIC in the tested MDR/XDR-TB strains and may be able to use in treatment of XDR-TB.

PS02 Community engagement to reach and support people with tuberculosis

PS02-412-25 Community involvement supports successful treatment outcomes among patients with TB: evaluation of community-based TB care projects in Myanmar

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Background: Myanmar is one of the 30 high TB burden countries. National TB control program has been striving towards the goal of ending TB epidemic (< 10 cases/100,000 population) by 2035. Ensuring completion of anti-TB treatment is one of the key strategies in reducing transmission and preventing development of drug resistant TB. Since 2011, non-governmental organizations (NGOs) have been implementing community-based TB care (CBTC) projects with support from Global Fund in conflict-affected and migrant areas with limited health care services. Trained community volunteers serve as DOTS supervisors, providing home visits, psycho-social support, side effects monitoring, and support for follow up visits.

Methods: This descriptive analysis uses data from progress reports of four NGOs implementing community-based TB care with the support of Global Fund in 31 townships in Myanmar in 2016. Treatment outcomes of patients who were supported by CBTC projects were evaluated.

Results: In 2016, 5,384 patients were provided with anti-TB treatment under DOTS supervision by community volunteers. Among supported patients, treatment success rate (TSR) was higher (92%) than the national TSR (87%). Loss to follow-up (LFU) among CBTC-supported patients was 2%, lower than the 6% LFU seen among TB patients notified nationally. Among 1,063 bacteriologically confirmed patients, TSR was 83% (including patients from areas with active armed conflict) while the national TSR among patients with bacteriologically confirmed TB was 85%. Loss to follow up among volunteer-supported bacteriologically confirmed TB was 3% as compared with the national LFU of 6% observed during the same period.

Conclusions: Involvement of community volunteers in TB care enhanced treatment outcomes and reduced loss to follow-up. DOTS supervision is effective in promoting drug adherence and supportive positive TB patient outcomes. CBTC projects support national program in achieving higher treatment success rates and therefore should be expanded to a larger scale.

PS02-413-25 Local NGO engagement in the fight against TB: experience of eight provinces in Democratic Republic of Congo

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Background and challenges to implementation: According to WHO 2017 Report DRC noted among 30 high TB burden countries where TB remains a public health priority. One of the challenges is case detection where half of the TB cases remain undetected. The findings reflect the challenges of NGO involvement in TB screening in hard to reach and conflict settings.

Intervention or response: International Union against TB and lung Diseases (The Union) through Challenge TB (CTB) project in DRC is supporting four local NGOs to improve community activities for TB diagnosis and care since 2014. Members of three NGOs are mostly cured TB patients and the members of fourth NGO are working with the persons living with HIV.

Local NGOs interventions included: sensitization activities, screening for identification of presumptive TB cases in the community (door-to-door, household contact visits, health facilities) and refer (person referral or sputum transportation) for diagnosis and treatment to "centre de diagnostic et de traitement" CSDT).

The results of the first 3 years of this project are reported below.

Results and lessons learnt: The number of presumptive TB cases referred by NGO members increased each year: 6,202 in year 1, 23,687 in year 2 and 43,451 in Year 3 with a consequently increase of. The number of notified TB: respectively 1250, 3853 and 6049.

The contribution of NGOs among all TB cases notified in 8 provinces increased each year of the project: 3% (1250/35811) in year 1, 9% (3853/40970) in year 2 and 13% (6049/47967) in year 3. 99% of these patients were put on treatment.

The followings difficulties as sample transportation, security situation and financial issue were noted.

Conclusions and key recommendations: Community engagement is ongoing and can contribute significantly to the national case detection. Local NGO involvement gave positive results in case notification and treatment outcome even in hard to reach and under conflict settings.

PS02-414-25 Tremendous increase of community contribution in tuberculosis case detection in Tanzania, 2016-2017

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Background and challenges to implementation: Globally, Tanzania is among the 30 high burden countries with TB. The prevalence is 528 cases per 100,000 (WHO, 2013). The average country notification is estimated at 62,000 cases per year equivalent to 36% of all estimated TB cases. Through Global Fund support, Tanzania has intensified its efforts to look for missed TB cases in health facilities and at community level in thirteen regions with low TB case notification.

Intervention or response: Community Health Workers and Sputum fixers were identified, trained and supported with transport, monthly allowances and enablers for Active TB case finding at community level. Activities conducted include TB education, identification and referral of Presumptive TB cases for diagnosis, contact tracing and Active TB case finding in the general population. In hard to reach areas, sputum fixers were supported to perform initial stages of microscopy at dispensaries, then transport slides with fixed smear to diagnostic centers for microscopy. Feedback results were communicated to the dispensaries for TB treatment initiation for confirmed TB cases. Referrals from community were captured in Electronic TB data system.



[Tremendous increase of community contribution in TB case notification in Global Fund supported regions from 2016 - 2017]

Results and lessons learnt: From 2016, country TB case notification is notably to be significantly increasing after a five years period showing low TB case notification. Total of 68,864 TB cases were notified in 2017, showing an increase of 6% (3962) compared to 2016. Implementation of community interventions was among the ma-

ior contributing factors to this success. Fourth quarter of 2017, TB cases attributed from community referral raised to 14.5% (9,949) from 6.0% (first quarter 2016) of all TB cases notified in the country. Significant community contribution has been realized in GF supported regions where notification has raised from 7% (first quarter 2016) to 16% (fourth quarter) in 2017.

Conclusions and key recommendations: Community engagement in high TB burden countries, highly contributes to TB case detection increase and reduction of TB problem.

PS02-970-25 A Community-Based Active Tuberculosis Case Finding Program in the Philippines: Social Capital predictors of positive outcomes

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Background: Screening, or active case-finding, among high burden populations has become an important strategy to locate active tuberculosis (TB) in a timely manner [1]. The results of an active case-finding program, implemented by International Care Ministries (ICM) in the Philippines, were examined to understand how social capital affects active case-finding outcomes.

Methods: This study was nested within ICM's 16-week poverty reduction program among extremely poor Filipinos. ICM staff carried out symptom screening and suspected cases were referred to the closest rural health unit (RHU) for testing. Program monitoring data was collected and repeated cross-sectional surveys were conducted through one-on-one interviews at the beginning and end of the program.

Results: A total of 4635 individuals were screened. 1290 (27.8%) were symptom positive and required referral of whom 336 (7.2%) underwent RHU testing for TB. Statistically significant difference in one social capital measure was found among RHU attenders versus non-attenders. The range of each measure was very narrow between the two groups, falling between 3.7 and 4.3 (scale 1-5). The means of "family satisfaction", "friendship satisfaction", and "trust in relatives" were higher by 0.1 among RHU attenders. In multi-level regression analysis, each increase in baseline level of "trust in relatives" was associated with a 1.08 times increase in likelihood of getting tested at an RHU. Though not statistically significant, "Family Satisfaction" and "Friendship Satisfaction" showed a small increase of 1.04 and 1.01 times, respectively.

Conclusions: These findings suggest that social capital plays an important role in an individual's health seeking behaviour. Individuals who perceive a higher sense of

security or stronger ties with their close relatives, were more likely to be tested for TB. Future studies need to explore in detail what individuals in low socio-economic group regard as “trust” and how this can be used to positively change health seeking behaviour.

	satisfaction in family	satisfaction in friends	trust in relatives	trust in neighbours	trust in religious leaders	trust in community leaders
log odds	0.04	0.01	0.08	-0.03	-0.01	-0.02
exp (odds)	1.04	1.01	1.08	0.97	0.99	0.98
p value	0.07	0.79	0.01	0.20	0.72	0.42

[Social Capital and RHU Attendance Outcomes, Multi-level Regression results]

PS02-415-25 Community contribution to halting the lost to follow-up phenomenon of TB cases: efforts in Maputo city, Mozambique

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Background and challenges to implementation: Mozambique Capital, the Maputo city, faces high TB burden ranked among top 3, with more than 6,760 cases detected in 2017 among 1.1 million inhabitants. There is an agreement between public TB diagnostic facilities and a university-based operational research (The Eduardo Mondlane University or UEM APOPO Project), running a rat-based technology to re-examine all bacteriologically negative sputum within facilities performing microscope testing. APOPO also compares rat testing sensitivity to GeneXpert testing. Among additional cases, around 50% of yield, about 25% to 30% cases were lost to follow up (LTFU) and not claiming their results.

Intervention or response: To address the LTFU-related challenges, APOPO Project and Associação Kenguelekezé, a community-based organization (CBO), began a collaboration relied on tracking daily enlisted cases (i) to ensure collection of correct and complete identifiers, and (ii) to track TB confirmed through cell-phone calls/sms, followed by household visits, involving community leaders.

Results and lessons learnt: During 2017, APOPO had an additionality of 393 TB cases, which Kenguelekezé traced 373 (95.0%) of them, of whom 336 (85.5%) started treatment. Remaining were found died 12 (3.1%) or refused treatment 25 (6.4%), alleging at least one of the following:

- (i) fear of stigma and discrimination,
- (ii) religious faith in the cure, or;
- (iii) children dependent on third parties.

Community activists, collecting sputum deliverers' identifiers correctly and completely combined with cellphone contacting services, and household visits has the potential for tracing or even for halting the LTFU phenomenon in Maputo city.

Conclusions and key recommendations: APOPO and Kenguelekezé added more clients for diagnosis and patients on treatment. LTFU phenomenon can efficacy addressed by establishing sentinel efforts, at TB diagnostic sites, for correct and complete client identity collection and consented household visits. This strategy of preliminary and correct identification of clients should be expanded to other provinces countrywide.

PS02-416-25 Contribution of community health committees in detecting new TB cases in the Sughd Oblast, Tajikistan

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Background and challenges to implementation: Based on WHO estimates, there are about 1260 ‘missing’ cases in Tajikistan. These are either cases which have not been reported to the NTP or have not been detected and initiated on treatment. In addition, Tajikistan is one of WHO’s high burden MDR-TB countries with growing XDR-TB.

Intervention or response: The USAID TB Control Program (2014-2019) implemented by Project HOPE is supporting Tajikistan in finding these missing cases with innovative approaches. The Program builds the capacity of community referral and support networks to ensure early diagnosis, timely treatment initiation and adherence to treatment. 95 Community Health Committees (CHCs) were established in Sughd oblast and linked with Healthy Lifestyle Centers under MOH in the first year. CHCs are rural community-level health committees, which include representatives of local authorities, women’s committees, religious leaders, youth committees, medical workers. 570 CHC members were trained on TB issues and community mobilization, and supported in community activities. CHCs conduct educational activities to reduce stigma and discrimination towards TB patients and their families, identify and refer people with presumptive TB symptoms for diagnosis, provide socio-psychological support to those diagnosed with TB. CHCs specifically target their outreach towards migrants and women.

Results and lessons learnt: Since July 2015, 95 CHC contributed 17% (420 of 2,447) of new TB cases detected in Sughd oblast. During the last year, CHC added to the detection of one in four new TB cases in Sughd, a 2.5-fold increase from the first six months of their operation (Figure-1).

Conclusions and key recommendations: Engaging the community in TB response and active case finding is critical. The increasing contribution of CHCs to newly detected TB cases offers evidence of the success and effectiveness of the approach. However, further studies are needed to understand contribution of CHCs to the overall yield of TB case detection, cost-effectiveness and sustainability of the piloted approach in Tajikistan.



[Figure 1. Increasing contribution of Community Health Committees in new TB case detection, USAID TB Control Program districts in Sughd, Tajikistan]

PS02-417-25 Community engagement a highly effective approach to increase TB case finding in four districts in Nias Island, Indonesia

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Background and challenges to implementation: Nias Island consists of 5 Districts and known as most under-developed regencies in North Sumatera. It contains over 105 islands, inhabited by indigenous people. With this geographical condition, the transportation cost is very high between the islands or villages, poor of existing health facilities and local government limitation, many people with TB do not have access to health service.

Intervention or response: Community volunteer were recruited and trained to screen for symptoms of TB in each village. Individuals suspected of having TB were then referred to a health facility to smear microscopy. Community health volunteer's facilitated transportation to ensure testing occurred. When a patient was detected, the volunteers helped to initiate and follow up treatment in the village. In addition to these community-based activities, laboratory technicians were trained and monitored to improve the quality of diagnostic services and advocacy to government to increase their budget for TB.

Results and lessons learnt: In a span of just 9 months, community volunteers screened over 88,000 people for symptoms of TB across 301 villages. These activities resulted in the detection of 5,500 of people presumptive TB who were referred for testing. Over 446 smear-positive TB were diagnosed and 22 of these newly detected patients were among children aged less than 14 years. With the same approach increase active case finding activities resulted +200% increase in new smear-positive case notifications compared with the same quarters in the prior year.

Conclusions and key recommendations: This project demonstrates that approach community health volunteers can be a highly effective solution to reach people with TB in hard reach populations.

Considering the significant of this result, initiatives which are able to expand services and demonstrate increases in anti-TB treatment uptake should be prioritized for scale-up.

PS02-418-25 Community-based active tuberculosis case finding in rural settlements in Homa-Bay County, Kenya: a feasible and effective strategy to find missing TB cases

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Background: Emerging from the limitations of the current case finding strategies and the global urgency to increase Tuberculosis case detection, a renewed interest in active case finding (ACF) has risen. WHO calls for more evidence on innovative ways of TB screening, to inform global guideline development.

We aimed to assess the feasibility of community-based ACF for TB diagnosis among the rural and beach settlements of Suba zone during World TB day period and determine its impact on case detection and treatment uptake.

Methods: Between 19/03/2018 to 23/03/2018 the clinical team in Homa-Bay conducted targeted community based TB screening in Suba Sub County. Health workers and community health volunteers performed symptom based TB screening alongside chest Xray screening. Sputum samples were collected and specimen transported to Sub county hospital through rider networking system. The Gene Xpert MTB/RIF assay was performed and positive results relayed to clinicians. Health care workers contacted diagnosed TB patients and linked them to respective facilities for treatment.

Results: Out of the 1,073 clients screened, 396 (37%) became presumptive and were investigated using mobile Xray and Gene Xpert. From the presumptive cases identified, 23 TB patients (5.8% yield) were diagnosed using the combined tests.

Conclusions: The cascade from our findings show that targeted community TB screening using mobile Xray and networked Gene Xpert sputum testing improves

case detection of Tuberculosis, shortening the diagnostic delays and successfully identifying the missing TB cases for prompt treatment.

PS02-419-25 Targeted outreach to uplift community health (TOUCH) for active case finding and treatment adherence

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Background and challenges to implementation: While implementing Tuberculosis Health Action Learning Initiative (THALI) it was realised that there was a disconnect between health facilities and the community in Kolkata. Cost of care-seeking for patients and health services was high. Active case finding was not there. Adherence management and Public Health Action including household visits during IP phase for counseling; and follow-up in CP phase and end of treatment was nearly absent.

Intervention or response: 16 Civil Society Organisations (CSOs)/NGOs are engaged to increase active case finding through community engagement, health camps, and media campaigns with key community level stakeholders. TOUCH Agents are the local community volunteers who work on incentive basis. 230 TOUCH agents were trained on using simple cell phone based tools for screening suspect patients and tracking the patient through complete treatment cycle. They establish family DOTS and have a game changing role in active case finding and treatment adherence through THALI ICT platform.

Results and lessons learnt: Present records of THALI ICT platform shows that 412 presumptive cases are registered on the ICT platform by 92 TOUCH Agents, of which 20 are, confirmed cases. Thus, the suspect to patient conversion rate is 4.85%. Reaching out to community opens up pandora's box. Cases that were not getting recorded or notified were coming to the system. Treatment adherence of patients improve.

Conclusions and key recommendations: The Govt. of West Bengal has taken up this model and are using TOUCH agents in government active case finding drive. They have also paid towards the remuneration of these TOUCH agents. If the government buy-in and ownership is there this is a good sustainable model for community engagement.

PS02-420-25 Community-based DOTS to find missing cases: experience in four provinces in Mozambique

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Background and challenges to implementation: Mozambique, with 1550 health facilities (HFs) for 27 million inhabitants, is ranked 11th among the TB high burden countries in the world. The USAID Challenge TB (CTB) project operates in four provinces (Nampula, Sofala, Tete and Zambézia) that contributed 49% of all TB cases in Mozambique in 2016. Community sensitization for TB is mostly done at the health facility level, and not all people have access to it. There is a need to spread TB information at the community level and to use community-based approaches to identify potential TB patients for screening.

Intervention or response: The Mozambique National Tuberculosis Program (NTB) introduced community DOTS in 2007 as a part of a DOTS expansion initiative. CTB works with partners to implement innovative approaches to support the NTP in finding missing TB cases, including holding monthly cough days, active house-to-house case finding, index contact referral, prison-based DOTS, using the "Finding cases Actively, Separating safely and Treating effectively (FAST) approach where TB messaging is provided by trained activists, screening for presumptive TB, and referral to HFs when presumptive TB is identified. These approaches bring the community and health care workers closer together and are implemented in coordination with the NTP in four of the country's nine provinces.

Results and lessons learnt: Each of the four provinces where CTB works saw an increased contribution of community-based activities to the total number of TB cases notified by NTP. Community-based activities contributed 12% of all TB cases reported in these provinces in 2015, 26% in 2016 and 36% in 2017. These improvements resulted in each province reaching NTP targets for overall case contribution of community-based activities.

Conclusions and key recommendations: Community-based DOTS proved to be efficient in finding TB missing cases and increasing case notification.

PS02-421-25 Community engagement to enhance case detection of people affected by tuberculosis in Burundi

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Background: In 2016, Burundi has an estimated incidence of 118 new tuberculosis (TB) cases/100.000population, and 72new-TB-cases/100.000 population of notification rate. As 90% of around 10.4 million population lives in the rural area, where the geographical access to health-facilities is difficult, the National Tuberculosis Programme (NTP) of Burundi implemented in 2011 a community-engagement strategy to improve case-detection. We analyse here the results of six-years of implementation of this strategy.

Methods: The community-engagement strategy consisted in: 1) Training of selected community-volunteers(CV), 2)Financial incentives, 3)Supervision and 4) Monitoring and Evaluation. 5836 CVs were trained, financial incentives were provided up to 2013, supervision was conducted quarterly by NTP staff and community-specific monitoring and evaluation forms were introduced to assess CVs contribution to TB case-detection. Target of community-engagement contribution was at least 15% of total number of TB-cases bacteriologically-confirmed. All TB-cases bacteriologically-confirmed detected from 2012-2017 detected or not by CVs were included.

Results: Patients were notified by 170 TB-Clinics. A total of 44,365 TB-cases were detected from 2012-2017, from which 25,761(58%) were bacteriologically-confirmed, from which 4,415(17%) were detected by CVs. The proportion of TB-cases detected by CVs were 25%, 30%, 19%, 13%, 9% and 8% in 2012, 2013, 2014, 2015, 2016 and 2017 respectively. Due to financial constraints financial incentives were stopped after 2014.

Conclusions: From 2012-2017, the goal of community-engagement contribution for detecting at least 15% of bacteriologically-confirmed TB was attained. However, annual-completion of this goal was not achieved during last three years probably because of the elimination of financial-incentives. A comprehensive strategy that includes financial-incentives seems to be important to maintain community-engagement for TB-detection.

PS02-422-25 Contact Investigation by community cadre in public primary health care in Surakarta city and Jember district in Indonesia

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Background and challenges to implementation: In Indonesia, primary health centers (Puskesmas) is responsible for TB contact investigation (CI). Community cadres are rarely engaged. In July to September 2017, Challenge TB project facilitated CI in Surakarta (7/17 Puskesmas) and Jember (10/50 Puskesmas).

Intervention or response: Each Puskesmas selected 4-6 cadres to be trained and allocated their operational funds, which were not accessible for community cadres. Index cases were mainly smear positive TB patients. In Jember, contacts were all occupants of 10-15 houses around the index' house. In Surakarta, contacts were 10-15 household members or close contacts (similar intensity as household member). Cadres conducted home visit to verbally screen adult contacts, and refer screen positives and child contacts to Puskesmas for evaluation.

Results and lessons learnt: In Surakarta, 861 contacts from 72 index patients were identified, 821 (95%) screened, 35 screen positive, 13 tested and 3 confirmed with TB. The main diagnostic tool was GeneXpert (85% of all presumptive and 100% of all confirmed TB). Of all confirmed TB, none (of 257 screened) were household contacts and 3 (of 564 screened) were close contacts. In Jember, 14,426 contacts from 421 index patients were identified, 13,567 (94%) screened, 394 screen positive, 269 tested, and 21 confirmed with TB. The main diagnostic tool was microscopy (82% of all presumptive and 71% of all confirmed TB). Of all confirmed TB, 3 (of 1,207 screened) were household contacts and 18 (of 13,219 screened) were other contacts. Number needed to screen (NNS) to find 1 TB patient was 273 among screened and 5 among tested contacts in Surakarta. In Jember, NNS was 646 among all screened and 11 among the tested contacts.

Conclusions and key recommendations: Collaboration with cadres supported by local funding are effective for CI. To increase yield, expansion should limit screening to household and close contacts instead of those with limited exposure; and use more sensitive screening and diagnostic tools.

PS03 Clinical aspects of multidrug-resistant tuberculosis treatment safety and toxicity

PS03-423-25 Trends in CRP, D-dimer and fibrinogen during therapy for HIV-associated multidrug-resistant tuberculosis

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Background: HIV positive adults on treatment for multidrug-resistant tuberculosis (MDR-TB) experience high mortality. Biomarkers of HIV/MDR-TB treatment response may enable earlier treatment modifications that improve outcomes.

Methods: To determine whether trends in C-reactive protein (CRP), D-dimer and fibrinogen predict treatment outcome among those with HIV/MDR-TB co-infection we studied 20 HIV positive participants initiating therapy for MDR-TB. Serum CRP, fibrinogen, and D-dimer were measured at baseline and serially while on treatment.

Results: At baseline, all biomarkers were elevated with median CRP 86.15 mg/L (IQR 29.25-149.32), D-dimer 0.85 µg/mL (IQR 0.34-1.80) and fibrinogen 4.11 g/L (IQR 3.75-6.31). CRP decreased significantly within 10 days of treatment initiation and fibrinogen within 28 days; D-dimer did not change significantly. 5 (25%) participants died. Older age (median age of 38y among survivors and 54y among deceased, $p=0.008$) and higher baseline fibrinogen (3.86 g/L among survivors and 6.37 g/L among deceased, $p=0.02$) were significantly associated with death. Higher CRP concentrations at the beginning of each measurement interval were significantly associated with a higher risk of death during that interval.

Conclusions: Trends in fibrinogen and CRP may be useful for evaluating early response to treatment among individuals with HIV/MDR-TB co-infection.

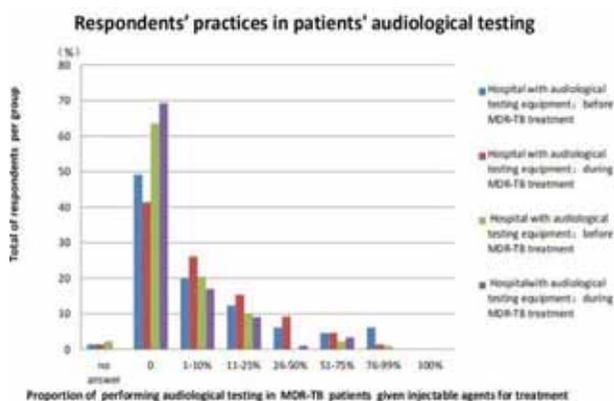
PS03-424-25 Ototoxicity monitoring in patients given injectable agents for treatment of multidrug-resistant tuberculosis in China: a survey of eight TB centers

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Background: China is one of the high MDR-TB burden countries where injectable agents (IAs) are widely used. However, reports on side effects of IAs in Chinese patients are very limited.

Methods: This survey was focused on IAs usage, hearing monitoring and incidence of ototoxicity, using a questionnaire distributed to doctors in 8 TB centers across China in March 2018. Response rate was 89.9%.

Results: All 156 respondents had used IAs in the past year, and most (153/156, 98.1%) for MDR-TB treatment. Amikacin was the most commonly used IAs (155, 99.4%), followed by capreomycin (102, 65.4%), streptomycin (71, 45.5%), and kanamycin (2, 1.3%). Audiological testing was available in 3 hospitals with 65 respondents, but 32 (49.2%) and 27 (41.5%) of these respondents had never performed hearing testing for the patients before and during MDR-TB treatment (Figure 1).



[Respondents' practices in patients' audiological testing in MDR-TB treatment]

The remaining 5 hospitals with 88 respondents did not have audiological testing equipment. In the hospitals with audiological equipment, the top three reasons for not performing hearing assessment were doctor's opinion that patient's complaints can reflect ototoxicity (67.7%), patient rejection (33.8%), doctor's estimation of low hearing impairment risk (27.7%). Among the 153 respondents, 118 (77.1%) estimated that the incidence of injectable agents-induced ototoxicity during MDR-TB treatment was less than 10% upon their own clinical experience.

Conclusions: The data indicated that hearing monitoring is commonly lacking in MDR-TB management in China, which is mainly attributed to the absence of audiological testing equipment and low clinical vigilance. Measures to improve hearing monitoring and researches in this area are urgently needed.

PS03-425-25 The incidence of leukopenia in patients treated for drug-susceptible tuberculosis

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Background: The incidence of leukopenia in patients treated for tuberculosis (TB) is related to certain factors¹. One factor could be the duration of anti-TB treatment. The goal of the current study was to gain an insight in the incidence of leukopenia in patients treated for TB in a Dutch TB center.

Methods: Patients treated in TB center Beatrixoord for TB between January 2016 and December 2017 were included. They had to have at least one leukocyte count value in the time period between start of treatment ($t = 0$) and 12 weeks later ($t = 12$). Leukopenia was defined as a leukocyte count $< 4.0 \times 10^9$. Only patients with drug susceptible TB that tested HIV negative were enrolled. All leukocyte counts from T0 to T12 were included and percentages of leukopenic values were calculated.

Results: In the study period, a total of 219 patients were screened of which 133 were included in the study. The incidence of leukopenia at single time points ranged from 7.8% ($t = 0$) to 22.9% ($t = 9$). Furthermore, the percentage of patients who experienced an episode of leukopenia at some point in the time frame was 26.3% ($N = 34$). Also, 64,7% of leukopenic patients had more than 40% of the measured values regarded as leukopenic. See figure 1.

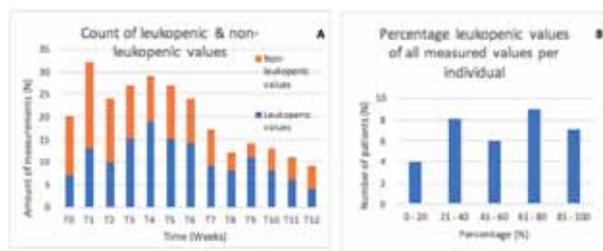


Figure 1. A: Count of values that are considered leukopenic and non-leukopenic for every weekly measurement of leukopenic patients displayed as stacked bars. B: Portion of values that is considered leukopenic, displayed as a percentage of total measurements for every leukopenic patient.

[Count of leukopenic and non-leukopenic values & percentage of leukopenic values]

Conclusions: The overall incidence of leukopenia was higher than expected. However, the course of the leukocyte count was different for every patient included, so that a conclusion for a steadier, consistent or rather declining leukocyte course could not be made. This suggests that multiple factors are associated with the incidence of leukopenia and further research in the causes is required.

PS03-426-25 Implementation of a national ototoxicity monitoring program in Swaziland

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Background and challenges to implementation: In 2016, Swaziland initiated a total of 384 patients on multi-drug-resistant tuberculosis (MDR-TB) treatment. The country's national treatment MDR-TB cases treatment policy includes injectable agents of the aminoglycosides group, which are known to be associated severe adverse events affecting the auditory system often resulting progressive to permanent sensorineural hearing loss.

In 2016, there was a national scale up of DRTB services from 5 to 13 sites, thus, it was paramount to scale up audiological services to all DRTB facilities nationally.

Intervention or response: Facility readiness assessments was conducted in all the DRTB sites and audiometry equipment installed. A national training of 50 nurses and doctors in conducting hearing screenings and 115 HCWs capacitated on monitoring of ototoxicity theory in correlation with the regional DRTB training. A standard training plan, curriculum and SOPs were developed. Training of facility administrators in order for them to motivate clinicians. Mentoring and supportive supervision was provided.

Results and lessons learnt: A total number of 343 patients were monitored for ototoxicity with documented baseline assessments, monthly monitoring assessments and exit assessment. 70/343 patients who developed a hearing loss during treatment were initiated on the new TB drugs. 90% of nurses were able to conduct hearing screenings, interpret the audiogram and make recommendations accordingly. Patients were reluctant to be monitored for ototoxicity thus counselling was conducted.

Conclusions and key recommendations: The implementation of national scale up of ototoxicity monitoring program has ensured that majority of DRTB patients have access to audiological services. Conducting supportive supervision is essential in providing support to the clinicians as well as verifying audiograms and be assured that clinicians are conducting hearing assessments according to the SOPs. With ototoxicity monitoring, the country's national treatment MDR-TB cases treatment policy could be re-evaluated as new TB drugs are readily available in the country.

PS03-427-25 Treatment and pregnancy outcomes of pregnant women exposed to second-line anti-tuberculosis drugs in South Africa

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Background: Rifampicin resistant tuberculosis (RR-TB) in pregnant women is a cause for concern globally due to the teratogenicity of parts of the TB treatment regimen. The literature on outcomes of women exposed to second-line anti-tuberculosis drugs during pregnancy is sparse making it difficult for clinicians and TB programmes to provide guidance on this important issue. The aim of the study is to characterise maternal, and pregnancy outcomes for pregnant women receiving second-line anti-tuberculosis treatment for drug-resistant TB (DR-TB).

Methods: We conducted a retrospective record review of pregnant women who received treatment for RR-TB between 01/2010-08/2016 at two outpatient treatment sites in Johannesburg, South Africa. Demographic, treatment and pregnancy outcome data were collected from available medical records. Premature labour (< 37 weeks), and miscarriage were categorized as adverse pregnancy outcomes.

Results: Out of 538 women of child-bearing age who received DR-TB treatment at the two study sites, 22 (4.1%) pregnancies were identified (median age 30.5 years IQR 24.0-35.0). The HIV co-infection rate was 55.0% (11/20). Most of the women (95.5%) were pregnant at the time of RR-TB diagnosis and one woman became pregnant during treatment.

Pregnancy outcomes were available for 13/22 (59.1%) women, which included 10 live births (7 occurred prior to 37 weeks), 1 miscarriage and 2 elective pregnancy terminations. Overall, 8/13 (61.5%) had an adverse pregnancy outcome. Of the 17 women with known TB treatment outcomes 5 (29.4%) successfully completed treatment (1 was cured and 4 completed treated), 5 (29.4%) transferred out, 3 (17.6%) were lost to follow-up, 4 (23.5%) died.

Conclusions: Pregnant women with RR-TB suffer from high rates of adverse pregnancy outcomes and fewer than a third achieve a successful TB treatment outcome. These vulnerable patients require close monitoring and coordinated obstetric, HIV and TB care.

PS03-428-25 Multidrug-resistant tuberculosis and concurrent hepatitis C virus infection: an additional challenge in the complex management of patients

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Background: Multidrug-resistant tuberculosis (MDR-TB) requires lengthy use of second-line drugs, burdened by many side effects. Hepatitis C virus (HCV) chronic infection increases risk of liver toxicity in these patients. New direct-acting antivirals (DAAs) changed chronic hepatitis C from a barely manageable to a curable condition.

Methods: We describe a case of successful treatment of pulmonary MDR TB and concurrent HCV chronic infection.

Results: A 39 years old woman of Romanian origin affected by MDR-TB (also resistant to amikacin) and HCV chronic infection was transferred to our unit for a severe liver enzymes alteration (more than 4-fold upper normal value). MDR-TB regimen was stopped. HCV viral load was 253.336 U/L, genotype 1b. Liver biopsy showed chronic hepatitis, mild necroinflammatory activity and portal fibrosis (grade 5 and stage 2 on Ishak score). Sofosbuvir/ledipasvir 400/100 mg once daily was started. After 2 weeks liver enzymes normalized and HCV RNA was undetectable, so standardized WHO MDR-TB regimen was re-started with ethambutol, moxifloxacin, cycloserine, ethionamide, linezolid, clofazimine. Cure was declared after 24 months of antitubercular therapy with a sustained HCV virologic response after 12 weeks of DAAs treatment and no hepatic adverse events.

Conclusions: HCV infection is an additional challenge in the already complex management of MDR-TB. Treatment with DAAs should be promptly started in HCV chronic infected patients with MDR-TB. This allows to complete antitubercular regimen also using second-line potentially hepatotoxic drugs and minimizing the risk of prolonged treatment's interruption.

PS03-429-25 Role of clinical features, microbiology, histopathology and molecular diagnostic test in the diagnosis of cutaneous tuberculosis

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Background: Cutaneous involvement is an important extrapulmonary manifestation of tuberculosis. It is a paucibacillary condition and has diverse clinical pre-

sentations. Conventional microbiological techniques have limitations and often delays its diagnosis. Recently molecular methods have emerged as diagnostic tool for various forms of tuberculosis. Sufficient data is not available regarding the role of GeneXpert MTB/RIF in skin tissue samples of cutaneous tuberculosis.

Methods: In this study BacT/ Alert 3D culture, Real time polymerase chain reaction (RT-PCR) and GeneXpert MTB/RIF were used along with histopathological features for diagnosis in forty seven patients with clinical features suggestive of cutaneous tuberculosis. Patients with previous history of tuberculosis were excluded from the study.

The study was carried out in the department of Dermatology of a tertiary care hospital.

Results: 36.17% patients belonged to the age group 11-20 years with male to female ratio of 1.6:1. None of the forty seven patients tested were seropositive for HIV. The commonest clinical presentation was scrofuloderma (42.6%) followed by lupus vulgaris (40.4%). All patients had a strong response to Mantoux test except two. Granulomatous inflammation was seen in 75.51%. Six patients had extracutaneous focus of tuberculosis. In fourteen (29.79%) patients culture of skin biopsy was positive for *M. tuberculosis* by BacT/Alert3D method. *M. tuberculosis* was detected in skin biopsy samples by RT-PCR in 8.51% (4 out of 47) patients and by GeneXpert MTB/RIF in 8.7% (4 out of 46) patients. None of the sample was found to be Rifampicin resistant by GeneXpert MTB/RIF. All forty seven patients showed significant improvement to anti tuberculosis treatment (ATT) within 6 weeks of initiation of therapy.

Conclusions: Clinico-histopathological examination with response to ATT for confirmation of the diagnosis of cutaneous tuberculosis still remains the best option due to low sensitivity of RT-PCR, BacT/ Alert 3D culture and GeneXpert MTB/RIF.

PS03-430-25 Serum uric acid levels in patients on anti-tuberculosis treatment in Douala, Cameroon

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Background: Tuberculosis remains a high public health concern in sub-Saharan Africa. Its treatment needs the use of 4 drugs which are generally well tolerated. However, pyrazinamide and ethambutol are known to generate hyperuricemia with or without joint pain. The aim of this study was to determine the prevalence and the risk factors for hyperuricemia in patients undergoing tuberculosis treatment.

Methods: We carried a cohort study between February and July 2017 in the respiratory unit of the Douala Laquintinie hospital. Newly diagnosed TB patients aged 18 years and above were included in the study. Demographic characteristics and clinical were recorded. Venous blood samples for serum uric acid (SUA) levels were collected before the start of the TB treatment, at the end of the first month and at the end of the second month. A SUA ≥ 60 mg/l was considered as hyperuricemia. Logistic regression was computed for the identification of factors associated with hyperuricemia.

Results: Of the total of 145 patients included, 51% were men. The mean age of the participant was 35.5 years. The prevalence of hyperuricemia at the end of the first month and the second month of the treatment were respectively 60% and 69%. The mean value of SUA was $76,49 \pm 37,83$ mg/l at the end of the first month and $74,44 \pm 27,92$ mg/l at the end of the second month. The socio-demographic and clinical characteristics were not associated with hyperuricemia. A body mass index less than 18.5 kg/m² was associated with the hyperuricemia as a protective factor.

Conclusions: Hyperuricemia is frequent in patient on antituberculous treatment during the intensive phase of the treatment. Further studies should correlates serum uric acid levels with with the occurrence of joint pain.

PS03-431-25 Alarming levels of ototoxicity among hospitalized multidrug-resistant tuberculosis patients in the intensive phase of treatment at specialist treatment centers in South Western, Nigeria

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Background: Management of multi drug resistant tuberculosis (MDR-TB) patients remains a challenge in the control of tuberculosis worldwide. MDR-TB patients require long term treatment with drugs that cause various adverse effects especially ototoxicity associated with aminoglycoside use. However, there is dearth of information regarding ototoxic effects of MDR-TB treatment in Nigeria. This study explored the prevalence of ototoxicity and associated factors among hospitalized MDR-TB patients during the intensive phase of treatment.

Methods: A retrospective review of records of MDR-TB patients admitted at two specialist treatment centers in South West Nigeria from 2012 - 2017 was conducted. Using a structured proforma, socio demographic characteristics and clinical history were extracted. Ototoxicity was assessed as any abnormality reported from a pure tone audiometry.

Discrete data were summarized with frequencies, proportions while bivariate analysis was done using ² test to identify associated factors. Multivariate analysis was

performed to identify independent predictors of ototoxic effects. All statistical significance was set at 5%.

Results: A total of 383 records were extracted, however only about a fourth (37.3%) had audiometry performed. Of these 143 MDR-TB patients, mean age was 36.2 ± 11.3 years and prevalence of any ototoxic effect was 72.7%. This was higher in older age groups, females and those underweight. ($p > 0.05$) Patients who did not sputum convert at the end of treatment and HIV co infected had higher proportions with ototoxic effects. ($p < 0.05$). However, on multivariate analysis only age remained a significant independent predictor of ototoxic effect. (AOR: 8.7; 95% CI: 1.4-52.2).

Conclusions: High rates of ototoxic effects as seen in this study could affect successful management of MDR-TB patients. Adverse effects are main deterrents to compliance and completion of long term treatment regimen. Auditory monitoring and rehabilitation should be recommended for MDR-TB patients even after completion of the intensive phase of treatment.

PS03-432-25 Adverse drug events in patients receiving treatment for multidrug-resistant tuberculosis in a tertiary referral hospital in Italy

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Background: Treatment of multidrug-resistant tuberculosis (MDR-TB) requires the use of expensive and toxic second-line anti-tubercular drugs which are given for a long time. Adverse drug events (AEs), and especially severe adverse drug events (SAEs) of second-line anti-tubercular drugs affect compliance and treatment outcome. With this study we want assess AEs in a cohort of MDR-TB patients at the National Institute for Infectious Disease "Lazzaro Spallanzani", a tertiary care center for infectious diseases care and research in Italy.

Methods: 76 MDR-TB patients receiving standardized WHO regimen between 2005 and 2016 were consecutively enrolled in an observational retrospective study. Data regarding socio-demographic profile, diagnosis, and treatment as well as AEs were recorded and analyzed statistically.

Results: 252 AEs were reported among 65 patients (85.5%); 47 AEs (18.7%) in 32 patients (42.1%) were classified as SAEs and required discontinuation of the offending drug. Most commonly observed SAEs were hearing loss (28.9%), acute liver injury (10.5%), gastrointestinal (6.6%), peripheral neuropathy (5.3%), nephrotoxicity (2.6%), hypothyroidism (2.6%), anemia (2.6%). Permanent discontinuation was commonest in patients receiving injectable drugs (26.3%).

Conclusions: AEs occurred commonly during MDR-TB treatment, often resulting in treatment modification, and impact on adherence. Our study confirm description and analysis of SAEs reported in literature with special concern about long term disability and loss of quality of life due to injectable drugs. Even if most of AEs reported in our study were not severe, our results show that MDR-TB patients have to tolerate a burden of side effects during the entire treatment period.

PS03-433-25 Clinical risk factors associated with multidrug-resistant tuberculosis in Mali: a ten-year cross-sectional study

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Background: MDR-TB is a major threat to global TB control. Among the 10.4 million new TB cases in 2015, 580 000 were enrolled in MDR-TB treatment. GeneXpert MTB/RIF®'s contribution has made substantial progress globally in the diagnosis and isolation of MDR-TB patients. In countries where first-line TB drug resistance testing is not routinely available, predictors can help clinicians target and prioritize suspected patients for screening and treatment. We aimed to determine clinical factors associated with MDR-TB in patients suspected of having MDR TB in Mali.

Methods: We analyzed cross-sectional data from 214 TB patients suspected of having MDR TB and admitted to Point-G hospital between 2007 and 2016. We computed crude odds ratios using SPSS version 25.0.

Results: Our data showed that age ≤ 40 years (OR = 2.56, 95% CI: 1.44 - 4.55), two previous courses of TB treatment (OR = 3.25, 95% CI: 1.44-7.30), history of TB treatment failure (OR = 3.82, 95% CI 1.82-7.79), sputum microscopy 3+ (OR = 1.98, 95% CI: 1.13-3.48) and history of contact with TB patient (OR = 2.48, 95% CI: 1.11-5.50) were significantly associated with microbiologic confirmation of MDR-TB. However, HIV was not an independent risk factor for MDR-TB (OR = 0.82, 95% CI: 0.34-1.94)

Conclusions: We identified predictor factors that may be used to help identify MDR TB suspects and prioritize them for a microbiological confirmation test. Prospective cohort studies are needed to fully understand factors associated with the incidence of MDR TB and MDR TB outcomes.

Keywords: Multi-Drug Resistant Tuberculosis, risk factors, Mali

PS04 Staying ahead of tuberculosis: a life's journey

PS04-434-25 Do hospitalized DR-TB patients at treatment initiation achieve better treatment outcomes than those under ambulatory care? Experiences from Uganda

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Background: Despite drug-resistant tuberculosis (DR-TB) medicines being increasingly available, its treatment remains a challenge. Globally, less than half of patients receiving therapy for DR-TB are successfully treated, with poor outcomes compared to Uganda's treatment success rate of 74% among 2014 cohort. There is little information available on treatment outcomes of DR patients hospitalized on treatment initiation compared to those under ambulatory care in resource limited settings. The DR-TB burden is estimated at 1.4% among all new and 12.1% among previously treated TB cases. This study aimed at comparing treatment success among these two groups in Uganda.

Methods: We conducted a retrospective study at all the 15 DR TB treatment initiation sites in Uganda. We analyzed treatment outcomes of DR-TB patients enrolled for treatment in 2013 and 2014 from electronic registers. We tested for the relationship between treatment type and treatment outcome (success rate, cured, completed, died) at 95% confidence interval.

Results: A total of 408 DR-TB patient's records were reviewed, of which 151 had complete results on type of care at treatment initiation and were included in the study. Patients either received ambulatory care (48.3%) or were hospitalized at treatment initiation (51.7%). The treatment success rate for hospitalized patients was higher (80.8%) when compared to those receiving ambulatory care (63.0%).

Treatment Outcome	Hospitalized at Treatment initiation n (%) (78)	Ambulatory care n (%) (73)	OR	95% CI	P-value
Treatment Success Rate	63(80.8)	46 (63.0)	2.46	1.18-5.15	0.02
Cured	54 (69.2)	59(53.4)	1.96	1.01-3.82	0.04
Completed	9 (11.5)	7 (9.6)	1.23	0.43-3.49	0.69
Died	8 (10.3)	23 (31.5)	0.24	0.10-0.60	<0.05

[Table 1: Treatment of DR-TB patient hospitalized at treatment initiation compared to those receiving ambulatory care]

Furthermore, hospitalized patients were strongly associated with treatment success and cured (OR = 2.46; p=0.02) and (OR =1.9; p=0.04) respectively. They were also at lower odds to die (OR = 0.24; p=< 0.05).

Conclusions: This study suggests that patients hospitalized at treatment initiation were more likely to achieve better treatment success. The study was limited to a small number of patients; we recommend a similar study on a large cohort to understand treatment success among these groups.

PS04-435-25 Pre-treatment loss to follow-up among people with bacteriologically confirmed tuberculosis in four regions of Cameroon

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Background: Rates of pre-treatment loss to follow-up among people diagnosed with TB vary significantly by setting, and little is known about this important population in Central and West Africa. We aimed to determine the proportion of people with bacteriologically-confirmed TB who were lost to follow-up prior to treatment initiation in Cameroon and to assess factors contributing to this outcome.

Methods: We performed retrospective record linkage of the NTP laboratory and treatment registers to quantify pre-treatment loss to follow-up using the WHO guidelines for TB inventory studies. The study area covered 4 of the 10 geographical regions of Cameroon (Northwest, Southwest, West, Littoral), representing ~40% of the country's population, and we included people registered with bacteriologically-confirmed TB from October 1st to December 31st 2015. Data from the paper-based lab and treatment registers were double-entered into EpiData (www.epidata.dk) databases, and then these data were linked using probabilistic linkage (Link Plus v. 2.0) with subsequent manual review of all potential matches. Anyone with a bacteriologically-confirmed lab result who was not documented as starting treatment within one month of lab diagnosis was considered as pre-treatment lost to follow-up.

Results: Data were obtained from 76 of the 100 NTP diagnostic and treatment centers in the assessment area, which notified 93% of the TB cases in this area during the study period. In these sites, 180 (14%) of 1,293 bacteriologically-confirmed TB cases from laboratory registers were lost to follow-up prior to entry in TB treatment registers. In univariable analysis, age, sex, geographical region and smear positivity grade were not significantly associated with pre-treatment loss to follow-up.

Conclusions: One in seven people with a laboratory confirmed TB diagnosis were lost to follow up before notification and initiation on TB treatment in Cameroon. Ensuring that all people diagnosed with TB are immediately started on treatment may reduce both transmission and TB-related mortality.

PS04-436-25 Is the profile of TB patients in India changing?

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Background: India plans to eliminate TB by 2025. With highest burden of TB, limited resources and a billion population to cover, India's TB Control Program needs to take stock of its progress and re-design its strategies to achieve its goal. In the current context, we analysed data from three serial surveys among TB patients in 2011, 2013 and 2017 with an aim to identify changes in key indicators for TB control.

Methods: As part of Project Axshya, three Knowledge Attitude and Practice (KAP) surveys were conducted over a seven year period (baseline-2011, midline-2013, endline-2017). The surveys were conducted across same 30 districts in randomly selected sampling units. The rural: urban ratio was as per the Census 2011 data. TB patients were identified through a line-listing process. All the identified patients were interviewed after obtaining consent using a pre-tested questionnaire.

	Baseline N=609 Year - 2011		Midline N=496 Year - 2013		Endline N=323 Year - 2017	
	N	%	N	%	N	%
TB patients who were male	389	64	302	61	214	66
TB patients who were illiterate	264	43	167	34	117	36
Patients with household income less than Rs.2000	212	35	75	15	30	9
Aware that TB is caused by micro-organisms	201	33	219	44	140	43
Heard of free diagnosis and treatment of TB	426	70	351	71	248	77
Aware of Govt health facility for free diagnosis and treatment	366	60	337	68	196	61
Visited Two or less providers for diagnosis of TB	411	67	400	81	284	88
Patients diagnosed within 1 month of the onset of symptoms	448	74	401	81	223	69
Patients initiated on treatment within 7 days of diagnosis	418	69	233	47	171	53
Receiving free treatment under DOTS	324	53	295	59	176	54
Aware that treatment has to be taken regularly	488	80	378	76	261	81
Aware that the duration of treatment is for 6-8 months	356	58	275	55	177	55

[Table 1. Key indicators of TB related knowledge among TB patients and their practices regarding diagnosis and treatment across three KAP surveys during 2011 - 2017]

Results: In baseline 609, midline 496 and endline 323 TB patients were identified (Table 1). The reducing number of patients is due to decreasing prevalence or selection of PSUs is not clear. Male patients continue to be the major affected gender ranging between 61-68%. The proportion of patients aware that TB is caused by microorganism is grossly low at less than 50%. Marginal gains were observed in patient's awareness on treatment duration, receiving DOT, aware of free diagnosis and treatment and awareness about regular treatment. We still have only half of the patients taking treatment under DOTS. Patients diagnosed within one month staggers at 70% and those initiated on treatment within one week at about 50%.

Conclusions: With half of the key indicators hovering around 50%, it's a daunting task for India to achieve its goals of TB elimination. The good part is that there are marginal gains; we need to now build on these to move forward steadily.

PS04-437-25 Treatment success rates for patients with tuberculosis receiving care in health facilities severely affected by Hurricane Matthew, Haiti, 2016

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Background and challenges to implementation: On October 4, 2016, Hurricane Matthew struck southwestern Haiti as a category 4 hurricane, causing over 1,000 deaths and extensive damage to infrastructure. The goal of this study was to conduct an assessment of tuberculosis (TB) health facilities, track patients who had been registered in care, and compare treatment outcomes in these three departments before and after hurricane Matthew.

Intervention or response: We developed a standard questionnaire to evaluate TB health facilities in the affected areas and a line list to help healthcare providers track all patients who were registered six months before the hurricane. We used the routine surveillance system of the National TB Program to determine outcomes for all notified cases in Sud, Grand'Anse, and Nippes in 2015 and 2016.

Results and lessons learnt: We assessed 33 (44.6%) of the 74 TB health facilities in Sud, Grand'Anse, and Nippes after the hurricane. One facility (3.0%) was destroyed, 14 (42.4%) had partial damage, and 18 (54.5%) were intact. Loss/damage of the TB registers occurred in 6 (18.2%) sites and damage to the microscopes in 5

(15.2%) sites. Eight facilities (24.2%) had no service interruption, whereas 18 (54.4%) sites were closed for < 1 week, and 7 (21.2%) for >2 weeks. A total of 466 TB patients were registered at the 33 facilities when Hurricane Matthew struck. Within an average of 21 days (SD 3.3) after the hurricane, 335 (71.9%) of the patients were accounted for and had visited the TB providers. Treatment success rates for the three departments were 80.3% and 82.5% in 2015 and 2016, respectively, ($P = 0.054$).

Conclusions and key recommendations: Despite major challenges, most TB patients continued to seek care in southwestern Haiti following the hurricane. The results highlight the need to design preparedness plan in the wake of natural disasters in order to ensure adequate follow up of patients with TB.

PS04-438-25 Improvement of DR-TB detection and management in the 8 provinces supported by Challenge TB in DR Congo

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Background and challenges to implementation: 8 Provinces of Democratic Republic of Congo supported by Challenges TB (CTB) project. The population of these provinces represent among 30% of the DRC total population.

Intervention or response: This study is a retrospective analysis of DR-TB detection and management in the 8 provinces from 2014 to 2017. The aim is to measure the impact of CTB support on DR-TB management in these provinces.

Results and lessons learnt: Since the beginning of the support given by CTB in 2014, the number of RR-TB confirmed cases increase from 71 in 2014 to 250 in 2017. The percent of RR-TB cases detected in these provinces in 2014 represented only 16% of the total RR-TB cases detected at national level, and in 2017 this proportion was 28% (table).

Year	Notification of RR-MDR TB cases at national level	Notification of RR-MDR TB cases in 8 CTB supported provinces	%
2014	436	71	16%
2015	501	91	18%
2016	661	152	23%
2017	880	250	28%

[Contribution to RR-MDR notification by Challenge TB project in DR Congo, 2014-2017]

The success rate of patients treated with long conventional MDR since 2014 varied between 73% and 75%. In 2016, short regimen for DR-TB was introduced in the 8 CTB-supported and the success rate for the first cohort of 39 patients analyzable in 2017 was 93%.

The main supports given by CTB during these years are the following: equipment with 3 Xpert machines, training and formative supervision of health care workers, transport and distribution of cartridges and second line drugs, publication of DR-TB guide.

Conclusions and key recommendations: Between 2014 and 2017, the number of DR-TB detected increase more quickly in CTB-provinces than at national level and the introduction of short course regimen in these provinces improved patient's treatment results. The support given by CTB was crucial for the improvement of DR-TB management in these 8 provinces.

PS04-439-25 The impact of TB retreatment regimens in treatment and post-treatment outcomes: a 7-year follow-up study in China

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Background: The treatment effect of previously treated TB regimens is far from satisfactory. This study aimed to examine the correlation between re-treatment regimens and therapeutic effects, and factors associated with recurrence or death after successful treatment.

Methods: We conducted a cohort study in 9 regions of China and enrolled previously treated TB patients from October, 2008 to December, 2010. Patients were randomly divided into four treatment regimen groups including standard, high-dose, long-course and individualized treatment groups. After treatment, those with successful treatment outcomes were followed up to 7 years by clinicians. The therapeutic effects of different regimens and the information of recurrence or death were recorded. Odds ratios relating risk factors to poor treatment outcomes were calculated by using logistic regression model, while hazard ratios relating risk factors to recurrence or death were calculated by using Cox proportional hazards model.

Results: Overall, 419 patients were included in our analysis of treatment effects. The treatment success rate is 75.9%, and the recurrence and death rate is 6.9% and 3.8%, respectively. Reduced risks of poor outcomes were observed in high-dose and individualized regimen

groups, and the adjusted ORs were 0.3 (0.1-0.6), 0.2 (0.1-0.5), respectively. Other independent predictors for poor outcomes include patients aged 45 or older, lower BMI, patients with an educational level of middle-high school, elementary school or below, non-local patients, resistance to single or multiple anti-TB drugs. In our analysis of factors associated with TB recurrence or death, all documented variables showed no statistical significance including treatment regimens and diabetes status.

Conclusions: High-dose and individualized retreatment regimens have better therapeutic effects compared to standard retreatment regimen in treating retreated TB patients, but they were not associated with lower risk of TB recurrence or death. Systematic cost-effectiveness evaluation of different treatment regimens should be taken into account in previously treated TB control program.

PS04-440-25 Tuberculosis among household contacts of drug-resistant TB patients in TB centre in Gaborone, Botswana

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Background and challenges to implementation: Princess Marina Referral Hospital (PMH) TB clinic is the centre of excellence for management of Drug Resistant TB (DR-TB) cases in the Southern Region of Botswana since 2006. All close contacts of patients diagnosed with DR-TB are screened for TB regularly, which has led to identification of several additional patients with, and particularly with DR-TB.

Intervention or response: Symptom screening for DR-TB contacts is carried out by TB clinic and DOT sites nurses at regular intervals over approximately two years after the diagnosis of the index case. In the first year after diagnosis of the index case, the contacts are screened every three months during the initial phase and every six months during continuation phase until index case completes TB treatment. If any of the contacts are found to be symptomatic, sputum is collected for Xpert MTB/RIF as well as for culture and drug susceptibility testing. Those symptomatic contacts diagnosed with TB are treated according to the drug susceptibility profile of the index case. This approach to contact tracing is common in most of African settings: however, it is usually only effectively implemented. For DR-TB implemented the approach which prevents it from being followed for all index patients with TB, regardless of susceptibility profile.

Results and lessons learnt: From 2010-2017, seventy-one contacts of nine DR-TB index cases at PMH TB clinic were screened whereby fifteen (21%) were found to be symptomatic. All these symptomatic contacts were eventually diagnosed with smear positive DR-TB, confirmed by culture. More than half (8/15) were under five years and the median age was 20 years (3 months-48 years). Four were HIV positive and already on ART.

Conclusions and key recommendations: Active contact tracing amongst contacts of patients with DR-TB is an effective active case-finding method that led to the diagnosis and treatment of almost twice as many DR-TB patients as initially diagnosed.

PS04-441-25 Population pharmacokinetic model and limited sampling strategies of levofloxacin in tuberculosis patients

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Background: Therapeutic drug monitoring (TDM) of levofloxacin has been recommended to prevent acquired drug resistance due to interindividual variability in drug exposure. Adequate estimation of drug exposure using a small number of appropriately timed samples is key. This study aimed to develop a sampling strategy for levofloxacin in MDR-TB patients using a Bayesian approach as well as multiple linear regression.

Methods: Three datasets of levofloxacin pharmacokinetic curves in tuberculosis patients were included in this study. First a population pharmacokinetic model and a sampling strategy using a Bayesian approach were developed based on data of 30 TB patients and externally validated with data from 20 different TB patients. The sampling strategy based on multiple linear regression was validated using a jack-knife analysis. Only clinically suitable sampling strategies (1-3 samples) were tested.

Results: A one-compartment model described the data the best. Levofloxacin exposure was non-clinically relevant underestimated (-7.9%, SE 1.7%). The Bayesian approach using 0 and 5 h post-dose samples adequately estimated the levofloxacin exposure with a mean underestimation of -4.4%, SE 2.7%. The sampling strategy based on multiple linear regression used 0 and 4 h post-dose samples as optimal sampling strategy showing a mean underestimation of -0.46%, SE 2.0%.

Conclusions: In this study, we successfully developed two sampling strategies, i.e. Bayesian approach (t=0 and 5 h), and with multiple linear regression (t=0 and 4 h). Both strategies are suitable to be implemented in clinical practice to facilitate TDM of levofloxacin in MDR-TB patients.

PS04-442-25 Comparison of pulmonary impairment after tuberculosis in patients treated with moxifloxacin-based regimens vs. standard rifampin-isoniazid-pyrazinamide-ethambutol

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Background: Approximately 60% to 70% of patients cured of Drug Sensitive Pulmonary Tuberculosis (DS-PTB) develop Pulmonary Impairment after Tuberculosis (PIAT). PIAT occurs despite successful treatment completion with standard RIPE regimen (Rifampin, Isoniazid, Pyrazinamide, and Ethambutol). Moxifloxacin-based regimens have shown effectiveness curing DS-PTB and may have superior effect mitigating the frequency and severity of PIAT.

Methods: We compared results of Pulmonary Function Test (PFT) in 166 patients with DS-PTB. Twenty-three were treated with a Moxifloxacin-based regimen and 143 with RIPE regimen. Pulmonary impairment (frequency and severity) was assessed following AMA criteria. FVC, FEV₁, and FEV₁/FVC ratio values were compared with predicted values considering gender and race standards. Lung restrictive defect was FEV₁/FVC ratio >70% with an FVC < 80%. Airway obstruction was FEV₁/FVC ratio < 80% with FVC >80%. Mixed pattern was FVC < 80% and FEV₁/FVC ratio < 70% of predicted values. Pulmonary Function Test was conducted after culture results were negative. (Approximately after 20 weeks of treatment). Demographic and risk factors for lung impairment were collected.

Results: Both groups had similar risk factors for lung impairment. PIAT was present in 35% of patients receiving Moxifloxacin and 57% receiving RIPE regimen (p = 0.0510). Mean FVC, FEV₁, FEV₁/FVC ratios flow, and FEF 25-75 showed no significant difference between the two groups. Patients treated with RIPE regimen showed predominately restrictive pattern compared with Moxifloxacin group. Twelve patients treated with RIPE regimen had 50% less of their expected vital capacity vs. none in the Moxifloxacin group. Patients receiving RIPE regimen had 2.5 more risk of having abnormal PFT in comparison with those receiving Moxifloxacin (95% CI (1.03-6.18)).

Conclusions: Patients treated with Moxifloxacin regimen had less impairment than those treated with standard regimen. Restrictive pattern of disease was pre-

dominant in patients treated with standard regimen. Further research is required to assess the effect of Moxifloxacin on PIAT.

PS04-443-25 How do tuberculosis patients really take their treatment? A detailed, quantitative, approach

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Background: Compliance with tuberculosis (TB) chemotherapy is at the crux of treatment success. Simplistic percentage thresholds to define non-compliance - commonly 80 or 90% - are frequently used in trials and other studies, but mask substantial complexity. This can be described using three domains: initiation, implementation and discontinuation.¹ Knowledge of how patients take their TB treatment relative to these domains is critical, yet data on precisely how patients take their medication are lacking.

Methods: A pragmatic cluster-randomised trial in pulmonary TB patients in China sought to improve medication compliance using electronic reminders.² Treatment was over six months (180 days) and dosed every other day (90 doses). Within the control arm, medication monitor boxes recorded compliance (the box being opened) without promoting drug-taking.

Patterns of compliance were described statistically using geometric means adjusted for county and graphically using lasagne plots. Logistic regression models examined factors associated with per-dose compliance, adjusting for clustering by participant.

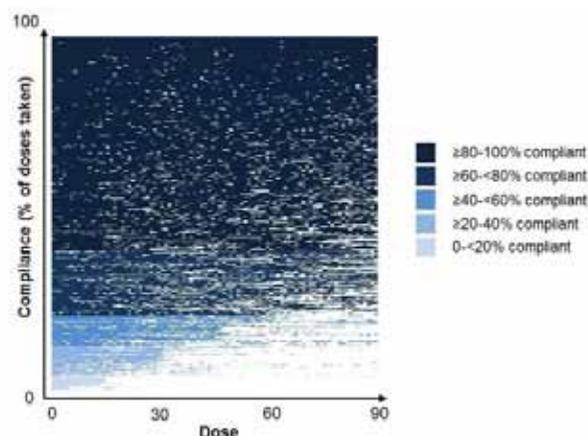
Results: Data for 780 control arm participants were available. The geometric mean percentage of doses taken was 75.6% i.e. 68/90 doses. The average duration on treatment (last dose taken before permanently non-compliant) was 80 doses. 58.8% took ≥80% of their doses and 38.2% ≥90% (Figure 1). During the initiation phase, patients took an average of 88.9% of doses, compared to 68.7% in the continuation phase.

Univariable models demonstrated associations between the continuation phase, weekends, and holidays and increasing odds of non-compliance (odds ratio 6.65 (95% confidence interval 6.27-7.05), *P* value < 0.001; 1.11 (1.06-1.17), < 0.001; 1.44 (1.33-1.56), < 0.001). Results were similar in multivariable models.

Conclusions: Knowledge of how precisely patients comply with their treatment can aid the effective design of behavioural interventions promoting compliance and regimens more 'forgiving' of non-compliance.

¹ Vrijens B, et al. *Br J Clin Pharmacol* 2012; 73(5): 691-705

² Liu X, et al. *PLoS Med* 2015; 12(9): e1001876



[Figure 1. Lasagne plots of patient compliance over time. Compliance expressed as a percentage of all 90 doses taken over the 180 day period. White indicates for each does that the medication monitor box was not opened.]

PS04-444-25 Pre-treatment loss to follow-up among smear-positive TB patients in tertiary hospitals, Quetta, Pakistan

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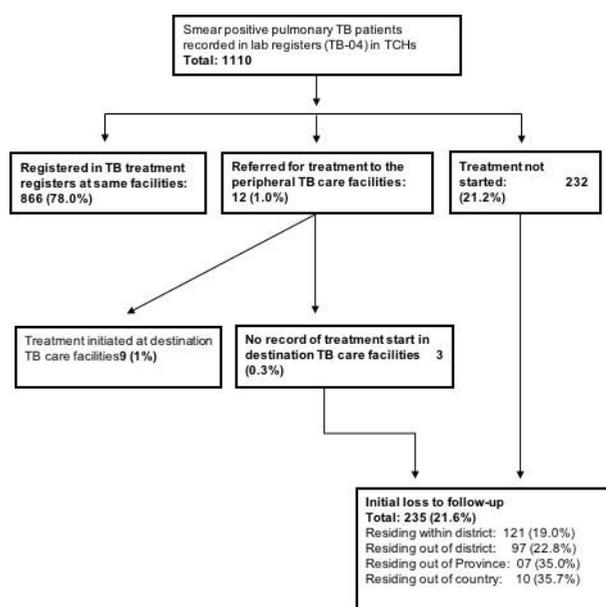
Background: Pre-treatment loss to follow-up (LTFU) of diagnosed tuberculosis (TB) patients is one of the major reasons behind missing TB cases. Here we conducted this study to assess the magnitude of pre-treatment LTFU among smear-positive pulmonary TB patients diagnosed in public sector Tertiary Care Hospitals (TCHs) and to identify the associated socio-demographic factors. The study was carried out in three out of five public sector TCHs in Quetta, Balochistan, Pakistan.

Methods: This was a retrospective cohort study involving the review of laboratory and TB treatment registers. The period of data review was January-December 2015. The study population included all the smear-positive pulmonary TB patients aged > 5 years diagnosed in 2015. For study purposes, 'pre-treatment LTFU' is defined as any smear-positive TB patient who was diagnosed (as documented in laboratory register TB-04) but who had no documented evidence of treatment initiation (TB Treatment register TB-03) or referral by the censor date (31 January 2016). Data was collected using a pre-structured data collection tool from May to August 2016.

Results: Of 1110 smear-positive pulmonary TB patients diagnosed (58% female, median age 40 years, 5% from outside the province or the country), 235 (21.2%) were

lost to follow-up before starting treatment. Pre-treatment LTFU was higher among males; in patients residing far away, in rural areas, outside the province or the country; and in those without a mobile phone number.

Conclusions: About one fifth of the smear-positive TB patients were lost to follow-up before starting treatment. Strengthening the referral and feedback mechanisms and using information technology to improve the tracing of patients is urgently required. Further qualitative research is needed to understand the reasons for pre-treatment LTFU from the patient's perspective.



[Flow diagrams of LTFU smear positive pulmonary TB patients in TCHs, Quetta, Pakistan 2015]

PS05 Latent tuberculosis infection screening: challenges and opportunities

PS05-445-25 Coverage and yield of voluntary LTBI screening among asylum seekers in Stockholm County: a record linkage study

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Background: Screening for LTBI in low-incidence countries is important to reduce TB burden and move towards elimination. The objective of this study was to determine coverage and results of LTBI screening among asylum seekers in Stockholm County.

Methods: A retrospective cohort of all asylum seekers in Stockholm 1 January 2016 -30 June 2017 was established through data extraction from the Stockholm County

Council (SLL) data base of asylum seekers eligible for a voluntary health examination (HE) and linkage through id-numbers to medical records from seven healthcare centers responsible for HE. The percentage of eligible asylum seekers completing HE, positive on IGRA and chest X-ray were analyzed by disaggregation for country of origin, age and sex.

Results: Among 10922 asylum seekers the five most common countries of origin were Afghanistan (1970, of which 1323 were men aged 15-19), Syria (1328), Iraq (1150), Mongolia (745) and Georgia (578). Out of the entire cohort, 73% completed an HE. However, HE completion among people from Georgia, Ukraine, Kyrgyzstan and Kazakhstan was below 50%. TB screening with IGRA (recommended in individuals from countries with TB incidence >100/100 000) was administered to 5226 persons, of which 1030(20%) were found positive. Chest X-ray examinations were performed in 918 cases with positive IGRA whereof 47(11%) had abnormalities.

Conclusions: Even though TB screening in Sweden is voluntary, the majority of eligible asylum seekers complete it. About 1/5 of those screened had a positive IGRA test. Further disaggregated analyses, may determine additional differences in IGRA positivity distribution, which could help refine targeting strategies in TB screening policies. Record linkage studies on LTBI screening coverage and yield are possible, but challenging because individuals have often more than one unique id-number.

PS05-446-25 Mediators of pediatric tuberculosis infection in Mbabane, Swaziland

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Background: Each year, globally, there are over 191,000 pediatric deaths due to tuberculosis, thus ranking tuberculosis as one of the top 10 most common causes of death in children under 5 years of age. Targeted prevention efforts and chemoprophylaxis have the ability to drastically lower infection rates and subsequently to lower the rates of disease and death in children. This study aimed to identify risk factors *Mycobacterium tuberculosis* for infection (Tbi), in order to guide prevention efforts and cost-effectively identify children at greatest risk.

Methods: Using a standardized measure of tuberculosis exposure, a cohort of pediatric tuberculosis contacts (n=83) at significant risk of Tbi was identified from

within a larger immunologic study conducted in Mbabane, Swaziland. Risk factor analysis was performed to measure associations between Tbi and child characteristics including baseline demographics, clinical data, and characteristics of the tuberculosis exposure. Tbi was measured via interferon gamma release assays.

Results: Of the 83 participants (mean age 6.7 years; range 0.73-14.87), 58% (48/83) were female and 42% (35/83) had Tbi. Multivariate analysis suggested that exposure to household tobacco smoke (OR 4.4, 95% CI 1.09, 18.21) and time spent in a kombi (minibus providing public transportation) (OR 1.44, 95% CI 0.92-2.25) were associated with an increased risk of Tbi in children under the age of 15 years. Age, HIV-status, and nutritional status were not associated with Tbi.

Conclusions: Our current evidence suggests that public health efforts targeting smoking cessation in the general population and improved air-flow within kombis could help to prevent the spread of TB and decrease rates of Tbi in Swaziland.

PS05-447-25 Estimated prevalence and distribution of latent tuberculosis infection in Australia, 2006-2016

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Background: The World Health Organization's End TB strategy calls for TB elimination (< 1 case per million population) by 2050. In Australia and many other low-incidence settings, the large majority of TB cases occurs among residents born in high-incidence countries and are predominantly attributed to reactivation of latent TB (LTBI) acquired overseas.

Methods: To estimate the LTBI prevalence and distribution among Australian- and overseas-born residents in Australia, we applied annual risks of tuberculosis infection (ARTI) estimates to population cohorts (by country of birth, year of arrival and age) in Australian census data in 2006, 2011 and 2016.

Results: Both the absolute number and proportion of Australian residents with LTBI increased - from 4.6% (IQR [interquartile range] 4.2-5.2%) in 2006 to 5.1% (IQR 4.7%-5.4%) in 2016, representing between 1.0 and 1.1 million persons in 2016 - due to the increasing proportion of the population born overseas (23.8% in 2006 to 28.3% in 2016). Risk of LTBI was highest in major

metropolitan centres. Of all residents estimated to have LTBI in 2016; 93.2% were overseas born, 21.6% were < 35 years of age and 31.3% had migrated to Australia since 2007.

Conclusions: The overall prevalence of LTBI in Australia is low. Some Australian residents, particularly migrants from high incidence settings, may have considerably higher risk of LTBI, and these findings allow for tailored public health interventions to reduce the risk and impact of future TB disease.

PS05-448-25 Exploring the prevalence of tuberculosis infection among health care workers in Afghanistan: a cross-sectional study

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Background: Health care workers (HCWs) are at risk of TB infection because of their constant exposure to TB patients. Inadequate use of preventative, poor ventilation at the work place, exposure during procedures like sputum induction and bronchoscopy are the risk factors. Systematic review revealed that the prevalence of latent TB infection among health care workers ranges from 33% to 79%. The aim of this study was to estimate the prevalence of TB infection among health workers in Afghanistan.

Methods: This was cross-sectional study conducted in 23 provinces of Afghanistan in Sep-Dec 2017. We selected both private and public health facilities using systematic random sampling. The study subjects were health care workers. Tuberculin Skin Test (TST) administered and read as per CDC Atlanta guidelines in forearms of study subjects and read after 48-72 hours.

Results: In total, 2,221 health care workers like doctors, nurses, midwives, lab technicians, vaccinator and pharmacy technicians enrolled in study. The mean age was 33.93 years, mean years of experience was 7.83 year. Also, the mean induration in millimeter (mm) was 11.25(SD=6.6) for all cadres. 207 (9.32%) of health care workers had skin induration of less than 5 mm, 432 (19.45%) between 5 mm-9 mm and 1,582 (71.23%) had induration of more than 10 mm (table 1). Moreover, 25th percentile mean induration was 6 mm, for 50th percentile it was 11 mm and at for 75th percentile it was 15 mm.

Variables	Value, # (%)	Standard Deviation
Mean Skin Induration in millimeter (mm)	11.25 mm	6.6
Study Subjects With Skin Induration < 5 mm	207 (9.32)	1.00
Study Subjects With Skin Induration 5 mm-10 mm	432 (19.45)	1.50
Study Subjects With Skin Induration > 10 mm	1,582 (71.23)	4.5

[Table 1: Key Study Findings]

Conclusions: The study finding shows that the prevalence of TB infection among health care workers is higher than WHO estimates for general population. Thus, it is strongly recommended to implement TB infection control measures across health sector during design of health facilities and also to promote TBIC practices among health care workers.

PS05-449-25 Screening and treatment for latent tuberculosis infection in a small Public Health Service department of TB control (Zaanstreek-Waterland) in the Netherlands

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Background and challenges to implementation: In recent years the number of patients with active tuberculosis (TB) has diminished in the Netherlands. The overall TB incidence rate is 5,2 .

For foreign born inhabitants however the incidence TB rate is 33,8.

Immigrant screening in the Netherlands is done by a chest X-ray :only once (incidence of TB in country of origin is >50 and < 200)or every six months for two years (TB incidence> 200).

The WHO (World Health Organisation) published in oktober 2017 recommendations for the management of latent TB infection in low TB burden countries. One of the recommendations involves testing immigrants from high burden countries with a Tuberculin skin test (TST) or interferon-gamma release assay (IGRA).

Intervention or response: Since 2017 newly arrived immigrants who are referred for post-entry TB screening to our Public Health Service (GGD) are tested for LTBI with a Tuberculin skin test (TST) and if the result is ≥ 10 mm followed by interferon-gamma release assay (IGRA) and chest-X ray. LTBI treatment with 3 months Rifampicin and Isoniazid (Rifinah) was offered to those with a positive IGRA and no signs of active TB.

Results and lessons learnt: In total 124 of 124 eligible immigrants were tested for LTBI, of whom 48 had a TST ≥ 10 mm. 48 were tested with IGRA, of whom 24 had a positive result. No immigrants had abnormalities on the chest X-ray, of 24 immigrants eligible for LTBI treatment 24 started and completed treatment successfully. Only 20% of the target group for TB screening was tested positive and diagnosed with LTBI and thus at risk to develop TB.

Conclusions and key recommendations: Screening and treatment for latent tuberculosis in newly arrived immigrants in a small Public Health Service is possible, and could contribute to diminishing the amount of tuberculosis in immigrants living in the Netherlands.

PS05-450-25 The impact of home visits on screening of child TB contacts and subsequent initiation of IPT: the experience of a clinic in Dili, Timor-Leste

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Background and challenges to implementation: Timor-Leste has a high burden of tuberculosis (TB). Household contact tracing and provision of isoniazid preventive therapy (IPT) for contacts aged ≤ 5 y are recommended in national guidelines, but implementation is difficult. We have previously reported on challenges to IPT delivery in Timor-Leste. Subsequently, we instituted a new program of household contact tracing and IPT at Bairo Pite Clinic (BPC), a non-government organisation (NGO) clinic providing free health care in Dili, Timor-Leste.

Intervention or response: The BPC TB program was expanded to provide a renewed focus on community education, household contact tracing, and IPT provision for high risk child contacts. Four new community healthcare workers were trained, and education materials translated into Tetum. Healthcare workers were supported to do home visits for education, symptom-based screening and treatment support for IPT. Following this, contacts aged ≤ 5 y and symptomatic individuals, were referred for medical review; children aged ≤ 5 y with TB excluded were offered IPT.

The program's impact was evaluated using prospectively collected data from August 2014 - July 2015, to enable comparison with outcomes prior to implementation of the program.

Results and lessons learnt: 92% of 309 bacteriologically proven TB cases were seen by healthcare workers. 270 household contacts aged ≤ 5 y were identified of which 212 (79%) were seen by healthcare workers. 10 of the 270 (5%) child contacts screened were diagnosed with active tuberculosis; 85% were commenced on IPT. Completion rate of IPT was 56%. The proportion of contacts screened, number of secondary TB cases identified, and proportion of children commenced on IPT, increased significantly following initiation of the new program.

Conclusions and key recommendations: Healthcare worker programs that facilitate home visits increase screening of child contacts and subsequent initiation of IPT. Barriers to treatment completion remain. Overcoming these challenges, including consideration of shorter course regimens for treating presumed latent TB infection, may further improve contact tracing and IPT outcomes in Timor-Leste.

PS05-451-25 Contact tracing at a large referral hospital in Papua New Guinea

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Background: Papua New Guinea is a high-burden Tuberculosis (TB) country. Port Moresby General Hospital (PMGH) is the largest hospital in the capital city and has the nation's highest TB case burden. This abstract describes efforts to improve contact tracing, through a Child-TB Project.

Methods: The project was supported by a dedicated project coordinator and health extension Officer (HEO). The HEO identified newly diagnosed adult TB index cases (ICs) receiving treatment within routine services and completed screening for household contacts.

Results: From October 2016 through September 2017, 343 household contacts of 81 ICs were identified, of which 53% (183/343) were < 5 years old. Contacts received symptom screening and radiography. In total 58% (206/343) completed screening, including 55% (101/183) of children and 57% (91/160) of those > 5 years.

Among contacts screened, 33% (68/206) were clinically diagnosed with TB. This included 44% (44/101) of children < 5 and 26% (24/91) of those > 5 years. TB was excluded in 67% (138/206), of which 56% (57/101) were children < 5 years. Of these 57 children, 46% (26/57) were placed on preventive therapy (PT) with INH for 6 months. Outcomes of PT included 42% (11/26) who completed PT, 23% (6/26) were lost to followup, and 34% (9/26) currently on treatment.

MDR-TB was diagnosed in 2.4% (2/81) of ICs. Screening of their contacts identified two additional cases of MDR-TB in adolescents and two asymptomatic children. The 2 child contacts completed 9 months of levofloxacin PT and remain healthy 4 months after completion.

Conclusions: In our setting, facility-based contact tracing yielded high TB and MDR TB case detection, affording opportunities to provide PT. Despite high patient volume and limited staff, use of a dedicated HEO

enabled our program to successfully introduce new tools and a novel contact tracing program tailored to the needs of our setting.

PS05-452-25 Latent tuberculosis infection in health care workers in low- and middle-income countries: an updated systematic review

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Background: Health care workers (HCWs) are at increased risk of latent tuberculosis infection (LTBI) and TB disease. We conducted an updated systematic review on the prevalence and incidence of LTBI in HCWs in low and middle-income countries (LMICs), along with associated factors, including studies using the tuberculin skin test (TST) and/or interferon-gamma release assays (IGRA).

Methods: We searched Medline, Embase, and Web of Science for observational studies from 01 January 2005 to 20 June 2017, published in any language. We used random effect methods to pool the data and did stratified analysis and meta-regression analyses to investigate heterogeneity.

Results: We included 85 studies with 32,630 subjects from 26 LMICs. For TST, prevalence ranged from 14-98% (mean 49%) in HCWs, 1-44% (mean 32%) in health care students (HCSs), and 1-98% (mean 46%) overall. For IGRA, prevalence of LTBI in HCWs ranged from 9-86% (mean 39%), 1-74% (mean 24%) in HCSs, and 1-86% (mean 38%) overall. TB incidence was the only factor associated with the prevalence of positive TST or IGRA. Those from countries with annual TB incidence of >300/100,000 had the highest prevalence of LTBI (TST: 34-84%, mean 55%; IGRA: 48-69%, mean 56%). For annual incidence of LTBI, when estimated from serial TST, this ranged from 1-38% (mean 17%) in HCWs, 3-8% (mean 5%) in HCSs, and 1-38% (mean 10%) overall. When estimated with IGRA, the annual incidence ranged from 10-30% (mean 18%) in HCWs, 8% in HCSs (1 study) and 8-30% (mean 15%) overall. The incidence of positive TST or IGRA was associated with several occupational factors including years of work, work location, contact with a TB patient and job category.

Conclusions: HCWs in LMICs in high TB incidence settings remain at increased risk of acquiring LTBI. There is an urgent years for robust implementation of TB infection control measures.

PS05-453-25 Prevalence of positive interferon gamma release assays and one-year conversion rates in nursing and medical students in Bandung, Indonesia

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Background: Nursing and medical students in high tuberculosis (TB) incidence countries are at risk for *Mycobacterium tuberculosis* infection and TB disease. We undertook a study to estimate Interferon Gamma Release Assay (IGRA) positivity and conversion rates for latent TB infection (LTBI) and to identify associated risk factors.

Methods: A cohort study was conducted at Universitas Padjadjaran, Bandung, Indonesia. All new nursing and medical students who started their clinical program in Hasan Sadikin Hospital between September 2016 and March 2017 were recruited. QuantiFERON-TB Gold Plus (QFT-Plus) was used for the IGRA. Those who had IGRA negative result at baseline had a repeat test after one year. A questionnaire and a log book were used to identify the associated risk factors.

Results: Of the 461 students, 414 (89.8%) were eligible. The prevalence of positive IGRA at baseline was 21.3% (95% CI 17.4 to 25.5). Positive IGRA was associated with older age (per year) (OR: 1.08, 95% CI 1.02-1.15), while history of BCG vaccination was protective (OR: 0.48, 95% CI 0.26-0.91). Of the 325 who were IGRA negative at baseline 302 (92.9%) had a second IGRA one year later of whom 26 (8.6%) underwent IGRA conversion. Being a medical student and participation in bronchoscopy procedures or sputum collection were associated with IGRA conversion (OR: 3.66, 95% CI 1.24-10.82 and 3.37, 95% CI 1.35-8.36, respectively). There was a non-significant trend to lower conversion among those with history of BCG vaccination (OR 0.72, 95% CI 0.23-2.23). One student developed pleural TB during one year follow up.

Conclusions: Nearly a quarter of students were positive for LTBI. The annual risk of TB infection was high and showed concordance with the occupational exposure. An effective program for TB infection control will need to be implemented to help protect students from acquiring TB infection in health care facilities.

PS05-454-25 Tuberculosis risk by time since U.S. entry among foreign-born residents of Washington State

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Background: The U.S. Centers for Disease Control and Prevention recommends targeted testing and treatment for latent TB infection (LTBI) for non-U.S. born individuals from high tuberculosis (TB) incidence countries during their first five years in the U.S. However, in 2010-15, among non-U.S. born residents the median interval from arrival in the U.S. to developing TB was 9 years. The objective of this study is to identify TB risk by region of origin and time since immigration to better target LTBI testing in Washington State.

Methods: The Washington State Department of Health disclosed all reported TB cases from January 1, 2005, through December 31, 2014. Estimates for the population denominator were derived from the American Community Survey. Annualized crude weighted TB rates were calculated and weighted for population size by year and by World Bank (WB) region (per 100,000). A Poisson model was utilized to estimate TB rates for non-U.S. born individuals for time since arrival and WB region (per 100,000).

Results: The crude TB rate ratio (RR) across all countries of origin was highest among recent immigrants (RR < 1 year: 54.3); however, there was also an increased RR observed at 21-25 years (RR: 8.5) and 31-35 years (RR: 7.1). When stratified by WB region, the crude RR is highest among countries of origin in the South Asia region during later years of immigration (RR 21-25 years: 18.8; RR 31-35 years: 18.3). The Poisson model estimated the expected TB rate as highest among recent immigrants from sub-Saharan Africa (RR: 176.2) and similarly observed the increasing trend during the same later years of immigration across all regions.

Conclusions: This analysis supports further investigation of non-U.S. born sub-populations at high risk for TB despite long-term U.S. residence and consideration of changes to the LTBI guidelines in order to achieve TB elimination in the U.S.

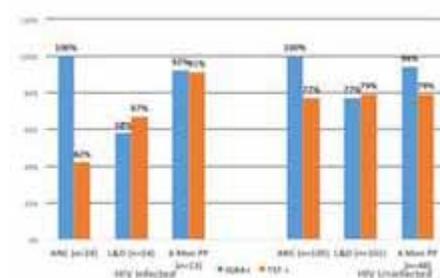
PS05-455-25 Challenges in TB diagnosis in pregnant women: findings from a cohort study in Pune, India

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Background: Immunological changes during pregnancy increases the risk of progressing from latent TB to active TB. The objective of this study was to compare the performance of the tuberculin skin test (TST) and interferon gamma release assay (IGRA) in pregnant women with and without HIV.

Methods: We are conducting a longitudinal observational cohort study of HIV-infected and -uninfected pregnant women with latent TB, in Pune, India. Pregnant women between 13 to 34 weeks of gestation are screened with the IGRA and TST. Women with a positive IGRA are enrolled and followed for two years postpartum to assess for active TB.

Results: We enrolled 223 pregnant women. The median gestational age was 23 weeks (IQR 17 to 29). 27% had a household whose income < \$3/day. HIV-infected women were virologically suppressed with a median CD4 of 445 cells/mm³. Initial LTBI prevalence differed by test (IGRA 36% vs. TST 30%, p:0.04). Among enrolled women, discordance varied depending on HIV status and stage of pregnancy (see Figure 1).



[Prevalence of LTBI varied by test used, stage of pregnancy and HIV status]

After TB antigen stimulation, IFN-g was significantly higher postpartum compared to delivery (2.91 vs. 6.9, p=0.003) and higher in HIV-uninfected vs. HIV-infected women at delivery (3.39 vs. 1.32, p=0.006) and postpartum (7.48 vs. 6.08, p=0.004). Five (2.3%) women (2 HIV infected and 3 uninfected) developed active TB postpartum; all 5 were IGRA positive but only 2 were TST positive.

Conclusions: The TST was more unreliable than the IGRA in detecting latent TB infection in pregnant women, especially HIV infected. The IGRA may be a bet-

ter test for predicting active TB in this population. Systematic screening with sensitive tests during pregnancy and postpartum are required to identify TB infection in women in TB-endemic countries.

PS06 Latent tuberculosis infection: treatment considerations

PS06-456-25 Uptake of and adherence to tuberculosis preventive therapy: are challenges and opportunities the same everywhere? A comparison between two Asia-Pacific countries

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Background: This study is part of a two-year initiative to strengthen health systems in Malaysia, Indonesia and Papua New Guinea in the management of malaria and tuberculosis. Here we focus on barriers to the successful delivery of tuberculosis preventive therapy, and compare these between Malaysia and Indonesia.

Methods: A multi-component intervention to improve tuberculosis contact management and treatment is being implemented at three primary healthcare centres (PHC) and two hospitals in Indonesia and two PHC in Malaysia. Barriers and enablers of IPT are investigated for both countries separately using qualitative research methods (semi-structured interviews with clinic staff and individuals eligible for IPT, records of meetings and workshops with tuberculosis staff, monthly activity reports and observations) which will be triangulated in an iterative process until saturation of data is reached. Records will be subjected to thematic analyses. Data from both countries will be analysed separately then compared.

Results: Data collected from tuberculosis registers in both countries demonstrated that during the baseline period, IPT was rarely prescribed. Multiple challenges to uptake of preventive treatment were documented and highlighted in the steps of the cascade of care. Examples include that national target in one setting is to screen ten contacts per case regardless of household size or infectivity of the index case; contacts need to visit the clinic

up to five times before being able to start IPT; transport costs are high; time away from work is needed; staff are unaware of guidelines and unfamiliar with the benefit of IPT. In both countries, the policy-practice gap is now being successfully closed using interventions such as workshops, peer support for staff, and use of continuous quality improvement processes.

Conclusions: This study reveals site-specific and universal challenges in up-scaling tuberculosis preventive therapy, and describes strategies to successfully overcome these.

PS06-457-25 Factors associated with completion of IPT in a cluster-randomized trial of symptom-based vs. TST-based screening of household TB contacts aged under 5 years

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Background: Isoniazid preventive therapy (IPT) is highly-effective at preventing tuberculosis (TB) disease in children under-5. Worldwide, IPT is poorly implemented, only 13% of TB-exposed children initiated IPT in 2016. Little is known about completion of IPT under routine conditions.

Methods: From October 2015 through February 2017 we conducted a cluster-randomized trial in all 16 primary health clinics in the Matlosana sub-district of North West Province that compared screening methods for initiation of IPT in children under-5. IPT was provided to child contacts via decentralized TB services within each clinic. We introduced a standardized child contact file and register from which outcome data were abstracted. Feedback on the IPT care continuum was provided to each clinic every 4-6 weeks for the first six months and then quarterly for the duration of the trial. Here we use multivariable logistic regression to identify factors associated with completion of therapy.

Results: Overall, 1002 IPT-eligible TB contacts under-5 were identified, 500 started IPT and 169 (34%) completed six-months of IPT. 325 (65%) were lost to follow-up (median duration follow-up 121 (IQR 84, 154) days). No child deaths or discontinuations due to side effects were reported, 4 (0.8%) were diagnosed with incident TB. Among children lost to follow-up, 176 (54%) completed ≥ 90 days of IPT. A clinic TB notification rate of < 8 cases/month was associated with a 3.6-fold increased odds of IPT completion (95% CI: 2.3-5.8; $p < 0.001$). Maintaining the same TB nurse for the duration of study increased the odds of IPT completion 2.9 fold (95% CI: 1.90-4.46; $p < 0.001$). Other child and index-level characteristics were not predictive.

Conclusions: Completion of IPT was abysmal. Clinic-level factors were more important in predicting completion of therapy than individual level child or index-level factors. If a 3-month regimen were available, twice as many children may have completed therapy. Further research is needed to evaluate interventions that ensure TB-exposed children are better protected against developing TB disease.

	Crude			Adjusted*		
	Relative odds of IPT completion	95% CI	P-value	Relative odds of IPT completion	95% CI	P-value
Index Demographics						
Male	1.0					
Female	0.83	0.58, 1.24	0.38			
Age <10 years	1.0					
Age 10-14 years	0.90	0.41, 1.94	0.18			
Age 15-19 years	0.61	0.32, 1.24	0.18			
Age 20-24 years	0.55	0.27, 1.10	0.09			
Age 25-29 years	0.63	0.29, 1.34	0.24			
Age ≥ 30 years	0.26	0.09, 0.76	0.11			
TB disease						
Latent/pulmonary TB disease	1.0					
Pulmonary TB disease	1.05	0.86, 1.30	0.51			
Sputum smear Result						
Smear negative	1.0			1.0		
Smear positive	0.88	0.58, 1.33	0.51	0.68	0.40, 1.08	0.10
Child-level factors						
Male	1.0			1.0		
Female	0.81	0.54, 1.18	0.27	0.69	0.41, 1.06	0.09
Relationship to Index						
Son (nephew)	1.0			1.0		
Grandchild	1.51	0.31, 7.55	0.10	1.51	0.83, 2.79	0.18
Niece/nephew	0.76	0.64, 0.90	0.22	0.85	0.42, 1.70	0.64
Other (sibling, etc.)	1.18	0.35, 4.8	0.68	0.90	0.36, 2.34	0.81
Sleep location						
Same bed	1.0			1.0		
Same room	0.89	0.61, 1.30	0.57	0.89	0.53, 0.99	0.05
Same house	0.88	0.64, 1.20	0.35	0.70	0.38, 1.27	0.24
Different house	1.28	0.35, 4.8	0.20	1.87	0.35, 8.09	0.19
Time Between Index and Child Initiation						
<60 days	1.0			1.0		
>60 days	1.49	0.89, 2.49	0.05	2.11	1.0, 4.48	0.05
Clinic-level factors						
TB nurse changed	1.0			1.0		
TB nurse unchanged	1.21	2.56, 4.36	<0.001	2.94	1.90, 4.56	<0.001
TB notification rate <16 cases/month	1.0			1.0		
TB notification rate 16-18 cases/month	0.26	0.16, 0.41	<0.001	0.32	0.20, 0.53	<0.001
TB notification rate ≥ 19 cases/month	0.18	0.11, 0.34	<0.001	0.20	0.11, 0.37	<0.001
Learning Effort						
First six months	1.0			1.0		
Second six months	1.10	0.72, 1.69	0.56			
Last 6 months	1.80	0.80, 4.11	0.28			

[Logistic regression of having completed IPT by individual and clinic-level factors]

PS06-458-25 Quality of life of patients on treatment for latent tuberculosis infection: a mixed-methods study in Stockholm, Sweden

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Background: Latent tuberculosis infection (LTBI) has been assumed to have no impact on health-related quality of life (HRQoL). This study aimed to quantify HRQoL and explore experiences of diagnosis and treatment in a population of mainly foreign-born LTBI patients in a low-TB incidence setting.

Methods: A mixed method study was conducted, including a survey using EQ-5D-3L, a generic instrument for HRQoL, and Refugee Health Screener-15 (RHS-15) that screens for distressing symptoms of anxiety, depression and PTSD. 78 patients filled the survey. A subgroup of 13 patients diagnosed during their pregnancy were

interviewed to explore their experience and attitude toward the screening and treatment.

Results: The average EQ-5D score was 0,87 (SD=0,22), and the VAS score mean was 82,65(SD=20,94). Patients at the beginning of LTBI treatment (first 2 weeks) scored very similar to patients at the middle or the end of the treatment. Regression analysis shows no significant difference when accounting for sex, age and country of origin. Concerning the RHS-15 results, 37% scored positive indicating a mental health problem. Among pregnant women, 41% screened positive for RHS-15, and the qualitative interviews showed that the main reasons of stress and anxiety among these women are being afraid of transmitting the disease to their family, the need to wait to deliver before starting the treatment and taking the medication while breastfeeding.

Conclusions: This study supports the previous evidence of no decrease in the HRQoL among LTBI patients, which has implications for economic evaluations of LTBI screening programs. However, the results raise concerns about the mental health status of this specific group, especially patients diagnosed during pregnancy, and indicates that special attention to psycho-social needs is important for optimal case management.

PS06-459-25 Isoniazid preventive therapy uptake in under five children using TB contact investigation as entry point over a 5-year period in Amhara region, Ethiopia, 2013-2017

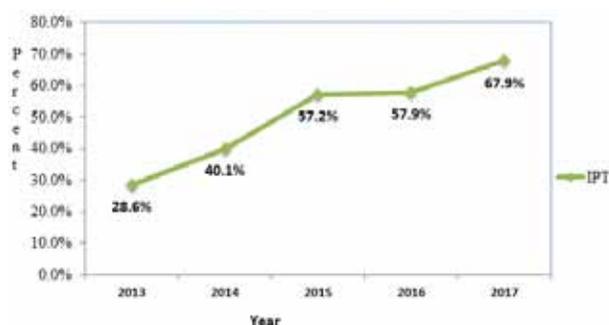
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Background and challenges to implementation: Young children living in close contact with a case of smear-positive pulmonary TB (SS+) are at higher risk of TB infection. Isoniazid preventive therapy (IPT), if administered properly, reduces the risk of developing TB among children 15 years and younger. Low coverage of IPT for children under five has been a major challenge. We described the trend of IPT coverage and TB contact screening through routine program based implementation.

Intervention or response: With support from consecutive USAID-funded projects since 2011, we developed standard operating procedures, trained health care providers, provided recording and reporting tools, and ensured an adequate supply of the pediatric formulation of isoniazid. We then monitored progress through regular review meetings and provided on-site support by deploying technical officers who provided on-site coaching and mentoring. We analyzed routine data for the period 2013-2017.

Results and lessons learnt: Of the 3,412 under-five child contacts of 17,999 SS+ index cases registered, nearly all (3,342/97.9%) were screened. Of those screened, 3,116 (93.2%) were symptomatically screen negative and 1,624 (52.1%) children received IPT. The IPT utilization increased from 28.6% in 2013 to 67.9% in 2017. In the most recent reporting quarter (July-September 2017), 74.1% of all eligible children received IPT.

Conclusions and key recommendations: The IPT uptake among under-five children more than doubled over the last five years. More effort is needed to further improve the IPT uptake rate.



[Trends in proportion of eligible <5 year children put on IPT, Amhara Region, Ethiopia 2013-2]

PS06-460-25 Modelling the cost-effectiveness of testing and treating for incipient TB

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Background: Incipient TB (ITB) is defined as the asymptomatic phase of early disease during which pathology evolves, prior to clinical presentation as active disease. Targeting ITB may be a better strategy than targeting latent TB infection (LTBI). Our objective was to estimate the public health impact and cost-effectiveness of screening for and treating ITB, assuming an ITB test meeting the WHO Target Product Profile performance targets.

Methods: We adapted a published deterministic dynamic transmission model, to include an ITB stage and 4 age groups. A cohort model variant was applied for screening close contacts of TB patients, HIV infected and other immunocompromised persons in 4 countries. Patients with a positive ITB test were assumed to be treated with preventive or full TB therapy. The model allowed for repeating the ITB test at specified intervals. Data on TB, demography and costing were collected for the Netherlands, Portugal, Viet Nam and South Africa. Quality adjusted life years (QALY) were used as effectiveness measure. For cost-effectiveness a willingness-to-pay threshold of 2x average income was applied.

Results: The model fitted reasonably well to age specific TB incidence and LTBI prevalence data in the 4 countries. Testing and treating for ITB among close contacts can be cost-saving in low incidence countries when testing costs US\$20-40, and is not cost-saving but highly cost-effective in high incidence countries. Testing and treating of PLHIV and other immunocompromised persons in low incidence settings is never cost-saving but will be highly cost-effective in high incidence settings. Cost-effectiveness was strongly dependent on assumptions on mortality and prevention of secondary cases and is robust for comparison with no LTBI screening or with recommended LTBI policies.

Conclusions: Testing and treating for ITB among contacts could be cost-saving for low incidence countries at low ITB testing cost. For high incidence countries substantial QALYs are gained.

PS06-461-25 Evaluation and follow-up of the cause of adverse events with latent tuberculosis treatment by single nucleotide polymorphism

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Background: Most newly diagnosed tuberculosis cases with a low incidence of tuberculosis are most caused by reactivation of latent tuberculosis infection (LTBI). The advantages of high dose INH and RPT for 3 months weekly (3HP) are short-courses, high-acceptance, -completion, but the adverse drug reactions (ADR) occurrence rate of hypersensitive reaction especially the flu-like syndrome in Taiwan is higher than western countries. This study aims to investigate the relationship between genetic variant of single nucleotide polymorphism (SNP) and tuberculosis susceptibility.

Methods: Inclusion criteria are over 12 years old, LTBI diagnosed and receiving 3HP treatment. Each patient was observed and recorded ADR once occurred. Metabolic enzymes from blood sample including cytochrome P450 2A6 (CYP2A6), CYP2B6, CYP2E1, CYP2C19, N-acetyltransferase 2 (NAT2) were analyzed by SNP at the same time.

Results: There are 1/3 of 285 cases had ADR and 80% of them are flu-like syndrome. There are 18 events of skin syndrome. Besides, the peak period of ADR occurred in the third week, and about 70% events occurred within three weeks.

The results of SNP, the ADR risk of AA genetic type of NAT2 rs1495741 is 2.562 times than GG type ($p=0.004$); the GA type of NAT2 rs1799930 is 1.815 times than

GG type ($p=0.02$); the risk of combination of GA and AA type of rs1495741 is 1.673 times than GG type ($p=0.049$); the risk of combination of GA and AA type of rs1799930 is 1.698 times than GG type ($p=0.03$); and the risk of A allele of rs1495741 is 1.684 times of G allele ($p=0.002$).

Conclusions: The ADR risk is significant higher than others while the rs1495741 and rs1799930 have allele changes that may have relation with flu-like syndrome. However, more sample size is needed to clarify and that could be applied in clinical in the future.

PS06-462-25 Latent tuberculosis infection treatment outcomes with daily isoniazid: consistent improvement in British Columbia, 1989-2013

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Background: As low-incidence populations tackle tuberculosis (TB) elimination, more individuals will be treated for latent TB infection (LTBI). Historically the adherence and safety of nine-months of daily isoniazid, the standard LTBI treatment regimen, have been suboptimal. However as quality of care improves over time, LTBI treatment outcomes are expected to improve. Using data from foreign-born persons in British Columbia (BC) from 1989-2013, we analyzed improvement of LTBI outcomes with isoniazid preventative therapy (INH).

Methods: Multiple administrative database and disease registries linked to the provincial TB registry identified foreign-born individuals treated with INH in BC between 1989 and 2013. Patient characteristics included age at diagnosis, sex, and presence of co-morbidities such as HIV, diabetes, dialysis, cancer, and transplant. Outcomes evaluated were treatment completion and physician-identified adverse drug reactions (ADRs) resulting in treatment cessation from 1989-2000 and each year thereafter. Generalized logistic regression was employed to evaluate outcomes adjusted for year of treatment and patient characteristics.

Results: A total of 7443 LTBI patients were treated with INH; an average of 176 per year from 1989-2000 and an average of 411 per year from 2001-2013. Treatment completion steadily improved over time. From 1989-2000 treatment completion was 61.3% (1290/2103) and ADR incidence was 10.3% (217/2103). From logistic regression (Table 1), each subsequent year post-2000 resulted in increased odds of treatment completion (aOR 1.05; 95% CI 1.03-1.06) and reduced odds of ADRs (aOR: 0.95; 95% CI 0.93-0.97). These improvements resulted in 77% treatment completion and an ADR incidence of only 6.7% in the 1000 most recently treated patients.

Covariate	aOR Treatment Completion (95% CI)	aOR Adverse Drug Reaction (95% CI)
Each Year After 2000	1.05 (1.03-1.06)	0.95 (0.93-0.97)
Age: Per 1 Year Increase	1.00 (1.00-1.00)	1.03 (1.02-1.03)
Sex: Male	1.25 (1.13-1.38)	0.67 (0.57-0.78)
HIV-Infected	1.64 (0.86-3.40)	0.60 (0.12-1.77)
Other Medical Co-Morbidity	1.14 (0.93-1.40)	0.89 (0.64-1.20)

[Table 1. Results of Logistic Regression for LTBI Treatment Outcomes]

Conclusions: LTBI treatment outcomes in the BC foreign-born population have steadily improved over a 25-year period. This analysis suggests that experience with LTBI and sustained focus on LTBI treatment outcomes can lead to clinically significant improvements in LTBI treatment completion without the introduction of new treatment regimens.

PS06-463-25 Improved coverage of IPT among household contacts of PTB cases: lessons learnt from Malawi

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Background and challenges to implementation: WHO recommends Isoniazid preventive therapy for children who are household contacts of pulmonary TB cases. This depends on a successful implementation of contact investigation in the country. The program reviewed progress in implementation of IPT over the last 3 years. **Intervention or response:** NTP in collaboration with partners developed standard operating procedure and a training package for contact investigation. The contact investigation register was revised, printed and distributed. Health care workers were trained on implementation of contact investigation. Site-specific mentoring activities were carried out tailored to support this intervention. All supportive supervisions were used to improve the quality and quantity of implementation. Data was routinely collected from IPT (Isoniazid Preventive Therapy), contact investigation registers, and used to monitor implementation of this intervention.

Results and lessons learnt: The IPT uptake has increased to 3,068 cases in 2017 from 2,303 in 2016. This is a 33% increase from previous year. The coverage improved to 47% of estimated eligible children. The coverage of contact investigation has also shown a substantial increase during the period. Nearly 51% of estimated household contacts were screened for TB through this intervention. **Conclusions and key recommendations:** The Uptake of IPT has increased substantially over the review period. The improved coverage of contact investigation and other system strengthening efforts contributed to improved coverage.

Item	2015	2016	2017
Number new Pulmonary cases(index cases)	11,288	11,111	11,114
Number screened for TB	NA	13,337	19,807
Estimated number of under five children eligible for IPT	6,400	6,299	6,477
Number started IPT	1,947	2,303	3,068

[Contact Investigation and IPT coverage]

PS06-464-25 Drug interactions in patients treated for latent TB infection

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Background: In LTBI treatment we use rifampicin and isoniazide. Rifampicin is potent inducer of drug metabolism, isoniazide is inhibitor of drug metabolism. LTBI patients have concomitant drugs and their efficacy could be changed due to LTBI drugs.

Methods: We conducted retrospective analysis of all patients treated at the University Clinic of Pulmonary and Allergic Diseases Golnik, Slovenia for LTBI during 2013-2015. We excluded patients which had not received any concomitant therapy and patients where concomitant therapy was changed before introduction of LTBI treatment due to drug-drug interactions. We performed analysis of clinical importance of drug-drug interactions with tool Lexi-Comp. We investigated if potential drug-drug interaction resulted in clinical consequences.

Results: 140 patients received concomitant therapy when treated for LTBI. 51,4% (72/140) were female. Average age was 58,2 years (range 27 - 86 years). Average LTBI treatment lasted for 3,2 months. Average number of concomitant drugs per patient was 6,6 (range 1-16).

Possible drug-drug interactions were identified in 118/140 (84,3%) patients. Lexi-comp identified 356 potential drug-drug interactions (2,54 per patient). Rifampicin was identified as primary cause in 309/356 cases (86,8%). Potential drug-drug interactions of LTBI drugs were identified mostly with pain medications (54/356), proton pump inhibitors (33/356), antihypertensive drugs (33/356), methylprednisolone (25/356), and methotrexate (24/356). 22/140 (15,7%) patients experienced important clinical effect of drug interactions. Out of 356 possible interactions only 40 (11,2%) resulted as clinically important, mostly with pain medications (15/40), methylprednisolone (7/25), methotrexate (6/24) and antihypertensive drugs (6/33). Interactions with proton pump inhibitors resulted only in 4/33 cases.

Average time between introduction of LTBI treatment and result of drug interaction was 23,5 days (range 1-76).

Conclusions: Patients treated for LTBI are at risk due to drug-drug interactions. Important limitation of our study is that we were not able to divide drug-drug interactions from exacerbation of the disease itself.

PS06-465-25 When prevention is dangerous: perceptions and experiences of isoniazid preventive therapy in KwaZulu-Natal, South Africa

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Background: As a result of changes to global recommendations for initiating isoniazid preventive therapy (IPT) to presumptively treat latent tuberculosis infection in low-resource, high-burden settings, the South African government began to offer IPT free of charge to people living with human immunodeficiency virus in uMgungundlovu District of KwaZulu-Natal in 2011. KwaZulu-Natal province has a tuberculosis notification rate of 808 per 100,000 population with 70% HIV co-infection. We aimed to describe community perceptions and experiences of IPT in three Zulu communities in uMgungundlovu during early implementation.

Methods: We utilised a hybrid of community based participatory research and ethnographic methods. Between October 2014 and May 2015, we undertook eight group interviews with community members and nine individual interviews with people accepting, discontinuing, or declining IPT. We met regularly with grassroots research advisory teams and key informants in each community between March 2012 and December 2016 to ensure the accurate descriptions of cultural concepts.

Results: Participants reported multiple ways in which IPT was perceived or experienced as dangerous. IPT became dangerous when costs related to pill collection or consumption were unsustainable for the household, or when daily pill consumption resulted in stigma or was seen to introduce excess dirt, "ukungcola," to the body. Theorist Mary Douglas explained that 'dirt' can represent 'matter out of place' in society. IPT in this setting was at times perceived as 'matter out of place' when given to people who identified as otherwise healthy, suggesting 'prevention as tablet' does not fit within existing explanatory models of health and disease.

Conclusions: Implementing IPT without understanding the social, cultural, and economic realities of community stakeholders can unintentionally undermine TB preventive efforts and introduce excess burden on people who already encounter a number of daily struggles related to health, access, safety, and basic needs.

PS07 Child tuberculosis: leaping forward

PS07-466-25 Performance of a novel stool-based TB diagnostic test in children diagnosed with TB in in-patient and out-patient settings in Mbeya, Tanzania

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Background: A highly sensitive, non-sputum based diagnostic test for tuberculosis (TB) in children is urgently needed. We evaluated the performance of a novel stool-based quantitative polymerase chain reaction (qPCR) for the diagnosis of TB in children.

Methods: Children newly diagnosed with TB at the Baylor College of Medicine Centre of Excellence in Mbeya, Tanzania were enrolled. Stool samples collected at diagnosis were analyzed for *M. tuberculosis (Mtb)* using a novel stool-based qPCR at NIMR-MMRC TB lab. Sensitivity, specificity, and additive yield of the stool qPCR was calculated using microbiologic confirmed TB as reference standard. To calculate specificity, a single stool qPCR was performed in asymptomatic, healthy controls.

Results: Between September 2017 and January 2018, 23 children diagnosed with TB were enrolled. Median age was 7.1yr, 52.2% (12/23) female, 47.8% (11/23) HIV positive, 82.6% (19/23) malnourished, and 52.2% (12/23) inpatient status. 78.3% (18/23) had pulmonary TB, and 12.5% (3/23) had microbiologically confirmed TB. Healthy controls (n=21) had median age 11.5yr, 47.6% (10/21) female, 23.8% (5/21) HIV positive, and 61.9% (13/21) with known TB contact.

Stool qPCR was positive in 39.1% (9/23) of children with TB. Among microbiologically confirmed TB cases, stool qPCR demonstrated 100% sensitivity and 94.1% sensitivity. Among non-confirmed, clinically-diagnosed TB cases (n=20), stool qPCR detected an additional 6 cases (including 2 cases of extrapulmonary TB), providing an additive diagnostic yield of 30.0% to routine sputum testing. Among children with TB, those with positive stool qPCR (n=9) were more outpatient (77.7% vs. 35.7%, p=0.05) and confirmed TB cases (33.3% vs. 0.0%, p=0.02) compared to those with negative stool qPCR (n=14).

Conclusions: Stool-based qPCR testing for TB showed high sensitivity and specificity among microbiologically confirmed TB in children with TB in inpatient and out-

patient settings, as well as offered 30.0% additive diagnostic yield over routine sputum testing in this population.

PS07-467-25 Identification of new cerebrospinal fluid and blood-based biomarkers for the diagnosis of tuberculous meningitis in children

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Background: Tuberculous meningitis (TBM) is the most severe form of extrapulmonary tuberculosis (TB). It mostly affects young children and results in high morbidity and mortality, mainly due to diagnostic delay. There is an urgent need for new tests for the earlier and accurate diagnosis of the disease. We previously showed that host biomarkers were potentially useful in the diagnosis of TBM. In the present study, we show that cerebrospinal fluid (CSF) and blood-based biosignatures may be useful in the diagnosis of TBM.

Methods: CSF and serum samples were consecutively collected from 47 children that were admitted to the Tygerberg Academic Hospital in Cape Town, South Africa, with signs or symptoms suggestive of TBM. Using a multiplex platform, the concentrations of 69 host markers were evaluated in the CSF and serum samples from all the study participants, followed by statistical analysis to ascertain the usefulness of these biomarkers as diagnostic candidates for TBM disease.

Results: Out of the 47 study participants, 23(48.9%) were finally diagnosed with TBM and 6 (12.8%) were infected with HIV. Several CSF and serum biomarkers showed potential individually as diagnostic candidates for TBM as ascertained by area under the receiver operator characteristics curve (AUC). However, the main findings of our study were the identification of a four-marker CSF biosignature which diagnosed TBM with an AUC of 0.97 (95% CI, 0.92-1.00), and a 3-marker serum biosignature which diagnosed TBM with an AUC of 0.84 (95% CI, 0.73-0.96). We also validated a previously identified 3-marker CSF biosignature (VEGF, IL13 and LL37) in the study.

Conclusions: CSF and serum biosignatures may be useful in the diagnosis of TBM in children. Our findings require further validation in larger, multi-site studies after which the biosignatures may be incorporated into point-of-care diagnostic tests for TBM.

PS07-468-25 Potential of the urine lateral flow lipoarabinomannan assay to improve the diagnosis of tuberculosis in symptomatic HIV-positive children in Cameroon

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Background: Rapid diagnosis of tuberculosis (TB) in HIV positive children remains difficult because specimens are often paucibacillary and symptoms are typically nonspecific. The urine LF-LAM assay has been shown to improve the rapid detection of TB in severely ill or severely immunocompromised adults, but there is a lack of data on its performance in symptomatic HIV positive children.

Methods: From October 2013 to January 2015 we prospectively recruited all HIV positive children ≤ 15 years with symptoms of active TB presenting at the Regional Hospital in Bamenda, Cameroon. Each patient received a systematic work up including TB contact history, clinical examination, chest x-ray, TST and microbiological testing using microscopy, Xpert MTB/RIF and culture on at least one sputum, gastric aspirate (GA) and/or stool specimen. Urine LAM testing was performed using the Determine LF-LAM assay. Anyone with a positive culture or Xpert result was defined as a bacteriologically-confirmed TB case. Patients were assigned to diagnostic subgroups based on the clinical case definitions proposed by Graham et al.

Results: Of 83 children who were enrolled and had urine specimens available for testing, 10 (12%) had bacteriologically-confirmed TB, 17 (20%) had probable TB, 40 (48%) had possible TB, 10 (12%) were unlikely to have active TB and 6 (7%) were unclassifiable because of missing x-ray, early death or loss to follow up. LAM was positive in 2/10 (20%) of confirmed, 4/17 (24%) of probable and 1/40 (3%) of possible TB cases; 1 of the unlikely TB and 2 unclassifiable patients also had a positive LAM result. As shown in the table, the LF-LAM sensitivity was higher in hospitalized and severely immunosuppressed children.

	Confirmed TB	Probable TB	Confirmed and probable TB combined
No severe immunosuppression	0/4 (0)	1/6 (17)	1/10 (10)
Severe immunosuppression	2/6 (33)	3/11 (27)	5/17 (29)
Not hospitalized	0/2 (0)	0/6 (0)	0/8 (0)
Hospitalized	2/8 (25)	4/10 (40)	6/18 (33)

[Sensitivity of the LF-LAM assay in HIV positive children with symptoms of TB, by degree of immunosuppression and hospitalization status]

Conclusions: Our preliminary analysis suggests that urine LF-LAM testing can improve the rapid diagnosis of active TB in HIV positive children, particularly among those who are severely immunosuppressed and/or hospitalized.

PS07-469-25 Incidence and factors associated with susceptibility to anti-tuberculosis drug-induced liver injury in children during the two-month intensive phase of therapy

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Background: As one of the most frequent and serious adverse reactions during TB treatment, antituberculosis drug-induced liver injury (ATLI) in children has been studied insufficiently compared with adults. Thus, our objective was to determine the incidence and risk factors of ATLI in children during the first two months (intensive phase) of therapy.

Methods: We performed a prospective observational study among 41 children with tuberculosis at the M. Djamil Hospital, Padang, Indonesia. Liver function tests were performed at baseline and after two weeks of therapy. Subsequent tests were conducted at 4, 6 and eight weeks if the initial 2-week measurement was abnormal, or if symptoms of hepatotoxicity were reported. ATLI was defined as elevation of aspartate aminotransferase (AST) or alanine aminotransferase (ALT) to more than three times the upper limit of normal, or a rise in total bilirubin to more than 2 mg/dL in the presence of jaundice.

Results: ATLI was detected in 27% of the patients within 14 to 42 days (median: 14 days) from the start of therapy. Univariate analysis showed that ATLI was significantly associated with extra-pulmonary tuberculosis (TB meningitis) ($p < 0.05$), hypoalbuminemia ($p < 0.05$) and hepatotoxic comedications ($p < 0.01$). However, age, gender, nutritional status, HIV status, and baseline liver function abnormalities (ALT, AST, bilirubin) were not associated with ATLI. Multivariate logistic regression analysis identified hypoalbuminemia ($p < 0.05$) and hepatotoxic comedications ($p < 0.01$) as independent risk factors of ATLI.

Conclusions: Hypoalbuminemia and concomitant use of hepatotoxic drugs were predominant risk factors of ATLI in children treated with first-line antituberculosis drugs. Physicians should be aware of the problem

particularly in patients with hypoalbuminemia, and it could be beneficial if hepatotoxic drugs can be avoided during therapy.

PS07-470-25 Outcomes of empiric tuberculosis treatment in children in Kampala Uganda, 2010-2015

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Background: Providers are often required to initiate treatment for childhood tuberculosis (TB) based on a clinical rather than a microbiological diagnosis. We describe the five-year outcomes of children initiated empirically on therapy in Kampala, Uganda.

Methods: We conducted a retrospective cohort study of children aged 0-14 years initiated on TB treatment at the Mulago National Referral Hospital Pediatric TB Clinic between January 2010 and December 2015. Children were followed every 2 weeks in the first month of treatment and then monthly thereafter. We extracted demographic, clinical, and treatment outcome data from the clinic electronic database.

We considered children to have a favorable outcome if they completed treatment and had documented clinical improvement, and to have an unfavorable outcome if they died, failed treatment or were lost to follow-up prior to treatment completion.

We performed multivariable regression analysis to identify demographic and clinical characteristics associated with an unfavorable outcome.

Results: Of 535 children started on TB treatment without microbiologic diagnosis, 294 (55%) were male, the median age was 36 months (IQR 15-74), and 7% were HIV positive (34 of 463 available results). Most children (N=439, 82%) had a favorable treatment outcome. Of the 96 unfavorable outcomes, 58 (60%) were due to loss to follow-up, 36 (38%) to mortality and 2 (2%) to treatment failure. No children were reported to experience an adverse event requiring permanent discontinuation of any anti-TB drug. In multivariable analysis, age 9-14 was significantly associated with unfavorable outcome (aOR 7.0, 95% CI 1.8-26.7, p =0.004).

Conclusions: Despite lack of microbiological confirmation, the majority of children started on empiric therapy had favorable outcomes and did not experience serious adverse events related to treatment. These findings sup-

port increased use of empiric treatment among children with symptoms and signs of TB when a microbiologic diagnosis cannot be established.

PS07-471-25 Xpert MTB/RIF implementation leads to more accurate diagnosis and rational use of antibiotics among children in Oromia, Ethiopia

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Background and challenges to implementation: Diagnosing tuberculosis (TB) among children is challenging because of the low sensitivity of smear microscopy and failure to produce sputum by younger children. Gene Xpert is believed to be a suitable, rapid, and specific method for diagnosis of childhood TB with better sensitivity than smear microscopy. Our objective was to assess the impact of Xpert MTB/RIF implementation on diagnostic accuracy, time taken for treatment, and rational use of antibiotics among children evaluated for TB.

Intervention or response: In 2016 we facilitated placement of Xpert machine in Assela hospital in southeastern Ethiopia, trained health workers, ensured supply of consumables, and monitored utilization rate monthly. We then reviewed trend data over a four year period; two years before and two years after the introduction of Xpert as part of routine program monitoring. We then analyzed the data in SPSS version 21.

Results and lessons learnt: During the pre-intervention period (2014-2015), 404 children under 15 were evaluated for TB, of whom 64 (15.8%) had sputum microscopy-confirmed TB. 200 (49.5%) were treated as 'probable or possible' TB cases and trials of broad spectrum antibiotics were prescribed for a total of 301 (74.5%) patients. During 2016-2017, 383 children were evaluated, of whom 93 (24.3%) tested positive for MTB, while 111 (29%) were treated as 'probable or possible' TB cases and 242 (60.0%) patients were given a trial of broad spectrum antibiotics. The mean time to start anti-TB treatment for 'probable and possible' cases was shortened [2.6 days (95% CI 1.5-3.5) versus 5.5 days (95% CI 3.7-7.4); P< 0.05].

Conclusions and key recommendations: Xpert MTB/RIF use was associated with a significant increase in the proportion of confirmed TB case detection; reduction in prescription rates for unconfirmed TB; and quicker starting of TB treatment among children. Its wide-scale use can contribute to improving TB diagnosis and treatment among children.

Variable	Pre-intervention	Post-intervention	P-value
Total evaluated	404	383	--
# confirmed TB detected	64 (15.8%)	93 (24.3%)	<0.001
# (%)Received anti-TB for unconfirmed TB	200 (58.8%)	111 (38.8%)	<0.001
# (%) Received antibiotics for unconfirmed TB	301 (74.5%)	242 (60.0%)	<0.01

[TB diagnosis and treatment initiation among children before and after introduction of Xpert/MTB RIF, 2014-2017]

PS07-472-25 Accuracy of two non-sputum based tuberculosis diagnostic tests (Xpert MTB/RIF in stool and urine LAM) in children at increased risk of severe or disseminated tuberculosis

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Background: Diagnosis of tuberculosis (TB) still relies on testing respiratory specimen. Severe TB is more common among young children and those with comorbidities and these are less likely to produce sputum. We assessed the diagnostic accuracy of two non-sputum based tests, Xpert MTB/RIF in stool and urine lipoarabinomannan (LAM), in children at increased risk of severe or disseminated TB in Uganda.

Methods: Children with clinical suspicion of TB and either age < 2 years, HIV infected, severely malnourished or had severe pneumonia were eligible. Xpert MTB/RIF and TB culture were performed on one gastric aspirate, one nasopharyngeal aspirate (or sputum) and necropsy samples when available, and were used to define the TB reference standard. Xpert in stool and urine LAM were performed on two specimens.

Results: Of 235 included children, 164 (69.8%) were < 2 years, 74 (31.5%) HIV infected, 18 (7.7%) had TB contact history, 157 (66.8%) severe malnutrition and 66 (28.1%) severe pneumonia. TB was confirmed in 12 cases (5.1%): 10 from respiratory specimens and 2 from necropsy samples. TB was detected by Xpert in stool in 9 (3.8%) cases. Sensitivity and specificity of Xpert in stool was 50% (6/12) and 99.1% (214/216), respectively. Urine LAM was positive in 64 patients (27.2%). Sensitivity and specificity of urine LAM was 50.0% (6/12) and 73.7% (157/213). It was 50% (2/4) and 76.1% (51/67) in HIV-infected children, and 80.0% (4/5) and 71.5% (103/144) in severely malnourished children, respectively. Of 56 false-positive LAM results, 80% were grade 1.

Conclusions: Proportion of confirmed TB was very low among these sick children. Xpert in stool identified half of the cases and could be a good option in these children. The low specificity of the urine LAM requires further investigations.

PS07-473-25 The impact of a childhood tuberculosis training program on knowledge among front-line health workers and childhood TB notifications in the provinces of The Gambia

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Background: Lack of training of frontline health workers is a major contributing factor to the persistence of childhood tuberculosis (TB) epidemic in Africa. This study aimed at determining the impact of a 2-day training program on childhood TB on the knowledge of front-line health workers and notification of childhood TB in provincial Gambia.

Methods: This was a prospective study involving delivery of a locally developed childhood TB training Module to front-line health workers. Training targeted all cadres of clinical healthcare staff. Two rounds of training were conducted in each region, four months apart. All areas of childhood TB diagnosis and management were covered. Impact of training on knowledge was assessed by pre and post training tests, highest possible score totalling 15 in each case. Childhood TB notification data was collected 1 year post-training and compared with the pre-training data.

Results: Overall, 326 frontline health workers from 89 health centres and 8 hospitals were trained; 122 (37.4%) of these were females. Nurses were the majority of trainees (128, 39.3%). The least number of trainees (67, 20.6%) was from the Lower River Region.

Overall, there was a significant improvement in the knowledge status of the trainees from a mean score of 6.3 (SD 2.5) pre-training to 9.6 (SD 2.6) post-training. Community health workers recorded the most improvement in knowledge post-training.

Referral rates of presumptive TB and overall TB notification increased only in the Lower river region, compared to pre-training levels. High attrition rate among trainees was observed during the 1-year post-training data collection.

Conclusions: Training led to increase in child TB knowledge of frontline health workers but to only limited improvement in detection of childhood TB in the regions.

Strategies to improve retention of trained health workers and inclusion of other non-clinical health workers in training could improve impact of subsequent trainings.

PS07-474-25 TB diagnostic methods in children and adolescents: evaluation of Brazilian Health Ministry and Keith Edwards Scoring Systems

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Background: Tuberculosis in paucibacillary individuals, particularly children, is difficult to diagnose. The clinical presentation is usually non-specific, pulmonary radiological images are generally inconclusive, a difficult to interpret the tuberculin test, mainly by BCG vaccination and low positivity in the detection of bacillus through bacteriology, making it difficult early treatment and control of transmission. The objective of this study was to evaluate the scoring system recommended by the Brazilian Ministry of Health (MH) (pulmonary TB) and the described by Keith Edwards (pulmonary and extrapulmonary TB) in the diagnosis of tuberculosis in children under 15 years of age, in the search for greater accuracy in the early detection of cases.

Methods: The study was carried out in Recife / PE / Brazil, with 209 patients under 15 years of age, from different health services in the state of Pernambuco, who were referred for diagnostic investigation with varied clinical complaints, with suspected tuberculosis infection or disease and history of contact with a bacilliferous patient. The diagnosis of tuberculosis (infection or disease) was carried out by two doctors separately, one of them being the researcher, using a diagnostic key to represent the gold standard of the research.

Results: The results showed that the criteria adopted by Brazilian Ministry of Health for pulmonary TB and those of Keith Edwards for pulmonary and extrapulmonary TB are satisfactory diagnostic tools (sensitivity 94.6% and 81.0% and specificity 93.4% and 91.9%, respectively) for the screening of tuberculosis cases in children and adolescents.

Conclusions: The study evaluated the possibilities of using simple and useful diagnostic tools, allowing a faster onset of treatment, increasing the chances of success and reducing morbidity and mortality.

PS07-475-25 Molecular detection of Mycobacterium tuberculosis in pediatric stool samples

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Background: Laboratory confirmation of pulmonary tuberculosis (TB) in children is challenging due to the difficulty of obtaining adequate sputum samples. Molecular detection of *M. tuberculosis* (*Mtb*) in stool, a non-invasive and easily obtainable sample type has been attempted with variable results (especially among sputum smear-negative cases). We assessed *Mtb* detection in stool using a novel procedure and platform in a cohort of children with TB symptoms and a close household TB contact in Lima, Peru.

Methods: This pilot study included 66 children between 0-14 years of age. Based on the outcomes of a tuberculin skin test, chest X-ray, smear microscopy and culture (sputum or gastric aspirate), we used standardized case definitions to classify children as having either confirmed, probable TB, or unlikely TB. Additionally, each child was evaluated by a physician and TB was diagnosed or ruled out. Stool (5 grams) collected from each child was homogenized, filtered and concentrated. DNA was extracted and purified by the TruTip platform (Akonni Biosystems), followed by amplification of MTB IS6110 via qPCR. We determined assay positivity based on the same threshold used for sputum ($C_p < 37.0$ and fluorescence ≥ 10.0).

Results: We detected *Mtb* in stool in all smear+/culture+ children (N=5; 100% sensitivity), all of whom were above 12 years of age (Table). *Mtb* was detected with low sensitivity in much younger children who were smear-/culture+ or diagnosed by clinical criteria (Table). Among 31 children in whom TB was ruled out by a provider, specificity was 87% (27/31). Results for 6 children were indeterminate (ind. Table); these results are pending.

Conclusions: Our data suggest that stool may be a promising sample type for rapid pediatric TB diagnostics. We are currently optimizing sample preparation and extraction procedures to improve assay performance in children with smear- and culture-negative TB and will evaluate the test in a larger cohort.

Confirmation group (N)	Culture TB confirmed, smear-positive (N=5)	Culture TB confirmed, smear-negative (N=12)	Culture TB confirmed (N=17)	Probable TB according to standardized case definition (N=18)	Unconfirmed, clinically diagnosed TB (N=11)
Sensitivity	5/5 (100%)	1/12 (8%) (2/12 ind.)	6/17 (35%) (2/17 ind.)	4/18 (22%) (1/18 ind.)	1/11 (9%) (2/11 ind.)
Median age [Min-max]	14.2 [12.7-14.3]	6.2 [0.6-13.4]	7.7 [0.6-14.3]	4.9 [1.3-9.7]	4.0 [1.3-9.7]

[Sensitivity estimates for *Mtb* detection from stool across different groups, according to lab results]

PS07-476-25 Under-reporting of childhood tuberculosis in Indonesia: subsample analysis of inventory study in Indonesia in 2017

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Background: Indonesia is the second highest TB burden country globally, with an estimated TB incidence of 1,020,000 cases in 2016. However, the number of TB cases notified in 2016 was only 360,565 and 32,604 (9% of total reported cases) were children. Indonesia has conducted TB inventory study in 2017 to estimate the level of under-reported TB cases in the National Surveillance System. The study shows under-reporting of TB cases was 41%. We analyze the under-reporting of childhood TB using the subsample of the study data.

Methods: The samples of 23 districts which represents nationally, were selected proportionally to the number of notified smear-positive TB, stratified by region. All health facilities in selected districts were enumerated. The lists were obtained from MoH's Data and Information Center, district health offices, and medical associations. Facilities that diagnosed or treated TB cases in the last three months since mapping were considered as eligible. The matching of two databases applied probabilistic record linkage. The analysis was done for cases under 15 years old.

Results: Of the total 21,320 cases, 3,942 were under 15 years old, of which 53% was under 5 years, 32% were 5-9 years and 15% were 10-14 years. The cases were found at public health centers (30.7%), hospitals (49.9%) and other health care facilities (19.4%). Only 2.5% of the TB cases in children were bacteriologically confirmed. The level of under-reporting was 54% (95%; CI 44%-64%). The level of under-reporting in primary health centers was 19% (12%-27%) and 71% (57%-81%) in other health care facilities.

Conclusions: Children with TB are often overlooked and more likely to be under-reported. This level of under-reporting is increased if children with TB seek for

treatment in hospitals or other health care facilities. The country needs to address this by engaging the private sector in order to increase child TB case notification.

PS08 Patient-centred care

PS08-477-25 Effect of a patient support model for patients with MDR-TB and introduction of bedaquiline in China: a pilot study

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Background: China is a country with a high burden of multidrug-resistant tuberculosis (MDR-TB). MDR-TB patients' adherence to treatment is poor, and irregular treatment leads to extensive drug resistance. Therefore, taking measures to improve patient adherence is crucial to avoid drug resistance to new anti-tuberculosis drugs. The purpose of this pilot study was to investigate the effect of patient support on patient TB related knowledge, medication adherence, and nursing services during the introduction of the new drug bedaquiline.

Methods: Thirty-seven MDR-TB patients taking bedaquiline from six pilot hospitals were selected. Support work was used to perform nursing interventions to improve patient care and included: management of adverse events, infection control and adherence. The intervention also included team building and various health education methods (posters, brochures, one-on-one health education, and use of social media platforms such as WeChat and QQ), and follow-up management for one-month after initiating treatment. Patients completed a TB knowledge questionnaire to assess their knowledge about TB at baseline and at one-month and a Medication Adherence Scale to assess treatment adherence. Patients also completed a survey on nursing service performance to assess satisfaction with education materials, staff attitude and quality of care.

Results: After one month of intervention, the patients' TB knowledge score increased from 13.05 out of 18 (± 1.12) at baseline to 16.97 ± 0.83 ($P < 0.05$). The medication adherence score was 6.25 ± 0.44 at baseline and increased to 7.73 ± 0.26 ($P < 0.05$). Patients rated their satisfaction of nursing service effectiveness to be 98% after one month of treatment.

Conclusions: The patient support model can effectively improve patient TB-related knowledge and medication adherence of MDR-TB, as well as improve patients' satisfaction with nursing care services. It not only helps to improve the treatment effect, but also to avoid further occurrence of drug resistance. It is recommended to promote in clinical practice.

PS08-478-25 Organization of patient-centred TB services: experience in Tajikistan

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Background and challenges to implementation: Tajikistan is among the 30 highest multidrug-resistant tuberculosis (MDR-TB) burden countries with 85 new notified TB cases per 100,000 (2016). 10% of MDR-TB patients have extensively drug-resistance tuberculosis (XDR-TB). This study assessed patients' perspectives on the quality of TB services.

Intervention or response: The study utilized *Quote-TB Light*, a qualitative standardized research method that includes focus group discussions (FGDs) and individual interviews to assess health facilities' performance. Fifteen sites assessed and sixteen FGDs (211 patients) and 292 individual (DR-TB patients) interviews held.

Assessments focused on nine quality dimensions of TB services (Professional competence; Availability of TB services; Patient Provider interaction and counseling; Support; Affordability; Communication and Information; Infrastructure; TB-HIV; Stigma).

FGD and interview results were combined into Quality Impact (QI) scores ranging between 0 and 10. The higher QI score indicates greater need for improvement, QI score above 0.75 indicates heightened need for improvement.

Results and lessons learnt: Patients ranked professional competency and psycho-social support as the most important dimensions of TB care, with importance scores at 83%. This was followed by the affordability (74%), availability of services and infrastructure (62%). TB-HIV was indicated as one of the least important dimensions (13%).

Based on QI above 0.75 focus should be placed on: easy to reach TB services to provide patient centered care (0.72), infrastructure (2.72), improvement on mutual decision making on TB treatment options (1.07) and confidentiality (0.86) as well as support for TB-HIV patients (1.01).

Conclusions and key recommendations: These assessment results were shared with NTP and other stakeholders, and possible improvement action plan for each facility was developed.

PS08-479-25 Strengthening patient satisfaction through ancillary patient care services in Wuhan, China

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Background and challenges to implementation: Treatment for multidrug-resistant tuberculosis (MDR-TB) patients is often challenged by a longer course of treatment, greater severity of the disease, and greater susceptibility to mental health problems such as anxiety and depression. Providing a comprehensive package of supportive services to address patients' educational, physical, psychosocial and financial needs may improve treatment completion, but the effectiveness of individual interventions requires greater understanding. With support from the USAID Control and Prevention of Tuberculosis Project as part of a National Action Plan pilot study, we assessed whether psychological support can strengthen patients' adherence and potentially improve treatment efficacy.

Intervention or response: Forty-two MDR-TB patients received the supportive services package in Wuhan from July 2017 to March 2018, including an individualized care plan developed with and for patients; face-to-face and online education and counseling for patients and their families provided by nurses and peer counselors; and other support. Included were six small-group participatory sessions to address the patients' psychosocial needs utilizing peer educators. We placed the patients in separate participatory groups according to their age and comorbidity: 1) comorbid group; 2) elderly, non-comorbid group; and 3) younger, non-comorbid group. All 42 patients participated in self-administered online satisfaction surveys before and after the interventions.

Results and lessons learnt: In the post-intervention survey, the 42 patients reported more satisfaction with care provided to them (9.55 ± 0.59) compared with the baseline (7.69 ± 0.87), which was statistically significant ($t=11.24, P < 0.001$). No patients were recorded as loss-to-follow-up (LTFU) during the intervention; in comparison, of 333 MDR-TB patients treated under a Global Fund program 2006-2014, 48 (14.5%) were LTFU during treatment.

Conclusions and key recommendations: Participatory patient support group activities can promote psychosocial health among patients and increase patients' satisfaction with care providers. This may result in better treatment adherence and a greater likelihood of successful treatment as the study cohort completes its treatment regimen.

PS08-480-25 Engaging private providers for TB screening, treatment and reporting in Ho Chi Minh City, Viet Nam

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Background and challenges to implementation: Drug inventory studies indicate that fewer people are treated for TB in the private sector of Viet Nam than other Asian countries. Yet, anecdotal evidence indicates large numbers of people are still accessing private-sector TB care owing to its convenience and privacy.

Intervention or response: We established a public-provider interface agency (PIIA) with a network of over 167 private providers across two districts of Ho Chi Minh City. Participating providers can distribute vouchers to their clients for reduced-rate chest X-rays (CXRs) at private radiology labs. Anyone with an abnormal CXR is then eligible for a free Xpert MTB/RIF test. Sputum samples are collected at private provider clinics or radiology labs and then transported to a gov't laboratory for testing. People with lab-confirmed TB can choose treatment with their private provider or at a nearby gov't facility. The PPIA also collected private-sector TB treatment initiation and follow up care data from a subset of participating providers.

Results and lessons learnt: Over six months, 1,754 reduced-rate CXRs were performed, resulting 556 people being tested and the detection of 41 lab-confirmed TB patients. Despite 167 providers signing agreements with the PPIA, 97% of CXR referrals came from just 11 clinics, and all of these patients chose to initiate treatment at gov't health facilities. A subset of 7 private providers reported treating 95 people for TB, most of whom (58%) were diagnosed clinically after a negative sputum test and abnormal CXR. Including these privately treated people in district notifications would increase TB treatment rates by +26.1% in project areas.

District	Baseline period all forms notifications (16-Q4 & 17-Q1)	Intervention period all forms notifications plus private-sector Tx (17-Q4 & 18-Q1)	Additional notifications	Percent change from baseline
D10	145	164	19	+13.1%
Go Vap	368	483	115	+31.3%
Both Districts	513	647	134	+26.1%

[Estimated impact of including private-sector TB treatment in district notifications]

Conclusions and key recommendations: A substantial proportion of people treated for TB receive care in the private sector in urban Viet Nam, but these practices re-

main un-notified. The NTP should formally recognize the PPIA model to facilitate reporting of notifications and treatment outcomes and to scale up this approach to other urban settings across the country.

PS08-481-25 Satisfaction of tuberculosis patients with the service provided by the health system

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Background and challenges to implementation: Patient satisfaction is a key factor in ensuring compliance to treatment regimens and clinic appointments which in turn impact treatment success rates in TB care. However, routine programmatic data often do not provide information on this important determinant of treatment outcomes. We present data on the level of and factors affecting patient satisfaction in TB services in Ethiopia.

Intervention or response: This cross-sectional survey was conducted in 11 regions of Ethiopia from October 25 to November 18, 2018. A multistage sampling technique was used to select study participants. Eight variables were used to assess the satisfaction of different aspects of health services provided to TB patients. To minimize bias, data was collected in a private area out of earshot of the service provider after the objective of the study clearly communicated and confidentiality of the information was assured. Patients were categorized as having high or low satisfaction using the median satisfaction score as cut-off point. Kruskal Wallis test used to assess factors associated with satisfaction level.

Variables	Satisfaction		Crude Odds Ratio (95% CI)	Adjusted Odds Ratio (95% CI)*
	High # (%)	Low # (%)		
Stigma score				
High	208 (58.4)	148 (41.6)	0.63 (0.47-0.84)	0.53 (0.38-0.73)*
Low	323 (69.2)	144 (30.8)	1	1
Age group in years				
18-30	263 (59.4)	180 (40.6)	1	1
31-60	236 (69.8)	102 (30.2)	1.58 (1.17-2.14)	1.7 (1.25-2.33)*
Above 60	32 (76.2)	10 (23.8)	2.19 (1.05-4.57)	2.34 (1.05-4.48)*
Wealth				
Lowest	93 (58.9)	65 (41.1)	1	1
Second	109 (66.5)	55 (33.5)	1.39 (0.88-2.18)	
Third	117 (67.6)	56 (32.4)	1.46 (0.93-2.29)	NA
Fourth	102 (62.6)	61 (37.4)	1.17 (0.75-1.83)	
Highest	110 (66.7)	55 (33.3)	1.4 (0.89-2.2)	
Setting				
Rural	219 (64.4)	121 (35.6)	0.99 (0.74-1.33)	
Urban	312 (64.6)	171 (35.4)	1	NA
Knowledge score				
High	257 (65.1)	138 (34.9)	1.05 (0.79-1.39)	
Low	274 (64.0)	154 (36.0)	1	NA
Region				
Oromia	109 (64.9)	59 (35.1)	1	1
Amhara	130 (76.5)	40 (23.5)	1.76 (1.09-2.83)	1.52 (0.93-2.49)
SNP	92 (56.4)	71 (43.6)	0.7 (0.45-1.09)	0.51 (0.32-0.83)*
Tigray	59 (68.6)	27 (31.4)	1.18 (0.68-2.06)	1 (0.57-1.77)
Benshang	27 (64.3)	15 (35.7)	0.97 (0.48-1.97)	0.8 (0.39-1.66)
Gambella	18 (64.3)	10 (35.7)	0.97 (0.42-2.25)	0.7 (0.3-1.68)
Addis Aba	58 (70.7)	24 (29.3)	1.31 (0.74-2.32)	0.92 (0.5-1.69)
Dire Daw	17 (40.5)	25 (59.5)	0.37 (0.18-0.74)	0.3 (0.15-0.62)*
Harari	21 (50.0)	21 (50.0)	0.54 (0.27-1.07)	0.43 (0.21-0.89)*

[Factors associated with satisfaction (on health services) score among TB patients.]

Results and lessons learnt: The vast majority, 786(95.5%) of 823 respondents were satisfied with the availability of drugs at the health center. The mean service satisfaction score was 31.6 (SD±4.9). 64.5% of TB patients had high satisfaction score. Meanwhile, supportive and respectful health care had the lowest proportion of satisfaction (78.5% and 76.9%). The internal consistency of satisfaction items was high with Cronbach's alpha of 0.87. High stigma score and younger age were associated with low satisfaction score

Conclusions and key recommendations: The vast majority of patients were satisfied with the TB services in Ethiopia. Availing youth friendly services and addressing stigmatizing practices at health facilities can further enhance the level of satisfaction.

PS08-482-25 Patient-centered nurse care plan as a successful intervention in complicated tuberculosis patients

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Background and challenges to implementation: Mexicali shows one of the highest tuberculosis incidence rate in Mexico, our biggest barriers represents social determinants and access to services which let to loss of follow up (20%).

Mexico actively seeks to standardize nursing care nationwide with the PLACES (Patient Centered Nurse Plan) strategy. This instrument is used to document and communicate the patient needs, expected outcomes, strategies, indications, interventions and the individualized monthly evaluation.

Intervention or response: We have applied the standardization with modifications with The Virginia Henderson model of the 14 needs, and identify the NANDA diagnoses, NIC Interventions and NOC Results.

We selected Patients with life-threatening complication (2) and with moderate risk of follow up (1), using dichotomous operational variables.

We carry out an initial evaluation to determine the status of the NOC Likert scale and initiate the application of the NIC, managing the resources required for their specific attention, assessing the treatment term and the impact of the interventions.

Results and lessons learnt: We identified social and physiological factors that represent a threat to therapeutic success allowing specific interventions. Social factors comprised an average 37.5% mainly social isolation, willingness to improve and ineffective health management; the physiological ones represented on average 50.9%, with large variations. All the patients benefited by this methodology where cured and showed a overall improve of 10.02 in the NOC Likert scale

Conclusions and key recommendations: A bridge between clinical activities and social work to optimize the impact on the patient in an individualized way, improve the outcomes of Tuberculosis affected people, the impact of PLACES in social affected areas is remarkable and measurable and the interventions designed on this plan let to improve of the quality of life and adherence to treatment.

PS08-483-25 Engaging private sector in TB care and control: a sustainable and scalable approach across 7 cities in India under urban interventions of project Axshya

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Background: The systematic involvement of all relevant health care providers in delivering effective TB services to all segments of the population is an essential component of the Global Plan to End TB.¹ Since, private health care providers are the first point of contact, they have a vital role to play in TB control. Their vigilance helps in identifying TB cases early and ensuring initiation of appropriate treatment for these patients. For diagnosis and treatment, private health care providers can link their patients to the RNTCP services or provide patient-centred care consistent with the standards of TB care in India.²

Methods: The Intervention was implemented across 7 cities of India where a unique and innovative approach was followed by trained urban coordinators to do mapping, sensitization and engagement of Qualified Private Practitioners, Private hospitals, Private labs in providing TB care and notification to Revised National Tuberculosis Control Program as per Standard of TB care in India guidelines. 1001 Qualified private practitioners, 129 private hospitals and 117 private labs were sensitized.

Results: During the project period, across 7 cities of India, 508 qualified Private practitioners, 59 Private Hospitals and 11 Private Labs got engaged in providing TB Care & Control as per STCI. Out of 19293 TB notifications from Project during Oct 2015-Dec 2017, 7451 (38.62%) notifications were by these private sector providers. Of these, qualified private practitioners contributed 80.84%, private hospitals 15.6% and private labs 3.5%.

Conclusions: Private providers can contribute immensely in successful care and control of TB by providing care ,early referral and notifications consistent with standards of TB care in India. Being the preferred first level of contact for patient seeking care in private sector, early referral and notification by them to Revised National Tuberculosis Control Program will prevent anticipated delay in diagnosis, referral and linkages of patients to RNTCP. The intervention needs to be scaled up all across india.

PS08-484-25 Coordination and partner support improved the performance of tuberculosis control in Tigray, Ethiopia

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Background and challenges to implementation: The performance of the tuberculosis (TB) programme depends on its capacity to deliver standard of care in the health system. However, baseline assessment by USAID/Challenge TB (CTB) showed there is limited programmatic supportive supervision and review meetings, training, infection control, community TB care external quality assurance and data quality. Hence, CTB categorized its support package into three levels, labeled as full package for poor performing, medium package for moderate performing, and minimal package for good performing zones. The seven zones in the region were categorized based on predefined set of criteria composed of 8 HMIS selected outcome performance indicators: case detection rate (CDR), cure rate (CR), treatment success rate (TSR), death rate, lost to follow up (LTFU), community contribution to TB cases notification, directly observed treatment (DOT), and testing TB patients for HIV.

Intervention or response: From April 2016 to Dec 2017 we provided 32 LED microscopes and conducted sensitization workshops with 1,211 participants, and program specific training for nearly 700 other health workers, plus conducted regular supportive supervision and quarterly performance review meetings.

Results and lessons learnt: At baseline, from January-March 2016, 29% (2/7) of zones in Tigray regions performed good, 29% (2/7) moderate, and 43% (3/7) were poor performing. After 18 months of intervention, 71% (5/7) of the zones performed good while 14% (1/7) were moderate and 14% (1/7) were poor performing zones.

Conclusions and key recommendations: The strong coordination and collaboration with TRHB to implement the prioritized zonal support package and the systematic interventions to address the pre-identified gaps have significantly contributed to improved TB program performance in the region. These support approaches need to be strengthened to sustain the gains made.

Overall rating	baseline - # (%) of zones	after intervention -# (%) of zones
Good performing (Green) zones	2 (28.6%), West, South	5 (71.4%), West, South, East, Northwest, Mekelle
Moderate performing (Yellow) zones	2 (28.6%), East, Northwest	1 (14.3%), Central
Poor performing (Red) zones	3 (42.9%), Mekelle, Southeast, Central	1 (14.3%), Southeast

[Table: contribution of coordinated support to the TB performance of zones in Tigray, Ethiopia]

PS08-485-25 Greater patient satisfaction achieved with a drug-resistant tuberculosis supportive care package in China

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Background: Treatment of drug-resistant tuberculosis (DR-TB) is complicated and challenging. Providing patients with a supportive care package including services such as better management of adverse reactions, specialized counseling, and peer support may improve treatment outcomes by improving patient engagement and satisfaction with their care. With support from the USAID Control and Prevention of Tuberculosis Project and as part of a National Action Plan pilot study, we assessed patient DR-TB care satisfaction before and after implementation of a supportive care package at facilities in five provinces in China.

Methods: We administered an electronic survey to two cohorts of patients who had received at least six months of DR-TB treatment: the baseline cohort received standard programmatic DR-TB care, while the pilot cohort received care enhanced by the supportive package. Results were quantified using descriptive epidemiology.

Results: Complete surveys were obtained from 139 baseline and 185 pilot patients. Comparing baseline and pilot cohorts, respectively, they were similar in terms of overall demographics such as sex (36% vs. 38% female), age (51% vs. 47% more than 40 years old), unemployment rates (65% vs. 58%), and travel time to their facility (two hours median for both). More pilot than baseline patients strongly agree that their healthcare providers treat them with respect (70% vs. 27%), make them feel at ease (75% vs. 27%), and educate patients and their families about TB (61% vs. 24%). More patients in the pilot cohort report greater participation in their care decisions (59% vs. 25%) and are overall very satisfied with their TB care (90% vs. 64%).

Conclusions: DR-TB patients in China report higher levels of satisfaction and greater involvement in their care with a supportive care package. Scale-up of this package should be considered at other sites in China and similar settings elsewhere.

PS08-486-25 Comprehensive reform of the TB health care system in Kyrgyz Republic

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Background and challenges to implementation: The Kyrgyz Republic has one of the highest MDR-TB burdens in the world. Until now, TB care was delivered through a vertical system of 26 TB hospitals. The hospitalization of patients was long and mandatory, and 60% of them were unnecessary. Other shortcomings hampered adequate TB care: hospital infection controls were weak, and TB hospital average occupancy rates were only 54%. Despite trainings and clinical guidelines improvement, the country lacked a plan to expand outpatient treatment. Additionally to this, due to lack of transportation system TB laboratories were ineffective and unable to provide quality tests.

Intervention or response: In 2015 the MoH began to reform the TB health care system. The following year, a ten year Road Map for TB system optimization was adopted. This document represented a concrete plan to move towards WHO-recommended fully outpatient treatment models. Since then, three TB hospitals with low bed occupancy rates were closed, and the number of TB beds was reduced by 25%. At the same time, the proportion of ambulatory treatment increased by 30%, and hospitalizations decreased by 35.9%. Up to date, this resulted in about half a million USD in savings.

Results and lessons learnt: Overall, the implementation of the Road Map is resulting in \$1 million in savings annually. This amount is being used for the procurement of TB drugs, incentive payments of PHC care providers, and a new sputum and drug transportation system. The ongoing sputum transportation system is being closely monitored with a view expand it to the TB labs can will be able to meet certain quality standards.

Conclusions and key recommendations: The implementation of the Road Map is proving successful. The MoH should continue its support to allow Kyrgyzstan in meeting national TB control targets.

PS08-487-25 Different patient management models in TB designated hospitals in China: a national survey

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Background: China is now in transition period from previous CDC-centered TB care to an integrated TB control network, in which hospitals plays great role on diagnosis, treatment and patient management. However,

patient-management is a new public health responsibility to most of transited hospitals, therefore they are facing great challenges.

Methods: A standard questionnaire survey was conducted to all provincial and prefecture designated TB hospitals in China in 2015. The information relate to patient management model were collected. 20% of questionnaires were randomly selected and re-confirmed via telephone interview for quality control purpose.

Results: Questionnaires from 350 TB hospitals nationwide were received and analyzed. Four different patient management models were reported from the survey. (1) Hospital-based model which means all patients are followed and managed in out-patient-department of the hospital. This model account for 21.4% of all 350 hospitals; (2) Transferring model (23.1%, 81/350) means that all patients are referred to CDCs or community health centers for follow-up; (3) Combined model which mixes above 1 and 2 according to actual situation of individual patients. 54% (189/350) of surveyed hospitals belong to this model; (4) No management: 1.4% (5/350) hospitals has no existing mechanism for patient follow-up and management. For 264 hospitals in model (1) and (3), 40.5%, 36.4% and 17.8% hospitals rely on nurses, clinicians and other dedicated full-time staff to carry out patient follow-up, while 14 hospitals (5.3%) has no full-time staff to do this work. For above 4 models, proportion of patients lost follow-up during previous year were 13.1%, 7.6%, 7.6% and 52.3% respectively.

Conclusions: Patient management is an important components in TB control program. Effective, patient-centered management model rely on good collaboration between different players. Our survey shows that in system transition stage, patient management in still weak for many TB hospitals in Chia and urgently need to be enhanced.

PS08-488-25 Patient-pathway analysis of tuberculosis services in Cameroon

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Background: According to the WHO, in 2016 Cameroon had a TB treatment coverage of 55% (range, 38-84%), which was higher than the African region but lower than the Global estimate and means that many people sick with TB are missed by the routine services. Cameroon has 248 health facilities that provide both TB diagnostic and treatment services under the supervision of the National TB Program (NTP), including 172 public, 67 confessional and 9 private facilities. An evaluation of patient care seeking behavior as compared with the existing TB services in the country may help to inform strategies to improve treatment coverage.

Methods: We performed a patient-pathway analysis to assess the alignment between patient initial care seeking and the availability of tuberculosis services in the country. We used the approach described at <http://links-bridge.com/work/tb-ppa/>.

Results: Based on this analysis, only an estimated 4% of people who seek care in Cameroon attend a health facility equipped with TB services during initial care seeking. While a large proportion of hospitals (Level 2 facilities) provide TB services, most people initially seek care instead at primary care (Level 1) facilities or through the informal private sector. Among people with TB that are notified to the NTP, 64% are notified by public structures, 37% by confessional entities and 1% by private facilities, and 87% have successful treatment outcomes.

Conclusions: While people with TB that are effectively notified and linked to care in Cameroon have generally good treatment outcomes, many people do not have access to TB services in their initial encounters with the health system. This situation likely leads to delays and drop outs along the patient pathway. Access to TB services may be improved by strengthening the specimen referral network to include primary care facilities and through better collaboration with the informal provider network.

PS08-489-25 Effectiveness of a motivational interviewing approach in a directly observed therapy program on tuberculosis outcomes among patients with tuberculosis and diabetes in Kelantan, Malaysia

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Background: Incidence of tuberculosis (TB) among diabetes mellitus (DM) patients in Malaysia is rising. Non-adherence to treatment has been identified as one of the barriers in achieving successful TB treatment outcomes and good glycemic control. The study was aimed to evaluate the effectiveness of an integrated TB and DM education using Motivational Interviewing (MI) approach within the directly observed therapy program (DOT) on TB treatment outcomes and glycemic control among patients with TB and diabetes.

Methods: Ten districts in Kelantan, a northeastern-state in Malaysia, were cluster-randomized into intervention (5 districts, 15 TB treatment centers and 50 TB/DM patients) and control group (5 districts, 12 TB treatment centers and 47 patients receiving standard health education). The intervention, MID-DOT, was a 30 minute-session of TB and diabetes self-care education using MI approach conducted weekly over 6 months (24 sessions) by TB nurses throughout DOT course. Primary endpoint was proportion of successful TB treatment out-

comes at 6 month while secondary endpoints included changes of HbA1C and diabetic self-care scores. Primary analysis relied on intention to treat using multilevel modeling analysis.

Results: Successful TB treatment outcome was 94% (cured 77%, completed 17%) in the intervention group versus 73% (cured 53%, completed 19%) among controls [relative risk (RR) = 5.99, 95% CI 1.56-22.67]. A significant mean difference in HbA1c was seen in intervention (0.82%, 95% CI 0.66-0.98) but none in controls (0.10, 95% CI -0.10, 0.31). Diabetes self-care score was significantly higher in the intervention group (8.49, 95% CI 7.38-9.59, $p < 0.05$).

Conclusions: This innovative MID-DOT as an adjunct to the standard health education for TB/DM patients is an effective tool on successful TB treatment as well as diabetic outcomes. Integrating this dual TB/DM strategy is recommended to be scaled up in national TB program to reduce TB and diabetes burden in similar burden countries.

PS09 Social, mental and behavioural determinants and tuberculosis

PS09-490-25 India, tuberculosis, and poverty: changes over time and mediating variables

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Background: Tuberculosis incidence is inversely correlated with economic status in India. A number of individual- and household-level risk factors mediate the relationship between poverty and tuberculosis. Whether disparities in tuberculosis burden, and mediators, are changing over time is unknown.

Methods: We analysed individual-level data on self-reported tuberculosis from participants in the National Family Health Survey (NFHS)-3 (2005-2006) and NFHS-4 (2015-2016). All analyses were weighted to adjust for survey design and disproportionate and non-response sampling. A wealth index was constructed and set up into quintiles (poorest, poorer, middle, rich, richest). We used multivariable logistic regression to examine the association between diabetes, smoking, indoor air pollution, alcohol, and malnourishment with tuberculosis. We compared the distribution of these risk factors across wealth quintiles.

Results: In all, 198754 and 811808 individuals between age 15-49 were included in 2005-2006 and 2015-2016 surveys. Overall tuberculosis rates in 2005-2006 and 2015-

2016 were 545 and 244 per 100,000 persons. In 2015-2016, tuberculosis among the poorest, poorer, middle, rich, and richest were 469, 300, 223, 167, and 109 per 100,000 persons ($P_{trend} < 0.0001$). The strongest risk factors were diabetes (Adjusted Odds Ratio [AOR], 1.82 [95% Confidence Interval (CI), 1.30-2.54]) and malnutrition (AOR, 2.69 [95% CI, 2.32-3.11]). The poorest wealth strata had higher rates of malnutrition, smoking, alcohol, and indoor air pollution compared to the richest (all $P < 0.0001$). Diabetes was over three times more common in the richest strata compared to the poorest (AOR, 3.20, 95% CI, 2.79-3.66).

Conclusions: Economic disparities in tuberculosis have decreased in India over the past decade, but remain large, with the poorest quintile having over four times greater tuberculosis prevalence compared with the wealthiest. Malnutrition, smoking and indoor air pollution partially mediate these disparities. Efforts to make treatment and prevention services accessible to the poor are critical to address the outsized burden of tuberculosis that they bear.

PS09-491-25 Proximate risk factors in patients with bacteriologically confirmed drug-resistant TB in South Africa

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Background: Actions to address the social determinants of TB combined with reducing proximate risk factors are essential to curb the global DR-TB pandemic and constitute a pillar of the new World Health Organization (WHO) End TB Strategy.

Proximate risk factors other than HIV infection receive less focus, and include physical and biomedical factors that govern bacterial exposure, the risk of acquiring infection and the risk of progression from tuberculosis infection to disease.

Methods: As part of a larger study evaluating models of care for DR-TB we evaluated proximate risk factors amongst patients with DR-TB within South Africa. A random sample of 102 RR-TB patients was obtained in from July-September 2016 from 13 urban and rural districts in 3 provinces. Exposure information was collected from laboratory, patient folder & geospatial sources from the time of the first RR-TB lab sample registration until 9-months after diagnosis.

Results: Results indicate that of 102 patients (62% male, 53% in urban residence), 90% had one or more proximate risk factors recorded. Patients who had ≥ 3 risk factors comprised 29% of the total sample and only 10% had no recorded risk factors.

HIV-infection, informal household type, overcrowding, previous TB diagnosis or interruption, alcohol abuse and smoking were the most commonly identified proximate risk factors.

Conclusions: While HIV is a significant comorbidity amongst patients with DR-TB in SA, other important proximate risk factors were common, including modifiable risk factors such as smoking and alcohol abuse. Very high exposure pressure was documented, with many patients living in crowded households (or prisons) with other family members suffering from TB. The co-occurrence of high exposure pressure and risk factors for progression to active TB is a strong argument to enhance the implementation of preventive chemotherapy for high risk individuals.

PS09-492-25 Tobacco smoking and tuberculosis treatment outcome in a West African setting

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Background: The objective of this study was to investigate if smokers with tuberculosis had more advanced disease at time of diagnosis and poorer treatment outcome compared with non-smokers with tuberculosis.

Methods: A prospective observational study was conducted at the health and demographic surveillance site located in urban Guinea-Bissau, West Africa. Newly diagnosed adult patients with tuberculosis were enrolled from three health centres and the national tuberculosis reference hospital, between February 2004 and February 2017. Patients were classified as non-smokers (never-smokers and ex-smokers who stopped smoking > 6 months prior to diagnosis) or smokers (current smokers and ex-smokers who stopped smoking < 6 months prior to diagnosis). Disease severity was assessed at time of diagnosis using the Bandim TBscore, a symptom-based score developed for low-income countries. Treatment outcome, including default and death, were registered at the end of treatment. Multivariate ordered logistic and Cox proportional hazard regressions were used to analyze data.

Results: A total of 1,139 patients were eligible for this study. Exclusion criteria were: treatment start > 14 days prior to inclusion, missing smoking status, and missing TBscore. On average smokers had smoked 9 (4.5-20) years. No difference in disease severity (TBscore) was observed between non-smokers and smokers (OR 1.2,

95% CI 0.9-1.5) at inclusion. Smokers had a significantly increased hazard ratio of 2.0 (95% CI 1.3-3.2) for default on treatment compared with non-smokers, but did not have an increased hazard ratio of mortality (HR 0.8, 95% CI 0.4-1.6). Analyses were adjusted for age, sex, HIV status, and civil status.

Conclusions: Smokers in Guinea-Bissau did not have more advanced disease at diagnosis and did not have a higher mortality during treatment. They did however have a higher risk of default, suggesting that smokers in Guinea-Bissau represent a patient group with difficulties adhering to treatment.

PS09-493-25 Alcohol consumption affects successful treatment outcome among tuberculosis patients in Guinea Bissau, West Africa

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Background: Tuberculosis (TB) and alcohol abuse are two major health issues. While it is well established that alcohol abuse is a risk factor for acquiring TB the data on alcohol as a risk factor for outcome of TB-treatment contradictory.

We aimed to investigate the association between alcohol consumption and outcome of TB-treatment and mortality during the first two years after treatment initiation, in an area with high prevalence of TB.

Methods: Data were collected from 2003-2016 in a prospective cohort of pulmonary TB patients in Guinea Bissau. Patients were diagnosed with TB according to WHO criteria. Background-information, including alcohol consumption, was obtained at inclusion. Based on consumption of different beverages and frequency of drinking alcohol, patients were divided into non-drinkers, drinkers and everyday drinkers. Patients were followed for six months to assess treatment outcome and for 24 months to assess survival.

Results: We included 1712 patients (63% male), 994 non-drinkers, 545 drinkers and 173 every-day drinkers (89% male). Patients consuming alcohol were more likely to be male; 14% of the males were heavy drinkers against 3% among the females ($p < 0.001$). Disease severity at treatment start, as measured by the Bandim TBscore, was not affected by alcohol consumption.

For both genders, the percentage of every-day drinkers was highest among the higher age groups and drinking was associated with having employment for both males and females. Male drinking was further associated with low educational status. Every-day drinkers had signifi-

cantly higher odds for unsuccessful outcome of treatment (i.e. failure, lost to follow-up or death) (OR 2.5 (95% CI 1.3 - 5.0), adjusted for sex, age group, ethnicity, HIV-status and smoking) while there was no significance in mortality between the groups.

Conclusions: While self-reported alcohol consumption was associated with unsuccessful outcome, it did not affect mortality among TB patients in Guinea Bissau.

PS09-494-25 Alcohol use disorder, drinking patterns, and tuberculosis treatment failure in Indian patients

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Background: Alcohol use disorders (AUD) are associated with tuberculosis disease (TB) and death. However there has been limited characterization of the severity of alcohol use on patterns of use during and after TB treatment, and TB outcomes.

Methods: We evaluated alcohol use severity and associated factors in the CTRIUMPH cohort of adults (18+) with pulmonary and extra-pulmonary TB followed for up to 24 months after treatment initiation in Pune and Chennai, India.

An AUD questionnaire (AUDIT) was administered at 0, 2, 6, 12, 18, and 24 months. AUDIT score > 8 was defined as AUD. Prevalence of AUD and patterns of alcohol misuse was assessed as well as associations with treatment failure using logistic regression.

Results: Of 627 adults enrolled, 242 (39%) reported alcohol use and 55 (9%) had treatment failure; only two women (1%) ever reported using alcohol. Overall, 42 (17%) of participants who reported alcohol use had an AUDIT 1-7; 68 (28%) with 8-15; 21 (9%) with 16-19 and 41 (17%) with > 19 . AUD was associated with increasing age, sex, low education, marital status, being unemployed, tobacco use, and rural residence.

In univariate analysis, being underweight (RR=2.20, 95% Confidence Interval [CI] 1.03-3.74), smoking (RR=1.79, 95% CI 1.03-3.09) and increasing AUDIT score (RR=2.93, 95% CI 1.18-7.30 for AUDIT 16-19 and RR=2.26, 95% CI 1.03-4.96 for AUDIT > 19) were associated with higher risk of failure.

Using a mixed-effects logistic regression model, AUDIT score decreased significantly at Week 8 to Month 6 ($p < 0.001$), Month 6 to Month 12 ($p = 0.01$), and Month 12 to Month 18 ($p = 0.04$), but rebounded to pre-treatment levels after 18 months of follow up ($p = 0.95$) (Figure 1).

Conclusions: Prevalence of alcohol use and AUD were high in our male TB cohort participants and heavier drinking and smoking are associated with treatment failure. Tailored interventions for tobacco users with high AUDIT scores are urgently needed.

PS09-495-25 The impact of alcohol consumption on tuberculosis treatment outcomes: a systematic review and meta-analysis

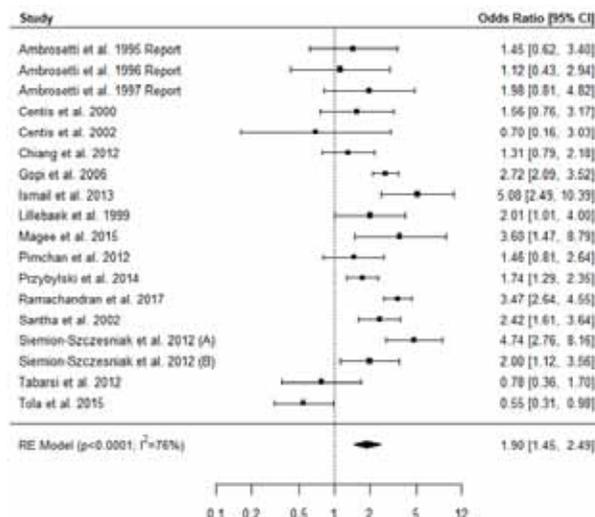
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Background: Alcohol consumption, particularly at hazardous levels, has been shown to increase risk of developing tuberculosis (TB) disease. The impact of alcohol use on TB treatment outcomes, especially independent of treatment loss to follow-up, is less clear. We performed a systematic review and meta-analysis to quantitatively summarize evidence of alcohol’s impact on TB outcomes.

Methods: We searched PubMed, EMBASE and Web of Science January 1980 - June 2017 for studies reporting risk factors associated with TB treatment outcomes. We reviewed 2828 abstracts and 998 articles. After excluding those without alcohol terms, we reviewed 528 full-text papers and included 104 which reported World Health Organization’s (WHO) TB treatment outcomes. We documented varying definitions of high or problem alcohol use and defined ‘high quality’ studies as those using a validated hazardous/harmful alcohol screener or quantifying drinking. We examined treatment outcomes of death, failure, and loss to follow-up individually and as two aggregated poor outcomes, including and excluding loss to follow-up. We ran separate analyses for studies reporting outcomes for drug susceptible (DS) versus multidrug resistant (MDR) TB.

Results: Any alcohol consumption was associated with increased risk of poor outcome among those treated for DS (OR 1.90; 95% CI, 1.45-2.49) and MDR TB (OR 2.02; 95% CI, 1.66-2.47). This association persisted after excluding loss to follow-up (OR 2.30; 95% CI, 1.65-3.20 and OR 1.61; 95% CI, 1.30-1.98 respectively). The proportion of studies using high quality alcohol definitions was only 19.2%, precluding sensitivity analysis on this variable after we stratified by outcome and drug susceptibility status.

Conclusions: Alcohol consumption significantly increases the risk of poor outcomes among DS and MDR TB patients, even after removing loss to follow-up. This study highlights the need for studies that investigate biologic reasons for the relationship between alcohol consumption and TB treatment response, that include more nuanced measurement of alcohol use.



[Figure Odds of poor outcome for patients with versus without documented high alcohol consumption.]

PS09-496-25 TB among alcoholics in informal settlements of Nairobi, Kenya

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Background: Alcoholism has been associated with development of active TB disease in Kenya due to congregate settings in which alcohol is partaken particularly in informal drinking dens.

Additionally, chronic alcoholism causes immunosuppression and increases the risk for TB disease. TB among alcoholics in informal settlement in Nairobi has been a major contributor to TB in Nairobi, with numbers increasing from 62 (0.5%) in 2016 to 252 (2%) in 2017. An assessment was conducted to determine burden of TB among alcoholics in informal settlements of Nairobi, Kenya.

Methods: Descriptive cross sectional study was conducted between 9th and 22nd March 2018. Twenty six informal settlements in 17 sub counties in Nairobi were identified. Mapping of dens within informal settlements was conducted. Community outreach was then conducted with owners of the dens used to encourage their clients to accept TB screening. WHO guidelines on Systematic Screening for Active Tuberculosis was used.

Presumptive TB cases had their sputum sent for Gene Xpert testing. Data was analysed to determine prevalence of TB in this high risk populations.

Results: Of 6480 people screened, 4295 (66%) were male, 2185 (34%) female. Presumptive cases were 2117 and 1395 (66%) were male, 722 (34%) female. Those who produced sputum from presumptive were 1418 (67%) with 911 (64%) male and 507 (36%) female. There was 4% positivity rate (61 cases) of whom 46 (3%) were male, 15 (1%) females. Of those who had TB, 4 (7%) were Rifampicin resistant, all being male.

Conclusions: There is high undiagnosed burden of tuberculosis among alcoholics in informal settlements of Nairobi. Drug resistant TB is an emerging issue in this population.

There is need for scale-up of collaborative activities between the County TB program, Community Based Organizations and Informal sector aimed at Active Case finding in drinking dens and messaging in these settings to find missing cases.

PS09-497-25 Determination of the initial level of IFN- γ in patients with disseminated forms of MDR-TB in combination with alcohol dependence syndrome

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Background: The antituberculosis immune response to a large extent depends on the activity of T-lymphocytes and the production of interferon-gamma, followed by the activation of macrophages and natural killers.

The development of disseminated forms of MDR-TB in patients with alcohol dependence syndrome is accompanied by immune system dysfunction effect.

The aim of work. To assess the level of endogenous IFN- γ in patients with disseminated forms of MDR-TB combined with alcohol dependence syndrome.

Methods: 41 patients with disseminated forms of MDR-TB were examined. Group A - 20 patients with disseminated forms of MDR-TB with alcohol dependence syndrome and group B - 21 patients with disseminated forms of MDR-TB without significant risk factors. Patients of both groups were comparable in age and sex, characteristics of the tuberculosis process in the lungs.

The control group consisted of 33 practically healthy persons for fixing of the intralaboratory level of IFN- γ . The serum level of IFN- γ was determined by ELISA. The statistical processing of the data was carried out using STATISTICA 10.0.

Results: It has been revealed the level of IFN- γ in blood serum in patients with disseminated forms of MDR-TB from both groups was significantly lower (by 24.7% - group A; by 26.4% - group B, respectively) in comparison with healthy persons from the control group ($p_{1,2}=0,02$).

No differences were established in the baseline level of endogenous IFN- γ in MDR-TB patients between groups A and B (146.1 (182.0-246.7) and 142.9 (146.4-212.1), respectively ($p = 0.4$)).

Conclusions: An initially low level of endogenous IFN- γ in patients with disseminated forms of MDR-TB in comparison with healthy persons from the control group was established. Based on the preliminary results obtained, it was established absence of significant effect of the alcohol dependence syndrome on the level of endogenous IFN- γ in patients with disseminated forms of MDR-TB.

PS09-498-25 Substance use trends among people with tuberculosis, United States, 2007-2016

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Background: Substance use complicates tuberculosis (TB) control. We hypothesized that drug use among TB patients has risen alongside the growing U.S. opioid epidemic.

Methods: We assessed Cochrane-Armitage trends for non-injection drug use (NIDU), injection drug use (IDU), and excess alcohol consumption (EAC) among patients aged ≥ 15 years by birthplace and among select subpopulations using the National Tuberculosis Surveillance System from 2007-2016.

For U.S.-born NIDU, we calculated 10-year period prevalence ratios (aPR) from multiple log-binomial regression models adjusted for age, sex, race-ethnicity, urbanicity, and homelessness.

We estimated recent transmission from 2011-2017 using a plausible-source case algorithm.

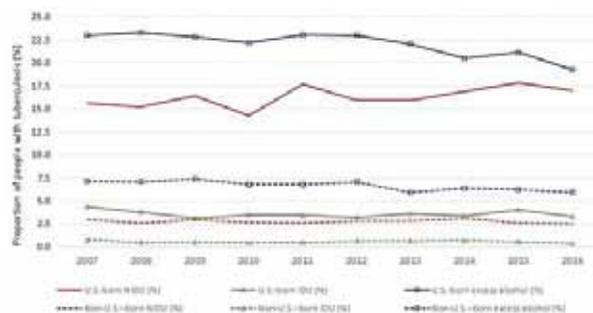
Results: Prevalence was high for EAC (22.6%), NIDU (16.4%), and IDU (3.7%) among 35,273 U.S.-born patients compared to 65,958 non-US—born patients: 6.8%, 2.8%, and 0.6%, respectively.

Among U.S.-born patients, NIDU rose 8.8% during 2007-2016 (trend $P=0.002$), whereas IDU (-22.7%, trend $P=0.123$) and EAC (-15.8%, trend $P=<0.001$) decreased. All substance use decreased for non-US—born.

For US-born, we found higher NIDU among those who were male (19.1% versus 11.2% for females; aPR=1.4, 99% CI 1.3-1.5), black (20.8% versus 11.8% for non-Hispanic whites; aPR=1.2, 99% CI 1.2-1.3), aged 25-44 years (25.1% versus 16.7% for those ≤ 24 years; aPR=1.1, 99% CI 1.0-1.3), large central metropolitan area residents (20.0% versus 12.0% for non-urban residents; aPR=1.2, 99% CI 1.0-1.4), and homeless (42.1% versus 13.1% for non-homeless; aPR=1.1, 99% CI 1.1-1.2).

Among U.S.-born, NIDU was associated with smear-positive pulmonary TB (20.4% versus 16.5%; aPR 1.2, 99% CI 1.1-1.3) and recent transmission (28.2% versus 14.6%; aPR 1.4, 99% CI 1.3-1.5).

Conclusions: NIDU increased among U.S.-born TB patients, was associated with recent transmission, and varied across subpopulations. Without opioid use data among TB patients, we can only speculate that the opioid epidemic may have contributed to the coincident upward NIDU trend. Interrupting transmission among NIDU populations is essential for U.S. TB elimination.



[Figure. Excess alcohol use (EAU), non-injection drug use (NIDU), and injection drug use (IDU) among people with tuberculosis aged ≥ 15 years by birthplace - United States, 2007-2016]

PS09-499-25 Prevalence of depression among patients with tuberculosis and diabetes/prediabetes in Lima, Peru

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Background: Current evidence suggests that there is an association between depression and tuberculosis (TB), lower adherence to treatment and morbidity and mortality increased. Nevertheless, the influence of glucose metabolism disorders (GMD) in this comorbidity is understudied. Our aim was to assess the association between depression and tuberculosis in a cohort of TB and diabetes/prediabetes patients from primary care health centers in North of Lima, Peru.

Methods: A prospective study of TB patients with GMD, including DM and pre-DM, and their household contacts (HHC) was initiated in Feb-2017. DM and pre-DM patients were diagnosed following American Diabetes Association definitions. To depression diagnosis, PHQ-9 was used in 272/277 study participants. Additionally, we assessed other socio-demographic and clinical factors. Some factors related with depression-TB in patients with GMD were analyzed by χ^2 test and finally with Mantel-Haenszel (MH) test ($p < 0.05$).

Results: The depression prevalence was 35.97% (95% CI: 30.34% - 41.60%) among TB patients and 20.29% (95% CI: 15.54%, 25.04%) among HHC. We haven't found significant differences between depression-TB and Non GMD group (54.3%) vs. depression-HHC and Non

GMD (45.7%) ($p=0.2$). We have significant differences between depression-TB and GMD group (78.1%) vs. depression-HHC and GMD (21.9%) ($p=0.008$). In the MH stratified analysis, significant differences were observed between the depression-TB and GMD group (78.1%) vs. depression-TB and Non GMD (54.3%) ($p = 0.006$) with an OR: 2.2 (95% CI: 1.3 - 3.7).

Conclusions: High rates of depression were found in TB patients and domiciliary contacts. Depression is associated with more glucose metabolic disorders in TB patients. We recommend a better diagnose and control of depression in all TB patients in order to improve treatment outcomes.

PS09-500-25 Alcohol use and clinical presentation of tuberculosis at the time of diagnosis in Puducherry and Tamil Nadu, India

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Background: Alcohol use increases the risk of developing tuberculosis (TB) disease and is associated with worse TB treatment response. The effect of alcohol use on disease severity at diagnosis is not well understood. Our objective was to assess the association between alcohol use and TB disease severity and presentation at time of diagnosis.

Methods: Study participants were smear-positive TB patients enrolled prospectively in Puducherry and Tamil Nadu, India. TB disease severity was assessed in four ways: 1) high versus low smear grade, 2) culture time to positivity (TTP), 3) cavitation on chest radiograph (CXR), and 4) percent lung affected on CXR. Alcohol use was assessed using the Alcohol Use Disorders Identification Test. Exposure was categorized as 1) alcohol drinker versus non-drinker, and 2) at risk for alcohol use disorders (AUD) versus not at risk. Associations were studied through univariate and multivariable linear and logistic regression, controlling for known risk factors.

Results: Among 948 patients, 565 (59.6%) were alcohol drinkers, of which 420 (74.3%) were at risk for AUD. High smear grade (aOR 1.11, 95% CI: 0.77, 1.56), cavitation (aOR 0.97, 95% CI 0.34, 2.74), and TTP (mean difference 0.43 days, $p=0.15$) did not differ between drinkers and non-drinkers, nor between those at risk for AUD compared to those not at risk (smear: aOR 0.95, 95% CI 0.68, 1.33; cavitation: aOR 1.07, 95% CI 0.42, 2.70; TTP: mean difference 0.04 days, $p=0.89$). Drinkers had greater percent lung affected than non-drinkers (adjusted mean difference 11.83%, $p < 0.001$), but this did not differ by AUD risk (adjusted mean difference 5.51%, $p=0.088$).

Conclusions: Alcohol drinkers had significantly greater percent lung affected on CXR at time of diagnosis than non-drinkers. Although there were no differences for other clinical characteristics, our findings warrant further investigation of potential biologic or behavioral pathways between alcohol use and TB disease.

PS10 Innovative diagnostics—looking into the future

PS10-501-25 Diagnostic performance of loop-mediated isothermal amplification for tuberculosis

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Background: Smear microscopy is still being used in the country as the primary diagnostic tool for tuberculosis (TB), despite of its observed poor sensitivity. A viable and better alternative is already available in the form of the loop-mediated isothermal amplification test (TB-LAMP), one of the newer World Health Organization-recommended rapid diagnostics (WRD) for TB detection. TB LAMP, however, has not been evaluated in the Philippine setting, and the test might perform differently for local strains. The current study is the first local evaluation of this WRD.

Methods: The study aimed to evaluate the diagnostic performance of TB-LAMP against a phenotypic reference standard, comparing the performance of the test with smear microscopy and Xpert[®] MTB/RIF. End user appraisal was also conducted to receive feedback from its operators as well as to estimate difficulties in uptake of the technology. Sputum samples collected from participants enrolled from Muntinlupa and Las Piñas were used for the study.

Results: Results from 277 samples collected were included in the final analyses. Results show TB-LAMP to have good diagnostic performance, better than smear microscopy (sensitivity: 86.1 vs 66.3) and comparable to Xpert[®] MTB/RIF (no significant difference with sensitivity and specificity, $p=0.109$). The test also received positive feedback from its end users, citing as benefits its ease of interpretation of results, lesser strain on the eyes, shorter hands-on time, and perceived ease of use when compared to smear microscopy.

Conclusions: TB LAMP has good diagnostic performance and has received positive feedback from its end-users. Values observed for its diagnostic performance were comparable to those observed from studies con-

ducted in other countries, if not better. Further study validating its diagnostic performance at the point-of-care setting and with a larger number of samples involved is recommended for a more precise and robust measure of how TB-LAMP will perform in local field conditions.

PS10-502-25 Phenotypic discrimination of mycobacteria using fluorescence staining techniques

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Background: Finding early biomarkers of long-term tuberculosis (TB) treatment outcome are essential to speed up the development of better therapies and to improve patient management. *M. tuberculosis* accumulates intracellular lipid bodies containing triacylglycerides a feature that is associated with a lowering of metabolic state (dormancy). The pathogen is antibiotic tolerant and these cells may be responsible for relapse of the infection. A high percentage of bacteria containing intracellular lipid bodies (lipid-rich phenotype) in clinical samples may predict poor treatment outcome. Current methods of measuring these cells are unwieldy and we developed a fluorescence microscopy method to improve monitoring so that it could be used as a predictor for TB treatment outcome.

Methods: We have reviewed and tested the currently available fluorescent staining techniques that are generally used to diagnose TB and monitor treatment response. We developed novel techniques using new but commercial fluorescent dyes to detect *M. tuberculosis* and intracellular lipid bodies in sputum samples.

Results: We developed a fluorescence microscopy assay in which Mycobacteria is dual labeled with two different fluorophores. We demonstrated that these two chemicals have good fluorescence spectral properties and can be successfully used to simultaneously detect intracellular lipids and the pathogen. With our new staining technique, we were able to observe and measure the proportion of bacterial subpopulations present in sputum and it can be used to further investigate the relationship between lipid status of the *M.tuberculosis* and treatment outcome.

Conclusions: We demonstrated that by using fluorescence microscopy it is possible to detect and count phenotypically antibiotic tolerant bacteria that are potentially responsible for relapse. Our technique can be used for phase II clinical trials, for research purposes or in routine clinical practice.

PS10-503-25 Evaluation of PURE-TB-LAMP for the diagnosis of pulmonary tuberculosis in Lusaka, Zambia

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Background: Zambia is one of the high tuberculosis (TB) burden countries and microscopy is still the main tool for screening TB. Although, economical, this test has poor sensitivity. Nucleic acid amplification technique (NAAT) is employed by molecular based assays and detects *Mycobacterium tuberculosis* complex (MTBc) with a reliable sensitivity. However, the utilization of current NAAT based methods is limited by their costs, particularly in low income settings with high TB burden. The objective of this study is to demonstrate the performance of PURE-TB LAMP (a low cost NAAT) compared with smear microscopy test among TB presumptive patients in Lusaka.

Methods: This ongoing study which commenced in January 2018 is utilizing leftover sputum samples (after routine fluorescent microscopy) to perform PURE-TB-LAMP assay at three health institutions. The PURE-TB-LAMP results are compared to the routine smear results as definitive method. Samples with discrepant results in the two methods are being cultured at the University Teaching Hospital and National TB reference laboratories. In these instances, culture results are considered gold standard.

Results: Of the 1500 estimated sample size, 1319 samples have been tested.

- The positivity rate for smear microscopy is 15.6% (206/1319)
- The positivity rate for PURE-TB-LAMP is 23.2% (306/1319).
- Of the available culture results for “smear negative, PURE-TB-LAMP positive samples”, MTBc has been isolated in 90.6% (48/53) cases.

Conclusions: So far PURE-TB-LAMP has shown high positivity rate (23.2%) demonstrating the potential to increase TB case detection. The significant proportion (90.6%) of smear negative but PURE-TB-LAMP positive cases that yielded MTBc upon culture, underpins an urgent need to adopt a profound method for screening TB among presumptive patients in Lusaka.

PS10-504-25 Thin-layer chromatography to support therapeutic drug monitoring of moxifloxacin in resource-limited settings

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Background: Moxifloxacin (MFX) is an important 2nd line anti-tuberculosis drug. Patients with low exposure or less susceptible *M. tuberculosis* strains risk treatment failure and may therefore benefit from concentration monitoring. However, advanced bio-analytical techniques are often not feasible in resource-limited settings. We describe a thin layer chromatography (TLC) method, a simple low tech procedure.

Methods: For technical validation, six MFX oral fluid concentrations were determined by TLC and independently classified by five lab technicians into the following categories (0; 0.5], (0.5; 1.0], (1.0; 2.5], and (2.5; ∞) mg/L, using fluorescent detection. Weighted kappa values and an intraclass correlation coefficient (ICC) were calculated to determine extent of correct classification and overall level of agreement. For clinical evaluation, paired concentration-time curves in plasma and oral fluid were obtained from tuberculosis (TB) patients and analysed by liquid chromatography-tandem mass spectrometry (plasma) and TLC (oral fluid). Patients' plasma area under the concentration-time curve up to 24 hours post dosage (AUC_{0-24h}) was calculated and oral fluid spots were categorized.

Results: The average weighted kappa was at least 0.84. An ICC of 0.968 (95% confidence interval, 0.714 - 0.997) suggested a moderate to strong agreement. Geometric mean MFX plasma AUC_{0-24h} in seven patients was 25 (range, 21 - 40) mg^{*}h/L. The oral fluid maximum concentration was > 0.5 mg/L in all patients. A possible decision-supporting table for clinical practice, using TLC, is presented in Table 1.

Conclusions: Our validated TLC method may enable clinicians to quickly personalize MFX dose in resource-limited settings. This simple, non-invasive test may contribute to global TB management.

Oral fluid Cmax (mg/L)	Predicted plasma AUC400 (mg*h/L)	MIC 0.125 mg/L	MIC 0.25 mg/L	MIC 0.5 mg/L	MIC 1 mg/L
>0.5	>20	maintain dose	maintain dose	600	800
<0.5	≤20	maintain dose	600	800	consider another anti-tuberculosis agent or revise co medication influencing plasma AUC (e.g. rifampicin).

[Table 1. Clinical decision-supporting table based on oral fluid data.]

PS10-505-25 Mycobacterium tuberculosis complex growth in sputum cultures with and without supplementation of resuscitation promoting factors

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Background: *Mycobacterium africanum* (*Maf*) causes about 50% of human tuberculosis (TB) in West Africa and grows slower in culture compared to *M. tuberculosis* (*Mtb*) lineages. A high content of lipid-body positive bacilli (LBPB) in sputum has been associated with slow growth in liquid culture. Nevertheless, it has been shown that supplementing sputum cultures with Rpf reduces culture time to detection (TTD).

Methods: Sputum smear microscopy positive samples were decontaminated and divided into four homogeneous aliquots for culture in BACTEC MGIT system. In the control tube, PBS (100mL) was added and 100mL of Rpf B, D or E was added in each test tube at the optimized concentration of 20 nM. The TTD of Rpf-supplemented tubes were compared to the control tube for each sample. The number of LBPB in sputum was determined by Auramine O and Lipid-Tox Red dual-staining and bacilli were genotyped by spoligotyping.

Results: Out of 117 cultured sputa, 78 were positive and uncontaminated. Overall, TTD was lower by at least 1 day in 13/78 samples supplemented with Rpf compared to the control tube, 11 were identified as *Maf* and 2 *Mtb*-Euro-American lineages. Only Rpf D induced a significant TTD reduction in 8 samples ($p=0.01711$). LBPB numbers in sputum were not correlated to TTD in *Mtb*-Indo-Oceanic ($r=0.05$) and *Maf* ($r=0.02$) lineages, whereas TTD decreased as LBPB increased in *Mtb*-Euro-American ($r= -0.2853$) and *Mtb*-Beijing ($r= -0.8617$) lineages.

Lineages	Number (%)	Average %LBPB	Average TTD (days)
Euro-American	41 (53.9)	37.14	9
Indo-Oceanic	12 (15.8)	24.21	7.5
<i>Maf</i>	19 (25)	42.61	21.5
Beijing	4 (5.3)	42.77	8.5

[Table: Average LBPB% and TTD of MTBC lineages]

Conclusions: Rpf D has the potential to reduce culture TTD particularly for *Maf* lineage strains that have high LBPB contents and slower growth rates. Since the growth enhancing effect was not observed in *Mtb*-Beijing strains which also have known high LBPB contents, it suggests that the growth enhancing effect of Rpf is mainly determined by MTBC lineage rather than LBPB content.

PS10-506-25 Quantifying Mycobacterium tuberculosis RNA in mask samples of pulmonary tuberculosis patients

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Background: Bioaerosols from pulmonary Tuberculosis (TB) patients could serve as a quantitative predictor of infectiousness and transmission. An earlier study described a patient mask sampling approach coupled with GeneXpert to detect expectorated *Mycobacterium tuberculosis* (*Mtb*). However, DNA based methods are unable to distinguish between live and dead bacteria whereas isolated RNA can be directly linked to the presence of viable bacteria and eventually infectivity. We carried out a feasibility study to quantify the *Mtb* and RNA from bioaerosols retained on patients' masks.

Methods: GeneXpert positive, pulmonary TB patients with a persistent cough were recruited from Sai Hospital, Dharavi, Mumbai before starting chemotherapy. Masks worn by these patients, for a period of either 1 hour (5 patients) or 3 hours (5 patients) were collected. The *Mtb* retained on the mask were released by vortexing the mask strips in 7H9 broth for two minutes and analysed for bacterial recovery and isolation of RNA and DNA.

Results: Bacterial recovery and RNA yield from patient masks were low (maximum- 2×10^3 *Mtb*/ml) from both groups (1 hour and 3 hours) with high variability among the patients. The quantity of extracted RNA and DNA was not significantly affected by the duration for which the mask was worn (1 hour-16-27 ng/ μ l; 3 hours: 21-38 ng/ μ l). Real-time PCR targeting *rpoB*, *sigA*, and *fgd1*, as well as sequencing, confirmed the presence of *Mtb* specific RNA in the mask samples. The level of expression of *Mtb* specific genes within patients may relate to the bacterial load and hence infectivity.

Conclusions: Patient masks can be used to sample bioaerosols to detect viable Mtb through a molecular approach. To our knowledge, this is the first study to demonstrate RNA isolation in patient mask samples. Further research will focus on enhancing RNA yield from the mask and analysing the relationship between aerosolized Mtb and treatment

PS10-507-25 Validation of the FluoroType® MTBDR assay using respiratory samples

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Background: The global prevalence of isoniazid (INH) resistant, rifampicin (RMP)-susceptible (HrRs) tuberculosis (TB) is estimated at 8.1% in new and 14.0% in previously treated cases. The World Health Organization has recently published new recommendations for treatment of HrRs-TB. However, rapid diagnosis of HrRs is not widely available. This study evaluated a new semi-automated molecular diagnostic test for detection of INH and RMP resistance using respiratory samples.

Methods: The study was conducted at the National Reference Laboratory in Germany using 343 stored decontaminated respiratory samples of patients not receiving TB treatment. Sensitivity and specificity of the FluoroType® MTBDR for detection of *Mycobacterium tuberculosis* complex (MTBC), RMP and INH resistance was calculated using culture as the reference standard.

Results: Of the 343 samples, 65 (19.0%) were culture positive for MTBC, 52 were smear positive (80.0%). The FluoroType® MTBDR revealed invalid results for 9 samples, one of those showed growth of MTBC in culture. Sensitivity of the FluoroType® MTBDR for detection of MTBC was 93.8% (60/65, 95%CI 84.8-98.3) and specificity was 99.6% (270/271, 95%CI 98.0-100). The number of indeterminate results was 13/60 (21.7%), 15/60 (25.0%) and 14/60 (23.3%) for *rpoB*, *katG* and *inhA* respectively. pDST revealed 60% (39/65) and 52.3% (34/64) INH and RMP resistance. INH susceptibility and resistance correctly identified in 18/18 and 15/22 samples, respectively. For RMP the FluoroType® MTBDR correctly identified 21/21 as susceptible and 26/27 (96.3%) as resistant.

Conclusions: The sensitivity of the FluoroType® MTBDR for detection of MTBC was high. However, the high rate indeterminate results for resistance detection limits the usefulness of this assay in determining resistance from primary samples so far. Further samples should be analyzed in order to increase the accuracy of the machine learning interpretation software.

PS10-508-25 Drug susceptibility testing of smear-negative samples using line-probe assay

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Background and challenges to implementation: Pakistan is a high MDR-TB burden country and fluoroquinolone resistance is reported in >40% of RR/MDR cases. Introduction of short course treatment for DRTB without developing capacity for rapid second line DST was not a feasible option. WHO endorsed the use of SL-LPA in May 2016 on RR detected cases for both smear negative and positive samples contrast to its earlier recommendation of testing FL-LPA on smear positive samples only.

Intervention or response: National TB Reference Laboratory (NRL) started offering services for rapid DST using LPA in May 2017. Patient diagnosed having Rifampicin resistant TB on Xpert MTB/RIF are referred to PMDT sites. On the very first day when patient reports to PMDT sites, a fresh specimen is collected and transported to Laboratory for DST. All samples are tested both for FL-LPA (Genotype MDRplus) and SL-LPA (Genotype MDRsl).

Results and lessons learnt: A total of 1316 direct samples were tested on FL and SL-LPA in 10 month period (May'17 to March'18). Among 1316 specimens tested, 656 (49.8 %) were smear positive. 239(18.2%) scanty and 421(32%) negative.

Among all tested valid results for FL-LPA and SL-LPA, were obtained respectively on 73.3% and 71.2% tested. For assays proportion of valid results was significantly higher in smear positive (97.3%, 97.9%) and scanty samples (82.8%, 77.4%) compared to smear Negative (29.5%, 27.1%).

Smear Result	Test performed	Valid Results MTBDRplus n % (95%CI)	Valid Results MTBDRsl n % (95%CI)	Test performed / Valid results
Negative	421	124 29.5% (25.3-33.9)	114 27.1% (23.1-31.5)	3.7
Scanty	239	198 82.8% (77.6-87.1)	185 77.4% (71.7-82.3)	1.3
Positive	656	642 97.9% (96.5-98.7)	638 97.3% (95.7-98.3)	1.0
All	1316	964 73.3% (70.8-75.6)	937 71.2% (68.7-73.6)	1.4

[First and second line -LPA valid results on direct sample correlation with smear result of samples]

Conclusions and key recommendations: We report no difference in proportion of valid results between first and second line LPA on direct sample. However there was a significant difference in valid results performed on positive and scanty smear compared to smear negative samples. For smear negative samples on average one valid results was obtained on testing of four sample.

PS10-509-25 Performance of new diagnostic tests for tuberculosis in hospitalized patients in Rwanda

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Background: In tuberculosis (TB), diagnostic performance of sputum microscopy is unsatisfactory. Sputum Xpert MTB/RIF tests are more sensitive but not always available. Simple low cost, non-invasive point-of-care tests are needed. Sensitivity of the lateral flow-Lipoarabinomannan test (LF-LAM) is too low to be recommended in ambulatory care, but may speed up diagnosis in hospitalized HIV coinfecting patients suspected with TB.

Methods: Adult hospitalized patients with bacteriologically proven or presumed TB and initiating TB treatment at Kigali University Teaching Hospital were included. Routine diagnostic workup included sputum auramin stain for Acid-Fast Bacilli (AFB) microscopy, sputum Xpert MTB/RIF, Urine Xpert MTB/RIF and Urine LF-LAM tests, HIV coinfection and TB dissemination status using medical imaging with chest X-ray and ultrasound.

Results: From November 2016 to September 2017, 116 patients, 58 (50%) HIV coinfecting and 47 (41%) with disseminated TB, were included. TB was confirmed by sputum AFB microscopy in 51/104, (49%), by sputum Xpert MTB/RIF in 47/84 (56%), by urine LF-LAM in 56/114 (49%) at cutoff =1, and by urine Xpert MTB/RIF in 16/83 (19%). All urine Xpert MTB/RIF positive samples were also LF-LAM positive at cutoff =1. TB diagnosis was confirmed by at least one technique in 88/116 (76%). In 82 patients having results for all three tests, combining sputum AFB with sputum Xpert MTB/RIF results confirmed TB in 52 (63%). Adding urine LF-LAM at cutoff =1 increased yield to 65 (79%). HIV coinfection was associated with a higher urine LF-LAM cutoff reading, but not with a positive LF-LAM test at cutoff=1.

Conclusions: In hospitalized patients treated for TB, urine LF-LAM at cutoff =1 provides a useful diagnostic addition to sputum AFB microscopy and Xpert MTB/RIF, both in HIV co-infected and in HIV negative TB patients. Performance of urine Xpert MTB/RIF is disappointing.

PS10-510-25 Performance of RealTime MTB RIF/INH resistance and GenoType MTBDRplus V2 assays for identification of drug-resistant Mycobacterium tuberculosis complex using isolates

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Background: The GenoType MTBDR^{plus} (HAIN Lifesciences, Nehren, Germany) line-probe assay (LPA) is well used for the diagnosis and confirmation of DR-TB. LPA requires 3 separate work areas to prevent contamination and a high degree of skill in interpreting results. An alternative molecular method is the highly automated RealTime MTB RIF/INH Resistance assay (RT-MTB/RIF-INH) [Abbott Molecular, Des Plaines, IL, USA], which can be used as a standalone or to reflex DNA extracts from MTBC-positives identified with the RealTime MTB assay on the Abbott *m2000* System, providing automated result interpretation and reporting. RealTime MTB tests can be performed outside a BSL-3 laboratory and the *m2000* System is currently used for HIV VL testing in countries requiring VL monitoring. In this study, RT-MTB/RIF-INH was investigated as an alternative to the in-country LPA.

Methods: Stored isolates (n=60) and laboratory isolates (n=33) from the NHLS TB Referral Laboratory with the following resistance profiles: 32% MDR, 24% RIF mono-resistance and 12% INH mono-resistance, were tested on both assays. Concordance was assessed using percent agreement and the kappa statistic and discordant isolates were analysed by sequencing.

Results: Both assays provided concordant resistance profiles for 78/93 isolates (kappa values: RIF 0.64, INH 0.89). The RT-MTB/RIF-INH reported "below limit of detection" in 10/93 (11%) of the isolates while the LPA reported 5/93 (5%) "negative" and 4/88 (5%) "indeterminate". Based on sequencing of the 15 discordant results, RT-MTB/RIF-INH misclassified 6 resistant isolates (5 MDR; 1 RIF mono-resistant) while LPA misclassified 13 (9 MDR, 3 RIF mono-resistant, 1 fully-susceptible).

Conclusions: This study demonstrates the potential for the Abbott *m2000* multi-purpose platform to be applied to identify RIF and INH resistance, with good performance compared to predicate technology. Further investigation is required on the assays 'cost and workflow for routine clinical patient care.

PS10-511-25 Online resource for GWAS analysis for large annotated DR-TB database: identification of unique genomic markers for *M. tuberculosis* strains circulating in Belarus

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Background: The Office of Cyberinfrastructure and Computational Biology of the National Institute of Allergy and Infectious Diseases (OCICB NIAID), National Institutes of Health (USA) spearheaded creation and growth of collaborative TB Portals network of clinical and research centers in countries with the heaviest burden of drug-resistant tuberculosis (DR-TB). The portfolio of TB Portals projects is proposed, revised and defined by the Network's Steering Committee. OCICB NIAID develops and supports the IT infrastructure of the TBP Network, including cloud databases, advanced analytics portal (DEPOT) and sites hosting clinical, radiological and genomics data analyses apps. Currently, the main database holds annotated and documented clinical histories of more than 1200 patients, and all anonymized data is available through user-friendly, open access Web interface (see <https://tbportals.niaid.nih.gov>).

Methods: Comparative analysis of genomic variations was performed with virtual cohorts chosen to represent *M.tuberculosis* Beijing strains circulating in different countries. GWAS analysis is performed using PLINK algorithm, results are evaluated using Fisher's test and t-test, ranked and visualized through TB Portals DEPOT. **Results:** Comparative analysis of Beijing strains circulating in Belarus, Romania, Moldova, Georgia and Azerbaijan found that Belarus genomes possess unique variations in several genes potentially implicated in virulence and interactions with the host organism. Results might reveal region-specific genomic basis for dire situation with tuberculosis in Belarus, and suggest new targets for TB diagnostics and drugs.

Conclusions: We identified several highly specific genomic variations in *M.tuberculosis* strains circulating in Belarus, that might be used for epidemiological and clinical purposes. The approach and tools we used for the analysis can be generalized for testing multiple hypotheses about the common factors and specific variations of on-going worldwide epidemics of DR-TB.

PS10-512-25 Does effective heat inactivation of sputum specimens compromise detection of *Mycobacterium tuberculosis* via real-time PCR?

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Background: Molecular detection of *M. tuberculosis* (MTB) is crucial for tuberculosis control. Working with MTB, even for molecular techniques implies risk. For reducing risks, labs perform DNA extraction into BSL3; however, this space is precious, and risk increases for cross-contamination with highly concentrated cultures. Heating or boiling would help to inactivate MTB but this procedure could reduce the performance of a real-time PCR. Here, we evaluated the survival of MTB after a heat inactivation protocol and the effect on extraction efficiency and real-time PCR amplification after the heating.

Methods: Twenty clinical sputum samples from adults with smear and culture negative for MTB, were spiked 1:10 with a 1.0 McFarland MTB H37Ra cell suspension. Half of the volume of the 20 samples were liquefied at 56°C for 20 minutes, then heat-inactivated at 90°C for 5 min, the remaining volume was the control; all samples were then cultured in duplicate by MGIT up to 56 days. DNA was extracted from both control and heat-inactivated sputum samples containing a 1;1000 dilution of MTB H37Ra cells using the protocol of TruTip System (Akonni Biosystems) and amplified by Real Time PCR (IS6110 targeted). We calculated the median time to positivity on MGIT and compared median Cp values from the PCR in both 20 samples of controls and heat-inactivated groups using Wilcoxon signed-rank test.

Results: All heat-inactivated and cultured group were negative after 56 days of incubation, while 100% of control group were culture positive with a median of 4.96 days (IQR = 4.71-5.67). The median of Cp values for control vs heat-inactivated samples was 28.97 (IQR: 26.57-30.01) and 28.91 (IQR 26.48-30.22), respectively (p=0.97).

Conclusions: This simple and easy procedure successfully inactivated MTB contained in sputum and showed no difference in PCR amplification after the heating. We recommend this inactivation procedure for sputum samples before leaving BSL3 for DNA extraction.

PS11 Dutch courage: how resistant are we to diagnosing drug resistance?

PS11-513-25 Pyrazinoic acid, a biomarker for pyrazinamide resistance in *Mycobacterium tuberculosis* using NMR

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Background: Currently pyrazinamide (PZA) is the most effective drug against latent bacilli. However, microbiological and genetic tests are not reliable. Most of PZA-resistant *Mycobacterium tuberculosis* (MTB) are unable to convert PZA to pyrazinoic acid (POA), the active compound. Wayne test determines pyrazinamidase (PZAse) activity by detecting POA in isolate which indirectly determine PZA resistance.

In this study, POA was detected in sputum liquid cultures by using Nuclear Magnetic Resonance (NMR).

Methods: 231 remanent-sputum samples were decontaminated and cultured in liquid media according MODS methodology. After 6 days of MTB-cord formation, PZA at 800 mg/ml was added to the well and incubated 3 days to allow POA production. 300 ml of PZA-culture supernatants were heated for 30 min at 98°C. Randomly, 48 sputum-positive samples were analyzed by NMR. PZA susceptibility was assayed by MGIT-PZA. The kinetics of POA production was assessed in a sample at 1, 3, 6, 7 and 8 days after adding PZA.

Results: In our preliminary results, 48 from 108 MTB-culture positive were evaluated by NMR (POA percentage over the PZA total found. 3 samples were resistant to PZA by MGIT-PZA, all of them were correctly detected by NMR. 45 samples were sensitive to PZA by MGIT-PZA, 40 were correctly detected by NMR. The sensitivity (PZA-resistant strains by MGIT-PZA) was 100% (3/3) and the specificity 88.9% (40/45). NMR percentages in PZA-sensitive samples were from 0 to 71% and in PZA-resistant samples were 1.07 to 1.4%.

In the POA kinetics, 5% of POA according NMR, was visually observed from day 1. POA reached 70% (560 ug/ml) at day 8.

Conclusions: PZAse activity could be verified from NMR in 40 PZA-sensitive samples. POA was detected from 5% (40ug/ml) in sputum-liquid culture using NMR. POA detection directly from sputum culture could be a biomarker that permits rapid and reliable PZA-resistance detection.

PS11-514-25 The era of pre-XDR and XDR-TB in Mozambique: mutations in genes associated with resistance to fluoroquinolones and injectables

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Background: The emergence of extensively drug resistant Tuberculosis (XDR-TB) is of major concern in national efforts towards ending TB in Mozambique. The usage of genetic drug susceptibility test is crucial to ensure prompt information for proper patient care. Surveillance of Pre XDR and XDR is important to control and prevent the spread of drug-resistant TB.

Methods: A retrospective study was conducted to determine the distribution of Pre- and XDR-TB cases and mutations in genes associated with second line drugs resistance tested by Genotype MTBDRsl Version 2 at Mozambique's National TB Reference Laboratory between July 2017 and March 2018.

Results: During the period of evaluation 291 patients were tested for second line TB drug resistance. From those, 58% (170/291) were male with median age of 32 (IQR: 1 - 82) years old. About 89% (259/291) of the patients were previously identified as Multidrug resistant TB (MDR-TB), 9% (27/291) monoresistant to isoniazid and 2% (5/291) susceptible by Genotype MTBDRPlus Version 2.

Twenty four percent (61/259) of the MDR-TB were confirmed as pre-XDR-TB and 10% (25/259) of XDR TB. Additional 15% (4/27) of pre-XDR were isolated from Isoniazid resistant strains. The 63 fluoroquinolones resistant cases showed only occurrence of gyrA mutations with more frequency to A90V (52%, 33/63), D94G (22%, 14/63), D94A (14%, 9/63) and S91P (10%, 6/63). Among the 27 strains resistant to injectable drugs, 93% (25/27) had mutations type a1401g and 7% (2/27) had mutations, a1401g and g1484t.

Conclusions: One third of Pre- and XDR-TB were found in Mozambique. All fluoroquinolone mutations identified, except D94G, enables the use of the drugs at higher doses whilst the mutations on injectables drugs calls for no use of this group of drugs. Strengthening the knowledge and skills of clinicians on the interpretation of mutations will improve management of TB patients and reinforces the need of drug resistance surveillance in Mozambique.

PS11-515-25 Genetic mutations associated with isoniazid resistance in tuberculosis in Mongolia

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Background: The National tuberculosis (TB) prevalence Survey, 2014-2015, revealed that TB prevalence in Mongolia was much higher than what WHO previously estimated. Third nationwide drug resistance survey (DRS) conducted in 2016 reported that the prevalence of isoniazid resistance was 22.5% among new and 34.1% among retreatment cases, and that the prevalence of multidrug-resistant tuberculosis (MDR-TB) was 5.3% among new cases and 16.5% among retreatment cases. Isoniazid resistance is usually associated with *katG* and/or *inhA* mutations. The *katG* mutation predominates in isoniazid resistance in most countries. The objective of this study is to assess the relative frequency of *katG* and *inhA* mutations among isoniazid resistant isolates and factors associated with *katG* mutation in Mongolia.

Methods: The study population was 409 isoniazid-resistant isolates, including 64 isolates from TB prevalence survey and 345 isolates from the third DRS in Mongolia. Drug resistance patterns and specific gene mutations of INH resistance were determined using GenoType® MTBDR_{plus} at the National Reference TB Laboratory, NCCD of Mongolia.

Results: Of the 409 isoniazid-resistant isolates, 71.9% (95% CI 67.3-76.0) had *inhA* gene mutation without *katG* mutation and 28.1% (95% CI 24.0-32.7) had *katG* mutation with or without *inhA* mutation. The proportion of *inhA* mutation without *katG* mutation was 83.0% (234/282) among isoniazid-resistant rifampicin-susceptible strains, which decreased to 47.2% (67/127) among MDR-TB. *katG* mutation with or without *inhA* mutation increased from 17% (48/282) among isoniazid-resistant rifampicin-susceptible strains to 52.8% (67/127) among MDR-TB. *katG* mutation was associated with rifampicin resistance (adjusted OR [aOR] 5.5, 95% CI 3.4-8.7, $p < 0.001$) and previously treated cases (aOR 1.8, 95% CI 1.1-2.9, $p < 0.05$).

Conclusions: *inhA* gene mutation predominated in isoniazid resistant TB in Mongolia. However, *katG* mutations increased substantially in strains with rifampicin resistance and in previously treated TB cases.

PS11-516-25 Prevalence of isoniazid resistance and mutations associated with isoniazid resistance in rifampicin-resistant and -susceptible clinical isolates

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Background: Short course treatment regimen (STR) for MDR TB was endorsed by WHO in 2016, and guideline for INH resistant TB treatment has been recently published. Drug resistance survey Pakistan was conducted in 2012-13 which informed that rifampicin resistance (RR) is associated with INH resistance in >90% of the cases and 8% of rifampicin sensitive cases are associated with INH resistance. First line LPA was introduced in 2016 at National TB reference laboratory (NTRL) Pakistan. We present prevalence INH resistance and distribution of *katG* and *inhA* mutations determined on Line Probe Assays.

Methods: Retrospective study, Line probe assay (Hain MTBDR_{plus} V2) performed in 2016-17 was analysed for proportion of INH resistance in Rifampicin resistance (RR) and sensitive (RS) strains and prevalence of *katG* and *inhA* mutation.

Results: A total of 3610 strains were tested including 64.4% (2325) RR strains. INH resistance was reported in 80.2% of RR and 11.8% of RS strains. Among RR cases 87.3% of INH resistance was due to *katG* and 7.9% promoter *inhA* mutation and 4.8% had mutations both at *katG* and *inhA*. Compared to RR strains prevalence of *inhA* mutation was significantly higher in RS strains.

SL-LPA results was available in 1468/3610 strains tested. No difference was seen in molecular characterization of INH resistance in MDR strains associated with and without FQ resistance. Among RS strains, 49/401 (12.2%) were INH resistant and of these 8/49 (16%) were resistant to Fluoroquinolone resistance.

	All Strain n=3610	Rif Resistant strains n=2325	Rif Sensitive strains n=1285	p-Value
INH Resistant; ALL N:%(95CI)	2016;55.8% (54.2-57.5)	1865;80.2% (78.5-81.8)	151;11.8% (10.0-13.6)	<0.005
KatG-Mutation N:%(95CI)	1737;86.2% (84.6-87.6)	1628;87.3% (85.7-88.8)	109;72.2% (64.3-79.1)	<0.005
inhA-Mutation N:%(95CI)	189;9.4% (8.1-10.7)	147;7.9% (6.9-9.2)	42; 27.8% (20.8-35.7)	<0.005
katG & inhA- Mutation	90;4.5% (3.6-5.5)	90;4.8% (3.9-5.9)	0; 0.0% (0.0-2.4)	0.006

[Prevalence of INH resistance and distribution of *katG* and *inhA* mutation in Rifampicin resistant and sensitive strains in Pakistan]

Conclusions: Among MDR cases having FQ sensitive on DST, 4% of patients will have to be excluded from short course because of mutation at both *katG* and *inhA* promoter region. Among rifampicin sensitive strains, there

is high level of FQ resistance in INH resistant cases, and second line DST will be required before including FQ in treatment of INH resistant cases as per WHO recommendation.

PS11-517-25 Validation of the Genoscholar® NTM+MDRTB assay for screening of rifampicin and isoniazid resistance in *Mycobacterium tuberculosis*

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Background: Multidrug resistant tuberculosis (MDRTB) remains to be a challenge in the control and elimination of TB. The method most utilized for detection of resistances to anti-TB drugs consists of phenotypic culture-based drug susceptibility tests (DST) which takes considerable amount of time, causing delays in determining the most suitable treatment regimen. The Genoscholar® NTM+MDRTB v2 line probe assay (LPA) provides an alternative method for rifampicin (RIF) and isoniazid (INH) DST, detecting mutations known to confer resistances to these drugs in significantly lesser time. This assay has already been recommended by the World Health Organization but may perform differently for the country's predominant TB strains. A local evaluation of the test is thus warranted, hence the conduct of this study.

Methods: This study aimed to validate the diagnostic accuracy of the Genoscholar® NTM+MDRTB assay using automated liquid culture DST as a reference standard. Biobanked isolates were used. DNA sequence analyses for *rpoB*, *inhA*, and *katG* were done for isolates found to have discrepant RIF and INH resistance profiles.

Results: 206 isolates had complete results and were included in the analyses. Sensitivity and specificity for RIF resistance detection are 100.0% and 65.06%, respectively. For INH resistance detection, sensitivity is 96.48% while specificity is 90.91%. Sequencing data for isolates with discrepancies in RIF resistance (n=23) reveal mutations in *rpoB* known to confer RIF resistance. For isolates with discrepancies in terms INH resistance (n=11), mutations were found in *inhA* and/or *katG* but for only six of them.

Conclusions: The Genoscholar® NTM+MDRTB v2 LPA performed reasonably well in terms of sensitivity, but a low specificity for RIF resistance detection was observed due to resistances that are detected only by genotypic methods. A further study evaluating the test using sputum samples, complemented by whole genome analysis for isolates with discordant test results, is recommended.

PS11-518-25 Baseline fluoroquinolone resistance among MDR-TB isolates. Are we armed enough to eliminate TB disease?

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Background: Emergence of fluoroquinolone (FQ) resistance in Multiple Drug Resistant Tuberculosis (MDR TB) isolates has become the major health issue in the treatment of MDR-TB. The present study was initiated to assess the percentage of FQ mono-resistance among MDR-TB isolates and to determine its cross-resistance between FQs (ofloxacin, levofloxacin and moxifloxacin) group of antibiotics.

Methods: Among 1619 MDR TB suspects tested, 249(15%) confirmed as MDR-TB along with 14(0.8%) rifampicin-resistance (RR-TB) isolates. To analyze the FQ drug resistance among MDR-TB isolates DST was performed using *Mycobacterium* growth indicator tube (MGIT-960) and their minimal inhibitory concentrations (MIC) were also determined.

Results: Ofloxacin mono-resistance among MDR-TB isolates were found to be 27.3% (68/249). A total of 68 ofloxacin mono resistance isolate was further evaluated for their MICs for ofloxacin, levofloxacin and moxifloxacin. Only 13% (9/68) MDR-TB isolates along with FQs resistance showed complete cross resistance for ofloxacin, levofloxacin and moxifloxacin by MIC.

Conclusions: Occurrence of 27.3% of FQs resistance among MDR-TB is a matter of great concern. The MIC for Ofloxacin was higher than its critical concentration pointing the prevalence of baseline resistance to FQs due to its irrational use.

PS11-519-25 The dynamics of *M. tuberculosis* drug resistance isolated from pulmonary TB patients at the Central TB Research Institute, Moscow, 2012-2017

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Background: Drug resistant TB poses a serious threat to the world countries, including Russia. However, the official statistics do not take into account detailed spectra of drug resistance, only considering its relation to MDR/XDR. The objective of this study is to evaluate resistance spectra of *M. tuberculosis* (MTB) isolated from patients at the Central TB Research Institute (CTRI) in 2012-2017.

Methods: We studied 1907 MTB strains isolated at admission of pulmonary TB patients (206 isolates in 2012, 322 - 2013, 378 - 2014, 385 - 2015, 304 - 2016, and 312

- 2017). Susceptibility to INH, RIF, EMB, PZA, ETH, AMK, CAP, LFX was determined in the BACTEC MGIT 960 system.

Results: The study of clinical isolates demonstrated that resistance to most TB drugs remained practically the same from 2012 through 2017: about 70% of strains were resistant to INH, 60% to RIF, 50% to EMB, PZA, ETH, 30% to AMK, 25% to CAP. We noticed growing resistance to LFX from 22% in 2012 to 34% in 2017. The analysis of MDR structure revealed that the number of strains resistant to INH and RIF, but not to AMK, CAP and LFX, decreased from 39-40% (2012-2013) to 31% (2017). We observed the growing number of isolates resistant to INH and RIF plus AMK, CAP and LFX from 18% in 2012 to 27% in 2017. The dynamics of resistance by the number of drugs in the resistance spectrum is represented in the table.

Conclusions: The stable level of resistance to first- and second-line drugs has been a favourable epidemiological indicator for 6 years. It reflects efficient policy of management of drug resistant TB patients at CTRL. The tendency to increasing resistance to fluoroquinolones and, as a result, an increasing number of strains with simultaneous resistance to 8 TB drugs are determined.

Resistance to	2012	2013	2014	2015	2016	2017
1-3 TB drugs	18.97%	21.74%	18.78%	17.66%	15.79%	15.71%
4-6 TB drugs	35.38%	34.78%	38.62%	31.69%	33.88%	34.62%
7 TB drugs	14.87%	8.07%	8.73%	9.09%	8.22%	8.97%
8 TB drugs	7.69%	9.32%	8.99%	10.39%	12.17%	12.18%

[Table]

PS11-520-25 Linezolid resistance amongst patients with treatment failure for drug-resistant tuberculosis at two sites in South Africa

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Background: There are limited data on clinical and genotypic correlates of linezolid resistance in TB. We aimed to describe patient characteristics and mutations associated with phenotypic linezolid resistance in *M tuberculosis* isolates from patients with drug-resistant TB at two public sector TB facilities in South Africa.

Methods: Adults and adolescents with treatment failure on a linezolid-containing regimen were retrospectively identified. Treatment failure was defined as positive sputum culture for *M tuberculosis* after at least 4 months of linezolid-based therapy. Retrieved isolates were subcultured onto Lowenstein-Jensen media, and those with observed growth underwent minimum inhibitory concentration (MIC) testing using broth microdilution. Targeted sequencing for mutations in *rrl* and *rplC* was performed on all isolates.

Results: *M tuberculosis* isolates were obtained from 58 patients with linezolid-based treatment failure, and we were able to successfully subculture isolates from 38 patients on solid media. Thirteen patients (34.3%) had phenotypic linezolid resistance (defined as MIC > 1 µg/mL): median age 36 years (IQR 30 to 47), 6 (55%) female, and 7 (64%) HIV-infected. The median duration of linezolid therapy prior to the identification of resistance was 23 months (range 9 to 32), with exposure to a median of 11 (range 5 to 14) other antituberculosis drugs. Mutations were identified in all resistant isolates with available sequencing results, with the *rplC* T460C mutation predominating. A *rrl* G2270C mutation was detected in one isolate (MIC 2 µg/mL), which has not been previously described in *M tuberculosis*. No mutations were detected in isolates from the remaining 25 patients with linezolid MICs ≤ 1 µg/mL.

Conclusions: Linezolid resistance occurred in a third of patients with linezolid-based treatment failure for drug-resistant TB, and all of these were associated with mutations in *rrl* or *rplC*. We identified a novel *rrl* resistance mutation, but this requires confirmation.

Patient ID	Baseline isolate resistance profile	Duration on linezolid (months)	Linezolid MIC (µg/mL)	<i>rrl</i> mutation	<i>rplC</i> mutation
2007	XDR	10	8	G2814T	
1007	XDR	18	4		
1008	MDR	25	4	Sequence analysis ongoing	
1010	XDR	21	2	G2270C	
1011	XDR	28	4	G2814T	
1013	XDR	25	8		T460C
1014	XDR	23	8	G2814T	
1015	Pre-XDR (injectable)	9	8		T460C
1023	XDR	No data	16		T460C
1032	XDR	32	4		T460C
1040	XDR	No data	4	Poor sequence quality	
1043	XDR	11	8		T460C
1050	XDR	28	16		T460C

[MICs and mutations in *M tuberculosis* isolates from 13 patients with linezolid treatment failure]

PS11-521-25 Susceptibility to streptomycin in extensively drug-resistant strains isolated from tuberculosis patients in Peru, 2011-2017

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Background: Streptomycin (SM), an aminocyclitol glycoside antibiotic, has not been used for treatment of tuberculosis (TB) in Peru for more than 10 years. However, in some cases, patients with extensively drug-resistant tuberculosis (XDR) and childhood TB could benefit from this drug. The aim of this study is to evaluate the susceptibility to streptomycin XDR strains during 2011 to 2017 in Peru.

Methods: This is a descriptive cross-sectional study. We selected from the database of the National Laboratory of Mycobacteria (LRNM) of Peru all the strains with XDR (according to standard criteria) diagnosed from 2011 to 2017. The drug susceptibility was tested through the Proportion method on agar. We quantified the percentage of patients with susceptibility to streptomycin.

Results: From 2011 to 2017, 890 patients were diagnosed with XDR through the proportion method on agar. The number of diagnosed patients was 121, 130, 111, 158, 116, 161 and 93 from 2011 to 2017, respectively. 20% of the samples corresponded to strains of patients never treated, 25% to patients treated before and in 55% we did not have clinical information.

Concerning the susceptibility to streptomycin, it has been steadily decreasing from 21% in 2011 to 16% in 2015, in which we have observed an unexpected increase in the susceptibility to 26% in 2016 and 29% in 2017 respectively.

Conclusions: Globally, the resistance to streptomycin in the XDR strains diagnosed in the LRNM of Peru during the 2011- 2015 period was approximately 85% while that in the last 2 years it fell to 73 %. The use of streptomycin should be confined to certain cases prior to a susceptibility analysis, and not as standard treatment for XDR patients. If we continue to see a decrease in resistance to this drug, it could become an important tool in the future for the treatment of these patients.

PS11-522-25 First- and second-line drug resistance pattern in new extra-pulmonary TB cases: prospective study in a tertiary care hospital in Pakistan

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Background: There is little information on prevalence of drug resistance in new Extra-pulmonary TB (EPTB) cases. The study was conducted in a tertiary level, spe-

cialized Tuberculosis care hospital in capital city of Punjab Province to determine the prevalence and pattern of first and second line drug resistance in new EPTB case.

Methods: Prospective cross-sectional study, clinical specimen from presumptive EPTB cases with enlarged lymph node or plural effusion was tested for AFB smear, Xpert MTB/Rif assay and culture. Indirect drug susceptibility testing (DST) was performed for Rifampicin (R), Isoniazid (H), Ethambutol (E), Pyrazinamide (Z), Fluoroquinolone (FQ), Second line Injectables (SLI) on MGIT and R,H, FQ, and SLI on LPA (HainLife sciences).

Results: Among 672 cases enrolled, 255 were bacteriologically confirmed and culture based DST and LPA results was available for 182 and 181 cases. 91.7% of strains were susceptible to all four FLD, MDR was detected in 2.2% (95% CI; 0.9-5.5%) on MGIT and among these four cases, two were resistant to Ethambutol, three to PZA and two to FQ. Among 178 RMP sensitive cases, 5.6% were resistance to H and 5.1% to Ofloxacin. No resistance to SLI drug was detected. Estimated sensitivity of LPA for R, H, FQ was 80.0%, 78.6% and 81.8% and specificity was 99.4%, 98.8% and 98.2% respectively. Of five cases reported Rifampicin resistant on Xpert, none on MGIT and only one on LPA was reported resistant.

	N-Resistant/N -DST	% Resistant (95%CI)
Any resistance to FLD	15/180	8.3% (5.1%-13.2%)
Any resistance to R	4/182	2.2% (0.9-5.5%)
Any resistance to H	14/182	7.7% (4.6-12.5%)
Any resistance to E	2/181	1.1% (0.3-3.9%)
Any resistance to Z	4/181	2.2% (0.9-5.5%)
Any Resistance to OFX	11/180	6.1% (3.45-10.6%)
MDR	4/181	2.2% (0.9%-5.5%)
MDR+FQ	2/4	50.0% (15.0%-85.0%)

[Drug resistance pattern for first-line and second line anti-tuberculosis drugs in new EPTB cases]

Conclusions: Prevalence of R, H, MDR and FQ in new EPTB cases is low compared to that in new PTB cases reported in drug resistance survey. LPA has high sensitivity and specificity both for first and second line drugs.

PS11-523-25 Drug resistance detection in M. tuberculosis strains isolated during a national TB prevalence survey in Mongolia

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Background: According to the First National TB Prevalence Survey in Mongolia the prevalence of bacteriologically-confirmed PTB among adults was 559.6 (95% CI: 454.5-664.7) per 100,000 population in 2014-2015. This was three times as high as previously estimated. Accordingly, we aimed to perform drug susceptibility

test on strains isolated from this study and to determine the proportion of drug resistance TB among prevalent cases.

Methods: All 242 MTB strains isolated from the survey TB cases were tested GenoType *MTBDRplus* test and conventional 1st line DST on solid medium. Also, second-line DST using Genotype *MTBDRsl* test were done for those multidrug resistant cases.

Results: Conventional DST and GenoType *MTBDRplus* tests done for 93.8% (227/242) of them and 6.2% (15/242) were tested by GenoType *MTBDRplus* only. A 61.6% (95% CI 55.3-67.4) of all cases were susceptible to first line anti-TB drugs, any isoniazid and any rifampicin resistance detected as 31.0% (95% CI 25.5-37.1) and 9.5% (95% CI 6.4-13.9), respectively. Prevalence of MDR-TB was 7.8% (95% CI 4.9-12.4) among new and 17.9% (95% CI 9.0-32.7) among previously treated cases. All of 23 multidrug resistant strains were susceptible for second line injectable and 2 (8.7%) were resistance to fluoroquinolone.

Conclusions: In Mongolia, drug resistance is high among prevalent TB cases. Prevalence of MDR-TB among new cases seems to be increased since drug resistance survey in 2007.

PS11-524-25 First national anti-tuberculosis drug resistance survey in Burkina Faso

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Background: The prevalence of drug-resistant tuberculosis (DR-TB) is poorly known in patients in Burkina Faso, hence this survey to evaluate it with the associated factors in new and previously treated tuberculosis patients.

Methods: Two sputum samples were collected from presumptive and previously treated TB patients in all 86 diagnostic and treatment centers of Burkina Faso. A questionnaire was administered to smear-positive patients to collect their socio-demographic characteristics and disease history. Smear positive sputa were further analyzed by the GeneXpert MTB/RIF test (Cepheid, Sunnyvale, CA, USA). Sputa from MTB+RIF+ patients were treated with *OMNIGene•SPUTUM* (DNA Genotek, Ottawa, Canada), transported to the national reference laboratory, and analyzed using the GenoType *MTBDR plus v2.0* test (Hain Lifescience, Nehren, Germany). HIV serology was performed in consenting patients. Thresholds of statistical significance $p < 0.25$ (univariate analysis) and $p < 0.05$ (multivariate analysis) were used to assess the association between patient characteristics and DR-TB.

Results: Of the 1,140 tuberculosis patients included, 995 were new and 145 previously treated; 74.1% of the total

population tested were men. The median age was 36.5 years old. HIV serology was positive in 75 (7.6%) of the 987 patients who accepted the test. In new patients, HIV status was a factor associated with DR-TB [OR=3.6 (95% CI:1.1-12.06), $p=0.031$]. The prevalence of DR-TB was 14.5% (21/145) (95% CI:8.7-20.5) in previously treated patients, and 2.0% (20/995) (95% CI:1.2-2.9) in new patients. Previous treatment was significantly associated with DR-TB ($p = 0001$).

Conclusions: The level of DR-TB is low in new patients, but high in previously treated patients. Previous drug treatment and HIV infection are associated with DR-TB.

PS12 Why tuberculosis kills in the 21st century? Lessons learnt from Brazil and beyond

PS12-525-25 Human Development Index and its associations with tuberculosis mortality in a Brazilian municipality: an ecological study

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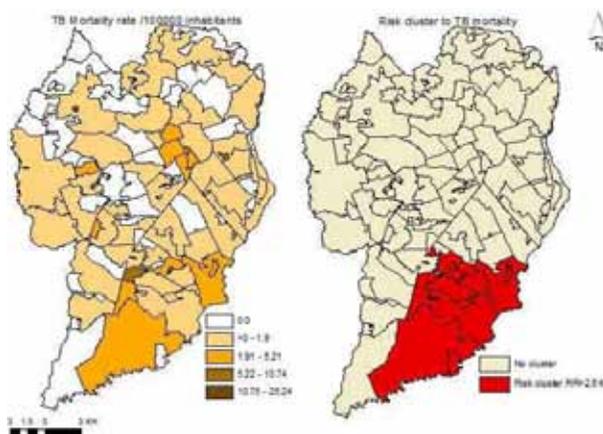
Background: Tuberculosis and life conditions have always been related. Human Development Index (HDI) aggregates the three main dimensions of human development: an opportunity to live a long and healthy life, to have access to knowledge and to have a standard of living represented by health, education and income. The goal of this study was to analyze the spatial pattern of tuberculosis mortality in Curitiba, Brazil (considering 138 spatial units) and their association with HDI and its three dimensions: education, longevity, and income.

Methods: An ecological study was developed, based on data from Mortality Information System (2008-2014). Crude and Bayesian rates were computed and Spatial Scan Statistics was used to identify high critical areas in both rates. Moran's I Global Bivariate (MGB) was used to assess associations between both rates and HDI (globally and considering the three components).

Results: Mortality rates ranged between 0 and 25.24/100.000 with a mean (standard deviation) of 1.07 (2.77). The corresponding values for Bayesian rates were: 0.49-1.66 and 0.90 (0.19). Using Crude rates, a critical area was identified in south (Relative Risk 2.64, $p=0.01$) and with Bayesian rate was not possible to identify critical areas. MGB between the HDI (and its components of HDI) and mortality crude rate were -0.039

($p=0.06$ (Education $I=-0.034$, $p=0.11$; Longevity $I=-0.039$, $p=0.06$; Income $I=-0.043$, $p=0.043$). Similar values were obtained when using Bayesian rates: $I=-0.060$ ($p=0.03$), Education $I=-0.057$ ($p=0.04$), Longevity $I=-0.068$ ($p=0.02$), Income -0.059 ($p=0.04$).

Conclusions: Spatial relations were found between mortality crude rates and income. Bayesian rates shown correlation in all analyses. These correlations were negative and significant (but not strong). In methodological terms, the use of both mortality rates (crude rates and Bayesian) have shown minor differences that should be better explored. These results demonstrate that social development variables are important in this challenge but other individual/contextual variables must be additionally incorporated in further studies.



[Tuberculosis mortality rate and risk cluster]

PS12-526-25 Mapping progress toward elimination of TB deaths in Brazil, 2001-2015

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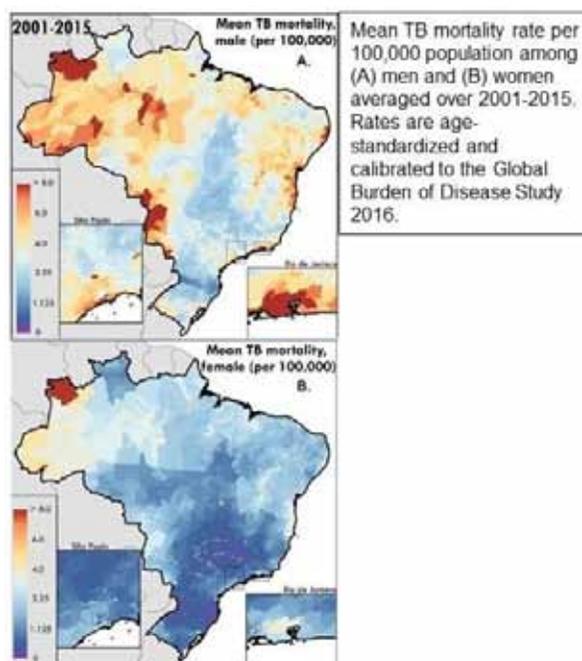
Background: Brazil has high burdens of tuberculosis (TB) and HIV-TB co-infection, as previously estimated for the 26 states and the Federal District. We improved the geographic detail of burden estimation by modeling deaths due to TB and HIV-TB co-infection and TB case fatality ratios for the more than 5500 municipalities in Brazil.

Methods: This ecological study used vital registration data from the national mortality information system and TB case notifications from the national communicable disease notification system from 2001 to 2015. Comprehensive cause of death assignment was performed us-

ing the methods of the Global Burden of Disease Study 2016. TB and HIV-TB mortality and incidence were modeled separately by sex using a Bayesian spatially explicit mixed effects regression model. Case fatality ratios were calculated for TB.

Results: There was substantial inequality in TB mortality rates within the nation and within states. National-level TB mortality in people without HIV infection declined by nearly 50% during 2001 to 2015. TB mortality rates for municipalities in the 90th percentile nationally were more than twice rates in the 10th percentile, with more than 70% of the worst-performing municipalities for male TB mortality and 80% for female mortality in 2001 also in the worst decile in 2015. Within states, the TB mortality rate ratios for municipalities in the worst decile versus the best decile varied from 1.4 to 2.8 for both males and females. The World Health Organization target case fatality rate for TB of less than 10% was achieved in 22.1% of municipality-years for males versus 46.4% for females, without clear trends over time.

Conclusions: Mortality rates in municipalities within the same state exhibited as much relative variation as within the nation as a whole. Monitoring the mortality burden at this level of geographic detail is critical for guiding precision public health responses.



[TB mortality by municipality and sex in Brazil, 2001-2015]

PS12-527-25 Undiagnosed tuberculosis deaths in Antananarivo; Madagascar, from 1996 to 2015

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Background: Tracking progress in the fight against TB in Madagascar is difficult because the case detection rate is unknown and the coverage of death registration is low at the national level. Yet, in the capital city, the death registration system is virtually complete. We use this system to evaluate the performance of tuberculosis notification between 1996 and 2015, by comparing deaths due to TB and cases notified to the national TB program.

Methods: Information on sex of the deceased, dates of birth and death, and underlying cause of death were transcribed from death registers maintained in Antananarivo. Causes of death were coded in ICD-9 to identify TB deaths and estimate cause-specific mortality rates. Tabulated data from Tuberculosis Diagnostic and Treatment Centers were obtained for the capital city. We estimated incidence based on notified cases of smear positive pulmonary TB, and examined treatment outcomes.

Results: Notification data suggest that the TB incidence has remained stable in the period 1996 to 2015, while treatment success rates gradually increased (from 62% in 1996 to 77% in 2015). According to death registration data, there has been only a modest decline in TB mortality. The ratio of deaths notified to the TB program to the number of deaths recorded in death registers has decreased over the period, from 1 death notified for every 5 deaths registered in the period 1996-2005 to 1 death notified for 9 deaths registered in the vital statistics system since 2005. The percentage of TB deaths occurring at home also increased to reach 66% in 2015.

Conclusions: A growing proportion of deaths are not notified in Antananarivo, possibly because they are undiagnosed, leading to discrepancies between TB notification and death registration. TB burden estimates could be improved with death registration data covering urban centers in Madagascar.

PS12-528-25 Social determinants, their variation in the urban space and association with tuberculosis deaths in the Amazon region, 2006-2015

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Background: Brazil is a signatory of the End TB Strategy, which aims to reduce tuberculosis deaths by 95% by 2035. The State of Amazonas is one of the Brazilian regions with the highest number of cases and, in turn, mortality, which makes fulfilling the goal a great challenge. There are variations of the social determinants in the urban space that can explain deaths due to tuberculosis. The study sought to investigate social determinants, their variation in the urban space and association with tuberculosis deaths in the Amazon region.

Methods: An ecological study was conducted, in which the units of analysis were the Human Development Units. Gross TB mortality rates were calculated and smoothed using the Global Empirical Bayes Method. Multiple linear regression was applied and tested using the Global Moran's index. The Lagrange multiplier test was used to identify the best model (whether Spatial Lag or Spatial Error). The Type I error of 5% was set as statistically significant.

Results: A mortality rate of 3.87, varying from 0.69 to 30.0, was found. From the OLS model, there was a statistically significant relationship between indicators of social determinants related to the Municipal Human Development Index and education, and the TB mortality rates ($R^2=0.04$, $p=0.03$). Observing the three models, it was verified that spatial dependence (Spatial Lag and Spatial Error) was better when compared to the classic model (OLS).

Conclusions: The study advances the knowledge by evidencing differences between the areas with respect to the social determinants, noting that more deaths occur in the areas with less social development, which was confirmed by the multivariate analysis. Advances in the distribution of income and social opportunities have a significant impact on tuberculosis mortality.

Variable	OLS	Spatial Lag	Error Lag
R2	0.044	0.064	0.072
Log-Likelihood	-579.772	-583.972	-583.476
AIC	1181.54	1177.94	1174.95
Moran's (I) - Residue	0.075	0.001	-4.899

[R2 indices, log-likelihood and Akaike information criterion for the three models studied]

PS12-529-25 Impact of living conditions on tuberculosis mortality in Brazil, 2002 - 2015

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Background: Objective: To verify the impact of living conditions on tuberculosis mortality in Brazil, from 2002 to 2015

Methods: Ecological study with data on panel of spatial aggregates and temporal surveys conducted in 1,614 municipalities with satisfactory quality of information. System of Mortality Information and the Brazilian Institute of Geography and Statistics were the data sources. The proxy variable for Living Conditions (CV) was the Urban Health Index (ISU), a composite indicator constructed from socioeconomic and health indicators. Potential determinants of TB mortality were considered as covariates. Negative binomial regression models estimated the effect of ISU (crude and adjusted) on the TB mortality rate and the impact was calculated from the Relative Risk Reduction $(1 - RR) \times 100$.

Results: From 2002 to 2015, the mortality rate for TB decreased by 23.5% and the ISU indicated an improvement in CV. Continuous model analysis resulted in $RR = 0.89$ (95% CI = 0.82 - 0.96), so RRR was 11.0%. The categorized model showed effect of 0.92 (95% CI = 0.83-0.95) in municipalities of intermediate CV, and of 0.83 (95% CI = 0.82-0.91) in those with low CV, that is, relative risk for TB mortality of 8.0% and 17.0%, respectively.

Conclusions: Improved living conditions had an impact on mortality from TB even when other determinants of mortality were considered. This impact was two times greater in the stratum of municipalities of low CV than in that of intermediate CV. This can be explained by the fact that social interventions have been directed mainly to the poorest and most impoverished populations.

PS12-530-25 Predictors of mortality in a cohort of hospitalized patients treated for tuberculosis in Rwanda

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Background: In subsaharan Africa, mortality rates for tuberculosis are high. HIV co-infection, a low CD4 count, TB dissemination and treatment delay are well recognized factors associated with excess mortality. In hospitalized TB patients, predictors of mortality are less well documented.

Methods: Data from two consecutive cohorts of patients who initiated TB treatment when hospitalized at the Internal Medicine wards, Centre Hospitalier Universitaire de Kigali in 2013 and 2017 were pooled (age, sex, BMI, HIV co-infection, CD4 count, temperature, dyspnea, abdominal tenderness, hemoglobin, white blood cell and platelet count, sputum mycobacterial confirmation, TB dissemination status) and plotted against mortality status at 2 months from TB treatment initiation.

Results: 295 patients were included, of whom 169 (57%) were HIV co-infected, 158 (53%) had disseminated TB and 91 (31%) died. TB was bacteriologically confirmed in sputum from 153/247 (62%) patients. Gender, Body Mass Index, HIV status, CD4 count (in HIV co-infected), TB dissemination status, TB confirmation status, temperature, cough, abdominal tenderness, hemoglobin and white blood cell count were not significantly associated with mortality. Mortality was significantly higher in patients with dyspnea (65/190, 34% vs. 22/101, 22%, $p = 0.04$, OR 1.86), older age (median 38 vs 35 years, $p = 0.01$) and lower mean platelet count (median 160.000/ μ L vs 222.000/ μ L, $p < 0.001$). When stratified for HIV coinfection, a lower platelet count was associated with higher mortality only in HIV co-infected TB patients (median 120.000 vs. 208.000, $p < 0.001$).

Conclusions: In hospitalized TB patients, mortality rates are very high. HIV status and TB dissemination are not associated with excess mortality. Only dyspnea, higher age and a low platelet count are (weak) predictors of mortality. Further research in etiology of mortality in this subgroup with high mortality risk is urgently needed.

PS12-531-25 Epidemiological profile of tuberculosis mortality in southern Brazil

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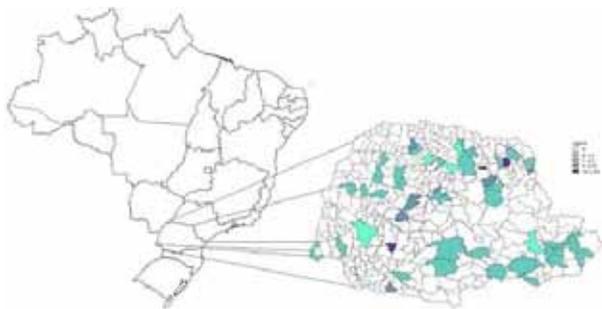
Background: The World Health Organization (WHO) notes tuberculosis (TB) is the infectious disease that kills most people in the world. Incidence and mortality are declining in Brazil, however in the Parana State, southern Brazil, has not yet reached the goals for TB elimination. The objective of this study was to identify the epidemiological profile of people who died with TB in the Parana State.

Methods: Observational study of death certificates with basic cause A15, A16, A17, A18 and A19, according to the International Statistical Classification of Diseases and Related Health Problems (ICD). Data were extracted from the Mortality Information System. Inclusion criteria were deaths in Paraná from 2008 to 2015.

Residents in other states were excluded. The descriptive statistical analysis included the variables gender, age, ethnicity, schooling, marital status, occupation and basic cause of death.

Results: A total of 949 deaths by TB were identified in the period. The mortality rate was 1.4/100,000 inhabitants in 2008, reaching 0.9 in 2012, however it had an increase to 1.1 in 2015. Men represent 75.8% (720/949) of deaths. The age ranged from 4 months to 95 years old with median of 53.7 years old. Respiratory TB (ICD A15 and A16) was the cause of 88% (837/949) of deaths. The diagnoses of TB were made by bacteriological or histological examination in 30% of cases (ICD A15 and A16.0). According to the death basic cause, 96% (246/255) of those who performed the diagnostic tests were positive for TB. Women had a higher proportion (12/22) of tuberculosis deaths in the nervous system (ICD A17).

Conclusions: Respiratory TB killed more white men aged from 15-59 years old and without bacteriological or histological confirmation. The results indicate that the records of basic cause of TB deaths might be qualified with laboratorial surveillance.



[Tuberculosis mortality rates by municipality of residence, Parana State, Brazil, 2015.]

PS12-532-25 Evaluation of tuberculosis patients who died during 2010-2015 in Samsun Province, Turkey

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Background: TB is among the first 10 death reasons worldwide. TB deaths in Turkey is below 1 in 100,000 population. Aim of this study is to evaluate tuberculosis (TB) cases with treatment outcome registered as "death"; death reasons, patient and disease characteristics and their differences during years.

Methods: From the national surveillance data, death registries sent from TB control dispensaries in our province between 2010-2015 were obtained: number,

involved organ system, treatment duration, detected by active surveillance system were collected retrospectively. Data from patient files and from national surveillance system were used. Death notification system initiated at 2013 in Turkey, so the death reasons in patient files are obtained from this system is more reliable.

Results: Among 1,624 TB cases 114 (7.0%) were registered as death. Their mean age were 67.2 (between 12 and 93), 56% were males and 72% had pulmonary involvement. 93 cases (81.5%) died during 82th day of treatment. Patients diagnosed after death were 21 (18.4%) and detected by active surveillance. Patients' death reasons and mean ages are shown in Table 1. One multi-drug resistant TB case died at 7th month. From 2010 to 2015, percentages of death numbers to total TB case numbers were 6.4%, 4.6%, 6.9%, 8.0%, 8.9%, and 8.1%, respectively. Cases detected by active surveillance were 0, 0, 5, 7, 4, 5 in the same years, respectively.

Conclusions: Cardiopulmonary diseases and malignities were the most common reasons for death among TB cases in our province. Patients died mean 2.7 months of treatment. Ages of persons died because of TB, cerebrovascular disease and cardiopulmonary reasons were high. Patients died with accidents were the youngest group. Case death rates in Samsun Province were higher than Turkey, because deaths registries were better. After 2013, all TB deaths were included to this registries which resulted an increase in case fatality rates.

	Number	Percent	Mean age
Cardiovascular diseases	54	47.4	69.3
Malignancy	23	20.2	64.0
Renal failure	10	8.8	63.2
Natural death	8	7.0	67.3

[Table 1. TB deaths in Samsun Province, with death reasons and mean ages, first 4 reasons (n=114).]

PS13 Found-not found reported-not reported with and without private providers

PS13-533-25 Under-reporting of tuberculosis by private providers in Indonesia: subsample analysis of an inventory study, 2017

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Background: The improved economic situation is driving factor of the rapid growth of the private health providers in Indonesia. However, most private providers do not engage with NTP, in 2016 only 10% of TB cases

were reported to the TB surveillance database. The aim of the study is to estimate the level of under-reported TB cases from private providers in the National TB Surveillance System.

Methods: Nationally representative sample of 23 districts were included in the study proportional to the number of notified smear-positive TB and stratified by region. All health facilities in selected districts were enumerated. The health facility lists were obtained from MoH's Data and Information Center, district health offices, and medical associations. Facilities that diagnosed or treated TB cases in the last three months since mapping were eligible for inclusion in the study. The matching of two databases applied probabilistic record linkage.

Results: Of 7,323 TB cases in private providers, 5,099 cases were underreported to National TB Surveillance System. The estimated proportion of under-reported cases was 25.4% (95% CI 20.8-30.7%) The under-reporting in private hospitals was 41.1% (95% CI 31.8-51.2%) while in other private providers was 95.5% (95% CI 90.9-97.8%). Only 18.6% of TB cases in private providers were bacteriologically confirmed.

Conclusions: The level of under-reporting in private providers was high particularly in non-hospital facilities, i.e., clinics, private practitioners and laboratories. The NTP should engage with all types of private TB service providers and strengthen TB surveillance system ensuring that all cases in private providers are diagnosed, receive standard treatment and notified.

PS13-534-25 Is private sector a contributor to missing TB cases? An experience from India

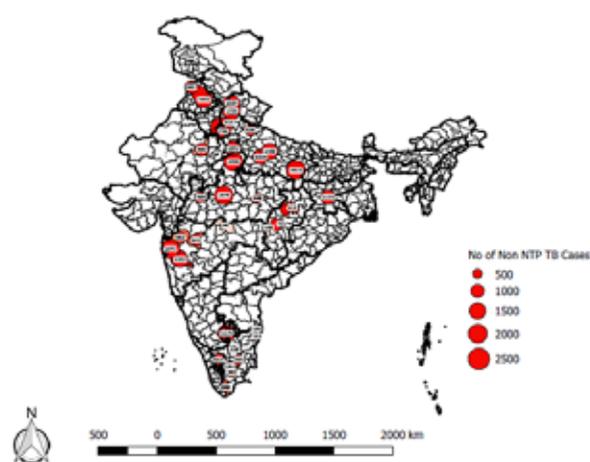
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Background and challenges to implementation: In India, tuberculosis remains a major public health challenge with an incident of 2.8 million with over 1 million cases are 'missed' annually. Low case detection and notification are two of the major challenges facing the National Program. The reasons could be attributed to limited access to TB treatment, private sector engagement and weak social support system. More than half of the TB patients approach the private practitioners, who often lack formal training and treatment is initiated without proper TB diagnosis. Often the TB cases from private sector not being reported to Government. This paper focuses on the efforts of The Union in engaging the private sector for increased case notification.

Intervention or response: The Union led project Axshya is implementing urban TB control in 40 urban sites of India. The project has mapped and provided formal

training /sensitisation on standards of TB care in India (STCI) guidelines to the health care providers. Linkages were also established with public and private for diagnosis and treatment. The project has developed innovative software and mobile app which facilitates notification of TB patients from private sector in Nikshay.

Results and lessons learnt: During the period Oct 2015 - Dec 2017, the project has sensitised and engaged 3715 qualified practitioners, 595 private hospitals and 733 labs in 40 urban sites and facilitated notification of 63568 TB patients from the private sector. It also offers treatment adherence support through daily SMS and interactive voice calls. Over 10,000 TB patients have benefited from this service.



[Notification patterns from private sector]

Conclusions and key recommendations: This model has proved sustained successful engagement of private providers results in improved TB case notification. A similar model on a national scale can rapidly accelerate TB control effects and bring the majority of patients treated in the private sector under the national surveillance system.

PS13-535-25 Patient health care system interactions before and after tuberculosis diagnosis in Taiwan: an individual patient pathway analysis using health insurance data

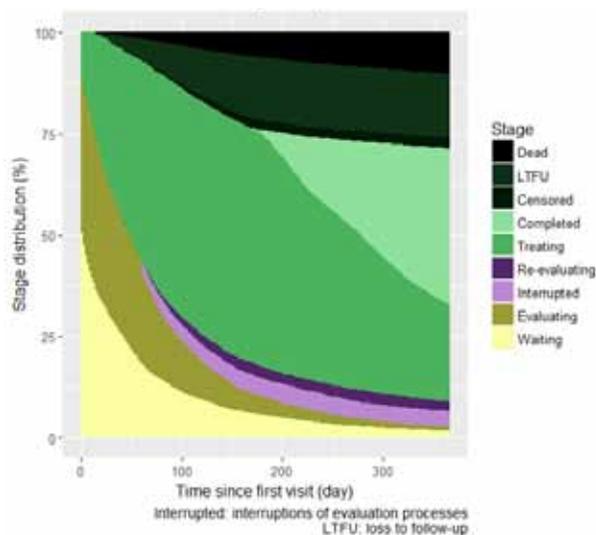
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Background: There is increasing interest in the health-care pathways of tuberculosis (TB) patients. Patient Pathway Analysis has highlighted mismatches between system capacity and patient access-points. These analy-

ses have so far been cross-sectional, do not reconstruct individual patient histories of interaction with health services, and thus have not quantified delays to first evaluation for TB or heterogeneity in pathway characteristics. We introduce methods to reconstruct and analyse individual patient pathways using data from compulsory health insurance in Taiwan.

Methods: We analysed a nation-wide retrospective cohort of one million individuals sampled from health insurance records in Taiwan after 2001 (Nation Health Insurance Research Database). Data captured all events relevant to individuals' insurance claims, including date and location. An algorithm was developed that interpreted events in the context of all other events for that patient and their relevance to TB, using evidence of relevant comorbidities, diagnostic procedures and anti-TB treatment.

Results: 6,410 care pathways were reconstructed for 5,700 TB patients treated between 2003 and 2010. Around 40 percent of the pathways started care-seeking at clinics; for 60 percent of the pathways initialised treatment at regional hospitals or medical centres. The median delay from a first care-seeking visit to beginning anti-TB treatment was 48 days. During this period, 26 percent of patient-healthcare interactions were before TB-related evaluations started. During the evaluation processes, 20 percent of pathways were at some point considered as other respiratory diseases. However, 11 percent of the pathways started on anti-TB treatment at their first healthcare visit. 80 percent of all patient-healthcare interactions prior to evaluation were in 26 percent of patients.



[Figure. Proportion of cohort in each stage by time since first care-seeking attempt]

Conclusions: We have introduced a novel methodology to reconstruct patients individual care pathways for TB from routine insurance data, detailing the delays and patient-healthcare interactions between stages and finding substantial heterogeneity in the pathway complexity.

PS13-536-25 Placement of TB screeners in large private practices as part of an enhanced case-finding intervention to increase TB case notification in Punjab, Pakistan

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Background and challenges to implementation: Pakistan ranks 5th among the 30 high TB burden countries. Private healthcare sector in Pakistan is the first point of contact for more than 70% of the population^[1]. Therefore, engagement of private sector to provide TB care services is essential. Mercy Corps (MC) has been working with small private practices through Public Private Mix (PPM) intervention since 2010, however, to ensure that a large proportion of missing TB cases are diagnosed and reported into the national TB case reporting, MC initiated an Enhanced Case Finding (ECF) intervention in 15 medium to large private practices in six districts of Punjab in 2016.

[1] Pakistan Social and Living Standards Measurement Survey [PSLM (2004-05)]

Intervention or response: Out of 15 selected private practices, five were already working under the PPM intervention. Two doctors, two paramedics and a lab technician were trained on National Guidelines for TB case management from each private practice. TB screeners were placed in each practice to do symptomatic screening of patients presenting in outpatient department, identify presumptive TB cases and direct them to the doctor for clinical evaluation and diagnosis. These practices were also provided with LED microscopes and six of them were equipped with GeneXpert machines.

Results and lessons learnt: From 15 practices about 75,000 patients were screened, 3,978 presumptive TB cases tested and 1,240 were diagnosed, of which 297 were bacteriologically positive. Of 78 RR cases 65 were registered at the public sector PMDT sites. In the five practices already providing TB care, 53 TB patients (Jan-Sep 2016) got registered and the yield increased to 419 (Jan-Sep 2017) after the start of intervention.

Conclusions and key recommendations: Engagement of medium to large private practices enabled with trained TB screeners is an effective strategy in finding the missing TB cases as well as early diagnosis among the population seeking healthcare from private sector.

PS13-537-25 Involving retail private pharmacists in tuberculosis care: preliminary findings from randomised cluster trial, South Indian district

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Background and challenges to implementation: In India, Retail Private Pharmacists (RPPs) are often primary care givers and dispense drugs over the counter, including chest symptomatics. Revised National Tuberculosis (TB) Control Program (RNTCP) is engaging with RPPs to refer chest symptomatics to nearby RNTCP centers for sputum examination. Government also recommends RPPs maintain register to document details of patients purchasing anti-TB drugs from them. We conducted this study in a south Indian district to optimise the involvement of RPPs for referral of presumptive pulmonary TB (PPTB) cases to RNTCP and improve RPP's reporting of anti-TB drugs sales.

Intervention or response: Cluster randomised trial. We carried out a census using GPS to map RPPs in the study area. We allocated eligible RPPs practicing in a sub-district to an intervention group (n=56) and other sub-districts to the control group (n=66). The intervention implemented between November 2016 to January 2018, included two sets of activities; one targeted at RNTCP strengthening and other at intervention RPPs. Number, proportion of referring RPPs and median number of referrals were calculated.

Results and lessons learnt: RPPs referred a total of 166 presumptive TB cases during the study period and 122 (73.5%) were males. Of the total 56 RPPs in the intervention arm, 75% (n=42) referred PPTB cases to RNTCP, compared to zero referrals made by RPPs in the control arm. Median number of referrals made by referring RPPs was 3. Among the 166 referrals made by intervention arm RPPs, 97 (58.4%) reached RNTCP and underwent sputum examination. Among the 97 cases, 5 (6%) were diagnosed with bacteriologically confirmed TB. In the intervention arm, 8 RPPs became DOT providers. No RPP documented details of patients purchasing private anti TB drugs from them.

Conclusions and key recommendations: Package of intervention implemented by RNTCP staff was successful in involving RPP's in RNTCP. TB control regulations need to be publicized and strictly enforced.

PS13-538-25 The level of under-reporting of tuberculosis cases in Indonesia in 2017

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Background: Indonesia is the second highest TB burden country globally, with an estimated TB incidence of 1,020,000 cases in 2016. However, the number of TB cases notified in 2016 was only 360,565. The aim of the study is to estimate the level of under-reported TB cases in the National Surveillance System.

Methods: Cross sectional with stratified cluster sampling was applied to this study. The samples of 23 districts which represents nationally, were selected proportionally to the number of notified smear-positive TB. All health facilities, i.e. hospitals, public health centers, clinics, private practitioners and laboratories in selected districts were enumerated. The health facility lists were obtained from MoH's Data and Information Center, district health offices, and medical associations. Facilities that diagnosed or treated TB cases in the last three months since mapping were considered as eligible to participate in this study. The matching of two databases applied probabilistic record linkage.

Results: 1,681 health facilities from 23 districts participated in the study and 21,320 TB cases of first quarter of 2017 were found. These numbers were matched with NTP data base in the same quarter. Of 22,681 TB cases identified after record linkage, 11,850 were registered with the NTP. The estimated proportion of under-reported cases was 41% (95% CI 36%-46%). The under-reporting in public health center was 15% (11%-20%), while in others was 71% (61%-79%). Clinically diagnosed TB patients were 55% (49%-61%) under-reported and in bacteriologically confirmed TB patients were 21% (16%-26%). Extra-pulmonary TB were more under-reported (58%; 49%-66%) compared to pulmonary TB (38%; 33%-44%). The level of under-reporting in children (54%; 44%-64%) was higher than in adults (39%; 34%-44%).

Conclusions: The level of under-reporting was still relatively high; especially in non-public health centers, clinically diagnosed TB patients, extra-pulmonary TB, and children. TB surveillance system should be strengthened to reduce under-reporting.

PS13-539-25 Socio-demographic and health care profile of hospitalized TB patients

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Background: With an annual incidence of 2.75 million TB cases, India is home to a quarter of global TB cases. In this context, this study identifies the socio-demographic and healthcare profile of hospitalized TB patients in India.

Methods: The National Sample Survey Organization (NSSO-2014) data on social consumption - health was analyzed using R-software survey-design package. Stratified analysis of various socio-demographic and healthcare covariates was done with respect to the inpatient care for TB diseases during last one year preceding the survey.

Results: TB accounted for 1% of all inpatient care. Majority of TB patients were male (71%), adults (15+ years: 88.6%), illiterate or primary educated (68.8%), rural residents (71.2%), socially backward castes (75.6%), Hindu (81.5%), uninsured (79.2%), and belonged to low socioeconomic status (52.6%). Majority of TB patients were treated in a public hospital (63.3%), admitted to free wards, (57.9%), received radio-diagnostic services on payment (52.9%), treated on medical advice (72.4%) before hospitalization, and treatment on medical advice continued (57.0%) after discharge from hospital. During hospitalization, only 16.6% received free medication. A majority (94.3%) of TB patients didn't receive any surgical intervention during hospitalization.

Conclusions: As the majority of TB patients are socio-economically disadvantaged, and use public hospitals, the government should expand universalization of free or subsidized TB inpatient care including free medication and free diagnostic services. Limited medical supervised treatment during pre-hospitalization and post-hospitalization period need to be addressed under the national TB control program, which in turn can reduce the need for hospitalization and associated morbidity.

PS13-540-25 Ecological study of changes in the pulmonary tuberculosis epidemic in the Shanghai registered population, 1992-2016

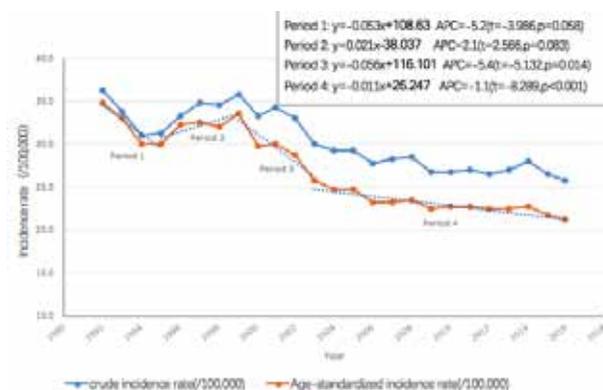
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Background: To estimate whether target set in WHO's End TB Strategy can be achieved by analyzing the incidence trend of pulmonary tuberculosis (excluding tuberculous pleurisy) in registered population in Shanghai during 1992-2016.

Methods: The incidence of tuberculosis(TB) was calculated annually based on the data obtained from TB patient registration system of Shanghai municipal center for disease control and prevention(SCDC), and rates were age-adjusted to standardized population (China Population Censes, 2010) through direct method using 5-year age groups. Linear regression analysis method was applied to analyze the trend of epidemic during 25 years, together with the statistical indicator of annual percent change(APC).

Results: The overall age-standardized rate decreased from 34.8/100,000 in 1992 to 21.2/100,000 in 2016, or 2.15% ($t=-13.258$, $p<0.05$) annually. After a resurgent in period 2(1995-1999)(2.2%/annum), the rate in the third period declined(1999-2003) rapidly(-5.4%/annum), after which the epidemic remained at a stable level with a lower annual declining rate(-1.1%/annum). It is estimated that the incidence will be 17.22/100,000 in 2035 based on the APC in period 4. There were two peaks in average incidence of total population, 30.9/100,000 in group 20- and 66.4/100,000 in group 70-, respectively, and gender(male/female) ratio was 1.6 and 4.6 in in two groups. In all cases, the constituent ratio of new cases increased from 81.7% to 89.3% and the ratio of new/retreated cases continually rose and eventually reached 8.36:1 in 2016. The constituent ratio of smear-positive cases ranged from 35.9% to 47.8% without rising or decreasing trend($p=0.065$), among which the proportion was high from 2002 to 2013, all over 40%.

Conclusions: Epidemic of TB in Shanghai has steadily declined during last two decades. However, there's still a gap to achieve the goal set in End TB Strategy. New strategy should be developed to rapidly reduce the incidence rate to achieve the Goals in 2035.



[Incidence trends for pulmonary tuberculosis in registered population in Shanghai: Year 1992-2016]

PS13-541-25 Tuberculosis among foreign-born persons in Japan

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Background: Japan has yet to achieve tuberculosis (TB) low-incidence countries (TB incidence < 10 per 100,000 population), and TB is still one of social problems. The Guidelines for the Prevention of Particular Infectious Diseases in Relation to TB (preventive guidelines for TB) revised in 2016 aims to become a country with low TB burden until 2020, the year of Tokyo Olympic and Paralympic, but the decline in TB incidence has slowed in recent years. TB in the elderly has been drawing attention in Japan, while in other developed countries, an increase in the proportion of foreign-born TB patients has been recognized. Therefore, in this study, the foreign-born TB and its burden was analyzed to illustrate this problem in Japan.

Methods: Based on data on TB case notifications made to the Japan TB Surveillance System, which was mentioned in the annual statistics of TB in Japan, we analyzed TB in foreign-born persons in Japan over the last 10 years.

Results: During 2007-2016, the number of TB cases among foreign-born persons in Japan increased by 3.5%, from 842 cases (22% of the national total) to 1,338 cases (7.9% of the national total). They occupied a large percentage especially in younger age groups (42.3% in 15-19 years old, 57.7% in 20s and 25.4% in 30s, respectively). About the birth countries of foreign-born TB patients, the top six countries account for 80% of the total in 2016 (Philippines, 23.8%; China, 20.3%; Vietnam, 15.8%); Nepal, 10.1%; Indonesia, 6.7%; Myanmar, 4.3%, respectively).

Conclusions: As the percentage of notified TB cases among foreign-born persons continues to increase, the achievements of the targets set in the preventive guidelines for TB 2016 and the elimination of TB in Japan will depend on TB among foreign-born persons. The necessary countermeasures for it including effective legislation should be considered.

PS13-542-25 Evaluation of the impact of TB bacteriological confirmation on case notification rates in Swaziland

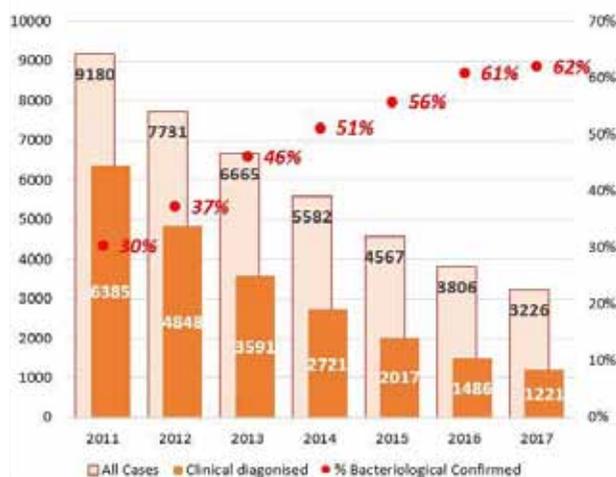
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Background: Swaziland has one of the highest HIV burden in the world with 27% of adults aged 15 and above living with the HIV virus. The country also has a high TB-HIV coinfection rate 70%. Delayed diagnosis of TB in the setting of HIV contributes to high mortal-

ity rates. However, the adoption of Xpert® MTB/RIF as the initial TB diagnostic test by the country has led into a substantial increase in TB case detection particularly bacteriological confirmed pulmonary TB cases. However, no studies have been done to explore the trends in bacteriologically confirmed TB cases and clinically diagnosed TB cases to determine whether TB cases are being missed whilst ensuring bacteriological confirmation. **Methods:** A secondary data analysis of data from TB and HIV Annual program reports for the period January 2011 to December 2017 was conducted. Data from the National TB Control Program (NTCP) DHIS 2 platform and the APMR from the HIV program was also used. Frequencies and proportions were used to describe trends in TB case notifications and bacteriological confirmation of TB cases.

Results: Bacteriological confirmed TB cases increased from 30% in 2011 to 62% in 2017, resulting in reduction in clinically diagnosed TB cases from 70% to 38% showing an inverse relationship. The number of notified TB cases also declined on average by 15% per annum over the same period, consequently paediatric TB cases declined from 12% to 5% between the period.

Conclusions: While bacteriological confirmation is important for airborne infection control measures, enrolling patients on TB treatment based on clinical symptoms is still needed. This will assist in bridging the gap between TB incidence estimates and cases notified, and hence improve case detection in Swaziland particularly paediatric cases.



[Trends in Bacteriological Confirmation of TB Patients in Swaziland 2011-2017:]

PS13-543-25 Modelling the impact of India's national strategic plan for tuberculosis

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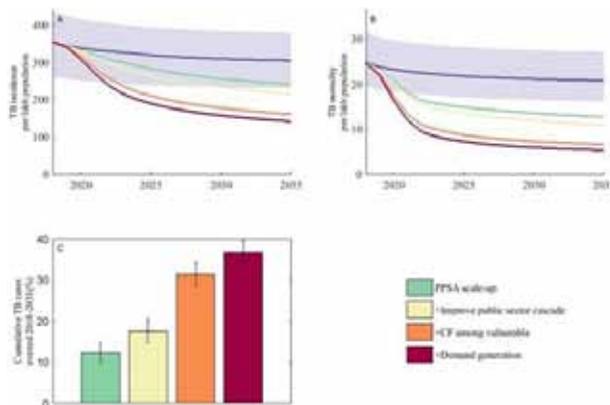
Background: Despite a declining trend in incidence, TB still represents a major health challenge in India, the country with the world's largest TB burden. India's recent National Strategic Plan (NSP) for TB elimination in India sets out an ambitious strategy for addressing this burden. Here, we present a mathematical modeling approach to assess the population impact of these interventions contained in the NSP.

Methods: We developed a mathematical model that reflects the natural history of disease and engagement into TB care. The model incorporates epidemiological variations between urban and rural settings, as well as vulnerable populations. Different components of the NSP package were simulated in additive combination, as follows:

- 1) Engage 85% of the private healthcare sector, to improve TB outcomes in this sector;
- 2) Improve treatment initiation and completion rates to 90% in the public sector;
- 3) Active case finding in vulnerable populations 3 times a year;
- 4) Demand generation measures to reduce patient delay in seeking care by 25%.

Impact was assessed as the cumulative averted cases between 2018 and 2035.

Results: A combined intervention scenario could have a substantial impact on TB transmission, averting 37% (95% CrI 34.5 - 39) of TB incidence, and 58% (95% CrI 55 - 61) of TB deaths by 2035 (Fig. 1). Individually, the highest impact on incidence can be attributed to private sector engagement 9% (95% CrI. 5.4 - 13) and active case finding 8.4% (95% CrI. 6 - 11).



[Incidence and mortality reductions under scenarios of India's NSP implementation]

Conclusions: These components of India's NSP could bring about dramatic reductions in India's TB burden. Other measures discussed in the NSP, such as addressing social determinants of TB, will be critical in bringing down burden still further: further work is needed on the potential epidemiological impact of these measures.

This work was funded by the Bill and Melinda Gates Foundation.

PS14 Away from home: tuberculosis in migrants

PS14-544-25 Association between prior incarceration and tuberculosis in Lima, Peru

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Background: In many settings, incarceration has been described as a risk factor for tuberculosis (TB) infection and disease. People who become infected with TB while incarcerated may develop disease once they are back in the community. Limited data are available on how TB within the prison system affects TB incidence in Peruvian communities. We conducted a nested case-control analysis within a TB household study to determine the association between former incarceration and TB disease in Lima, Peru.

Methods: Our analysis was nested within a longitudinal cohort study of household contacts (HHCs) of pulmonary TB cases in Lima, Peru (2009-2012). We considered as cases index patients or HHCs with TB detected at the baseline visit. Controls were HHCs who were TB-free at baseline and had no prior history of TB. Analyses were limited to individuals ≥ 18 years of age and only households with controls available. We use multilevel logistic regression modeling to estimate the association between self-reported former incarceration in the previous five years and TB.

Results: From a study cohort of 4500 index patients and 14044 HHCs, we identified 9657 individuals (2879 cases and 6778 controls) in 2783 households that met inclusion criteria for our study. In total, 132 (4.6%) cases and 77 (1.4%) controls reported former incarceration. After controlling for possible confounders and accounting for household clustering, household members who reported former incarceration had over 3 times the odds of having TB disease as those who did not (adjusted odds ratio, 3.33; 95% confidence interval, 2.30-4.84; $P < 0.001$).

Conclusions: We observed an association between former incarceration and TB disease within households in Lima, Peru. This finding identifies a high-risk group for whom targeted screening may prove beneficial. More research is necessary to establish the extent to which incarceration contributes to TB incidence in communities in Peru.

PS14-545-25 Cross-border tuberculosis patient referral from Japan to the Philippines, 2009-2018

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Background: Cross-border tuberculosis (TB) patient referral has become an issue because quite a few foreign-born patients on TB treatment intend to return to their countries of origin once they become non-infectious. The Research Institute of Tuberculosis (RIT), Japan, and the RIT/JATA Philippines, Inc. (RJPI) has been coordinating referrals of TB patients between the local health offices in Japan and the TB treatment sites in the Philippines. This study aimed to describe cross-border referral process among TB patients from Japan to the Philippines.

Methods: It is a retrospective descriptive document review. The data on the pathways of Filipinos with TB or Latent TB Infection (LTBI) initially treated in Japan from 2009 to 2018 were summarized. The RIT starts communicating with the RJPI soon after the local health offices in Japan contact for a TB patient referral. The RJPI makes initial coordination with the health workers in the Philippines, follows-up through any form of communication with the patient and health staff to track and ensure access to and completion of patients' TB treatment.

Results: Among 31 patients referred, 61% were males, median age was 34 years old, 52% were new bacteriologically-positive TB including three multi-drug resistant TB patients (MDR-TB). 81% (25 patients) were successfully referred to the health facility. Among these, 23 patients were proved that they started TB / LTBI treatment. Treatment success rate among these 23 patients indicated 78.2% (18 patients. Additional three patients were still on treatment upon writing). Two out of three MDR-TB patients accessed on any of the health facilities, only one patient successfully started MDR-TB treatment and was declared successfully treated afterward.

Conclusions: The current cross-border referral process between Japan and the Philippines indicated successful results. However, it has to be enhanced further in consideration of strengthening mechanism to track the referral outcomes especially of MDR-TB patients referred.

PS14-546-25 Tuberculosis among internally displaced persons in North-Eastern Nigeria

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Background and challenges to implementation: Three States of Nigeria (Adamawa, Gombe and Yobe) are affected by massive movement of IDPs due to ongoing Boko Haram insurgency. There are over 298,300 IDPs in 7 Camps and Host Communities (HC) in 12 of 49 LGAs in these 3 States (IOM, 2016). This has placed a remarkable strain on already overstretched health services. Inadequate access to health services, inadequate housing, overcrowding and malnutrition are known to influence transmission of TB among IDPs. Although Nigeria has one of the highest TB burdens in Africa, case detection rate was 24% in 2017. With support from Stop TB Partnership through its Wave 5 TB Reach grant in 2017, TB control service was launched in IDP camps and host Communities of these 3 States.

The **objective** of this paper is to demonstrate results of Active TB Case Finding (ACF) among IDPs in Adamawa, Gombe and Yobe States of Nigeria.

Intervention or response: ACF among IDP populations in 7 camps and HCs was implemented from 1st June to 31st December 2017 in 3 States. The process involved mapping, advocacy, training and engagement of Community Volunteers (CVs) and Health Workers. Sputa were tested by Xpert MTB/Rif while children were screened using paediatric desk-guides and X-Rays. CVs transported sputum and provided treatment support for diagnosed TB cases.

Results and lessons learnt: 180 CVs, 30 HWs, 30 lab staff and 12 TB supervisors were trained on TB control using NTP guidelines. 7 IDP Camps and 81 HCs were screened for TB; 10,007 (7%) presumptive TB cases were tested with Xpert MTB/Rif out of which 602 (6%) had B+ TB including 18 Rif resistant cases which represents 33% of all TB cases and 100% of Rif resistant TB cases notified by the 12 LGAs respectively.

Conclusions and key recommendations: Large-scale ACF interventions among IDPs could improve TB and HIV case detection.

PS14-547-25 Syrian refugees in Jordan: TB control for displaced vulnerable populations, 2012-2017

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Background and challenges to implementation: The National Tuberculosis Programme (NTP) of Jordan faces challenges hosting large numbers of Syrian refugees requiring access to TB services. 5.5 million Syrian refugees worldwide mainly hosted in Turkey, Lebanon, Jordan, Iraq and Egypt. Jordan hosts 1.3 million—the largest number of refugees per capita in the world. Majority Syrian refugees (>80%) live with host communities, scattered across the country, frequently change their locations. TB diagnosis, treatment and follow-up are complicated by the insecurity and inaccessibility in areas near the Syrian border.

Since the Syrian crisis started in 2012, IOM—The UN Migration Agency has been working in close partnership with the NTP addressing challenges in Syrian TB case detection and treatment.

Intervention or response: Awareness raising, active case finding (ACF) with symptom screening, mobile X-ray and Xpert testing in refugee camps, hard-to-reach areas, and urban communities by Community Health Workers (CHW) and Mobile Medical Unit (MMU). MMU facilitated referrals, diagnostic tests and hospitalization. NTP TB centers were supported with diagnostic equipment (Xpert, X-ray, microscope), lab consumables, anti-TB drugs and additional staff.

Results and lessons learnt: From March 2012-December 2017, 358 Syrian refugees were diagnosed having TB disease, 211(59%) male and 147 (41%) female; 37 (10%) pediatric(>15yrs) and 4 MDRTB cases.

342 (95% of total Syrian) TB cases detected through ACF by screening 8,554 presumptive cases.

CHWs and MMU were essential in reaching out Syrian refugees.

Patient (n)	Treatment success n(%) cure/tx completed	Mortality n(%)	Lost to follow up n(%)
326	310 (95%)	13 (4%)	3 (1%)

[Treatment outcome of 2012-17 Syrian TB patients cohort*]

*32 patients are still on treatment

Conclusions and key recommendations: Joint innovative approaches are essential to increase TB case detection, reducing morbidity and mortality among displaced vulnerable populations. The outcomes confirm that extensive collaborative effort of NTP and IOM leads to successful TB control programme in a humanitarian context.

PS14-548-25 Innovative approaches to identifying migrant mineworkers with TB: experience from a pilot program

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Background and challenges to implementation: Providing access to and continuity of care for TB and HIV for persons who migrate for work is challenging. We describe a program to facilitate consistent access to TB and HIV services for Mozambican mineworkers who migrate to South Africa for work.

Intervention or response: Several approaches were used to identify Mozambican mineworkers currently working in South Africa. In South Africa, Kawena, a goods supply distributor, provided TB-HIV education and referrals to mobile screening conducted in mining areas. In Mozambique, TB registers at 18 health facilities in areas where mineworkers reside were reviewed (January 2017-March 2018). During the December 2017 holiday, we worked with traditional healers and community leaders to conduct house-to-house TB and HIV screening among mineworkers returning to their family residence. A cross-border program was established to find mineworkers with TB, link them to care on either side of the border, and facilitate treatment adherence. The program utilizes community health workers in Mozambique and a nurse call-center and field staff in South Africa.

Results and lessons learnt: Demand creation for TB screening was mobilized through 13,000 text messages to mineworkers registered with Kawena and 200,000 flyers distributed to mineworker communities. A total of 674 mineworkers were screened over 6 screening days; 259 were Mozambican. Three Mozambicans were identified with TB and 28 of 259 were identified with HIV and included in the program. In Mozambique, 35 mineworkers identified through TB registers, 6 through traditional healers, and 4 through house-to-house case finding have been referred into the cross-border program.

Conclusions and key recommendations: Active review of TB registers, and partnerships with private companies, traditional healers, and community leaders helped to identify Mozambican mineworkers with TB and/or HIV. Establishing a cross-border program for linkage and care retention is the first step in improving access and provision of TB and HIV services in this mobile population.

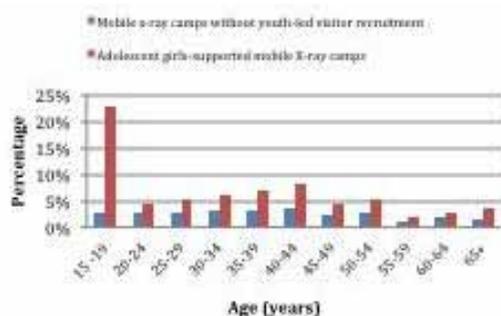
PS14-549-25 Engaging adolescent girls to increase the uptake of TB screening services among females

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Background: Engaging youth in community mobilization for development programs has been deemed as an effective strategy for social change. Currently, there is no evidence for engaging youth in TB screening programs. In Pakistan, rates of notified TB cases are 20-30% higher in young females compared with males, however females are more susceptible to stigmatization, limiting uptake of services. Aim of this study was to understand the effectiveness of engaging adolescent girls to increase uptake of TB screening services among females in Pakistan.

Methods: Under the *Kiran Sitara* (KS) program, adolescent schoolgirls are engaged and trained to identify people with presumptive TB in the community. They are then referred for chest x-ray and Xpert MTB/RIF testing (in case of abnormal x-ray) to mobile x-ray vans. This abstract analyzes retrospective data from Nov-Dec 2017, from mobile x-ray camps supported by adolescent girls for generating referrals for chest x-ray based screening and compares it with camps without any youth-led visitor recruitment.

Results: During the study period, a total of 5,462 and 35,196 individuals were screened at mobile x-ray camps conducted through adolescent girls-supported and routine visitor recruitment strategies respectively. For all age groups, a higher proportion of female visitors were screened at the adolescent girls-supported camps where out of all visitors, 71.2% were females, 22.8% were females aged 15-19 years, 5.8% were males aged 15-19 years. At camps without youth-led visitor recruitment, out of all those screened, a total of 27.7% were females and only 2.9% were females aged 15-19 years (Fig 1). Out of all the females with abnormal chest X-Rays, sputum was collected from 25.9% females from adolescent girls-supported camps and 27.4% from routine camps.



[Proportion of females visiting adolescent girls-supported mobile x-ray camps and routine mobile x-ray]

Conclusions: Engaging adolescent girls for community mobilization is an effective strategy for recruiting higher numbers of females for TB screening compared to routine mobilization strategies.

PS14-550-25 Tuberculosis incidence and treatment outcome among marriage and labor migrants following pre-entry screening in Taiwan

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Background: The annual incidence of tuberculosis (TB) of Taiwanese was median. One (before obtaining citizenship) or Four post-entry mandatory screenings (at post 0, 6, 18 and 30 months) were respectively targeted to marriage migrants or labor migrants from South-east Asian during first- 4- year following the pre-entry screening. TB incidence and treatment outcome among these high risk migrant groups is a matter of public health concern.

Methods: A nationwide, retrospective and cross-sectional study of TB surveillance among migrant based on 4-year (2012-2015) notification data was conducted. TB data on these migrants were obtained from the national TB registry database for further analysis. The data of migrant population was obtained from the official publications of the Ministry of the Interior and the Ministry of Labor, respectively.

Results: The TB incidences were ranged from 11-90 per 100,000 with 61% bacteria positive and 31% sputum smear-positive (ss+) cases as well as 67-120 per 100,000 with 41% bacteria positive and 17% ss+ cases respectively during their first post- entry 0-4 year among marriage and labor migrants origin from Southeast Asia following pre entry screening for permission health ones, 2012-2015. The cured/completed treatment rate of >90% was above the WHO target of >85% among both labor migrants and marriage migrants; moreover, the completed treatment rate of labor migrants with TB of post (2014-2015)- vs. pre(2012-2013)- implementing friendly policy with no compulsory repatriation was increased to 4.6 folds higher of 30.9% (95% CI 37.6-24.3) versus 6.7% (95% CI 3.8-9.7); i.e., interrupted treatment due to transferred out including back to origin countries was largely decreased.

Conclusions: Earlier case detection with less SS+ were observed among labor migrants due to multiple post-arrival screenings. Furthermore, the pragmatic and patient-friendly approaches that could encourage migrants to access to treatment and could play a significant role in preventing the re-emergence of TB in the receiving country.

PS15 "On the job" and tuberculosis

PS15-551-25 Intensifying TB screening among healthcare workers: lessons learnt from Mozambique

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Background and challenges to implementation: According to the Ministry of Health (MoH) of Mozambique, health care workers (HCWs) should be screened at least twice a year for tuberculosis (TB). The MoH has instituted special provider consultation services in all main health facilities (HFs) to improve service delivery for HCWs and their families. However, the majority of HCWs do not use these consultations. The number of TB reported among HCWs was 182 cases in 2014, 231 in 2015 and 376 in 2016.

Intervention or response: The National Tuberculosis Program (NTP), in collaboration with the USAID Challenge TB (CTB) Mozambique project and provincial directorates of health, initiated quarterly campaigns to sensitize and screen HCWs at all levels. These were preceded by consultative meetings with provincial and district senior health personnel for buy-in. HCWs were voluntarily screened using standardized questionnaires. Presumptive cases were investigated using GeneXpert and chest x-rays.

Results and lessons learnt: From January to March 2018, 4 campaigns were conducted in 37 HFs across 7 districts in Sofala, Tete, Zambézia and Nampula provinces. From 1,811 registered HCWs, 1083 (60%) were screened and 282 (26%) identified as presumptive TB cases. All 282 (100%) were investigated and 8 (3%) confirmed with TB (7 drug sensitive and 1 Rif+). All were put on treatment. The remaining presumptive cases were treated according to the national protocol and will be actively followed up. The number of registered HCWs participating limited by the association providers had of the campaign with HIV testing.

Conclusions and key recommendations: The results from the intervention will be vital to strengthen sensitization campaigns and to identify existing gaps in TB infection control at HFs. There is a need of increase awareness among HCW to regularly get screened for TB.

PS15-552-25 Barriers and solutions to TB and HIV care: lessons from current and past Mozambican mineworkers

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Background: Mozambicans migrate to South Africa (SA) to work in mines and are at higher risk for TB and HIV but little is documented about how they access care. We aimed to understand mineworkers' perceptions of TB services and differences in health-seeking behavior between SA and Mozambique.

Methods: We conducted semi-structured knowledge, attitudes, and practice (KAP) surveys and focus group discussions (FGDs) among current and ex-mineworkers who migrate to SA for work. Data was collected in Gaza Province through convenience sampling in June-August 2017. Frequencies of survey responses were generated using SAS (9.4). Key themes in FGDs were determined applying inductive and deductive codes using NVivo.

Results: A total of 102 mineworkers (n=29 current, n=73, ex-mineworkers) completed the KAP survey. Of the 95 persons who responded to a question regarding barriers to obtaining healthcare in SA: 34 (36%) reported no issues obtaining care, 28 (29%) reported not being allowed to use the public healthcare system, 29 (31%) reported mistreatment by SA healthcare workers due to citizenship, 4 (4%) reported other issues. These barriers also emerged as key themes in FGDs. Many mineworkers reported no problems with obtaining healthcare in Mozambique (74, 73%), though 19 (19%) identified fear of job loss due to a need to stay in Mozambique for TB treatment. Of 26 HIV positive individuals diagnosed while working in SA, 7 (27%) described sending antiretroviral therapy from Mozambique to SA through public transportation. FGD participants reported returning to Mozambique for initial TB treatment and sending medications to SA as means of overcoming barriers to healthcare.

Conclusions: Mozambican mineworkers identified barriers to obtaining healthcare in SA and described self-generated solutions for overcoming these barriers. Further research is needed to identify best practices for quality patient-centered TB and HIV care delivery within SA to ensure continuity of care for Mozambican mineworkers living in SA.

PS15-553-25 Workers' compensation for occupational tuberculosis in health workers in South Africa: a survey and qualitative study

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Background: Workers' compensation (WC) is an important component of social security for health workers (HWs) suffering from active TB, and includes reimbursed medical expenses, special ("WC") sick leave, and income replacement for persistent work incapacity. In South Africa, as elsewhere, TB exposure to HWs is often from undiagnosed patients. South African WC legislation allows a presumption of TB work-relatedness in HWs in such environments. Our study aimed to assess the functioning of the WC system for TB in HWs.

Methods: Three hundred cases of occupational TB reported in 2003-2016 among employees of the Western Cape Province public sector formed the sample. Progress of WC claims was sought from the statutory Compensation Fund. Fifty-one cases in the sample were interviewed telephonically with closed and open-ended questions to ascertain experience and outcome.

Results: Of the 300 reported claims, 46% could not be found on the Fund website implying process failure. Median waiting time of unresolved claims was 5.8 years. Of the interviewees, 29% did not use WC leave provision, and 76% incurred medical expenses personally or through their medical insurance despite treatment being free in state services; 42% reported ongoing medical problems and only one received incapacity compensation. Emergent themes included poor communication from the Fund and employer, stigma, surprise at contracting TB, and financial stress.

Conclusions: We conclude that the WC system functions poorly with long delays in resolution which undermine trust in the system. Employees are poorly informed of their rights and use their ordinary (capped) benefits rather than the benefits for which WC legislation was intended. There is little if any follow up for residual incapacity. These findings are probably generalisable to many countries and more research is needed. Besides social security, since WC is an incentive to TB disclosure by HWs which is needed for prevention, these findings merit attention.

PS15-554-25 Targeted Intervention amongst truckers: key achievements and learning to strengthen TB prevention and care in mobile populations

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Background and challenges to implementation: Despite being recognized as an economically productive labour force, health of truckers is often neglected. Extreme stress, prolonged separation from families and exposure to high-risk environment makes them vulnerable to TB either as co-infection or independently. German Leprosy and TB Relief Association (GLRA India) in collaboration with Apollo Tyres Foundation implemented a pilot during 2017-18 to improve the health and well-being of truckers affected by TB in Sanjay Gandhi Transport Nagar (a major trans-shipment location) of Delhi.

Intervention or response: Target population included truck drivers, helpers and allied population (local shopkeepers/ vendors) who are approached through different community outreach activities like one-to-one interpersonal interactions, group meetings, street plays, public announcements and monthly health camps. Project team enabled referral for free chest X-ray to nearby clinic and sputum collection and transport.

Results and lessons learnt: Through these initiatives, 1168 presumptive TB cases were identified- 675 among truckers and 479 in allied populations. However, a mere 50% underwent diagnostics- 596 for sputum examination and 569 for chest X-ray. There was insecurity among truckers to leave their trucks unattended while going for diagnostics. Moreover, due to frequent mobility, truckers immediately travel out-of-station for long duration. Many felt that after getting confirmed for TB, they might lose their employment due to highly prevalent stigma. A total of 30 TB cases were confirmed; 10 being truckers. While treatment was initiated for 23 cases; six patients are being followed up and one has died.

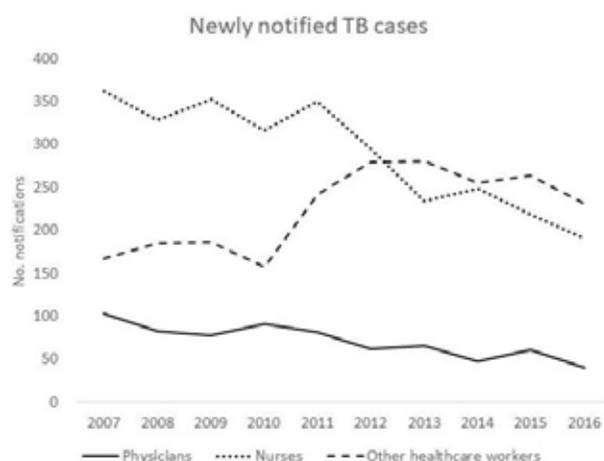
Conclusions and key recommendations: Experience from project suggests that diagnosis of TB and subsequent initiation of treatment remains key challenges among truckers. The need for ensuring rapid point-of-care diagnostics for this key affected population cannot be overemphasized. Efforts to build an enabling environment, continuous awareness and advocacy with transporters/ proprietors to facilitate screening among truckers along with improving linkages with treatment services will contribute to strengthened TB prevention and care among mobile populations.

PS15-555-25 Recent epidemiological trend of TB and LTBI among health care workers in Japan

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Background: The increasing contribution of immigrant in the healthcare workforce in Japan poses an opportunity to reevaluate TB control policy among healthcare workers (HCWs), including screening and treating latent tuberculosis infection (LTBI). This descriptive study was conducted with the aim of projecting an updated epidemiological overview of TB and LTBI among HCWs in Japan.

Methods: Data from the Japan TB Surveillance was analyzed over a period of 2007 to 2016. Trends of TB and LTBI and treatment outcomes were analyzed and compared by the three categories of HCWs i.e. physicians, nurses and other HCWs, and by country of birth.



[Figure 1 TB notification among healthcare workers in Japan]

Results: Figure 1 shows the number of newly notified TB cases among the HCWs. The estimated notification rate per 100,000 was the highest among other HCWs, at 37.1 in 2016, as compared with 9.4 among physicians and 12.2 among nurse. Both the number and the proportion of foreign-born among the other HCWs have steadily increased. As for treatment outcome, compared with other professional categories, lost to follow-up was high for all three categories of HCWs, with physicians being the highest at 11.3%.

A cumulative total of 6849 LTBI cases were notified among the HCWs. Notifications for other HCWs steadily increased, unlike for physicians and nurses - this was caused by the continuous increase in the notifications from foreign-born. The proportion of those terminating LTBI treatment due to "treatment completion" was 89.1%, 85.9% and 85.6% for physicians, nurses and oth-

er HCWs respectively. However, among those who have apparently completed treatment, the proportion of those whose treatment duration fell short of the recommended 180 days was especially high among the nurses, at 18.5%.
Conclusions: Treatment outcome for TB needs to be improved for HCWs. In the light of increasing number of foreign-born for both TB and LTBI, discussions regarding systematic screening for LTBI ought to start.

PS15-556-25 Targeted interventions led to improvements in TB case finding among selected mining workers in six high-priority districts in Ethiopia

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Background and challenges to implementation: Nomadic and pastoral populations comprise a significant proportion of the population in Africa, but they are difficult to estimate, reach, and track. This results in serious issues of TB case finding and treatment follow-up. This is compounded by a high number of other mobile populations, such as migrant workers. In the Guji and Borena zones of the Oromia Region of Ethiopia, the population is predominantly pastoralist. Our objective was to assess the impact of targeted interventions on TB case finding in this community.

Intervention or response: The USAID/CTB project identified six districts where 42,678 migrant workers are estimated to be engaged in informal gold mining activities. Health workers who have experience in TB programs were deployed in the six regions to support TB program implementation in the mining and surrounding community in collaboration with the district TB focal persons. Health education and sensitization on TB and TB-HIV was provided to 22,525 migrant workers. The health workers were also engaged in screening for TB among the mining workers and surrounding community, treatment support for TB patients on DOT, and TB contact screening.

Results and lessons learnt: A total of 10,538 mining workers were screened for symptom of TB, of whom 981 (9.3%) were found to be presumptive TB cases. Laboratory testing was offered for 948 presumptive TB cases, of whom 165 were diagnosed with active TB. This translates to a case notification of 1,565 per 100,000 mining workers screened.

Conclusions and key recommendations: The case notification among migrant workers was 11.3 times the case notification in the general population in the region. The targeted intervention was paramount in reaching the mining workers and diagnosing a significant number of TB patient who would otherwise have remained undiagnosed.

Characteristics	Frequency	Percentage
# of mining workers screened for TB	10,538	N/A
# of mining workers with presumptive TB	981	9.3%
# of presumptive TB cases evaluated for TB	948	96.6%
# of active TB cases diagnosed	165	1.6% [CNR = 1,565 per 100k]

[Results of screening for TB among mining workers, Nov 2015-June 2016 in Ethiopia]

PS15-557-25 Systematic TB screening in communities of mineworkers: lessons from a regional intervention in Southern Africa

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Background and challenges to implementation: Mineworkers in Southern Africa present a higher TB incidence than any other working population in the world. Is systematic screening in mining communities a successful strategy to identify TB cases and reduce the TB burden amongst mineworkers?

Intervention or response: The TB in the Mining Sector Programme (TIMS) was a Global Fund-funded intervention covering ten Southern African countries. Systematic screening was undertaken by local NGOs through community door-to-door and workplace strategies in collaboration with NTPs, mining companies and local stakeholders. It was combined with awareness raising campaigns through context specific IEC materials. Key populations (KPs) included mineworkers, ex-mineworkers and their families and communities. Diagnosis was primarily done at public health facilities and occupational health centres. Case finding results after one year of implementation in Botswana, Lesotho, Malawi, Mozambique, Namibia, Swaziland, Lesotho and Zambia have been analysed.

Results and lessons learnt: TIMS screened 226,960 KPs (52% male) in 22 areas of intervention across the eight countries. 45,683 (or 20%) people screened by the project were current or ex-mineworkers from formal and informal mining sectors. The rest were community and family members. 38% of TB cases (all forms) identified were mineworkers or ex-mineworkers. 80% of them were found in the three countries where more mineworkers were screened (Lesotho, Tanzania and Zambia).

Conclusions and key recommendations: 38% of TB cases identified were mineworkers/ex-mineworkers although mineworkers only made up 20% of KPs screened confirming that TB affects them disproportionately. Factors affecting success in case finding include: numbers of key populations in project area, efforts to ensure diagnostic (only 59% presumptive cases were actually tested) and capacity of collaborating health facilities.

The availability of occupational health centres in the areas of intervention in Lesotho, Tanzania and Zambia are likely to have had an impact on increasing access to diagnosis and case finding amongst mineworkers

PS15-558-25 TB outreach screening at Karatina Town bus stage, Nyeri County, Kenya

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Background: Kenya TB prevalence survey result suggested that the proportion of incident TB cases that are not notified is at 55% translating to 93,000 cases being undiagnosed and untreated. Recommendation was that in order to reach the END TB strategy goals, there is need to accelerate case finding. High yield interventions that were fronted for prioritization were: institutionalization of health facility based active case finding, special strategies for reaching men and private-public partnership in TB. Targeted outreaches at high influx areas for men (matatu stages) provide a unique opportunity to maximize the gains of TB screening.

Methods: A two-day screening exercise was organized targeting the drivers, conductors, hawkers, mechanics and small scale business people within Karatina stage. Community mobilization with the help of social mobilization and stakeholders meeting was done two days prior to the intervention. Screening was conducted by HCWs (clinicians, laboratory technologists) from the nearby health facilities using a structured questionnaire with key cardinal symptoms.

Results: Total people screened for TB were 311 with 73% of them being males and 23% matatu crew plying various routes. 135(43%) people presented with cough plus/minus other key symptoms, 80(59%) people produced sputum for Xpert and 8 TB cases were confirmed through genexpert 12 others reported having all the 4 key TB symptoms but could not produce sputum; linkage to chest X-ray services is still ongoing to aid in clinical diagnosis., 11% of 311 screened reported having been treated for TB previously with 23% of them being the matatu crew; 8.5% among the previously treated defaulted on medication.

Conclusions: Targeted outreaches is key in reducing the transmission cycle and can complement the current strategy of facility based active TB case finding. Moreover, incorporation of chest X-ray in screening heightens the sensitivity of the exercise.

PS15-559-25 How workplaces can address TB care and prevention for workers: a field report from Bihar

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Background and challenges to implementation: TB is an occupational risk, augmented by crowded living and working conditions, increased vulnerability to HIV, malnutrition, poor health seeking behaviours, stigma and fear of loss of wages. Sensitizing and engaging employers on TB presents an opportunity to improve access to accurate information on TB prevention and knowledge of TB services.

Intervention or response: In the state of Bihar in Eastern India, at an orientation programme organized by REACH and the Department of Industries, Government of Bihar, 20 small and medium industries were sensitized about the need to join India's response to TB. A pilot initiative was launched with BATA industries, Asia's largest footwear company, employing more than 250000 workers throughout the country, including workers from the formal and informal sectors. The workshop was conducted with an objective to promote the participation of employers in the TB response and the adoption of the Employer Led Model for TB. Orientation meetings for BATA employees provided opportunities to understand access to health services for their informal workers.

Results and lessons learnt: BATA Industries adopted the Employer Led Model for TB and incorporated TB-related activities in their annual action plan. BATA printed & displayed banners & hoardings, arranged film shows on TB as well as TB awareness workshops and camps for their 650 informal workers and are committed for similar workshops in a scheduled manner.

Conclusions and key recommendations: The engagement of BATA is a demonstration of a low-cost model for engagement of industries for TB care and prevention. This has resulted in increased interest from the management of other leading industries as well as discussions around adopting employee-friendly workplace health policies. This will have an impact on the health of employees, reducing delays in diagnosis and improving access to the correct providers. It will also result in reducing absenteeism and reduced performance on account of diseases like TB.

PS15-560-25 Tuberculosis control in the garment industries through partnership programme: achievements and challenges in Bangladesh perspective

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Background and challenges to implementation: The garment sectors of Bangladesh have about six million workers, mostly woman and poor. They often work in crowded situation in poor ventilated housing structures which is favorable for spreading TB infection. To deal with this situation, BRAC initiated a partnership programme with Bangladesh Garment Manufacturers and Exporters Association (BGMEA) and Bangladesh Knitwear Manufacturers and Exporters Association (BKMEA) to diagnose and treat TB cases among workers under DOTS strategy.

Intervention or response: Advocacy and health education forum has been conducted to raise awareness among factory owners, management authority's health care providers, and workers. If anyone had cough for more than 3 weeks considered as TB presumptive and sent for microscopy; among them those who were negative in microscopy and with poor socioeconomic status get free investigation support for other tests such as X-ray, FNAC, biopsy etc. to confirm tuberculosis.

Results and lessons learnt: In BGMEA working area through 545 orientation events, a total of 9,238 workers and manager/owners of corporate sectors were orientated on TB from 2013 to 2017. TB cases detection increased from 600 in 2013 to 1194 in 2017; among them 646 TB presumptive got financial support for investigation and 320 were diagnosed among factory workers. In the BKMEA working area 24 sensitization meetings with business associations were conducted with 1184 management level staff from 2014 to 2017. TB cases detection increased 146 to 200 from 2016 to 2017; among them 265 TB presumptive got financial support for investigation and 63 were diagnosed among factory workers. In 2016, overall treatment success rates were 95.74% and 94.29% among registered new smear positive TB cases of BGMEA and BKMEA respectively.

Conclusions and key recommendations: Different sensitization meeting and orientation with financial support to poor workers for diagnosis leads to increase in case notification, treatment adherence and treatment success rates. Effective follow-up and proper referral linkage need to be developed.

PS15-561-25 Mineworkers on the move: implications for TB control in Zambia

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Background: Zambia's mining sector has expanded in recent years, and persons are migrating across the country to pursue work in the mines. Mobile populations pose a challenge to TB control efforts by both fostering transmission to multiple communities and disrupting continuity of care. Thus, a better understanding of practices, perceptions, and understanding of TB is needed in this critical population.

Methods: Knowledge, attitudes and practices (KAPs) surveys were administered to mineworkers residing in the Copperbelt and North-Western Provinces in Zambia as part of the Zambia Assessment of TB and HIV in the Mines (ZATHIM) project. Population proportional to size was used to determine the study sample and convenience sampling was used to recruit participants in mining communities. KAP surveys were also conducted among healthcare workers (HCWs) at government and mining company facilities providing TB and HIV services. Proportions were calculated to summarize the findings.

Results: One thousand nine-hundred and fifty-six (N=1,956) current mineworkers and 94 HCWs completed KAP surveys. Mineworkers worked a median of 9 years in the mines (interquartile range [IQR]: 5-13); 31% of mineworkers with < 10 years of experience had worked for >2 different mining companies, and 7% had worked at >3 different companies. Over one-third (34%) of mineworkers maintained both a mining residence and a family home elsewhere. Surveyed mineworkers visit their family residence a median of 6 (IQR: 3-12) times in a 3-month period. Only 30% of HCWs stated they had a formal referral system in place for transferring TB patients to another community; and most (94%) agreed that such a system would enhance national TB control.

Conclusions: Mineworkers in Zambia today often undergo transitions in employment and in residences. These data highlight the need to implement a comprehensive, national program with coordinated notifications and referrals in order to provide continuity of TB care for mineworkers.

PS16 Factors associated with tobacco use: have they changed with time?

PS16-562-25 Smoking among medical interns and their perceptions about training on tobacco smoking in the medical curriculum, Bangladesh

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Background: Tobacco use related deaths could be prevented by reducing tobacco use. Evidence suggests that advice from physician acts as catalyst for smoking cessation among patients; therefore undergraduate students should be equipped with knowledge and skills to promote smoking cessation among their patients. This study aimed to measure prevalence of smoking among medical interns, their perceptions and attitudes towards tobacco use and practices of interns towards patients' tobacco use, and problems affecting teaching about tobacco in medical colleges.

Methods: This cross-sectional study was conducted in nine medical colleges in Bangladesh. Self-administered questionnaires were used among 515 interns and 24 in-depth interviews were conducted among teachers. Data were analyzed to see the prevalence of tobacco use; content analysis was done to identify the inadequacies in the current curriculum regarding tobacco use.

Results: Most interns opined that the physicians should be a role model by being non-smoker and more than half believed smoking among doctors is main obstacle for tobacco cessation. Among the male interns 41 percent were current smoker. In terms of current practices, most doctors asked their patients about history and duration of tobacco consumption but only around half of the doctors (55%) informed patients about the health effects of smoking. More than three quarters of doctors (78%) mentioned they were either not taught or could not recollect the clinical guidelines of tobacco cessations. Teachers opined that lack of a specific module on tobacco control affected the interns' tobacco control practices.

Conclusions: Smoking prevalence among the male interns is very high and should be addressed urgently. Attitudes of doctors towards physicians' role in smoking cessation among their patients were quite positive but the ability of the doctors to deliver tobacco cessation techniques was rated inadequate by the respondents themselves. Tobacco education should be included in the medical curriculum.

PS16-563-25 Tobacco consumption among Class III & IV employees of health care setup in Gujarat: a cross-sectional study

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Background: Both smoking and smokeless form of tobacco is widely prevalent & serious public health problem in India. Hospital workers are usually aware of dangers of tobacco products. Present study was conducted to describe prevalence & pattern of tobacco consumption, cessation practices, exposure to media & health morbidities among health care employees in Gujarat.

Methods: A cross sectional study was conducted among Class III and IV employees of two big government hospitals of Ahmedabad & Rajkot city. Total 200 workers were included by stratified random sampling. Personal interview was conducted & information about socio-demographic profile, tobacco use, health morbidities etc. was collected using W.H.O.'s tobacco questions for surveys (TQS). Data was compiled in excel & analyzed by appropriate statistical methods.

Results: Overall prevalence of tobacco use was 82.5%. Prevalence of smoking & smokeless tobacco was 31.5% (31% male & 0.5% female) & 59.5% (47% male & 12.5% female) respectively. Mean age of smokers & non-smokers was 43.0±11.8 & 36.5±13.0 years respectively ($Z=3.51$, $P<0.001$). Majority (73.0%) were smoking daily & 62.2% were using smokeless tobacco daily. Majority (60.3%) were not smoking inside home but 63.5% were consuming tobacco at work place. 54% of smokers & 44.5% of smokeless tobacco users had tried to quit during past year, 23.8% were consulted doctor for the same & 81% of them were advised to quit smoking. Workers have noticed dangers of tobacco quitting information in TV (81.5%), Newspaper (72%) and Cigarette package (43.5%) while 19% have noticed signs of cigarette promotion. Smoking is significantly associated with history of pneumonia (85.7%) & Asthma (77.8%).
Conclusions: Prevalence of tobacco consumption among health care employees is very high compared to general population. Intervention program should be planned for health care employees to reduce burden of tobacco related morbidities & to set up example for community visiting health care facilities.

PS16-564-25 A cross-sectional study on tobacco use and stress among professional cab drivers in New Delhi

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Background: In recent years, professional cab driving has seen a revolution with the advent of application based cab services, which are extremely time-bound. This poses a great burden on the service providers - the cab drivers. The drivers are at an increased risk of contracting physical and mental diseases and becoming habituated to use of habit-forming substances like tobacco due to the stress that they are exposed to.

Methods: A cross sectional study was conducted on 111 cab drivers between February to May 2017. Their demographic characteristics, lifestyle, use of habit forming substances was determined using a semi structured questionnaire. Their stress level was measured with the help of DASS-21 (Depression Anxiety Stress Scale) questionnaire. Data was analyzed using SPSS.

Results: In the current study, 55.9% drivers worked for more than 12 hrs a day, 31.5% worked on all 7 days of a week and only 39.6% get the required 8 hours of sleep on most days. Notably, one-fourth of the drivers are irritated while driving. It was noted that 53.2%, 36.9% and 32.4% drivers had some degree of depression, anxiety and stress, respectively. The number of drivers who smoke is 40 (36%), the average duration of smoking is 9.48 (5 months to 40 years). Out of them 29 (72.5%) said that they wanted to quit and have attempted leaving smoking in the last one year but were unsuccessful.

Conclusions: Majority of cab drivers are suffering from physical and mental morbidities. They are getting addicted to tobacco and other habit forming substances. There is a need to address to their healthcare status by the companies that have hired them.

PS16-566-25 Prevalence of tobacco use among priests and their willingness to spread anti-tobacco messages among devotees in Delhi

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Background: Tobacco use has increased in India in recent times. Hence, need for intensification of tobacco control efforts become pertinent. Tobacco cessation involves behavior change and evidence suggests that religious professionals may be helpful in community based smoking cessation programs.

Objective: To assess the prevalence, knowledge and practices related to tobacco use among priests and their

willingness to spread anti-tobacco messages among their devotees.

Methods: It was a community based cross-sectional study conducted amongst 159 head priests of Delhi. A semi-structured interviewer based questionnaire containing items to assess socio-demographic characteristics, tobacco use behavior, their knowledge about harmful effects of tobacco and willingness to spread anti-tobacco messages among devotees, was used for data collection.

Results: Out of the total 159 participants, 86.2% (n=137) were males. There were 61% (n=97) Hindus followed by 18.2% Muslims (n=29). Thirty seven respondents (23.3%) reported to be the current users of tobacco. Among the current tobacco users, 32 (86.5%) were using more than one form of tobacco. The most common form of tobacco being used was 'Chillum' (n=31; 83.8%). The knowledge about harmful effects of tobacco use was less among tobacco users as compared to that of non-tobacco users. However, majority of them (n=152; 95.6%) expressed their willingness to spread anti-tobacco messages to their devotees irrespective of their smoking status and also desired to be trained in the same.

Conclusions: The prevalence of tobacco use was low among the priests. Majority of them expressed their willingness to spread anti-tobacco messages. Therefore, religious leaders should be motivated through training in tobacco use prevention and helped in implementing tobacco use cessation activities.

PS16-567-25 Tobacco use and its consequences: perceived health effects among adolescents

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Background: Tobacco use is one of the most important causes of premature death in its role as risk factor for cancer, stroke, ischemic heart disease and respiratory diseases. Initiation into tobacco use is rooted in adolescence and therefore, its elimination appears to be a great opportunity for preventing Non-Communicable Diseases. This investigation assessed perceived health effects and social support for cessation behaviour among adolescent tobacco users in Mangalore taluk.

Methods: Study population comprised high school students selected by stratified cluster sampling after obtaining necessary permissions from concerned authorities and parental informed consent. Data on current tobacco use, use in family, perceived health effects, awareness of harm, quitting behaviour, recognition of habit by health professionals, and familial and professional support in habit cessation were obtained using a pre-tested questionnaire. Chi squared test was used for data analysis.

Results: Of the 1340 participants, 12.8% reported current use and it was higher among boys ($p < 0.001$). One-third users (35.7%) revealed tobacco use by family members. Perceived health effects of tobacco use such as cough, halitosis, loss of appetite, burning sensation in mouth, stained teeth, etc. were reported by all the female and 68.8% male users ($p = 0.007$).

A majority of users (88.9%) were aware of dangers of tobacco use but only 31.6% expressed a desire to quit. Unsuccessful past quitting attempts were described by 60.9% boys and 32.6% girls ($p = 0.021$).

Among users, 32.2% stated that their families were aware of their habit and had advised quitting, and 29.2% had been offered help for quitting by health care personnel after recognition of habit during a routine checkup.

Conclusions: Rising tobacco use among adolescents and an inability to quit, in spite of high prevalence of perceived ill-effects and availability of familial and professional support in quitting, is a cause for concern.

PS16-568-25 Knowledge, attitude and practice of Georgian population regarding the MPOWER measures

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Background: As part of *The Bloomberg Initiative To Reduce Tobacco Use* project "Supporting endorsement and enforcement of strengthened legislation on tobacco demand reduction in Georgia in order to meet WHO FCTC requirements", Public Opinion Poll has been completed. The aim of the polling was to identify the knowledge, attitude and practice of population regarding the harm of tobacco products, their smoking status, opinion on tobacco tax increases, prohibiting smoking inside public places, banning all advertising for tobacco products, and smoking status.

Methods: Public Opinion Poll has been performed using street-intercept survey methodology with stratified multistage random sampling approach. Sample size of 1200 was distributed by 11 regions evenly except for Tbilisi, with 100 participants in each region and 200 in Tbilisi. In regions 70 participants were selected from the regional centres (urban settlement) and 30 from the randomly selected rural settlement in the given region. As a result of the survey, a total of 1205 people were interviewed, 16% of them in Tbilisi. Majority of respondents represented 17-59 age group.

Results: 98.2% of respondents answered that smoking cigarettes is very or somewhat harmful. 94.9% consider tobacco use in Georgia to be a very or somewhat serious problem. 71.9% consider tobacco product advertising; 87.1% - easy access to tobacco products; 75.9% - low

tobacco prices; 89% - adult smoking as an example and 93.8% - peer pressure as factors that might contribute to youth smoking.

69% thinks that tobacco use in Georgia can be decreased by increasing the price; 65.1% - by increasing the tax; 66.3% - by banning all advertising and 57.9% by strengthening the health warning labels.

Conclusions: The results show that Georgian adult population is quite aware regarding the tobacco harm. They are ready and willing tobacco control to be strengthened according the MPOWER measures.

PS16-569-25 Factors influencing the tradition of smokeless tobacco use in rural communities of Bangladesh

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Background and challenges to implementation: Smokeless tobacco (SLT) is a kind of tobacco product in which nicotine is intended to be directly absorbed in an unburnt state rather than burning tobacco and inhaling the smoke. World Health Organization (WHO) reported that there is an increased likelihood of SLT use among the illiterate and less educated Bangladeshis. The aims of the research are to identify the current situation of SLT use among rural community and the influential socio-cultural factors.

Intervention or response: To identify the factors of SLT use in rural communities of the southwestern part of Bangladesh 6-villages were selected from each of 2-districts, namely Khulna and Kushtia. A total of 552 SLT users were surveyed through using semi-structured questionnaire. About 8-FGD and 20-IDI was also conducted. Respondents were selected through systemic random sampling technique. Comparative analyses were performed to test for statistical association. Content analysis of the qualitative findings was conducted that supplemented the quantitative results.

Results and lessons learnt: The mean age of the respondents was 47.2±23.1 with no formal education. The result indicated that a good proportion of the respondents were influenced by their family members to take up SLT use. Only 5% respondents were influenced yet by the indirect advertisements. Half of the respondents were influenced by social peer groups. Qualitative findings showed that people provided SLT during marriage ceremonies or for welcoming guest, which is a culture in Bangladesh. About 84% respondents believed that SLT has harmful effect on health and they received information about it from television, medical professionals and from SLT packs.

Conclusions and key recommendations: The study results indicated that majority of the respondents had knowledge about harmful effects of SLT use but social factors and traditional beliefs encouraged them to accept this product. Promotional activities should be fur-

ther controlled through effective monitoring by proper authorities. Availability of SLT may be restricted at social events through awareness campaigns.

PS16-570-25 Cigarette use among female sex workers in selected local government areas in south-western Nigeria

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Background: Smoking is an important public health issue and FSWs are exposed to various risk factors including cigarette use. This study was carried out to determine the prevalence and factors associated with cigarette use among FSWs.

Methods: The design was a quasi-experimental study among 645 brothel based FSWs aged 18 years and above in selected LGAs in Ibadan and Ogbomosho health zones of Oyo State. A multi stage cluster sampling technique was employed and a semi-structured interviewer administered modified questionnaire was used. This questionnaire was pretested and validated prior to administration. Data was analysed using SPSS version 22. Logistic regression was used to determine independent predictors of cigarette use and all statistical test was set at a *P* value < 0.05.

Results: Mean age of respondents in years was 31.3 ± 7.6. Among respondents, 303 (46.9%) were single, 341 (52.8%) attained secondary school education, 591 (91.6%) earned above the Federal Government minimum wage, 241 (37.4%) were current smokers, 44 (6.8%) were former smokers, 408 (63.2%) consumed alcohol, 110 (17%) used and 44 (6.8%) formerly used other substances. Age, educational level, duration as FSWs, alcohol and substance use were significant factors associated with cigarette use. Independent predictors of cigarette use were alcohol and substance use. (OR=1.7; 95% CI=1.19-2.56 and OR=11.8; 95% CI=7.13-19.53 respectively).

Conclusions: The higher prevalence of cigarette use among FSWs when compared to the female and male national prevalence (0.3% and 7% respectively) could be a means of coping with intrapersonal and interpersonal experiences, thereby eliminating inhibitions, desensitizing and detaching them from the stigma associated with the job. Interventional programs with a view to regularly educate FSWs who belong to a population referred to as "hard to reach."

PS16-571-25 How the Philippine government tracked results relative to the Sin Tax Law of 2012

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Background and challenges to implementation: The measurement of where the incremental revenues from Sin taxes were spent is critical to ensure continued funding for health as decided by the Congress during annual reviews. The Department of Health was tasked to show results of use and effectiveness of the tax measure.

Intervention or response: A monitoring and evaluation framework was developed. Following the framework, we analyzed the national health budget to identify earmarks from the tax. We also collected information on expenditure items funded by the tax and analyzed data trend on tobacco use.

Results and lessons learnt: The health budget exponentially increased from \$1B in 2013 to \$3B in 2018. The additional budget were distributed among public health programs. In particular, the Tuberculosis Control Program was allocated \$20M which funded the treatment of 200,000 people with TB from 2014-2018. The resources also resulted in the procurement of 200 Gene Xpert machines. Other major funded programs are: the National Insurance Program resulting in the increase in population coverage from 79% in 2013 to 91% in 2017, the Facilities Enhancement Program resulting in the construction of 5,862 health facilities, and the Human Resources for Health Program resulting to an additional 1,188 HRH deployed. There was also a significant decline in tobacco use among adults from 31% in 2012 to 23% in 2015, among the poor from 38% in 2012 to 27% in 2016, and among the youth from 5.7% in 2013 to 4.2% in 2015.

Conclusions and key recommendations: The Sin tax M&E framework allowed the Philippine government to effectively track the effects of the incremental revenue for health. This practice provided a way to link increases in budgets to actual expenditures therefore quantifying its use. At the end of the results chain is data on smoking prevalence which reflect the law's primary objective of reducing tobacco use being met.

PS16-572-25 Impact analysis and changing attitudes of smokers after implementing graphic health warnings in Bangladesh

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Background: Bangladesh is one of the world's most densely populated countries with 170 million people among these 43% live below poverty. Bangladesh has a fairly young population with 34% aged 15 & younger and 19.36% population in the age of 15-24. In Bangladesh 43.13 Million (GATS-2009) people are using tobacco and the rate is higher among the age between 11to20 that is 58%. For reduce tobacco use Bangladesh has enacted tobacco control law in 2005 and amended in 2013 along with notification of the revised rules in 2015. As per rules Graphic Health Warnings (GHWs) has been implemented from 19 March 2016 on 50% principal display area of all tobacco packs in Bangladesh.

Methods: Cross sectional study design, quantitative and qualitative approaches, purposive sampling method and semi-structured questionnaire and in-depth interview used to conduct the survey. The objectives of the study was to identify the impact of GHWs implementation to quit smoking attitude. SPSS 21, Microsoft Excel used to analysis the data.

Results: 100% respondents are well known the visual impact of GHWs implementation on Cigarette pack among these 88 % low income and 92% young population feel that the smoking is very harmful for health and they should quit smoking after seen the GHWs on the time of smoking. Total 68% low income and 60% young generation tried to quit smoking after implement the GHWs but they again start smoking among these 47% shows that their relatives/friends/family totally quit smoking.

Conclusions: Tobacco Company still trying to increase their sales. Most of the respondent share their ideas that the appeal of the image is weak and they said that strong/more dangerous appeal should be incorporate. So that related authority/government agency should take initiative to increase the size of image of GHWs and also select the dangerous appeal image for GHWs.

PS17 Curbing the tobacco epidemic: policy and practice

PS17-573-25 Government school teachers' knowledge on FCTC and the NATA Act in Gampaha district, Sri Lanka

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Background: The public school network in Sri Lanka is vast, ranging up to 4.2 million children enrolled in over 9,790 public schools. The number of teachers extends to around 200,000. The objective of the study is to assess the government school teachers' knowledge on FCTC and the NATA Act (National Authority on Tobacco and Alcohol) in Sri Lanka.

Methods: A descriptive study design method was employed. Using the simple random sampling method, 3 schools were selected from the Gampaha district. Sample size is 162; A self-administration questionnaire was used to obtain data.

Results: Only 43.3% were aware that Sri Lanka had ratified and signed the FCTC. Out of that, only 27.2 % were aware of the articles of FCTC. 65.4% correctly responded to the legal age for buying tobacco products (21years old). 67.9 were aware that tobacco promotion is banned. Only 45.1% knew that any sponsoring by tobacco industries was prohibited. However, 85.8% responded that smoking in enclosed areas is prohibited. Only 39.5% were aware that free distribution of tobacco is banned.

The Sri Lankan Tobacco industry has launched a subtle campaign targeting children, "Cigarettes are not for Minors". Although 84.6 % respondents have seen this notice in shops, only 29.2% respondents have recognized it as a tobacco industry tactic. Only 19.8% respondents have encountered situations that provoke smoking in media within the last month. However ADIC media research ascertains that tobacco promotion is prevalent in media every day.

Cross tabulation analyses were done but there were no significant differences within schools.

Conclusions: FCTC and NATA has been dominant in policy implementation from 2003 to date. Yet, among the teachers, the knowledge regarding those policies is not substantial. Hence the teachers must be well informed about such policies.

PS17-574-25 Psychological empowerment for tobacco control in a rural low-income setting in Sri Lanka

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Background: Tobacco, a vector of poverty and disease, is portrayed as a powerful determinant difficult to be controlled. "Psychological empowerment for tobacco control" encompasses an individual's sense of control over tobacco related issues, the foundation for strengthening community actions against tobacco. This study aimed to describe the psychological empowerment for tobacco control in a rural low-income community in Sri Lanka.

Methods: The study used a cross-sectional descriptive study design. Empowerment was operationalised based on literature into 27 item scale under intrapersonal, interactional and behavioural domains. The tool was developed using a modified Delphi technique and validated for the local context. The interviewer administered tool assessed participants recruited via a multi-stage cluster sampling technique using a household (N=1160) survey.

Results: Response rate was 98.6% (N=1144). The majority (92.1%; n=1054), felt they have a responsibility to involve in tobacco control even though only 21.9% (n=251) has ever participated in such activities at least once in their lifetime. Perceived mastery, motivation, competence, awareness and efficacy for tobacco control among participants were satisfactory. Interactional domain, assessing participants' preparedness to act, received the highest scores (M=23.5; SD=5.9) among all the domains.

Conclusions: Perceived mastery, motivation, competence, awareness and efficacy for tobacco control among participants were satisfactory. Level of action did not match the levels of intrapersonal empowerment and preparedness to act. Unused potential for tobacco control exists among the community to act against tobacco.

PS17-575-25 Second-hand smoke practices among schoolgoing adolescents in a hilly district in the Himalayan region

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Background and challenges to implementation: There is no safe level of exposure for second hand smoke. The link between SHS and several health outcomes, such as respiratory infections, ischaemic heart disease, lung cancer and asthma, has long been established. However according to WHO, 40% of children, 33% of male non-smokers and 35% of female non-smokers are exposed to second-hand smoke. The study was undertaken to estimate the prevalence of SHS exposure and to identify the various factors related to SHS.

Intervention or response: This was a descriptive school-based cross-sectional study conducted among students 13 to 19 years studying in classes 8th to 12. Multi stage cluster random design and PPS sampling methodology was adopted. A sample of 900 students both from rural and urban areas studying in 10 government and private senior secondary schools was selected. An anonymous, pre tested, self-administered questionnaire was used to collect relevant information.

Results and lessons learnt: Self reported tobacco use was reported by 19.6% of the participants. It was seen that 35.1% participants were exposed to second hand smoke. Nearly 71.1% of the participants perceived it to be harmful for health, while 59.6% were aware about the current ban on smoking in public places. The participants whose family members smoked or who themselves reported self use were at greatest risk.

Conclusions and key recommendations: The high knowledge about deleterious effects of second hand smoking among the participants did not translate into any beneficial behavioural change. Hence scaling up of IEC activities focussed on school going adolescents is imperative. Further, the negative influence of family abuse practices highlights the necessity to include parents in any awareness campaign being planned.

PS17-576-25 Relationship between selling tobacco products and tobacco consumption of child vendors in Dhaka

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Background: Tobacco consumption is a leading risk factor for disease and death. Marketing and distribution of any kind of tobacco products to under 18-year-olds is a punishable offense by law, nonetheless, tobacco products are being distributed to child vendors for selling. The vulnerability of this child vendor group for tobacco consumption risk has not yet been explored in Bangladesh. This study aimed to determine the relationship between selling tobacco products by children and their attitude and practice regarding tobacco consumption.

Methods: A retrospective cohort study was designed where a calculated 133 tobacco sellers and 133 non-tobacco sellers were selected as exposed and non-exposed group respectively based on predetermined inclusion criteria. The study was conducted in the capital city Dhaka. Respondents were interviewed using a pretested

semi-structured questionnaire near respondent's workplaces. A scoring system was developed to assess the overall attitude and practice of child vendors. Descriptive and inferential analysis was also performed to explore the vendors' attitude and practice regarding tobacco consumption and also to identify factors significantly associated with their tobacco consumption status. All research steps were conducted in an ethically appropriate manner.

Results: Children selling tobacco products were found three times more likely to consume tobacco products than those who did not sell tobacco products ($p < 0.05$). When the scoring criteria were imposed, tobacco selling children's mean score was significantly higher than the non-tobacco selling children both in attitude ($p < 0.01$) and practice ($p < 0.001$) which implies that tobacco trading children practice and favor tobacco use more than the other child vendors.

Conclusions: Selling tobacco by children is directly associated with their tobacco consumption practice and attitude. Tobacco selling children are more likely to consume tobacco products than non-tobacco selling children due to this particular exposure. This study recommends the policymakers to emphasize on tobacco control initiatives for this specific group.

PS17-577-25 Anti-tobacco legislation and youth tobacco use: comparison of Kenya Global Youth Tobacco Surveys 2007 and 2013

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Background: Tobacco is a major risk factor for non-communicable diseases globally. Anti-tobacco legislation has been used to reduce burden of disease from tobacco use. Kenya passed the tobacco control act (TCA) in 2007. The country also conducted the Global Youth Tobacco Survey (GYTS), used to monitor tobacco use among students in seventh to tenth grades, in 2007 and 2013. This study aimed to compare the two surveys to determine the impact of the legislation on youth tobacco use.

Methods: Kenya GYTS 2007 and 2013 were multi-stage, clustered, nationally representative surveys of youths ≤ 15 years. We conducted secondary analysis of the data-sets to determine change in tobacco use between the surveys. Accounting for complex survey sampling, we calculated prevalence of different tobacco use parameters in 2007 and 2013.

Results: The survey participants were 11,069 in 2007 and 1895 in 2013; 51.7% and 48.7% were female, respectively. Tobacco products use decreased from 18.6% in 2007 to 9.9% in 2013 (difference 8.7%, $P < 0.001$). Cigarettes smoking prevalence decreased from 9.6% in 2007 to 5% in 2013 (difference 4.6%, $P < 0.001$) while smokeless tobacco use fell from 12.6% in 2007 to 6.2% in 2013 (difference 6.4%, $P < 0.001$). Prevalence of second-hand smoke exposure remained unchanged over the period (39.1% vs. 37.0%, $P = 0.083$). Exposure to tobacco advertisement decreased from 81.1% in 2007 to 27.0% in 2013 (difference 54.1%, $P < 0.001$). Morning smoking urge decreased by 11.5% to 6.5% in 2013 ($P < 0.001$). In 2007, 24.4% of participants had experimented with cigarettes, compared with 15.3% in 2013 (difference 9.1%, $P < 0.001$).

Conclusions: Decrease in youth tobacco use may be attributed to enactment of TCA 2007; its full implementation, including the proposed tobacco regulations, can further reduce tobacco use in Kenya.

PS17-578-25 Effective use of provisions under the Drugs and Cosmetics Act of India for curbing the use of Electronic Nicotine Delivery Systems in Punjab, India

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Background and challenges to implementation: ENDS popularly known as e-cigarettes are highly addicting products, detrimental to health of the users. It is mostly being used by children and youth because these are glamorised by the tobacco industry. They are widely promoted and sold through E commerce sites. These products are unapproved under Drugs and Cosmetics Act of India. Eight States of India have already declared these products as unapproved for sale under Drugs and Cosmetics Act. Punjab was the first state in India to declare E-Cigarettes as unapproved under Drugs and Cosmetics Act of India in 2013. All the Drug Inspectors were instructed to initiate action if any vendor is found selling ENDS. There is a provision of fine of up to Rupees one Lakh (about US \$ 1700) and imprisonment of three years for violation of this Act.

Intervention or response: Regular monthly monitoring of sale of ENDS at state level by Commissioner FDA and at District level by Deputy Commissioners is being done in Punjab. Strict implementation of the Act is being done all over Punjab, by the enforcement teams. Seizure of these products was done in 5 districts and court cases were launched against seven violators contravening Drugs and Cosmetics Act.

Results and lessons learnt: Two court cases in Districts Mohali and Sangrur have already been decided and sellers of E-Cigarettes were penalised with fine and imprisonment as per provisions in the Drugs and Cosmetics Act of India for sale of unapproved products. These are the first such cases decided by the court anywhere in India and amongst very few globally.

Conclusions and key recommendations: The provisions under Drugs and Cosmetics Act can be effectively used for containing the increasing popularity of ENDS in India. This case vignette can be successfully replicated in other states of India, and other countries with similar problems of growing use of ENDS.

PS17-579-25 Did the Gutkha ban impact sale of other smokeless tobacco in the states of West Bengal and Kerala in India?

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Background: India is the second largest producer and the third largest consumer of tobacco. 28.6% adults use tobacco and 21.4% currently use smokeless tobacco (GATS 2, 2017).

Following the Supreme Court's order and amendment in the food safety regulation, Gutkha - mixture of areca nut, lime and scented tobacco was banned across in India with states of Kerala banning it in September 2012, in West Bengal in June 2013.

Methods: One state each from East and South India have been selected for this cross-sectional study along with the District Head quarter and two Blocks. In West Bengal 90 and in Kerala 83 vendors were selected. Transect survey method was used for collection of data.

Results: The study reveals that 100% of the respondents in Kerala know about the Gutkha ban as against 62.2% in West Bengal. 82.2% of Vendors from West Bengal did not know that Gutkha sale is a punishable offence whereas in Kerala the percentage is only 4.8. Gutkha was found unavailable in 48.8% of the shops in Kerala, in West Bengal Gutkha is available in 68.5% of shops. 49.4% of shops in Kerala and 75.3% shops in West Bengal sale Gutkha to the minors. Only 16.9% of vendors from West Bengal reported fall in sale of Gutkha or like products whereas in Kerala the figure is 61.4%. Sale of gutkha per month in Kerala is significantly lower than that of West Bengal whereas enforcement of the ban in Kerala is highly significant ($p < 0.01$) than that of West Bengal.

Conclusions: Overall, the ban on Gutkha has had significant effect in Kerala but lower impact in West Ben-

gal. Lower education, porous borders which permit illicit trade and lack of enforcement were cited as the key reasons for the persistence of gutkha in West Bengal.

PS17-580-25 Curbing the prevalence of beginner smokers by enacting national regulations on a total tobacco advertising, promotion and sponsorship ban in Indonesia

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Background and challenges to implementation: Government of Indonesia targets to reduce the prevalence of smokers aged ≤18 years in 2014 from 7.2% to 5.4% in 2019 but in 2016 the prevalence rate is still increasing to 8.8%. This happen because the policy on Tobacco Advertising, Promotion and Sponsorship (TAPS) are restrictive. Parliament are still believe with the constitutional court decision that cigarettes are legal products so they can be advertised .

Our policy advocacy program that supported by The Union focus on advocacy government and parliament members to enact a national regulation on total TAPS ban through providing data and information. This policy target about 261 million of Indonesian people national wide. While the case studies was taken in 6 big cities in Indonesia

Intervention or response:

- Research The relationship of smoking status to students with TAPS
- Developed Policy Paper Of TAPS ban
- Direct advocacy meeting with related stakeholders
- Press Conference, Media Briefing and social media campaign
- Judicial Review of broadcasting law and Press law at constitutional court

Results and lessons learnt:

- 99 % of the students watch the tobacco advertising, 68,91 % agree that cigarette advertisements affect a person to try smoking.
- Policy document has been delivered to related stakeholders
- Tobacco industry interference and lobbying is very strong
- Media and public awareness was important to give information about the importance of TAPS ban
- Tricky and unfair lawsuit practices in the Constitutional Court

Conclusions and key recommendations:

- Significant correlation between exposure of TAPS to the smoking status of students
- Total TAPS ban is more effective than just the restrictions.
- TAPs ban issue in the revision of the Broadcasting Bill

- The Parliament and government should have strong political will to enact national regulation on total TAPS ban.
- Voice of youth to remind the constitutional court that exposure of TAPS harming citizens' constitutional rights.

PS17-581-25 Tobacco advertisements, promotion and sponsorships: tobacco companies continue the business of lies and deception in India

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Background: Tobacco companies have been using all possible tricks to market their deadly products and earn profits at the expense of lost lives. Companies are continually applying manipulative tactics and circumventing the Indian tobacco control law (COTPA). It is important for tobacco control advocates and law implementers to have an understanding how tobacco companies market their deadly products. This information is important in designing tobacco control efforts and get better prepared to counter the industries tactics. The researcher did the present study with the objectives to keep a track on tobacco industry's tactics and overview range of the ongoing TAPS violations in India.

Methods: Researcher did the newspaper scans, market survey and company's website search in 2015, 2017 and January 2018. The marketing materials at point of sale (PoS) were also analyzed.

Results: Tobacco companies are utilizing PoS as a strategic location for carrying out TAPS. Companies are paying retailers to display the advertisement billboards; tobacco products are placed strategically to give an ambience of power walls. Most cigarette brands are offering price discounts and encouraging single cigarette sale. Contests, giveaways and coupons for gift catalogs are other gimmicks. Special edition packages of cigarette brands are common in India. Surrogate advertisements as trademark diversification and brandstretching are most rampant. Industry has been successful in product placement in movies and promoting tobacco through film stars. As part of the image building exercise, most tobacco companies are doing CSR activities. The industry effectively and discreetly is using social networking sites like "facebook" to promote its products.

Conclusions: Tobacco companies in India are carrying out aggressive advertising and promotion and sponsorship campaigns to glamorize its deadly product through indirect advertising and deceitful tactics. There is an urgent need to enforce legislation to contain all common types of TAPS violations in India.

PS17-582-25 Assessing the policy attention accorded to tobacco control in Uganda's health policies over a 10-year period, 2004-2014

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Background: Implementation of WHO Framework Convention on Tobacco Control (FCTC) is constrained by a lack of high-level political commitment in low-income countries. Even within the national health agendas of low-income countries, tobacco control (TC) is assigned a low priority. We aimed to assess policy attention towards tobacco control in Uganda's health sector policies and plans over a 10-year period (2004-2014).

Methods: A qualitative research design was adopted. In phase one, a desk review was conducted of all available health sector policies and plans between 2004-2014 based on on-line searches and documents archived in Uganda's Ministry of Health. In phase two, in-depth interviews ($n=36$) were conducted with national-level health policy planners in government. In stage three, a workshop was conducted with key tobacco control stakeholders in Uganda ($n=56$) to analyze data generated from the previous two study phases. Interview data were analyzed by coding and thematic analysis while the content thematic analyses were performed on identified health policies and plans.

Results: A total of 17 health sectors policies and plans were identified for analysis. Out of the 17 health sector plans selected, only 6 explicitly mentioned 'tobacco control'. Of the 17 plans reviewed, only 3 explicitly mentioned TC as a program objective. Uganda's national health policies and plans were skewed towards infectious diseases responses particularly HIV, Malaria, and Tuberculosis with resource allocation and programming commitments aligned accordingly. National policy responses were inclined towards disease treatment rather than prevention. Uganda's health policies were predominantly derived from global health agendas.

Conclusions: Tobacco control was assigned a low priority in Uganda's health sector policies and plans for the period under review. Efforts to integrate tobacco control in Uganda's successor health policy and planning instruments is recommended. The inclusion of TC in global health policy has potential for trickling down into national health policy and planning in low-income countries.

PS17-583-25 Tobacco-free school and colleges: a study of the adoption and implementation of tobacco free policies in the Punjab, India

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Background and challenges to implementation: Tobacco use among the youth reached new highs in the country. Most interventions for school and colleges on tobacco control emphasized on knowledge, attitudes and beliefs of individual student. There is scarcity of published data on statewide campaigns to accelerate the adoption of tobacco-free policies in school and colleges along with hostels.

Intervention or response: The State Tobacco control cell, Punjab developed a multilevel strategy to accelerate the adoption of tobacco-free policies in Government school and colleges along with hostels. Instructions were issued by the Director General School and college Education to all the schools and colleges to adopt Tobacco free guidelines in year 2015. Seminars and street plays in schools and colleges were done for awareness generation among the students. Tobacco Control Cell, Punjab tracked process and policy outcomes as well as the diffusion of policy adoption from January 2015-December 2017.

Results and lessons learnt: All the Government schools and colleges along with hostels declared themselves as Tobacco Free. A written declaration was given by the Principal of school and College regarding the same to protect students, faculty, staff and visitors from Tobacco. The Tobacco free school and colleges along with hostels have also banned the sale of tobacco within the 100 yards radius from the outer boundary of the campus.

Conclusions and key recommendations: The school and college setting is a key system to impact tobacco use in students. This policy will help to curb the menace of Tobacco as this will go a long way in deterring young children & youth from initiation & also motivate current users to quit.

PS17-584-25 Articulating children and human rights violations from tobacco production to consumption in India

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Background and challenges to implementation: Child labour in many countries in the tobacco-growing areas exposes children to many hazards, notably long working hours, heat exhaustion, respiratory disorders, injuries, accidents, poisoning and health problems from being exposed to pesticides, musculoskeletal injuries, and green tobacco sickness, which is caused by nicotine absorbed through the skin from contact with wet tobacco leaves which is a threat to public health and violates the rights of children for Health and for Health Information.

Tobacco Production Would be bidi factories in which boys work and bidi rolling where girls work at home with mothers, Women constitute ~75 percent of the total bidi workforce. Production is 750 billion to 1.2 trillion sticks every year. Women and girls work from dawn to dusk rolling bidis for piecework, paid in pennies They sit in a crouched position all day.

Intervention or response: We analysed the sample of 100 children from four cities of India and found major factors associated with violations of human rights as well as for severe health related issues. Most of them are suffer from Backache and knee problems, Dizziness due to tobacco dust. Chronic bronchitis, asthma and even tuberculosis Burning sensation in eyes and throat. Rheumatic syndromes, allergies. Stomach troubles and haemorrhoids.

Results and lessons learnt: After analysis, we find that violation of Right to Education, adequate rest, play, entertainment--joys of childhood. Consumption of Tobacco due to influence of atmosphere. Tobacco industry luring children by advertisements, Free samples Selling cheap products (Not using warnings) Luring by point of sale. Also Violating rights to information.

Conclusions and key recommendations: Children are being used in Tobacco business from beginning to end. This presentation will draw the attention of the Global community to protect the children from exploitation by the industry and minimise the possibility of violation of human rights in India.

ABSTRACT PRESENTATIONS FRIDAY 26 OCTOBER 2018

ORAL ABSTRACT SESSIONS

OA10 Cooling down tuberculosis hotspots: innovative trials

OA10-267-26 Effect of population-wide screening on the prevalence of TB: a cluster randomised controlled trial in Viet Nam

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Background: Active case finding for TB is being evaluated in many settings but there are three important limitations to the existing strategies: 1) symptom-based screening has a low sensitivity; 2) chest radiography is complex to implement in remote settings; and 3) in high burden settings most TB cases occur in people who are not “high-risk”. Hence, we assessed the role of community-wide active case finding, using Xpert[®] MTB/RIF (Cepheid) testing of sputum, as a strategy for reducing the prevalence of TB in a high-burden setting.

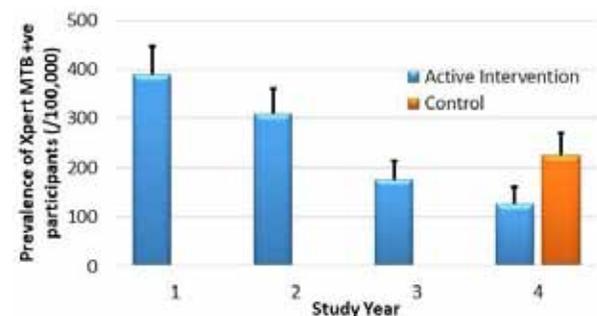
Methods: We conducted a cluster randomised controlled trial in Ca Mau province, Vietnam. Clusters were sub-communes (population ~1000 adults). Active intervention clusters were screened annually for three years (2014-16). Screening involved collecting spontaneously expectorated sputum from all adults, regardless of symptoms. Sputum was tested by Xpert[®] MTB/RIF. There was no intervention in control clusters. The primary study endpoint was the prevalence of pulmonary TB in persons aged 15 years and over in the fourth year of the study.

Results: There were 60 active intervention clusters and 60 control clusters. The number of participants screened / eligible population (% participation) in the three annual screens were 43,425 / 51,453 (84.4%), 44,085 / 55,069 (80.1%), and 44,317 / 56,888 (77.9%), respectively. In the fourth year prevalence survey (2017), these numbers were 42,161 / 56,629 (74.5%) and 41,649 / 48,221 (86.4%), in the active intervention and control clusters,

respectively. The prevalence of MTB positive results on Xpert[®] testing of sputum are shown in the Figure. The prevalence ratio (active intervention : control) in the final year survey was 0.56 (95% confidence interval 0.40 to 0.78, P=0.0009).

Conclusions: Population-wide screening using Xpert testing of spontaneously expectorated sputum from all adults capable of producing a specimen, repeated annually for three years, resulted in a 44% reduction in the prevalence of TB.

Funding: Australian NHMRC



[Figure: Population prevalence of TB by randomised group and study year]

OA10-268-26 Disparities in access to diagnosis and care identified through enhanced citywide tuberculosis surveillance and spatial analysis in Blantyre, Malawi

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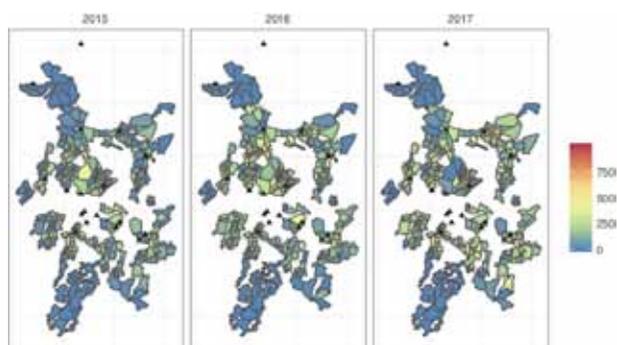
Background: A sizeable fraction of TB cases go undiagnosed. By implementing citywide enhanced TB surveillance, we aimed to identify modifiable predictors of poor access to diagnosis.

Methods: The population of Blantyre, Malawi residing within 315 Health Surveillance Assistant (HSA) catchment areas was enumerated between 10/10/2015 and 30/12/2015. From January 2015, TB Officers implemented an enhanced TB surveillance system at all TB registration centres, comprising collection of demographic and clinical characteristics TB cases, collection of sputum for culture, and geolocation of cases' place of residence using a satellite map application. We estimated annual

case notification rates (CNRs), stratified by microbiological status. To identify population and areal-level factors predictive of HSA catchment area TB case notifications (including poverty, estimated from Worldpop data), we constructed Bayesian spatially-autocorrelated Poisson regression models.

Results: A total of 753,489 people were enumerated in 315 catchment areas. Between 2015 and 2017, 4009 TB cases (63% male; 97% HIV tested; 67% HIV-positive; 59% culture-confirmed) were registered (3723 [93%] resident within a city HSA catchment area, crude CNR per 100,000 per year: 2015: 131.9; 2016: 174.4; 2017:187.8). There was strong evidence supporting a negative correlation between greater distance to the nearest TB clinic and case notification rate (relative rate [RR] per \log_{10} increase in clinic distance [in metres]: 0.82, 95% credible interval [CI]: 0.70-0.97). We additionally found strong evidence for negative correlations between CNRs and poverty (RR per percentage point increase in proportion living on less than \$US2 per day: 0.04, 95% CI: 0.01-0.18), and lower adult male:female ratio (RR: 0.24, 95% CI: 0.10-0.59).

Conclusions: We found strong evidence of the “inverse care law”, with people living in poorer neighbourhoods, further from TB clinics and with lower male: female adult ratios having poor access to TB diagnosis. Pro-poor strategies to facilitate equitable access to TB diagnosis and treatment are required.



[Annual TB case notifications in Blantyre, Malawi: 2015-2017]

OA10-269-26 Identification of potential TB hot-spots through a mobile X-ray supported community-based mass screening program in Karachi, Pakistan

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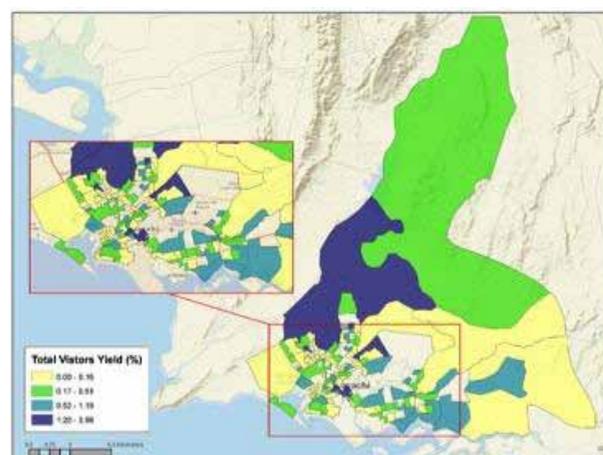
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Background: High-incidence hot-spots of TB transmission can have a significant impact in propagating the TB epidemic within a city. Identification of these hot-spots and interventions to reduce local transmission, have been described as a cost-effective strategy for TB control.

Methods: We analyzed retrospective data from mobile X-ray camps conducted in Karachi, Pakistan as part of an active case-finding intervention from July 2017-March 2018. Data was analyzed at the Union Council (UC) level, the smallest geographically defined unit in the city. Yield for TB, was defined as the number of bacteriologically confirmed TB cases identified per total number of individuals screened. The mobile x-ray camps visitors were screened using Chest X-ray supported with Computer-Aided Detection for Tuberculosis (CAD4TB). Individuals identified with CAD4TB score >50 were referred for Xpert MTB/RIF testing. Global Moran's I statistic was used to test spatial autocorrelation overall in Karachi. Population density of UCs were utilized to carry out geographically weighted regression and identify potential clusters of high TB yield identified during mass-screening.



[Union Council wise TB yield in Karachi, Pakistan]

Results: A total of 337 MTB+ve were identified out of 102,785 individuals screened for TB over the study period. The highest MTB+ve yields were reported from UC-13 Safooran (3%), (Gulshan), followed by UC-7 Water Pump (2%) (Gulshan) and UC-6 P.E.C.H.S 1 (1.8%) (Bahadurabad). Global spatial analysis of MTB+ cas-

es in Karachi city suggested overall clustering of cases (Moran's $I=0.0578$, p value=0.02). A total of 7 UCs located in Bin Qasim, Malir and Gadap towns of Karachi were identified as clusters with high yield of TB.

Conclusions: There was evidence of heterogeneity in TB yield identified through mass-screening in Karachi and UCs with clustering of TB were identified. Further data from the city required to appropriately identify areas with higher risk of transmission.

OA10-270-26 Private health sector engagement in national tuberculosis control programme: preliminary findings from a cluster randomised trial, India

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Background and challenges to implementation: In India, Private Practitioners (PPs) and Retail Private pharmacists (RPPs) play an important role in provision of Tuberculosis (TB) care. Government is making efforts to involve them in Revised National TB Control Programme (RNTCP). TB is a notifiable disease in India, mandatory for all private health facilities to notify TB cases to RNTCP.

Intervention or response: Cluster randomised trial, implemented between November 2016 and January 2018 in a south Indian district. One set of interventions targeted towards strengthening of RNTCP and other towards intervention PPs and RPPs to refer presumptive pulmonary TB (PPTB) cases to RNTCP. GIS mapping of PPs and RPPs was done. Of total 57 PPs identified, 34 and 23 PPs were enrolled in intervention and control arms respectively. Similarly, 122 RPPs identified; 56 enrolled in intervention and 66 in control arm.

Results and lessons learnt: Total 812 PPTB cases were referred from PPs, of which 733 (90.2%) were from the intervention arm. There was significant difference in the proportion of referring PPs between intervention arm (88.2%) and control arm (52.2%). Intervention PPs had significantly higher median number of referrals (median=3) than control (median=1) arms. 82.2% of the cases referred by intervention PPs underwent sputum examination, of which 32 (5.3 %) were bacteriologically positive, compared to 79 cases referred by control arm, of which 7 (9%) were detected positive. Among RPPs, intervention arm referred 166 cases compared to none from the control arm. Intervention PPs and RPPs contributed to 22.5% to the total sputum examinations done in study area, compared to 2% from control arm. Overall, intervention PPs and RPPs contributed 31.3% to total case detection and control arm contributed 4.4%. None of PPs or RPPs notified TB cases to RNTCP.

Conclusions and key recommendations: Our study successfully involved PPs and RPPs in RNTCP by utilising local resources in RNTCP. The regulation for notification needs to be strengthened.

OA10-271-26 Risk factors associated with case clustering of Mycobacterium tuberculosis based on whole-genome sequencing in northern Thailand

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Background: Thailand is one of the high tuberculosis (TB) burden countries. Understanding the risk of clustering could provide useful information for public health interventions to control TB. Whole-genome sequencing (WGS) identified transmission chains accurately and can be used to identify epidemiologically linked clusters. We determined the risk of WGS-based clustering in Thailand.

Methods: *Mycobacterium tuberculosis* (MTB) culture positive cases between 2002-2011 in Chiang Rai province, northernmost Thailand, were included in this study. We extracted DNAs of MTB from culture samples and performed WGS on Illumina HiSeq 2000 platform. The single nucleotide variants (SNV) as compared to *M. tuberculosis* H37Rv genome (GenBank NC_000962.3) were identified. The socio-demographic data and clinical information were collected at their enrollment. Clusters were determined by SNV of less than 10 between two isolate pairs. The risk of clustering was assessed calculating the adjusted odds ratios (aORs) compared with non-clustered cases by a multivariate logistic regression model. The proportion of cluster size was calculated by MTB genotypes.

Results: Among 1298 culture-confirmed TB cases, 394 (30.4%) of them were clustered with at least one other cases. Hill-tribe ethnicity (aOR 1.43 (vs Thai ethnicity), 95% CI:1.05-1.94), Beijing genotype (aOR 4.11 (vs East African-Indian (EAI)), 95% CI:3.00-5.62) and other types of genotype (aOR 2.02 (vs EAI), 95% CI: 1.33-3.07) were increased the risk of clustering in the multivariate analysis. Older age (≥ 65 years of age) showed a lower risk of clustering than the youngest age group (< 35 years of age) (aOR 0.35, 95% CI: 0.21-0.57). Only Beijing genotype created large clusters with more than 10 people in a cluster.

Conclusions: Not only host socio-demographic risk factors but also the pathogen genotype was associated with TB case clustering in Thailand. People with the risk of clustering could be a target of public health interventions to prevent TB outbreak.

OA10-272-26 Estimation of national tuberculosis incident cases using capture-recapture method based on inventory study data in Indonesia in 2017

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Background: Current national tuberculosis (TB) incident estimates in Indonesia was indirectly estimated using the 2013-2014 Indonesia TB Prevalence Survey, notification data, and non-Indonesia specific duration of TB disease. The WHO Global TB Report showed that the estimation of TB incident in Indonesia in 2016 was 1,020,000 cases (660,000-1,460,000) and 430,000 cases were notified in the National TB Control Program. Indonesia just finished the TB inventory study to measure level of under-reporting of TB cases. With appropriate selected model on national surveillance (NTP) and inventory study (IVS) data matching, we might be able to estimate the number of undetected TB cases. Using the estimated proportion of undetected cases, the total TB incidence might also be extrapolated.

Methods: Capture-recapture analysis based on 22,681 NTP-IVS unique cases used to estimate undetected TB cases and extrapolate to total incidence TB cases. Poisson regression models were performed to estimate the number of undetected TB cases. The best model was selected with the smallest value of Akaike Information Criterion (AIC). The uncertainty level was estimated using propagation method.

Results: We estimated 5,114 (95% CI 4,257-6,143) TB cases were undetected. It was equivalent to the proportion of undetected cases was 18.4% (15.6-21.1%). Based on the under-reporting of 41.3% (36.4-46.4%), the estimate of total detected TB cases was 733,000 (677,000-795,000) cases. The national estimate of TB incident cases was 898,000 (821,000-984,000).

Conclusions: The estimated number of detected TB cases but not notified to national surveillance system was 303,000 (34%), as twice as number of undetected TB cases (165,000 (18%)). Most of TB cases in Indonesia had already been detected (82%). Improving the recording and reporting system, simpler system for private practitioners and enlarging notification system to all health care providers are immediately needed. Active and intensified case finding are also still in the national TB control program priority.

OA10-273-26 Enhanced case finding of tuberculosis in The Gambia: a cluster randomized trial

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Background: Worldwide, TB case notifications have stagnated and tuberculosis (TB) surveys report undetected TB in communities. With the current trajectory of declining TB incidence, global WHO TB control targets will not be achieved. These suggest the need for a more active approach to TB case detection but the evidence base of different case finding strategies is slim.

Methods: We conducted a cluster randomized trial of enhanced case finding from 2012-2014 (ClinicalTrials.gov NCT01660646). Intervention communities received three 6-monthly visits during which sensitization with an educational lecture and video on TB symptoms was followed by provision of sputum cups (2 each) for those who sought to be tested. These were collected the following day for fluorescent microscopy. Persons with smear positive TB were referred to the nearest TB clinic (TBC). Recruitment into the trial was population-based at all TBCs, and patients who provided informed consent were visited at home and classified as living in an intervention versus control area. We compared the direct yield of the sputum collection and the indirect self-referral to the TBCs by comparing case notifications over time between intervention and control communities.

Results: 3052 patients were recruited into the trial, 1482 from intervention and 1570 from control communities. The direct yield of the intervention was minimal as only 35 (0.34%) of 10,185 individuals who had sputa screened after community sensitization had smear positive TB. In addition, TB case notifications did not significantly differ between intervention and control areas.

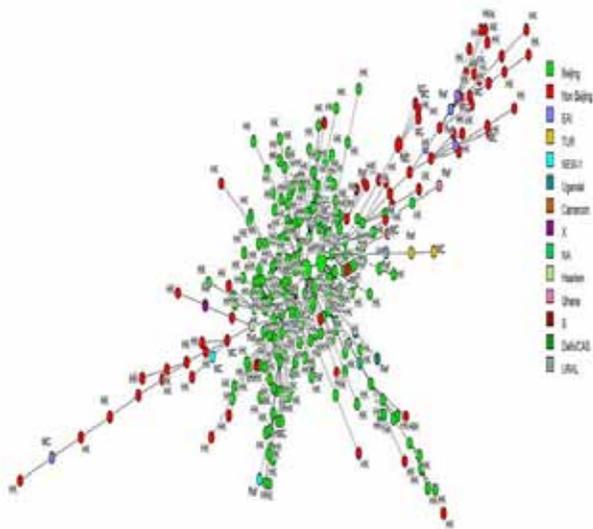
Conclusions: The intervention did not significantly improve TB case detection in The Gambia. This might be the result of a lower-than-expected community prevalence of smear positive TB (53 per 100,000 population) and high case detection (70%) as reported by a parallel nationwide TB prevalence survey. Alternative case finding approaches should be piloted and formally tested to inform public health guidelines.

OA10-274-26 Molecular relatedness of Mycobacterium tuberculosis strains isolated from Hong Kong and Macao: so far and yet so near

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Background: Both Hong Kong (HK) and Macao (MC) are tuberculosis(TB) intermediate-burden areas with notification rates in 2016 of 60.1 and 67.0 per 100,000 population respectively. Both places have many foreign visitors year round, including frequent travelers who shuttled between the two places. Using molecular genetic markers as genotyping tool for studying *Mycobacterium tuberculosis* complex (MTB), we investigated genetic relatedness and possible recent transmission(s)/outbreaks involving these two cities.

Methods: Non-duplicate patients' isolates of MTB were collected over a 2-year period(2015-16) from new pulmonary TB, sputum culture-positive cases in a large regional hospital in Hong Kong(254 strains) and Public Health Laboratory in Macao(40 strains). Using a 24-loci set of variable number tandem repeat(VNTR)-mycobacterial interspersed repetitive units (MIRUs) for analysis, their genetic relatedness and possible clustering in Minimum Spanning Trees (MSTs) were constructed.



[Figure 1. Minimum Spanning Trees constructed by VNTR MIRU 24-loci.]

Results: Patients' age ranged from 9 to 99 (median 59) years old, with 70% male and 30% female. Genotyping of patients' MTB isolates showed that Beijing family strains were prevalent in Hong Kong (77.2%,196/254) and Macao (62.5%,25/40). With 24-loci VNTR-MIRU

analysis, only two of 254 (0.79%) strains from Hong Kong and 12 out of 40 (30.0%) from Macao displayed clustering. Clustered rate for Macao cases was significantly higher than Hong Kong (p< 0.001). A total of five clusters could be identified amongst all strains isolated from Hong Kong and Macao, with one cluster involving two non-Beijing family strains, while Beijing family strains were in other four clusters (of 4,2,4,2 cases each).

Conclusions: This genotyping study simultaneously examined strains isolated from two TB intermediate-burden areas, and attempted to show their possible genetic relatedness. We showed that useful VNTR-MIRU clustering information could be generated and MSTs constructed, thus demonstrated possible intercity transmission of TB cases. Public health epidemiological investigations, plus next-generation sequencing (NGS) studies, will confirm their clustering and transmission potential between the two areas.

OA12 Allocating funds for impact

OA12-275-26 Insights from four allocative efficiency studies: evaluating the current and potential impact of national TB budgets and responses

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Background: TB is a leading cause of death globally. There is a need to evaluate the impact of National TB Programmes and current levels of spending. This paper compares findings and lessons from allocative efficiency modelling studies in Belarus, Gauteng Province of South Africa, Moldova, and Peru.

Methods: We used Optima TB to conduct integrated analyses of epidemiological, intervention impact, and cost data sourced from TB surveillance systems, literature, and local experts. Optimisation analyses were conducted across sub-populations by age-group, co-morbidities (HIV, diabetes), and prisoner status, as well as different screening strategies, treatment modalities, and drug-resistant regimens.

Results: Estimates from all four studies show that improvements in key TB indicators can be achieved by optimally re-allocating TB funding across new and existing interventions. Significant reductions in active prevalence and TB deaths of 30%-45% were projected by 2035 whereas impact on TB incidence was gener-

ally smaller. The largest estimated health impacts from re-allocations were in Belarus, a treatment response focussed on tertiary care, where optimised allocations could achieve up to 50% reductions in prevalence and deaths by 2035. Contact-tracing was consistently funded in all studies, compared to mobile outreach for which investments were only recommended for high-burden areas. Intensified case finding in primary health care received significant allocations in the Gauteng analysis given the high-incidence context, particularly among people living with HIV, but was partially scaled-down in Peru where incidence is lower. New drug-resistant treatment regimens were consistently funded in all studies as their modelled impacts offset their costs.

Conclusions: Re-allocating TB budgets to cost-effective interventions like contact-tracing, new drug-resistant regimens, and investing savings into linkage-to-care can significantly improve TB outcomes. Overall, study results suggest most national TB targets could be reached but not the global End TB targets, indicating more investment and new technologies are required to meet the latter.

OA12-276-26 Sub-national priority setting for TB control in South Africa: results from a cost-effectiveness model

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Background: Sub-national differences in TB burden and cost of interventions can be used to inform appropriate geographically-targeted TB control interventions. The objective of this study was to determine the most cost-effective intervention strategies to be implemented in South African provinces to reach the 90-90-90s targets for TB control by 2035.

Methods: We developed a cost-effectiveness model in Microsoft Excel to determine which of three TB control interventions, or their four possible combinations, should be adopted in KwaZulu-Natal, Western Cape and Limpopo provinces; and at national level. The interventions were: (1) intensified case finding; (2) initial loss to follow-up reduction and (3) improved treatment success. Mathematical modelling for interventions and combinations was carried out using the 'TIME Impact' TB transmission model and unit costs were attached to model outputs to assess the relative cost-effectiveness of the different strategies. Intervention costs were obtained from different sources including published literature,

expert communication and primary data collection. Interventions were deemed cost-effective if their cost per disability-adjusted life-year (DALY) averted fell below the South African reported Gross Domestic Product (GDP) per capita.

Results: All interventions and combinations in all regions fell below cost-effectiveness threshold. In KwaZulu-Natal and Limpopo, intervention 3 was the most cost-effective and was cost-saving in KwaZulu-Natal. It was, however, the least cost-effective nationally. At national level, intervention 2 was the most cost-effective whilst interventions 2 and 3 combined were most cost-effective in Western Cape. The combination of all three interventions averted the most DALYs in all regions, but was also the most expensive strategy.

Conclusions: National-level modelling for priority setting might overlook regional variations that call for a targeted approach if TB control targets are to be achieved. Using regional disease burden and cost differences, cost-effectiveness models can inform suitable interventions to prioritise in different geographical areas.

OA12-277-26 Cost-outcomes analysis of decentralised care for drug-resistant tuberculosis in Johannesburg, South Africa

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Background: In South Africa, hospital-based treatment for drug-resistant tuberculosis (DR-TB) has been estimated to cost \$9,385 per patient treated. In 2011 the country adopted decentralized, outpatient treatment to reduce barriers to and costs of treatment. To evaluate the latter, we estimated the cost per outcome in a decentralised model of care in a high-HIV prevalence outpatient DR-TB clinic in Johannesburg.

Methods: Data are from a prospective cohort study. Costs of DR-TB treatment from initiation to outcome were estimated from the provider perspective using bottom-up costing and included drugs, laboratory tests, staffing, equipment, supplies, infrastructure, and other overheads. Costs were estimated as patient-level resource use multiplied by resource unit costs. Quantities of clinic visits, TB and non-TB drugs dispensed, laboratory tests performed, and total days hospitalised were collected from patients' medical records. Staff time was estimated through a time and motion study. Average 2017 costs/patient are reported in USD (13.31 ZAR/\$1). The cost of antiretroviral therapy (ART) was not included.

ed. A successful treatment outcome was defined as cure or completion of the regimen. Average cost to achieve a successful outcome = total cohort costs/number of successful patients.

Results: From 03/2013 to 09/2014, we included 127 patients in the study, of whom 52% had a successful outcome. The average cost/patient for all patients was \$2,621(\$3,665 successful, \$1458 unsuccessful). The largest contributors to total cost across all outcomes were drugs(48%) and staff (36%).The average effective cost to achieve a successful outcome in the cohort was \$5,045.

Conclusions: Decentralised, outpatient MDR/RR-TB care under South Africa’s 2011 strategy costs 61% less than under the previous strategy of inpatient care. The total cost of DR-TB treatment to the national TB programme will depend on the proportion of patients who achieve a successful TB outcome; as outcomes improve over time, costs are likely to increase substantially.

Cost in 2017 USD	Staff cost	Drug costs	Labs and monitoring	Equipment	Consumables	Over-heads	Hospitalization	Total
All patients (n=127)	877 (36%)	1,173 (48%)	331 (14%)	68 (3%)	29 (1%)	63 (3%)	54 (2%)	2,449 (100%)
Treatment success (n=66)	1,213 (33%)	1,724 (47%)	434 (12%)	106 (3%)	30 (1%)	93 (3%)	63 (2%)	3,665 (100%)
Loss to follow-up (n=37)	593 (35%)	593 (35%)	254 (15%)	43 (3%)	20 (1%)	46 (3%)	78 (5%)	1,717 (100%)
Died (n=24)	370 (35%)	369 (35%)	271 (26%)	22 (2%)	15 (1%)	29 (3%)	0 (0%)	1,059 (100%)

[Cost breakdown by outcomes (in 2017 USD)]

OA12-278-26 Tuberculosis care reform in Belarus: an allocative efficiency analysis supporting the policy dialogue

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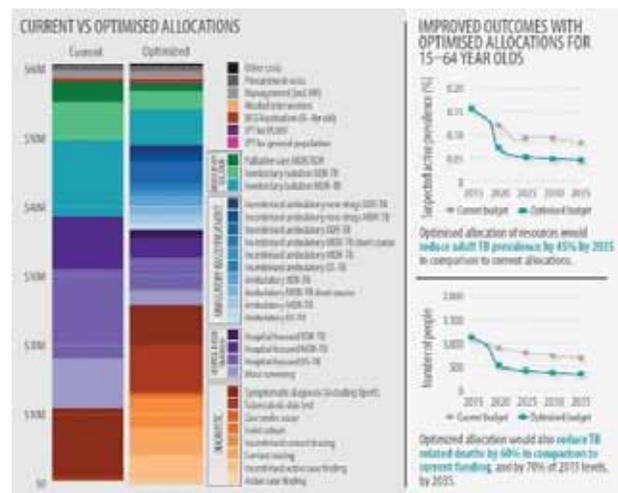
Background: Despite reductions in TB incidence and mortality achieved in the past decade, Belarus’ national TB response is faced with the need to address an epidemic characterized by high levels of multi-drug resistant (MDR-TB) and extensively drug resistant tuberculosis (XDR-TB). In 2015, investment in the tuberculosis response was US\$62 million. Calls for TB care reform have been made.

Methods: A multi-method allocative efficiency study was carried out using epidemiological, program and cost data for 34 TB program categories. Analyses were performed in Optima-TB, a model of TB transmission and disease progression. The expected impact of dif-

ferent program bundles were compared using scenarios and a formal mathematical optimization algorithm applied to establish how available resources could be allocated optimally to minimize TB incidence, prevalence and deaths.

Results: The analysis confirmed the need and scope for reform of the Belarus TB response. Treatment costs could be reduced by as much as 40% by expanding ambulatory care, without a reduction in overall treatment effectiveness. Treatment in involuntary isolation departments absorbed 27% of TB resources in 2015, while only covering 6% of TB patients. Provision of alternative drug regimens for people with XDR-TB was estimated to reduce prevalence of XDR-TB by 65% by 2035. Optimization analysis showed that the same budget available for TB-related activities in 2015 (US\$ 61.8 million) could - if allocated optimally - reduce TB prevalence in the general adult population by 45% and reduce the total number of TB deaths 60% compared to current allocations.

Conclusions: Optimizing investment in Belarus’ TB response requires a reduction in hospitalization, involuntary isolation and mass screening. These resources should be refocused on strengthened ambulatory care, treatment scale-up including new drugs for MDR-/XDR-TB and enhanced active case-finding for high-risk populations. Findings from the study are used in the policy dialogue surrounding Belarus’ TB care reform process.



[Belarus optimized allocations]

OA12-279-26 Active case finding of pulmonary tuberculosis in the Russian Federation: how to save costs

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Background: In Russia, mass chest X-ray (CXR) screening for tuberculosis (TB) is mandatory for the whole population. The objective of this study was to compare the cost of mass CXR screening with other approaches to find pulmonary TB in adolescents and adults in the Arkhangelsk region, Russia in 2013-2017.

Methods: This is an ecological study using aggregated data to compare cost of three approaches to detect pulmonary TB: mass CXR screening, passive case-finding and contact tracing. Coverage, yield, proportions, mean cost of examinations and per TB case detected were calculated. Health system costs included: a cost of a local general practitioner's vs. TB-doctor's visit (labour costs), cost of CXR screening, microscopy, travel expenses (diesel fuel, travel allowance of a driver and a laboratory assistant). For analysis all data were obtained from official medical, economic documents and reporting system used for registration of TB cases.

Results: TB cases detected and the corresponding yields (proportion of examined population with TB) were: by mass CXR screening 684 (28 per 100000), contact tracing 61 (753) and passive case-finding 743 (960). Correspondingly, the mean cost per examination (and per detected tuberculosis case), were: 2.39 USD (in a municipal hospital; 8458 USD) and 5.31 USD (in a TB hospital; 14903 USD); 20.28 USD (2693 USD), and 11.85 USD (1234 USD). In targeted groups the highest yields but the least costs per TB case detected were in HIV-positive persons 645 per 100000 (370 USD), homeless 461 per 100000 (518 USD), and migrants 441 per 100000 (542 USD).

Conclusions: Mass CXR screening (excluding targeted groups of HIV-positive, migrants and homeless) has low yield and high cost per TB case detected, indicating that it should be stopped while resources should rather be used to strengthen the screening of targeted high-risk groups, contacts and passive case-finding.

OA12-280-26 Cost-effectiveness of interventions to improve TB contacts' cascade of care in Rio de Janeiro, Brazil

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Background: Recently, WHO stated that latent tuberculosis infection (LTBI) treatment is one of the most effective health interventions for tuberculosis prevention. In Brazil, all pulmonary tuberculosis contacts are supposed to be investigated for active tuberculosis, but preventative treatment for contacts is not a priority. We conducted a cost-effectiveness analysis to evaluate interventions to increase the number of individuals who initiate treatment for LTBI.

Methods: The number of contacts reaching each step in the cascade-of-care were collected at baseline in two clinics participating in a research trial (ACT-4) in Rio de Janeiro. Associated health system costs were estimated using a questionnaire at those clinics. Types of costs included personnel, building overhead, supplies and services. Interventions evaluated included 1) healthcare worker (HCW) training 2) patient education leaflets and 3) both. Interventions' costs were obtained from pilot studies in Brazil and their effectiveness from a systematic review. A hypothetical cohort of 1000 contacts was evaluated using a discrete event simulation model, designed to estimate total health system costs associated with the cascade, as well as the cost-effectiveness of introducing interventions aimed at strengthening the cascade. The incremental cost effectiveness ratio (ICER) used to compare interventions was cost per additional contact initiating LTBI therapy.

	Number of contacts initiating treatment per 1000 eligible contacts	Cost per 1000 eligible contacts	Increase in effectiveness (vs. Base case)	Increase in cost (vs. Base case)	ICER (US\$ per additional contact initiating LTBI treatment)
1) No intervention (Base case)	7.7	US\$ 25,798	-	-	-
2) Patient education	10.2	US\$ 35,296	2.5	US\$ 9,498	US\$ 3,799
3) Health Care workers' training	184.3	US\$ 75,087	176.6	US\$ 49,289	US\$ 279
4) Both interventions combined	225.0	US\$ 92,953	217.3	US\$ 67,155	US\$ 309

[Table 1. Cost, effectiveness and incremental cost-effectiveness ratio of different interventions to improve the cascade-of-care of contacts in Rio de Janeiro]

Results: Total cost for each scenario and cost-effectiveness of different interventions are shown in table 1. The no-intervention scenario cost US\$ 25,798 per 1000 eligible contacts. The most cost-effective scenario was when HCW training was applied (ICER US\$ 279).

Conclusions: The current policy for contact investigation in Brazil presents a missed opportunity to treat LTBI. Huge resources are spent to identify contacts and exclude active tuberculosis, yet very few contacts will initiate LTBI treatment. We have shown that several simple solutions are highly cost-effective and can potentially have a big impact on improving contacts' cascade-of-care, which will further reduce costs by preventing active TB.

OA12-281-26 But at what cost? The cost of implementing mobile-health facilitated tuberculosis contact investigation

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Background: Mobile health (mHealth) applications are utilized to improve timely access to health services and improve communication between patients and providers, but little is known about the costs of executing such a program. We therefore measured the costs of implementing a multifaceted mHealth-facilitated household contact investigation strategy in Kampala, Uganda.

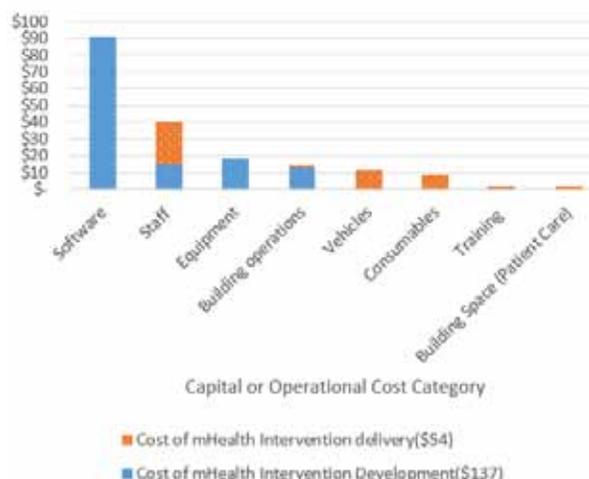
Methods: We conducted a cross-sectional micro-costing study nested within a randomized controlled trial testing community health worker (CHW) led home-based specimen collection and automated SMS messages for delivery of TB test results among household TB contacts. CHWs used self-reported time-and-motion (TAM) surveys to estimate time-related costs. We conducted interviews with key informants to estimate capital and operational costs including information technology (IT) costs. We calculated absolute costs of the mHealth intervention delivery and estimated costs per household member screened for TB over five years. Costs reported in 2017 US dollars.

Results: CHWs spent 44% of their time conducting clinic-based activities, 6% performing mHealth-facilitated household activities and 20% on travel. Total labor costs were estimated at \$0.60/household member at risk for TB. CHWs spent a median of 15 minutes/household member at risk for TB (IQR 6.5-29.0) conducting home-

based procedures. Median travel time was 60 minutes (IQR 35.0-91.0).

Over 5 years, 1928 household contacts were screened for TB at a total cost of \$191/ household member. Costs were primarily driven by IT which comprised the development of an mHealth intervention at \$137/household member screened of which \$91 was an overhead software cost. The mHealth intervention delivery cost \$54/household member screened of which \$25 reflected staff time.

Conclusions: The primary drivers for implementing mHealth-facilitated contact investigation strategies lay in software development, rather than in the delivery of the intervention itself. More attention must be paid to these cost components if mHealth-facilitated interventions are to be widely implemented in resource-limited settings.



[Cost Per Household Member Screened for TB]

OA12-282-26 Early-phase implementation success of isoniazid preventive therapy for people living with HIV, Malawi, 2017

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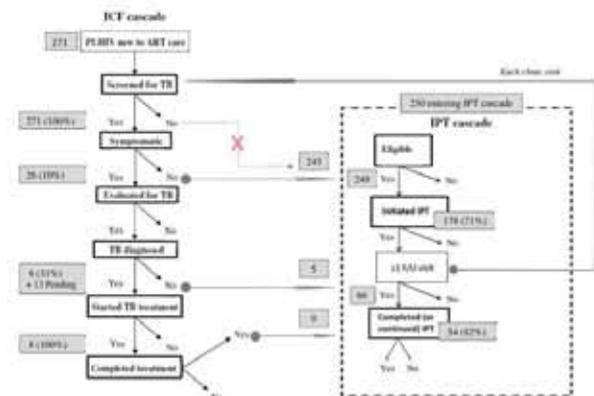
Background: Isoniazid (INH) preventive therapy (IPT) for TB is a life-saving intervention for people living with HIV (PLHIV). In late 2017, Malawi began to scale-up IPT to eligible PLHIV in the five highest TB-HIV—burden districts, and we aimed to measure the frequency and timeliness of early-phase IPT uptake in a programmatic setting.

Methods: We conducted a two-stage cluster survey using systematic probability-proportional-to-size sampling of six CDC-affiliated antiretroviral therapy (ART) centers operating in the urban areas of Lilongwe and Blantyre,

Malawi. ART clinic patient volume determined cluster size. Within each cluster, we systematically sampled approximately 50 medical records for cross-sectional review. We also illustrated a comprehensive quality-of-care cascade for IPT in PLHIV.

Results: We sampled 271 new-to-care PLHIV. All underwent TB screening and 26 (10%) had a positive four-TB-symptom screen. Among eligible PLHIV, the overall weighted IPT uptake was 70% (95% CI 46-86%). Weighted uptake for children with HIV < 15 years of age (30%, 95% CI 12-55%) was significantly lower than for adolescents ≥15 years and adults (72%, 95% CI 47-89%; Rao-Scott χ^2 F=10.9, P=0.03). PLHIV < 5 years had weighted uptake of only 13% (95% CI 1-79%). For pregnant women, weighted uptake was 67% (95% CI 32-90%), which was similar to that for non-pregnant women ≥15 years (72%; 95% CI 49-87%). 82% (95% CI 76-87%) of those with a follow-up visit were continuing IPT (Figure 1). Lastly, we measured excellent timeliness of quality-of-care indicators, as 96% started ART within one week of HIV diagnosis, and 91% of IPT starts occurred on the same day the person began ART.

Conclusions: These results demonstrate an effective early-phase scale-up of IPT among new-to-care PLHIV in Malawi, which may serve as a model for similar national programs. Malawi also underscores the utility of early assessments, as doing so can lead to prompt quality improvement interventions.



[Figure 1: Intensified Case Finding (ICF) and IPT Quality-of-Care Cascades for New-to-Care PLHIV]

OA14 Pharmacokinetics and pharmacodynamic sciences to accelerate development of new drugs and vaccines

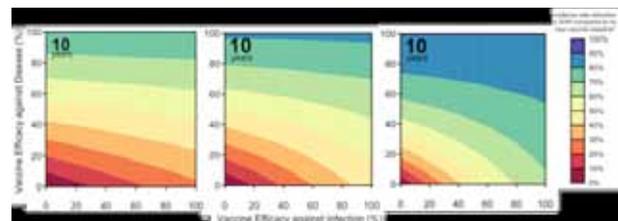
OA14-283-26 Maximising impact of the TB vaccine pipeline: mathematical modelling to inform TB vaccine development

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Background: Target Product Profiles (TPPs) guide strategic development of new TB vaccines to maximise future epidemiological impact. Currently, insufficient evidence exists to guide decisions on future TB vaccine characteristics. To inform TPP development by BMGF, WHO and others, we estimated the influence of new TB vaccine characteristics on potential impact in China, India and South Africa (SA).

Methods: An *M.tb* transmission model was calibrated, to available age- and HIV-stratified estimates of population, TB prevalence, notification, incidence and mortality rates, for China, India and SA. We explored vaccine efficacy (VE) for prevention of infection (POI) and disease (POD) (0-100%), duration of protection (2yrs-life), and efficacy pre- and post-infection. Vaccine was implemented in 2025, with 80% routine coverage of 9 year olds, and 70% coverage of ≥10 year olds in 10-yearly mass campaigns. Primary outcome was percentage incidence rate reduction in 2050 compared to no-new-vaccine baseline.

Results: In all 3 settings, POD vaccines would have greatest impact over 2025-50. In China, POD efficacy was imperative to achieve at least ~25% impact in 2050, whereas in India and South Africa POI efficacy could also have substantial impact due to greater ongoing transmission (Fig.1).



[Figure 1. Median incidence rate reduction in 2050 by VE against infection & disease (P&PI, 10yrs protection)]

Post-infection vaccines provided similar impact in each setting, whereas pre-infection vaccine impact was highest in India and lowest in China. Minimum duration of protection to achieve ~25% reduction in 2050 was 5 years for China and SA, and 2 years in India. Safety and efficacy in HIV-positive populations was important for achieving substantial impact in SA.

Conclusions: Population-level impact of future vaccines was dependent upon underlying epidemiology - ‘one size won’t fit all’. Whether an epidemic is reactivation- or transmission-driven may influence trial endpoint selection. Where feasible, trials should include *M.tb*-infected populations, and extend beyond the usual 2-3 years. This research is imperative for data-driven TPP development and policy, to maximise future vaccine impact.

OA14-284-26 Proteomic analysis of *Mycobacterium tuberculosis* lineages 3, 4, 5 and 7 reveals differentially abundant proteins involved in DNA repair, lipid metabolism, oxidative phosphorylation and virulence

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Background: Despite *Mycobacterium tuberculosis* (*M. tuberculosis*) was discovered more than a century ago, the fundamental mechanisms underlying its physiology and pathogenesis are not adequately understood. The objective of this study was to compare and characterize the differentially abundant protein profiles of *M. tuberculosis* lineages 3, 4, 5 and 7.

Methods: Peptide identification and quantitation were performed by label-free quantification LC-MS/MS using a Q Exactive hybrid quadrupole-orbitrap instrument. MaxQuant (MQ) software package was used to perform the MS/MS data analysis. Bioinformatics analysis was performed using the Perseus software. Proteins assigned to enriched term categories ($p < 0.05$) were grouped according to the Kyoto Encyclopedia of Genes and Genomes (KEGG) classification. The GO and KEGG categories of proteins identified were added using the Uniprot annotation for the *M. tuberculosis* reference proteome database (Gene ontology).

Results: A total of 38,346 unique peptides were identified which correspond to 3092 proteins. This represents 77% coverage of the predicted protein-coding genes. More than 81% of the proteins were present in all four *M. tuberculosis* lineages. Compared to other lineages, lineage 7 exhibited downregulation of proteins involved in various metabolic pathways including DNA repair, inorganic phosphate uptake, lipid metabolism, ESX-3 and ESX-1 secretion systems. Proteins involved oxidative phosphorylation and CRISPR/Cas system were up-regulated in lineage 7 than other lineages.

Conclusions: This study presented novel findings regarding the differentially abundant protein profiles of *M. tuberculosis* lineage 7 versus other clinically relevant lineages. The observed less abundant proteins involved in DNA repair, lipid metabolism, ESX-3, ESX-1 secretion systems in lineage 7 strain may contribute to its slow growth and less virulent phenotype. The up regulation

of proteins involved in CRISPR/Cas system and oxidative phosphorylation in lineage 7 may contribute to the reduced drug resistance phenotype and metabolic flexibility observed in Lineage 7 to survive adverse growth conditions during its life cycle, respectively.

OA14-285-26 Matrix metalloproteinases are associated with lung inflammation in HIV-TB co-infected patients initiating ART in South Africa

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Background: HIV-infected patients with pulmonary tuberculosis (pTB) often present with atypical lung involvement, but can develop an inflammatory response with impairments in lung function after antiretroviral therapy (ART) initiation. By highlighting areas with increased metabolic activity, ¹⁸F-FDG PET-CT imaging can identify both pulmonary and extra-pulmonary TB-associated inflammation. We evaluated the association between lung inflammation and

- 1) pro-inflammatory cytokines and
- 2) matrix metalloproteinases (MMP), which degrade lung extracellular matrix, in HIV-TB co-infected patients initiating ART in Johannesburg, South Africa.

Methods: In this prospective cohort study of ART-naïve, HIV-infected patients with GeneXpert positive pTB, PET-CT was used to capture changes in body and lung total glycolytic activity (TGA) before ART initiation (baseline) and at week 4 post-ART. Circulating MMP-8, MMP-9, TNF-, and IL-6 levels were measured by Luminex. Pearson’s and Spearman’s correlation coefficients were used in analyses.

Results: Among 28 participants with biomarker data and a PET-CT at baseline, the median pre-ART CD4 count and viral load were 51 cells/ μ l (IQR: 33-115) and 5.29 log₁₀copies/ml (IQR: 4.96-5.80), respectively. The median time between TB treatment start and ART initiation was 27 days (IQR: 16-41). At baseline, higher lung and body TGA both correlated with higher MMP-8 and MMP-9, with stronger correlations in the lung (MMP-8: $r=0.57$, $p=0.0016$; MMP-9: $r=0.63$, $p=0.003$). TNF-correlated only with body TGA ($r=0.42$, $p=0.025$), while IL-6 was not correlated with either. After 4 weeks of ART, MMP-8 correlated with increases in lung, but not body, TGA ($r=0.57$; $p=0.041$). MMP-9, TNF- and IL-6 did not correlate with increases in lung or body TGA ($p>0.1$).

Conclusions: Elevated MMP-8 levels are associated with high levels of lung-specific inflammation in HIV-TB co-infected patients initiating ART. Analyses evaluating the association between MMPs and lung function are pending. Given the role of MMPs in lung extracellular matrix degradation, these proteases may drive TB-associated lung injury.

OA14-286-26 Acute phase proteins and IP-10 as a first step screening test for TB: could they increase the pre-test probability of a follow-on test?

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Background: Acute-phase proteins (APP) and Interferon-gamma-inducible-protein 10 (IP-10) are non-specific markers associated with inflammation and part of the innate response to injury and infection. APPs are detectable in blood in response to *Mycobacterium tuberculosis* infection and are often used to support a clinical diagnosis of tuberculosis. We speculated that APPs could also be used as triage tests to rule-in or rule-out individuals who should undergo further confirmatory tests for diagnosis.

Methods: We conducted a systematic review and meta-analysis of publications describing APPs and IP-10 for screening or diagnosis of Tuberculosis using Pubmed, Web of Science and Scopus. Authors were contact to request disaggregated information of non-stimulated IP-10. Data of selected papers was extracted using predefined tables and data was analysed using standard systematic review methods.

Results: Fourteen studies were selected for C-Reactive protein (C-RP), six for IP-10 and one for alpha-1-acid glycoprotein (A1AG). C-RP pooled sensitivity/specificity was 88% and 57%, respectively. Sensitivity/specificity were higher in high TB-burden countries (90%/66%), HIV-infected individuals (91%/61%) and community-based studies (91%/65%).

IP-10 studies included diverse populations, precluding the estimation of pooled sensitivity/specificity. The sensitivity/specificity of IP-10 comparing TB vs Non-TB were 85%/68%, TB and HIV co-infection vs. other lung conditions were 90%/55% and TB vs. healthy controls >90%/>90%. A1AG had 86% and 93% sensitivity/specificity.

Conclusions: Most studies used cut offs defined for diagnosis and could be optimised when used for triage purposes. C-RP and IP-10 have high sensitivity and moderate specificity and are potential markers for triage. There are no studies assessing their combined performance and prospective studies are needed.

OA14-287-26 Use of resuscitation promoting factors to screen for tuberculosis infection in exposed children in The Gambia

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Background: Tuberculosis (TB) diagnosis in children remains a challenge and there is a need for more sensitive and specific diagnostic tests for TB infection in endemic regions with diverse *Mycobacterium tuberculosis* complex strains. Whole blood stimulation with Resuscitation promoting factor (Rpf) proteins has been shown to enhance TB diagnosis in adults, but data in children is scarce.

Methods: Whole blood collected from 44 household MTBC-exposed Gambian children below 15 years was stimulated overnight with Phytohemagglutinin (PHA), ESAT-6/CFP-10 (EC), Purified protein derivative (PPD), and RpfA, B, C, D and E. The IFN- production was measured in the supernatant using ELISA in order to detect infected and uninfected children eligible for further TB screening. A parallel stimulation assay with the antigens PPD, EC, RpfD and RpfE was setup to study T cell responses using multiparameter flow cytometry by analysing surface (CD3, CD4, CD8, CD45RA and CD27) and intracellular (IFN-, TNF- and IL-2) marker expression. All the children received a Tuberculin skin test (TST) before providing blood samples.

Results: Based on TST and EC stimulation results, children were classified as truly infected TST+IGRA+ and truly uninfected TST-IGRA-. The AUC of PPD, RpfB and RpfD was respectively 0.90, 0.91, 0.92. RpfB had 70% specificity and 91% sensitivity based on a 40.4 pg/mL IFN- cut off and RpfD had 62% specificity and 100% sensitivity with a cut off of 81.6 pg/mL IFN-. The overall CD4+ and memory CD4+ T cells production of IFN-, IL-2 and TNF- was significantly different between infected and uninfected children in response to PPD but not for RpfD and RpfE.

Conclusions: In conclusion, RpfD could detect infected children with higher accuracy than PPD and the other RpfS based on IFN- response. This result is particularly important within the current global shortage of PPD and needs further investigation.

OA14-288-26 Contribution of pretomanid to the BPamZ regimen in different murine models of tuberculosis

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Background: The BPamZ regimen (Bedaquiline + Pretomanid + Moxifloxacin + Pyrazinamide) shortens the treatment duration needed to cure TB in BALB/c mice by 2.5-3.5 months compared to the first-line regimen and produced nearly 100% sputum culture conversion in MDR-TB patients in a recent phase 2 trial. However, the specific contribution of the investigational new drug pretomanid to the regimen's efficacy has not been examined. We compared the efficacy of BPamZ and BMZ in 3 different mouse strains.

Methods: BALB/c mice and immunodeficient athymic nude mice were aerosol-infected with *M. tuberculosis* H37Rv and C3HeB/FeJ mice were aerosol-infected with the Beijing strain HN878. Treatment with BPamZ or BMZ began 2 weeks (BALB/c, nude) or 6 weeks (C3HeB/FeJ) post-infection. Outcomes included lung CFU counts, relapse rates and selection of bedaquiline-resistant mutants.

Results: After 1 month of treatment, addition of pretomanid to BMZ resulted in additional 1, 1, and 2.4 log₁₀ CFU reductions in BALB/c, nude and C3HeB/FeJ mice, respectively. Although nude mice responded slower than BALB/c mice, 10/10 BPamZ-treated and 7/10 BMZ-treated nude mice were culture-negative after 2 months of treatment. Relapse rates were higher in BMZ-treated vs. BPamZ-treated BALB/c and nude mice. At baseline, 5/5 nude mice harbored bedaquiline-resistant sub-populations of *Rv0678* and/or *pepQ* mutants.

Frameshift mutations in *Rv0678* caused 2-fold higher MICs than SNPs and *pepQ* mutations (0.25 µg/ml). Bedaquiline-resistant isolates were found at relapse in 2 BMZ-treated mice and no BPamZ-treated mice. Among severely-ill C3HeB/FeJ mice with caseous pneumonia and cavitation, median survival was longer with BPamZ vs. BMZ (≥60 vs. 21 days).

After 2 months of treatment, only 2 BMZ-treated mice survived, whereas 9/10 BPamZ-treated mice were culture-negative and the other had 1 CFU detected.

Conclusions: Pretomanid contributed significantly to the efficacy of the BPamZ regimen in 3 different mouse models of TB and reduced the selection of bedaquiline-resistant mutants.

OA14-289-26 Discontinuing universal bacille Calmette-Guérin vaccination in Taiwan: a dynamic modelling study

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Background: *Bacillus Calmette-Guérin* (BCG) is a widely-used vaccine for tuberculosis (TB) control, although its quality of protection has been reported inconsistently. In Taiwan, recent surveys suggested that burden of BCG-induced osteomyelitis/osteitis (BCGO) can be nontrivial. Thus, the risk of BCG might outweigh its benefit, and there is a need to consider the value of discontinuing universal BCG vaccination.

Methods: We developed an age-structured compartmental model to assess health and cost implications of BCG discontinuation in an intermediate TB burden setting like Taiwan. We adopted 'pessimistic' and 'optimistic' scenarios for BCG protection, with distinct assumptions on the duration of protection, and efficacies against infection, progression to pulmonary TB, and progression to extrapulmonary TB. After calibrating the model to the TB notification rates during 2005-2016 in Taiwan, we simulated the effect of discontinuing BCG in 2018, by estimating averted disability-adjusted life years (DALYs) and incremental costs over the subsequent 10 years.

Results: Discontinuing BCG would result in 3.53 (95% uncertainty interval: 1.05 - 7.77) and -0.61 (-3.37 - 3.83) net averted DALYs over 2018-2027 in the pessimistic and optimistic scenarios, respectively. In the pessimistic scenario, health benefits were robustly observed because the additional TB-burden was offset by the avoidance of BCGO, whereas the net health impact was uncertain in the optimistic scenario. In financial terms, regardless of vaccine protection scenarios, the foregone cost of the vaccination programme substantially outweighed the incremental cost for TB treatment. The sensitivity analysis further revealed that the vaccine protection against pulmonary TB was crucial for estimating the health impact.

Conclusions: In Taiwan, the net health impact of discontinuing universal BCG vaccination is particularly sensitive to the quality of protection that BCG provides. These findings are relevant to other intermediate TB burden settings, where modelling analysis and local data on BCG efficacy could be similarly useful in informing future vaccination strategies.

OA15 Finding and treating latent tuberculosis infection

OA15-290-26 Improving the quality of care of TB contacts: a pilot study in Brazil

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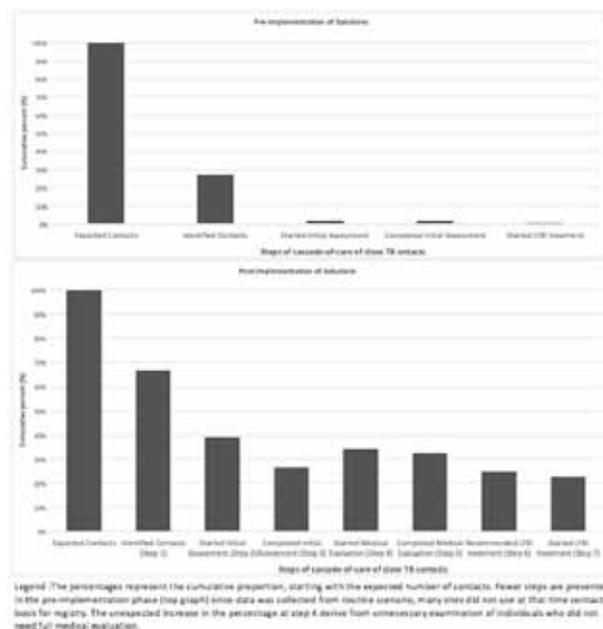
Background: Losses in the cascade-of-care of close TB contacts limits the public health benefits of prevention of active disease through latent TB infection (LTBI) treatment. We conducted a pilot study to develop and evaluate a public health approach to identifying and improving problems in the cascade-of-care of TB contacts in Brazil (Dec2015-Apr2017).

Methods: Twelve clinics in three Brazilian cities underwent a standardized assessment of barriers to identifying, investigating and treating contacts of newly diagnosed index-cases. In order to identify key gaps, questionnaires regarding knowledge, perceptions and practices were administered to TB patients, their contacts and healthcare workers (HCW). Data on TB contact investigation at baseline was also retrospectively collected from clinics. Clinics were then randomized to either implement solutions to address observed gaps or to do nothing. Solutions targeted at specific LTBI cascade gaps were selected by local stakeholders, supported by the investigators. They included the implementation of contact management registry, education and sensitization of HCW, service organization, supervision and training with ongoing feedback related to improvements (or lack of improvement) to the LTBI cascade (Figure). The change in the proportion of contacts starting LTBI treatment pre- and post-implementation of solutions was compared.

Results: The largest gap in the baseline LTBI cascade was identification of contacts. Over time, new bottlenecks appeared as previous steps of the cascade improved. A slow but steady improvement in all steps of the cascade was ultimately observed; treatment initiation increased from 0.5% to 23% of expected eligible contacts ($p < 0.000$, Figure).

Conclusions: Lessons learned in this pilot were the basis for an on-going cluster randomized international trial (ACT4 Trial). After the implementation of solutions

and LTBI program strengthening activities, close follow-up and ongoing in-service training was essential to reinforce new procedures, and to deal with evolving problems in the LTBI cascade. This public health approach seems a promising strategy.



[Cumulative percentage of contacts in the cascade of care pre and post solution implementation]

OA15-291-26 Effective approach: TB screening among close contacts

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Background and challenges to implementation: TB incidence in Cambodia is estimated at approximately 55,200 cases. In 2016, 33,736 cases were notified and 29% (24,164) were missed. Cambodia has adopted contact investigation (CI) at community level to systematically and actively search for TB. CI implementation is limited in scale across the country.

Intervention or response: The USAID Challenge TB project aims to improve early TB case detection and treatment among close contacts of TB patients. Close contacts of all smear positive TB index patient are recorded on a CI form at health facilities where they are registered. This is used by village health support groups (VHSG) from the same villages as the TB index patients. On an appointed date, health center (HC) staff visit the household and perform TB symptom screening. Sputum is collected on site from all those with presumptive TB, including children. Children under five without TB symptoms are given isoniazid preventive therapy (IPT)

in the community. Test results are given to HC staff who then inform the clients. Those with negative smear results are sent to referral hospitals for further evaluation, including chest x-ray

Results and lessons learnt: From July 2015 through December 2017, 81,089 close contacts of smear positive patients were screened for TB, of whom 3,212 (4%) were found to have active TB and initiated treatment, including 1,779 children. In addition, 5,558 under 5 children commenced IPT. TB prevalence among close contacts was therefore 3,961/100,000, which is 6.3 times the national prevalence in the general population.

Conclusions and key recommendations: CI is an effective approach to identify TB cases and initiate treatment to reduce transmission. It provides an opportunity to ensure IPT for children. The assistance of existing VHSG enhances HC staff efforts in case finding and reduces barriers to access for both the poor and key populations.

Year	# of close contacts	# of close contacts met and screened	# of Presumptive TB	# of TB diagnosed	# of IPT initiated
2015	11,910	9,767	1,172	127	1,104
2016	27,910	22,126	5,825	603	1,877
2017	56,191	49,196	12,965	2482	2,577

[Table: Results of contact investigation, July 2015 - December 2017]

OA15-292-26 Enhancing the public health impact of latent tuberculosis infection management (ACT4): results from Ghana

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Background: Latent tuberculosis (LTBI) management for household contacts (HHC) of patients with pulmonary tuberculosis has been recognized as a priority by the World Health Organization. Among existing LTBI management programs, large gaps (patient losses) throughout the LTBI cascade of care have been demonstrated. The largest proportion of losses occurred prior to treatment start.

The primary objective of the ACT4 study was to evaluate a programmatic package to increase the proportion of HHCs starting LTBI treatment. Interim results from the intervention site at St. Patrick's hospital in Offinso, Ghana are presented here.

Methods: The ACT4 study is a pragmatic cluster randomized trial at 24 health facilities in 5 countries. The intervention group received a complex two-phase inter-

vention lasting 18 months (November 2016-April 2018). In Phase 1, sites performed a standardized public health evaluation to identify and understand local gaps and barriers to care. Context-specific "solutions" were then developed at each site in collaboration with the main study personnel. In Phase 2, sites implemented program strengthening activities and their site-specific solutions. **Results:** Identified barriers for LTBI management in Ghana included knowledge, stigma, and cost. Implemented solutions included community stigma reduction activities, home visits for HHC identification and testing, and reimbursement for x-ray and travel costs. Interim analyses performed in February 2018, 6 months after implementation of the "solutions", demonstrated a significant increase in the proportion of HHCs who completed initial assessment (13/108 (12%) versus 136/145(94%) (p <0.05)) and who started on LTBI treatment (0/13(0%) versus 79/80(98%) (p <0.05)) at baseline versus 6 months after solution implementation, respectively.

Conclusions: Using a programmatic approach to develop and implement context specific solutions and program strengthening successfully increased the proportion of HHCs who completed initial testing and started on LTBI treatment. This approach may support improvement and scale-up for LTBI management in other settings.

OA15-293-26 Integrated care and patient choice enable treatment completion of isoniazid preventive therapy in Swaziland

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Background: Despite Ministry of Health endorsement, uptake and treatment completion of Isoniazid Preventive Therapy (IPT) in Swaziland had been poor. To improve IPT uptake and outcomes, we conducted a prospective cohort study in 2015-16 at five HIV care facilities to determine an effective model for IPT delivery using patient preferences. Our findings showed that a model of self-selected community- or facility-based IPT delivery aligned with antiretroviral therapy (ART) refills achieved high rates of adherence (94.8%) and treatment completion (89.4%). We conducted an immediate follow-up study to identify the key factors that favorably influenced patient adherence and treatment completion.

Methods: In this retrospective, mixed methods study, trained researchers interviewed participants who completed IPT during the prior study stratified across delivery model, enrollment site, and basic demographics. Qualitative data were analyzed using thematic analysis.

Results: Between June and October 2017, we interviewed 150 participants who completed IPT in the prior year. Fourteen participants did not recall being offered a choice and were excluded from analysis. Of the remaining 136, 56.6% were female and median age was 42.5 years (IQR 26.5 - 42.5 years). All participants (100%) reported that being offered a choice was important to their treatment completion. Nearly all (98.5%) reported that linking their IPT refills with ART pick-up was very important to facilitate taking IPT. Participants were knowledgeable about the benefits of taking IPT and valued the education they received from the nurses. The results also revealed a high rate of disclosure (95%) to friends and family members among those that completed IPT.

Conclusions: Offering patients a choice in IPT delivery, linking ART and IPT pick-up, emphasizing patient education and engagement with healthcare workers, and supporting appropriate disclosure of IPT are critical factors to enabling IPT completion. These interventions should be incorporated elsewhere in Swaziland and in other similar high TB-HIV burden settings.

OA15-294-26 Active case finding of tuberculosis among household contacts in Bangladesh: lessons learned from Challenge TB contact investigation pilot

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Background and challenges to implementation: Despite the success of tuberculosis (TB) control in Bangladesh, about 39% of estimated TB cases remain undetected every year. Globally, growing evidence suggests the effectiveness of active case finding (ACF) and contact investigation (CI) for TB in high burden settings. The Challenge TB (CTB) Project collaborated with NTP to conduct a pilot in the Sylhet and Faridpur districts of Bangladesh to explore a systematic CI implementation and reporting strategy.

Intervention or response: CTB jointly with NTP conducted a baseline CI assessment in seven divisions and developed a draft Standard Operating Procedure (SOP) and recording/reporting formats for both drug-sensitive TB (DS-TB) and drug-resistant TB (DR-TB). A CI pilot was conducted in two selected districts from January to

June 2017 using the draft formats where 774 government and NGO health care workers (HCWs) who conducted household CI in intervention districts were trained.

Results and lessons learnt: Over a period six months, a total of 4,862 contacts of 1,314 index TB cases were screened in pilot areas and 476 (10%) TB presumptive cases were identified. Among the presumptive cases, 240 (50%) contacts underwent clinical and diagnostic evaluations and 20 (4% of the presumptive) DS-TB cases were diagnosed and enrolled for treatment. Further, 187 contacts of 37 DR-TB index cases were screened, but no DR-TB cases were found among those contacts. Prevalence among the adult contacts screened was 287/100,000, the same as the national prevalence 287/100,000. (Ref: National TB prevalence survey, 2014-15.

	Total screened	Total presumptive	Clinically evaluated	Total diagnosed
Male	2,436	242	129	7
Female	2,426	234	111	13
Total	4,862	476 (10%)	240 (50%)	20 (% of the presumptive)

[Sex distribution of the cases from contact investigations]

Conclusions and key recommendations: The pilot data indicates that targeted household contact investigation substantially increased missing case notification during the intervention period. Based on the experience of the pilot, NTP is now expanding ACF and CI approaches countrywide with minor revisions in SOP and reporting systems.

OA15-295-26 Family matrix-guided HIV and tuberculosis case finding using index patients as an entry point at four urban sites in Ethiopia

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Background and challenges to implementation: Both HIV and TB are family diseases, but approaches to case finding in the programs for them have often followed distinct strategies. In HIV programs, family members of people living with HIV (PLHIV) are screened for HIV but not for TB, and the reverse is true for TB patients. We combined HIV and TB screening for family members of both TB patients and PLHIV to assess the yield of dual TB-HIV screening in selected clinics in four urban areas of Ethiopia.

Intervention or response: We conducted this study in 14 clinics of four towns of Ethiopia between August 2017-January 2018. Towns with TB-HIV co-infection

rate >10% were selected for this intervention. Trained health workers visited homes of patients and conducted TB screening and HIV testing on the household contacts of patients. TB screening was symptom-based and diagnosis was confirmed by Gene Xpert. We used rapid HIV test kits for HIV diagnosis. We computed TB case detection rates and HIV sero-positivity rates, and conducted multivariable logistic regression analysis to identify factors associated with the yield of TB and HIV.

Results and lessons learnt: We screened family members of 114 TB patients, 80 PLHIV and 20 TB-HIV co-infected index cases. Of 527 family members screened, 198 (38%) presumptive TB and 44 (8.3%) definitive TB patients were detected. The proportion of family members diagnosed with TB was 9.4%, 1.2% and 5% respectively among TB only, HIV+ only, and TB-HIV co-infected groups respectively (Table). HIV positivity rate was same (2.6%) both for contacts of “TB only” and “HIV only” index cases while the rate was 11.6% among contacts of TB-HIV co-infected index cases. There was no significant association between type index cases and TB case ($p>0.1$).

Conclusions and key recommendations: Family members of both TB patients and PLHIV should be targeted as key population groups both for TB and HIV.

Variables	TB only index cases	HIV+ only “index cases”	TB/HIV “index case”	All HIV + (HIV only & TB/HIV) index cases	All PTB (TB only & TB/HIV) index cases
Number of “index” cases	114	80	20	100	134
Number of family members screened for TB	406	163	121	284	527
Number (%) of TB cases identified	38 (9.4)	2 (1.2)	6 (5.0)	8 (2.8)	44 (8.3)
Number (%) HIV positive among tested	3 (2.6)	4 (2.6)	8 (11.6)	12 (5.5)	11 (5.9)

[The proportion of TB and HIV among the screened and tested families and contacts of PLHIV and TB patients, August 2017-January 2018]

OA15-296-26 ‘Contact tracing’ beyond household in MDR TB patients: how effective?

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Background and challenges to implementation: Pakistan is among the world’s high-burden countries for drug-susceptible (DS) and DR-TB, with an estimated 14000 new DR-TB patients (respectively 4.2% and 16% of new and retreatment patients) in 2016. Approximately 4 million of the global estimated TB patients are missed from care, and Pakistan ranks third among the

12 countries that contribute 75% of missing TB cases. Several innovative interventions are being recommended to detect the remaining ‘missed’ TB cases. One such intervention involved expanding contact investigation to the community.

Intervention or response: Passive case finding and household contact investigation was routinely done. In this prospective cohort study contact investigation beyond household was done in two districts Islamabad and Rawalpindi. All people staying within a radius of 50 metres (using Geographical Information System) from the household of Drug Resistance (DR) TB patients were screened for tuberculosis using the GIS technologies. Those with presumptive TB were investigated using Xpert MTB/RIF test. All the diagnosed TB patients were linked to TB treatment and care.

Results and lessons learnt: A total of 4571 contacts were screened for tuberculosis symptoms, of whom 703 were household contacts and 3868 were close community contacts. A total of 461 (10.1%) presumptive TB patients were identified and of whom, 367 (79.6%) presumptive TB patients were investigated for Xpert testing. Among investigated, 78 (21.2%) were bacteriologically confirmed TB patients. Of the diagnosed TB patients detected as a result of this intervention, 77 (98.7%) were initiated on treatment.

Conclusions and key recommendations: Community contact investigation beyond household not only detected additional TB patients but also increased TB case detection. However, further long term assessments and cost effectiveness studies are required before national scale-up.

OA15-297-26 Contribution of sustained contact investigation for case notification in North Western Sidama Zone in Southern Ethiopia

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Background: Contact investigation (CI) is a proven means to identify new Tuberculosis (TB) cases in the community. However, the practice of conducting CI at community level is gaining momentum only recently. The objective of this study was to determine the level of contribution towards case notification.

Methods: An observational study was conducted from January 2011 to December 2013 using unit TB registers in health facilities (HFs) in Sidama Zone, Southern Nations Nationalities and Peoples Region (SNNPR) of Ethiopia. Health extension workers (HEWs) identified presumptive TB cases during their routine house to house visits. HEWs in the health posts, collected two sputum specimens and referred smeared slides to HFs for diagnosis. HEWs and district TB supervisors conducted household visits at treatment initiation for index

TB cases to conduct CI for household contacts (HHCs) whenever pulmonary TB positive (PTB+) cases were identified either through active or passive case finding. HEWs frequently screened and followed up symptomatic HHCs. TB cases diagnosed among HHCs during the first visit were considered prevalent and excluded from analysis. Follow-up started from treatment start date for index cases and ended when HHCs developed TB or were last observed. Diagnosis of TB was made using smear-microscopy, chest X-rays, or clinically according to the national guideline.

Results: 1,421 HHCs of 325 index cases were screened and followed-up for a median of 1.2 years (IQR: 0.59-1.83) with 1,673 cumulative PY observations. CI identified 46 additional TB cases. It contributed to 12% (46/371) of all TB cases diagnosed in this period making TB incidence among HHCs 2,750/100,000 PY observations.

Conclusions: Contribution of contact investigation to case finding was found to be significant even after implementing intensified TB case finding by HEWs through routine household visit to identify TB cases.



[Contribution of Contact Investigation for Case Notification in North Western Sidama Zone in SNNPR, Ethiopia 2011 - 2013]

OA16 Air pollution and ecology of illness

OA16-298-26 Association between household air pollution and lung function among rural women: a population-based study in Odisha, India

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Background: Currently, about 70% of India's population lives in rural areas and most of the households use some form of solid fuels for domestic energy, resulting in widespread exposure to household air pollution (HAP). Despite the high burden of disease from HAP, it has not received the same attention as other disease risk factors in India.

We examined the relationship between indoor particulate matter (PM₁₀ and PM_{2.5}), exposures and lung function among women.

Methods: A population based cross-sectional survey was conducted in rural Odisha, India. 1250 women (aged 18-49 years) were included for lung function measurements. Basic socio-demographic information was collected by using standard questionnaire and lung function was measured by spirometric tests. 70 representative households were included for measurement of 24-hour concentrations of indoor PM₁₀ and PM_{2.5} using portable air samplers. Associations between household particulate matter concentrations and lung function were assessed by multivariate regression models, controlling for the effects of age, height, weight, tobacco smoke, asthma diagnosis, and socioeconomic status.

Results: 24-hour mean \pm SD PM₁₀ and PM_{2.5} level was 88.6 ± 31.2 and $126.3 \pm 18.4 \mu\text{g}/\text{m}^3$ respectively, and primarily associated with household cooking behaviour. Study participants living in homes that use solid biomass fuel had lower peak expiratory flow (PEF), forced vital capacity (FVC) and lower forced expiratory volume in 1 s (FEV₁) ($P < 0.05$). In multivariate analysis, PM_{2.5} (per interquartile range increase) was associated with a 1.25% decrease [95% confidence interval (CI), -3.2% to -1.1%] in FEV₁, a 0.5% decrease (95% CI, -1.8% to 0.7%) in forced vital capacity, and a 2.8% decrease (95% CI, -5.3% to -0.7%) in PEF.

Conclusions: In this study, household PM_{2.5} levels independently predicted decreased lung function and urged for public health interventions.

OA16-299-26 Household air pollution and tuberculosis in India: analysis of District Level Household Survey-IV, a nationally representative survey in India

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Background: In developing countries, air pollution tends to be highest indoors, where biomass fuels are burnt by 80% of households for cooking and space heating. Globally, 4.3 million deaths were attributable to household air pollution (HAP) in 2012. In India, about three-quarters of households use unprocessed biomass (like wood, charcoal, dung cakes, kerosene, crop waste etc.) as their primary fuel for cooking food.

Although a known risk factor for several respiratory diseases, the relationship between cooking smoke and tuberculosis has not been conclusively established. Therefore the present study was planned to study the association between use of solid/biomass fuels for cooking in households and the prevalence of tuberculosis in a nationally representative sample of households in India, after statistically controlling for the effects of several potentially confounding variables.

Methods: We analyzed data from 1, 80, 917 households in the District Level Household Survey IV conducted in India to investigate the association between household use of cooking fuels (liquid petroleum gas/electricity, kerosene, biomass) and the risk of Tuberculosis. Prevalence ratios were obtained using Poisson regression with robust standard errors after controlling for potential confounders.

Results: Households using firewood/biomass (PR 1.4; 95% CI: 1.2-1.7, $p=0.001$) were more likely to have a TB case compared to electricity. Other household level actors associated with occurrence of TB were place of residence, religion, caste of the head of the household, wealth index, smoking at home, presence of separate room for kitchen, presence of windows and overcrowding. The population attributable risk of firewood as cooking fuel for TB in India was 13%.

Conclusions: Biomass cooking fuels are associated with TB occurrence. Assuming these associations are causal, about 13% of TB in India could be prevented by providing access to cleaner cooking fuel.

OA16-300-26 Heat effects of ambient apparent temperature on respiratory disease mortality in six major cities in South Africa: 2006-2010

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Background: Due to climate change, an increase of 3-4°C in ambient temperature is projected along the South African coast and 6-7 °C inland during the next 80 years. Very few epidemiology studies have been conducted in Africa on heat effects of ambient temperature indicators on human health and none which also controlled for possible confounding by air pollution.

Methods: Six cities were included in the study: Cape Town, Durban, East London, Port Elizabeth, Pretoria and Johannesburg. The cities are located in different Köppen-Geiger climatic zones. Individual level respiratory disease (RD) (ICD10: J00-J99) mortality data were obtained from Statistics South Africa, after ethics approval. PM10, temperature and relative humidity data were obtained from the South African Weather Services. The time-series and case-crossover epidemiological study designs were applied. The heat effect was investigated for Tapp above the city-specific thresholds. Lag0-1 was applied in the models, i.e. average Tapp on the day before and on the day of death. The regression models were adjusted for PM10 (lag0-1); if available. The effect estimates of the six cities were combined in a meta-analysis.

Results: A total of 79 217 RD deaths occurred in the six cities. No heat waves occurred. The city-specific Tapp thresholds were in general close to the 75th city-specific Tapp value, and ranged from 6.6°C to 26.4°C. The

daily mean PM₁₀ level was 32.7, 33.9 and 59.5 µg/m³, respectively in Cape Town, Durban and Johannesburg. PM₁₀ levels regularly exceeded the WHO daily guideline (50 µg/m³). RD mortality increased by 0.50% (95% CI 0.03%, 1.03%) [J1] in the six cities per 1°C increase above city-specific Tapp thresholds. Stronger associations were observed for the elderly (≥65 years).

Conclusions: This study is very relevant in stressing the importance of increasing Tapp on RD mortality risk in South Africa, especially among the elderly.

OA16-301-26 Associations between solid fuel use and low birth weight in Indonesia

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Background: Nearly 3 billion people live in household's dependent on polluting solid fuels for cooking. Women and children are most exposed to the resulting household air pollution, which causes low birthweight, still-birth, pediatric pneumonia, and adult cardiopulmonary disease. Despite expanded access to clean energy, 40% of households in Indonesia still rely on polluting solid fuels for cooking and heating. This study assessed the population-level impact of household air pollution on household risk of having a low birth weight child in homes using clean fuels compared to homes using polluting solid fuels for cooking in Indonesia.

Methods: Household data from the 2012 Demographic and Health Survey was analyzed to determine type of cooking fuel used and the birth weight of all children born in the household in the 5 years prior to the survey. Type of cooking fuel was dichotomized as clean fuels (liquefied petroleum gas, or LPG) and biomass or dirty fuels (wood). Birthweight was also dichotomized as at or above average (≥2.5 kg) and below average (< 2.5 kg). A ² analysis and multiple logistic regression were performed to assess associations between fuel type and birth weight status.

Results: 11.8% of households that cooked or heated their homes with clean fuels (LPG) had a low birth weight baby, compared to 17.1% of households that cooked or heated their homes with dirty fuels (wood). Furthermore, respondents in households cooking with biomass fuels had 1.4 times the odds of having a low birth weight baby compared to those in households who cooked with clean fuels. .

Conclusions: Low birth weight is associated with increased risk of infant mortality and can impact healthy childhood development. Households should therefore be educated on the dangers of exposure to smoke from solid fuels and cleaner technologies should be made accessible and scaled up to ensure sustained use.

OA16-302-26 Citizen science on air pollution

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Background and challenges to implementation: In the Netherlands air pollution levels, i.e. for particulate matter and nitrous oxides, have been decreasing over the past decades and this is expected to continue in the coming years. Although almost everywhere in the Netherlands the European Union Air Quality Limit Values (AQLV's) are met, there is an increasing awareness of the health impact of long term exposure to these remaining levels of air pollution.

A growing group of citizens is expressing their concern about this health impact and wants to be involved in the discussion on air pollution levels, possible measures and policies, behavioural change, et cetera.

Intervention or response: One of the developments is 'citizen science', where people actively participate in data gathering and analysis, e.g. by measuring air pollution levels in specific local situations on a regular basis applying low cost methods. This raises the awareness and involvement of people regarding their own contribution to possible solutions, ultimately lowering the threshold for the acceptance of new measures by government actors. At the mean time this evolution challenges authorities to deal with this new source of information and subsequently the people's demand for action.

Results and lessons learnt: Different practical examples of citizen science approaches are presented, focusing on:

- Involving citizens to raise the level of awareness, stimulate clean healthy behaviour and support air quality policy measures
- Application of smart sensing systems and monitoring of effectiveness of the applied technical measures.
- Application of an online toolbox, allowing citizens to measure the air quality and the effectiveness of measures taken by themselves.

Results show the commitment of the people involved, but also raises discussion among scientists and policy makers.

Conclusions and key recommendations: The possibilities and challenges of citizen science need to be further explored. This is one of the subjects in the EU Interreg project "Clean air" (2018-2020) through cooperation between partners in the Netherlands and Belgium.

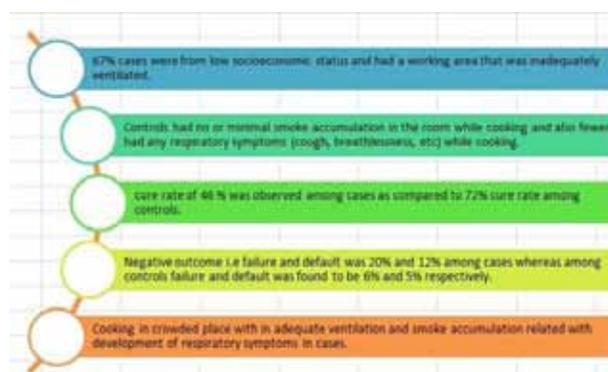
OA16-303-26 Is indoor air pollution derailing the efforts of the TB control programme? Impact study of indoor air pollution on pulmonary tuberculosis patients in rural India

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Background: Indoor air pollution (IAP) from combustion of solid biomass fuel (SBF) such as dried-dung, wood and crop residue for cooking, has emerged as an important risk factor in the pathogenesis, prevalence, morbidity and mortality from chronic respiratory diseases, frequent occurrence of respiratory infections and lung function impairment. In spite of all advances, SBF is being used by more than 70% rural females. The objective of the study was to ascertain impact of IAP on pulmonary TB treatment outcome of females.

Methods: 200 female new sputum positive TB cases who were exposed daily to smoke from SBF for at-least 4 hours from 10 rural districts of Maharashtra, India were prospectively followed from 1st quarter 2017 till treatment outcome was declared according to NTP guidelines. Control of 100 females having pulmonary TB not exposed to daily smoke from SBF was also included. The questionnaire elicited information regarding the demographic data, type of SBF used, average hours exposed to smoke, socio economic status, use of separate kitchen and respiratory symptoms during cooking. This was followed by interview of the patients.

Results: Please refer to Figure-1



[Figure 1. WLC-4]

Qualitatively, it was found out that due to IAP, there was continuous symptoms related to cough and breathing problems which aggravated patient's lung health leading to disbelief in current treatment and defaulting due to no improvement in patient's lung condition.

Conclusions: IAP from SBF is a major concern in developing countries in relation to lung health. In the present study we observed association between exposure to smoke by SBF and negative outcome amongst

TB patients. The study is important as it brings out the pathway in which a TB patient loses hope in the system due to environmental effects not under the control of TB programme.

OA16-304-26 Relationship between daily air pollutants and emergency room visits of children with acute respiratory symptoms in Delhi, India

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Background: Air pollution is one of the leading causes for acute and chronic respiratory disease exacerbations and frequent emergency visits. However, epidemiological studies on air pollution in relation with acute respiratory symptoms in Delhi, India are limited. Therefore, we aimed to evaluate the association between daily air pollutant levels and daily emergency room (ER) visits of children with acute respiratory symptoms (ARS).

Methods: Cross-sectional study was carried out from June 17-December 17. Daily data for children (< 15 years of age) visiting Pediatric ER of the All India Institute of Medical Sciences, Delhi, India with physician diagnosed acute onset (less than 2 weeks) of respiratory symptoms (ARS) - were obtained. Daily air pollutant levels for particulate matter (PM) 10, PM 2.5, oxides of nitrogen, nitric oxide, sulphur dioxide and carbon monoxide were obtained from the Delhi Pollution Control Committee. Data on daily number of visits to ER of children with ARS were correlated with daily air pollutant levels using Spearman correlation coefficient.

Results: A total number of 17192 patients were screened who attended ER; of these 3080, patients with ARS were enrolled. Number of children with ARS attending ER daily were significantly and positively associated with daily levels of PM 2.5 ($r=0.136$, $p=0.047$), oxides of nitrogen ($r=0.159$, $p=0.020$), nitric oxide ($r=0.201$, $p=0.003$), sulphur dioxide ($r=0.161$, $p=0.018$) and carbon monoxide ($r=0.167$, $p=0.015$).

Conclusions: These observations suggested that daily air pollutant levels are directly associated with emergency room visits of children having acute respiratory symptoms. Results of this preliminary study can help in developing respiratory health management measures for children residing in Delhi, India.

OA16-305-26 Severity of air pollution in New Delhi and burden of paediatric respiratory illnesses - an ecological study

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Background: The air pollution is becoming a serious public health problem in India. New Delhi is considered as one of the most polluted cities in the world. There is paucity of data on its relationship with pediatric respiratory illnesses. This study was conducted with objective to determine correlation between severity of air pollution levels in New Delhi and burden of childhood respiratory illnesses over a period of six years - 2011-2016. **Methods:** An ecological study was conducted by collecting secondary data on air pollution levels and childhood respiratory illnesses in Delhi over a period of 2011-2016. Data on air pollution was taken from Delhi Pollution Control Board. Total and month wise distribution of number of cases of childhood respiratory illnesses as per ICD-10 classification reported from a period of year 2011-2016 in a secondary level hospital in a rural area in Delhi was collected. Data was analyzed to find any correlation between the average air pollution levels over the years and proportion of cases of childhood respiratory illnesses out of total number of patients reported.

Results: The mean PM10 levels was 249.5 microgram/m³ while mean Nitrogen oxide (NO₂) was 58.6 microgram/m³ which were higher than permissible levels in India. Overall Air Quality Index (AQI) fell in the category of poor/very poor. The average air pollution levels was increasing from 2011-2016. There was significant correlation ($p < 0.05$) between PM10 levels and proportion of childhood respiratory illnesses out of total cases reported in the hospital.

Conclusions: There was a significant correlation between air pollution levels and childhood respiratory illnesses. There is urgent need to make policy changes to control air pollution.

OA18 Innovative treatment for multidrug-resistant tuberculosis

OA18-306-26 Characteristics of patients with drug-resistant TB in Eastern Europe/Central Asia and determinants of their treatment outcome

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Background: DR-TB is a major challenge in Eastern Europe/Central Asia and its treatment outcome has been poor.

Methods: Charts of patients with DR-TB registered in 2013 were reviewed in health facilities in Ukraine, Romania, Belarus, Tajikistan and Azerbaijan.

Results: Data from 212 patients (77 from Romania, 65 from Ukraine, 30 from Azerbaijan, 23 from Tajikistan, and 17 from Belarus) were analysed.

71% were male and 25% were employed when they were diagnosed with DR-TB. At baseline, 30.2% had history of regular alcohol consumption, 5.2% used illicit drugs, 10.8% had a history of detention and 7.1% were homeless. The table presents additional findings.

At baseline, 47% had resistance to RH plus some other first-line drugs, 16% were resistance to RH only and 2.4% were resistant to R only. 21.7% had pre-XDR, 9% had XDR-TB.

81% of the patients were hospitalised, 65.2% for at least two months. During ambulatory care, 78.5% of the patients had health facility-based DOT and 10.3% home-based DOT.

The culture status at two months was available for 191 cases; 34.4% were still culture-positive.

For 191 patients there was a definite treatment outcome; 58.6% were successfully treated, 19.4% failed, 12.6% died, and 9.4% lost to follow-up.

Univariate analysis found five significant risk factors for poor treatment outcome: homelessness (odds ratio 10.7); body mass index below 18.5 kg/m² (OR 4.7); previous treatment with second-line drugs (OR 3.8); culture-positivity at two months of treatment (OR 3.1);

and bilateral disease with at least one cavity (OR 2.4). HIV-positivity was clearly not significant (OR 1.4). Independent risk factors were homelessness (adjusted OR 9.6; 95% CI 2.3 - 66); culture-positivity at two months of treatment (aOR 2.5; 1.2 - 5.1); and previous treatment with second-line drugs (aOR 2.9; 1.3 - 6.9).

Conclusions: Social support, patients-centred treatment and regimens with new TB drugs could improve DR-TB treatment outcome.

Patient feature	Yes	No	Unclear / not available	Remarks
HIV-positive	20 (9.4%)	181 (85.4%)	11 (5.2%)	16 of the 20 were from Ukraine
Bilateral disease with at least 1 cavity	76 (35.8%)	132 (62.3%)	4 (1.9%)	
At least one previous TB treatment episode of at least 1 month	137 (64.6%)	75 (35.4%)	0	14.2% had between 3 and 9 previous treatment episodes
At least one previous DR-TB treatment episode of at least 1 month	42 (19.8%)	169 (79.7%)	1 (0.5%)	

[Characteristics of the 212 patients at baseline]

OA18-307-26 Efficacy, safety and tolerability profile of linezolid containing regimens in the treatment of drug-resistant pulmonary tuberculosis in Georgia

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Background: WHO guidelines include linezolid among core second-line drugs for patients with limited therapeutic options; however, close monitoring for toxicity is recommended. We sought to assess efficacy, safety and tolerability of linezolid containing regimens in the treatment of DR-PTB in Georgia.

Methods: A retrospective cohort study was conducted among DR-PTB patients who started treatment with linezolid containing regimens from July, 2014, through June, 2015, within the National TB Program. Treatment regimens varied but also included standard second-line drugs as well as other new and re-purposed drugs including bedaquiline, delamanid, clofazimine, and imipenem/cilastatin. Patients with XDR-TB or treatment non-responsive/intolerant MDR-TB were eligible for linezolid therapy. Initial linezolid dose was 600 mg once daily. Treatment drug monitoring was provided according to WHO recommendations.

Results: A total of 60 patients with mean age of 38 years started linezolid-containing regimens; 47 (78%) were male, 46 (77%) had a previous history of TB (33

of whom had failed prior treatment), 38 (63%) ≥ 1 comorbidities, and 44 (73%) had XDR-TB. Linezolid was prematurely discontinued in 1 patient (2%) due to peripheral neuropathy on the 6th month of treatment. Linezolid dose was reduced to 300 mg in 3 patients (5%) due to peripheral neuropathy (on 6th, 3rd and 13th month respectively) and in 2 (2%) cases due to thrombocytopenia (on 4th and 16th month respectively). Hepatotoxicity developed in 12 (20%) cases, which was not related to linezolid. Culture conversion was achieved in 54 (90%) cases with mean time of 77(SD 63) days. Overall, forty-five (75%) patients had successful outcome, 44 (73%) of whom finished a full course of linezolid (up to two years), 8 (13%) were lost to follow-up, and 7 (12%) died. **Conclusions:** Long treatment regimens of linezolid were well tolerated with few limiting side effects and were associated with high rates of culture conversion and favorable outcomes.

OA18-308-26 Bedaquiline containing regimens in the treatment of multi- and extensively drug-resistant tuberculosis at the programmatic level: prospective cohort study

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Background: To improve treatment outcomes in patients with multi- and extensively drug-resistant tuberculosis (M/XDR-TB) bedaquiline (BDQ) was programmatically introduced in Belarus in July 2015.

Methods: The national TB program developed measures to monitor safety and effectiveness BDQ containing regimens prospectively in the cohort study in line with the World Health Organization recommendations.

Results: Currently by March 31, 2018 181 patients had final treatment outcomes: 73% males; 42% new and 58% previously treated; 64% XDR-TB; 31% pre-XDR-TB (17% FQ and 14% Injectables resistant); 5% MDR-TB. After exclusion 3 dead and 8 lost in the rest 170 patients sputum culture conversion rates were at: 2 months (mo.) - 70%; 4 mo. - 94%; 6 mo. - 97%. All patients experienced adverse events (AE). The most common adverse events were: hyperuricemia, liver function tests abnormalities, hypokalemia, hypomagnesaemia, cardiac arrhythmia, nausea, vomiting, abdominal pain, anemia, low platelet count, creatinine clearance decrease, paresthesia, hearing loss. Most of the AE were mild and moderate and did not cause BDQ withdrawal or regimen stop. The following final treatment outcomes were recorded: treatment success - 168 (93%): cure - 144 (80%), treatment completed 24 (13%); treatment failed 2 (1%); lost to follow up - 8 (4%); death - 3 (2%).

Conclusions: The results of our large prospective cohort study showed fast bacteriological conversion, satisfactory safety profile, and excellent final treatment outcomes even in the cohort with a significant proportion of XDR-TB cases.

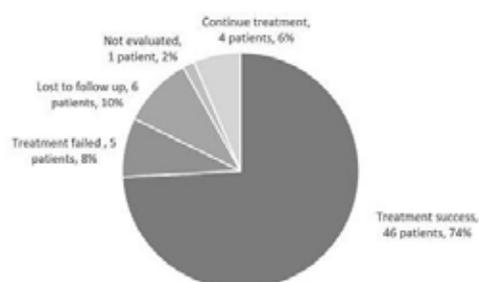
OA18-309-26 Shorter treatment regimen for multidrug-resistant tuberculosis: first outcomes in the Kyrgyz Republic

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Background: Many countries in the World Health Organization (WHO) Euro region were hesitating to introduce the shorter treatment regimen (STR) for multidrug-resistant tuberculosis (MDR-TB) as WHO recommendations were based on data from settings with lower levels of resistance to second line drugs (SLD). The Kyrgyz Republic (KR) is one of 25 high MDR-TB burden countries; 25% of new and 60% of retreatment cases have MDR-TB (2016). From the 2014 MDR-TB cohort, only 55% were successfully treated, 22% patients were lost to follow-up (LTFU). The objective of this analysis was to evaluate treatment outcomes for MDR-TB patients enrolled on treatment with STR in KR.

Methods: MDR-TB treatment with STR in KR was initiated in January 2017 in two pilot sites - Bishkek city and Chui oblast. MDR-TB patients with confirmed baseline susceptibility or considered at low risk of resistance to fluoroquinolones (FQ) and second line injectables (SLI) according to pre-set criteria were enrolled on STR. We describe treatment outcomes of MDR-TB patients started on STR in 2017.

Results: In 2017, 129 patients, including 20 children and 8 adolescents, started treatment with STR. Among the 62 patients who started treatment in January-June 2017, 46 (74%) were treated successfully (see Figure).



[Treatment outcome of MDR-TB patients initiated on the STR in KR in January-June 2017. Data as per April 1, 2018]

After two months of treatment, 60% of patients had negative culture results, and 84% patients after six months. For 37 patients (60%), the intensive phase was extended, mainly because culture results were not known on time to fulfill requirements.

Conclusions: Although these are just preliminary results, the experience in KR shows that with the proper evaluation of eligibility criteria, the efficiency of STR is good under programmatic conditions, even in a country with a high level of resistance to SLDs. Based on these experiences, STR will be introduced in all regions of KR in 2018.

OA18-310-26 First results of shorter treatment regimen use in treatment of multidrug-resistant patients in Tajikistan

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Background: Multi-drug-resistant tuberculosis (MDR-TB) occurs frequently among both new and previously treated patients in Tajikistan. Levels of resistance to first-line drugs and to fluoroquinolones and second-injectable drugs are high. Therefore, the introduction of the shorter treatment regimen (STR) was facing some skepticism in the country.

Methods: The KNCV Patient triage approach was introduced under the USAID Challenge TB project for enrolment on STR based on results of the second line Line probe assay (SL LPA) and/or risk factors for SL drug resistance. We analyzed treatment outcomes of MDR-TB patients enrolled on STR in 7 CTB pilot sites (Dushanbe and 6 suburbs) from December 2016 to December 2017.

Results: In total, 75 patients were enrolled on STR. Among them, 69 (92%) were new TB cases, while 6 (8%) had been previously treated for TB. Forty patients (53%) started outpatient treatment from the first day. Three patients (4%) were HIV positive. Nine (22%) patients were switched to individualized regimens (excluded from STR outcome analysis) upon obtaining DST results confirming drug resistance to SLDs - as SL LPA was not available at that time results were obtained after on average two months after enrolment. Final STR treatment outcomes for 32 patients who started treatment between December 15, 2016 and June 30, 2017: 23 (72%) successfully completed treatment, 5 (16%) are still on treatment, 2 (6%) were lost to follow up and for 2 (6%), treatment failed.

Conclusions: Preliminary treatment results of first TB patients on STR are promising and show that it is possible to implement STR even in countries with high levels of drug resistance. It does require very precise analysis

of patient information (history of disease, contacts with TB patients, treatment tolerability) in order to assess the risk of resistance to SLDs.

OA18-311-26 A comparison of medical versus medical and adjunctive surgical treatment of patients with cavitary multidrug-resistant tuberculosis

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Background: Available data suggest adjunctive surgical resection may improve treatment outcomes among patients with multi and extensively drug-resistant pulmonary tuberculosis (M/XDR-PTB); however, most studies are case series. We sought to evaluate the impact of surgery by comparing outcomes among patients with cavitary disease who received medical versus medical and surgical treatment.

Methods: A retrospective observational cohort of patients with cavitary M/XDR-PTB treated in Tbilisi, Georgia between 2008-2012. Indications for surgery included:

- i) failed medical treatment with persistent sputum positivity,
- ii) extensive drug-resistance where failure was likely and
- iii) persistent localized cavitary disease among medically treated sputum negative patients. We used ² tests to compare proportions achieving favourable treatment outcomes (cured or completed).

Results: A total of 408 patients were included; 299 receiving medical treatment alone and 109 receiving medical treatment along with adjunctive surgical resection. Patients in the non-surgical group were older, had higher rates of tobacco and alcohol use, were more likely to be retreatment cases and had higher rates of bilateral disease compared to the surgical group (all with $p < 0.05$). Patients in the surgical group had higher rates of XDR disease, ($p < 0.05$). Favorable outcomes were higher among the surgical versus non-surgical group in the overall cohort (80% vs. 41%, $p < 0.01$) and when removing patients with loss to follow up (91% vs. 64%, $p < 0.01$). Among the surgical group 92% achieved final culture conversion compared to 53% among the nonsurgical patients ($p < 0.01$). At the end of treatment, CXR revealed the presence of a cavity in 4% ($n=4$) of surgical patients versus 69% ($n=204$, $p < 0.01$) patients in the nonsurgical group.

Conclusions: Adjunctive surgery may improve the effectiveness of treatment among patients with cavitary M/XDR-PTB. A clinical trial or other adaptive study designs would more completely determine the impact of surgery.

OA18-312-26 Sensititre MYCOTB MIC plate for testing *Mycobacterium tuberculosis* susceptibility to first-line, second-line and new drugs in Georgia

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Background: *M. tuberculosis* drug susceptibility testing (DST) data are essential for constructing treatment regimens; however, limitations of standard DST include only one concentration used per drug. More data is needed on the performance of minimal inhibitor concentration (MIC) testing which provides more comprehensive data that may be helpful in developing the most effective individual patient treatment regimens.

Methods: Patients enrolled in a prospective observational cohort study evaluating the pharmacology of anti-TB drugs in Tbilisi, Georgia were enrolled. All patients had multidrug- or extensively drug-resistant TB confirmed through standard first and second-line DST. MIC testing was performed on subcultured Mtb isolates using customized Trek Sensititre™ Mycobacteria Plates including a dry (standard drugs plus linezolid, tedizolid and clofazimine) and frozen plate (bedaquiline and sutezolid); this included baseline Mtb isolates and selected isolates recovered after one month of treatment. For each antibiotic, a range of 5-7 concentrations per drug were used and the lowest concentration with no visible growth was the MIC.

Results: Among 100 patients with M/XDR-TB enrolled, 141 Mtb isolates had MIC testing including 95 baseline and 46 follow up Mtb isolates. The mean time to results was 10 days. Among all isolates, MIC testing revealed 9 Mtb isolates with rifampin resistance and rifabutin susceptibility; and 19 and 49 Mtb isolates resistant to ofloxacin and susceptible to levofloxacin and moxifloxacin, respectively. In the nine Mtb isolates with linezolid resistance (MIC \geq 2 mcg/ml, (range 2-32), the MICs of tedizolid and sutezolid were \leq 1 mcg/ml. No bedaquiline resistance was detected.

Conclusions: The implementation of the Sensititre MYCOTB MIC assay was feasible, had a fast turnaround time, and provided much data relevant for clinical case management that was not available through traditional DST methods. Further roll out and use for patient management should be considered.

OA18-313-26 Active tuberculosis drug safety monitoring and management results in the country of Georgia

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Background: Multidrug-resistant and extensively drug-resistant tuberculosis (MDR and XDR-TB) remain a major challenge for Tuberculosis (TB) control in Georgia, despite the universal access to second-line treatment. In 2015 programmatic use of Bedaquiline (BDQ) and Delamanid (DLM) has started in Georgia. In parallel, active TB drug safety monitoring and management (aDSM) framework implementation for all Serious Adverse Events (SAEs) took place. SAEs for all drug resistant TB patients are reported to the National Center for Tuberculosis and Lung Diseases (NCTLD) Pharmacovigilance (PV) Committee.

Methods: Analysis of SAEs reported from April 2015 to December 2017 among patients with MDR and XDR-TB was performed and descriptive characteristics were evaluated.

Results: Total of 141 SAEs have been reported. Overall 102/516 (19.7%) patients had at least 1 SAE. Among them, 70 (13.5%) had 1 SAE, 25 (4.8%) had 2 SAEs, and 7 (1.4%) had 3 SAEs. Out of the 102 SAE patients 84% are male, Mean Age - 41. 36 were on DLM with 49 SAEs, 57 were on BDQ with 70 SAEs, and 9 were on other drugs (22 SAEs). Majority of the patients developing the SAEs had bilateral TB disease with extensive drug resistance (>60% FQ resistant). 41 (40%) had Hepatitis C virus (HCV) co-infection, 17 (17%) had HIV and 8 (8%) had diabetes. 78% of SAEs were of severity grade 3 or 4, 68% of SAEs have resolved or resolved with sequelae, 15% not resolved and 17% were fatal. In 66% of the SAE cases TB drug doses were either changed or drugs were permanently withdrawn. 3 most frequent SAEs were: Increased liver enzymes/hepatitis (34%), QTc prolongation (11%) and gastro-intestinal disorders (7%).

Conclusions: Good reporting practice of SAEs has been observed, although 68% was resolved. Two-third of patients required treatment change or interruption. Hepatitis is common and requires attention to co-morbidities. QTc prolongation was never fatal.

SHORT ORAL ABSTRACT SESSIONS

SOA08 FCTC (Framework Convention on Tobacco Control) at the crossroads: implementation and sustainability of its impact

SOA08-1076-26 Sub-national monitoring of tobacco advertisement, promotion and sponsorship at point of sale in India

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Background and challenges to implementation: A total ban on direct and indirect advertising, promotion and sponsorship, as provided in guidelines to Article 13 of the WHO Framework Convention on Tobacco Control, can substantially reduce tobacco consumption and protect people, particularly youths, from industry marketing tactics. New industry documents have emerged that emphasise the importance of the retail environment to support sophisticated tobacco industry point of sale marketing to attract youth and newer users. Therefore, TAPS ban policies must be comprehensive including product display at PoS and should be supported through rigorous enforcement mechanism and monitoring system to ensure compliance to the law.

Intervention or response: The studies to assess compliance to laws on prohibition of PoS advertisement of tobacco products were conducted between 2012 and 2017 across jurisdictions in India under Grants Programme supported by Bloomberg Initiative to Reduce Tobacco Use. A robust protocol developed by The Union in consultation with experts was used to assess the compliance conducted by third party assessment.

Results and lessons learnt: 28 jurisdictions (Districts and cities) in states of Karnataka, Bihar, Punjab and Himachal Pradesh conducted both base line and end line compliance assessment of PoS advertisements viz presence of boards, posters, stickers, banners, danglers, product display and showcase, LCD/Video Screen showing tobacco products. The level of compliance increased from 55% in the baseline to 76% in the end line survey. As per the end line survey the most important violation seen at PoS were advertisement boards, posters, product showcase and stickers at 62%, 26%, 20% and 16% respectively.

Conclusions and key recommendations: PoS is an important channel for tobacco industry to advertise its products. Effective enforcement and monitoring of laws related to prohibition of PoS advertisement of tobacco products is crucial to achieve high level of compliance.

SOA08-1077-26 Effective enforcement of the Tobacco Control Act in the Shahjadpur sub-district of Sirajganj district, Bangladesh

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Background and challenges to implementation: Bangladesh is implementing several measures to reduce tobacco use. Bangladesh enacted tobacco control law in 2005 and in 2013 the law was amended for more befitting to FCTC including Graphic Health Warnings (GHW) on 50% of tobacco packets, ban on all of Tobacco Advertisement, Promotion and Sponsorship (TAPS) etc. Government formed taskforces at national, district and sub-district levels with the task of tobacco control including enforcement of law under their jurisdiction. Law implementation became big challenge due to interference of Tobacco Industries (TIs), providing a large sum of cash to farmers by TIs for tobacco production etc.

Intervention or response: Sub-District Administration (SDA) of Shahjadpur of Sirajganj District took various initiatives with the help of NGOs to ensure enactment of tobacco control law including seminars with stakeholders, disseminate law gazettes among owners of PoS and to students. SDA conducts Mobile Courts (type of summary trial, conducted by Executive Magistrates at the place of offence by imposing spot punishment like imprisonment, fine etc.) for effective enactment of law at the PoS, public places, and offices of TIs. Beside this, with the help of Agriculture department alternative crops has been provided to tobacco farmers as government subsidy.

Results and lessons learnt: Taken initiatives ensured smoke free environment at public places and tobacco advertisements from PoS had been removed, TIs were fined and became cautious to follow law. Tobacco farmers are now encouraged to cultivate alternative crops. For this remarkable work on law implementation, Shahjadpur SDA rewarded 'Best Sub-District in tobacco control in 2017' by Sirajganj District Administration. This initiatives has been replicated all other districts in Rajshahi division through a letter circulated from Divisional Head of Administration.

Conclusions and key recommendations: At Sub-district level, SDA holds full legal power on law implementation, so, if concern district instructed every SDA, it will ensure effective tobacco control in Bangladesh.

SOA08-1078-26 Perceived effectiveness of pictorial health warnings in South Jakarta

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Background: Previous research has shown that pictorial health warnings on tobacco packs were perceived as an effective way to prevent adolescents from smoking, motivate smokers to quit, and convince former smokers to keep quitting smoking. Currently, the pictorial health warnings in Indonesia included graphic pictures at the top 40% of the package. The Minister of Health's Decree No. 40/2013 mandated that the size of pictorial health warnings should be increased to a minimum of 75% during 2015-2018 period. This study aimed to assess perceived effectiveness of the different sizes of pictorial health warnings.

Methods: A cross sectional study was carried out from November to December 2017 in South Jakarta. A total of 462 individuals were successfully interviewed using a structured questionnaire. The sample size was determined using Multistage Cluster Sampling method.

Results: Most respondents (97,6%) stated that 90% pictorial health warnings on tobacco packs were highly perceived to be effective scare people. A total of 35,1% of smokers stated that graphic warnings were very effective to motivate them to quit smoking. Besides, 75% of pictorial health warnings effectively convinced 98,5% of adolescents not to start smoking, and prevented 90% of ex-smokers from smoking again. The most effective size perceived by majority of the respondents was 90% pictorial health warnings.

Conclusions: Most respondents, including smokers, support the larger size of pictorial health warnings. Therefore, Indonesian Government, especially the Ministry of Health should overcome the political barriers to implement a larger size of pictorial health warnings as mentioned in the roadmap of tobacco control in Indonesia.

SOA08-1079-26 Affordability of smoke tobacco products in India

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Background: Tobacco industry implement a range of pricing tactics to increase the affordability of tobacco products. Easy affordability of tobacco products is responsible for increased tobacco consumption. The objective of this study is to analyze the affordability of cigarette and bidi in India in four scenarios of increased taxation from years 2017 to 2025.

Methods: A mathematical model was used to calculate the price of cigarette and bidi and also the per capita Gross Domestic Product (GDP) from 2017 to 2025 in four different scenarios (0%, 25%, 50% and 100%)

based on increase in incremental tax on tobacco products. The model used the retail price of most sold brand of cigarette and bidi, inflation rate, the annual GDP growth rate and the per capita GDP. Affordability was calculated by dividing the price of pack of cigarette/ bidi (multiplied by 100 packs) by the per capita GDP and is further expressed in terms of Relative Income Price (RIP).

Results: The affordability of cigarette and bidi is very high (10.80) for India. Our model projected that the affordability of cigarette and bidi is getting easy over a period of time with a decrease of (6.9%, 3.5%), (13.6%, 7.1%), (16.4%, 14.6%) for cigarette and bidi respectively in scenario 2, scenario 3, and scenario 4 respectively (as compared to scenario 1) by the year 2025. Further the model projected that bidis are far more affordable than cigarettes for the same increase in taxation rates.

Conclusions: Since affordability of smoked tobacco products, especially bidi, is quite high, the governments should take adequate measures to lessen it for overall reduction of ill effects of tobacco use.

SOA08-1080-26 Legislative courtesy notices by NGOs - a step towards elimination of TAPS ban violation by Tobacco Industries

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Background: TAPS ban has been found out to be an effective way to reduce Tobacco Use and various Legislation have been adopted in different countries to counter the promotion and advertising in their regions. However, restricted advertisement is allowed on packages of tobacco products, entrances of places where tobacco products are sold. Thus, a very important component of effective TAPS ban is regulating Point of Sales, as advertising and promotion of Tobacco Products account for more than 75% of Tobacco Company marketing expenditure.

Methods: POS were randomly selected in 22 districts of Punjab in 6 months. Out of them, the point of sales violating either component of TAPS ban a "Legislative Courtesy Notice" was issued, removing all the boards, posters, frames, displays present at POS. The violating instruments were quantified by taking the costing of manufacturing and installing such advertisements at the POS to study the financial loss made to the industry in 6 months.

Results: Total POS visited 1200, among them 1000 were violating either component of ban with more violations being of brand boards and posters.

A total of 900 display boards of average dimensions 7 feet x 3 feet.

Every shop violating had an average of 3 posters of the new products totaling 1800.

The Vendors were paid a monthly average rental of INR 5000 (\$76.92).

Total loss made to tobacco industry in reference to just point of sake advertisement removal by a single NGO by way of legislative courtesy notices within 6 months amounted to INR 12,222,000 (\$188,030).

Conclusions: Legislative Courtesy Notices is an effective, cost efficient and sustainable tool of implementing TAPS ban. Enforcement of TAPS ban can be made more effective with involving more NGOs for the drive. The loss made to the industry in respect to the input cost is huge.

SOA08-1081-26 'Tobacco shops': trade and product characteristics

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Background: Recently there has been an increase in the tobacco retail outlets with the label of "tobacco shop" in Turkey. This study aims to investigate the legality, product portfolio and compliance to legislation of these premises.

Methods: This is an observational study carried out in four districts of Istanbul with a high trade density. The observation was carried out using shadow reporting method for point of sales developed by the Framework Convention Alliance.

Results: Of the 21 shops observed none had the license to sell tobacco products issued by Tobacco and Alcohol Regulatory Authority. The legally required warning labels were not found in any of the shops. The frequency of product types sold were as follows: roll your own tobacco 95.2 %, unfilled cigarette paper rolls filter, cigarette paper, side products 95.2 %, cigar and cigarillo 90.5 %, water-pipe, water-pipe tobacco, accessories 85.7 %, electronic cigarette liquids 57.1 %, electronic cigarettes 52.4 %.

Conclusions: The "Tobacco shops" sell various tobacco products, devices, flavours, including loose tobacco and empty cigarette shells without any tobacco trade license. These illegal shops, at the heart of the city, clearly indicate the extend of illicit tobacco manufacturing and production, as well as lack of enforcement. Electronic cigarettes which are not legal in Turkey, can also be marketed through these channels. Tobacco control cannot be fully achieved unless all products and marketing outlets are inspected.

SOA08-1082-26 Sustainable funding for tobacco control through implementation of an operational plan under the Non-Communicable Disease Control Program of the Government of Bangladesh

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Background and challenges to implementation: The Health Services Division (HSD), under the Ministry of Health and Family Welfare, is responsible for government tobacco control program. The National Tobacco Control Cell is operating nationwide tobacco control activities under HSD. But neither HSD, nor NTCC has revenue budget for tobacco control activities. Although government imposed 1% Health Development Surcharge on retail prices of all tobacco products either manufactured in Bangladesh or imported in 2014-15 financial year to ensure sustainable finance for tobacco control. But, almost end of FY2017-18, money collected as surcharge is not been transferred to HSD. Lack of sustainable finance hampered nationwide tobacco control activities and weakened law implementation across the country.

Intervention or response: The Non Communicable Disease Control (NCDC) Program, Directorate General of Health Services (DGHS), under HSD prepared and implementing five year long operational plan (OP) on NCDs prevention. The NTCC linked with NCDC, DGHS and pushing them in several meetings to include tobacco control activities effectively and allocate budget for various types of tobacco control activities. NTCC is also formed a committee to provide guideline for implementation of tobacco control activities and to monitor and follow-up the OP, NCDs prevention.

Results and lessons learnt: This is first time in Bangladesh that government allocated 25 crore (more than \$3.1 million) for various types of activities on tobacco control including awareness on health hazards of tobacco use and law, capacity building and World No Tobacco Day celebration etc. Already first year of OP activities is successfully implementing that reached 12 million people directly.

Sustainable finance for tobacco control is ensured.

Conclusions and key recommendations: Allocating revenue budget not only strengthened tobacco control law implementation and tobacco control movement, but it also change government officials attitudes from the feeling of donors activities to government own activities. This is huge change at the mindset of government officials across the country.

SOA08-1083-26 Cigarette selling to and by the minors in Bangladesh: policy gaps and implementation challenges

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Background: Minors who smoke cigarettes which contain harmful additives are most susceptible to health injury. In compliance with WHO Framework Convention on Tobacco Control, Government adopted Tobacco Control Act emphasizing ban on selling tobacco products to and by the minors in Bangladesh. But reality shows that minors are still easily buying and selling cigarettes. Hence, this study aimed to explore the flaws and implementation related loopholes of the Act.

Methods: Mixed method approach and primary data were utilized. Data was collected through questionnaire surveys from a representative sample of 398 minor cigarette buyers (207) and sellers (191). In addition, 50 in-depth interviews and information from 10 key informants was obtained. Along with descriptive statistics, comparative analysis among the respondent groups was performed.

Results: Overall 63% of the respondents were found smokers. Prevalence of smoking among the buyers was significantly higher ($p < 0.001$) than sellers. A majority of the buyers (79%) and sellers (85%) had never been prevented from buying and selling cigarettes by any authorized personnel, even general public. Majority of the respondents (86%) had no knowledge about any law on tobacco control in the country. Even a majority of the adult sellers were not familiar with the law regarding restrictions on sale to the minors. About one quarter of the respondents (24%) perceived that the main causes of non-implementation of the law were the citizens' reluctance to obey and negligence of the concerned authority to implement the law.

Conclusions: Lack of effective enforcement measures is one of the greatest loopholes of the law. Socio-economic context of country is another challenge which has direct influence on minor sellers. However, campaigns for anti-tobacco marketing, delegating adequate power to concerned authority, monitoring, and promoting social movements against tobacco use can definitely have a positive impact on ending cigarette selling to and by the minors in Bangladesh.

SOA08-1084-26 Tobacco industry's interference challenging public health in India; it is time for strict and strategic implementation of FCTC article 5.3

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Background: There is an irreconcilable conflict between the tobacco industry and public health. Tobacco companies use their enormous wealth and power to influence policies. Industry usually takes the shield of government's constitutions, international bilateral investment treaties, corporate property rights and adult autonomy to oppose any move by tobacco control advocates. It is important for tobacco control advocates to know the manipulative tactics of tobacco companies to get better equipped for countering the tobacco industries' interference. Present study was conducted to examine the common tactics adopted by tobacco industry to interfere in public health in India.

Methods: Investigators did a snowball retrieval research from websites of major tobacco companies in India, accessed UCSF truth tobacco industry documents online library and MOH website and referred to available literature between 1st October 2017 to 31st March 2018.

Results: Tobacco industry manipulated political and legislative process; delayed notification of national legislation (COTPA 2003) and subsequent rules. Industry took legal measures for challenging TAPS ban in the name corporate property rights and delayed new pictorial health warnings. Industry intimidated government with litigation on Gutkha ban. Industry created fronts groups of farmers, traders and film industry and argued in the name of livelihood and individuals rights of expression. New Company's act 2013 is now grossly misused by tobacco companies in the name of social responsibility.

Conclusions: Tobacco industry will keep doing all possible manipulation and interference in public health to carry on their business. Tobacco control advocates and law implementers to tackle each case of industry interference using provisions in the existing legislation. It is a right time for national and state government to develop a model code of conduct and clear policy document that aligns with principle of FCTC article 5.3.

SOA08-1085-26 Unresolved issue: point of sales tobacco advertisements

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Background: Advertising is crucial avenue to recruit new customers for the tobacco industry. Since most tobacco control legislations do not allow advertisements, the industry has been using point of sales (POS) for this pur-

pose. Turkish law prohibits advertising at POS and visibility of the products from outside the shop. The aim of this study is to investigate the compliance to the legislation at POS and compare the results with previous years.

Methods: Framework Convention Alliance (FCA) shadow reporting methodology is used for this observational study. The study is carried out in four trade districts of Istanbul in August 2017 by filling observation forms and taking pictures during 1 km-diameter walking tour.

Results: Advertising violations were noted in all of 202 POS observed. The products were on visible shelves in 100 %. The breakdown of the violations was as follows: illegal price tags in 100 %, overt advertising and brand preference in 96.5 %, more than one display area in 91.6 %, shelves of cigarette companies in 70.8 %, no warning about sales to minors in 45%, physical accessibility in 41.6%, pictorial warning not displayed in 39.1 %, sales by stick in % 39.1 %, lighters carrying cigarette brand names in 22.8 %.

Conclusions: Advertising at POS in Istanbul, clearly violates Turkish tobacco control act and Framework Convention on Tobacco Control. The results of 2017 observation showed an increase in violations compared to the previous years (2014-2016). The infrastructure for inspection and enforcement must be reviewed and improved.

SOA09 Catastrophic costs vs. social protection: measuring digesting and addressing patient-level economic drivers of TB

SOA09-1086-26 Social protection for patients with tuberculosis in Uganda, a significant gap in efforts to attain the Sustainable Development Goals

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Background: Sustainable Development Goals and “End TB Strategy” emphasize addressing social determinants of Tuberculosis, including poverty alleviation and social protection programs in a bid to End TB by 2030 and 2035 respectively. There is paucity of research on the relationship between social protection and TB, especially in LMICs like Uganda. We document the state and access to forms of social protection by TB patients in Uganda.

Methods: We used a validated WHO TB “patient cost tool” to collect demographic, cost and social protection data from 1,181 participants under the National Tuberculosis and Leprosy Program, at 67 health facilities across the country. A random cluster sampling approach was used to ensure national representativeness of the data.

Results: Of the 1,181 participants, 69.4% were male, 3.4% attained college or University education and 18.9% were unemployed. 47.4% were below poverty line at the time of interview and the median annual income estimated based on consumption data was USD 1,179. More than half of participants had at least sold assets, used up savings or borrowed money to defray TB costs. 51.0% of participants reported food insecurity, 7.7% were divorced, 37.9% lost a job and 12.5% reported that their children had school interrupted after contracting TB. Despite the immense sensitization campaigns, stigma is still a tremendous challenge to TB patients, 52.4% experienced a form of social exclusion. Only 38 (3.2%) had received some form of social protection as disability grant, paid sick leave, cash transfer and pension.

Conclusions: In Uganda, social protection among TB patients is still very limited. Only a small percentage of TB patients have access to forms of social protection. This underscores the urgent need to address the social determinants of TB especially alleviating and fighting stigma in order to achieve the END TB strategy goals.

SOA09-1087-26 Prevalence and risk factors for catastrophic health expenditure due to tuberculosis in Kaduna State, Northwest Nigeria

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Background: Despite providing free tuberculosis (TB) diagnosis and treatment, TB patients and their households still incur catastrophic health expenditure (CHE) while seeking for care. WHO has set a target of eliminating CHE due to TB by year 2020. There is a dearth of information on the prevalence of CHE due to TB in Nigeria. We assessed the prevalence and risk factors for CHE due to TB in Kaduna State, North-Western Nigeria.

Methods: A cross-sectional study was conducted involving 274 pulmonary TB patients recruited using a multi-stage sampling technique. Data was collected using a pre-tested semi-structured interviewer administered questionnaire adapted from a tool developed by USAID. CHE was defined as out of pocket health expenditure

≥40% of non-food expenditure. Bivariate and multivariate analysis were used to identify risk factors by estimating the adjusted odds ratio (AOR) and 95% confidence interval (CI).

Results: Of the 274 TB patients, 171 (62.4%) were males, 41 (15.0%) were unemployed and 218 (79.6%) were within the first and second wealth quintiles. The prevalence of CHE due to TB in Kaduna State was 17.2%. TB patients were at a higher risk of incurring CHE when they are unemployed (AOR = 2.31; 95% CI: 1.02-5.23), had TB diagnosed more than two weeks after first time treatment was sought (AOR = 2.56; 95% CI: 1.19-5.53), collected drugs more frequently (AOR = 2.82; 95% CI: 1.36-5.84) and had sputum smear negative TB (AOR = 2.70; 95% CI: 1.03-7.08).

Conclusions: The prevalence of CHE due to TB in Kaduna State was above the target set by WHO and is associated with delay in diagnosis of TB, frequent collection of TB drugs, employment status and having sputum smear TB. We recommended that the TB Control Programme explore strategies to reducing frequency of drug collection and diagnosing TB earlier to reduce CHE due to TB.

SOA09-1088-26 Catastrophic costs of tuberculosis illness and treatment in rural South Africa: a risk factor analysis

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Background: Eliminating the experience of catastrophic costs due to tuberculosis (TB) is a key goal of the WHO's End TB Strategy. We evaluated factors contributing to catastrophic costs among individuals treated for TB in rural South Africa.

Methods: From October 2017 through January 2018, we interviewed consecutive patients being treated for TB across 55 clinics in Limpopo Province, South Africa. We ascertained costs and income during pre-diagnostic, diagnostic, and treatment phases. We defined catastrophic costs as those meeting two criteria: (a) loss of 20% or more of a household's annual income in out-of-pocket costs, lost wages, and lost time due to TB illness, care-seeking, and treatment; and (b) a minimum loss of 100 South African Rand (ZAR, 100 ZAR = US\$8.30) or 20 hours of care-seeking time. We assessed risk factor associations through multivariable Poisson regression.

Results: Among 326 participants interviewed, total estimated TB episode costs (mean 5410 ZAR = US\$416) consisted of 58% out-of-pocket costs, 24% lost time during care-seeking, and 17% lost wages. Using the first criterion, 105 (32%) participants experienced a loss of at least 20% of household annual income. Of these 105

participants, we re-classified 9 (3%) participants as not experiencing catastrophic costs per the second, "minimum loss" criterion. Therefore, 96 (29%) participants met our primary definition of catastrophic costs. Factors associated with catastrophic costs included heavy smoking, greater travel distance from clinic, and fewer household members (see table).

Conclusions: Catastrophic costs are common among people diagnosed with TB in rural South Africa, though inclusion of a minimum loss threshold reduced this proportion. Smoking tobacco, longer trips to clinics, and fewer household members were factors associated with catastrophic costs in this setting. Further research is needed to better describe "catastrophic" costs for patients with little or no income.

Potential Risk Factors	Travel Distance to Clinic (min) [1]			Pack-years of Smoking Tobacco [2]			Number of Household Members [3]		
	15 to 59	60 to 89	≥90	0 to 5	5 to 15	≥15	3 to 4	5 to 6	≥7
Prevalence of CC, n (%), N=298	50 (26%)	18 (43%)	10 (38%)	21 (29%)	10 (25%)	10 (53%)	29 (28%)	18 (22%)	24 (32%)
Adjusted Prevalence Ratio, Sig. level: *0.10 ≤ P < 0.05	0.9	1.7*	1.5	1.1	0.9	2.0*	0.8	0.6*	0.9
95% CI	0.6 - 1.6	0.9 - 3.1	0.8 - 2.9	0.7 - 1.9	0.4 - 1.8	1.0 - 3.9	0.5 - 1.3	0.3 - 1.0	0.5 - 1.5

[Risk factors associated with experiencing catastrophic costs (CC). Ref. groups: [1] <15: n=17 (28%); [2] Never-smoker: n=54 (29%); [3] 1-2: n=25 (36%)]

SOA09-1089-26 Which subgroups of TB patients in Kenya suffer the 'triple burden' of catastrophic expenditure, dissaving and a disruption of social life during treatment?

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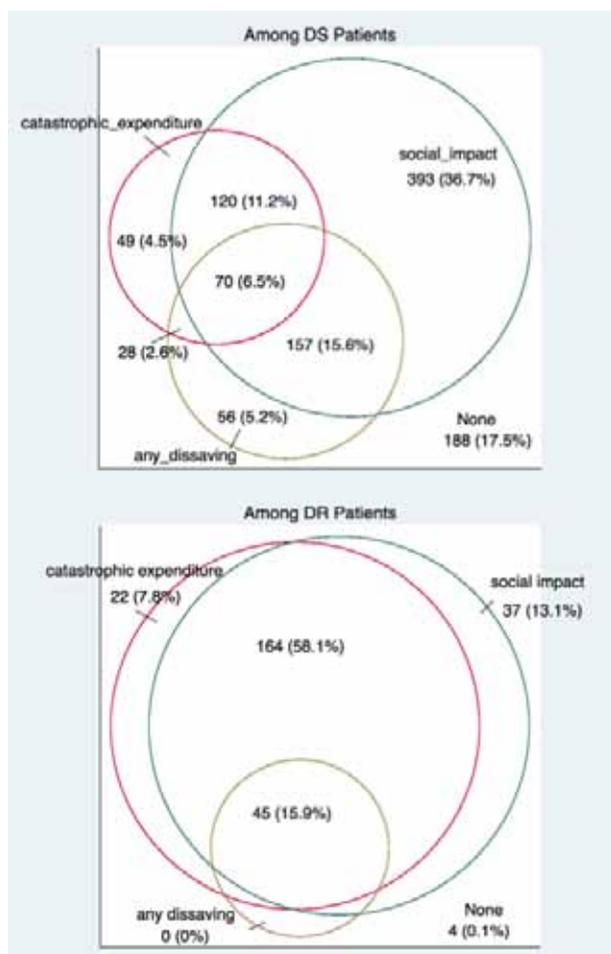
Background: Kenya has committed to achieve UHC by 2030. The 2016 Kenya TB Prevalence survey revealed a prevalence of 588 (455 - 662) adults per 100,000. Using the First Kenya TB patient cost survey data, this study describes the TB patients that are most likely to suffer from the 'triple burden' of catastrophic expenditure, dissavings and disruption of social life.

Methods: Data was obtained from a two-stage cluster sampled patient survey conducted in 2017, which reached 1071 drug sensitive (DS) and 282 drug resistant (DR) patients. Patients were asked about the costs they incurred, dissavings incurred during TB care, plus the social consequences that their households experienced (school dropout, social exclusion, loss of jobs) due to

taking TB treatment. Catastrophic costs were computed at a 20% threshold of household expenditure.

Results: From the study, 14.2% (CI 8.6, 22.6) of DR and 5.8% (CI 4.5, 7.6) of DS patients experienced the triple burden of catastrophic expenses, dissavings and disruption of social life. Survey-adjusted multivariate logistic regression found that the odds of incurring the triple burden increased 2.8 (CI 1.2, 6.8) times for DR patients, 2.6 (CI 1.0, 6.6) times for patients in the lowest expenditure quintile compared to the highest quintile, and increased 2.8 (1.2, 6.0) times when the TB patient was a child below 15 years. There was no significant difference across gender, HIV co-infection, nutritional status nor across public or private facilities.

Conclusions: Although Kenya has expanded provision of TB treatment across public and private facilities, poor households and households with children undergoing treatment are more likely to suffer the triple burden. Furthermore, due to the prolonged treatment regimen, households with DR patients are more likely to incur catastrophic expenditure, dissavings and social consequences. Countries including Kenya need to explore mechanisms for deepening social protection for such subgroups of TB patients.



[Venn diagram of intersection of catastroph, dissavings and social consequences for DS patients]

SOA09-1090-26 Evaluating catastrophic costs for tuberculosis patients in Brazil: a multicentre study in five state capitals

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Background: High costs for tuberculosis (TB) treatment may be impoverishing for families. Costs care above 20% of pre-illness annual family income are considered catastrophic. This study aimed to evaluate the family-level economic impact of TB disease in Brazil.

Methods: We conducted a multicentre survey during 2016-2018 in 13 healthcare [WR1] units located in 5 state capitals of 4/5 [WR2] regions of Brazil (North East, North, South East, and South). The survey questionnaire was adapted from the WHO Tool to Estimate Patients' Costs. The study population was newly diagnosed patients with drug sensitive TB that had completed at least one month of treatment. Total costs included direct and indirect costs incurred pre-diagnosis, and during diagnosis and treatment. Patients' household cost burden was calculated as the sum of direct and indirect costs divided by pre-illness annual household income, with a threshold for catastrophic cost $\geq 20\%$. Poverty was measured using the World Bank threshold of US \$ 5.5 per day.

Results: 344 patients were enrolled in the study period. Average [WR1] direct costs were US\$ [WR2] 126.49 (SD: US\$ 368.67), and indirect costs were US\$ 1030.65 (SD: US\$ 1358.57). Overall, 101 (29%) of study participants were characterized as poor before TB, and 131 (38%) after, with impoverishment of 9%. The percentage of participants' experiencing catastrophic cost was 46%. Analyzing pre-illness income, 69 (44%) of the poor, and 87 (55%) of the non-poor had a catastrophic cost above 20%, $p < 0.001$. Analyzing income after illness, 89 (57%) of the poor had catastrophic cost above 20%, $p < 0.001$.
Conclusions: Although treatment is funded by the government, TB continues to result in catastrophic costs and impoverishment for many households in Brazil. There is a need to evaluate ways to reduce the costs generated by illness prior to diagnosis and during treatment.

SOA09-1091-26 Out-of-pocket costs for patients diagnosed with tuberculosis in Bandung, Indonesia

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Background: Costs related to tuberculosis (TB) can impose a significant impact on patients and their families and create barriers to diagnosis and treatment. Our study aimed to quantify health care pathways, out-of-pocket pre-diagnosis costs and coping mechanisms of TB patients in Bandung, Indonesia.

Methods: This cross-sectional study consecutively recruited adults diagnosed with pulmonary TB in 30 randomly selected public Community Health Centres (CHCs) and 5 hospitals in Bandung, Indonesia (January - March 2018). Following informed consent, patients completed an in-person interview with a research nurse. Costs were converted to US dollars (US\$). Student t-test and chi² test were used to estimate differences.

Results: A total of 264 TB patients completed the interview (CHC n=114; Hospital n=150): mean age 38 years; 57% male. The median number of visits to any healthcare provider up to the time of diagnosis was 6 for CHC patients and 5 for hospital patients (p=0.001). Median overall time from first symptom onset to starting TB treatment was 67 days (CHC 85 vs. hospital 52 days; p=0.022). The median total cost per healthcare provider visit was US\$3.34 (CHC \$2.40 vs. hospital 4.36; p<0.001). The main expenditure was for sputum and other diagnostic tests (mean \$11.50; median \$4.72; range \$1-\$167), and x-ray (mean \$9; median \$7.27; range \$0.50-\$21.80), with no difference between CHC and hospital patients. Sixty-three patients had hospitalisation costs ranging from \$4-\$1381 (median \$58). A greater proportion of hospital patients had government insurance (81% vs. 47%; p<0.001). Overall, a third of patients (34%) had to borrow money to cover costs with no difference between CHC and hospital patients.

Conclusions: Despite much of TB care being free, patients in this Indonesian setting experienced delay in diagnosis and substantial out-of-pocket costs that is likely to have an impact on them and their families well beyond the time of their treatment period.

SOA09-1092-26 Effect of financial support on reducing the incidence of catastrophic costs among tuberculosis-affected households in Indonesia: eight simulated scenarios

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Background: The World Health Organization's End Tuberculosis (TB) Strategy mandates that no TB-affected families face catastrophic costs due to TB. To achieve this target, providing adequate social protection is essential. However, few studies have evaluated social protection programs to see whether the target is indeed being reached. We assessed the effect of financial support on the incidence of catastrophic costs due to TB in Indonesia.

Methods: We interviewed adult patients receiving treatment for TB or multidrug-resistant (MDR) TB in three districts in Indonesia to measure the incidence of catastrophic costs, socioeconomic impact due to TB, and patients' perceived needs for social protection. Based on the needs assessment, we developed eight scenarios of social protection. For each simulated scenario, we assessed the effect by measuring reductions in the incidence of catastrophic costs.

Results: We analyzed data from 282 TB and 64 MDR-TB patients. The respective incidences of catastrophic costs in TB and MDR-TB-affected households were 36% and 83%. Patients who experienced income loss lost almost all their income. Patients' prominent needs for social protection were financial support to cover costs related to income loss, transportation, and food supplement. Of eight scenarios of financial support, the optimal scenario could reduce the respective incidence of catastrophic costs in TB and MDR-TB-affected households by 25 and 55 percentage points, but could not eliminate the incidence of catastrophic costs to zero percent.

Conclusions: Indonesia's current level of social protection remains insufficient to mitigate the socio-economic impacts due to TB. Financial protection that covers a combination of income loss, transportation costs, and food supplement costs would offer optimal protection. However, providing financial support alone will not eliminate the incidence of catastrophic costs to zero percent. Achieving this target requires more innovative social protection policies and higher levels of domestic and external funding.

SOA09 Catastrophic costs vs social protection: measuring digesting and addressing TB's economic drivers at patient level

SOA09-1093-26 Catastrophic health expenses and their determinants for tuberculosis in-patient care in India

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Background: Tuberculosis (TB) often results in catastrophic health expenses (CHE), particularly in an out-of-pocket (OOP) health financing scenario such as India. This study quantifies OOP expenditure and CHE arising out of TB inpatient care and identifies determinants of CHE in India.

Methods: Relevant data from National Sample Survey Organization (NSSO), India (2014) including TB inpatient care expenses during one year preceding the survey were analyzed using R-software survey-design package. In absence of household income data, CHE was defined as health expenses exceeding one-fourth of the household expenses. Logistic regression analysis was done to identify CHE determinants.

Results: About 565676 TB patients were received inpatient care during 2013-14 in India. The median OOP expense during TB inpatient care was USD 89 (IQR: 31-229 USD). The incidence of CHE was 16% (95%CI: 11.2-20.5). An inverse association was observed between CHE and household expense level. Significant determinants of CHE were household size, service provider (private/public), insurance coverage, and source of financing. Factors including age, gender, educational level, residence, caste and religion had no significant associations with CHE.

Conclusions: One in six hospitalized TB patients is suffering from CHE in India. India with huge TB patients needs to provide free care packages through public facilities and ensure universal coverage of TB patients. Financial and social protections are essential to reduce the CHE in India.

SOA09 Catastrophic costs vs. social protection: measuring digesting and addressing patient-level economic drivers of TB

SOA09-1094-26 Socioeconomic determinants and economic outcomes for tuberculosis patients in Taiwan: an individual patient pathway analysis using health insurance data

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Background: Tuberculosis (TB) is associated with poverty: low socioeconomic status (SES) is a risk factor for TB, and in addition, diagnosis and treatment for TB can often impose catastrophic costs on affected households. Taiwan has compulsory health insurance, but procedures incur small cover charges. We investigated the influence of SES on features of individual patient pathways constructed this health insurance data.

Methods: We analysed a nation-wide retrospective cohort of one million individuals sampled from health insurance records in Taiwan after 2001 (Nation Health Insurance Research Database). Data captured all events relevant to individuals' insurance claims, including date and location. We algorithmically extracted complete TB care pathways. We then analysed determinants of delay to treatment prescriptions, interruption of TB evaluation, treatment outcome, and out-of-pocket patient costs in terms of socioeconomic variables. We included individual income, social groups, and job types as well as SES in region levels.

Results: 6,410 care pathways were constructed for 5,700 TB patients. We found employed patients had longer delays to TB evaluation. Patients in low-income households tended to have longer evaluation periods and more frequently interrupted evaluation processes. But patients in poorer areas had shorter evaluation periods and diagnosis to treatment delays. 80% of out-of-pocket costs before anti-TB treatment were incurred by 17% of the care pathways; during anti-TB treatment, 11% of the care pathways incurred 80% of out-of-pocket costs.

Conclusions: In this setting with compulsory health insurance, the effects of SES on TB care were complex, with SES impacting distinct features of care pathways differently. Out-of-pocket costs to patients are strikingly heterogeneous.

SOA09-1095-26 Patient and household costs of tuberculosis services among the rural-to-urban migrant population in Shanghai, China

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Background: Catastrophic costs incurred by TB patients and their households could worsen their socio-economic and health status, particularly for rural-to-urban migrants in China. We estimated the costs incurred during TB services among both migrants and residents in an urban setting and the associated factors with catastrophic costs.

Methods: We conducted a cross-sectional study of culture-confirmed TB patients (≥ 15 yo) in Songjiang district, Shanghai, from January 1 to December 31, 2014. Direct and indirect costs before and after the diagnosis of TB disease were collected by a standardized questionnaire. We defined catastrophic costs as the annual expenses of TB care for the entire illness course that exceed 20% of total household income. We used logistic regression to identify factors associated with catastrophic costs.

Results: 248 drug-susceptible TB patients were enrolled. Migrants accounted for majority (70%, 174 of 248) of the TB patients. Patients among migrants were significantly younger and had a lower education level compared to resident patients. The total costs were USD \$4103 and \$2158 among resident and migrant patients, respectively. The medical direct cost comprised about 70% of the total costs among both migrants and residents. 22% (55 of 248) of the TB patients faced household catastrophic costs. More than half of the migrants had no feasible health insurance in local healthcare system (51%) to pay the costs by themselves. In contrast, most of the residents (95%) had health insurance. Meanwhile, residents were more likely than migrants to be hospitalized for TB (OR, 4.4, 95% CI, 2.3-8.1). Hospitalization was the significant determinant of catastrophic costs after adjusting for household status, age and gender.

Conclusions: Catastrophic financial burden of TB service cannot be neglected despite of the free TB service policy. Internal migrants have difficulties benefiting from health insurance in cities, and interventions such as financial assistance are needed to secure the universal TB care.

SOA10 Tuberculosis, safety, outcomes and innovation

SOA10-1096-26 The burden of clinical, spirometric and HRCT abnormalities at pulmonary TB treatment completion: a cross-sectional study

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Background: Little is known about the prevalence and pattern of residual structural lung damage amongst adults completing pulmonary TB (PTB) treatment in sub-Saharan Africa (sSA). This large cross-sectional study comprehensively characterised post-TB lung damage (PTLD) in HIV-infected and uninfected adults in Malawi. **Methods:** We recruited 405 adults completing treatment for a first-episode of PTB from urban Blantyre, Malawi (February 2016 - April 2017). Investigations included the St George's Respiratory Questionnaire, ATS-standard spirometry and low-dose high-resolution computed tomography (HRCT) chest imaging.

Results: Median age was 35-years (IQR 28-41), and 68.1% were male. 77.7% had microbiologically proven TB disease at diagnosis, 61.4% were HIV-infected, and 29.6% were ever-smokers (median 2.7 pack-years (IQR 0.7-6.0)).

Monthly or weekly respiratory symptoms (breathlessness, cough, sputum production) were reported by 60.7% and 7.6% of participants, and spirometry was abnormal in 34.1% (125/367) (19.9% low FVC / 14.2% obstruction).

Moderate to severe bronchiectasis was a dominant feature on HRCT, seen in 44.2% (170/385) of scans. Bronchiectasis severity was positively correlated with the extent of parenchymal damage, and other airway pathologies (bronchial wall thickening, airway plugging, tree-in-bud). Parenchymal abnormalities were widespread: 96.6% had some abnormality, with >50% of tissue abnormal in 15.1% of patients. 9.4% had ≥ 1 non-functioning lobe, extensively damaged by atelectasis / cavities or cystic airspaces / banding.

Conclusions: This is the largest study to describe PTLD amongst HIV-infected and uninfected adults in sSA to date, including the use of HRCT imaging. Over 1/3rd of

patients had abnormal spirometry and almost all had residual structural pathology at PTB treatment completion, with a high burden of bronchiectasis and lobar destruction. This is a young population with a high prevalence of HIV co-infection and a surprisingly high smoking rate, who are at risk of poor outcomes. Targeted clinical services to identify and manage these patients may be required.

SOA10-1097-26 QT prolongation in multidrug-resistant tuberculosis patients on high dose moxifloxacin in Taiwan

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Background: Taiwan multidrug-resistant tuberculosis (MDR-TB) consortium (TMTC) has been established in 2007 for programmatic management of drug-resistant tuberculosis and has achieved more than 80% treatment success of MDR-TB in Taiwan. Shorter MDR-TB regimen has been piloted in TMTC since 2016 and active tuberculosis drug-safety monitoring and management (aDSM) has been introduced in 2017. This study aims to evaluate electrocardiographic QT prolongation in MDR-TB patients treated with high dose moxifloxacin (Mfx) as compared to normal dose Mfx and levofloxacin (Lfx) in the first 6 months of treatment.

Methods: MDR-TB patients enrolled in TMTC and treated with high dose Mfx in 2016-2017 were enrolled. MDR-TB patients treated with normal dose Mfx or Lfx and enrolled in aDSM between May-Sep 2017 were included as a comparison group. 12-lead electrocardiogram (ECG) was done at base line, month 1, month 3, month 6 and as needed for all patients with additional ECG at month 4 for patients on high dose Mfx. The Fredericia Formula was used for QT interval correction (QTcF). Patients without ECG during the first 6 months of treatment were excluded.

Results: Sixty MDR-TB patients with a mean age of 56.3 (range 17-95) years were included; 44 (73.3%) were males. 13 (21.6%) were on high dose Mfx, 31 (51.7%) on normal dose Mfx and 16 (26.7%) on Lfx. The mean frequency of ECG measurements in 6 months of treatment was 5.9 (range 5-6) in patients on high dose Mfx, 2.7 (range 1-5) in normal dose Mfx, and 2.8 (range 1-4) in Lfx (ANOVA $P < 0.001$). Use of high dose Mfx (46.1%; adjusted odds ratio 12.61, 95% confidence interval 1.26-126.74) were significantly associated with QTcF ≥ 500 ms. (Table 1).

Conclusions: A substantial proportion of MDR-TB patients receiving high dose Mfx had QTcF prolongation. Regular ECG monitoring in MDR-TB patients treated with fluoroquinolones is essential.

	% (number)	Adjusted odds ratio*	95% confidence interval
Peak QTcF ≥ 450 ms			
Levofloxacin, (n=16)	37.5 (6)	1	
Moxifloxacin normal dose, (n=31)	35.5 (11)	0.88	0.24-3.18
Moxifloxacin high dose, (n=13)	76.9 (10)	6.96	1.25-38.63
Peak QTcF ≥ 480 ms			
Levofloxacin, (n=16)	6.3 (1)	1	
Moxifloxacin normal dose, (n=31)	19.4 (6)	3.57	0.39-32.63
Moxifloxacin high dose, (n=13)	61.5 (8)	25.15	2.43-259.78
Peak QTcF ≥ 500 ms			
Levofloxacin, (n=16)	6.3 (1)	1	
Moxifloxacin normal dose, (n=31)	9.7 (3)	1.62	0.15-16.99
Moxifloxacin high dose, (n=13)	46.1 (6)	12.61	1.26-126.74

* adjusted for age

[Table 1. Peak QTcF during the first 6 months of treatment of MDR-TB patients in Taiwan]

SOA10-1098-26 Decentralisation of a short-course MDR-TB regimen in a low middle-income country. What worked? What didn't? Why?

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Background and challenges to implementation: Cameroon manages multidrug-resistant tuberculosis (MDR-TB) with alternative treatment regimens inspired by Bangladesh experiences since 2005 and started decentralization of treatment with the 9-month short-course regimen in 2015. We measured progress by key indicators and analysed obstacles to this process through interviews and participating observation.

Intervention or response: During the period 2015-17, the number of diagnostics facilities (Xpert machines) increased from three to seventeen and treatment facilities from three to sixteen units, country-wide.

Results and lessons learnt: Three flexible models of care were introduced (hospitalization, ambulatory, mixed), depending from patients, provider, and setting characteristics. Coverage of target population diagnosed increased (from 67% to 81%), delay to treatment initiation decreased (median from 15 days to 11 days), treatment success rates were maintained ($>80\%$). However, management of the main preventable undesirable side-effect, hearing impairment, did not improve. Social aid disbursement to patients under treatment remained in-

consistent. Systematic investigation of contacts did not cover more than 20% of index cases. An automatized data base was inconsistently actualized. - Key obstacles to more consistent progress were:

- a) lack of implication and, perhaps, motivation by program deciders to consequently develop the component (accountable only to performance framework indicators of the Global Fund (GF));
- b) lack of a fully functional management unit with authority to give instructions and follow them up;
- c) the financial unit of the program failing largely to make available in a timely way funding for activities (though funding through GF was available throughout the period studied).

Conclusions and key recommendations: Essential components of a MDR-TB component in evolution are a fully functional MDR-TB management unit with defined and monitored performance indicators, piloted by fully accountable program deciders, and existing funding made readily available.

SOA10-1099-26 Preliminary treatment outcomes of the shorter MDR-TB regimen using levofloxacin: an operational pilot study in Viet Nam

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Background: Vietnam has a high MDR-TB burden with 75% treatment success for conventional MDR treatment (2015). Three provinces piloted a levofloxacin-based shorter treatment regimen (STR) for rifampicin-resistant (RR) TB.

This was an observational study of standard 9-month regimen for RR-TB patients containing high-dose levofloxacin, clofazimine, ethambutol and pyrazinamide throughout treatment, with 4-6 months kanamycin, prothionamide and high-dose isoniazid during the intensive phase.

Methods: Xpert-confirmed pulmonary RR-TB patients underwent eligibility criteria (absence of confirmed/presumed resistance or intolerance to STR drugs, pregnancy, advanced disease, etc). Baseline and monthly smear, culture and safety monitoring tests were done. Baseline second-line drug (SL) susceptibility (DST) for fluoroquinolones (FQ) and SL-injectables (SLI) was performed; if resistant, patients were shifted to 20-month bedaquiline (Bdq)-containing regimens.

Results: During April-December 2016, 116 RR-TB patients started STR treatment; SL-DST coverage was 84 %; 17 patients (15%) were subsequently shifted to a Bdq-containing regimen. Of 99 patients retained on STR, 64% were male, 81% aged 25-55 and 99% HIV

negative. The success rate was 80%, 6 patients failed, 6 were lost to follow-up, 8 died.

There was no significant difference in deaths among sexes and age groups; 3 occurred within < 1 month of treatment, 5 at 2-6 months; one was HIV positive; FQ DST was unknown in 3 (one died on enrolment, 1 culture negative, 1 contaminated), 4 were susceptible, one resistant.

Failure was declared between months 6-10 in 6 patients aged 31- 58 (5 male); in 2 FQ DST was unknown (1 culture negative, 1 contaminated), 3 were susceptible, one resistant.

Conclusions: This study showed the good preliminary treatment outcome of 9 months regimen using Levofloxacin for RR-TB patients in Vietnam. To fully evaluate the treatment outcome of RR-TB patients, longer post-treatment follow-up is needed. More complete and rapid bacteriological testing is likely to reduce unfavorable outcomes.

SOA10-1100-26 Factors associated with aminoglycoside-induced ototoxicity in HIV-co-infected drug-resistant tuberculosis patients in the intensive phase of therapy

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Background: Ototoxicity following second line Injectables therapy for DRTB is a significant challenge in HIV co-infected DRTB patients.

Studies have documented aminoglycoside induced ototoxicity with HIV infection established to be a risk factor for ototoxicity in DRTB patients treated with aminoglycoside.

The study objectives were to determine the prevalence of ototoxicity amongst DRTB-HIV co-infected patients and to assess the factors associated with this outcome.

Methods: A retrospective analytical study was conducted involving the review of case notes of patients admitted to the DRTB treatment centre for the intensive phase of therapy (4 months) over a 2 year period.

Baseline Pure Tone Audiometry including CD4 count of HIV co-infected DRTB patients were documented. Serial PTA were done monthly to determine the onset of ototoxicity in affected patients.

Univariate and multivariate analyses were done on the data at *P* value < 0.05 using SPSS 21.

Results: 172 patients were recruited for the study. Mean age of patients was 38 ±12.9years. Majority had normal baseline audiometry. About one fifth (21.6%) of the patients were co-infected with HIV of which 5.2% developed ototoxicity during the intensive phase of treatment.

HIV co-infection was associated with higher prevalence of ototoxicity (18.9% vs. 1.5%, $P < 0.001$) compared to non-HIV DRTB patients. In the HIV group however, those with CD4 count < 200 cells/ μ l developed ototoxicity (50% vs. 0%, $P < 0.001$) compared to those with CD4 count > 200 cells/ μ l.

HIV co-infected patients with CD4 count < 200 cells/ μ l on kanamycin developed ototoxicity (87.5% vs. 0%, $P < 0.001$) compared to those on capreomycin.

Conclusions: HIV co-infection in DRTB patients with CD4 count < 200 cells/ μ l and kanamycin therapy are significant factors associated with ototoxicity.

Capreomycin is therefore recommended for use in all DRTB-HIV co-infected patients to prevent aminoglycoside induced ototoxicity.

SOA10-1101-26 High prevalence of ototoxicity in successfully treated rifampicin/multidrug-resistant tuberculosis patients in Uganda: results from the initial 2013/2014 rifampicin/multidrug-resistant tuberculosis cohorts

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Background: Uganda initiated programmatic management for rifampicin/multidrug-resistant tuberculosis (RR/MDR-TB) in July 2012 with a mixed model of care using WHO recommended second-line TB treatment regimens. Early treatment outcomes were impressive with treatment success rate of 74% against global averages of 50%. Unfortunately, successfully treated patients reported hearing loss. We evaluated the 2013/2014 RR/MDR-TB cohorts to profile side effects, prevalence of ototoxicity, and associated demographic characteristics.

Methods: This was a retrospective cohort study, among RR/MDR-TB patients enrolled in second-line TB treatment care in Uganda between January 1, 2013 and December 31, 2014.

We analysed data from routine patient records collected the 14 national second-line TB initiation hospitals. A total of 407 patient record were reviewed and 396 were included in the study.

Results: 396 individuals were evaluated, 63% males, median age 35 years (IQR=27 - 43), HIV positive 48% (191/396), all HIV positive were on treatment. 62% (246/396) reported at least one side effect. 31% had arthralgia, 30% reported gastro-intestinal symptoms, 20% reported ototoxicity including 10% complete hearing loss, 15% reported peripheral neuropathy, 7.1%

developed psychiatric manifestations, 8.0% reported dermatological complications, 1.8% reported visual disturbances, 1.5% developed hypothyroidism, 1% developed nephrotoxicity, and hepatitis and convulsions were reported in 0.5% each.

Males had 2.04 times odds of ototoxicity as compared to females $OR_{ad}=2.04$ (95% Confidence Interval [CI]=1.05 - 3.98), the odds of reporting ototoxicity increased with age 25 - 34 years $OR_{ad}=1.78$ (95% CI=0.58 - 5.46), 35 - 44 years $OR_{ad}=2.6$ (95% CI=0.89 - 7.8), and 45+ years $OR_{ad}=4.2$ (95% CI=1.29 - 11.5).

Conclusions: This study demonstrated presence of several side effects including complete hearing loss in 10% of the cohort of RR/MDR-TB patients. Aggressive monitoring and management of side effects associated with second-line TB treatment should be emphasized, including use of audiometers for monitoring hearing function. Males and older patients should be followed up more closely.

SOA10-1102-26 Interim outcome of DR-TB patients treated with bedaquiline- or delamanid-containing regimens under programmatic conditions in Ethiopia

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Background: Bedaquiline (Bdq) and Delamanid (Dlm) were introduced in Ethiopia under programmatic conditions. The efficacy data of regimens containing these new drugs is being systematically collected through endTB observational study. The objective of this study is to describe interim outcomes of MDR-TB patients treated with regimens containing Bdq or Dlm in Ethiopia.

Methods: We report sputum culture and sputum smear conversion from positive to negative during the first 6 months of treatment with Bdq or Dlm. To allow for six-months of follow-up, we included patients initiating a Bdq- or Dlm-containing regimen prior to March 1, 2017. We also describe the timing of smear and culture conversion.

Results: Of 21 MDR-TB patients who were enrolled during the study period, 20 consented to participate in the observational study. Of these, nine (45%) had culture positive sputum and 11 (55%) had smear positive sputum at the time of Bdq or Dlm initiation. Rates of HIV and malnutrition were high in these patients (HIV prevalence of 55%; BMI < 18.5 in 100% and 82% of

patients included in culture and smear analyses, respectively). All but one patient had received prior MDR-TB treatment with second-line drugs. Culture and smear conversion rates were 89% (8 of 9; 95% CI: 52 - 100%) and 82% (9 of 11, 95% CI: 48%- 98%), respectively. We conservatively classified the two patients who did not have follow-up smear data as having not converted. The median times to culture and smear conversion were 78.5 days [interquartile range 38-121] and 35 days [interquartile range 32-64], respectively.

Conclusions: High rates of smear and culture conversion were achieved in this small cohort of patients with a high rates of HIV, malnutrition and prior treatment with second-line drugs.

SOA10-1103-26 The role of bedaquiline and linezolid in the management of toxicity from rifampicin-resistant tuberculosis treatment in Johannesburg, South Africa

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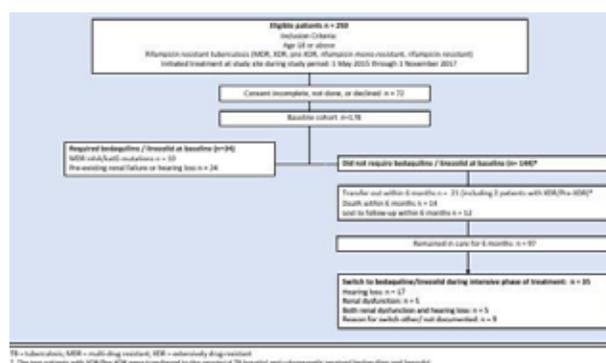
Background: Bedaquiline and linezolid are substituted for aminoglycosides in the management of rifampicin-resistant tuberculosis (RR-TB) in South Africa in patients with baseline or incident hearing-loss or renal dysfunction or multi-drug-resistant TB (MDR-TB) with *inhA* and *katG* mutations. We describe reasons for baseline use of bedaquiline/linezolid and risk factors for switch during the first 6 months (intensive-phase) of therapy.

Methods: Prospective cohort study at an outpatient RR-TB treatment site in Johannesburg, South Africa. Patients with RR-TB, age >18, who consented to study participation and enrolled between 1/5/2015 and 1/11/2017 were included. A log binomial regression model was applied to determine risk factors for switch to bedaquiline/linezolid during intensive-phase. Patients received monthly monitoring for hearing-loss and renal dysfunction. Bedaquiline/linezolid are co-prescribed for all patients requiring an aminoglycoside-sparing regimen.

Results: Of 250 eligible patients, 178 consented to enrol in the study. 143/178 (80.3%) were HIV-infected with a median age of 29 (IQR 18 - 36) and median of CD4 54 cells/mm³ (IQR 19 - 191). Bedaquiline/linezolid were prescribed at treatment start in 34/178 patients: 24 had baseline hearing-loss or renal dysfunction and 10 had MDR-TB with *inhA* and *katG* mutations. Amongst the 97 patients who completed the intensive-phase of treat-

ment an additional 35 switched to bedaquiline/linezolid and discontinued kanamycin (figure): 17/35 developed hearing-loss; 5/35 renal dysfunction; and 5/35 both (reason for switch was not documented in 9/35). The following risk factors for switch to bedaquiline were examined using a log-binomial logistic regression analysis: gender, age, HIV status, CD4, body mass index, baseline anemia. Only baseline anemia (hemoglobin < 12) was significantly associated with subsequent regimen switch (RR 1.71 95% CI 1.01 - 2.91).

Conclusions: In an outpatient RR-TB treatment site, close to 40% of patients required a bedaquiline/linezolid based regimen during the intensive-phase of therapy: 19% at baseline and 20% developed aminoglycoside-induced treatment toxicity requiring treatment switch.



[Description of cohort]

SOA10-1104-26 Factors associated with loss to follow-up and mortality in public sector MDR-TB treatment in western Maharashtra, India, 2015-2016

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Background: Poor treatment outcomes for multidrug-resistant tuberculosis (MDR-TB) are a continued challenge for patients, clinicians, communities and TB programs. Leveraging programmatic data provides an opportunity to identify local challenges and barriers to TB care. In the present analysis, factors associated with mortality and loss to follow-up (LTFU) from MDR-TB treatment in Western Maharashtra, India were examined.

Methods: For this registry analysis, individuals starting public sector MDR-TB treatment in 5 districts of Western Maharashtra between 2015-2016 were included. LTFU was defined as treatment interruption ≥2 months. Baseline factors associated with LTFU were assessed

using subdistribution hazard (SH) models, accounting for the competing risk of death. Factors associated with mortality were assessed using Cox proportional hazards regression.

Results: In total, 684 individuals initiating MDR-TB treatment were included with 759 person-years (PY) of follow-up. During follow-up, 89 patients were lost to follow-up and 140 died. After adjusting for district, year of treatment registration and baseline covariates, factors significantly associated with increased LTFU were older age (>55 years vs. ≤25 years, aSHR 2.65), history of alcohol addiction (aSHR 2.37), and extrapulmonary TB (vs. pulmonary TB, aSHR 3.24). Severe anemia (vs. no anemia, aSHR 0.16) and prior private TB treatment (aSHR 0.55) were marginally associated with lower rates of LTFU. Mortality during MDR-TB treatment was associated with severe underweight at baseline (body mass index < 16 vs. ≥18.5 kg/m², aHR 3.23), severe anemia (aHR 4.55) and any prior LTFU from TB treatment (aHR 1.65).

Conclusions: An understanding of the factors associated with mortality and LTFU from treatment has the potential to inform the development and implementation of flexible, patient-centered support programs. Efforts to address several of the identified risk factors are underway through the public sector TB program in India, including: decentralized drug susceptibility testing and integrating TB counseling activities with de-addiction services.

SOA10-1105-26 Impact of nutritional status on outcome of treatment and mortality among MDR TB patients

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Background: Despite of adoption of multiple strategies for prevention and treatment of multidrug resistant (MDR) tuberculosis over the past decade, MDR TB still continues to challenge mankind with high treatment failure and mortality rate especially among the Asian countries. It is important to identify the modifiable risk factors that may have adverse impact on MDR TB treatment outcome.

Methods: A retrospective cohort study was conducted in 323 MDR tuberculosis patients registered at the DOTS Plus site of a tertiary care teaching hospital between April 2010 to March 2012. Variables identified as risk factors were BMI, extreme age, Female gender, Hypoproteinemia, anaemia and type of prior antitubercular treatment.

Data is expressed as mean ±SD or percentage. The χ^2 test was used to compare categorical variables. Student's t-test, was used to compare continuous variables. Multivariate logistic regression analysis was used to evaluate

the association of independent variable and outcome of treatment and all cause mortality.

Results: 86.7% of the study population was underweight, 54.5% was moderate to severely anemic and 60% were hypoproteinaemic at the time of starting treatment for MDR tuberculosis. Outcome of treatment was unsuccessful in 62.3% of the patients with all cause mortality 28.5% during the treatment period. Underweight patients were at greater risk of unsuccessful treatment outcome with AOR 1.17(95% CI 1.06, 1.28, P< 0.0001) and mortality AOR 1.34(95% CI 1.18, 1.52 P< 0.0001) compared to those with normal weight. Risk of all cause mortality further increased significantly among patient with severe malnourishment crude OR 5.03 (95% CI 2.42, 10.48 P< 0.0001).

Conclusions: Adequate nutritional supplementation as an adjuvant to antitubercular therapy should be considered for high risk patient population to overall improve the outcome of treatment and mortality rate among MDR TB patients.

SOA10-1106-26 Is the current practice of using response to empirical broad-spectrum antibiotic treatment as an exclusion diagnostic for tuberculosis supported by evidence? Systematic review and meta-analysis

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Background: Suboptimal diagnostics for pulmonary tuberculosis (PTB) drives use of "trial-of-antibiotics" to distinguish PTB from bacterial lower respiratory tract infection (LRTI), particularly in low-resource settings. The underlying assumption ---that patients with LRTI will improve after taking broad spectrum antibiotics, while those with PTB will not--- has an unclear evidence-base for such a widely used intervention (~26.5 million prescriptions/annum). Numerous potential causes of misclassification include bacterial superinfection of PTB, placebo effect, and antimicrobial resistance (AMR). This systematic review and meta-analysis aimed to collate available evidence on diagnostic performance of trial-of-antibiotics.

Methods: We searched (24Nov2017) MEDLINE, Embase, and Global Health for studies investigating diagnostic performance (sensitivity and specificity) of trial-

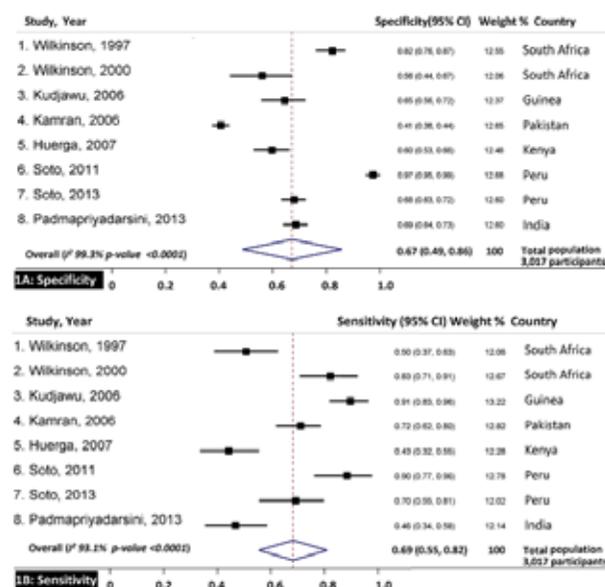
of-antibiotics against mycobacteriology in adults with TB symptoms, including studies published 1993-2017. QUADAS-2 was used to assess risk of bias. Meta-analysis included random-effects modelling.

Results: After screening 7,064 abstracts, 12 eligible studies involving 3,809 participants were included. Study quality was low, with small sample sizes. Most were conducted in hospital or specialised clinic settings (9/12), used mycobacterial culture (8/12) reference standards, and amoxicillin for trial-of-antibiotics (7/12) but with variable duration and number of antimicrobial courses, and definition of response-to-treatment. Eight studies (3,017 participants) with adequate data for meta-analysis yielded 69% (95% Confidence Interval [CI] 55-82%; I^2 93.1%) sensitivity and 67% (95% CI 49-86%; I^2 99.3%) specificity for trial-of-antibiotics against reference mycobacteriology (Figure 1), but with substantial heterogeneity.

Conclusions: The current level of evidence to support trial-of-antibiotics in PTB diagnostic algorithms is weak, with worryingly poor and highly inconsistent methodologies and performance estimates. Given the extent of use and potentially serious consequences of misclassification and AMR, well-designed studies are urgently needed to rigorously evaluate broader benefits and harms.

Systematic review registration:

PROSPERO: CRD42017083915.



[Figure 1: Meta-analysis of the diagnostic performance of trial-of-antibiotics versus mycobacteriological reference standard in the 8 studies with meta-analysable data.]

SOA10-1107-26 Using quality Improvement science to improve rifampicin-resistant TB surveillance through GeneXpert weekly reporting, Uganda, May 2016-November 2017

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Background and challenges to implementation: Despite the deployment of over 100 GeneXpert machines in Uganda, monitoring their performance had been a challenge as only 45% reported on a weekly basis in 2016. The machines are deployed with GxAlert, a remote monitoring solution, with ability to transmit results. GxAlert reporting had been problematic for almost all the 100 machines. We implemented an intervention to improve rifampicin resistant tuberculosis (RR-TB) surveillance through weekly reporting.

Intervention or response: An improvement team was formed at the Uganda National TB and Leprosy Program, with data officers, epidemiologist, genexpert coordinator, and MDR-TB coordinator. The team analyzed and identified lack of internet for GeneXpert machines as the challenge hindering reporting. Use of other means of reporting (SMS, email and phone calls) as a change for testing, and was communicated to the GeneXpert-site-coordinators during a meeting in June 2016 in Kampala. A weekly reporting tool capturing samples tested, results, reporting rates and means of reporting was developed, and it would be populated and shared on a weekly basis on Thursdays via email. During the initial 3 months, the team met bi-weekly to review implementation and there after meetings were as when needed.

Results and lessons learnt: Reporting rates increased significantly from 45% in week 24 (June 16) to 90% in week 43 (November, 2017) ($X^2 = 120$, $p < 0.001$), thereafter remained between 70-80%. In the same period, 178028 samples were tested, and 21384 TB patients were diagnosed, weekly 286 (range 124 - 437) patients were diagnosed. TB positivity rate was 12% (21384/178028) [range 9 - 18%] and 373 RR TB cases were diagnosed; RR rate among TB patients was 1.7% (373/21384). All reported RR TB patients were initiated on treatment.

Conclusions and key recommendations: Reporting through other means led to increased reporting rates from 45% to about 80%. We recommend use of other means of reporting in countries with challenges with internet connectivity.

SOA11 Solutions to improved case finding and early treatment OR Find and treat

SOA11-1108-26 Intensifying tuberculosis control interventions in urban slums: a patient-centered approach from BRAC

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Background and challenges to implementation: Urban areas are characterized by densely populated settlements where TB possesses a greater threat due to its pervasive nature, and was reflected in the National TB prevalence survey 2015-2016, which reported that for every 100,000 population 316 cases were prevalent in Urban areas as opposed to 270 in Rural areas. Cases were most concentrated amongst migrants and floating populations residing in urban slums. Despite the success of active case finding in various communities, a more integrated patient centered approach combining various diagnostic centres and private sector engagement can enhance case detection.

Intervention or response: BRAC, a non-government organization, has intervened with TB management in 132 slums of Dhaka city by establishing an out-reach sputum collection centre in each. The centres are responsible for building community awareness, and sputum collection which is followed by transfer to diagnostic laboratories. Community health workers (CHW) overlook community mobilization for active case findings and contact investigation, within the catchment area, in addition to operating the out-reach centres. Many slum dwellers take their primary complains to physicians and pharmacy holders who are mapped by the CHW to create referral linkages that connect patients to TB diagnostic centres. Diagnosed patients are registered and tagged to a DOT provider to take medicines under supervision.

Results and lessons learnt: A significant increase was observed in the number of cases notified from 2014 to 2017. The number of cases confirmed bacteriologically nearly doubled from 313 (in 2014) to 598 in 2017. Clinically diagnosed cases increased from 164 to 175, while extra-pulmonary cases leaped from 198 to 373. 83 cases of relapse were recorded in 2017 displaying much higher figures from 2014 (35 relapse cases).

Conclusions and key recommendations: Integrating technologies into the current strategy can optimize the reporting and supervision system which promotes efficiency in active case finding and contact investigation.

SOA11-1109-26 Impact of the patent medicine vendor engagement drive on the identification, referral and diagnosis of presumptive TB cases in a TB control program

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Background: Identification and prompt referral for diagnosis is a key component of TB management. This study, undertaken across 7 local government areas (LGAs) in a state in northern Nigeria, examined the results of the patent medicine vendors (PMVs) involvement in TB diagnosis between January 2017 and December 2017. PMVs sell over-the-counter medicines in informal settings.

Methods: In 2016, PMVs were mapped out by the state TB control team and the respective local government team based on client-burden across 7 LGAs after which they were trained on identification of basic TB symptoms and prompt referral for diagnosis. Meetings were held monthly thereafter to collate data generated and share best practices. They received routine mentorship and supportive supervision to ensure data accuracy and continuous improvement.

The data generated from this intervention in the year 2017 was weighed against total data generated in the seven LGAs in 2015 prior to the engagement of PMVs to measure the effectiveness of the drive.

Results: A total of 10,381 presumptive TB cases were referred across the 7 LGAs in 2017 as against 2865 (362.3% improvement). Of these, 16% (1663) were found to be positive for TB and enrolled on treatment with a 191% improvement from 871 in 2015. Overall, the PMV drive referred 7160 (69% of total) presumptive TB cases across the 7 LGAs with 625 (38% of total) cases diagnosed and successfully placed on treatment in the year 2017. Effective community entry and stakeholder engagement, strengthening community systems, advocacy visits as well as community enlightenment were some of the factors responsible for this success.

Conclusions: While efforts aimed at prompt diagnosis of TB in communities must be strengthened, efforts at further engagement of community players such as patent medicine vendors should be further encouraged for achievement of a TB-free Nigeria.

SOA11-1110-26 Private sector TB patients: counting the uncounted by engaging private providers in Mumbai

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Background and challenges to implementation: In India, half of the all TB patients seek care in the private sector and Since September 2014, Mumbai is started providing Diagnostic and treatment services to private sector patients through PATH (Sep 2014 to Dec 2017) and Patient provider support agency (From Jan 2018 onwards). From 1st Jan 2018, PPSA scheme is implemented By Municipal Corporation of Greater Mumbai for engaging the private providers to reach private sector TB patients.

Intervention or response: PATH supported MCGM to engage Private sector TB patients and free diagnostic & treatment services was provided which was later adopted by MCGM through by appointing PPSA agency.

Results and lessons learnt: Public sector in Mumbai has engaged total 689 Hospitals, 1653 private Doctors and 394 pharmacist to provide free diagnostics and free treatment services to the Private sector TB patients. 60000 private sector TB cases were notified from Mumbai in last 3 years. During Sept 2014 to March 2018, total 74697 CBNAAT test were offered to the private sector TB patients. Out of these 74697 tests, 63349 tests were performed by private sector CBNAAT sites which was supported by PATH and 11348 CBNNAT tests were performed through Public sector CBNAAT sites of Mumbai. More than 50000 private sector TB patients were offered free treatment services to private sector TB patients (50,000 patients through PATH and 450 through PPSA scheme). More than 19000 Xray services was provided to private sector TB patients.

Conclusions and key recommendations: To achieve the TB elimination goal by 2025, it is very much important to reach each and every TB patients. Mumbai Model has shown that TB diagnostic and treatment services can be made available free to private sector TB patients also and this model can be replicated across the nation.

SOA11-1111-26 Applying continuous quality improvement methods and monitoring weekly TB screening increases TB case finding in health facilities in Wakiso district, Uganda

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Background and challenges to implementation: Uganda remains one of the 30 TB-HIV high burden countries with a current TB incidence of 202 per 100,000 population but only 50% of estimated TB cases were detected in 2017. In Wakiso district in central Uganda only 36% (541 cases) were notified to the National TB and Leprosy Programme (NTLP) between October and December 2017. This performance is attributed to low index of TB presumption and a weak systemic approach for TB screening at care entry points in health facilities.

Since January 2018, the USAID Defeat TB project has been providing support to facilities in three urban districts of Kampala, Wakiso and Mukono to improve the quality of TB services using quality improvement approaches.

Intervention or response: In mid-February 2018, five health facilities contributing half of the total number of TB cases diagnosed in the district were selected. Improvement teams mapped out the processes for TB screening at different care entry points and identified bottlenecks which included a weak systematic process for TB screening and lack of regular monitoring. We oriented health workers on systematic TB screening, identified a triage volunteer to identify coughing patients and link them for diagnostic evaluation. For seven weeks (12 Feb- 31st March 2018) weekly data was collected and the number screened was plotted against the total outpatient department (OPD) attendance in a documentation journal.

Results and lessons learnt: The proportion of patients screened for TB increased from 35% in mid-February 2018 to 100% by 31st March 2018. TB case notification increased by 90% in the quarter of Jan-March 2018 from 125 to 238 new TB patients.

Conclusions and key recommendations: Using continuous quality improvement (CQI) methods for monitoring systematic TB screening improves TB case finding at health facilities. District and National programmes should target interventions that give support to health facilities to adopt this approach.

SOA11-1112-26 Social enterprise model to engage the private sector for improved tuberculosis care in metropolitan cities of Bangladesh

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Background and challenges to implementation: Bangladesh is both a high tuberculosis (TB) and Multi-Drug Resistant TB burden country and a large number of TB cases remain un-notified to National TB Control Program (NTP), mostly from private sector. Quality assured TB diagnostics and treatments are inadequate in the private sector. Innovative and sustainable approach to engage private sector were undertaken in Dhaka metropolitan area for increased detection of TB cases and improve the management of identified cases.

Intervention or response: The social enterprise model (SEM) intervention focused on developing a referral network of Private Physicians (PP) to refer patients to three icddr, TB Screening Centers (SC) equipped with digital chest X-ray (CXR) and Xpert MTB/RIF (GXP). From January 2017, DOTS were initiated in these SCs that operate beyond traditional business hours for patient convenience. To scale up the initiative, three more SCs in Dhaka and two in Chittagong were established in between November 2017 and February 2018. The SCs also served presumptive cases identified in outreach campaign, referred by networked drug seller, extra-pulmonary presumptive cases and self referred patients.

Results and lessons learnt: From July 2014 to April 2018, 65,399 CXRs were performed among the presumptive pulmonary TB cases, of whom 61,475 (94%) cases provided sputum for GXP. A total of 13,493 (21% of 65,399) pulmonary TB cases were identified, of which 87% were bacteriologically confirmed (B+). In addition, 1,104 extra-pulmonary TB cases were identified at these centers. Among the B+ cases, 486 (4% of 11,779) were rifampicin resistant cases. In the SCs, a total of 1,311 patients registered for treatment, of which 20% transferred in from private sector.

Conclusions and key recommendations: The icddr, SEM intervention was effective in engaging the urban private care providers for client referral. This model can be further scaled up to other metropolitan cities in similar settings to bridge the gap between the private sector and the national programs.

SOA11-1113-26 Achieving systemic and scalable quality assured private sector engagement in TB-HIV care and prevention in Nigeria: successes and lessons learnt

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Background and challenges to implementation: Since 2015 KNCV and PharmAccess implement the project “Improved TB-HIV prevention and care - Building models for the future”[1] in collaboration with the Lagos State TB Program. The objective is to increase access to quality TB screening, early diagnosis and treatment in the private sector.

Intervention or response: The project integrated the international SafeCare quality improvement standards with the International Standards for TB Care (ISTC) [1] into a quality improvement tool in 60 private facilities and started with a participatory baseline assessment. Active TB screening was introduced, SOPs, IEC materials, standard M&E forms provided along with targeted training sessions on TB-HIV, staff retention, quality management and “healthy business” with on-site support and mentoring during joint supervision with public TB officers.

Results and lessons learnt: We observed a five-fold and three-fold increase of presumptive and confirmed TB diagnosis respectively; improved access to diagnostics through a sputum transportation system and TB patients diagnosed using Xpert_MTB/RIF from 43% to 82%. Contact investigation tripled with eligible children placed on IPT. TB literacy of patients improved by introducing the patient charter and the TB literacy tool. Orientation of HCWs and District TB supervisors on the patient charter led to increased knowledge and referrals of presumptive TB patients. Treatment success increased from 59% at baseline to 87%. In less than one year 43% of facilities with poor adherence to ISTC standards reached 100% compliance.

Conclusions and key recommendations: The implemented model has contributed to a marked quality improvement in all facilities enrolled. A facility wide quality improvement approach that integrates TB-HIV quality standards into overall health care can increase TB-HIV case finding and quality care in the private sector. This model will build sustainable health systems, exploring health financing options and business models and integrate the ISTC quality tools into regulatory and National TB program supervision tools.

SOA11-1114-26 Creating demand for small-scale private clinics: results and lessons learnt from community active TB case finding using RAPPID-LINK intervention in Lagos, Nigeria

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Background and challenges to implementation: The public sector in Nigeria is larger than the private sector but contributes only 10% to annual case notification. In Lagos, small private clinics due to lower general patient load find fewer TB cases compared with larger clinics despite active TB screening. To increase demand of presumptive TB patients for these clinics, RAPPID-LINK (figure 1) was used, a community active TB case finding (ACF) approach.

Intervention or response: RAPPID-LINK interventions were implemented between July and August 2017 in 80 communities harboring 16 small-scale, low yield private health facilities. Community selection was done during initial research and review meeting with Lagos NTP and stakeholders. This was followed by advocacy visits to community heads, community mobilization and sensitization using information materials. The partnership with State's AIDS Program provided HIV and glucose test kits for screening of other TB comorbidities. Collected sputum samples were monitored by qualified laboratory staff and recorded by DOTS providers from the private clinics before being transported by standby sputum carriers. Diagnosed TB cases were promptly followed up and linked with the closest small-scale private clinics for TB medication.

Results and lessons learnt: 23.4% (1876) of the total 8021 screened were presumptive. 69% (1296) of the presumptives were tested for TB using genexpert. 61 TB patients were diagnosed, representing 4.7% of the tested presumptive TB, 2(3.3%) pre-treatment death, 2(3.3%) MDRTB, 2(3.3%) LTFU and 55(90%) were successfully linked for treatment with proximate small-scale private health facilities.



[Figure 1: Schema of the RAPPID-LINK for active community TB case Finding]

The total yield of 4.7% of diagnosed TB patients among those tested is higher than the yield from usual outreach approaches implemented in similar communities where only 2.6% (4/156) were confirmed among presumptive tested.

Conclusions and key recommendations: RAPPID-LINK is an effective community ACF approach engaging relevant service providers. It can increase demand with a higher yield of TB cases through community mobilization, quality TB screening, testing TB comorbidities and effective follow-up linkages to small scale private providers.

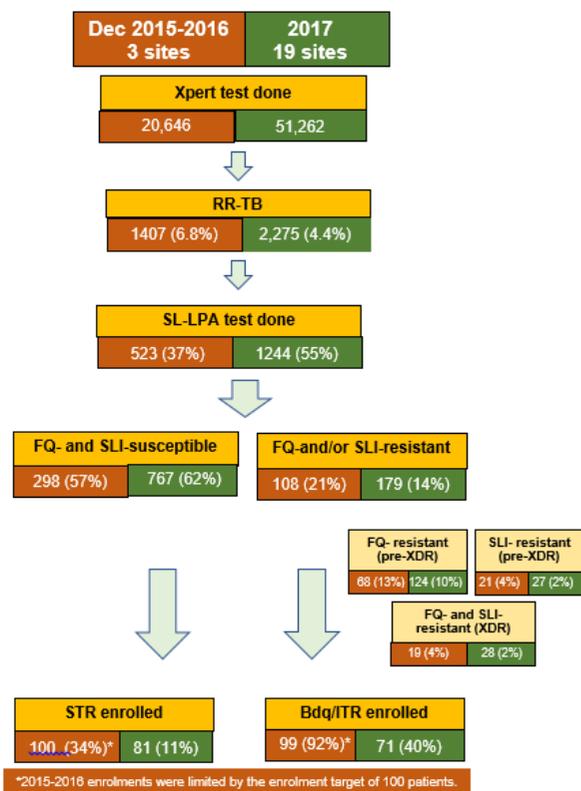
SOA11-1116-26 Right diagnosis and right treatment through the patient triage approach: challenges and lessons from pilot to expansion in Vietnam

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Background: Vietnam expands the use of rapid diagnostics, new drugs and regimens for rifampicin-resistant TB (RR-TB), and (pre-) XDR (extensively resistant) TB through patient triage. Xpert is the initial test for RR-TB detection, and SL-line probe assay (LPA) for detection of fluoroquinolone (FQ) and second-line injectable (SLI) resistance. Bedaquiline (Bdq) and the shorter treatment regimen (STR) were introduced in December 2015 and April 2016, respectively, in three pilot provinces. SL-LPA access was expanded to 19 provinces and STR to 8. **Methods:** Patient triage guides health providers in initiating the most appropriate, least toxic regimen in the shortest possible time: category 1 regimen for rifampicin-susceptible patients; STR for confirmed RR-TB without presumed or confirmed resistance to FQ and SLI, or intolerance to STR drugs, not pregnant and without extrapulmonary TB; individualized treatment regimen (ITR), mostly Bdq-containing for RR-TB with SL drug resistance and/or intolerances. SL-LPA results later guide regimen continuation or shift.

Results: After two years of triage implementation, among 51,262 patients tested, Xpert detected 4.4% (2,275), of whom 1244 (55%) were tested with SL-LPA. SL-LPA coverage increased from 37% to 55%; however, due to a 7-month interruption of STR and Bdq use pending Ministry of Health expansion approval, STR enrolment declined from 32% to 11%; and Bdq from 92% to 40% (Figure). Other factors were variability in policy uptake and management capacity of different provinces, specimen transport problems, and patient refusal for STR enrolment due to the required study conditions, like informed consent and hospitalization.

Conclusions: Implementation of the triage approach using rapid molecular diagnostics and new treatment regimens is feasible in Vietnam and can provide better tailored treatment for MDR patients. Engagement and mandate of top ministerial level for the introduction and expansion of the new treatment, patient centeredness, and continued clinical mentoring during scale-up are crucial.



[Patient triage approach, Vietnam, December 2015-2017]

SOA11-1117-26 Quality of care among adult pulmonary TB patients in The Gambia, West Africa: a cross-sectional survey

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Background: One of the major roadblocks in control of tuberculosis (TB) is the lack of early diagnosis. This can be hampered both by weak health systems in developing countries and stigma associated with TB. We investigated the care-seeking behaviour and causes of diagnostic delays among adult TB patients in The Gambia .

Methods: We conducted a cross-sectional survey of adult patients (age ≥ 15 years) with pulmonary TB in an urban setting of The Gambia. We investigated where TB patients had initiated care and the number of visits before TB diagnosis. TB diagnostic delay was defined as more than three health care visits before TB diagnosis. Univariate and backward stepwise multivariable logistic regression analysis was used to investigate factors associated with TB diagnostic delay.

Results: Overall, 224 smear-positive pulmonary TB cases were recruited; age range was 15 - 72 years and 170 (76%) were males. 115/224 (51.3%) of the TB patients initiated care in the formal and informal private sector, comprising 'traditional healers' (n=9), 'dispensaries' (n=8), 'pharmacy shops' (n=51) and 'private clinics' (n=47).

A total of 70 TB patients (31.3%) had more than three health care visits before TB diagnosis. Age ≥ 30 years (aOR 1.3 [95% CI 1.1 - 1.6]; p=0.019) and 'mixed care-seeking' at both private and public facilities (aOR 3.6 [95% CI 1.9 - 7.1]; p=0.000) were significant and independent predictors of TB diagnostic delays.

Conclusions: About half of adult TB patients in The Gambia initiate care in the private sector, where providers often have poor knowledge about TB symptoms and TB diagnostic facilities are frequently unavailable. There is need for improvement and better understanding of care-seeking behaviour of TB patients and full engagement of the private sector to improve quality of TB care in The Gambia.

SOA12 Digital technology to improve treatment adherence and outcomes

SOA12-1118-26 Comparing electronic directly observed therapy with in-person DOT: patients' perspectives

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Background: We are conducting a randomized controlled trial comparing traditional in-person directly observed therapy (ipDOT) with electronic DOT (eDOT) for tuberculosis (TB) treatment, in four TB clinics in New York City.

Methods: Participants are asked to complete 20 medication doses with one form of DOT (either ipDOT or eDOT), and then cross over to complete 20 doses with the other. The initial form of DOT is randomly assigned. eDOT uses recorded (eDOT-Rec) or live (eDOT-Live) video. After completing the two observation periods, participants are asked to complete an opinion questionnaire comparing the two types of DOT relative to independence, privacy, ease, care and support.

Results: Since July 2017, 79 persons have enrolled. Of 43 who completed both observation periods, 33 (77%) completed the questionnaire. Within this group, age ranges 18-86 years (average 41.8 yrs.), 61% (n=20) are male, 91% (n=30) are non-U.S. -born. There were no evident response differences between those using eDOT-Rec (n=15) and those using eDOT-Live (n=18). Overall, 72-93% of respondents felt that eDOT offered greater opportunity to:

- (a) maintain independence;
- (b) keep their schedule as it was prior to their illness;
- (c) keep diagnosis and treatment private; and
- (d) take treatment more easily.

In contrast, 52-64% of participants noted no difference between ipDOT and eDOT or rated ipDOT higher with regard to:

- (a) ability to talk to staff about treatment concerns;
- (b) emotional support from TB program staff;
- (c) staff listening to concerns or worries;
- (d) staff knowing and caring about my situation; and
- (e) staff checking on me for side effects of medications.

Conclusions: These limited preliminary observations suggest that different forms of DOT have different advantages and disadvantages from the perspective of the TB patient. Ongoing data collection will clarify these initial observations. Such information can guide TB programs' use of DOT.

SOA12-1119-26 Acceptability to patients and providers of 99DOTS, a cellphone-based TB adherence monitoring strategy

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Background: Poor adherence to TB therapy is associated with increased risk of treatment failure, disease relapse, and drug resistance. India's government TB program has introduced 99DOTS, a cellphone-based strategy, for monitoring medication adherence.

The purpose of this study is to evaluate:

- (a) patient and healthcare provider (HCP) acceptance of, and satisfaction with, 99DOTS;
- (b) barriers to using 99DOTS, and;
- (c) options for improving 99DOTS' acceptability.

Methods: We conducted in-depth qualitative interviews with 60 TB patients (HIV co-infected and un-infected) being monitored with 99DOTS and 30 HCPs in the government programs in Chennai and Mumbai. The RE-AIM framework (Reach, Adoption, Implementation, and Maintenance) structured our analytical approach. We coded interview transcripts using thematic analysis.

Results: Lack of availability and sharing of mobile phones within the family were voiced by some patients as barriers to the "reach" and "adoption" of 99DOTS. Some patients also described poor cellular network coverage as being a barrier. In the intensive phase of therapy, most patients with adequate cellphone access expressed relatively high satisfaction, because 99DOTS saved time that would normally be spent visiting health centers for facility-based DOT. However, some patients in the continuation phase expressed "fatigue" from having to call 99DOTS regularly and from depending on family members to call for those using shared phones. Overall, HCPs expressed satisfaction with 99DOTS, as they felt it saved them time that would normally be spent on home visits, which could now be used for updating records and providing better patient care at health centers. Many HCPs voiced a need for refresher training in 99DOTS.

Conclusions: Most patients and HCPs noted relatively high acceptability of 99DOTS. However, use of shared phones in the family, poor cellular network coverage, fatigue with calling in the continuation phase, and the need for refresher training for HCPs are barriers that need to be addressed.

SOA12-1120-26 Medication electronic reminding monitor used to guide differential patient management at community level in China

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Background and challenges to implementation: Directly Observed Treatment (DOT) cannot be fully implemented in managing TB treatment for various limitations. Medication Electronic reminding monitor (MERM) shows great promise as an alternative. However, due to cost and other consideration, MERM without real-time data transmission is always used, which limits timely access of doctors at all levels to the patient's dosing data and intervening any incorrect dosing behaviours.

Intervention or response: A small LED screen was developed in MERM to enable community doctors to know the patient's regularity of dose intakes and intervene as needed.

Community doctors are requested to visit patients using MERM once ten days in intensive phase and once a month in continuous. Based on MERM records in the previous month, if 20-50% doses were missed, the patient would be switched to "intensive management" for the rest of treatment. If at least 50% doses were missed, DOT will be conducted. The intensive management will require the community doctors to visit patients once a week. Mechanism was established between county and community to implement the differential management.

Results and lessons learnt: The MERM and interventions were piloted in 303 patients from 11 counties for 3 months. Only 2.7 % (8/303) of patients had to be switched to intensive management. Use of MERM greatly reduced the workload of community doctors compared to DOT. However, county clinics spent more resources on MERM configuration, data downloading, training and data-driven counselling.

LED screen was proved helpful for community doctors in knowing patient dosing pattern while the screen significantly increased the battery consumption of MERM, leading to increased costs for frequent battery changes.

Conclusions and key recommendations: TB patient will improve adherence to the prescribed regimen through using MERM and the differentiated patient management. By using MERM widely, the workload in patient management was partially transferred from community to county, which requires optimizing the resource allocation accordingly.

SOA12-1121-26 Effect of mobile app-based nursing health education on patients with pulmonary multidrug-resistant tuberculosis

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Background: To explore the role of nursing and health education based on a mobile app in the treatment of multidrug-resistant pulmonary tuberculosis (MDR-TB).

Methods: 224 MDR-TB patients admitted to Wuhan Pulmonary Hospital from April 2013 to October 2015 were randomly divided into intervention (N = 112) and control groups (N = 112). The control group received routine nursing health education and standard treatment. In addition to regular care, health education, and standard treatment, the intervention group continued to receive WeChat, QQ, and telephone communication after hospital discharge, and received health education from dedicated nursing staff for 2 years.

Results: A total of 167 cases completed the study; 57 cases did not complete the study (24 cases in the intervention group, including 6 deaths, 8 lost to follow up without mobile education, and 10 cases with treatment failure; 33 cases in control group, 8 deaths; 11 cases were lost to follow up and 14 cases failed treatment). The rate of sputum conversion was 69/88 (78.4%) in the intervention group and 33/79 (41.7%) in the control group ($p < 0.05$). Poor adherence was significantly more common in the control group 37/79 (46.8%) compared with the intervention group 6/88 (6.8%) over the two-year period ($p < 0.05$). Nearly all participants in the intervention group 80/88 (90.9%) had self-reported anxiety and depression scale scores < 50 compared with 32/79 (40.5%) in the control group ($p < 0.05$).

Conclusions: Mobile app-based nursing and health education can improve the treatment adherence of patients with MDR-TB and reduce the incidence of psychological problems such as anxiety and depression. The use of mobile apps and nurse-directed health education can improve treatment success of patients on MDR-TB treatment.

SOA12-1122-26 Patient acceptability of an electronic pillbox for monitoring adherence to MDR-TB therapy in India

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Background: The Medication Event Reminder Monitor (MERM, an electronic pillbox) has the potential to improve MDR TB care by providing patients with remote and real-time medication adherence monitoring. We report early findings of a study evaluating the MERM's acceptability to MDR TB patients taking therapy in the government TB program in India.

Methods: We are conducting in-depth qualitative interviews with MDR TB patients in Chennai and Mumbai. We present interim findings from 24 MDR TB patients in Chennai. We used thematic analysis of transcripts to understand the MERM's acceptability, perceived impact on medication adherence, and barriers to its use.

Results: Many patients reported helpful features of the MERM. These included internal storage compartments for organizing medications (e.g., "so much better than carrying loose medication strips, which can be misplaced") and an audiovisual pill-taking reminder that was largely appreciated by patients. Some patients reported that the audiovisual reminder facilitated fam-

ily engagement in their TB care (“*Every time the alarm rings my son would shout out at me saying the doctor is calling*”). Most patients perceived improvements in medication adherence and reduced visits to healthcare facilities. However, multiple patients also reported barriers to engagement with the MERM, including the large size of the box (leading one patient to store it in a chicken cage outside); poor durability of the box, such that the cardboard frame would “bubble out” during the humid monsoon season; and challenges in organizing medications due to overlapping partitions.

Conclusions: Most patients found the MERM to be acceptable and, in particular, the audiovisual alarm was found to be helpful as a reminder and for prompting family engagement in the patient’s care. However, concerns were raised about the size and quality of the pillbox which need to be addressed. Further research is needed to assess the MERM’s accuracy for measuring adherence.

SOA12-1123-26 TB medication adherence using patient-centered, self-managed wirelessly observed therapy is superior to directly observed therapy

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Background: WOT was designed as a patient self-management system. This FDA-cleared device, consisting of an edible ingestion sensor (IS), external wearable patch and paired mobile device, can detect and record medication ingestions, which are uploaded to a secure Internet server. The device records medication taking behavior and health indices on the patient’s mobile device and allows healthcare workers to view records remotely in near real-time to provide support as needed. WOT identifies ingestions with an accuracy equivalent to DOT. We conducted a randomized controlled trial in US DOT programs to compare adherence to TB medications in patients using WOT or DOT.

Methods: Sixty-one participants with active drug-susceptible TB in the continuation phase of treatment were randomized 2:1 to receive WOT or maximal DOT (5 days per week). In the WOT arm, if ingestions were not remotely confirmed, the participant was contacted by text or cell phone to provide support. The number of doses confirmed as taken were collected in each group, the number of doses prescribed followed standard of care (7 days per week); the length of observation varied. Non-parametric methods were used (Wilcoxon rank

sum test, permutation test (10000 permutations) for group comparisons, bootstrap approach (10000 bootstraps)) to estimate 95% confidence intervals for confirmed dose proportions in each group and the difference between groups.

Results: Demographic data included: median age 45 years, 54% male, 77% of reported income was < \$2000/month, 61% High school or less education. Table 1 shows intent-to-treat analysis. Daily medication adherence > 90% was confirmed in 100% of participants using WOT versus 0% in DOT. All participants expressed preference for WOT over DOT. WOT associated adverse events were skin rash and pruritus (< 7%).

Conclusions: Patient self-management supported by WOT was superior to DOT in providing confirmed adherence to TB medications and was overwhelmingly preferred by participants.

	WOT-DOTS (N=51)	DOT (N=20)	Difference	P-value	P-value
Doses confirmed	37/50	2/20			
Doses not confirmed	2/51	7/20			
Total	40/22	2/20			
Non-parametric tests: individual level mean					
Proportion confirmed	0.9236	0.1000	0.3047	<0.001*	<0.001*
(95% Confidence Interval)	(0.8872, 0.9600)	(0.3631, 0.6744)	(0.2396, 0.3699)		
Proportion witnessed ≥ 90%†	0.7825	0.0000		<0.001*	
Bootstrap estimation: group level mean					
Proportion confirmed	0.9294	0.1113	0.2981	<0.001	
(95% Confidence Interval)	(0.8873, 0.9692)	(0.5826, 0.6686)	(0.2431, 0.3551)		
Odds Ratio			7.69		
(95% Confidence Interval)			(4.51, 14.48)		

Method: *Wilcoxon rank sum test; †Permutation test; ‡CIs are based on Student’s t distribution; § Proportion of patients who have 90% or more of days with witnessed doses; ¶ Fisher’s exact test.

[Table 1. Intent-to-treat analysis. All data are used, no exclusions are applied.]

SOA12-1124-26 99 DOTS: a mobile phone based technology to monitor treatment adherence in TB-HIV co-infected patients in Himachal Pradesh State, India

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Background: DOT (Directly Observed Therapy) in India is a specific strategy of TB treatment adherence. There is no doubt that DOT ensured a fairly good treatment success rate; however, it came with a high cost and was often inconvenient for patients. Special groups such as TB-HIV co-infected patients have to cope with stigma related issues. National TB Program (NTP) endorsed 99 DOTS—a novel technology, which leverages mobile phones and innovative packaging to monitor and improve TB medication adherence. Present study was conducted with an objective to demonstrate the feasibility and effectiveness of 99 DOTS in treatment adherence among TB-HIV infected cases in Himachal Pradesh in India.

Methods: A desk review followed by patients and providers interview was done at a cross section in February 2018.

Results: Total 82 (94%) TB-HIV patients were initiated on treatment covered with 99 DOTS adherence mechanism. There was high acceptance rate of the technology;

over 90% of all doses till date were reported correctly using 99 DOTS. About 10-15% of patients required high attention because of inconsistency recorded in the missed calls; all such patients were contacted by the program supervisors following automated SMS from 99DOTS. Real-time adherence reports were also available on the web.

Conclusions: 99DOTS presented a promising approach for improving treatment adherence among TB-HIV co-infected patients at much low cost and high convenience. Considering high effectiveness of this technology, State Government has taken a policy decision to cover all TB patients with 99 DOTS from April 1st, 2018. This technology can also be implemented in other states and countries having similar settings.

SOA12-1125-26 Follow-up observation on the nursing effect of hemodialysis patients with pulmonary tuberculosis complicated with renal failure after WeChat video follow-up

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Background: The side effects using anti-TB were apparent in treating renal failure patients with the TB complications. The compliance of hemodialysis patients with pulmonary tuberculosis complicated with renal failure may affect the quality of patients' life and the patients' recovery. Follow-up with WeChat video is a good mode for health education.

Methods: Eighty-three patients with pulmonary tuberculosis complicated with renal failure, control group (43 cases) and experimental group (40 cases) were continuously included in our hospital from March 1, 2016 to March 1, 2017. The patients in the control group were given routine health education; the experimental group used WeChat video follow-up communication mode to carry out health education for the patients. The differences in disease awareness, medication accuracy, accuracy of urine volume records, and incidence of adverse reactions after dialysis were compared between the two groups.

Results: Experimental group (40): knowledge of disease was 93% (38/40), accuracy of medication was 100% (40/40), accuracy of urine volume record was 90% (37/40), the incidence rate of adverse reaction after dialysis was 54% (22/40), and the total awareness rate was 84% (138/160), which was higher than that of the control group (43): knowledge rate of disease knowledge was 66% (29/43), and medication accuracy was 73% (32/43), Accuracy of urine volume record 70% (31/43), incidence of adverse reactions after dialysis 61% (27/43), total awareness rate 68% (119/172), ($X^2=10.114$, $P = 0.001$; $X^2 = 11.55$, $P = 0.001$; $X^2 = 5.829$, $P=0.016$; $X^2=0.520$, $P=0.471$).

Except for the incidence of adverse reactions after dialysis was not statistically significant, the rest were statistically significant.

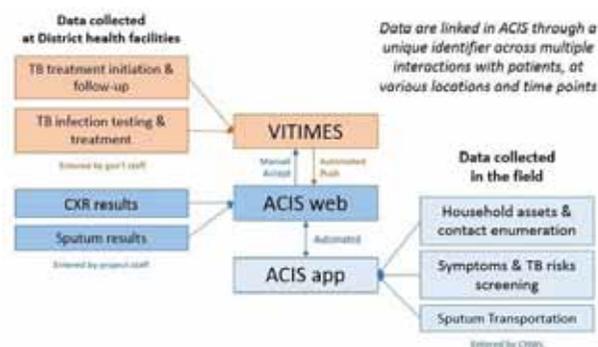
Conclusions: Follow-up with WeChat video can improve the compliance of hemodialysis patients with pulmonary tuberculosis complicated with renal failure, and the quality of patients' life is significantly improved.

SOA12-1126-26 Integrated mHealth tool for nationwide scale-up of community-based TB services

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Background and challenges to implementation: Mobile technologies in public health are commonly referred to as mHealth tools. They allow for real-time data analysis, which promotes data driven programming and have been shown to improve patient services. Though mHealth tools have many benefits, they are often developed as parallel systems and fail to reach scale.

Intervention or response: VITIMES, Vietnam's national electronic routine surveillance system, captures drug sensitive TB treatment initiation, monitoring and outcome data. By 2014, all districts in Vietnam were using VITIMES. In 2017, the Access to Care Information System (ACIS, tb.acis365.vn) was developed for the Zero TB Vietnam project. Through an Application Programming Interface, it bi-directionally links VITIMES to the project's community-based TB services.



[ACIS System Overview]

When a patient is recorded in VITIMES, ACIS receives and forwards the record to a CHW in the ward of the patient's residence and functions as a survey tool for verbal screening of patient contacts and other high-risk individuals. Records of individuals referred for X-ray screening are submitted to VITIMES prior to their arrival. ACIS tracks sputum transportation and allows project staff to record test results. Treatment monitoring and outcome data captured in VITIMES, update automatically in ACIS, removing double-entry of data.

Results and lessons learnt: The app was released in 2017-Q4 and currently has 384 active users; 83% are ward-level users. Over 200 Android tablets with the app were deployed in 13 districts in Hai Phong, Hoi An and Ho Chi Minh City. ACIS allows for the central monitoring of activities and currently stores 32,000+ patient records and 1,200,000+ unique data points. All of Vietnam's 63 provinces, 713 districts and 11,112 wards are mapped in ACIS and can be deployed nationwide.

Conclusions and key recommendations: Robust, electronic data systems are required to increase TB case detection and control the TB epidemic. This innovative tool from Vietnam provides a direction forward for integrated mHealth for active case finding in communities.

SOA12-1127-26 Implementing digital health solutions for monitoring mutations of *Mycobacterium tuberculosis* associated with drug resistance in high MDR TB burden Arkhangelsk Region of Russian Federation

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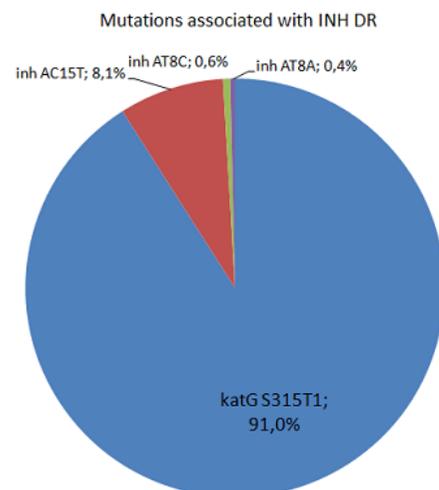
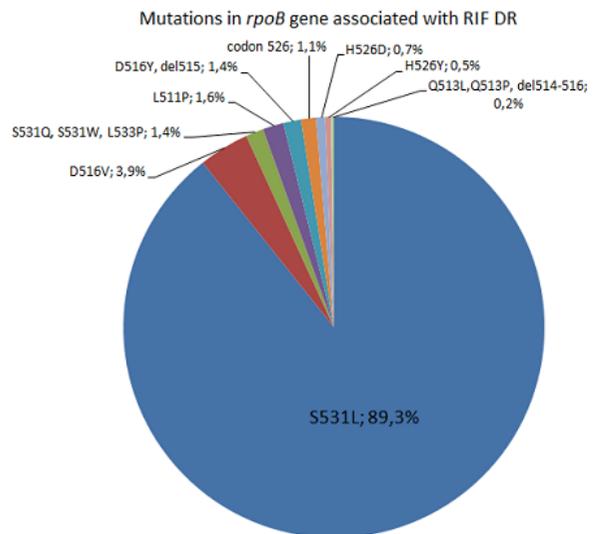
Background: Multidrug-resistant tuberculosis (MDR TB) is one of the main challenges in management of TB patients. In 2016 incidence of TB in the Arkhangelsk region was 26.9/100000 with 33.1% of MDR TB among 'new cases'. Nucleic acid amplification tests, such as line probe assay (LPA), detect mutations associated with drug resistance (DR) of *Mycobacterium tuberculosis* (MBT) and allow rapid detection of DR. Information on mutations might contribute to better management and control of transmission of MDR TB.

Regional electronic register of TB patients (inIT-TB) was developed and introduced as a part of digital health solutions in TB care and control in Arkhangelsk region. The system contains all information on diagnostics and treatment of all TB patients, but lacks information on mutations of MBT.

The aim of this study was to create an electronic system for registering MBT mutations associated with DR to rifampicin (RIF) and/or isoniazid (INH) and to determine the prevalence of those mutations among TB patients in Arkhangelsk region in 2014-2017.

Methods: All TB patients in Arkhangelsk region were routinely tested for MDR with LPA before treatment. The results of LPA were registered in inIT-TB where we introduced a module for recording mutations in *rpoB*, *katG*, *inhA* genes.

Results: Overall 1142 TB patients were tested with LPA In 2014-2017 in Arkhangelsk region. Among them 439 (38.4%) patients had mutations associated with RIF-resistance and 543 (47.5%) - with INH-resistance. Mutations detected among DR TB patients are presented.



[Mutations of MBT among patients with DR to rifampicin and isoniazid]

Conclusions: Mutations *rpoB* S531L and *katG* S315T1 associated with DR to RIF and INH respectively were detected in almost 90% of DR TB patients in Arkhangelsk region in 2014-2017. Electronic system for registering and monitoring of MBT mutations associated with MDR was developed and implemented in the high MDR TB region allowing for better understanding and further evaluation of MDR TB transmission.

SOA13 Tuberculosis, laboratory and epidemiology in Europe

SOA13-1128-26 Tuberculosis control and prevention in the EU/EEA: a survey of national TB programmes

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Background and challenges to implementation: TB incidence has declined across the European Union (EU) and European Economic Area (EEA), but projections show that intensified efforts are needed if WHO End TB targets are to be met. Well designed and robustly implemented national TB strategies are regarded as essential to TB control.

Intervention or response: We conducted a survey of all EU/EEA national TB programme leads to obtain information about the availability, implementation and content of national TB control plans, priority action areas and target groups, and barriers to programme implementation.

Results and lessons learnt: The response rate was 100% (31 countries). About 55% of countries have a national TB strategy, and all of these were implemented. A further five countries were preparing a strategy. 74% of countries have a clearly defined organisational structure and central coordination of TB control, and 19% have a costed programme budget; few programmes included patient and civil society representation. The most commonly (46%) identified priority group was undocumented migrants, because of their high unmet need for TB diagnosis and treatment. The most frequently mentioned priority actions were: reaching vulnerable population groups (80%); targeted screening for active TB in high risk groups (63%); implementing electronic case registries (60%); contact tracing and outbreak investigation (60%); and tackling MDR-TB (60%). 35% of respondents indicated insufficient government prioritisation of TB as a barrier to TB strategy implementation, but the most commonly cited barriers related to recipients of care (including lack of TB knowledge, treatment seeking and adherence), care providers (including need for specialist training of nurses and doctors) and health system constraints (including funding and communication between health and social care systems).

Conclusions and key recommendations: This survey has provided insight into TB strategy development and implementation in EU/EEA member states, and this evidence will be key to developing a TB strategy implementation toolkit for member states as part of the E-DETECT TB project.

SOA13-1129-26 The effect of tuberculosis patient and health care delays on the infectiousness of cases in London

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Background: In England, improving access to services and early diagnosis is a goal of the collaborative tuberculosis control strategy. Many factors affect the impact of reducing treatment delays, including changes in the infectiousness of cases over time. Smear-positive cases are more infectious than smear-negative cases and cavitary cases are more infectious than those non-cavitary, but little is known of how increasing patient delay affects the proportion with smear-positive and/or cavitary disease.

Methods: We calculated the proportion of pulmonary cases who were smear-positive and/or cavitary with increasing time since reported symptom onset among all cases notified during 1st January 2013-31st December 2015 in London. We used mathematical modelling to explore how the proportion changes with increasing time since symptom onset for different assumptions about the rate of onset of smear-positive disease and cavitation.

Results: 3783 pulmonary cases were notified in London during 2013-2015. Among cases with known cavitary and smear status, the proportion who were both cavitary and smear-positive was higher for those diagnosed at least 28 days after reported symptom onset, compared to those diagnosed within 28 days of onset (21% (333/1589, 95% CI: 19%-23%) and 14% (53/372, 95% CI: 10-18%) respectively, $p=0.005$). The corresponding percentages considering smear-negative cases without cavitation decreased from 50% (187/372, 95% CI: 45-55%) to 45% (710/1589, 95% CI: 42-47%) but the difference was not significant ($p=0.06$). The percentage of cases who were smear-positive but without cavitation (13%, 247/1961) or smear-negative with cavitation (22%, 431/1961) remained similar with increasing time since reported symptom onset. The findings are consistent with preliminary results from mathematical modelling.

Conclusions: Increases in delays to diagnosis and treatment may lead to increases in the proportion of cases that are infectious. The findings will be relevant for identifying population groups which might be targeted for maximum impact on incidence.

SOA13-1130-26 Experiences from the introduction of screening and treatment of tuberculosis among pregnant women in Stockholm 2016

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Background and challenges to implementation: Pregnancy and the postpartum period has been associated with higher incidence of active TB and as such an increased risk of maternal and fetal morbidity and mortality both in HIV negative and HIV positive women.

Intervention or response: We evaluated adherence to a newly introduced screening program for active and latent TB among pregnant women (PW) from TB high endemic countries ($\geq 100/100\ 000$) or with previous exposure to contagious TB visiting the Mother and Health-care (MHC) clinics in Stockholm in 2016.

Results and lessons learnt: Five active pulmonary TB cases were detected among all screened PW (229/100 000), where of only one had symptoms i.e. slight cough. About 10% of HIV negative PW were from TB high endemic countries, where of 70% were screened with Quantiferon (QFN) according to guidelines and 21% of these were positive. Only 23% of all PW with a positive QFN result started treatment for LTBI. Main reasons for not being screened, referred or treated were previously tested TST/QFN negative and thereafter no exposure, previously treated for latent/active TB, arrival to Sweden >10 years ago, poor routines, unwillingness and/or loss to follow-up.

Treatment of LTBI with mainly rifampicin postpartum was generally well tolerated and only 14% have discontinued.

About 80% of HIV positive PW were from TB high-endemic countries, where of 70% were screened with QFN and 23% of these were positive. None of these were treated for LTBI. No active TB cases were detected.

Conclusions and key recommendations: An incidence rate of $>200/100\ 000$ for active TB and 21% for LTBI among PW from high endemic countries clearly justifies TB screening for early detection and treatment to reduce the risk of severe TB infection and a possible transmission to the newborn child. HIV positive PW are more often from TB high endemic countries and are thus of special concern for TB screening and intervention.

SOA13-1131-26 Setting up the first TB-PRACTECAL trial site: experience from Uzbekistan

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Background and challenges to implementation: TB-PRACTECAL is a regulatory level phase II/III multi-centre randomised controlled trial studying six month exclusively oral regimens containing bedaquiline and pretomanid for the treatment of MDR- and XDR-TB. The trial is recruiting in Uzbekistan, Belarus and South Africa.

The Karakalpakstan Ministry of Health (MoH) of the Republic of Uzbekistan with support from Médecins sans Frontières, has been treating drug resistant TB for the past 17 years. In the years preceding TB-PRACTECAL trial, they had also successfully implemented an intervention study on the adapted Bangladesh regimen.

Intervention or response: Site selection by the sponsors was based on programmatic management MDR-TB experience, strong local collaboration and recruitment potential. A sponsor team provided regular trainings to the investigator lead team which were then cascaded to the rest of the site team. The effectiveness of training and functioning of trial systems was periodically reviewed throughout the trial by reviewing monitoring visit reports and weekly teleconferences between sponsor team and site staff.

Results and lessons learnt: Karakalpakstan was the first site to be activated in the TB-PRACTECAL trial. Between December 2017 and March 2018, the site has pre-screened 329 patients, screened 93 and recruited 79 patients. No critical protocol or SOP deviations have been reported and the safety and management of patients are recognized as satisfactory.

Conclusions and key recommendations: With the filling of new chemical entities in the TB pipeline, there is a continued need to develop new MDR-TB trial sites. Significant financial and logistic investment is required to set-up these sites. Extensive support is then also needed beyond the site activation up until ICH-GCP standards are consistently attained. This has successfully been achieved through strong commitment from the sponsor, the investigator team and government of Uzbekistan.

Practice	Site routines	ICH-GCP requirements	measures to meet standards
Administration, accountability and storage of medications	Medications are dispensed by the MoH nurses to patients in DOT corner and sometimes to relatives in certain cases in rayons (districts). MSF nurses evaluate by checking the drug administration records. Medications are stored in MoH facilities.	Medications are dispensed to named patients only after identifying the patient by study number and initials confirming the right patient. Complete drug accountability log. All medications are stored under strict temperature controlled environment	Central pharmacy with GMP compliant storage conditions renovated and staffed. Extensive dispensing training and documentation. Individualised packaging material, electronic label printers to facilitate drug administration.
Directly observed treatment (DOT)	MSF nurses conduct monitoring and evaluation activities monthly in MoH DOT corners. MSF support team not directly involved in DOT administration	Medications are provided by CT trained nurses in the Inpatient unit (IPD) and ambulatory care (DOT corners or home based) directly to patients and records in the Medication Administration Record.	Extensive training on DOT, GCP and patient safety. Monthly duty roster allows full coverage IPD and ambulatory care (DOT corners or home based) daily including Sundays and holidays.
adverse events: identification, recording and reporting	MSF Medical Doctors support the MoH Medical Doctors in adverse events identification and management. AEs and SAE are recorded into patient progress notes only.	AEs are identified from history, during clinical examination, reviewing lab reports, ECG and other investigations. All AEs are recorded, regardless of their frequency, severity or causality. Serious Adverse Events and Adverse Event of Special Interest are reported to the MSF Pharmacovigilance Unit within 24 hours.	Extensive training was provided to site staff. Guidance documents, forms and logs were developed. Supervision and support to ensure adverse events identification, recording and reporting requirements were met.
laboratory quality assurance	External quality assurance system in place. Procedures in the laboratory are not strictly controlled. Some practices passed on as word of mouth without detailed documentation. Lab results and data collated through locally developed electronic programme.	Quality system with an identified laboratory quality manager using approved laboratory technical manuals, quality manuals, biosafety manuals. A data collection system with secondary approvals for each lab report and an audit trail. Validation of each instrument or method before implementation. Reference organism (ATCC) and lyophilised control samples are used for the quality assurance in mycobacteriology and safety laboratory in line with GCLP requirements.	Guidance development, staff training and supervision. Laboratory quality manager position created. Regular teleconferences and site visits by sponsor TB lab specialists. Introduced paper lab report forms with data collated directly from source.

[Adaptations to site routines to comply with ICH - GCP requirements when treating multidrug resistant TB]

SOA13-1132-26 Social determinants of tuberculosis in Portugal

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Background: The socio-economic aspect of tuberculosis (TB) epidemiology is increasingly deserving of attention, as a solely curative approach to the disease is now

regarded as insufficient. Our objective was to identify and quantify the impact of social determinants of TB in Portugal and help guide national public health policies.

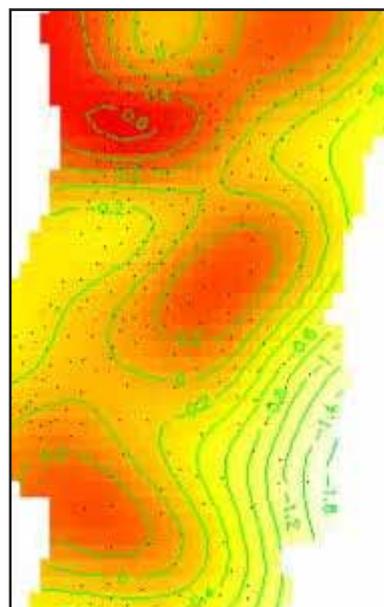
Methods: Data was gathered at the municipality level from the 2011 Census and national health institutions. A semiparametric negative binomial model was used to estimate TB incidence. The non-parametric part of the model was obtained by using thin plate smoothing splines defined on the spatial component of the data.

Results: Household overcrowding, human immunodeficiency virus (HIV) incidence, immigration from high-TB incidence countries and professional exposure to silica dust are each independently associated with high TB incidence. Three high incidence clusters with different contributions from these determinants are defined. The North cluster suffers from a high geographical influence, the Lisbon cluster has high immigration from high TB incidence countries and high HIV incidence and the South cluster also has high immigration from high TB incidence countries, combined with a high burden of professional exposure to silica dust. All three clusters have high and comparable levels of household overcrowding.

An association with high TB incidence is identified in the Porto Metropolitan Area.

Conclusions: With the help of cluster profiles, regional public health policies targeting the most relevant social determinants can be applied more effectively.

The apparently intrinsic geographical influence on TB incidence observed in the Porto Metropolitan Area may be attributed to historical or societal reasons or other unidentified social determinants of TB.



[Adjusted spatial effect on TB incidence.]

SOA13-1133-26 Risk of tuberculosis infection among health care professionals in non-tuberculosis hospitals in Estonia

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Background: Tuberculosis (TB) has long been considered as an important occupational hazard for health care workers (HCW), but recent studies recognized that TB in HCW is generally not acquired through a particular occupational exposure. These findings are supported by recent results from Estonia showing that the incidence of TB among HCW has equalized to the incidence of TB in the entire population. **OBJECTIVES.** To find the determinants of the risk of acquiring TB infection among HCW in non-TB hospital departments following contact with at least one infectious TB patient.

Methods: All HCW (N=87) having occupational contacts with an infectious TB patient were tested twice for latent TB infection (LTBI) in three departments of the Tartu University Hospital in 2016. Partial least squares regression analysis was performed to find relations between LTBI and HCW's gender, age, profession, duration of the contact, previous TB contacts and infectiousness and drug-resistance of the index case.

Results: Two smear-positive TB patients, MDR and drug-sensitive TB, died in separate intensive care units after 11 and 7 days of stay, respectively. A 3rd, culture-positive TB patient, was hospitalized in a department of radiotherapy during 38 days. Out of all tested HCW (N=87, 11 males and 76 females, aged between 22-65 years, spent 12-216 working hours with the infectious TB patients. The 1st post-exposure IGRA test was positive in 8 cases (9.7%). After 2 months, two additional IGRA-positive cases with were diagnosed at repeated testing (2 additional IGRA-positive cases out of the former IGRA-negatives (2 out of 79, 2.5%). Out of all cofactors, only the earlier-in-life TB contacts were significantly associated with IGRA-positivity.

Conclusions: The occupational risk among health-care workers of acquiring LTBI in non-TB departments of Estonia is usually not dependent on occasional contacts with infectious TB patients.

SOA13-1134-26 Prospects for preventing and closing undesirable adverse reactions in patients with lung tuberculosis and hepatitis C

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Background: Treatment of patients with tuberculosis in combination with hepatitis C is particularly difficult due to the poor tolerability of anti-tuberculosis therapy regimens (ATTR). The purpose of the study is to assess the tolerability of I ATTR in patients with pulmonary tuberculosis with hepatitis C in the appointment of Phosphogliv®.

Methods: 146 patients with tuberculosis and hepatitis C, with sensitivity to isoniazid and rifampicin, who were divided into 2 statistically homogeneous groups: the main n = 74 and comparison (n = 72) groups were observed. I ATTR was assigned to all patients. Patients of the main group were assigned Phosphogliv® for 4 months as an escort therapy, from the first day of chemotherapy appointment, the comparison group received standard treatment.

Results: In the main group, sputum abacylation was achieved in 65 (87.8%) people after the 4th month of treatment, in the comparison group in 27 patients (37.5%) (OR = 12.0; 95% CI 5.2 - 28.0, p < 0.05).

In the main group, adverse reactions were observed in 8 patients (10.8%), in the comparison group in 48 (66.7%) patients (OR = 16.5; 95% CI 6.9 - 39.9, p < 0.05).

In the main group, adverse reactions did not require the abolition of chemotherapy, in 24 patients of the comparison group (33.3%) required the abolition of chemotherapy.

In the patients of the main group, the number of viral copies decreased to $1.2 \cdot 10^6$ [95% CI: 0.9-1.5], in comparison group patients it did not decrease and remained at the level of $3.0 \cdot 10^6$ [95% CI: 2.8-3.2] (p < 0.05).

Conclusions: Use of Phosphogliv® prevents and significantly reduces the incidence of adverse reactions, as well as hinders the replication of hepatitis C viruses, which increases adherence to treatment and the effectiveness of antituberculous therapy.

SOA13-1135-26 Tuberculosis not prevented in contacts of infectious tuberculosis patients: a retrospective study of missed cases based on genotyping

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Background: In the Netherlands, contact investigation is carried out by the Municipal Public Health Services (GGDs). The National Tuberculosis Control Plan 2016-2020 recommends to systematically investigate cases that i) share similar DNA-fingerprints (clustered cases), ii) have a confirmed epidemiological link to a index patient in the Netherlands, and iii) were not detected by contact investigation.

Methods: The National Tuberculosis Register provided information on i) the DNA fingerprint (variable number of tandem repeats; VNTR) of the *M. tuberculosis* of the patient, ii) results of cluster investigation i.e. confirmed epidemiological link and iii) how the TB patient was identified i.e. not identified by contact investigation but by self-reporting. GGDs provided additional information on why patients were missed during contact investigation.

Results: In 2016, 889 TB patients were notified; 583 (66%) were confirmed by culture. Seventy-four (8%) patients were diagnosed by contact investigation. Twenty-three (3%) patients were epidemiological linked to a source patient (identical VNTR), but were not identified or prevented by contact investigation. Of these, 11 (48%) were not included in the contact investigation, 7 (30%) were (partly) investigated or had incomplete test results and in 5 (22%) LTBI was diagnosed; 4 were not treated and 1 was treated.

Three patients were infected during an outbreak in a congregate setting and three in coffeeshops (soft drugs) and a person-to-person link could not be confirmed. In the other situations, the secondary cases knew the putative source patient by name.

Conclusions: Genotyping and cluster investigation revealed that contact investigation in the Netherlands can be improved by better identification and examination of contacts and improving LTBI treatment initiation and completion.

SOA13-1136-26 Utility of whole genome sequencing (WGS) to study tuberculosis transmission

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Background and challenges to implementation: Since 2016, all culture positive *M. tuberculosis* complex isolates received at the RIVM have been subjected to both WGS and VNTR typing to allow comparison of tuberculosis transmission by these typing methods. Isolates were clustered by VNTR if they shared identical 24-loci VNTR patterns; isolates were assigned to a WGS cluster when the pair-wise genetic distance was ≤ 12 SNPs. Cluster investigation was performed by municipal health services (MHSs) on all isolates clustered by VNTR.

Intervention or response: In total, 535 isolates were genotyped in 2016, of which 25% (134/535) were clustered by VNTR and 14% (76/535) by WGS. The proportion of identified epidemiological links among WGS clustered cases (57%) was twice as high as among VNTR clustered cases (31%). Based on these results, a pilot study was initiated in 2018 in which WGS data was shared with MHSs, next to VNTR data, to support cluster investigation. Isolates of two relatively large VNTR clusters handled by the Amsterdam MHS were subjected to WGS.

Results and lessons learnt: Cluster 9000289 comprised four isolates from 2016/2017 for which no epi-links were found by the MHS. This was in line with WGS results, as there was 75 SNPs difference between the VNTR clustered cases. Cluster 9000293 comprised 29 isolates from 2016/2017. Three transmission chains were identified by the MHS in this cluster that were also identified by WGS. On the other hand, some patient isolates that could not be linked by the MHS did cluster by WGS. Eight isolates were not clustered by WGS and in line with this also not linked by the MHS, meaning cluster investigation could have been prevented for these patients if only WGS was applied.

Conclusions and key recommendations: The utility of WGS to trace tuberculosis transmission will allow more efficient investigations on transmission, as false clustering can be avoided more efficiently.

SOA14 Drug-resistant: disease burden outcomes

SOA14-1137-26 Short-course MDR-TB treatment in the high HIV prevalence setting of Swaziland: treatment and post-treatment follow-up outcomes and safety

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Background: TB and HIV are leading causes of death in Swaziland. In 2016 the WHO recommended a short course regimen (SCR) for multidrug resistant tuberculosis (MDR-TB). A success rate of 84% has previously been reported for a 9-11 month regimen. Evidence on SCR effectiveness is lacking in high MDR-TB and HIV co-infection settings. MSF and Swaziland Ministry of Health wished to study the safety and effectiveness of the SCR in HIV co-infected populations.

Methods: A prospective observational study was conducted in Swaziland, at Matsapha Health Center and Mankayane Hospital. All consenting MDR-TB patients diagnosed using molecular or phenotypic susceptibility testing were included in the study, initiated on SCR and were followed up with culture. The study underwent ethics review boards approval in MSF and Swaziland.

Results: We present outcomes of 140 patients starting treatment between January 2014 and September 2016. In the overall cohort, 113 (81%) were HIV co-infected, median age was 33.5 years (IQR 27-40) and 62 (44%) were male. End of treatment outcomes are shown in table 1. Overall success rate was 73.0% and 70.0% for the HIV co-infected cohort. 21 (15%) patients experienced failure of the SCR, either due to microbiological failure to culture convert or culture reversion (n=12, 8.6%) or due to severe adverse events (SAE) (n=9, 6.4%). 49 (34.8%) patients experienced a grade 3/4 side effect. Reported SAEs requiring treatment interruption and an alternative regimen were: 5 nephrotoxicity, 3 ototoxicity and 1 QTc prolongation. 2 relapses were identified after one-year post-treatment follow-up.

Conclusions: Our data suggest that short-course regimen for MDR-TB has satisfactory outcomes in high HIV prevalence settings. A small number of patients experienced serious adverse events or microbiologically failed with the SCR, underlining the need for new and repurposed drugs to manage such patients and future regimens with a lower side effect profile.

	Total (N=140)	HIV co-infected (N=113)
Success rate N, % (95%CI)	102, 73.0% (64.8-79.6)	79, 70.0% (60.7-77.7)
Death rate N, % (95%CI)	16, 11.4% (7.0-18.0)	16, 14.2% (8.8-22.0)
Failure rate N, % (95%CI)	21, 15.0% (9.9-22.0)	17, 15.0% (9.4-23.0)
Lost-to-follow up rate N, % (95%CI)	1, 0.7% (0.1-5.0)	1, 0.9% (0.1-6.2)

[Table 1. End of treatment outcomes in total cohort and amongst HIV co-infected patients.]

SOA14-1138-26 Determinants of mortality among patients with drug-resistant tuberculosis in Northern Nigeria

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Background: Drug-resistant tuberculosis (DR-TB) is estimated to cause about 10% of all TB deaths. Dearth of data on determinants of mortality in DR-TB patients in Nigeria exists. Treatment outcome data for death among DR-TB cohorts in Nigeria was 30%, 29%, 15% and 13% respectively from 2010 to 2013. Our objective is to identify factors affecting survival among DR-TB patients in northern Nigeria.

Methods: Demographic and clinical data of all DR-TB patients enrolled in Kano, Katsina and Bauchi states between 1st February 2015 and 30th November 2016 was used. Survival analysis was done using Kaplan-Meier and multiple regression with Cox proportional hazard modeling.

Results: Mean time to death during treatment is 19.2 weeks and for those awaiting treatment 3.9 weeks. Thirty eight of the 147 DR-TB patients analyzed died. HIV co-infection significantly increased probability of mortality, with a hazard ratio (HR) of 2.353, 95% CI: 1.047 - 5.287, p = 0.038. Duration from detection to treatment start showed significant association with survival (p = 0.000), not starting treatment significantly reduced probability of survival with a HR of 7.984, 95% CI: 2.832 - 22.511, p = 0.000. Starting treatment greater than 8 weeks after detection or within 2 to 4 weeks after detection, slightly approaching significance with respective p values of 0.056 and 0.092 is showed to have less than average hazard (beneficial). The model of care (facility vs. community-based) did not significantly influence survival.

Conclusions: Co-infected DR-TB patients and DR-TB patients that experience delayed treatment start after diagnosis are at significant risk of mortality.

Our study showed no significant association with mortality in either facility or community based model of care and emphasizes the need to address programmatic or operational issues causing delays with patient treatment initiation while strengthening DR-TB-HIV co-management as key strategies to reduce poor outcomes.

SOA14-1139-26 Innovative real time reporting system improves healthcare responses to drug resistant (DR)-TB in Nigeria

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Background and challenges to implementation: Nigeria, ranked as the 4th highest TB-burden and 11th DR-TB burden country in the world. Problem stems from the location to diagnosis across a country of over 160 million, continued reliance on paper records and slow data transit systems, resulting in lack of timely quality data to guide resource allocation.

Intervention or response: SystemOne developed an innovative mobile-based solution that sends GeneXpert diagnostic results to enable quick enrollment of newly diagnosed patients in a DR-TB treatment program. GxAlert is configured on GeneXpert and sends encrypted data to the secure web-based database in real time.

This rapid reporting system networks the GeneXpert labs with the capability to send diagnostic test results out to national programs, supervisors, clinicians and patients via SMS text, email, and web dashboard or by connecting into existing M&E, patient record, or case management tools already in use.

The system sends the results in a SMS alert to program decision makers at the state and national TB program, shortening the new-case reporting period from months to seconds.

Results and lessons learnt: The proportion of DR-TB patients enrolled for treatment based on GxAlert messages received from 200 GeneXpert facilities jumped to 85% in December, 2016 from only 50% enrolled in April 2014. SMS or text message alerts speed treatment initiation.

Weekly reports of all new TB+ cases are both emailed and sent by SMS to local health officials to ensure better connection between diagnosis, enrollment and treatment. GxAlert has demonstrated its potential to strengthen surveillance of DR-TB, TB in children and the HIV infected, speeding response and improving programmatic decision and reporting tens of thousands of test results for faster enrollment of patients in treatment programs

Conclusions and key recommendations: The use of GxAlert SMS notification of GeneXpert testing suggests a model for sustainability. Technology is kept simple as local telecom modems are readily available and affordable for GxAlert connectivity.

SOA14-1140-26 What are the factors contribute to Multi-drug resistant tuberculosis patients' survival in Yangon Region, Myanmar?

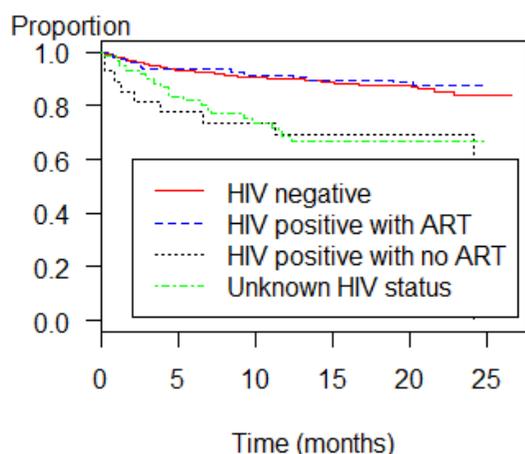
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Background: Myanmar is one of the 30 high Multi-drug resistant tuberculosis (MDR-TB) burden countries. About 60% of MDR-TB patients in Myanmar are located in Yangon Region and the death rate is the highest among unfavorable outcomes. The study aimed to assess MDR-TB patients' survival and associated factors in Yangon Region. The result can be used to improve the treatment care and guideline for the country.

Methods: Retrospective study involved all registered MDR-TB patients in Yangon Region (2015). The association between survival and associated factors were analyzed using ² test and variables having *p*-value less than 0.2 in bivariate analysis were included in the cox regression model and Kaplan-Meier survival curves were drawn.

Results: There were 992 (80%) successfully treated, 186 (15%) died, 42 (3%) lost-to-follow-up and 17 (2%) failure. The total of 1,237 MDRTB patients, 138 (11%) were HIV positive and 109 (79%) received Anti-retro-viral-therapy (ART). We categorized MDRTB patients as following age group: < 28, 24-47 and >48. We found age groups were associated with poor survival [HR=3.95 (95% CI= 2.10, 7.43)] and [HR=7.97 (95% CI= 4.25, 14.96)] respectively. History of previous TB treatment (">2 months" vs. "<2 months) were difference in survival with HR=1.59 (95% CI= 1.10, 2.31). Using HIV negative patients as the reference, HIV positive patients with no ART treatment and patients with unknown HIV status were associated with poor survival [HR=3.60 (95% CI= 1.82, 7.11)] and [HR=2.39 (95% CI= 1.49, 3.82)] respectively. Interestingly, the survival of MDRTB-HIV patients who received ART treatment had the same as HIV negative patients. Other factors such as sex and diagnosed sputum grading were not associated with survival of patients.

Conclusions: Although treatment success was high, we needed to emphasize the factors associated with poor survival. It is important to strengthen and start ART treatment early for all MDRTB-HIV patients.



[Survival of MDR-TB patients, by HIV status and ART]

SOA14-1141-26 What is the impact of Swaziland's TB program interventions on the treatment outcomes of DR-TB patients for the cohort 2009-2014?

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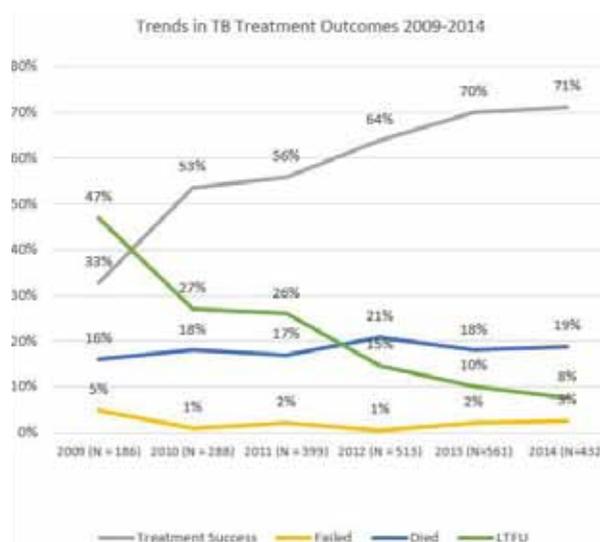
Background and challenges to implementation: The emergence of drug resistant forms of tuberculosis (TB) continues to threaten global efforts to end the TB epidemic due to its complicated management, longer duration of treatment, severe side effects and expensive medicines. From 2009, Swaziland through the National TB control program (NTCP) has worked towards improving DR-TB treatment success rates, reducing transmission with eventual decrease of DR-TB cases. For the first time, we describe the impact of Swaziland TB program improvement efforts on the treatment outcomes for DR-TB patients.

Intervention or response: From 2009-2014 the NTCP introduced key programmatic interventions which included introduction of rapid diagnostic test which allowed prompt diagnoses and initiation on treatment, decentralization of DR-TB services, adoption of community model, outreach teams, defaulter trackers and treatment supporters. The program has also introduced new drugs, shorter MDR-TB regimen and also optimized the existing tools to improve the management and treatment outcomes of patients with drug resistance TB. patients. To ascertain the impact of these interventions, we analysed routine collected data from 2009-2014 cohorts.

Results and lessons learnt: Treatment outcomes for DR-TB patients has significantly shown improvement over the years. DR-TB Treatment success rate has increased from 2009 (33%) to 2014 (71%). Consequently, lost to follow up rates have declined drastically from 2009 (47%) to 2014 (< 3%) cohort. Significant increase in enrolled DR-TB cases from 2009 (186) to 2013 (561) then dropped in 2014 (432). However, mortality has remained high above the WHO threshold ranging between 16% and 21%.

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Conclusions and key recommendations: Decentralization of DR-TB services, adoption of Community model with outreach teams, having defaulter trackers and treatment supporters could have resulted in improved lost to follow up and treatment success rate. Introduction of geneXpert could have resulted in increased case detection. The country hopes to see a change in deaths rate with the introduction of new drugs and institutionalisation of TB mortality reviews in 2015 and 2017 respectively.



[Trend of DR-TB outcomes for 2009-2014 cohort]

SOA14-1142-26 Baseline radiographic appearances in the STREAM MDR-TB trial and their association with treatment outcomes

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Background: In Stage I of the STREAM trial patients with multi-drug resistant tuberculosis (MDR-TB) were prospectively randomised to receive either the WHO 20-month treatment regimen or a 9-month experimental regimen. Patients enrolled in the trial had a baseline chest X-ray performed, and we investigated the association between radiographic findings and treatment outcome.

Methods: Each chest radiograph was classified according to extent of opacities and number of cavities. A favourable outcome was defined as achieving and retaining negative culture status. An unfavourable outcome included all deaths, early loss to follow-up, changes of

treatment or administration of 2 or more additional drugs. Outcomes were compared to baseline disease and cavitation status.

Results: A total of 260 patients were included in the analysis. "Far advanced" disease at baseline was seen in a higher proportion of males (39.3%, 66/168) than females (27.1%, 20/92), and in more patients ≥ 35 years old (44.4%, 48/108) than < 35 years old (25.0%, 38/152). However, 35 of 108 (32.4%) of patients ≥ 35 years had no cavities seen compared to 35 of 152 (23.0%) < 35 years. Fifty-five of seventy-three (75.3%) HIV-positive and 99 of 187 (52.9%) HIV-negative patients had "multiple" cavities, but similar proportions had "far advanced" opacities (29 of 73 [39.7%] and 57 of 187 [30.5%]) respectively. On the study regimen, there was a significant trend to increased unfavourable outcomes with increased opacities (table) and increased cavitation, $P < 0.01$ and $P < 0.05$ respectively. There was no such association with the control regimen, $P > 0.5$ and $P > 0.4$ respectively.

Conclusions: Older patients, males and HIV-positive patients presented with more advanced disease radiographically. A greater extent of disease and cavitation on baseline chest X-ray was associated with poor outcome on the 9-month treatment arm suggesting these patients may require longer treatment.

	9-month Regimen		20-month Regimen	
	n Assessed	n Unfavourable (%)	n Assessed	n Unfavourable (%)
Minimal Disease Extent	23	2 (9%)	11	1 (9%)
Moderate Disease Extent	88	12 (14%)	52	8 (15%)
Advanced Disease Extent	61	18 (30%)	25	4 (16%)

[Proportion of patients with an unfavourable outcome in the STREAM trial presented according to baseline chest X-ray findings and treatment arm]

SOA14-1143-26 Predictors of treatment outcomes among drug resistant tuberculosis patients in Swaziland

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Background: Drug resistant tuberculosis (DR-TB) is a critical threat to public health in Swaziland. Despite efforts that the Government of Swaziland has put towards the management of this disease, treatment outcomes for DR-TB patients remain poor. The study aimed to investigate predicting factors of treatment outcomes among DR-TB patients in Swaziland.

Methods: A retrospective cohort design was adopted where secondary review of medical records of all adult patients who initiated DR-TB treatment in Swaziland between January 2013 and December 2014 was done. A total of 800 DR-TB patients' records were included

in the analysis. Data was analyzed using SPSS version 24. ² test was used to determine difference among variables. We used multinomial logistic regression analysis to identify predictors of DR-TB treatment outcomes. Data with P value < 0.05 was considered significant.

Results: Of the 800 patients; 419 (52.4%) were cured, 157 (19.6%) completed treatment, 149 (18.6%) died, 52 (6.5%) were lost to follow up (LTFU) and 23 (2.9%) failed treatment. Predictors were compared to cured. Predictors of mortality were; age 40 years and older (OR 1.759, 95% CI 1.024-3.024, $P=0.041$); DR-TB treatment regimen with a combination of eight drugs (OR 2.962, 95% CI 1.107-7.926, $P=0.031$); Rifampicin resistance (OR 6.284, 95% CI 2.406-16.414, $P=< 0.001$). A predictor for treatment completion was being located in the Shiselweni region (OR 5.455, 95% CI 1.677-12.742, $P=0.005$). Protective factors for mortality and LTFU were: DOT (OR 0.017, 95% CI 0.008-0.035, $P=< 0.001$), provision of food and transport support (OR 0.0111, 95% CI 0.033-0.375, $P=< 0.001$).

Conclusions: This study revealed the large burden of DR-TB in Swaziland accompanied by high mortality. Intensification of interventions targeted at; early DR-TB identification and treatment, enhancing infection prevention and control measures, addressing social risks factors that limit adherence such as provision of material incentives in the form of food or transportation is necessary.

SOA14-1144-26 Improving DR-TB treatment interim outcomes - lessons learnt from Nigeria

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Background: Effective treatment of DR-TB patients using the conventional regimen in a mixed model of care includes monitoring sputum culture conversion during the intensive phase; however there has been poor access to sputum culture services and retrieval of test results due to limited number of TB reference laboratories.

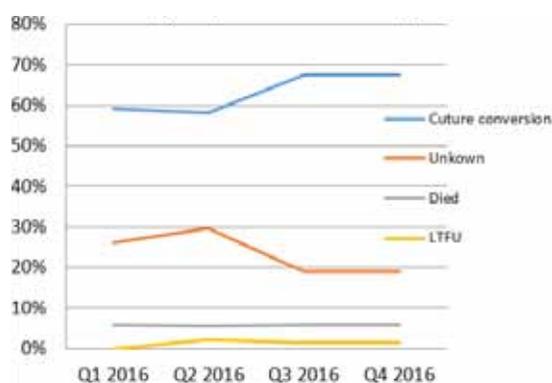
Objectives: This study aimed to improve DR-TB treatment interim outcomes for patients on conventional treatment regimen through coordinated sputum specimen collection, transportation, retrieval of test results and prompt update of patients' paper and electronic recording and reporting tools.

Methods: State DR-TB teams were established across 12 states from January to March 2016, 8 reference TB laboratories with capacity for TB culture/DST were mapped, effective mechanisms for sputum specimen collection were set up, a results relay system between TB reference laboratories and DR-TB treatment sites was established.

Periodic hands-on mentoring and supportive supervisory visits by technical staff from national and state TB programs to staff at facility-level and district-level was established including monitoring and validation of monthly culture results on patient treatment cards, treatment registers and the electronic e-TB manager.

Results: During the preceding quarters from April to December 2016, sputum culture conversion increased from 59% to 68%, patients whose culture results were not known dropped from 26% to 19%, actual LTFU dropped from 2% to 1% while proportion of deaths plateaued at 6%. Overall, there was sustained improvement in documentation of patient's medical records and on average 85% upload of sputum culture results onto e-TB manager.

Conclusions: Sustained coordination for sputum specimen transport and results retrieval systems during DR-TB treatment improves interim treatment outcomes. National and state TB programs should strengthen mentoring of HCWs and regularly monitor documentation of sputum culture results.



[DR-TB Treatment interim outcome (conventional regimen) across 12 states of Nigeria]

SOA14-1145-26 Burden, characteristics and treatment outcomes of patients treated for isoniazid mono-resistant TB in Cape Town, South Africa

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Background: Isoniazid mono-resistant tuberculosis is the most prevalent form of drug resistant tuberculosis in South Africa (TB). The South African National Department of Health recommends 6-9 months treatment with four drugs (rifampicin/Isoniazid/ethambutol/pyrazinamide). Few studies have reported the burden of disease and treatment outcomes of patients with INH mono-resistant TB in this setting. This study aim to characterise the burden of disease and identify risk factors associated with unfavourable treatment outcomes.

Methods: This is a retrospective cohort study of all adult patients (≥ 18 years) with microbiologically confirmed isoniazid mono-resistant TB recorded in the electronic drug-resistant register (EDRWeb) during 2013-2015 in the City of Cape Town, South Africa. Disease burden, basic demographics, routinely captured clinical characteristics and TB treatment outcomes are reported. Multivariate logistic regression were used to identify predictors of unfavourable treatment outcomes, and included age, gender, HIV status, treatment category and registration year.

Results: During the three-year period, 370 patients (226 [61%] males; 218 [59%] ≥ 35 years of age) were recorded in EDRWeb; 187 (51%) newly treated for TB with no previous isoniazid drug exposure. Of patients with a known HIV status, nearly half (180/364; 49%) were HIV infected. Favourable treatment outcomes were reported for only two thirds of patients (229/370; 62%). Unfavourable outcomes included 27 (7%) deaths, 93 (25%) loss-to-follow-up/unrecorded, 14 (4%) failed, and 7 (2%) moved/transferred out. Retreatment patients had an increased odds (aOR=1.7; 95% CI 1.1-2.6) of unfavourable outcomes compared to new patients in multivariate analysis.

Conclusions: In this high DR-TB burden setting, more than 50% of patients with isoniazid mono-resistant TB did not report any previous drug exposure, indicating high rates of community transmission. Overall treatment outcomes were sub-optimal, with 37% unfavourable outcomes observed. Optimal duration and dosing of treatment should be evaluated in this group, especially those with recurrent TB.

SOA14-1146-26 Pyrazinamide treatment is associated with shorter time to sputum culture conversion in multidrug-resistant tuberculosis

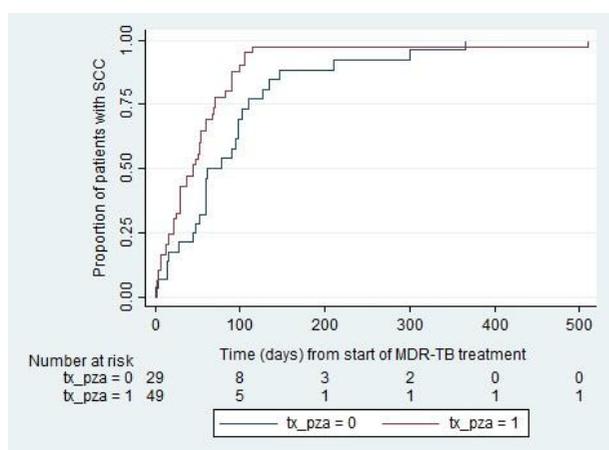
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Background: Pyrazinamide (PZA) is important in the treatment of susceptible tuberculosis (TB) and enables a shortened treatment from 9 to 6 months. However, results have been conflicting regarding the impact of PZA

treatment and resistance in multidrug resistant (MDR)-TB patients.

Methods: In this retrospective nationwide cohort study, all pulmonary MDR-TB patients in Sweden 1992-2014 (n=122) were included. Time to sputum culture conversion (SCC) was analysed with a proportional Cox regression model and adjusted for confounders. PZA drug susceptibility testing (DST) was performed by the proportion method in Bactec MGIT™ (Becton Dickinson, NJ, USA).

Results: Resistance to PZA was seen in 53.3% (65/122) *M. tuberculosis* (Mtb) isolates. Median time to SCC was 46 days and conversion was achieved for 96.5% (83/86) of patients with information of time to SCC. In a univariate analysis, PZA treatment, amikacin treatment, more recent year of diagnosis and increasing BMI were associated with shorter time to SCC, whereas PZA resistance, previous TB treatment, sputum smear positivity and poor adherence were associated with longer time to SCC.



[Kaplan-Meier curve of time to SCC from start of MDR-TB treatment and PZA treatment (tx)]

In a multivariate model, PZA treatment for patients with PZA susceptible Mtb isolates was significantly associated with a shorter time to SCC (aHR 2.24 95% CI 1.29-3.90 p=0.004). PZA treatment, for one month or more, was given to 32.3% of patients despite a PZA resistant Mtb isolate and in these patients, PZA treatment was not associated with shortened time to SCC.

Conclusions: Our results confirm the importance of PZA treatment MDR-TB treatment and highlights the need of a reliable DST of PZA. A high quality DST in combination with whole genome sequencing or novel generation line probe assays to detect PZA resistance, might optimise the use of PZA in MDR-TB treatment.

SOA14-1147-26 Challenges across four types of directly observed therapy

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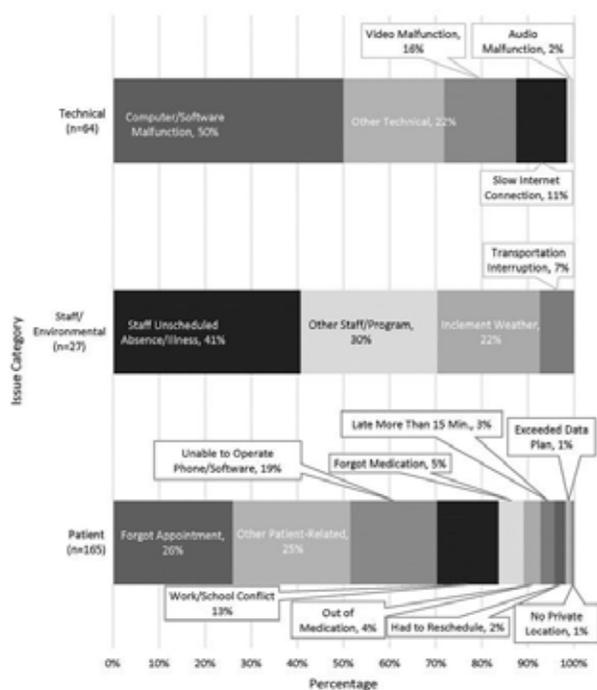
Background: Directly observed therapy (DOT) is the standard of care for treatment of tuberculosis (TB). However, challenges encountered during observations have not been well documented. As part of a randomized controlled trial comparing in-person to electronic DOT, for patients being treated for TB disease, we assessed challenges encountered among four DOT types.

Methods: Staff documented issues encountered during scheduled observations for four DOT types: clinic-based (CDOT), field-based (FDOT), live-video (LVDOT) and recorded-video (RVDOT). Issues were categorized as patient-related, staff-related, and technical. Issues were self-reported or determined by staff to have potentially hindered adherence or quality of a DOT session.

Results: For 79 participants enrolled to date, there were 6,293 prescribed medication doses with 4,251 planned DOT observations (excluded weekends and holidays). Fifty-six (70.9%) participants experienced issues with 344 (8.1%) DOT observations. Among these planned observations, 142 (41.3%) occurred with LVDOT; 101 (29.4%) with FDOT; 77 (22.4%) with RVDOT; and 24 (7.0%) with CDOT. FDOT observations experienced the greatest percentage of issues with 17.5% (101/576) having issues compared to 10.4% (142/1360) for LVDOT, 4.6% (77/1659) for RVDOT, and 3.7% (24/656) for CDOT.

The 344 observations had 415 different documented issues. Of the 415 issues, 220 (53.0%) were patient-related; 131 (31.6%) were technical; and 64 (15.4%) were staff-related. The most common issues were computer/software malfunctions (49), patient forgetting the appointment (44), miscellaneous patient-related issues (42), patient tardy for scheduled observations (40), patients' inability to operate the software/smartphone (37), and staff logistical issues (34). A total of 256 issues were associated with a medication doses not being observed as planned (Figure 1).

Conclusions: Patient-related and technical issues accounted for most hindrances to DOT. Issues occurred more frequently when patients were restricted by time or location to complete observations. Further follow-up will allow for better understanding of the impact of issues on patient outcomes.



[Issues by Category Associated with Non-Directly Observed Doses of Medication]

SOA15 Human immunodeficiency virus, diabetes and other comorbidities—association with treatment outcomes and risk of behaviour

SOA15-1148-26 Hyperglycemia and increased rate of all-cause mortality among people with HIV-TB co-infection in Myanmar (2011-2017)

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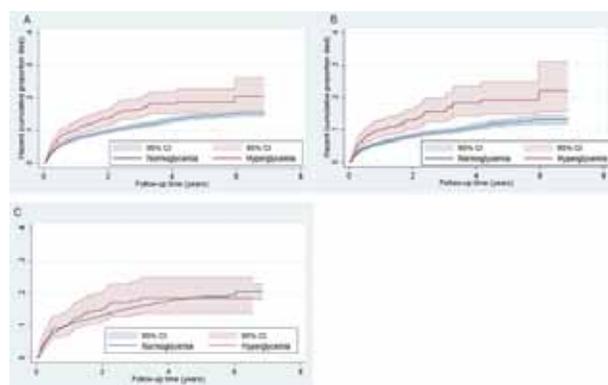
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Background: Hyperglycemia with or without diabetes mellitus increases the risk of mortality in non-TB hospitalized patients. In TB, hyperglycemia increases the risk of adverse outcomes, but this relationship is understudied among people living with HIV (PLHIV) and TB. We

aimed to estimate the association between hyperglycemia and all-cause mortality among PLHIV and determine if the relationship differs by active TB status.

Methods: We conducted a retrospective analysis of data from Integrated-HIV-Care Program, Myanmar. Eligible patients included adult (≥ 15 years) PLHIV with a baseline (test within one-month of enrollment into care) blood glucose test who enrolled into care from 2011-2016. Hyperglycemia was defined as random blood glucose measurement ≥ 140 mg/dl. Patients who received anti-TB treatment on or within one-month after enrollment were classified as having active TB. We used proportional hazards regression to estimate the association between hyperglycemia and rate of all-cause mortality through 2017.

Results: A total of 19,395 patients were included. Mean age was 37 (SD: 9) years, 40% were female, 32% had active TB at baseline, and median baseline CD4 count was 154 (IQR:63-305) cell/ μ l. Prevalence of baseline hyperglycemia was 7.0% (95% CI 6.7-7.4). The overall mortality rate was 6.7 per 100-person-years; the rate among patients with hyperglycemia (7.7; 95% CI: 6.8-8.8) was significantly higher than the rate among those without hyperglycemia (6.7; 95% CI: 6.4-6.9) (P value < 0.05). After adjusting for age, sex, body mass index, CD4 count, hepatitis C co-infection and antiretroviral therapy status, the mortality rate was higher among patients with hyperglycemia compared to those without hyperglycemia (adjusted hazard ratio [aHR]: 1.31; 95% CI: 1.1-1.6). In stratified analysis, hyperglycemia was significantly associated with mortality among patients without active TB (aHR: 1.59, 95% CI: 1.3-2.0) but not among patients with TB (aHR: 1.04, 95% CI: 0.8-1.4)



[Cumulative mortality among (A) all, (B) without active TB and (C) with active TB patients]

Conclusions: Studies that systematically measure glucose throughout the treatment to evaluate effects of hyperglycemia and diabetes on mortality are needed to inform the future clinical guidelines for HIV-TB.

SOA15-1149-26 Lung glycolytic activity on 18F-FDG PET-CT and pulmonary function among South African adults with TB and HIV

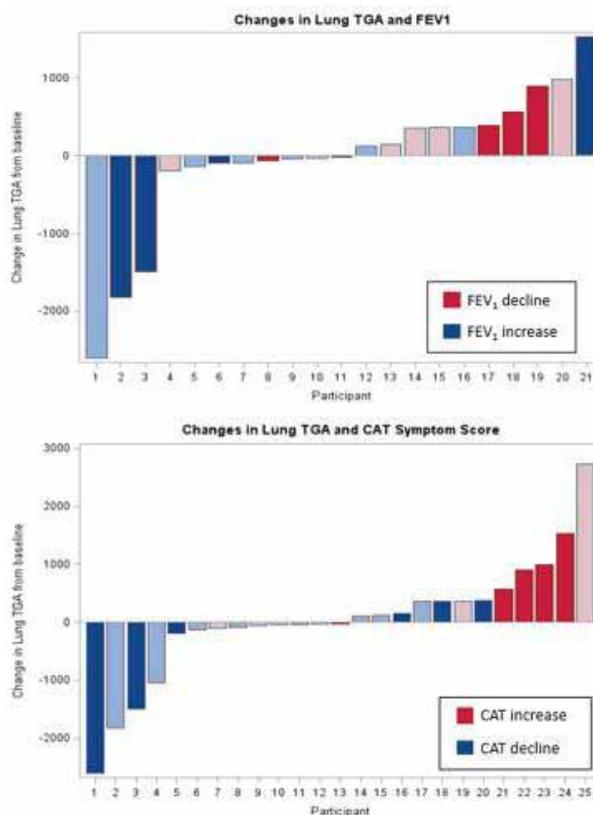
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Background: HIV-infected patients with pulmonary tuberculosis (pTB) often have less lung involvement than HIV-uninfected individuals with pTB. ART initiation restores immune function and may increase pulmonary inflammation. By comparing glycolytic activity on fluorodeoxyglucose (FDG)-positron emission tomography (PET)/CT scans with lung health indicators, we characterized patterns of lung injury among a cohort of HIV-infected adults with pTB initiating ART in Johannesburg, South Africa.

Methods: HIV-infected adults being treated for GeneXpert-positive pTB had PET/CT, spirometry (forced expiratory volume in 1 second [FEV₁], forced vital capacity [FVC]) and the COPD Assessment Test (CAT) for pulmonary symptoms performed prior to ART initiation; a sub-set repeated these tests after 4 weeks of ART. MIM software quantified lung total glycolytic activity (TGA) and data were compared using Spearman correlation coefficients (ρ) and the rank-sum test.

Results: Among 46 participants, the median age was 38 (IQR 33-43) and 54% were female. The median baseline CD4 count was 84 cells/μl (IQR 44-156), and increased to 185 cells/μl (IQR 103-318) at 4 weeks. At baseline, greater lung TGA was correlated with lower FEV₁ (ρ=-0.43, p=0.009), lower FVC (ρ=-0.43, p=0.001), higher CAT score (ρ=0.36, p=0.02), and higher CD4 cell count (ρ=0.68, p< 0.001). Among 25 participants with a week-4 PET/CT, 12 (48%) had an increase in lung TGA, which correlated with an increase in CAT score (ρ=0.51, p=0.009). Overall, change in lung TGA was not significantly correlated with change in FEV₁ (ρ=-0.37, p=0.09), but those whose FEV₁ decreased had larger increases in lung TGA than those whose FEV₁ increased (median change 358 [IQR -36-565] vs. -95 SUVs [IQR -1492-123]; p=0.05) and most with FEV₁ declines had increasing lung TGA (Figure).

Conclusions: Increases in lung TGA among adults with HIV-TB coinfection initiating ART are associated with worsening pulmonary function and respiratory symptoms. Research determining risk factors for and clinical implications of this phenomenon is needed.



[Change in lung TGA from baseline to 4 weeks vs change in (A) FEV₁ and (B) CAT symptom score.]

SOA15-1150-26 Mortality amongst HIV-positive female tuberculosis patients in South Africa

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Background: Studies show that antiretroviral therapy (ART) may reduce mortality among HIV-positive tuberculosis (TB) patients on treatment. In 2011, the South African National TB Programme changed its policy regarding ART for TB patients to initiate all HIV-positive TB patients on ART, irrespective of CD4 count. We investigated the impact of this policy on mortality, using data from the South African National electronic TB register (ETR.net).

Methods: ETR.net data from 2009-2013 were used in conjunction with the Thembisa model for population denominators. Newly registered adults who were not transferred or moved were included and individuals

with missing data excluded. An adjusted Cox regression model was developed, as well as the standardised mortality ratio (SMR) determined.

Results: 1,155,924 individuals were included. ART coverage increased from 36% to 87%, similar in both sexes; the Cox model showed a 23% reduction in mortality risk amongst TB patients between 2009-2013 (aHR 0.77 95% CI 0.75-0.78). In both sexes, the highest mortality risk reduction was seen in age groups 15-24 and 25-34 years. Mortality risk reduced by 22% in HIV-positive women and 25% in HIV-positive men; it was stable in both HIV-negative groups. However, in HIV-positive women, the SMR increased significantly each year from 9.62 (95% CI 9.38-9.88) in 2009 to 16.46 (95% CI 16.05-16.89) in 2013. In HIV-positive men, the SMR showed no significant difference.

Conclusions: A substantial decline of mortality was observed in HIV-positive TB patients, while among HIV-negative TB patients mortality was stable. The SMR showed mortality amongst HIV-positive women decreased at a slower rate in TB patients than in the general population.

This might be explained by women not accessing HIV care as early or frequently as men because of family commitments but the data are limited by not including time of ART initiation, CD4 count or ART adherence and should be further investigated.

SOA15-1151-26 Outcomes among a MDR TB cohort with high HIV co-infection treated with delamanid or bedaquiline in Lesotho

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Background: Lesotho has the second highest TB incidence in the world; TB mortality is estimated at 41% and 7% of incident cases have multi-drug resistant or rifampicin-resistant (MDR/RR) TB. HIV co-infection occurs in 73% of TB cases. Partners In Health has supported use of bedaquiline or delamanid in the Ministry of Health MDR TB program since October 2015 through its Unitaid-funded Expand New Drug Markets for TB (endTB) project. We describe treatment outcomes among a prospectively enrolled observational cohort of MDR/RR TB patients initiated on a bedaquiline- or delamanid-containing regimen between October 1, 2015-June 30, 2016.

Methods: Study participants had confirmed RR TB and were eligible to receive bedaquiline or delamanid based on World Health Organization guidance. Monthly follow-up occurred throughout treatment. Final outcome at the end of treatment, based on World Health Organization definitions, was assessed.

Results: Of 42 people who initiated a bedaquiline- or delamanid-containing regimen, 28 (67%) were male and 35 (83%) had HIV co-infection. Median age was 43.5 [range 18-84] years. Treatment success was achieved in 27 (64%); 13 (31%) died. One (2.4%) patient was lost to follow-up and another was not evaluated. HIV-positive individuals had reduced risk of death (23%) compared with HIV-negative individuals (71%) (p=0.02). The median CD4 cell count among HIV-positive participants was 194 [range 7-726] cells/mm³ at time of TB treatment initiation and 80% were receiving antiretroviral treatment. The five HIV-negative patients who died had extensive prior treatment histories and important comorbidities (see Table 1).

Conclusions: The majority of patients receiving a bedaquiline- or delamanid-containing regimen had a favorable outcome. The surprising finding of elevated mortality among HIV-negative patients may reflect the extreme vulnerability of this population. While HIV co-infected patients in Lesotho have broad access to antiretroviral treatment, and relatively well-controlled HIV disease.

Variable	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
Demographics	44 yr old male	61 yr old male	61 yr old male	63 yr old male	84 yr old male
Co-morbidities	- Chronic anemia - Malnutrition	- Chronic lung disease - Cor pulmonale	- None	- Diabetes mellitus (poorly controlled) - Hypertension - Chronic obstructive pulmonary disease - Chronic hepatitis B	- Congestive heart failure - Chronic kidney disease
CXR findings	Bilateral cavitory disease	Bilateral cavitory disease with fibrosis	- Bilateral disease with fibrosis	Bilateral disease, no cavities	Bilateral disease with emphysematous changes
Comments	- Received Bdq and/or Dlm for 854 days prior to death - Confirmed pre-XDR TB (FQ resistant) - Remained culture positive	- Confirmed pre-XDR TB (FQ resistance) - Converted culture on Bdq prior to death	- Remained culture positive - Died of acute respiratory failure 2 months after starting Bdq	- Died in 13th month of treatment - Culture negative for 9 months prior to death	- Died of decompensated congestive heart failure

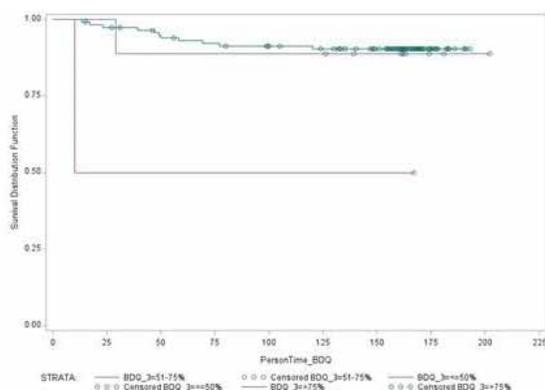
[Demographic and clinical characteristics of five HIV-negative participants who died during treatment with bedaquiline- or delamanid-containing regimen]

SOA15-1152-26 Adherence to bedaquiline and antiretroviral therapy predicts mortality in the treatment of multi- and extensively drug-resistant tuberculosis and HIV co-infected patients in KwaZulu-Natal, South Africa

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Background: Medication adherence is a critical to successful treatment but is poorly characterized. Bedaquiline is the first new medication licensed for drug-resistant TB treatment in over 40 years. The PRAXIS Study aims to quantitatively measure adherence in multi and extensively drug resistant tuberculosis (M/XDR-TB) HIV treatment (including Bedaquiline) using a next-generation electronic pill box (Wisepill RT2000).

Methods: Prospective cohort study of adult patients with M/XDR-TB HIV initiating treatment on Bedaquiline containing regimens and on antiretroviral therapy (ART). Adherence was assessed in real-time using Wisepill boxes separately for Bedaquiline or ART through 6 months. Percent adherence was calculated as observed compared to expected doses taken. Patients were assessed clinically in monthly study visits. Outcome was all cause mortality.



[Kaplan Meier Survival Curves: Stratified by Bedaquiline Adherence (<50%, 51-75%, >75%)]

Results: From November 2016 through March 2018, 200 M/XDR-TB HIV patients were enrolled. 153 had sufficient follow up time to be included in the survival analysis. Overall patients achieved an average of 92% (SD

11.7) adherence to Bedaquiline and 81% (SD 21.8) to ART. Mortality through 6 months was 16/153 (10.4%). In patients with >50% adherence to Bedaquiline survival was 50% while in those with the highest quartile of adherence survival was 100% (p=0.03). Adherence to ART similarly was associated with all cause mortality at 6 months but the difference was less and not statistically significant.

Conclusions: Adherence is a key indicator of mortality for patients with MXDR-TB and HIV. Next generation e-pill boxes to measure adherence may provide real-time feedback on adherence practices. Supporting optimal adherence may be an important intervention to improve mortality in MXDR-TB HIV treatment.

SOA15-1153-26 Whole genome sequencing of Mycobacterium tuberculosis from tuberculosis patients with and without diabetes mellitus

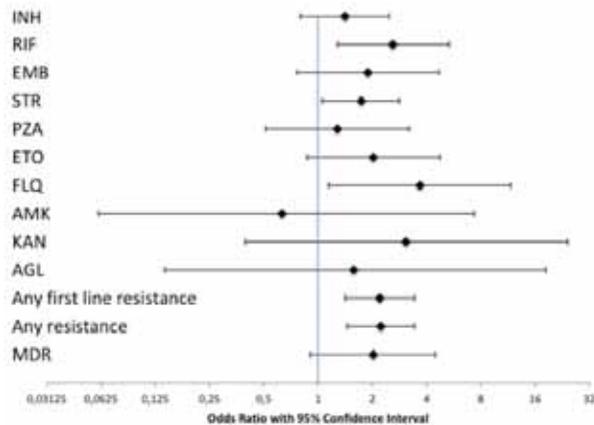
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Background: Diabetes is associated with an increased risk of tuberculosis (TB) treatment failure and relapse. Increased rates of drug resistance may be one contributing factor.

Methods: We used whole genome sequencing to compare the genomes of 904 *M. tuberculosis* isolates from TB patients with (n=162) or without (n=742) diabetes from Indonesia and Peru. We investigated differences in well-known drug resistance genes, as well as possible pre-resistance/adaptive mutations. We then used multivariable logistic regression to examine if the variants associated with diabetes comorbidity remain associated after adjusting for possible confounders.

Results: Drug resistance was strongly associated with diabetes comorbidity. The *M. tuberculosis* isolates of 40 of 118 (34%) Indonesian TB patients with diabetes had any well-known drug resistance mutations, compared to 68 of 298 (23%) of the patients without diabetes. In Peru this was 27 out of 44 (61%) for those with, compared to 204 out of 444 (46%) without diabetes; Mantel-Haenszel odds ratio (OR) adjusted for stratification by country = 1.8 (95% CI 1.2-2.6). Adjusted for age, gender, country, HIV co-infection, previous TB treatment, and *M. tuberculosis* lineage, drug resistance was even stronger associated with diabetes; OR = 2.2 (95% CI 1.44-3.43). Regarding individual drugs, diabetes was significantly associated with genotypic drug resistance against rifampicin, streptomycin, and fluoroquinolones (Figure 1).

Conclusions: Drug resistance mutations are significantly more frequent among *M. tuberculosis* strains from TB patients with, than from patients without diabetes, even when adjusted for confounders. Possibly, less fit drug-resistant strains may lead to active TB in individuals with diabetes who have impaired immunity against *M. tuberculosis*. To our knowledge this is the first study examining the role of *M. tuberculosis* genotype in relation to the interaction of TB and diabetes.



[Figure 1. Forest plot associating genotypic drug resistance and diabetes, adjusted for confounders.]

SOA15-1154-26 The effect of chronic non-communicable diseases and dyslipidemias on tuberculosis treatment outcomes

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Background: Non-communicable diseases are on the rise globally. Diabetes has now firmly been established as a risk factor for poor tuberculosis (TB) treatment outcomes; however, the effect of other chronic non-communicable diseases on TB treatment outcomes is not clearly known.

Methods: We conducted a retrospective cohort study comprising 2,949 patients aged ≥ 13 years undergoing treatment for culture-confirmed, drug-susceptible pulmonary TB at National Taiwan University Hospital from 2000 to 2016. We assessed the effect of the top 10 most prevalent non-communicable diseases worldwide and dyslipidemias on all cause and TB-specific mortality during TB treatment and 2-month TB sputum culture conversion using a multivariate logistic regression model.

Results: After adjustment, history of diabetes (OR 1.68, CI 1.36-2.07, $P < 0.01$), cancer (OR 3.04, CI 2.40-3.85, $p < 0.01$), myocardial infarction (OR 1.65, CI 1.05-2.60,

$p=0.03$), heart failure (OR 1.90, 1.25-2.87, $p < 0.01$), cerebrovascular disease (OR 1.60, CI 1.06-2.40, $p=0.02$), and high density lipid (HDL) < 40 mg/dl (measured within a year of TB treatment start [OR 3.23, CI 2.04-5.11, $p < 0.01$]) were associated with increased all cause mortality during TB treatment. After adjustment, history of diabetes (OR 1.74, CI 1.34-2.27, $p < 0.01$), chronic kidney disease (OR 1.37, CI 1.00-1.88, $p=0.05$), cancer (OR 1.93, CI 1.44-2.60), myocardial infarction (OR 1.92, CI 1.16-3.18, $p=0.01$), autoimmune disease (OR 2.41, CI 1.36-4.28), and HDL < 40 mg/dl (measured within a year of TB treatment start [OR 2.91, CI 1.81-4.67, $p < 0.01$]) were associated with increased TB-specific mortality during TB treatment. Only diabetes (OR 1.46, CI 1.41-2.14, $p=0.01$) was associated with decreased 2-month TB sputum culture conversion.

Conclusions: Non-communicable diseases have a large impact on TB treatment outcomes, especially those associated with cardiovascular disease. HDL < 40 mg/dl measured within a year of TB treatment start is significantly associated with increased mortality during treatment, warranting further investigation as a potential biomarker.

SOA15-1155-26 International research and guidelines on post-tuberculosis chronic lung disorders: a systematic scoping review

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Background: Pulmonary tuberculosis (TB) is an important risk factor for chronic respiratory disease due to lung damage. Yet, the WHO End TB strategy does not mention post-TB chronic lung disorders (PTBLD) and programmatic interventions to address PTBLD are lacking. This study assessed the scope of current guidelines and evidence on PTBLD to inform policy and research action.

Methods: A systematic literature search was conducted following PRISMA guidelines. Eight databases (TRIP, International Guideline Library, MEDLINE/PubMed, EMBASE, Web of Science, Global Health, Cochrane Library) were searched for records on PTBLD published between 1 January 1990 and 1 December 2017. Non-English records, case series, conference abstracts and letters to editors were excluded. Data was extracted and charted on: publication year, location, PTBLD condition(s) and main study outcome.

Results: A total of 212 guidelines and 3,661 articles were retrieved. After screening, only three international TB guidelines mentioned TB sequelae, but none described how to identify or manage the condition. A total of 156 articles addressed PTBLD: 54 (35%) mentioned unspecified TB sequelae; 47 (30%) specific post-TB conditions including aspergillosis, bronchial stenosis or bronchiectasis; 52 (33%) post-TB obstructive disease or lung function impairment; and 20 (13%) post-TB respiratory symptoms or chest x-ray abnormalities. The first two groups mostly assessed surgery and ventilation techniques for patient management, while the last two groups typically assessed prevalence and predictors of disease.

Conclusions: This is the first review to provide a comprehensive overview of the current literature on PTBLD. The scope of evidence around the burden of PTBLD warrants inclusion and recognition of the problem in international guidelines. Research is now needed on early detection of PTBLD as well as patient management options that are suitable for high burden TB countries.

SOA15-1156-26 End-stage renal disease and risk of tuberculosis: a nationwide population-based cohort study

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Background: The convergence of two epidemics, tuberculosis (TB) and end-stage renal disease (ESRD) causes global public health burden and difficulties in controlling TB, however, relationship between them are still poorly understood. We conducted a nationwide propensity score-matched cohort study in order to assess risk of developing TB among ESRD patients on dialysis.

Methods: From database of national health insurance program, ESRD patients on dialysis were identified to form the exposure cohort between 2004 and 2013. The control cohort comprised an equivalent number of subjects without dialysis. The incidence of TB was identified in the exposure cohort and control cohort between 2004 and 2013. A multivariable Cox regression analysis was used to determine hazard ratio of ESRD on development of TB.

Results: A total of 59,584 patients newly diagnosed with ESRD on dialysis between 2004 and 2013 were identified. The ESRD patients were associated with a significantly higher risk of tuberculosis compared to controls (incidence rate ratio 4.80). The risk of TB in the dialysis cohort was 4.39-fold (95% confidence interval 3.60-5.37) higher than in the control cohort.

Conclusions: We demonstrated an increased risk of TB among patients with ESRD on dialysis, which is consistent with previous studies. Attentive and well-organized guideline is necessary to detect and manage TB in ESRD patients.

SOA15-1157-26 Risk of tuberculosis in cancer patients in British Columbia, Canada: retrospective cohort study

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Background: Malignancy has been described as a risk factor for developing active tuberculosis (TB). Specific malignancies, including hematologic malignancies and head and neck cancers have been identified as TB risk factors, and incorporated into some guidelines for latent TB infection (LTBI) testing and treatment recommendations. Meanwhile, evidence to support TB screening in high risk populations with other malignancies is less robust.

Methods: We designed a population-based retrospective cohort study with a source population including all foreign-born individuals landing in Canada between January 1st, 1985 and December 31st, 2012 and established residency in BC during this period. We linked multiple health administrative databases and disease registries, and extracted data on TB treatment and diagnosis, immigration history, demographics, and co-morbidities. We used Cox extended proportional hazards regression to model hazard ratios (HR) to evaluate the impact of cancer on active TB risk, adjusting for patient characteristics.

Results: Of a total of 1,080,908 people entering the cohort, 30,331 (2.8%) were diagnosed with a primary malignancy in BC over the study follow-up period. The hazard ratio (HR) of TB in people with any cancer was 2.17 (1.67, 2.82), after adjustment for age group, gender, TB incidence in birth country, immigration classification, contact status, HIV, CKD, diabetes, transplant, medical immune-suppression and completion of LTBI treatment. Adjusted hazard ratios (aHR) were highest for lung cancers, aHR: 10.46 (6.83, 16.01), followed by hematologic cancers, aHR=2.80 (1.61, 4.88) and head and neck cancers, aHR=1.99 (0.75, 5.30).

Conclusions: Active TB risk was increased following a cancer diagnosis in our cohort, with the highest risk seen in people with lung, hematologic and head and neck cancers. These findings support guideline recommendations for LTBI screening, but point to lung cancer as a TB risk factor that requires further evaluation for inclusion into screening guidelines.

SOA16 Chest radiography—a key piece of the puzzle

SOA16-1158-26 Prevalence of Xpert-positivity is strongly associated with CAD4TB score in individuals screened for TB using mobile X-rays in hospital settings in Karachi

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Background: Mobile chest X-ray (CXR) based active-case finding, as part of the Zero TB initiative in Karachi, commenced in April 2017. The screening algorithm implemented at sites to triage number of Xpert® MTB/RIF (Xpert) tests was to request a single sputum sample in all individuals with a CAD4TB ≥ 70 . We present implementation data for the 1st quarter of 2018 when activities in hospital settings were being conducted at scale.

Methods: All patients and attendees visiting 11 public and 5 private, secondary and tertiary hospitals in Karachi between January 1 and March 31 2018 were offered CXR with CAD4TB, regardless of TB symptoms. Sputum samples in those with a CAD4TB < 70 were only submitted and tested based on clinical suspicion.

Results: 40,370 individuals were screened using CAD4TB, of whom 3790 (9.4%) had a CAD4TB score > 70 . A valid Xpert result was available for 4102/4326 samples submitted, of which 319 were Xpert-positive (7.8%).

Table 1a shows the screening cascade of numbers x-rayed using CAD4TB and number of sputum samples submitted. In those with a CAD4TB score > 70 , there was no significant difference between the proportion of individuals who submitted a sputum sample within each band. The prevalence of Xpert-positivity amongst samples tested increased with the increasing CAD4TB score (Table 1b).

(a) Screening cascade				(b) Prevalence of Xpert-positivity in those with a valid Xpert result		
CAD4TB score	Total no. x-rayed	Proportion of all CXRs by CAD4TB score (%)	No. of sputum samples submitted	Proportion of those x-rayed who submitted a sputum sample (%)	No. of sputum samples with a valid Xpert result	No. Xpert positive
> 70	3790	9.4	3790	100	319	7.8
60-70	3010	7.5	3010	100	230	7.6
50-60	2010	5.0	2010	100	150	7.5
40-50	1010	2.5	1010	100	80	7.9
30-40	510	1.3	510	100	40	7.8
< 30	3570	8.9	1000	28.0	100	10.0
Total	40370	100	3790	9.4	4102	319

[Table 1: (a) Screening cascade by CAD4TB category in all individuals x-rayed

(b) Prevalence of Xpert-positivity by CAD4TB Score in those with a valid Xpert result]

Conclusions: The currently implemented screening algorithm of using CAD4TB cut-off ≥ 70 in hospital settings is functioning well as a funnel to identify individuals eligible for sputum submission and Xpert testing. Further analyses will address the limitations of the lack of individual-level data on whether individuals screened were:

- referred by a clinician or actively screened and;
- presence or absence of symptoms and/or TB contact history.

SOA16-1159-26 The association between bacterial homoplasmy and radiological pathology in tuberculosis

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Background: Understanding how pathogen genetic factors contribute to pathology in tuberculosis disease would enable treatments to be tailored to the most pathogenic and infectious strains. New strategies are urgently needed to control drug resistant tuberculosis which requires longer, costlier and more toxic treatment. We hypothesized that the severity of radiological pathology on the chest radiograph in tuberculosis disease would be significantly associated with convergent evolutionary homoplastic polymorphisms in the *Mycobacterium tuberculosis* genome including those that confer drug resistance.

Methods: We performed whole genome sequencing using the illumina HiSeq2000 platform with 100bp paired end reads on sputum samples from 103 drug resistant tuberculosis patients attending clinics in Lima between 2009 and 2013. Variables including age, sex, HIV status, previous tuberculosis disease and the percentage of lung involvement on the pre-treatment chest radiograph were collected from health posts of the national tuberculosis program. Genomes were assembled and polymorphisms identified using standardized pipelines.

Results: Three mutations were significantly associated with more widespread radiological pathology in a multivariate regression model controlling for confounding

variables (Rv2828c.141, RR 1.3, $p < 0.01$; rpoC.1040, RR 1.9, $p < 0.01$; and katG.315, RR 1.2, $p = 0.01$). Those who had a previous episode of tuberculosis disease, male gender and those between 10-30 years of age also had significantly increased radiological pathology. The rpoB.450 mutation was associated with less extensive radiological pathology suggestive of a fitness cost for this mutation in vivo.

Conclusions: This study is the first to compare the *Mycobacterium tuberculosis* genome to radiological pathology on the chest radiograph. We identified 3 homoplasmic polymorphisms significantly associated with more widespread radiological pathology. Prospective cohort studies are warranted to determine if these mutations predict the spread of drug-resistant tuberculosis.

SOA16-1160-26 Baseline chest X-ray score identifies TB patients at greater risk of slower bacillary clearance and poor treatment response

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Background: Treatment for drug-sensitive tuberculosis is prolonged, and even with excellent adherence, is complicated by the risk of treatment failure. Identifying patients at higher risk of failure early may allow for treatment intensification or prolongation.

Methods: Malawian patients on standard first-line therapy for pulmonary TB were recruited to a longitudinal cohort study (n=157). Baseline postero-anterior chest radiographs were scored independently by a radiologist and a clinician using a simple scoring tool based on the extent of parenchymal involvement (%) and the presence or absence of cavitation. Serial sputum samples were collected over the intensive phase of TB treatment and cultured in liquid media. The time-to-positivity (TTP) in liquid culture was taken as a measure of bacillary load, and using mixed effects modelling, the sputum bacillary elimination rate estimated.

Results: Baseline smear grade and bacillary load (TTP) were closely related to both the chest X-ray (CXR) score and the presence of cavitation ($p < 0.001$). Participants with higher CXR scores were more likely to have a higher respiratory rate and white cell / neutrophil count ($p < 0.05$), and lower oxygen saturations and haemoglobin ($p < 0.001$). CXR score was closely related to rates of

two-month sputum culture conversion ($p < 0.001$), time-to-culture conversion ($p < 0.01$), and bacillary elimination rate ($p < 0.001$).

Conclusions: Use of a simple CXR scoring tool can identify TB patients with higher bacillary burdens and greater risk of poor response to treatment. These patients may benefit from treatment intensification or prolongation to reduce transmissibility or rates of failure. Future work will investigate the relationship between CXR score and rates of treatment failure or recurrent TB disease to 18 months.

SOA16-1161-26 Prevalence of 'scarring' on chest radiographs among foreign-born non-resident patients with microbiologically proven pulmonary tuberculosis: a retrospective study

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Background: CXRs are commonly used in the evaluation of pulmonary tuberculosis. Foreign-born non-residents applying for, or renewing permits to study, work or stay in Singapore require a CXR as part of their medical examination to evaluate for pTB. Reports of "scarring" on CXR often suggest inactivity, and if sputum cultures are not performed, active pTB may be missed, thereby posing a public health threat. This study aims to examine the prevalence of scarring on CXR of foreign-born, non-resident patients with microbiologically-proven pTB.

Methods: Foreign-born non-residents with microbiologically-proven pTB seen in the Tuberculosis Control Unit from November 2016 to October 2017 were extracted from the Singapore National TB notification registry. Demographics, clinical findings, sputum microbiology and CXR reports were obtained from casenotes review.

Results: A total of 297 patients with microbiologically-proven pTB were analysed; 192 (64.6%) were symptomatic and 105 (35.4%) were asymptomatic. Of the 297 patients, radiologic findings of scarring with or without other abnormalities were reported in 33 (11.1%) patients. 14 patients had isolated scarring, 4 of whom were smear positive. Radiology reports concluded inactivity in 11 (78.6%) patients with isolated scarring on CXR, 2 of whom were smear positive.

Subgroup analysis was also performed on 149 patients who were diagnosed with microbiologically-positive pTB during pass application/ renewal. Among these 149 patients, 12 patients had isolated scarring on CXR, 3 of whom were smear positive. 11 of these 12 patients were asymptomatic. Radiology reports concluded inactive TB in 10 (83.3%) of 12 patients with isolated scarring on CXR during pass application/ renewal, 2 of whom were smear positive.

Conclusions: Isolated scarring on CXR cannot be used to confidently exclude active pTB, especially in asymptomatic patients who are diagnosed during pass application/renewal. Sputum AFB smear and cultures remain key in the evaluation and diagnosis of active pTB.

SOA16-1162-26 Consistent high performance interpretation of pulmonary tuberculosis in chest X-rays using multi-label classification under the Deep Learning framework

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Background: The current proposal is an artificial intelligence based automated tool for consistent high performance interpretation of pulmonary tuberculosis (PTB) in chest X-rays (CXR) with a focus on classification of findings in CXRs which are suggestive of active PTB. These findings or manifestations are infiltration/consolidation, cavitory lesion, nodule, fibrosis, pleural effusion, opacities and masses and are represented as various instances or labels in a CXR. A multi-label deep learning framework under supervised learning is developed to generate the classifier for detecting presence of multiple labels or PTB manifestations in the CXR.

Methods: The first module is a preprocessing stage which involves several image processing steps to improve the quality of the CXR images. The parenchymal region in the CXR is automatically detected and used for the multi-label classification training. In the second module each CXR is resampled via scaling, translations, and rotations to increase the variation of the training data and to avoid overfitting. These multiple views of CXRs are used to train a deep learning network with a focus on novel feature-space representation to reduce complexity during training such that the label inter-dependencies are reduced and these labels become easier to model and predict at the inference time.

The training dataset comprised of 100908 and test dataset of 11212 CXRs and both sets representing the spectrum of PTB radiological manifestations.

Results: An overall accuracy of 92.192% is achieved using the proposed multi-label classifier which independently classifies multiple instances or radiological manifestations present in a CXR which are suggestive of PTB.

Conclusions: Our technique provides consistent automatic interpretation of digital CXR images for PTB, with a high sensitivity and high specificity as a screening tool from CXR before confirmatory molecular/microbiological tests.

SOA16-1163-26 Online resource for data explorations in large annotated DR-TB database. Comparative analysis of annotated CT scans of patients with drug-resistant forms of tuberculosis

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Background: The Office of Cyberinfrastructure and Computational Biology of the National Institute of Allergy and Infectious Diseases (OCICB NIAID), National Institutes of Health, spearheaded creation and growth of TB Portals (TBP), the collaborative network of clinical and research centers in countries with the heaviest burden of drug-resistant tuberculosis (DR-TB). More than 1200 anonymized records are available through a user-friendly Web interface (see <https://tbportals.niaid.nih.gov>).

We built Data Analysis and Exploration Portal (depot.tbportals.niaid.nih.gov) for the purposes of comparative analysis of virtual cohorts of patients, selected from TBP database. DEPOT allows to search for patterns in clinical, genomic, radiological data. DEPOT's main goal is to help in developing best clinical and diagnostic practices.

We present here analysis of 380 DR-TB chest CT images from our database, all annotated by radiologists. Every image is linked to history of disease (case definitions and outcomes), treatment regimen and drug sensitivity results.

Methods: Comparative analysis of radiological patterns was performed in DEPOT on virtual patient case cohorts from TBP. All queries for cohorts used in the study are reproducible, shareable and could be saved as is or modified for future studies. We compared groups of patients with distinct forms of tuberculosis (drug-sensitive, resistant, extremely resistant), as well as relapse patients, new patients, successfully and unsuccessfully treated etc.

Results: Our examination of CT chest images suggests that lung cavities, affected pleura, lung capacity decrease were frequently found with certain forms of drug-resistant TB and may be indicative of relapse cases.

Conclusions: Characteristic manifestations of DR tuberculosis, detected with chest imaging techniques, could help with rapid diagnostic and optimum treatment. Comparative analysis of characteristic patterns in lungs of patients with various forms of TB as well as for relapse vs. successfully cured may help establishing additional checkpoints before patients' release.

SOA16-1164-26 Diagnostic evaluation of an automated chest radiography reading software for TB among individuals with diabetes in Karachi, Pakistan

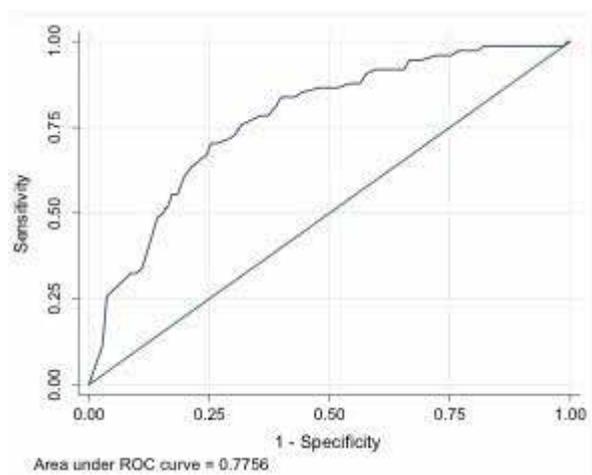
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Background: Pakistan has fifth highest burden of tuberculosis (TB) globally and an estimated Diabetes Mellitus (DM) prevalence of 6.8%. DM increases risk of developing TB and contributes to adverse TB treatment outcomes. Computer-Aided Detection for TB (CAD4TB) provides automatic readings of chest-X-ray and is currently being used as a triage tool in low-resource settings in mass-screening programs in several countries. However, diabetes is thought to influence radiographic manifestations of pulmonary TB and may lead to variation in CAD4TB scores and may affect diagnostic accuracy.

Methods: Between July 2016 and April 2017, bi-directional screening for TB and Diabetes was conducted at private health clinics and community screening camps in Karachi, Pakistan. Known diabetics and individuals with random blood sugar >200 mg/dl (tested during screening) were referred for chest X-ray supported by CAD4TB and Xpert testing to private TB treatment and diagnostic centers. Sensitivity and specificity were computed and receptor operator characteristic curves were constructed for CAD4TB.



[The Area under the ROC curve (AUC) using CAD4TB scores as predictor for MTB detection]

Results: A total of 694 diabetics and individuals with RBS>200mg/dl were screened with CAD4TB. The median age of participants was 54 (IQR 17) years and 374 (53.9%) were male. A total of 478 (68.9%) individuals had known history of DM while 74 had MTB+ve results on Xpert. The median CAD4TB score was 60 (IQR 33).

Out of all MTB+ individuals, 60.8% had a CAD4TB score >80. A high sensitivity (96.0%) and NPV (98.1%) were recorded for CAD4TB in diabetics while the area under the ROC curve (AUC) was 0.78. A larger study (unpublished) conducted by our group, evaluating CAD4TB among 6,845 individuals with presumptive TB in Pakistan, showed a diagnostic accuracy of 0.79.

Conclusions: CAD4TB offered high diagnostic accuracy among diabetics. Further studies are needed to compare the CAD4TB score distribution between diabetics and non-diabetics to identify CAD4TB threshold score to be used to screen diabetics.

SOA16-1165-26 Role of computer-aided diagnosis in chest radiography for TB: concordance with human readers

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Background: The first TB prevalence survey was conducted in 2017, with chest X-rays offered to all participants. This analysis compares the performance of computer aided reading of digital chest X-ray images for TB with that of trained medical officers.

Methods: Digital chest radiography was performed on individuals 15 years and older during the TB prevalence survey in 2017-18. Each image was read by a general medical practitioners (GP) and CAD4TB version 5 (Delft Imaging Systems) automated reading software. The GPs identified digital CXR images that had abnormalities compatible with TB, while blinded to the CAD4TB system. CAD4TB assigned a score of 0-100 to the same images based on probability of TB and an in-built algorithm. Blinded to both, a specialist radiologist re-read all abnormal, and 10% of normal images.

Results: 27,747 individuals had CXRs, 26,961 (97.2%) had results for both CAD4TB and GP reading. GPs assigned 3,578 images as probable TB. The CAD4TB scores ranged from 0 to 100 (median29; IQR 22-46). The ROC curve with the GP reading as standard had an AUC of 0.8372 (95% CI, 0.833-0.842) suggesting satisfactory concordance.

Against the radiologist as the reference standard, CAD4TB had the following sensitivity and specificity respectively at different thresholds; at 40 (95.1% & 50.5%); at 50 (90.1% & 58.3%); at 60 (79.3% & 70.8%) and at 70 (57.4% & 93.0%).

Against the same standard, GPs' reading had a pooled sensitivity and specificity for detecting TB of 89.6%

(95% CI 88.1%-91.0%) and 64.2% (95% CI 62.6%-65.8%) respectively. This was closest to CAD4TB at threshold 52; sensitivity 88.2% (95% CI 86.7%-89.7%) and specificity 61.5% (59.9%-63.1%).

Conclusions: At threshold score of 52, CAD4TB performed as well as humans when used for TB screening by CXR. This suggests that CAD4TB may replace trained humans for field reading of CXRs in TB prevalence surveys and active case finding.

SOA16-1166-26 The role of the chest x-ray in screening for tuberculosis in Uganda

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Background: Tuberculosis (TB) is a major cause of morbidity and mortality worldwide. The WHO END TB strategy indicates a need for $\geq 90\%$ TB case detection among others to combat TB. In order to achieve increased TB case detection there is need for a more sensitive and specific screening tool. Currently, symptoms are recommended for screening tuberculosis (TB) in resource-limited settings, however; they have been found to be sub-optimal. We evaluated the performance of the Chest-X-ray during the Uganda National TB prevalence survey.

Methods: 4512 complete records of participants ≥ 15 years who consented to participate in the Uganda National TB Prevalence Survey (UTPS) were analysed. In the UTPS, all participants who were positive for symptoms or had an abnormal chest x-ray (CXR) were requested to submit a sputum for analysis. In addition, all participants who declined a CXR were requested to submit a sputum for analysis.

Sputum Löwenstein-Jensen (LJ) culture results were used as the gold standard.

The performance of the symptoms or CXR was determined using 2 by 2 tables and reported as sensitivity, specificity, positive predictive value, negative predictive value, positive likelihood ratio and negative likelihood ratio.

Results: 160(3.5%) TB cases were prevalent.

The symptoms had sensitivity 76% (95% CI 70-83), specificity 31% (95% CI 29-32), positive predictive value 3.9% (95% CI 3.2-4.6), negative predictive value 97.2% (95% CI 96.2-98.0), positive likelihood ratio 1.1 (95% CI 1.0-1.2) and negative likelihood ratio 0.8 (95% CI 0.6-1.0).

The CXR had sensitivity 93% (95% CI 87-96), specificity 65% (95% CI 63-66), positive predictive value 8.9% (95% CI 7.6-10.4), negative predictive value 99.6% (95% CI 99.2-99.8), positive likelihood ratio 2.6 (95% CI 2.5-2.8) and negative likelihood ratio 0.1 (95% CI 0.1-0.2).

Conclusions: The CXR is a good screening tool for tuberculosis and performed better than symptoms in Uganda. Therefore, the CXR should be adopted in TB screening algorithms in resource limited settings.

SOA16-1167-26 Further evidence for a standardised chest radiograph scoring System for TB

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Background: Ralph *et al* proposed a standardised scoring system for chest X-rays (CXRs) in smear-positive tuberculosis (TB) patients in Western Papua. This calculates a single numerical score based on percentage of affected lung and presence of cavitation, and predicted baseline clinical and microbiological severity and treatment response in a predominantly HIV-uninfected population. We wished to assess the utility of this scoring system in clinical cohorts from Malawi with high rates of TB-HIV co-infection.

Methods: We analysed data from 2 cohorts of TB patients recruited to pharmacokinetic-pharmacodynamic studies in Malawi: the SPUTuM Study (n=147, 2010-2011) and the SPITT Study (n=156, 2016-2018). Both studies recruited adult patients with microbiologically-confirmed pulmonary TB, performed baseline postero-anterior CXRs, and collected serial sputum samples to monitor treatment response. CXRs were blinded before analysis and interpreted independently by a non-radiologist clinician and an external radiologist using the CXR scoring tool. Concordance between each element of assessment was reviewed using Lin's concordance coefficient for continuous variables and prevalence-adjusted, bias-adjusted kappa values for dichotomous variables; and discrepancies resolved by consensus.

Results: The CXR score was simple to use and allowed for rapid assessment of the radiological severity of disease. Both studies demonstrated good inter-reader concordance between radiologist and clinician, with a concordance coefficient of 0.71 and 0.79 in SPUTuM and SPITT respectively. Agreement on dichotomous variables was mainly "substantial" or "almost perfect". In both cohorts, CXR score and cavitation were associated with higher baseline bacillary load (by smear grade or time-to-positivity in liquid culture), and 2-month sputum culture conversion was less common in those with cavitation on CXR ($p < 0.05$).

Conclusions: We demonstrate that the use of a simple CXR score to grade radiological severity in pulmonary TB is transferrable to a population with high TB-HIV co-infection, and correlates well with baseline clinical and microbiological severity and treatment response.

E-POSTER SESSIONS

EP04 Progress in paediatric tuberculosis and lung diseases

EP04-127-26 Risk factors for TB infection after household exposure to a TB index case among household contacts aged less than 5 years, Kisumu County, Kenya, 2014-2015

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Background: Kisumu county of Kenya is a high-TB burden (TB CNR 228 vs. 170 nationally per 100,000 populations in 2016), densely-populated (464.5 persons per km²) region with 17% of its population aged < 5 years (children). The TB burden and the interaction of known risk factors for TB progression, among child contacts of TB index cases, have not been established because Contact invitation, rather than contact investigation is the norm. We determined prevalence and risk factors for TB infection among child household contacts.

Methods: A cross sectional survey, recruiting child contacts of TB index cases who underwent TB symptom, Tuberculin Skin tests (TST) and Chest X-ray screening, was conducted between 2014 and 2015 in Kisumu County. Prevalence of TB was identified using a cut off for TST positivity based on a bimodal peak. Hierarchical level modeling analyses, with children nested within households, was employed to describe TB index characteristics (including household information) and contact characteristics associated with TB infection.

Results: Of 257 child contacts linked to 183 TB index cases, 39.3% had TB infection based on a TST cut off of 5mm for positivity. This included 8 (3.1%) child contacts with TB disease. 37% of TB infection could be attributed to clustering. The probability of TB infection was significantly higher among child contacts of TB index cases, that had cough (OR 5.1, 95% CI 1.6-16.1), whose household size was < 25 m² (OR 3.7, 95% CI 1.0-13.3) and, that were 1st degree relatives of TB index case (OR 2.9, 95% CI 1.1-7.2), after fixing other contact and index characteristics.

Conclusions: Household clustering contributes to TB infection; a targeted contact investigation approach with 'watchful waiting' maybe employed for child contacts from specific households. Due to a high prevalence of TB infection, IPT administration among child contacts without TB is justified.

EP04-128-26 The pharmacokinetics of high dose isoniazid for the prevention or treatment of drug-resistant tuberculosis in HIV-infected and -uninfected children

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Background: Treatment options for multidrug-resistant tuberculosis (MDR-TB) in children are limited. High-dose isoniazid (hdINH) may overcome low-grade INH resistance. However, pharmacokinetic data to inform dosing in children is currently absent. The aim of this study was to characterize the pharmacokinetics of hdINH in children.

Methods: This prospective observational study in Cape Town, South Africa, included HIV-infected and -uninfected children routinely receiving hdINH for the prevention or treatment of MDR-TB. Pharmacokinetic sampling was performed after a 20mg/kg INH dose (maximum 400mg). Non-compartmental analysis and multivariable regression models were used to determine associations of key covariates with AUC_(0-∞) and C_{max} and to compare to proposed targets.

Results: Seventy-seven children were included. In the group <5 years (n=58), 32 received hdINH for MDR-TB disease and 26 for MDR-TB exposure. All children >5years (n=19) had MDR-TB disease. Overall, the median (IQR) AUC_{0-∞} was 17.9 µg*h/mL (9.9-48.6) and C_{max} was 5.14 µg*h/mL (2.69-12.2). In multivariable analysis in children <5 years old, MDR-TB disease (vs. MDR-TB exposure) was associated with both [GMR=0.19 (95 % CI 0.15-0.26), p<0.001] and C_{max} [0.20 (0.15-0.26), p<0.001]. In children with MDR-TB disease, the median (IQR) of 9.9 µg*h/mL (6.3-14.3) and C_{max} of 3.4 µg/mL (2.0-5.1) were well below those in the MDR-TB exposure group [µg*h/mL (43.2-102.7), C_{max} 16.0 µg/mL (12.9-20.5)] and also well below previously reported values in children receiving a 20mg/kg dose of INH for TB meningitis (19.1µg/ml at 1-2 hours). INH exposures seen here were below proposed targets for the majority of isolates with low and intermediate level resistance (Table 1).

MIC	AUC (0-∞)		C _{max} /MIC		C _{max} compared to MIC value	
	MDR-TB Disease (N=48)	MDR-TB Prophylaxis (N=26)	MDR-TB Disease (N=51)	MDR-TB Prophylaxis (N=26)	MDR-TB Disease (N=51)	MDR-TB Prophylaxis (N=26)
0.125	26 (54.2)	26 (100.0)	37 (72.6)	26 (100.0)	51 (100.0)	26 (100.0)
1.0	1 (2.1)	9 (34.6)	1 (2.0)	11 (42.3)	49 (96.1)	26 (100.0)
3.0	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	28 (54.9)	26 (100.0)
5.0	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	13 (25.5)	26 (100.0)

[Proportion of patients achieving target for AUC(0-∞)/MIC > 85 and C_{max}/MIC > 17.52 and C_{max} stratified by disease status]

Conclusions: INH concentrations in children treated for MDR-TB disease with hdINH were much lower than expected. However, concentrations in the MDR-TB exposed groups were comparable to previous reports. Further studies are needed to confirm these findings and explore causes including previously undescribed drug-drug interactions.

EP04-129-26 Adult-to-child transmission of tuberculosis within households in The Gambia

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Background: Childhood tuberculosis (TB) has significant impact on public health worldwide. It is believed that most children acquire TB from an adult smear-positive index case within their households. To further examine this hypothesis, we compared *Mycobacterium tuberculosis* (*Mtb*) complex (MTBC) lineages in adults and active TB children contacts, and examined the influence of bacillary burden and lineage in adult index case on the clinical outcome of exposed children.

Methods: Smear positive adult TB index cases were grouped as index cases of active TB, of tuberculin skin test positive (TST+) or of TST negative children (<15 years old) household exposed contacts. Bacterial genomic DNA was extracted from adults' and children's sputum culture samples and genotyped using the spoligotyping method.

Results: There was a clear relationship between sputum smear grade positivity of the adult index cases and outcome of the exposed children: AFB grade 3 was found for 54% of index cases related to children with active TB, 50.94% for those related TST+ve children, and 36.6% for TST-negative children.

Category	Total number of samples successfully genotyped	Mtb-lineage 4	Maf-lineage 6	Mtb-lineage 3	Mtb-lineage 2
Children with bacteriologically confirmed active TB	37	31(83.8%)	1(2.7%)	4(10.8%)	1(2.7%)
Adult index cases of children with active TB	49	39(80%)	8(16%)	1(2%)	1(2%)
Adult index cases of children who are TST +	53	35(66%)	11(21%)	5(9%)	5(9%)
Adult index cases of children who are TST -	87	44(51%)	33(38%)	8(9%)	8(2%)

[Proportion of MTBC lineages found in active TB children and different categories of adult index cases]

Conclusions: Our results show that higher bacillary burden in adult index cases increase likelihood of TB transmission to children contacts. Adult patients appear to be more likely to transmit TB if they were carrying *Mtb*-lineage 4 compared to the other lineages.

EP04-130-26 Implementation of a cascade training approach improved child TB case notification in Uganda

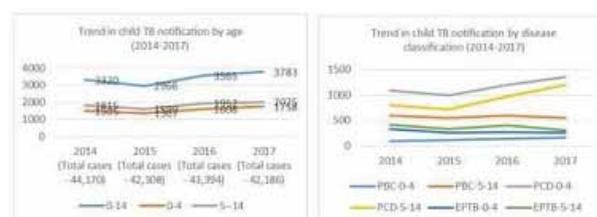
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Background and challenges to implementation: Limited health worker knowledge and skills contributes to low child TB case finding. Uganda notified only 7.5% of all incident TB cases (3,320) as children in 2014, against the estimated 17%. With support from national and regional stakeholders, the national TB program (NTP) implemented a cascade training approach to rapidly improve frontline health worker knowledge and skills in child TB case finding, management, and notification.

Intervention or response: From November 2015 to June 2016, a total of 106 national trainers had completed a 5-day competence based training of trainers' course on child TB management and used the same curriculum to train 740 regional/district trainers. The latter subsequently conducted health facility training and mentorship across the country using a compressed 3 day curriculum. The health facility curriculum focused on the knowledge/ skills required to perform NTP desired tasks. A national trainer observed training at each site for one day to strengthen quality. Knowledge gain was assessed by pre and post-test. Training coverage and child TB case notification were tracked using an NTP based online training reporting tool and routine quarterly TB reports respectively. Follow on mentorship was integrated into the quarterly regional mentorship and supervision activities. 74 health facilities implementing a child TB pilot project were excluded.

Results and lessons learnt: By December 2017, 9588 health facility staff from 76% of 1489 health facilities had been trained. Median knowledge gain was 20% (IQR10%-30%). Child TB case notification increased from 7.5% to 9% in 2017 (figure 1).



[Figure 1. Trend of child TB case notification by age and disease classification in Uganda (2014-2017)]

Conclusions and key recommendations: A cascade training approach is effective in rapidly reaching front-line health workers and facilitates the build-up of a pool of national, regional, and district trainers/ mentors. However, there is need to reinforce acquired knowledge and skills through continuous mentorship.

EP04-131-26 Non-communicable lung disease and exposure to household air pollution in rural Malawian children: a cross-sectional study

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Background: Non-communicable lung disease and exposure to high levels of air pollution are issues of major global health importance - particularly in low- and middle-income countries. Recent studies in Africa, including Malawi, reported a high burden of chronic respiratory symptoms and low Forced Vital Capacity (FVC) in adults. It is unknown whether these problems are present in childhood.

Methods: We did a cross-sectional study to measure the prevalence of chronic respiratory symptoms and spirometric abnormalities in children aged 6-8 years, living in Chikwawa, rural Malawi. Households previously enrolled in the Cooking and Pneumonia Study (CAPS), a cluster randomised controlled trial of cleaner-burning biomass-fuelled cookstoves were included, to explore the role of household air pollution (HAP) on lung health. Data collected during community field visits included; a respiratory symptom questionnaire, anthropometry, spirometry, and measures of personal exposure to HAP. Spirometric indices were compared to African-American predicted values, derived from the Global Lung Initiative equations. Analysis was stratified by CAPS intervention and control groups.

Results: 804 children were enrolled between February-October 2017; including 260 from CAPS intervention households, and 216 from control households. 16.6% of children experienced chronic respiratory symptoms; including 8.0% with regular cough, 7.1% with current wheeze (half with severe asthma symptoms) and 6.1% with difficulty breathing. Overall, lung function was reduced compared to predicted values, in the 522 children with technically acceptable spirometry (Table). 13% of children had spirometric abnormalities; 7.1% restriction and 6.3% obstruction. Children from CAPS intervention households had higher FVC z-scores (-0.22 vs. -0.44, $p=0.05$) and lower carboxyhaemoglobin levels (4.02% vs. 4.94%, $p=0.003$), than controls.

Conclusions: We found high rates of non-communicable lung disease in rural Malawian children and some evidence that the burden of low FVC was decreased in children from CAPS intervention households. Effective strategies to optimise lung health in the world's poorest children are needed.

	All participants n=522	CAPS intervention n=167	CAPS control n=133	Intervention vs control
FEV1 (Forced Expiratory Volume in 1s) z-score (SD)	-0.48 (0.93)	-0.41 (0.92)	-0.60 (0.97)	$p=0.10$
FVC (Forced Vital Capacity) z-score (SD)	-0.30 (0.96)	-0.22 (0.97)	-0.44 (0.98)	$p=0.05$
FEV1/FVC z-score (SD)	-0.38 (0.90)	-0.40 (0.91)	-0.34 (0.93)	$p=0.57$
Abnormal spirometry (FVC or FEV1/FVC below lower limit normal), n (%)	68 (13.0)	21 (12.6)	22 (16.5)	$p=0.42$

[Pre-bronchodilator spirometric indices]

EP04-132-26 Culture-confirmed tuberculosis in infants less than 3 months of age: clinical presentation and management

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Background: Published experience on the presentation and management of intrathoracic complications in perinatal tuberculosis (TB) is limited. We describe the presentation, medical management and surgical management of culture-confirmed TB in infants less than 3 months (< 3 months) of age.

Methods: We conducted a retrospective study including all infants < 3 months of age with culture-confirmed TB admitted to Tygerberg Hospital, Cape Town, South Africa from March 2003 through June 2015. We collected data on clinical presentation, clinical management and surgical management of intrathoracic complications in these infants.

Results: Of 2017 children < 13 years of age with culture-confirmed TB during the study period, 106 (5%) were infants < 3 months of age. The median age on admission was 67 days (IQR 40-79). Intrathoracic (lung and mediastinal nodes) TB was present in 101 (95%) infants; of these, 34 (32%) also had extrathoracic TB (ETTB). Two (2%) infants had ETTB only, while 3 (3%) infants were asymptomatic and retrospectively diagnosed as having TB infection only. Forty (38%) infants were HIV-exposed and 14 (13%) were HIV-infected. A source case was identified in 87 (82%) infants; the mother was the source case in 53/106 (50%) infants. *Mycobacterium tuberculosis* was cultured in a median of 2 (IQR 1-7) specimens per infant; 9 (8%) had drug-resistant TB. Bronchoscopy was done in 37 (35%) infants due to large airway complications and 27 (26%) underwent intratho-

racic lymph node decompression. Twelve (11%) infants died during admission, 81(76%) were clinically stable on transfer or discharge from the hospital and outcome was not documented in 13 (12%) infants.

Conclusions: TB in young infants often presents with severe intrathoracic complications, including large airway compression. Bronchoscopy may aid the diagnosis and management. Urgent decompression of mediastinal lymph nodes was common. Mortality in this age group remains high.

EP04-133-26 Demonstration of a successful model for diagnosing paediatric TB using upfront Genexpert testing

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Background and challenges to implementation: Clinical diagnosis of tuberculosis can be challenging in children, as signs and symptoms of TB can be very non-specific and similar to common childhood chest infections. Rapid, highly sensitive diagnostics are increasingly available in the public and private sector in India. Nevertheless, majority of the paediatric TB cases are empirically diagnosed because either samples are not accessible or microbiological testing is negative. In this large-scale implementation project in 10 major cities of India, reported here, GeneXpert testing was offered on available sample (pulmonary and extrapulmonary) thereby paving way for better TB care.

Intervention or response: A high throughput lab was established in each of the 10 cities, and linked to various providers in the public and private sector across the city, through rapid specimen transportation and electronic reporting. Free-of-charge GeneXpert testing was made available to all paediatric presumptive TB cases (both pulmonary and extra-pulmonary). Several low-cost outreach and education interventions were undertaken to increase diagnostic uptake by providers catering to paediatric population.

Results and lessons learnt: For the 88,289 paediatric presumptive TB cases tested across 10 cities under the project between Apr'14-Dec'17, a total of 96,514 specimens were tested on GeneXpert (table). A total of 5989 (6.8%, CI 6.6-7.0) TB patients were detected, of which 528 (8.8%, CI 8.1-9.6) were rifampicin resistant. Overall detection rates on GeneXpert were three-fold higher than smear microscopy (5989 vs. 1637). For >93% patients, results were reported within 24 hours of sample receipt at lab. The number of providers/facilities engaged and trained under the project increased from 43 in Apr'14 to 1329 in Dec'17 with engagement, both from public and private sector.

Conclusions and key recommendations: Project demonstrated the feasibility of rolling out rapid & upfront GeneXpert testing for presumptive paediatric TB cases. Rapid turnaround testing time in turn facilitated prompt treatment initiation. The project is now being scaled up by the National Programme in India.

Specimens	Total tests	Xpert positive	Xpert positive %	Rif resistance cases	Rif resistance % positivity
Induced Sputum/Sputum	47322	2975	6.3%	356	12.0%
Non-sputum	49192	3533	7.2%	383	10.8%
Total	96514	6508	6.7%	739	11.4%

[GeneXpert positivity in different types of specimens tested under the project]

EP04-134-26 Increasing paediatric TB case detection using the quality improvement approach: early results from the USAID Defeat TB project in Uganda

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Background and challenges to implementation: Despite the high burden of TB in children, it is estimated that at least two thirds of cases in Uganda go un-diagnosed or un-reported. At five health centers serving the urban population of central Uganda that participated in a quality improvement (QI) collaborative, the paediatric TB case notification was low at an average of 6 cases (50% clinically diagnosed) notified per month (August 2017-Jan 2018) yet the total number of expected cases per month is 55 per the population projections and average attendance. This low performance was mainly due to low coverage for paediatric TB screening at 12%, limited capacity and skills to screen and clinically diagnose paediatric TB, and poor documentation of the cascades of care.

Intervention or response: Since February 2018, the USAID Defeat TB project has supported the five health centers to implement changes to improve paediatric TB screening using QI and build capacity for clinical diagnosis and documentation through bi-weekly coaching sessions. Changes implemented as a package that led to improvement included assigning a staff as a focal person to oversee screening children at all entry points, displaying the diagnostic algorithm on paediatric TB in the clinical rooms, peer-peer mentorship on clinical diagnosis of paediatric TB, recording patients' clinical signs and symptoms for paediatric TB in the presumptive register and holding weekly review and audits to discuss each case.

Results and lessons learnt: As a result of this intervention, screening for paediatric TB increased from 12% to 78%, with 45 more paediatric TB cases (94% clinically diagnosed) notified in March 2018 from the five health centers. The completeness of the TB records has improved from 45% to 73% (August-March 2018).

Conclusions and key recommendations: Paediatric TB case detection can be increased through QI methods to improve screening, health worker capacity for clinical diagnosis and documentation of the cascades of care.

EP04-135-26 Could 'non-typical' chest radiographic features in children with culture-confirmed tuberculosis reflect early, less severe disease?

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Background: Children treated for pulmonary tuberculosis (PTB) are frequently not microbiologically confirmed. Clinicians typically rely on history, clinical findings and chest radiographs (CXR) to make a TB diagnosis. However, not all children diagnosed with PTB have 'typical' CXR features. Investigating children with culture-confirmed PTB and 'non-typical' CXRs could help refine the use of CXR as a diagnostic tool for TB in children. We compared clinical and microbiological characteristics in culture-confirmed children by CXR classification ('typical' and 'non-typical' of TB).

Methods: Children 0-14 years with a clinical suspicion of PTB who were enrolled in a diagnostic study and who had at least one respiratory specimen culture-positive for Mycobacterium tuberculosis were included. CXRs were read independently by 2 or 3 experts and classified by consensus as 'typical' or 'non-typical' of TB. Logistic regression was used to determine if TB exposure and infection status, culture time to positivity (TTP) and other clinical characteristics were associated with CXRs ('non-typical' vs 'typical'). Missing values were imputed using multiple imputation by chained equations.

Results: There were 95 children with culture-confirmed PTB: 21/95 (22%) had CXRs read as 'non-typical' of TB. Median age was similar between groups; children with 'non-typical' CXRs were more likely to be HIV positive (OR=3.30, 95% CI 1.00-10.93). The proportion of children with a positive tuberculin skin test (TST) and/or exposure to an adult source case was similar between groups. Children with 'non-typical' CXRs were less likely to be confirmed on Xpert MTB/RIF in addition to culture (OR=0.07, 95% CI 0.02-0.22), and had significantly longer culture TTP compared to those with 'typical' CXRs (OR=1.09, 95% CI 1.03-1.15).

Conclusions: The children in this well-defined culture-confirmed cohort who had 'non-typical' CXRs had microbiological test results suggestive of lower bacillary load. We hypothesize that this may reflect earlier and less severe disease presentation. This hypothesis warrants further investigation.

	CXR 'non-typical of TB' n=21	CXR 'typical of TB' n=74	Univariable OR (95% CI)
Median age in years (IQR)	1.8 (1.1-4.1)	1.6 (0.5-4.4)	1.02 (0.89-1.17)
HIV positive (%)	6 (28.6)	8 (10.8)	3.30 (1.00-10.93)
Median culture time to positivity in days (IQR)	26 (22-29)	17 (12-23)	1.09 (1.03-1.15)
Positive Xpert MTB/RIF (%)	5 (23.8)	60 (81.0)	0.07 (0.02-0.22)

[Univariable logistic regression estimating the odds ratio of 'non-typical' chest X-rays for children with culture-confirmed pulmonary tuberculosis]

EP04-136-26 Over a third of child tuberculosis patients diagnosed in a tertiary centre in Botswana are missing from the national Electronic Tuberculosis Register

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Background: Tuberculosis (TB) remains a global epidemic. Healthcare workers (HCW) in Botswana refer children from primary clinics to hospitals for TB diagnosis. Hospitals do not register patients in the national Electronic TB Register (ETR) expecting this to be done by the primary directly observed therapy (DOT) site following hospital discharge. The system of reporting cases at DOT sites was implemented to reduce double registration. However, there is a risk that children diagnosed with TB in-hospital may be missing from the ETR if they are lost to follow-up between diagnosis and registration at a DOT site.

Methods: We conducted an audit of all children (0-15 years) diagnosed with TB at Princess Marina Hospital, Botswana's largest tertiary hospital, located in Gaborone, between 2008-2012. All child TB cases recorded in the hospital TB register were matched using a step-

wise matching algorithm to assess for registration in the ETR. Demographics were summarized and comparisons made for year registered, district referred and age.

Results: 370 children were listed in the hospital TB register, with females comprising 178 (48%) and 214/328 (65%) under age 5 years. 216/370 (58%) were found in the ETR. Both younger age ($p=0.03$) and child living in Gaborone ($p=0.002$), the district around the hospital, were associated with being missing in the ETR ($p=0.03$). Year of registration was not associated with being missing from the ETR ($p=0.297$).

Conclusions: Over a third of children diagnosed with TB at this tertiary facility were missing in the ETR, suggesting underreporting at the national level of child TB cases. Younger children and those living in Gaborone were at highest risk. TB programmes need to ensure optimal case notification from all facilities to the national ETR to prevent under reporting, particularly for pediatric patients who are often diagnosed at secondary/tertiary facilities because of the challenges of TB diagnosis in this population.

EP04-137-26 Drug-resistant tuberculosis in children and adolescents: experience from the Indus Hospital, Karachi, Pakistan

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Background: An estimated 32,000 children (< 15 years) develop drug resistant TB each year, yet fewer than 1000 children have been ever reported in literature. An individual patient data meta-analysis describes 957 children with DR-TB who achieved good treatment outcomes. Data on adolescents is lacking.

Methods: We retrospectively analyzed the data of children and adolescents 0-18 years ever diagnosed, registered and treated at the Indus Hospital Drug resistant TB (DR-TB) program (2009-2018). Data on patient age and weight at diagnosis, type of resistant TB, exposure to TB drugs prior to diagnosis, and outcomes were extracted from our electronic DR-TB data base and analyzed using SPSS.

Results: A total of 287 children and adolescents, (94) 32% males and (193) 67% females, have been diagnosed, registered and started on treatment at the Indus Hospital DR-TB program since 2009. The youngest age group comprised only 3.8% of this group, children 5-9 years were 2.8%, patients 10-15 years were 36% and older adolescents 16-18 years age made up 57% of the cohort. The adolescent cohort (10-18 y) contained 2.7 times more females than males. Overall 57% (164) children had primary DR-TB. Severe malnutrition with

(wfa z-score of < -3) was present in 54% of the cohort and in 60% of the females. Outcomes were declared for 219 patients with favourable outcomes in 75% and death in 11%. Older adolescents experienced unfavourable outcomes in 32% (40/124) patients.

Conclusions: Drug resistant TB is massively under diagnosed in young children. Although outcomes for children with DR-TB are good, adolescents (particularly young women) present a high risk group with higher rates of severe disease and unfavourable outcomes.

EP05 Raising awareness about tuberculosis through community education

EP05-138-26 Co-creating an evaluation framework for tuberculosis extension for community health outcomes (TB-ECHO) model in New Delhi, India

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Background and challenges to implementation: The ECHO model™ expands capacity to manage complex diseases by sharing knowledge, disseminating best practices, and building communities of practice. Multidrug-resistant tuberculosis (MDR-TB), a deadly form of TB, is substantially more challenging than non-drug resistant TB. Many national TB control programs rely on highly specialized institutions and practitioners to manage MDR-TB centrally. The National Institute for TB and Respiratory Disease (NITRD), New Delhi manages greater than 1,000 MDR-TB patients annually. Since November 2016, NITRD provided expert consultation via virtual teleECHO™ sessions using case-based learning, and didactic presentations about the diagnosis, treatment, and management of complicated MDR patients with local TB officers and program staff. TB-ECHO clinics hold promise to decentralize MDR-TB management.

Intervention or response: An evaluation framework is needed to monitor project implementation, measure success, and ensure sustainability. We conducted a two-

day workshop to (1) identify facilitators and barriers to building a TB-ECHO community of practice for managing complex TB cases in India and, (2) inform the development of a comprehensive evaluation toolkit for TB-ECHO programs. A modified appreciative enquiry approach, SOAR (Strength/Challenges, Opportunities, Aspirations, and measurable Results), facilitated an interactive discussion amongst five homogenous groups (i.e., matched by professions and responsibilities). A systematic qualitative analysis summarized individual and group reflections.

Results and lessons learnt: Forty stakeholders, including government program leaders, state and district medical officers, laboratorians, and field staff, offered a multitude of perspectives. The key themes that emerged related to political advocacy, capacity building, establishing partnerships, measuring public health impact, and securing funding for replicability and sustainability. Technological, communication, and logistical challenges were also shared. These themes informed a broad set of process- and outcome-based indicators.

Conclusions and key recommendations: Purposeful facilitation using the SOAR methodology encouraged co-creation and empowered participants to share experiences openly, without inhibition. Developing an evaluation framework, identifying and addressing potential barriers to TB-ECHO implementation will support the dissemination of this model globally.

EP05-139-26 Tuberculosis-related knowledge in the general population: results from a cross-sectional survey in 11 regions of Ethiopia

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Background: Ethiopia is a high-burden country with significant missed tuberculosis cases. It has decentralized TB services to communities to improve community awareness and raise health-seeking behavior of the general population. However, no national population-based survey has been conducted to assess the knowledge of the general population. Our objective was to assess the knowledge of the general population about TB, its causes, and modes of transmission.

Methods: This was a cross-sectional population-based survey conducted in all 11 regions of Ethiopia between October 25 and November 18, 2017. A multistage sampling technique was used to select study participants. A semi-structured, pre-tested questionnaire was used to assess knowledge about TB, its causes, and transmission. Trained health professionals collected the data electronically and analysis was done using SPSS Version 20.

Results: Of 1783 participants interviewed, 46.8% were women. The mean age was 34.6 (SD±12), 48.7% were household heads and 66% were married. 94% of study participants had heard of TB, only 30.1% knew that germs cause TB, and 74.2% knew that it is transmitted by coughing or sneezing. 48.6% of the general population did not know the disease's cause. A majority reported that TB is preventable and curable 80.8% and 90.3% of respondents, respectively. 92.7% of the population want more information about TB. Only 20.9% the population had heard of drug-resistant TB and 76.2% of these knew that it is caused by non-adherence to treatment. The main source of information cited was family, friends, neighbors, and colleagues combined. High knowledge scores are associated with gender and wealth index, with regional variations.

Conclusions: This study showed that knowledge of TB within the general population is high. However, there is limited knowledge of its cause and high demand for more information. Therefore, community-based dissemination of TB-related information is crucial to improve performance of the TB program in Ethiopia.

EP05-140-26 Integrating tuberculosis into the primary school teaching curriculum in Malawi

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Background and challenges to implementation: There is generally big knowledge gap on Tuberculosis (TB) among primary school going children, teachers and the community at large in Malawi. Unlike TB; HIV/AIDS and Malaria have been integrated into primary school teaching curriculum in Malawi. Children are generally regarded as agents of change as they can easily disseminate information to the community.

Intervention or response: As one way of involving children in TB information dissemination to the community, Malawi Ministry of Education, Science and Technology (MoEST) in collaboration with the National Tuberculosis Programme (NTP) developed a TB sourcebook for primary schools. The sourcebook is designed to be integrated into primary school teaching curriculum in the country.

The NTP and MoEST organised a 5 days' workshop where the first draft of the TB sourcebook was developed. This was followed-up with another workshop where the draft sourcebook was refined and illustrations were included. Trial testing of the draft sourcebook was organised in selected 30 primary schools across the country, where teachers were given time to go through the sourcebook for their comments. Teachers were also

given chance to deliver TB lessons in 4 primary schools. These lessons were observed by both NTP and MoEST staff. After the trial testing, a 2 days' workshop was organised to consolidate comments from teachers.

Results and lessons learnt: Primary school teachers have generally welcomed the development of the TB sourcebook as it was perceived to improve TB knowledge among school children, teachers and community at large. Teachers gave valuable comments in areas they liked most and in areas that needed some improvements; especially in the content and illustrations. The lesson observation revealed that TB concepts are teachable and students can easily understand and apply in their everyday life.

Conclusions and key recommendations: Teachers and children were very enthusiastic to know more about TB. Similar intervention need to be considered in other education sectors in Malawi.

EP05-141-26 Study on the effect of health promotion on health behavior for newly diagnosed TB patients

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Background: China is one of the 22 countries identified by WHO as having a high burden of TB. The purpose of this study was to examine the influence of health promotion on the TB knowledge and health behaviors of newly diagnosed TB patients in a TB clinic.

Methods: Doctors conducted various forms of health promotion activities for 336 newly diagnosed TB patients in a TB clinic from June to December 2017 Ningxia Fourth People's Hospital, China. Patients were asked to complete a questionnaire and an interview to assess knowledge of TB and health behavior. TB patients acquired knowledge of tuberculosis and their health behavior were investigated during the health promotion sessions. The data were statistically analyzed in SPSS 11.0 statistical software. ² tests were used for group comparison.

Results: After health promotion sessions, patients basic TB knowledge regarding signs and symptoms, routes of transmission, diagnosis of TB, treatment, whether TB is curable and treatment costs improved from baseline ($p < 0.05$). Meanwhile, tuberculosis patients' health behavior such as diet and nutrition management, rational medication use, sputum management, wearing a surgical mask, cough etiquette, and emotional management, etc. improved over baseline ($p < 0.05$).

Conclusions: Health promotion and education can help newly diagnosed pulmonary TB patients to get core knowledge of TB, improve their health behavior patterns, increase the cure rate and reduce TB transmission efficiently. It has a promoting effect on tuberculosis prevention and control.

EP05-142-26 Communication in health to fight tuberculosis in the prison system: the Brazilian experience

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Background and challenges to implementation: In 2017, in Brazil, 10.5% ($n=7,317$) of tuberculosis (TB) new cases were in inmates. The risk of TB disease in this population is 28 times higher than in the general population. Recognizing this vulnerability, from 2014 to 2016, the Ministry of Health, and the United Nations Office on Drugs and Crime (UNODC), with funding from TB Reach Program/Stop TB Partnership, developed a project in prisons of Rio Grande do Sul and Rio de Janeiro, in order to carry out an educational TB campaign for prison community to increase TB knowledge and case detection.

Intervention or response: The communication strategies were developed considering the specificities identified in focus groups with prison community (prisoners, family members, health and safety professionals). Behavioral interventions with family members were performed through peer education and theater with health and safety professionals. The strategies and materials considered education level, the need for technical deepening on disease control recommendations, and addressed issues related to the stigma about TB.

Results and lessons learnt: The TB Reach Project contributed to the expansion of TB information in the prison units. Through reports from the prison community, the main differential was the development of different strategies specific to each public. During the 18 months of the project, 280 people with TB were identified in these units. The educational materials developed by the Project are available for use of the health and prison facilities.

Conclusions and key recommendations: In recognition of health communication actions importance and positive results of TB Reach Project materials and strategies, in 2017, the Ministry of Public Security in technical cooperation with the Ministry of Health, transferred R\$ 27.5 million to the Oswaldo Foundation Cruz (Fiocruz) to carry out a National Project for Health Education and TB in the Brazilian Prison System, aiming to increase the knowledge, detection and timely treatment of TB.

EP05-143-26 TB knowledge among general population across 30 districts in India: findings from three serial KAP surveys

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Background: Health related knowledge plays a key role in determining one's health seeking behavior. It helps general public to make choices about their health care practices and contributes to the larger sustainable development goals. Tuberculosis (TB) control program in India heavily depends on passive case finding i.e. people in need coming to the public health system for care. Unless the general population has adequate knowledge about TB, its symptoms or treatment options they will not be able to choose the right service providers. In this context, we assessed the TB knowledge about among general population in India at three different points in the last seven years and analyzed the changes.

Methods: Project Axshya supported by a Global Fund conducted knowledge, attitude and practice surveys in 2011 (baseline), 2013 (midline) and 2017 (endline) across 30 districts in India. Various TB related knowledge indicators were captured among the general population respondents. We compared these indicators across the surveys. The rural: urban ratio was as per the Census 2011 data. From each district 10 primary sampling units with approx. 250 households were covered. Respondents were selected randomly from the household list with equal male to female ratio and were interviewed using pre-tested questionnaires after obtaining consent.

Results: The key knowledge indicators revealed increase across baseline (N=4562), midline (N=4804) and endline (N=4912) in proportions of general population who knew that cough of over 2 weeks is key symptom for TB, mode of transmission, tests of diagnosis, treatment duration and heard of DOTS, (Table 1).

KEY INDICATORS	Baseline (N=4562)		Midline (N= 4804)		Endline (N=4912)	
	N	%	N	%	N	%
Heard of TB	3823	84	4211	88	3580	73
Having knowledge that cough of > 2 weeks is TB	2843	62	3443	72	2775	78
Having knowledge that TB is transmitted through air	2283	50	3008	63	2471	69
Having knowledge that TB can be diagnosed by sputum examination	2515	55	2778	58	2366	66
Having knowledge that TB is curable	3346	73	3526	73	3369	94
Having knowledge that the duration of TB treatment is 6-8 months	1724	38	2044	43	2091	58
Have heard of DOTS	1059	23	1094	23	1169	33
Know that TB treatment is free under DOTS	849	19	961	20	1070	22

[Table 1. Key indicators of knowledge about TB among opinion leaders across baseline, midline and endline KAP surveys.]

However, there is a considerable decline in population who heard of TB. The indicators regarding treatment duration or DOTS are still very low.

Conclusions: Though the general population is becoming more aware of TB, its symptoms and curability, knowledge on treatment aspects is poor and needs intensified awareness programs.

EP05-144-26 Opinion leaders of India and their knowledge about tuberculosis across 30 districts in India: findings from three serial KAP surveys

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Background: Opinion leaders (OL) are persons with significant influence in the community, people trust their opinions and seek their advice when needed. They range from a school teacher to a sarpanch of a village or a political leader for that matter! So is it important that they have good knowledge about a disease like tuberculosis (TB)? Yes of course!

When a community member is struggling with TB symptoms and is not sure what to do, he/she will surely approach one of these leaders. Hence these leaders not only have a responsibility to give right information but also follow up and make sure that the community members complete their treatment upon diagnosis. In this context, we assessed the TB knowledge about among opinion leaders in India at three different points in the last seven years and analyzed the changes.

Methods: Project Axshya supported by a Global Fund conducted knowledge, attitude and practice surveys in 2011 (baseline), 2013 (midline) and 2017 (endline) across 30 districts in India. Various TB related knowledge indicators were captured among OL. Respondents were identified based on the information provided by the community members and the study definition. OL were interviewed using pre-tested questionnaires after obtaining consent.

Results: The key knowledge indicators revealed increase across baseline (N=511), midline (N=611) and endline (N=752) in proportions of OL who knew that cough of over 2 weeks is key symptom for TB, mode of transmission and curability (Table 1).

However, many indicators showed decline. The indicators regarding treatment duration or DOTS are still very low. Very low proportions of them were involved in any TB related activity in the community.

Conclusions: Opinion leaders, such an important group of stakeholders are not having essential knowledge about TB. These leaders if trained and engaged in a systematic way can be instrumental in creating TB-free villages and communities!

Characteristics	Baseline (N=511)		Midline (N=611)		Endline (N=752)	
	N	%	N	%	N	%
Spontaneous recall (TB included in the top health priorities of their community)	113	22	191	31	300	40
Heard of TB	511	100	575	94	404	89
Mode of transmission: through the air when the infected person coughs or sneezes	422	90	456	75	589	78
Know that the major symptom of TB is cough of 2 weeks or more	400	78	538	88	587	78
Know that sputum smear test is necessary for the diagnosis of TB	407	80	423	69	436	58
Consider TB as fully curable disease	468	92	554	91	683	91
Heard of DOTS	300	59	351	58	456	61
Know that treatment of TB is through allopathic medicines	362	71	526	86	337	45
Know that the duration of TB treatment is 6-8 months	319	62	322	53	490	65
Know that the treatment of TB is available at government hospital	462	90	540	88	654	87
Have played a role in treating awareness for DOTS	113	22	106	17	180	24
Know that DOTS is free of cost	345	68	367	60	434	58

[Table 1. Key indicators of knowledge about TB among opinion leaders across baseline, midline and endline KAP surveys across the 30 districts in India.]

EP05-145-26 Effectiveness of TB information, education and communication display screen: a case at Naitiri sub-County Hospital, Kenya

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Background and challenges to implementation: Information Education and Communication (IEC) is a set of public health approaches aiming at changing, reinforcing health-related behavior in a target audience, concerning a specific problem and within a specified period of time, through a communication method and principles. The objective of the project was to assess the effectiveness of TB IEC display screen as a tool for igniting health action in TB control, empowerment of communities and social mobilization

Intervention or response: Animated short and specific TB Information, blended with pictures and videos, relevant background sounds and songs loaded in portable disks were prepared, displayed and played repeatedly on facility installed television screen since August 2017. Through a customer satisfaction survey, 190 participants were interviewed and rated the media on its effectiveness based on consistency, environmental friendliness and visibility at its two months of operation. Results were tabulated and analyzed.

Results and lessons learnt: TB IEC display screen was 67.5% effective according to the respondents with 56% consistency, 83.2% environmental friendliness and

68.5% visibility. Mounted strategically on a waiting area wall within the facility, the display screen attracted attention of most clients in the facility. It maintained facility wall cleanliness compared to print displays.

It can be duplicated to other facilities and institutions as it is affordable.

Conclusions and key recommendations: Generally, TB IEC display screen can be an effective innovation in health promotion. It will be source of TB Information, means of communication and education to communities. Developed contents for display being programmable, stored, transferable and secure will be a cost effective TB advocacy, communication and social mobilization. Inputs from experts in health promotion, Information and Communication Technology (ICT) and National TB control programs for advice on policy are key for a future TB IEC display screen. Further research and development on the material is recommended.

EP05-146-26 eHealth in tuberculosis: are we going in the right direction?

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Background: Despite modern medicine's advancements, tuberculosis (TB) remains in the top 10 world's most important causes of death. With the rise in internet and mobile usage, researchers are looking beyond the mycobacterium trying to find new approaches in order to fulfill the End-TB Strategy. One of these approaches is eHealth, the organization and delivery of health services and information using the Internet and related technologies.

Methods: A systematic review (SR) of eHealth in tuberculosis was performed in parallel with focus group interviews (FGI) on the same subject. SR, identified 2481 potential studies, out of which 80 were included in the final analysis. FGI were performed with tuberculosis patients and medical staff, in five countries over three continents.

Results: Previous work in eHealth in tuberculosis as revealed by SR has focused mainly on diagnosis and treatment and less on tuberculosis awareness (17.1% of selected studies). Most eHealth solutions concerned expert advice, sending SMS reminders, performing video-DOTS or enhancing patient-doctor communication. The few apps which performed awareness, send motivational or informational messages to tuberculosis patients.

In contrast with SR results, the interviews showed that the first priority for worldwide tuberculosis patients and medical staff is information: patients would like to have

more and share more information about tuberculosis and medical staff would like to offer patients more information, delivered even if there are time or distance constraints. Patients and staff across the board agree that video would be the optimum environment to offer information, in the form of short videos which patients can replay.

Conclusions: This study showed a clear gap between efforts made and priorities felt by the end-users of a tuberculosis eHealth solution. Future tuberculosis app targeted on patients and medical staff should focus on user preferences in order to be successful.

EP05-147-26 Study on level of tuberculosis knowledge among women in Aksu, China

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Background: In recent years, the incidence of tuberculosis (TB) in Aksu Prefecture, Xinjiang, has been at a high level. Women play important role in family to prevent and control TB. The objective of this study was to explore the level of TB knowledge among women in Aksu Prefecture and its influencing factors, in order to provide suggestions for TB-related health education.

Methods: A cross-sectional survey was conducted to collect data among 245 women in Aksu Prefecture, Xinjiang Uygur Autonomous Region. The self-administered National TB Knowledge, Attitude and Behavior Questionnaire was used to assess participants' knowledge about classic TB symptoms of cough/blood-tinged sputum, TB modes of transmission, management and control. The inclusion criteria were aged over 18, no cognitive impairment, able to complete questionnaires independently and informed consent. Kruskal-Wallis test and stepwise linear regression was used to identify the influencing factors on level of TB knowledge.

Results: 245 women returned questionnaire, 41 were excluded because they answered "never heard of TB", 14 didn't complete questionnaire, and thus the final sample included 190 women. Only 22.1% of them had knowledge of TB symptoms, 80.0% and 73.7% knew local dispensaries of TB and free TB treatment policy respectively, and 54.7% recognized that TB patients should not experience stigma. The univariate analysis revealed that place of residence, education level, occupational status, and type of medical insurance were variables with statistical significance ($P < 0.05$). The multiple regression analysis showed that the level of TB knowledge was positively associated with education level ($F=22.860$, $P < 0.001$).

Conclusions: The level of TB controlling knowledge among women in Aksu Prefecture should be further improved, especially in low-educated and low-income women, who would be the focus of health education in the future.

EP05-148-26 A holistic and self-sustainable approach to control TB in a rural area of Senegal

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Background: Effective, sustainable and reproducible projects are fundamental to decrease the burden of Tuberculosis (TB) and optimize resource allocation in low-resource settings. The objective of this study is to measure preliminary results of a self-sustainable programme, started in 2013, between Stop TB Italia Onlus and the Senegalese NTP in the district of Diofior, Senegal. The project aimed to:

- 1) enhance health education;
- 2) improve laboratory diagnostic capability;
- 3) reduce catastrophic costs for TB-affected households;
- 4) establish a parallel intervention to ensure the self-sustainable project.

Methods: A comprehensive educational programme supported by distribution of informative materials, organisation of public events and training of community-based workers was realized to raise TB awareness and to reduce accessibility barriers to health-care services. To strengthen TB diagnostic capacities, the Xpert MTB/RIF system and a mobile chest-X-Ray were implemented at the Health Care Centre of Diofior (HCD). Economic support (20.000 CFA) was provided to all patients who completed treatment. An agricultural cooperative, fully managed by former TB patients, was established to economically support families of former TB patients and ensure continuity and self-sustainability of the project.

Results: Fifty women were enrolled to detect chronic cough in the peripheral villages surrounding the HCD. In a pre-post study, the efficacy of the interventions resulted in a more favourable TB treatment outcome (treatment completed and cured): 29/43 (67.4%) vs. 176/196 (89.8%), ($p < 0.0001$). Patients' death during treatment decreased from 8/43 (18.6%) in 2012 to 11/196 (5.6%) in 2013-2016 ($p=0.009$). All patients received economic support and only 3 (1.5%) were lost to follow-up. Currently, 10 ex-patients are working the farmland and the number is expected to increase to reach enough incomes from harvest to fully sustain the project in 2020.

Conclusions: This holistic and self-sustainable approach to control TB in a rural setting may point to a model that could be scaled-up at national level.

EP06 Next-generation sequencing implementation: tools for the future!

EP06-149-26 Impact of whole genome sequencing versus GeneXpert and line probe assays on therapy selection for multi- and extensively drug-resistant tuberculosis

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Background: Rapid and accurate drug susceptibility testing (DST) is essential for the treatment of multi- and extensively drug-resistant tuberculosis (M/XDR-TB). We aimed to assess the impact of whole genome sequencing (WGS) versus Cepheid GeneXpert MTB/RIF (GeneXpert), Hain GenoType MTBDR*plus* 2.0 (LPA1) and MTBDR*sl* 2.0 (LPA2) line-probe assays in appropriately selecting treatment regimens for drug-resistant (DR)-TB.

Methods: We present preliminary data from the CAPRISA 020 Index study (Individualized M/XDR TB Treatment strategy study) on 24 adult patients with pulmonary TB (2 rifampicin (RIF) resistant, 18 MDR-TB, 3 pre-XDR, 1 XDR-TB) randomized to receive WGS-based individualized treatment enrolled between May 2017 and April 2018. A study therapeutics advisory committee informed drug selection based on WGS and patient clinical presentation. LPA 2 and WGS results were compared second-line phenotypic DST (capreomycin 2.5ug/ml; levofloxacin 1.5ug/ml; moxifloxacin 0.5 and 2.0ug/ml).

Results: GeneXpert detected rifampicin resistance correlating with LPA1 and WGS in 24/24 (100%) patients. LPA1 detected isoniazid and ethionamide resistance correlating with WGS in 23/24 (95.8%) patients. One patient with high-level isoniazid resistance was detected by WGS only. LPA2 detected fluoroquinolone and aminoglycoside resistance correlating with WGS and phenotypic DST in 23/24 (95.8%). LPA testing on sputum failed in smear-negative patients (n=5), however, subsequent culture-based testing correlated with WGS. WGS resulted in further regimen changes 19/24 (79.1%) patients. WGS in 18/19 patients showed resistance to ethambutol and pyrazinamide resulting in exclusion of these drugs. Ototoxicity was the predominant treatment modifying clinical feature resulting in regimen changes (14/24; 58.3%).

Conclusions: GeneXpert and LPA1/2 were effective to rule in M/XDR-TB and initiate standardized DR-TB treatment. LPA had limited impact in patients with smear-negative TB. WGS was the most accurate technique to guide the selection of individualized treatment, including selection of appropriate companion drugs. Additionally, clinical consequences of overlapping drug toxicities significantly impacts treatment selection, further complicating M/XDR-TB management.

EP06-150-26 Whole genome sequence based resistance prediction and molecular typing of Mycobacterium tuberculosis complex strains in BioNumerics

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Background: WGS has become an increasingly important tool for epidemiologic studies of TB, including outbreak detection. Furthermore, in contrast to the time-consuming phenotypic drug susceptibility tests, WGS enables rapid prediction of associated antibiotic resistance, crucial for TB control and treatment. In this study, we present BioNumerics MTBC genotyping plugin, predicting associated resistance to first and second line antibiotics, and determining the *Mycobacterium* species, lineage and spoligotype of the MTBCstrains.

Methods: All functionalities within the plugin are read-based. **Species decomposition** is based on the 16S rRNA gene sequence. The **lineage determination** component classifies MTBC strains in 8 lineages and 55 sublineages based on 62 SNPs. In addition, *in silico spoligotyping* is performed using the nucleotide sequences of 43 spacers as references in a mapping analysis. Lastly, **resistance prediction** for 12 antibiotics is based on known mutations in 28 resistance genes, and can be easily extended. Results were validated on 161 MTBC samples (PRJ-NA187550).

Results: The majority (98%) of the strains were correctly identified as being MTBC species and predicted lineage of all samples corresponded with previous reports. For 99% of the MTBC isolates, the tool predicted spoligotype identical to SpoTyping. The sensitivity for isoniazid (INH), rifampicin (RMP), ethambutol (EMB), kanamycin (KAN) ranged between 80 and 95%, while for ethionamide (ETH) this was only 50%. Specificity for INH, RMP, ETH, EMB and KAN, on the other hand, ranged between 70 and 100%. All samples were predicted to be resistant to streptomycin (SM) while this was only true in 52% of the cases according to phenotypic DST. The amount of false positive and negative drug resistance predictions indicated the need for an optimization of the current genotype-phenotype correlations, which is currently being implemented.

Conclusions: The BioNumerics MTBC genotyping functionality, is an effective and user-friendly tool for species identification, strain typing and prediction of resistance, useful for high-throughput molecular surveillance and control of TB.

EP06-151-26 Number of effective drugs in the short-course MDR-TB regimen according to standard of care drug susceptibility testing and whole genome sequencing

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Background: Patients with drug resistant tuberculosis (TB) should receive ≥ 4 effective drugs. The new short-course regimen consists of high-dose isoniazid, pyrazinamide, prothionamide, ethambutol, kanamycin, moxifloxacin, and clofazimine. It is unknown how many drugs are effective in individuals who empirically start this regimen. We compared knowledge on drug susceptibility obtained by standard of care (SOC) methods versus whole genome sequencing (WGS) in South African patients.

Methods: Pre-treatment *Mycobacterium tuberculosis* isolates of 318 patients with rifampicin resistance on Xpert MTB/RIF or Hain MTBDR_{plus} were assessed by SOC (Hain MTBDR_{plus}, isoniazid phenotypic drug susceptibility testing (DST) in case of genotypic isoniazid susceptibility, Hain MTBDR_{sl} V1) and WGS (using the genomic variants published in 2018 by Coll et al. to call resistance and variants in Rv0678 for clofazimine). Based on SOC or WGS data, isolates were classified as pan-susceptible, rifampicin mono-resistant, MDR, (pre)-XDR, or other. In absence of information, the strain was classified as susceptible to a specific drug. We estimated the proportion of patients receiving ≥ 4 effective drugs under the short-course regimen, with drugs with unknown resistance profiles classified as either effective or of unknown effectiveness.

Results: The distribution of resistance profiles based on SOC and WGS data is shown in Table 1. The proportion of patients receiving ≥ 4 effective drugs was 66% based on WGS data. This proportion was significantly overestimated by SOC methods when classifying drugs with unknown susceptibility as effective (77% vs. 66%, $p=0.002$), and significantly underestimated by SOC methods when only classifying drugs with proven susceptibility as effective (51% vs. 66% $p=0.001$).

	Pan-susceptible	RIF Mono	MDR	Pre-XDR	XDR	Other
	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)
SOC	0 (0%)	94 (29.6%)	123 (38.7%)	35 (11.0%)	38 (11.9%)	28 (8.8%)
WGS	30 (9.4%)	68 (21.4%)	94 (29.6%)	51 (16.0%)	49 (15.4%)	26 (8.2%)

[Table 1: Drug resistance profile as determined by SOC methods and whole genome sequencing in 318 South African patients]

Conclusions: One third of South African patients diagnosed with rifampicin resistance on Xpert MTB/RIF empirically started on the new short-course MDR-TB regimen may receive an insufficient number of effective drugs. SOC DST methods result in an inaccurate estimation of the number of effective drugs.

EP06-152-26 Whole-genome sequencing characterization of Mycobacterium tuberculosis drug resistance at a referral centre in Rome: implications for diagnosis and disease control

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Background: Although tuberculosis (TB) control has been effective especially in low-incidence countries, the increasing burden of multidrug-resistant (MDR) and extensively drug-resistant (XDR) disease pose a serious challenge.

The metropolitan area of Rome has recently experienced intense population movements, resulting in higher rates of TB compared to Italy as a whole.

A clear knowledge of the trends of drug-resistant TB in this area could contribute to a better management of the disease. The use of whole-genome sequencing (WGS) could help to identify *M. tuberculosis* mutations correlated with drug-resistance.

In this study we aimed to characterize, using WGS, the drug-resistance profiles of TB strains circulating in the great metropolitan area of Rome.

Methods: *M. tuberculosis* strains isolated from patients admitted at the National Institute for Infectious Diseases in Rome between 2011 and 2016 with TB, were subjected to DNA extraction (CTAB method) and to WGS by Illumina. Sequences were uploaded on PhyResSE 1.0 for identification of mutations correlated with drug-resistance.

Phenotypic drug-susceptibility testing for the first line drugs was performed on all strains, as part of the diagnostic routine.

Results: *M. tuberculosis* isolates were collected from 260 patients and sequenced. Of these, 193 (74%) were from foreign born (FB) patients. Mutations correlated to drug-resistance were found in 17% of the strains, and approximately half (54.5%) of these were MDR. Resistance profiles including single or multiple drugs were characterized and further compared to phenotypic results. Agreement of 94% was found on MDR strains, while second line drugs show more significant differences, although phenotypic DST was done on limited number of them.

Conclusions: This study, conducted in a TB referral hospital in Rome, provides information on drug-resistance related mutations found in strains circulating in the

area. Discordant results were evaluated. A panel of single and multiple drug-resistances was found and further investigation is ongoing.

EP06-153-26 Whole genome sequencing *Mycobacterium tuberculosis* directly from sputum identifies more genetic heterogeneity than sequencing from culture

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Background: *Mycobacterium tuberculosis* next generation whole genome sequencing (WGS) reveals the presence of genetic diversity within individual patients due to mixed infection or within-host evolution. WGS is usually performed on cultured isolates, even though this can alter the original population structure, because WGS directly from unenriched sputum yields insufficient DNA for deep genome coverage. Oligonucleotide enrichment technology SureSelect^{XT} (Agilent, USA) has successfully obtained purified *M.tuberculosis* DNA directly from sputum. Here we compare genetic diversity identified sequencing from enriched sputum and culture.

Methods: Paired sputum samples from 46 patients were analysed. DNA was extracted directly from one sample, with the other inoculated into MGIT (mycobacterial growth indicator tube) until flagging positive. DNA extracted from sputum underwent enrichment. All samples were sequenced on an Illumina NextSeq. Genetic diversity was measured using two methods. First, heterogeneous sites were identified using CLC Genomics Workbench v11.0 where >1 nucleotide mapped to a base with ≥ 3 supporting reads including one in each direction. Second, the probability that two reads have a different nucleotide at a given position within each sample was estimated using a locally-designed program.

Results: More heterogeneous sites were identified in direct sputum than MGIT samples as shown in the table. Mean genome coverage was similar between direct sputum and MGIT samples (184.3 vs. 191.1, $p=0.80$). Within-sample read variation probability estimated by the program was greater in direct sputum than MGIT samples (6.71×10^{-6} v 3.86×10^{-6} , $p < 0.001$).

Mutation type	Direct sputum	MGIT culture	p-value
Intergenic	2146	1039	<0.001
Synonymous	1767	511	0.014
Non-synonymous	3546	1375	0.001
Total	7459	2925	<0.001

[Heterogenous sites identified sequencing directly from sputum and MGIT culture across all samples]

Conclusions: Sequencing directly from sputum identifies more genetic diversity than from MGIT. This contrasts to a previous study that has sequenced directly from

sputum, but may be due to greater coverage depth and patient numbers included here. These results concord with other data suggesting that repeated subculture lead to a loss of diversity. Direct sputum sequencing may better represent true mycobacterial genetic diversity within patients and have a role investigating heteroresistance.

EP06-154-26 Ethical challenges in the use of whole genome sequencing for tuberculosis surveillance and drug resistance testing: a qualitative study of stakeholder perspectives

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Background: Advancements in whole genome sequencing (WGS) can aid in tuberculosis (TB) surveillance efforts, both nationally and globally, while also helping track drug resistance. However, the use of WGS raises ethical concerns that have not been examined. We present findings from a qualitative study exploring key stakeholder perspectives regarding ethical challenges associated with the use of WGS for TB.

Methods: We conducted 23 semi-structured interviews with policy makers and scientists working with WGS in TB, in Canada and globally. Interviews ran for approximately one hour, were audio-recorded, transcribed, and coded using NVivo 11. Data were analyzed using Braun and Clarke's thematic analysis.

Results: We identified five themes:

(1) Ensuring the safe use of WGS, e.g., balancing the value of the contribution of genomic data to assist in surveillance efforts with the protection of individuals and communities, and potential reputational harms to national TB programs;

(2) data sharing, e.g., logistical, political and ethical challenges associated with data sharing at local and global levels;

(3) equity challenges, e.g., WGS as a complex technology that requires expertise and infrastructure that low-burden, high-income countries may have but may not necessarily exist in high-burden, low-income countries;

(4) governance of WGS procedures and outcomes, e.g., a dearth in global and national policy for data stewardship and data sharing;

(5) Challenges with the science of WGS, e.g. the rapid evolution of molecular diagnostics poses challenges to the abilities of healthcare workers to understand the science but who are charged with using the technology.

Conclusions: While respondents agreed WGS may hold immense promise for future surveillance and diagnostic efforts for TB, underlying ethical challenges must be addressed to ensure the fair and just implementation of WGS into public health systems, particularly in those high-burden countries with marginalized populations.

EP06-155-26 Intrinsic genomic structure of Peruvian *Mycobacterium tuberculosis* strains

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Background: *Mycobacterium tuberculosis* (MTB) is the most common causative agent of Tuberculosis (TB). The aim of this research is to identify the intrinsic genomic architecture of MTB strains circulating in different areas of Peru, and to evaluate the diversity between them.

Methods: The study included 100 MTB strains coming from 16 "health networks" along the country: XDR-TB (49), Pre XDR-TB (15), MDR-TB (16), Isoniazid Mono-resistant (10), and susceptible to all drugs (10). Whole-Genome Sequencing using the Illumina Technology was performed. Arlequin v3.5.2.2 software to assess the genomic nucleotide diversity (π) and AMOVA analysis for several geographic hypothesized structures were used. A evolutionary tree was constructed using the Maximum-Likelihood approach by RAxML v2.8.10 with 1000 bootstraps. The genomic structure was performed through clustering and admixture analysis using BAPS v6.0 software. Additional substructure was achieved by Ade4 v1.7-10 and Poppr v2.6.1 R packages. Finally, *in silico* Spoligotyping was performed through the Spotyping v2 software and the results were contrasted to the SITVITWEB database.

Results: 8528 SNPs were obtained from the strains evaluated. There was a little bacterial genetic differentiation along different geographic settings (F_{ST} ranging between 0.027 - 0.053). The groups that included strains isolated in the capital of Peru showed to have a greater nucleotide diversity (0.09097, 0.09116 and 0.09163). We find that MTB strains were assigned to four, six and eight genomic clusters and there was no significant admixture between them. These clustering patterns were highly concordant with Maximum likelihood clades and Spoligotypes. The most prevalent Spoligotypes families were LAM (32%), T (32%), H (9%), X (9%), S (1%) and Beijing (5%). (Figure 01)

Conclusions: MTB families show a constant flow throughout Peru. However, there is a high centralization of them at the capital city. Finally, the predominant lineage in Peru keep being Euro-American one with a recent arrive of East-Asian lineage.

EP06-156-26 Detection of pre-XDR and XDR-TB by whole genome sequencing in Tunisia

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Background: Early detection of drug resistant tuberculosis (TB) is essential to prevent and control TB transmission. The aim of this study is to evaluate whole genome sequencing (WGS) for the rapid detection of fluoroquinolones (FQ) and aminosides (AG) resistance in multidrug resistant (MDR-TB) strains.

Methods: A total of 46 MDR-TB strains isolated in Tunisia from June 2012 to June 2016 were screened for second line drug susceptibility testing in BACTEC MGIT 960. Thirteen strains were identified as FQ resistant. Six among them had an additional resistance to AG (extensively drug resistant: XDR-TB). All isolates were tested with GenoType MTBDRsl assay (v1.0) (Hain Lifescience, Germany) and underwent WGS. The web tool PhyResSe was used to analyse genes involved in drug resistance.

Results: In comparison with MGIT 960, GenoType MTBDRsl assay (v1.0) had sensitivities of 84.6% (95%CI: 54.5-98.0), 66.6% (95%CI: 22.8-95.6) and 50.0% (95%CI: 11.8-88.1) to detect resistance to FQ, AG and XDR cases respectively with a specificity of 100%. However, WGS confirmed all FQ, AG resistance and XDR cases (100% of sensitivity and specificity).

All FQ resistant strains on MGIT (7 pre-XDR and 6 XDR) harboured at least one mutation conferring resist-

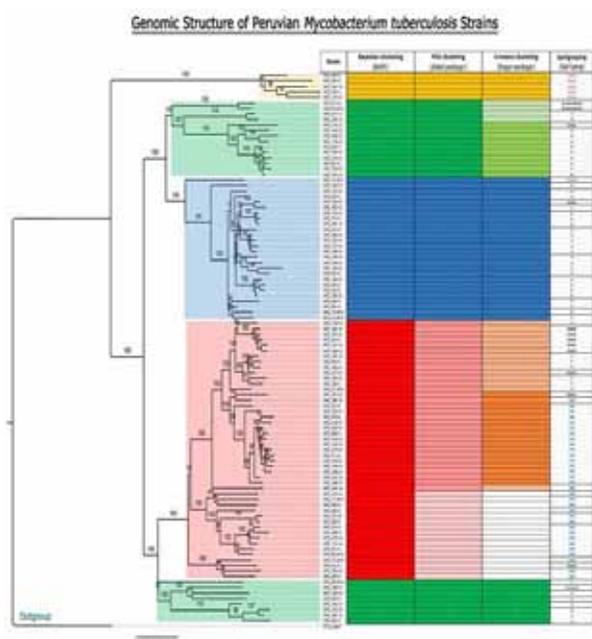


Figure 01: Genomic structure of peruvian *M. tuberculosis*. The Maximum-Likelihood Phylogenetic tree was constructed from 100 *M. tuberculosis* peruvian strains using 9739 whole-genome SNPs. This evolutionary tree was estimated by RAxML v2.8.10 using the General Time Reversible nucleotide substitution model plus Gamma distribution. Bootstrap supports were calculated from 1000 replicates and are indicated at nodes. The tree was rooted using the "Uruguai-7" (outgroup). Clades are highlighted according BAPS results. Bayesian clustering was performed using BAPS 6.0 software. Different colours represent the assignment of populations to different genetic clusters (K=4). Principal Component Analysis (PCA) and *k*-means clustering, showing additional genetic substructure, were performed in R v3.4.3 software using the Ade4 v1.7-10 and Poppr v2.6.1 packages, respectively. *In silico* Spoligotyping was performed using Spotyping v2.0 and contrasted with SITVITWEB database. Spoligotypes highlighted in red belong to East-Asian Lineage, whereas highlighted in blue belong to Euro-American Lineage. Scale bar indicate nucleotide substitution per site.

[Genomic structure of peruvian *M. tuberculosis*]

ance to FQ in the Quinolones Resistance Determining Region (QRDR) of *gyrA* or *gyrB* genes. Eleven strains carried a mutation in *gyrA* and 3 strains had a mutation in *gyrB* (codon 461). The codon 94 of *gyrA* was the most involved in FQ resistance (53.8%). For AG, 4 of 6 XDR strains presented the mutation A1401G of *rrs* gene (66.6%). One XDR strain was only Kanamycin resistant and harboured the mutation C-14T of *eis* promoter. The last XDR was phenotypically resistant to Capreomycin and presented a frame shift in *tlyA*.

Conclusions: WGS could be an attractive alternative to detect pre-XDR and XDR-TB strains with a short turnaround time.

EP06-157-26 From MDR to pre-XDR to XDR-TB: whole genome sequencing reveals several different evolutionary strategies

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Background: South Africa has one of the highest burdens of extensively drug-resistant tuberculosis (XDR TB) globally. XDR TB is difficult to treat, resulting in low treatment success and high death rates. XDR TB can evolve within a patient during treatment, but limited data exist on the evolutionary paths and genomic profiles of XDR *Mycobacterium tuberculosis* (*Mtb*) strains.

Methods: We performed whole genome sequencing (WGS) on 226 serial *Mtb* isolates from 41 patients resident in South Africa (range 2 to 9 isolates per individual patient). These strains were selected based on phenotypic drug susceptibility testing showing increasing drug resistance from multidrug resistance (MDR) to XDR during treatment. To identify mutations potentially involved in drug resistance or compensatory mechanisms, the type, frequency patterns and chronology of the genomic changes occurring within these strains were analyzed and compared.

Results: WGS data reveals the parallel existence of several hetero-resistant *Mtb* sub-populations with different combinations of genomic changes in almost all patients.

Twenty strains first acquired fluoroquinolone resistance and 19 strains first acquired resistance against the injectable drugs. For 2 strains, this chronology could not be determined. Apart from canonical drug resistance-conferring mutations, rare or potential novel resistance-conferring mutations were detected, accompanied by various other mutations either hitchhiking or potentially compensating for loss of fitness. WGS detected rare resistance markers not included in standard molecular diagnostic tools, and underlying resistant sub-populations were found earlier than by phenotypic susceptibility testing.

Conclusions: Our data demonstrates complex evolutionary dynamics during treatment of highly resistant *Mtb*. Although these evolutionary processes are not fully understood yet, they impact standardized, routine diagnostic procedures which may fail to determine the full drug resistance profile of a patient. Consequently, treatment outcomes might be affected. WGS will provide clinicians with more comprehensive drug susceptibility information on how to manage TB patients.

EP06-158-26 Pangenome analysis of *Mycobacterium tuberculosis* isolates disclosed accessory genome sequences specific to Beijing lineage

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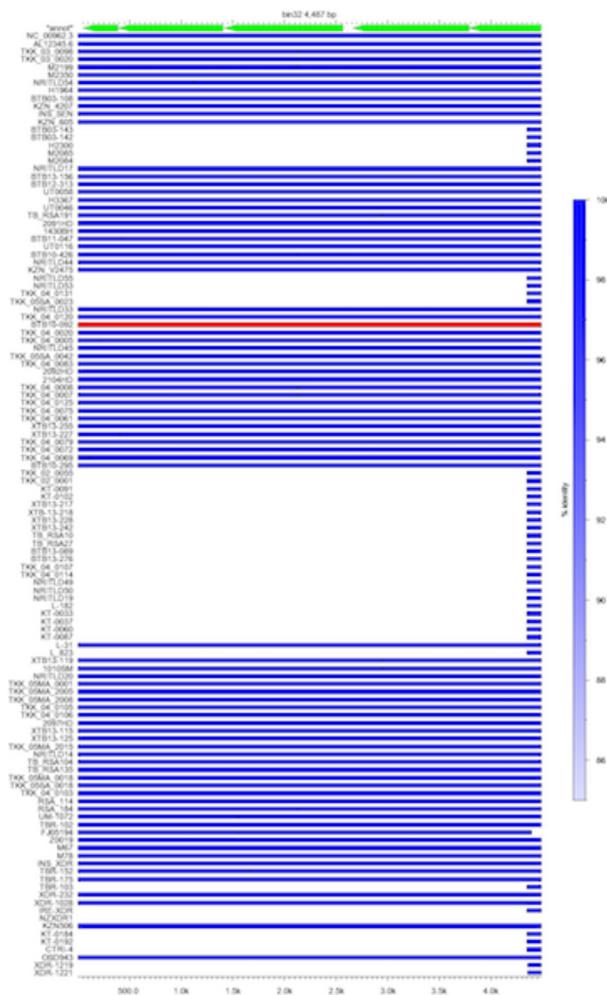
Background: Beijing lineage of *Mycobacterium tuberculosis* (MTB) is well known prone to drug resistance compared to non-beijing lineages. resistance compared to non-beijing lineages. The main aim of our study was to explore the core and accessory genome of 121 MTB lineages to attempt to characterize the complete gene repertoire.

Methods: Of total 121 genomes of MTB to define pangenome repertoire, three isolates were sequenced using Ion-Torrent PGM and draft assemblies of 118 isolates were downloaded from GenBank. Lineages (Beijing 40; Non-Beijing 81) for analysis in study belonged to globally diverse regions and drug resistant patterns. Pangenome analysis was performed using software Spine (V0.2.3), AGEnt (V0.2.3) and ClustAGE (V0.7.6).

Results: Total pangenome size was estimated to be 4,540,849 bp with 4,391 coding sequences (CDS), and a GC content of 65.4%. Estimated average size of the majority core genome (present in 100%) was 36,83,161 bp, contained 3,698 CDS and had an average GC content of 65.1% as compared to the average accessory genome size 6,96,320.9 bp, with 539.4 CDS and GC content of 67.9%. Among accessory elements an overall 4487 bp complete deletion of the CRISPR-associated endori-

bonuclease cas2 gene was found among 100% Beijing lineages part of the CRISPR-associated endonuclease cas1, CRISPR type-III-a/mtube-associated protein csm6 and CRISPR type-III-a/mtube-associated ramp protein csm4 were also deleted among 61.5% Beijing lineages and were present in all other lineages included in the collection.

Conclusions: CRISPR-Cas system in MTB associated with Cas1 and Cas2 genes perform endogenous DNA-repair along with Type-III-a-(CSM) effector arrangement, providing adaptive immunity to bacteriophages and plasmids. Deletion of these accessory sequences among Beijing lineage strains could suggest more defective DNA-repair genes in such strains. This could predispose the lineage developing drug resistance and transmission in the community. Such sequence markers could be useful in geographical regions where predominance of Beijing lineage is suspected.



[AGE graph output showing 4487 bp segment having deleted sequences in beijing Lineages]

EP06-159-26 Compensatory mutations in *rpoA* and *rpoC* gene regions in 121 *Mycobacterium tuberculosis* isolates disclose association with Ser531Leu mutation of *rpoB* gene

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Background: Mutations in the 81-bp region of *rpoB* gene is well known to confer rifampicin resistance in upto 95% isolates of MDR-TB. The role of compensatory mutations in *rpoA* and *rpoC* genes which restore the fitness of strains with mutations in *rpoB* gene region is less known. Hence this study was done.

Methods: A total of 118 MTB genome sequences were downloaded from the GenBank NCBI database and 3 strains were sequenced in our laboratory using Ion torrent PGM. The draft assemblies of all 121 MTB genomes were used in the analysis. Of the 121 genomes 40 belonged to Beijing and 81 to non-Beijing lineages. For the sequence reads of MTB genomes GATK version 3.8 was used for variant detection and annotated using SnpEff version 4.3p taking H37Rv genome (Accession: NC_000962.3) as reference.

Results: Rifampicin resistant strains were identified for non-synonymous and frame shift mutations mainly in 81bp (RRDR) region of *rpoB* (507-533 codon region). Of the 121 MTB genomes, mutations in RRDR region were found in 104 (85.9%). The Ser531Leu mutation was commonest (52, 50%) followed by Asp516Val (27, 25.9%). The *rpoA* mutation was found in 13 (10.7%) genomes, of which 9 (69.2%) were associated with Ser531Leu mutation. Beijing lineage was found to be statistically (P value 0.0009) prone for Ser531Leu mutation. Mutations in *rpoC* gene region were found in 58 (47.9%) genomes, of which 42(72.4%) were associated with Ser531Leu mutation. Four mutations (Lys-1135Arg, Thr480Ala, Arg908Cys, Ser493Ala) were outside the RRDR region. One mutation (Val183Gly) was in *rpoA* gene region while two mutations (Val1252Leu, Gly1261fs) in *rpoC* gene region were novel mutations discovered in our 3 genome sequences.

Conclusions: The Beijing strain was significantly associated with Ser531Leu in *rpoB* gene. This Ser531Leu mutation was associated with *rpoA* and *rpoC* mutations. This may explain their functional dynamics and compensatory repairing fitness and enhancing transmission.

POSTER DISCUSSION SESSIONS

PS18 The role of digital technologies along the patient pathway

PS18-585-26 Findings from the DrOTS Perceptions Study: patient and wider community engagement with a drone-observed therapy strategy for TB control in rural Madagascar

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Background: The DrOTS (Drone Observed Therapy Strategy) was launched in Madagascar's Androrangavola commune in autumn 2017. A proof of concept project, DrOTS aims to connect remote villages to TB diagnostic and treatment centers with drones, support and train patients and community healthcare workers with tablet-based educational material, and remotely monitor adherence with medical event reminder technologies or evriMED devices. The goal of DrOTS P.S. is to evaluate the cultural acceptability of DrOTS for enrolled villages, with particular attention to how those on the receiving ends of DrOTS understand and engage with its suite of technologies.

Methods: This mixed methods study involves administration of a questionnaire in 20 villages, ethnographic observation, as well as focus groups discussions (N=14) and semi-structured interviews (N=24) with a range of DrOTS involved individuals connected to three enrolled villages (patients, non-participant villagers, community health workers, village chiefs, DrOTS mobile health team members). An experienced medical anthropologist and epidemiologist are leading the data collection. Questionnaire analysis is being completed using Stata software version 13. Directed and thematic analysis of the qualitative data is being completed in Nvivo 11.0 (QSR).

Results: Findings suggest widespread enthusiasm for the technologies and health care made available to villagers through DrOTS. Nevertheless, also reported are a number of practical concerns vis a vis the continuity of the program, and uncertainty about whether more could

or should be done to maintain the status of DrOTS patients private. Questionnaire results are briefly presented to highlight some differences in results between different study sub-groups (e.g. patients *vs.* non-patients, most educated *vs.* least educated, etc.).

Conclusions: There exists no ethical or practical guidance on the contextually-sensitive use of drones for disease diagnosis and treatment at present. Attending to contextual and lived particularities of DrOTS is key to designing and planning feasible and effective scale-up.

PS18-586-26 Use of video-DOT in treatment of active tuberculosis in Norway

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Background: Norway is a low-incidence country for tuberculosis (6 cases/100000 inhabitants/year in 2016) and all TB-treatment is given as Directly Observed Therapy (DOT). North-Norway is sparsely populated and DOT frequently requires long travel-distances. No previous studies have investigated the use of Video-DOT (VDOT) in treatment of active TB in Norway and this study aims to fill this knowledge gap.

Methods: TB-nurses at University Hospital of North-Norway, Tromsø coordinate TB-treatment in 19 municipalities, serving as a link between the patient, municipal medical officer, homecare-nurses and medical specialists in the hospital. Based on defined criteria patients with active TB were enrolled in the VDOT-study from October 2016 (stop-date: October 2018). VDOT implies that the homecare-nurse daily contacts the patient via real-time video-call, observes the patient taking TB-medicine in real-time, and notes the time spent. As Norwegian health-legislation requires high security-levels to ensure privacy in patient-communication, commercial video-messaging-platforms (e.g. Skype) are not allowed. Accordingly, both parts are obliged to use a video-communication-line with personal password approved by national health-authorities, using iPad, mobile phone or computer. By the end of the TB-treatment period, the patient and homecare-nurses are interviewed individually.

Results: By April 2018, altogether 13 patients have been enrolled in the VDOT-study and 14 patients have been excluded. The ideal VDOT-candidate is ≥ 16 years, accepts the TB-diagnosis, is motivated, understands the need for TB-treatment, complies with ≥ 2 weeks initial in-person-DOT, has reliable internet-connection, masters digital technologies, and communicates effectively. Excluded patients were mainly children. Both the homecare-nurses and patients report that VDOT saves time and increases patient flexibility during the treatment period. Furthermore, both prefer VDOT ahead of in-person-DOT.

Conclusions: VDOT is a feasible, timesaving and acceptable method for observing real-time administration of TB-medicine in Norway and further implementation should be considered. However, we recommend increased focus on the development of improved communication-technology in accordance with Norwegian health-legislation.



[Taking TB-medicine using VDOT]

PS18-587-26 A randomized trial of in-person vs. electronic directly observed therapy for tuberculosis treatment

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Background: The use of electronic directly observed therapy (eDOT), as an alternative to in-person DOT (ipDOT), for monitoring tuberculosis (TB) treatment is increasing. However, studies of eDOT are limited to pilot programs or a select patient population. We initiated a randomized controlled trial to compare ipDOT with eDOT among patients undergoing treatment for rifampin-sensitive TB.

Methods: The trial is a cross-over, 2-arm, non-inferiority trial with broad eDOT inclusion criteria conducted in four New York City Health Department TB clinics. Participants are randomized to start outpatient treatment with either traditional ipDOT or eDOT; participants aim to complete 20 doses of medication and then switch to the other form of DOT for another 20 doses. Each patient serves as their own control. With ipDOT, patients choose clinic or community-based DOT; with eDOT, patients choose live or recorded videos. Following 40 doses, patients receive their preferred form of DOT for their remaining treatment. After randomiza-

tion, the study relies on the TB clinics' standard protocols and practices.

Results: Since July 2017, 79 (29%) of 271 eligible patients were enrolled. Participants are comparable to non-enrollees in age, gender, and birth within or outside the U.S. More Hispanic persons, but fewer Asian persons were enrolled. Primary reasons for non-enrollment include perceived inconvenience of ipDOT or eDOT (n=61), unwillingness to be randomized (n=57), and inconvenient number of study visits (n=38). Of participants' 4,251 scheduled DOT observations, 3,819 (90%) DOT observations occurred. Of 1,073 (28%) ipDOT observations, 622 (58%) were conducted in the clinic; 451 (42%) were conducted in the community. Of 2,746 (72%) eDOT observations, 1,198 (44%) were conducted using live eDOT and 1,548 (56%) using recorded eDOT.
Conclusions: Multiple studies have reported potential benefits and shortcomings associated with DOT that have informed TB programs' policies. This study's findings will help guide the implementation of eDOT.

PS18-588-26 Evaluating the accuracy of 99DOTS, a cellphone-based strategy for monitoring TB treatment adherence

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Background: Digital adherence technologies (DATs) have the potential to improve TB care by rapidly identifying patients with poor medication adherence. However, to serve this function, DATs must measure true adherence with reasonable accuracy. We report early findings of an evaluation of the accuracy of 99DOTS, a low-cost cellphone-based strategy for monitoring TB medication adherence that is being rolled out in India's government TB program.

Methods: We enrolled patients taking TB treatment in the government program in Chennai (HIV co-infected patients) and Mumbai (HIV un-infected patients). To minimize bias from short-term changes in patients' behavior, we waited at least three weeks after enrollment before conducting an unannounced home visit for each patient. During home visits, a urine sample was tested for isoniazid content using an IsoScreen test. We compared the patient's medication adherence as recorded by 99DOTS to the urine isoniazid test result to assess 99DOTS' accuracy for measuring doses taken in the last 48 hours.

Results: Out of 286 patients for whom unannounced home visits were conducted, 183 (64%) had called 99DOTS in the 48 hours before the home visit. Among these patients, 16 (9%) had a negative urine test result, yielding a positive predictive value of 91% (CI:86%—95%). Out of 103 patients who had not called 99DOTS, 77 (75%) had a positive urine result, yielding a negative predictive value of 25% (CI:18%—34%). 99DOTS had a sensitivity and specificity for measuring true medication adherence of 68% (CI:62%—74%) and 62% (CI:47%—75%), respectively.

Conclusions: For patients who call 99DOTS, a signal has a relatively high positive predictive value for true medication ingestion. However it is worrisome that three-fourths patients who do not call 99DOTS are actually taking their TB medications. Efforts must be made to strengthen patient engagement, if 99DOTS is to be an effective approach for monitoring TB medication adherence.

		Urine isoniazid test result		Total
		Positive for urine isoniazid	Negative for urine isoniazid	
Adherence as reported by 99DOTS	Adherent per 99DOTS	167	16	183
	Non-adherent per 99DOTS	77	26	103
	Total	244	42	286

[Operating characteristics of 99DOTS for measuring true TB medication adherence]

PS18-589-26 Advanced real-time electronic data system to improve turnaround time and data management in mobile screening: TaS4TB 2017 operational year

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Background: Zimbabwe adopted Active case finding as a strategy to end TB and health information system is needed strengthening so as to cope with lots of data generated during mobile TB screening. Data for every patient screened, was collected on four paged file, waiting to be captured at the end. 180 patients were screened per eight hours a day. Every patient would move through 6 stations, this meant the patient would start from registration, screening, HIV test, counseling, Chest X-ray and sputum collection desk and the corresponding sections were updated as they navigated through the process. Data entry and analysis for 4000 files would take 7 working days.

Methods: An electronic data system was developed for real time capturing as the patient moved from one desk to another using android devices. This System was designed using MySQL and connectivity was ensured using a wireless router for real time data sharing within the screening camp and previously captured informa-

tion would be ready for use at the next desk. The system does not use internet connection but uses wireless connectivity for file sharing. All the captured data is saved to local MySQL server.

Results: The number of patients Screened for TB increased from an average of 180 per day to 250. Previously, the total district files of patients screened for TB resulted in huge volumes of data in 2 big boxes weighing 15kgs but have been reduced to an excel file less than 1mega bytes. The whole data set of 37 570 patients screened for TB using the electronic system is 11.3 megabytes.

Conclusions: Electronic Data Management improves patient management and makes any data analysis easy and faster with a complete data-set. The roll out of real time electronic data management systems within the public health facilities will improve patient turn flow and time.

PS18-590-26 mHealth for home-based TB contact investigation in Kampala, Uganda: a household-randomized controlled trial

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Background: WHO recommends household tuberculosis (TB) contact investigation in low-income countries. However, the proportion of contacts completing TB evaluation is low.

Methods: We performed a randomized, controlled trial of home-based TB contact investigation in Kampala, Uganda, with sputum-testing results and follow-up instructions sent by SMS(Pan-African Clinical-Trials Registry #201509000877140). At seven public-sector, primary-care clinics, community-health workers(CHWs) approached consecutive index pulmonary TB patients who were bacteriologically confirmed or aged < 5 to screen their household contacts for TB at home. Consenting contacts/surrogates of consenting index patients/surrogates underwent concealed, variable, permuted-block, random, household-level allocation, stratified by index-patient characteristics and visiting CHW, to standard clinic-based or home-based evaluation. In the standard arm, CHWs referred “at-risk” contacts(symptomatic, aged < 5, and/or persons living with HIV) to clinics for TB evaluation. In the intervention arm, CHWs collected and delivered sputum from at-risk contacts aged ≥5 to clinic laboratories; sputum-testing results and/or follow-

up instructions were returned by automated SMS. The primary outcome was the household-adjusted probability of at-risk contacts completing TB evaluation.

Results: CHWs identified 213/448(48%) standard-arm and 186/471(39%) intervention-arm contacts as at-risk during screening. The cluster-adjusted probability of completing TB evaluation was similar among intervention-arm(24%) and standard-arm contacts(18%, $p=0.20$). Among intervention-arm contacts, SMS were sent to 92/186(49%) at-risk contacts, and sputum was obtained from 35/91(39%) at-risk contacts ≥ 5 years old. Symptomatic contacts aged ≥ 5 without HIV appeared more likely than other at-risk contacts to have SMS sent(58% vs. 46%, $p=0.12$) and sputum collected(45% vs. 4.9%, $p < 0.001$); the cluster-adjusted probability of completing TB evaluation for this subgroup appeared higher for intervention(43%) than for standard(24%, $p=0.076$) contacts.

Conclusions: Home-based TB evaluation facilitated by CHWs and automated SMS did not increase the probability of completing contact investigation in Uganda, likely because of implementation challenges. However, when well-implemented, home-based TB evaluation holds promise for improving household TB contact investigation in low-income settings.

PS18-591-26 Scaled deployment of ICT-enabled adherence monitoring for all public-sector TB patients in Mumbai

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Background and challenges to implementation: Intermittent regimen made it feasible to implement Directly Observed Therapy (DOT) for every dose. However, India's RNTCP program is now transitioning to daily dose (FDC drugs). As daily DOT is prohibitive for many patients, additional tools are needed to monitor adherence

Intervention or response: ICT-enabled adherence tool called 99DOTS implemented to enable some doses to be monitored remotely. 99DOTS wraps each medication blister pack in a custom paper envelope (see figure). When patients dispense drugs, they reveal an unpredictable phone number. They place a free call to this number (which is answered and acknowledged by a computer) to indicate that drugs are dispensed and taken. 99DOTS analyzes the calls and displays patient-wise adherence information on a mobile application (and Internet website), enabling providers to identify patients who need additional counseling

Results and lessons learnt: From 2017, daily regimen was launched in Mumbai. Since then all Drug Sensitive TB patients are enrolled on 99DOTS. As of April 2018, the deployment encompassed over 250 health centers and

over 22,000 patients. The vast majority of patients (88%) are able to make at least one call to 99DOTS. Of these patients, 78% are marked as adherent on at least 80% of days, based on a combination of calls and annotations by providers. Of these, the majority have at least 80% adherence based on calls alone. Remaining 20% patients need alternative ICT based Adherence tool. ICT Tool may impact home visits by Health worker staff.

Conclusions and key recommendations: We have shown that it is feasible to deploy ICT-enabled adherence monitoring (99DOTS) as a standard-of-care in a large-scale programmatic setting. While there is variable engagement with the system, many patients do call consistently and can benefit by proceeding independently. Future work can focus on further improving patient engagement and quantifying the benefits of engagement for patients and providers.

PS18-592-26 Effectiveness of a reusable tobacco prevention toolkit with online material to reduce availability in a lower middle-income country: a case study from Sri Lanka

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Background and challenges to implementation: Sri Lanka is a lower middle-income country with a 20.2 Million population. World No Tobacco Day (WNTD) celebrations are officially celebrated in Colombo, the capital, and the administrators of rural areas are requested to plan and conduct their own activities in the respective territories. Due to low resources, providing technical inputs for each and every local administrator on planning and conducting such programmes is an extreme challenge. Use of online resources in health-related activities and services is limited due to limited competencies of the government officials and field staff, especially the senior staff.

Intervention or response: Aim is to explore the acceptability and re-usability of a toolkit by field officers in the state institutions involved in implementing WNTD activities. The toolkit comprised of banners and posters to be displayed in public places; presentations, audio and video clips to be used in community advocacy programmes; leaflets to be distributed to tobacco retailers and two notices to be displayed at tobacco selling and non-selling retail shops. Letters were sent via regular post to all the field level administrative officers informing them about the toolkit and how to obtain it. Post assessment carried out via post.

Results and lessons learnt: Out of the 600 administrators contacted via post, 115(19.2%) responded positively and requested the material. 10,000 posters, 10,000

stickers, 30,000 leaflets and 200 banners were posted to them. Website statistics showed 150(25.0%) downloads of online material. Post assessment revealed that toolkit was used as a resource in community advocacy programmes to stop cigarette sales. Programmes were carried out in 160 locations. Cigarette sales were stopped in five cities as a result.

Conclusions and key recommendations: Toolkit has helped to save time and cost in planning. Results show that the toolkit was acceptable and reusable in prevention. Lower income countries can hugely benefit from developing similar toolkits to facilitate community engagement in tobacco control.



[World No Tobacco Day 2016 - Map]

PS18-593-26 Automated electronic sensing of TB health care facilities in Johannesburg, South Africa: Time and Motion Study

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Background: Developing knowledge to inform effective delivery of TB services in clinics require conducting time and motion studies. The objectives of this study were to investigate the feasibility of applying an automated electronic sensing technology that uses wearable devices to understand patient movement within TB clinics, measure patient waiting times for service and health care provider interaction during routine clinical visits.

Methods: The study was conducted at two clinics offering various TB services, in Johannesburg, South Africa. At each clinic, we enrolled patients coming for drug

pickup and medical checkup. Also, we enrolled nurses, pharmacists and administrative staff. The automated system was deployed as follows; to follow and document patient movement and waiting times, electronic locators were placed in rooms, corridors and booking stations. To measure patient and healthcare provider interaction both patients and staff were given wearable devices. Descriptive and analytical statistics were used to analyze the data.

Results: A total 90 TB patients were recruited, 86% females and 14% males. 72% had visited the clinic for drug pickup, 6% for medical visit, and 22% other visits. Waiting time was highest at the pharmacy with median of 54 minutes and IQR of 38 minutes. At the booking station, the median waiting time was 10 minutes with IQR of 34 minutes. Patient-patient interaction was observed with an average interaction of 10 minutes across multiple interactions. Amongst healthcare workers, most interaction was observed between pharmacists with median interaction time of 21 minutes and IQR of 33 minutes.

Conclusions: Our data demonstrate the utility of automated electronic sensing platforms to decipher operational inefficiencies within TB healthcare facilities, provide important data to build models for reducing patient waiting times, map out optimum patient flow within TB care facilities. Findings on patient-patient interactions can be used to understand nosocomial infections that may occur in TB care facilities.

PS18-594-26 Improved patient management through implementing an electronic surveillance system: a Kenyan TIBU experience

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Background and challenges to implementation: Decision making by organizations require data. To meet this need and since its inception, the National TB Program (NTP) utilized the traditional paper based system where reports were generated through manual aggregation of records from the hard copy facility registers. This transitioned to transcription of summary data into excel sheets to come up with case finding and cohort reports. While this option served the purpose, it posed a lot of challenges not limited to delays in case notification, difficulties in accessing case based data, matching TB cases notified with case holding and not all data collected at the facility and sub county level were relayed to the NTP. **Intervention or response:** An almost successful solution piloted by the NTP in 2010 saw the use of Personal Digital Assistant device to electronically relay TB data. Despite its potential of providing case based data, the system had no capability of transmitting data in real time and required rigorous training.

Towards the end of 2011, a robust solution, TIBU surveillance system was born through a multi-disciplinary team engagement lead by the NTP Kenya. This would address all these challenges.

Results and lessons learnt: Because of this great innovation, Kenya enjoys real time access to Tuberculosis data, case finding and case holding tabulation which imply that data, a very key resource to policy formulation, is available at a click of a button; Improved turnaround time in making payments and accountability (In supervision module and patient support) anchored in TIBU cash; Targeted provision of quality care; monitoring of adverse drug reactions; Generation of heat maps on disease density; and finally a tool which will continue to influence research.

Conclusions and key recommendations: The solution continues to grow with additional features which include linking patient diagnosed using genexpert and culture through to treatment completion and dashboard whose interaction extends to all the citizens.

PS18-595-26 Adhaar: an important link between government programs and TB patients in India to create an enabling environment

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Background: Government of India implemented 12 digit unique identification number viz., ADHAAR for every citizen, which simplifies the government delivery process, brings in transparency and efficiency and enables beneficiaries to get their entitlement directly. In 2015, Indian government urged for Adhaar details of all notified new TB case and this feature also incorporated in Nikshay, the electronic data portal for TB case surveillance, to further linked with PFMS for direct benefit transfer of cash to TB patients on their bank account. Earlier money was given in cash or cheque to ASHA workers and medical officers to disburse to beneficiary.

Methods: The paper used data of 2,748,327 usual residents living in 601,509 households during the Demographic Health Survey-4 (2015-16). Main goal of the paper is to understand how Adhaar played role among TB patients in India, in addition to its link to different health schemes or health insurances among TB patients in the country. Regression model was applied to understand significant effect of having Adhaar after controlling for other socio-economic factors on TB.

Results: In India, almost 70% of respondents have Adhaar and almost 29% household covered by a health scheme or health insurance and 90% households are having bank/post office account. Majority of TB patients are having adhaar and bank account. Almost all TB Patients with adhaar received treatment. However, health insurance coverage of TB patients is too low and

majority of them sought private health insurance facilities where benefits of Adhaar may not be applicable.

Conclusions: To provide create enabling environment and provide universal access to TB care to END TB by 2025, Adhaar is an important link between government programs and beneficiaries to systematise the whole mechanism from case notification to diagnostics, treatment adherence, and transfer of cash benefits to the patients without presence of any middleman.

PS19 Tuberculosis advocacy for political commitment and accountability and critical areas for tuberculosis care

PS19-596-26 Governance of tuberculosis programme in rural India: health providers and community perspective

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Background: The National Strategic Plan (2017-2025) for Tuberculosis (TB) has adopted a “bottom-up” approach for TB programme implementation in India. Understanding health actors (health providers and community) perspectives on different elements of this approach within the health system are essential for effective TB services delivery.

This study presents health actors perspective on governance mechanisms in the delivery of TB services in rural healthcare settings in India.

Methods: The present study was done in six high TB burden districts of Uttar Pradesh and Bihar in January 2018. Randomly sampled health providers and community members in 16 blocks covering 768 villages were interviewed using both quantitative and qualitative techniques. Author used Siddiqi et al. (2009) governance framework to assess the understanding of the accountability & governance principles in the delivery of TB services.

Results: A total of 258 community members and 93 health providers (68 Medical Officers in government primary health centers; 25 General Specialist doctors in private health facilities-at block level) were interviewed. Majority of the community (89%) and a third (53%) of the health providers were not clear of the expected roles within the health system-an element of strategic vision and direction. Transparency in decision making, efficiency, equity and fairness, and health system’s responsiveness were the major weak governance elements from the community perspective. Health providers suggested improving the elements of community participation (78%), evidence-based information generation (54%) and responsiveness (47%) for better TB services delivery. Regular awareness and information exchange

(86%) and community engagement in the planning process (51%) were the key suggestions to strengthen TB services at the grassroots level.

Conclusions: Governance mechanisms for TB services in rural India are weak. There is an urgent need for meaningful engagement of health providers and community for effective TB services delivery.

PS19-597-26 Zero TB Cities Initiative in Bangladesh: the power of advocacy in turning political commitment into action

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Background and challenges to implementation: The Zero TB Cities Initiative (ZTBCI) is committed to ending tuberculosis (TB) by utilizing an evidence-based comprehensive framework. The initiative facilitates a process to bring the TB epidemic into the elimination phase in mega cities. This paper focuses on the efforts that advocated the concept of ZTBCI declaration in Bangladesh signed and then immediately put into action.

Intervention or response: Bangladesh decided to join this innovative TB control platform in October 2017 when the health minister launched the ZTBCI with a strong political commitment, signing a declaration and calling for action to make Bangladeshi cities TB-free. Challenge TB (CTB) Bangladesh facilitated the process by laying the foundation of ZTBCI through advocacy on policy, provision of technical support, and implementing new evidence-based interventions.

Results and lessons learnt: Under National TB Program leadership, CTB conducted significant advocacy efforts to move stakeholders towards adopting this initiative. The ZTBCI Launch in Dhaka received huge print and electronic media coverage, reaching an estimated 106 million TV viewers through 18 major TV channels, including state-owned TV and radio channels, as well as 2.49 million newspaper readers through 21 newspapers. Social media and prominent websites (e.g. the Stop TB Partnership) also carried coverage of the event. Following the ZTBCI declaration, CTB, under the guidance of the NTP, communicated the concept of ZTBCI to other city corporations to generate a favorable environment. Further, health leaders of Bangladesh attended the Moscow Inter-Ministerial Meeting on Zero TB initiatives in November 2017 and shared their progress, which generated international recognition and support. By March

2018 the elected city Mayor and his Councilors along with the senior employees of the City Corporation sat together and started planning activities for implementation under ZTBCI.

Conclusions and key recommendations: The political commitment and progress so far indicates that CTB's advocacy initiatives played an important role aimed at producing action-oriented results for ZTBCI.

PS19-598-26 Community advocate to increase local funding allocation for TB control

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Background and challenges to implementation: While individual TB services are largely funded through health Insurance coverage, in the decentralized Indonesian setting, district action plans (DAP) for TB are essential to ensure sustainable funding programming at local levels. A DAP for TB is a local government policy document describing activities, tasks and roles of all local stakeholders in the elimination of TB, to achieve the objectives of the Indonesian National Strategic Plan 2016-2020 (NSP) and the (inter)national roadmap towards TB elimination. Whereas CSO's have rich experiences in the promotion of good governance, their capacity building is needed on TB specific matters to ensure effective participation in planning, utilization and public monitoring of these annual budgets.

Intervention or response: In 4 districts supported by KNCV-led, USAID-supported, Challenge TB project identified strong CSOs, willing to fulfill a central role in TB programming. With each organization an inception workshop was held, followed by training on TB awareness, needs of the NSP at district level, the role of community in TB prevention, diagnosis, treatment and care, the district planning cycle, and public monitoring of TB activities and budgets. A CSO forum was organized to involve local CSOs in district planning, discussing how to identify potential budgets, collaboration with the district parliament and other key persons, and how to discuss with government to increase funding for TB programming, monitoring and evaluation with the involvement of CSOs.

Results and lessons learnt: In the 3 out of 4 selected districts decentralized funding for TB programming was increase in 2016. 47 CSO's participated in District Action Planning and the development of local budgets. The DAP contains budget for CSO tasks, including public monitoring.

Conclusions and key recommendations: Empowerment of local CSO's regarding DAP for TB programming effectively contributes to increased local awareness, ownership and local budgets for TB elimination.

PS19-599-26 Involving TB survivors as TB champions and advocates: a report from India

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Background and challenges to implementation: TB responses have remained traditionally top-down with minimal engagement of those directly affected by TB. Their potential role as advocates with the capacity to improve public understanding and destigmatize TB has been largely ignored.

Intervention or response: A series of four capacity-building workshops for TB survivors were organised in New Delhi and in Bihar, Odisha and Jharkhand. Participants were identified through an open call for applications, followed by personal interviews. 55 TB Survivors from across India participated in these workshops which emphasized participatory learning and focused on knowledge and skills-building. 60% of workshop participants enrolled in an ongoing six-month advocacy mentorship programme, developing a work plan with clear goals, activities and intended outcomes. All workshops were organized in close coordination with the state TB offices.
Results and lessons learnt: The workshops resulted in the formation of two networks led by TB-affected people - Touched by TB as an outcome of the national workshop in New Delhi with over 100 survivors as members to date and TB Mukh Vahini from the Bihar workshop. Several TB Champions were invited as speakers at the Delhi End TB Summit and World TB Day observations and as members of different forums constituted by the National Programme. 60% of participants consented to feature in the TB Champions Video Series. 11 Videos disseminated to date through a pro-bono partnership with a digital news agency generated over 50,000 views on social media. Overall, the workshops resulted in the creation of a cadre of trained and committed TB survivors.

Conclusions and key recommendations: This year-long process of identifying and engaging with TB survivors has demonstrated the need for a sustained mechanism to involve affected communities. The increased involvement of survivors by the National TB Programme also indicates a shift in thinking and an acknowledgement of their role as TB Champions in supporting the response to TB.

PS19-600-26 Maximising the impact of cash transfers for TB control: when, how much, and for how long?

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Background: The WHO's post-2015 End TB strategy suggests that social protection programmes, such as cash transfers, can play a crucial role in TB prevention, care and control. However, it remains unknown how to maximise the impact of these programmes for TB patients, particularly in terms of timing of enrolment, duration enrolled, and value of cash received. We assessed the Bolsa Familia cash transfer programme in Brazil (BFP) and aimed to estimate whether there were associations between the proportion of patients cured and these programmatic elements.

Methods: Logistic regression analyses were conducted to assess these associations, adjusting for major clinical and socioeconomic confounders. The data included all new notified TB cases in Brazil in 2010 with clinical data linked to socioeconomic data from enrolment in the Social Registry (n=14760).

Results: After adjustment, compared to those who did not receive BFP, individuals who received it before treatment had 1.45 times the odds of cure (95% CIs: 1.24-1.69) and those who received the programme after treatment had 1.16 times the odds of cure (95% CIs: 0.94-1.45). Amongst those enrolled in the programme prior to treatment, there was no evidence for an association between time enrolled and proportion cured. Amongst BFP recipients (n=8095), our results suggest that for each additional R\$10 received per month, the odds of cure decrease (OR:0.985; 95% CIs: 0.973-0.997).

Conclusions: Taken together, this suggests that preemptively enrolling TB-vulnerable patients in a cash transfer programme improves cure outcomes, though enrolling patients after diagnosis may also be beneficial. Receipt of BFP acts rapidly to improve treatment outcomes. The unexpected direction of association of transfer value suggests that those receiving more money may be particularly vulnerable to TB in ways unaffected by cash. Cash transfers are a social and political solution to TB, but key operational aspects need to be better investigated to maximise their impact.

PS19-601-26 Awareness and knowledge of tuberculosis and predictive factors among urban slum dwellers in Lagos, Nigeria

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Background and challenges to implementation: There is little evidence on the level of awareness among urban slum dwellers on TB symptoms and mode of spread in Nigeria. This study was to assess level of awareness on TB, its transmission and where to find affordable care, as well as predictors of knowledge.

Intervention or response: The study took place in 2017 across 10 purposively selected Lagos communities classified as urban and having a high TB burden. A cross-sectional design using interviewer administered questionnaire was implemented. Questions were asked on knowledge of TB symptoms, its transmission and on awareness of the presence of TB treatment facilities. Data was entered in Excel imported into SPSS version 21 and analyzed for knowledge predictors using logistic regression.

Results and lessons learnt: 632 respondents participated in this study. The highest number of respondents was in the age group of 25-34 years (37.8%), an average of 3-4 persons per household (41%) and 1-2 persons living in one room (44.5%). About two-third (59.7%) of the respondents had heard of TB, while 41% have heard about DOTS. Only 31.5% knew what TB symptoms are and 48.4% knew that TB is curable. Only 27.2% were aware of a nearby existing TB facility, while 41.6% knew it is free of charge. The major sources of information about the availability of TB services is from a health worker (48.9%) followed by radio (20.4%). The predictors of correct knowledge of the symptoms of TB were male sex, older age > 45 years and having some education (compared to illiteracy). The predictors of correct knowledge on how TB is spread were smokers, high income and age > 45 years.

Conclusions and key recommendations:

The currently used TB communication strategies are not sufficiently reaching illiterate groups, females and the younger segment of the population (< 45). Alternative methods and communication channels should be explored targeting illiterate young slum dwellers.

PS19-602-26 Tuberculosis-related knowledge of family members of tuberculosis patients in Ethiopia

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Background and challenges to implementation: The family of a TB patient is the most important circle that defines the disease and shapes the decision to seek care prior to reaching health facilities. Therefore, understanding the position of family in relation to TB remains an important determinant. Therefore, this study aimed to assess the knowledge of family members of TB patients about TB, its causes, and its modes of transmission.

Intervention or response: This is a cross-sectional survey conducted from October 25 to Nov 18, 2017 in all 11 regions of Ethiopia. A multistage sampling technique was used to select study participants. We used a standardized pre-tested questionnaire to gather information on participants' TB knowledge, its causes and modes of transmission, and sources of TB information. Electronic data was collected by CSPro and analysed using SPSS Version 20.

Results and lessons learnt: Of 836 family members interviewed, 48.7% were women. The mean age was 34 (SD±13.8), 46.9% were heads of household, and 51.4% were married. The vast majority (97.5%) had heard of TB but only 32.9% felt well-informed and only 31.9% knew that germs cause TB. About 80% knew that coughing is a common symptom (80.6%) and that TB affects the lungs (79.9%). However, only a quarter of respondents had heard of drug-resistant TB. The most frequently cited source of information (54.2%) was family, friends, neighbors, and colleagues combined. Most family members (91.5%) wanted more information about TB. Community health workers and billboards were the most and least preferred sources of information, respectively. Higher levels of education attainment were associated with better knowledge.

Conclusions and key recommendations: We report high knowledge of TB among families of TB patients. There is limited knowledge about its cause and high demand for more information. Therefore, to improve health seeking decisions and provide support to the patients, more should be done to improve the knowledge of their families.

PS19-603-26 Additional nutritional support to TB and DR-TB patients provided under Chief Minister's Flagship Food Support Program improved treatment compliance and outcome of NTP in Chhattisgarh

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Background and challenges to implementation: Tuberculosis is one of the top-ten causes of illness, death, and disability worldwide and is the leading cause of death from a curable infectious disease in India. TB and Malnutrition are two sides of the same coin; TB makes malnutrition worse and malnutrition weakens immunity. Both cause major concerns in the underdeveloped regions of the world including India. There are significant financial barriers to access TB and MDRTB treatment in India.

With lasting undernutrition, lower BMI and Wasting (coupled with poor Human Development Index in general) among most of its diagnosed TB & DRTB patients, NTP in Chhattisgarh that tops the list of states in terms of poverty rate in India, faces huge challenge of poor treatment compliance and adverse outcome.

Intervention or response: Considering food assistance as a potentially influential means for increasing adherence to TB & DRTB treatment that reduces the costs to patients of staying in treatment, and for improving nutritional status; and also guided by the WHO's policy on nutritional care and support and End TB Strategy's emphasis on integrated patient centred care for management of co-morbidities, Chhattisgarh State introduced a *Flagship-Food-Support-Program* (FFSP) under 'Mukhyamantri-Kshyayposhan-Yojana' during 2017.

Enriched with energy, protein and micronutrient ingredients, monthly food baskets containing 3kg groundnuts, 1kg oil and 1kg milk-powder, specially packed by the accredited vendor (CGMSC, a certified government approved logistics body), was supplied to all treating TB & MDRTB patients under NTP through their respective Designated Microscopy Centres & individual Treatment Supporters. Regular counselling, weight & BMI monitoring and treatment adherence was followed up by NTP staff. Around 60% of them were additionally linked to Public Distribution System, a highly subsidized monthly food provisions scheme meant for extremely poor families available under the state Social Welfare Department.

Patients were counselled on an appropriate balanced diet with 3 meals and at least 2 snacks during treatment period. Inspired by the outcome, the Indian Prime Minister made special budgetary allocation of INR 500 per TB/MDRTB patient/month in the country from 2018.

Results and lessons learnt: 39,021 TB and 1,035 MDR-TB patients notified: a staggering 12% and 20% jump from the previous year respectively. With $\geq 97\%$ & $\geq 80\%$ treatment adherence, $\geq 95\%$ treatment complete

and zero loss to follow up, and around $\geq 85\%$ & $\geq 70\%$ gained weight substantially during treatment while $\geq 95\%$ & $\geq 80\%$ patients who completed treatment said to have had no side effects (common during first two months of drugs intake)

Poor weight gain/weight loss for around 15% of the cases was observed due to treatment failure, non-adherence to therapy, and other reasons. Around 30% cured patients and their family members advocated the benefits of the program within their communities.

A patient and provider feedback suggested that the program benefits offset the costs of treatment, motivated patients to seek treatment earlier, improved adherence to treatment and nutritional status, and reduced stress.

Conclusions and key recommendations: FFSP achieved the dual objectives of NTP and End TB Strategy. Nutrition is especially important in the Indian context when the NTP is increasing in scale to maximize TB & DRTB diagnosis and treatment.

Poverty, food insecurity and undernutrition being the key causes and consequences of poor adherence among most patients, it is essential that stronger political & administrative commitment is ensured for their optimal diagnosis and standard of care.

PS19-604-26 Assessing community knowledge and stigma perception about tuberculosis through stigma measurement scale in Pakistan

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Background: Stigma-associated with tuberculosis is known to affect health seeking and disclosure behaviors, which lead to poor health outcomes. The objective of the study was to measure perceived level of stigma associated with tuberculosis and to assess knowledge level of community members in Pakistan.

Methods: This is cross-sectional study of a convenience sample of 183 individuals who attended private health-care clinic for general ailments. A validated tool of Van Rie was adapted with slight modifications. The tool was pretested before actual data collection and included variables such as demography, perception of TB stigma and knowledge about it. The data was collected through ODK Collect and analyzed through SPSS version 20.0.

Results: 183 individuals (73% males; 27% females) participated in the survey with a mean age of 37 years (± 12). Majority were aware that TB is a curable disease (87%; n=159) and it spreads through coughing (91%; n=167). The respondents also thought that TB spreads through contaminated food (73%; n=134), sharing meal (55%; n=100), sharing utensils (53%; n=96) and by having sex with person infected with TB (51%; n=93). 57% (n=104) of the community members associated high stigma with TB. Individuals who had less than six years

of education (crude OR = 1.2; 95% CI: 0.89, 1.72) and lacked knowledge that TB is curable (crude OR = 3.42; 95% CI: 1.20, 9.70) were more likely to associate stigma with TB. In addition, females (crude OR = 1.33; 95% CI: 0.87, 2.04) and unemployed (crude OR = 1.06; 95% CI: 0.65, 1.74) individuals associated relatively more stigma with TB.

Conclusions: Study found association between lack of knowledge and presence of stigma. This highlights the need for reducing stigma through awareness activities with a particular focus on gender and disease specific knowledge.

PS19-605-26 Importance of community engagement in the STREAM Stage II trial in two study sites in India: a learning experience

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Background: Community engagement is a cornerstone of ethical medical research. Two sites in India namely National Institute for Research in TB, Chennai and BJMC Medical College, Ahmedabad have been chosen to undertake STREAM Trial Phase II study. The community engagement process for the STRAEM study has been initiated in both the sites as an important intervention to generate ownership of the research process in the country.

Methods: The community engagement process was initiated in August 2017. The key activity was to prepare line listing of key stakeholders who could possibly be engaged and invited for a workshop in September 2017. A mapping exercise was conducted prior to organising a workshop for the community engagement process in both the sites. Workshop on community engagement process was conducted with participation of civil society members, TB and HIV community, TB advocates and participants from the study sites.

Results: Community Advisory Board (CAB) formed in both the study sites with representation of community members in October 2017. The Community Advisory Board members agreed to work closely with the research study team. Further meeting of the Community Board members was held in December 2017 to discuss the coordination issues with the research team.

STREAM Stage I results were shared with the CAB members in March 2018 in both the study sites. Regular

teleconferences are being held with the CAB members. CAB members have prepared a work-plan and budget to implement community engagement activities from April-September 2018.

Conclusions: A mechanism has been formed to coordinate community input into the study. Concrete engagement with communities is needed from all TB scientists at each step of the R&D process, particularly in the pre-trial and post-trial phases. The formation of CAB in study sites has been very effective for the patient enrolment, visits to patient home for counselling and conducting support group meeting.

PS19-606-26 Monthly cough days to increase TB screening at the community level: experience from Sofala Province, Mozambique

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Background and challenges to implementation: Mozambique ranked 11th among the TB high burden countries has 1550 health facilities for 28.7 million inhabitants. Community sensitization for TB has been done at the health facility level, which limits access to information for most of the population. In response, the USAID Challenge TB (CTB) Project in coordination with the NTP, strategized on how best to ensure universal access to TB information for active case finding.

Intervention or response: Since October 1st, 2016, CTB has been implementing monthly cough days as one of its main approaches to increase TB case finding in the community. This activity brings together community DOTs supervisors, activists, local health facility staff, and local leadership. One day per month, a community sensitization session is delivered in preselected community locations. The team conducts TB screening and all presumptive TB cases are referred to health facilities for further investigation.

Results and lessons learnt: This intervention contributed to an increase in diagnosis of All Forms (AF) of TB. In 2016, 14% (8,989/64,204) of presumptive TB patients were referred to and received services from health facilities were diagnosed with TB; of which 13% (1,248/9,604) were diagnosed with TB AF. CB DOTS activities contributed to 27% (9,604/35,620) of total TB case notification in the supported provinces in Mozambique in 2016 and 36% (15,850 cases out of 44,223 cases) in 2017.

Conclusions and key recommendations: Monthly cough days improve access to TB care by bringing health services to the community, thus reducing the distance between the communities and health care.

PS19-607-26 Effect of decentralization of clinical and programmatic management of drug resistant tuberculosis services on enrolment of drug-resistant tuberculosis patients: Nigerian experience, 2013-2017

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Background and challenges to implementation: Nigeria commenced PMDT in 2010. The number of diagnosed RR/MDR-TB patients rapidly increased as Xpert/MTB/Rif assay increased. The initial programme policy of admitting all DR-TB patients to curtail ensure quality care creates the followings challenges: huge number of patients on the waiting list due to limited bed spaces; difficulties in accessing treatment due to long distant; separation of patients from their families and means of livelihood for several months. These challenges resulted in many patients refusing treatment; hence the need to decentralize PMDT services closer to patients piloted in Oyo State, Southwest-Nigeria.

Intervention or response: Electronic data base was evaluated and 18 confirmed RR/MDR-TB patients were enrolled in the community. To promote patient-centered approach and ensure quality care and infection control, measures taken included capacity building for LGA DR-TB teams for monthly patients reviews; engaging Adherence Counselors and Treatment supporters to ensure daily DOT; health education to patients/families on cough etiquette and home visits. Lessons learnt were used to scale-up the intervention across the country.

Results and lessons learnt: Out of 18 patients, 17 (94%) had negative sputum culture conversion at the end of intensive phase of treatment. The final treatment outcome revealed 8 patients (44%) were cured, 8 patients (44%) completed treatment, 1 patient (6%) died and 1 patient (6%) was loss to follow up. The treatment success rate was 88%.

Conclusions and key recommendations: Decentralization of PMDT services into the community improved enrolment of patients into care. There is need to maximize the gains of community-based PMDT approach.
 Fig.1: Community Enrolment vs. Treatment Centre Admission in Nigeria.

PS20 Anti-tuberculosis drugs, monitoring and optimising

PS20-608-26 Clinical efficacy of combined chemotherapy with clofazimine in the treatment of multidrug-resistant tuberculosis

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Background: To evaluate the clinical value of combined chemotherapy with clofazimine in the treatment of multidrug-resistant tuberculosis.

Methods: Sixty patients with MDR-TB were randomly divided into observation group and control group, 30 cases of each. Both groups were treated by traditional medicine with pyrazinamide, ethambutol, moxifloxacin, amikacin, amoxicillin and clavulanate potassium, isoniazid, observation group take clofazimine on this basis, and check stump for acid-fast bacilli monthly, cultures for tuberculosis and check lung CT every three months.

Results: The sputum negative conversion rates of observation group (51.1%) was better than control group (42%). Full course of negative conversion rate (63%, 45%). Lung CT examination showed that the lesion absorption rate (61%, 44%).

Conclusions: Clofazimine has a significant short term effect on MDR-TB, but the side effects of pigmentation which are generally unacceptable to young women.

PS20-609-26 Double dose rifampicin is well tolerated in first-line treatment for tuberculosis

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Background: Randomized clinical trial with double dose rifampicin in the standard first-line regimen (Cat1).

Methods: Smear-positive pulmonary TB patients were randomized to rifampicin 10 (controls) or 20 mg/kg/d (intervention) with biochemical screening for liver toxicity. Primary outcome definitions were smear-defined. Diagnostic sputum was sequenced a posteriori for rifampicin resistance (RR), and smear and culture were done 12 months after treatment end. Microscopy-defined late converters on smear, found RR on Xpert MTB/RIF were switched to MDR treatment. The intervention arm was moreover screened at two weeks for <1 log decline of acid-fast bacilli (AFB) on vital staining, followed by Xpert MTB/RIF.

Results: 468 control and 475 intervention patients remained after exclusion of two patients with non-TB mycobacteria from each arm. Excluding also one un-

der-dosed weight-band from both arms, 3.0% (8/267) of control patients developed a drug-related serious adverse event versus 3.5% (10/286) of intervention patients (non-significant). Hepatobiliary disorders comprised 0.7 (2/267) respectively 2.1% (6/286). Of eight primary RR, 2/3 intervention patients were switched to MDR regimen at two weeks, the third cured without regimen modification; of the five primary RR controls, three were switched at two months and two cured. Treatment success reached 82.8% (216/261) for control and 88.0% (249/283) for intervention patients, against failures 3.4 (N=9) versus 2.8% (N=8) and relapses 1.3% (N=3) versus 0.8% (N=2), smear-defined. Only three possible failures (two controls, one intervention), five proven relapses (2 controls, 3 interventions) and no acquired RR remained considering results of culture, vital staining and genotyping. **Conclusions:** Reservations made for too wide confidence intervals and smear-defined outcomes, double dose rifampicin Cat. 1 might be equally safe and more effective than standard. Screening for viable AFB decline after double dose for two weeks reduced Xpert MTB/RIF tests needed to 9% of the cohort, while detecting 2 out of 3 cases of primary RR.

PS20-610-26 High-dose rifampicin results in higher total and protein-unbound plasma concentrations but not in increased free fraction

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Background: A higher dose of rifampicin (35 mg/kg instead of 10 mg/kg daily) results in a more than proportional (nine-fold) increase in total (protein-unbound plus protein-bound) rifampicin exposure in plasma, which is associated with shorter time to culture conversion [Boeree et al., 2017]. However, since only protein-unbound drug is active, concentration-response evaluations are ideally based on protein-unbound concentrations. It is currently unknown if strongly elevated exposures to rifampicin cause a saturation in protein-binding, causing a misrepresentation of protein-unbound, active concentrations by the total concentrations.

Methods: Intensive pharmacokinetic sampling took place after 4 weeks of standard dose (10 mg/kg) and high-dose rifampicin (35 mg/kg), administered daily with other first-line TB drugs, in pulmonary TB patients in the PanACEA MAMS-TB-01 trial. Protein-unbound and total rifampicin plasma concentrations were measured for 10 patients on 10 mg/kg rifampicin and 10 patients using 35 mg/kg rifampicin, using validated ultrafiltration and HPLC techniques. Pharmacokinetic parameters were assessed using standard non-compart-

mental pharmacokinetic methods. Differences in total and protein-unbound drug exposures and free fraction were assessed with independent-samples t-tests on log-transformed pharmacokinetic parameters.

Results: The rifampicin geometric mean total and protein-unbound area under the plasma concentration-time curve from 0-24h (AUC_{0-24_total} and AUC_{0-24_free}) significantly differed between the 10 mg/kg and 35 mg/kg group: 22.0 (range: 11.7-37.2) h·mg/L versus 172.0 (128.8-269.2) h·mg/L ($P < 0.001$), and 2.8 (1.4-5.1) h·mg/L versus 18.9 (11.2-26.3) h·mg/L ($P < 0.001$), respectively. The resulting free fractions ($AUC_{0-24_free}/AUC_{0-24_total}$) were not significantly different and showed considerable inter-individual variability, with arithmetic mean free fractions of 13.3% (range: 8.1-24.9) and 11.1% (8.6-13.6) for the standard-dose and high-dose group ($p=0.214$), respectively.

Conclusions: A high dose rifampicin of 35 mg/kg results in strongly elevated total and protein-unbound exposures to rifampicin in plasma, without a change in free fraction. The inter-individual variability in free fraction suggests that protein-unbound drug concentrations are still preferable when performing concentration-response evaluations.

PS20-611-26 Therapeutic failure associated with low pyrazinamide exposure to MIC ratio using dried blood spot analysis

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Background: The objectives of our study were to evaluate whether low drug exposure of pyrazinamide is associated with delayed sputum conversion and to assess the feasibility of Dried Blood Spot (DBS) as method for Therapeutic Drug Monitoring.

Methods: Rates of sputum culture conversion were determined at weeks 2, 4, 8, 12, 16 after initiating therapy in patients with newly diagnosed drug susceptible sputum smear- and culture-positive tuberculosis (TB),

hospitalized in the Regional Clinical Center „Ftisiatria” Grodno, Republic of Belarus between January 1, 2014 and March 1, 2016. DBS samples obtained at steady state 1, 3, 6 hours after drug administration were measured by validated liquid chromatography-tandem mass spectrometry. The minimum inhibitory concentration (MIC) values of pyrazinamide were determined by the MGIT960 system. The area under the concentration-time curve (AUC) and AUC/MIC ratio was calculated and related to time of conversion.

Results: 35 of 55 examined patients (30 (86%) men and 5 (14%) women) with a median age of 56 years (interquartile range (IQR) 90-47) with complete data were included for pyrazinamide analysis. Only 1 of 55 patients was excluded because of too small size of blood spots. The median AUC_{0-24} , MIC and AUC/MIC were 401.8mg*h/L (IQR 330.1-905.3), 12.5mg/L (IQR 12-50) and 22.2 (IQR 14.4 -55.2) respectively. Twenty-six patients showed sputum culture conversion at the end of week 8. The median AUC/MIC of patients who converted was significantly higher than in those who not converted: 26.1 (IQR 16.2 -55.2) vs. 15.3 (IQR 9.6-32.1) [$P=0.027$].

Conclusions: The low pyrazinamide drug exposure together with relative high MIC values was associated with worse treatment outcome. Limited sampling by DBS was feasible and is ready to be implemented.

PS20-612-26 Assessment of rifampicin exposure using dried blood spot analysis: a pilot study

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Background: The objective of our study was to assess the effect of pharmacokinetic variability of rifampicin on sputum conversion rate, using Dried Blood Spot (DBS) as method of bioanalysis for Therapeutic Drug Monitoring (TDM).

Methods: Rates of sputum culture conversion were determined at weeks 2, 4, 8, 12, 16 after initiating therapy in patients with newly diagnosed drug susceptible

sputum smear- and culture-positive tuberculosis, hospitalized in the Regional Clinical Center „Ftisiatria” Grodno, Belarus between January 1, 2014 and March 1, 2016. DBS samples obtained at steady state 1, 3, 6 hours after drug administration were measured by validated liquid chromatography-tandem mass spectrometry. The MICs of rifampicin were determined by the MGIT960 system in the range of 0.125mg/L-2 mg/L. The AUC of rifampicin were calculated using MWPharm® version 3.82; Medi-ware, Netherlands, by the log-linear trapezoidal rule.

Results: Altogether, 18 patients - 16 males and 2 females - were included. The median age was 44,5 (interquartile range (IQR) 48-87) years and body mass index 22.8 (IQR 19.4-31.4) kg/m². All patient isolates had MIC < 0.125mg/L; median AUC_{0-24} 36.06mg*h/L (IQR 24.14-59.55) and AUC/MIC 576.88 (IQR 386.24-952.8). Six (33%) patients had sputum culture conversion at the end of the first month and 14 (78%) at the end of the second month of treatment. Two out of 4 still culture positive patients died during the treatment due to tuberculosis, one patient died because of co-morbidity and one had treatment failure. The median AUC/MIC ratio of patients with negative culture at the end of 8-th week (775.2 (IQR 381.92-952.8) was nearly 2 times higher compared to patients with still positive culture - 406.32 (IQR 410.08-611.68; $P=0.373$).

Conclusions: a trend was observed in the association between rifampicin drug exposure, culture conversion rate and treatment outcome. Limited sampling by DBS was conveniently used for TDM.

PS20-613-26 Delayed drug susceptibility results are associated with amplified drug resistance in M. tuberculosis isolates

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Background: Solid culture-based isolation and drug susceptibility (DST) of M. tuberculosis (Mtb) takes up to 6-8 weeks and even longer if contamination occurs. We wanted to examine how diagnostic delay may amplify drug resistance and affect TB treatment outcome.

Methods: We performed a prospective cohort study in eastern and western areas in China, including all registered TB patients within year 2016/2017. DST and minimum inhibitory concentrations (MIC) were performed on all 207 Mtb isolates cultured from sputum samples before treatment (at the time of diagnosis) and on 46 cultures that remained positive (during treatment) at the point DST results available for the initial isolates.

Results: The average time to obtain a solid culture-based DST result was 55 ± 9.8 days. Among the isolates cultured at the time of diagnosis, 18 were multidrug-resistant and 55 exhibited resistances to either rifampicin (RIF), isoniazid (INH) or pyrazinamide (PZA). DST/MIC was repeated on the 46 “follow-up” isolates (22.3%) that were still culture positive at the point DST results were ready for the initial isolates (55 days on average). By comparing the drug susceptibility profile between the 46 initial and “follow up” isolates, nine showed an increase in MIC to RIF (three with acquired RIF resistance), five had an increase in MIC to INH (four with acquired INH resistance) and 12 exhibited an increase in MIC to PZA (ten with acquired PZA resistance). In a multivariate analysis, the diagnostic delay was significantly associated with an increase in MIC and acquired drug resistance, especially for RIF and PZA. Previous TB treatment history and increasing age were other variables associated with unfavorable treatment outcomes.

Conclusions: This study shows that the delay in phenotypic DST data is associated with amplified drug resistance of Mtb isolates, highlighting the need of rapid DST for early guidance of an effective treatment strategy that reduces infectiousness time and improve treatment success.

PS20-614-26 Therapeutic drug monitoring for rifampin, isoniazid and pyrazinamide among newly diagnosed tuberculosis in Shenzhen, China

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Background: Therapeutic Drug Monitoring (TDM) has been proposed in an attempt to optimize treatment outcome and reduce the development of drug resistance in tuberculosis management. The aim of the study was to analyze plasma concentrations of RMP, INH and PZA at 2-h post-dose and 6-h post-dose samples in newly diagnosed Tuberculosis in Shenzhen, China, thus to discuss the potential role of TDM in tuberculosis management.

Methods: A retrospective analysis was performed of 148 new PTB patients, in whom early TDM at a 2-h post-dose sample and a 6-h post-dose sample were completed after more than 1 week standard four-drug treatment from 30/10/2016 to 30/10/2017. Drug were administered under DOT with dosage according to guideline. High performance liquid chromatography (HPLC) was used for TDM.

Results: 36 of 148 (24.3%) patients were found lower blood concentration for RFP compare to standard C_{max} which is 8-24ug/ml at a 2-hour post-dose samples. 13 of 36 (36.1%) reached standard C_{max} (8-24ug/ml) at a 6-hour post-dose samples, while 23 of 148 (15.5%) had lower concentration at both 2-hour and 6-hour post-

dose samples. 112 of 148 (75.7%) patients had standard C_{max} for RMP, while 13 of 148 (8.8%) were above standard C_{max} concentration. Plasma peak concentration of Isoniazid and pyrazinamide appeared at a 2-hour post-dose in all patients. 70 of 148 (47.3%) TDM of INH was lower than standard C_{max} concentration (3-6ug/ml). When 35-60ug/ml was taken as standard PZA C_{max} concentration, 17 of 148 (11.5%) was lower than 35ug/ml.

Conclusions: There is delayed absorption of RFP. For necessary accuracy, 2-h and 6-h post-dose samples should be collected for TDM to estimate for C_{max} of RFP. A 2-h post-dose TDM is mostly enough for estimation of C_{max} of INH and PZA. Low C_{max} is more commonly seen in INH than RFP and PZA.

PS20-615-26 Adverse reactions in the treatment of MDR-TB

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Background: The number of TB cases with MDR-TB is increasing both among newly identified patients and with chronic forms of tuberculosis. When using new modern drugs, such as bedaquiline, too, there are adverse reactions.

Methods: The study included two (N=84) groups of TB patients with MDR M. tuberculosis. The first group (n=47) received bedaquiline (Bq) in the therapy regimen, the second group (n=37) received standard chemotherapy regimen. The groups are comparable in clinical and radiological characteristics.

Results: The development of adverse events in the first group was found in 28 (59.6%) patients, which is significantly less ($p < 0.05$) than in the second group - 30 (81%). In the majority of cases (96.4% group and 90% in the second) there were adverse reactions of the mild and moderate severity. No serious adverse events were observed in the observation groups. Both groups were dominated by adverse reactions from the category of “gastrointestinal disorders” (50% (14) and 63.3% (19), which were eliminated without the abolition of anti-TB drugs. The frequency of cardiotoxic adverse reactions in both groups did not differ significantly ($p > 0.05$, $Y_2 = 0.21$) and amounted to 28.5% in the first group and 23.3% in the second. At the same time, in the group that took bedaquiline, most of reactions had a subclinical nature (cardiac pain, transient Qt prolongation). Only in two cases, the relationship of cardiac arrhythmias with the reception of bedaquiline was regarded as “probable” and in one case - as “certain”. All other undesirable phenomena are classified as “possible”.

Conclusions: The use of bedaquiline does not significantly increase the risk of cardiotoxic adverse events. Isolated cases of development of subclinical forms of

cardiac arrhythmias, do not lead to the appearance of subjective sensations in patients and do not affect the quality of chemotherapy.

PS20-616-26 Treatment of patients with extensively drug-resistant tuberculosis by administration of new anti-tuberculosis drugs

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Background: Introduction of new anti-tuberculosis drugs nowadays is an important and actual goal.

Main objective: To compare treatment efficacy of combined drug therapy including tioureidoiminometilpiridin perchlorate (Tpp) and bedaquiline in patients with XDR lung TB.

Methods: In phthisiopulmonology department 132 patients with XDR lung TB from 18 to 70 years old started treatment. Patients were divided into three groups: I group (n=47) - with inclusion of Tpp to standard combined therapy of 6-7 anti-tuberculosis drugs; II (n=40) - with inclusion of bedaquiline to combined therapy; and III (n=45) - standard combined therapy based on drug sensitivity. Patients were examined in 2, 4, 6, 8 months from treatment start. Statistical analysis was done by program Statistica 7.0. Chi-square criterion (χ^2) was applied. Differences were considered significant at $p < 0.05$.

Results: After 2 months of therapy cessation of bacterial excretion was observed significantly more frequently in II group (30.0% (12) (I), vs. 17,8% (8) (III) vs. 65,0% (26) (II), $p < 0,05$). In 4 months cessation of bacterial excretion was registered in 23 (48.9%) patients in I group and 28 (70.0%) - in II, in comparison with III group 13 (28.9%). In 6 months - 29 patients (61.7%) in I group, 31 (77.5%) in II group, III - 19 (42.2%). In 8-month culture negative results were observed in 65.9% (31) in I group, 82.5% (33) in II group, and 55.5% (25) - in III group.

Conclusions: Inclusion of bedaquiline in combined drug therapy in patients with XDR lung tuberculosis allows to reach early cessation of bacterial excretion. Administration of Tpp is also justified in patients with XDR lung tuberculosis.

PS21 Optimising regimens for multidrug-resistant tuberculosis treatment

PS21-617-26 Risk factors for poor treatment outcomes in patients with multidrug-resistant TB in Cambodia: a 10-year experience

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Background: Cambodia started pilot for Multidrug-resistant tuberculosis (MDR-TB) program in 2006 and then expended nationwide in 2011. GeneXpert testing was used for MDR-TB diagnosis since late of 2011.

Methods: To determine the factors associated with treatment outcomes in patients with MDR-TB in 10 years cohort. We retrospectively analyzed the clinical records of MDR-TB patients with culture-proven MDR-TB or MTBc/Rif detected by GeneXpert who were registered for TB second line treatment from 2006 to 2015 at 11 MDR-TB treatment sites of Cambodia. Poor outcomes was defined as a combination of death, treatment failed and lost to follow-up.

Results: A total of 682 patients were enrolled for second line treatment regimen: 567 patients were confirmed MDR-TB and 115 were confirmed DR-TB (mono or PDR-TB). For MDR-TB group (n=567): 210(37%) were female; 6(1%) were children less than 15years old; 121(21%) were HIV co-infection. Median age was 44 years old (IQR: 33-54), 94 (32%) median BMI was 17kg/m² (IQR: 15.0-18.8). 472 patients were previously treated TB; 12(2%) were closed contact to MDR-TB index. The success rate of DR-TB group (n=115) was 96(83%); died 10(9%); 4(4%) lost to follow up and 3(3%). The treatment outcome for MDR/RR-TB group are: 435(77%) cured/completed; 88(16%) died; 5(1%) failed; 33(6%) lost follow-up; 6(1%) transferred out. Poor outcomes (n=126) were significantly associated with previously treated TB patients (OR:2.7, 95% CI 1.4-3.5; $p=0.00$); HIV co-infection (OR:1.8, 95% CI:1.2-2.9, $p=0.00$), a BMI less than 18.5 kg/m² (OR:4.5, 95% CI: 2.3-8.9, $p=0.00$); resistance to RHES or XDR-TB/pre XDR-TB by confirmed DST (OR:2.5, 95% CI: 1.2-5.2, $p=0.00$).

Conclusions: The overall successful treatment outcome was achieved at least as high as in published studies. However, the presence of HIV coinfection, low BMI, patients who confirmed resistance to the 4 first line drugs or XDR/preXDR-TB are independent prognostic factors for poor outcomes.

PS21-618-26 Roll-out of the shorter treatment regimen for drug-resistant tuberculosis in Zambia: finding opportunities to strengthen programmatic gaps

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Background and challenges to implementation: Until 2017, programmatic management of drug-resistant TB (PMDT) in Zambia was centralised in two tertiary hospitals. PMDT has now been scaled-up countrywide, along with introduction of ambulatory care and adoption of the WHO-recommended shorter treatment regimen (STR).

Intervention or response: Introduction of STR began with detailed implementation planning and clinical guideline updates supported by international technical experts. A national DR-TB clinical expert committee spearheaded the training and clinical mentorship of 550 personnel countrywide - including clinicians, nurses, laboratory scientists, pharmacists and social workers - on appropriate selection of patients for STR based on clinical and line-probe-assay (LPA) results.

The roll-out was structured in a phased approach: phase 1 targeted four provincial sites with access to LPA and PMDT experience; phase 2 includes the remaining six provincial sites.

Results and lessons learnt: From October 2017 to April 2018, 106 DR-TB patients were notified; 67 patients were initiated on STR, 34 on conventional regimens, and 5 on individualised regimens. STR interim outcomes after 4 months include 52 active in care with 4 deaths and no loss to follow-up. Three deaths were attributable to disseminated disease and the fourth to malignancy. The deaths occurred at sites that did not adhere to STR eligibility criteria.

Low accessibility to LPA, limited social support, and difficult access to health facilities have been significant challenges; ambulatory care patients travel up to 20km to receive kanamycin injections. No trained community health workers are dedicated to the PMDT programme.

Conclusions and key recommendations: Introduction of the STR in Zambia has been feasible using a structured implementation plan, and has highlighted new and existing PMDT challenges that pose a threat to successful outcomes: the need for simultaneous expansion of LPA access; a lack of community support programmes; further decentralization of DR-TB care; and ongoing mentorship of clinicians on careful and appropriate selection of patients for STR.

Keyword: shorter regimen, scale up

PS21-619-26 Trends in treatment outcomes among MDR-TB patients in Tigray Region, Ethiopia

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Background and challenges to implementation: A baseline assessment of the drug-resistant TB (DR-TB) program in the Tigray region of Ethiopia identified gaps including a shortage of trained personnel, limited programmatic coordination, and suboptimal treatment outcomes. The Tigray Regional Health Bureau (TRHB) with support from the USAID-funded Challenge TB project took a series of improvement actions since June 2016. Here we assessed the progress in DR-TB treatment outcomes in the Tigray region of Ethiopia.

Intervention or response: To address the capacity gaps, we instituted regular monthly supportive supervision; strengthened multidisciplinary team meetings at each treatment site; and organized quarterly catchment area meetings. At the patient level, we introduced an individual-level excel-based patient outcome monitoring tool; organized quarterly cohort analysis; and ensured strict monthly clinic follow up days. We also organized semi-annual data verification workshops at the national level.

Results and lessons learnt: The 6-month interim culture conversion rate improved from 47% (9/19) at baseline between Apr-Jun'16 to 92% (11/12) between Jul-Sep'17 (Fig. below). Similarly the cure rate among cohorts of pulmonary MDR-TB patients significantly improved from 24% (4/17) at baseline between Apr-Jun'16 to 77% (10/13) between Jul-Sep'17 [OR=10.833, 95% CI (1.961-59.834), p=0.006]. Overall, the 24-month final treatment success rate (TSR) (i.e. cured or treatment completed) among all MDR/RR-TB patients was 81% (17/21) in the period Jul-Sep'17, improved from 74% (14/19) in Apr-Jun'16 (Fig. below).



[Figure: Trend of 6-months interim and 24-month treatment outcomes indicators of MDR TB pts. Enrolled]

Conclusions and key recommendations: This analysis indicated both the interim and final treatment outcomes among MDR-TB patients persistently improved over a period of time, mainly contributed through the patient level monitoring, and continuous and coordinated technical support to the TICs. Strengthening the patient level monitoring and enhancing the technical supports are mandatory to further improve favorable outcomes among MDR-TB patients.

PS21-620-26 Death and loss to follow-up among patients receiving out-patient care for drug-resistant tuberculosis in Johannesburg, South Africa

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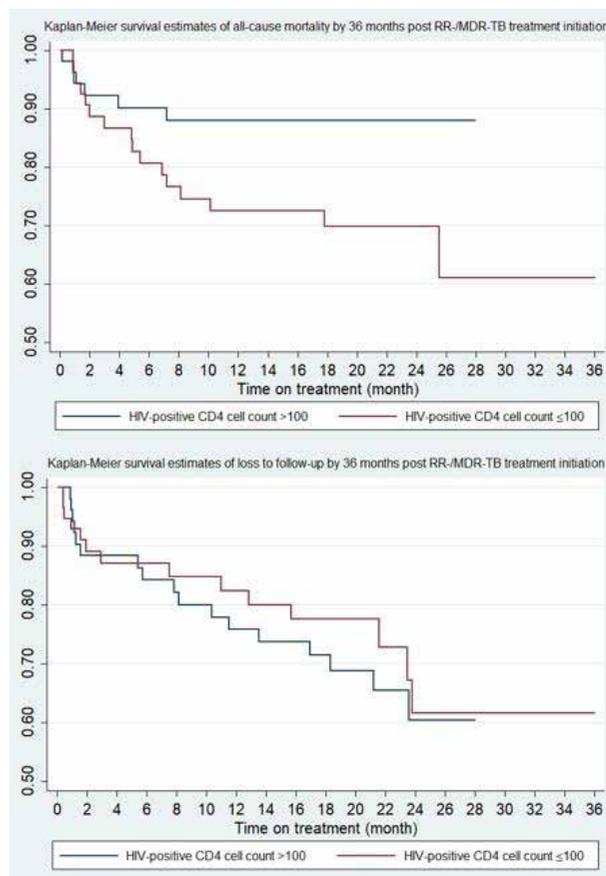
Background: South Africa adopted an outpatient treatment model for multi-drug (MDR) and rifampicin resistant (RR) tuberculosis (TB) in 2011. Treatment uptake and outcomes amongst individuals initiating care in the community remain poorly characterized. We evaluated outcomes, time to initiation, and risk factors for death and lost to follow-up (LTF) at an outpatient clinic in a cohort of patients with a high rate of HIV co-infection.

Methods: Adult patients newly initiating DR-TB treatment were enrolled in a prospective observational cohort from 3/2013-9/2014 and followed until transfer out, death, LTF or successful outcome (cured/completed). Cox proportional hazards were used to estimate hazard ratio and 95% confidence intervals.

Results: 127 patients were included in the analysis (51% female; median age 38 years (IQR 31- 43); 87% HIV co-infected). Among 107 patients with HIV the median CD4 count was 101 cells/mm³ (IQR 27-245). Of these patients 51% were on antiretroviral therapy prior to MDR/RR-TB diagnosis. 79/127 were diagnosed with MDR/RR-TB as outpatients and initiated treatment in a median of 12 days (IQR 7 - 40) after diagnosis. At the end of follow-up, treatment success (cured or completed) occurred in only 52% (66/127), 19% of patients had died and 28% were LTF. For those with HIV, 92% of deaths occurred during the first 10 treatment months, with higher rates seen in those with CD4 < 100 cells/mm³. In contrast, LTF occurred throughout the 24-month treatment period (Figure).

Increased risk of death and LTF were predicted by age <30 (aHR 2.68, 1.34-5.38) and unemployment (aHR 2.34, 1.16-4.70).

Conclusions: Outpatient treatment for MDR/RR-TB allows for rapid initiation on treatment. Overall outcomes are poor, but are similar to historical treatment success rates reported in hospital-based models of MDR/RR-TB care. Patients with HIV and low CD4 counts experience early high rates of death and LTF throughout the prolonged care course.



[Survival estimates of loss to follow-up by 36 months post RR/MDR-TB treatment initiation]

PS21-621-26 Mortality and associated risk factors of patients with extensively drug-resistant tuberculosis: an emerging public health crisis in China

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Background: Limited treatment options of extensive-drug-resistant-tuberculosis(XDR-TB) have led to its high mortality worldwide. However, relevant data about mortality of XDR-TB in literature are limited and likely

underestimate the real situation in China, we assume that the main reason is the majority of XDR-TB patients are lost to follow-up after discharge from hospitals. Our study was to investigate the mortality and associated factors of Human Immunodeficiency Virus(HIV)-negative XDR-TB in China.

Methods: All patients who were diagnosed with XDR-TB for the first time in four TB hospitals across China between March 2013 and February 2015 were consecutively enrolled. Active tracking through contacting patients or family members by phone or home visit was conducted to obtain patients' survival information by February 2017. Multivariable Cox regression models were used to evaluate factors associated with patients' survival.

Results: Among 67 patients enrolled, the mean age was 48.7 ± 16.7 years, 51 (76%) were men. Fourteen (21%) patients were treated naïve at diagnosis indicating primary transmission. The mean body-mass-index(BMI) was 18.9 ± 3.7 kg/m². During a median tracking period of 32 months, 20 deaths occurred, with an overall mortality of 128/1,000 person-years. Among patients who died during tracked, the median survival was only 5.4 months (interquartile-range [IQR]:2.2-17.8). Seventeen(85%) of them died at home, and the median duration from discharge to death was 8.4 months (IQR:2.0-18.2). In Cox proportional hazards regression models, BMI < 18.5 kg/m² (hazard-ratio [HR] = 4.5, 95% confidence-interval [CI]:1.3-15.7), smoking (HR=4.7, 95% CI:1.7-13.2), or a combination of underlying diseases (HR=3.5, 95% CI:1.3-9.4), such as serious heart, lung, liver, renal organ disorders and immune disease, etc., in addition to tuberculosis, were factors independently associated with a higher risk of death.

Conclusions: Our study suggested an alarming situation of XDR-TB in China with a sizable proportion of newly transmitted cases, high mortality rate, and long period in community. This observation calls for urgent actions in China to enhance XDR-TB case management, including better regimen, palliative care, community engagement, and infection control.

PS21-623-26 Evaluation of isoniazid-resistant tuberculosis cases in Istanbul, Turkey

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Background: Isoniazid (H) is one of the most important first-line medicines for the treatment of active tuberculosis (TB) and latent TB infection (LTBI), with high bactericidal activity and a good safety profile. About 8% of TB patients worldwide are estimated to have rifampicin-susceptible, isoniazid-resistant TB.

Methods: The treatment results of INH-resistant cases without Rifampicin resistance were compared with the control group which was sensitive to all drugs during the same years. Patient information The National TB control program was evaluated retrospectively from the registry system. In the treatment of the patients, the initial treatment first two months of 6-9 months were treated with standard therapy HRZE, continuation with HRE.

Results: 884 cases with INH resistance and 884 cases with no drug resistance were compared between 2011 and 2015. 607 (%68.7) men with INH-resistant cases and 605 (%68.4) men with susceptible cases. 138 (%15.6) of the INH-resistant cases and 235 (%26.6) of the susceptible were previously treated. Treatment success rates of INH-resistant cases were 688 (77.8%), 730 (82.5%) of sensitive patients ($p = 0.0008$). Treatment failure of INH-resistant cases was 21 (2.37%), and 6 (0.68%) of sensitized patients ($p < 0.0001$). 34 deaths (3.84%) in INH resistant cases and 26 (2.94%) in more sensitive patients ($p = 0.1132$). Poor outcome (death + treatment failure) in INH-resistant cases was 55 (6.22%) patients, poor outcome in sensitive patients 32 (3.61%) ($p < 0.0001$). In following years, 18 INH resistant cases had HR resistance.

Conclusions: The emergence of TB strains resistant to isoniazid threaten to reduce the effectiveness of TB treatment. Early detection and appropriate treatment is necessary for control TB program.

PS21-625-26 Factors affecting outcomes of drug-resistant tuberculosis in the Philippines

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Background: Programmatic Management of Drug-resistant Tuberculosis (PMDT) has been scaled-up across the Philippines since 2014. The objectives of the study were to describe PMDT outcomes and assess factors influencing treatment outcome among drug-resistant tuberculosis (DR-TB) patients in the Philippines.

Methods: We conducted a retrospective cohort study of patients confirmed to have pre-XDR or XDR TB and a random sample diagnosed with MDR TB between 2013 and 2016. For this analysis, we excluded patients still on treatment. We extracted demographic and clinical data from the central PMDT database (extraction of patient-level data from PMDT treatment cards is ongoing). We used descriptive statistics to summarize treatment outcomes for MDR TB and pre-XDR/XDR TB patients,

and performed multivariate regression to identify factors associated with unfavorable outcome (treatment failure, death, or lost to follow-up [LTFU]).

Results: Of 678 DR-TB patients included, 323 (47.6%) had MDR, and 355 (52%) had pre-XDR (N=343) or XDR TB (N=12). Unfavorable outcomes were more common among pre-XDR/XDR TB patients than MDR TB patients (58.6% vs. 45.5%, $p=0.001$). Unfavorable outcomes were due to death, treatment failure and LTFU in 7.7%, 1.0% and 27.8% of MDR TB patients, respectively, and in 15.6%, 5.2% and 30.14% of pre-XDR/XDR TB patients, respectively. There was no difference in the proportion with an unfavorable outcome at PMDT sites within and outside of Metro Manila (53.85% vs. 51.09, $p=0.47$). In multivariate analysis, older age (OR 1.01, 95% CI 1.00-1.02) and pre-XDR/XDR TB (OR 1.83, 95% CI 1.34-2.53) were associated with unfavorable treatment outcomes, but not gender or prior TB treatment status (Table 1).

	Male	Female	MDR	Pre-XDR/XDR	New Case	Relapse	Treatment Failure	Lost to follow-up
Unadjusted OR (95% CI)	1.0	0.73 (0.53 - 1.02)	1.0	1.69 (1.25 - 2.30)	1.0	Too few cases	1.06 (0.56 - 2.01)	1.72 (0.89 - 3.35)
p-value	--	0.07	--	0.001	--	--	0.86	0.11
Adjust OR (95% CI)	1.0	0.76 (0.54 - 1.06)	1.0	1.83 (1.34 - 2.53)	1.0	Too few cases	1.16 (0.60 - 2.25)	1.86 (0.94 - 3.69)
p-value	--	0.11	--	<0.001	--	--	0.66	0.07

[Table 1. Odds Ratio (OR) of Unfavorable Outcome]

Conclusions: PMDT has been scaled up successfully throughout the Philippines, with similar outcomes across PMDT sites. However, LTFU is a significant problem and further research is needed to assess outcomes among LTFU patients and identify strategies to maximize treatment completion.

PS21-626-26 Failing multidrug-resistant tuberculosis treatment with the short-course regimen: what next?

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Background: Shortened 9-12 months treatment regimens (SCR) for multidrug-resistant tuberculosis (MDR-TB) have shown promising results in observational cohorts. SCR has been implemented as pilot study in Swaziland since 2014 with promising success rate. Little has

been described about patients who are not successfully treated with SCR and optimal management strategies for them.

Methods: This is a retrospective analysis of the cohort of patients with microbiological failure of the study piloting SCR in two Swaziland sites (Matsapha and Manakayane), their management and early culture conversion results. SCR microbiological failure was defined as failure to convert by month 6 of treatment or culture reversion during continuation phase.

Results: 12 patients with MDR-TB who started SCR experienced microbiological failure (4 failure to convert, 8 culture reversions). Baseline resistance to Ofloxacin was identified in 3 patients and poor treatment adherence was noted in 4 patients. Follow up DST was available for 10/12 patients, 6 (60%) cases did not show amplified resistance, 4 (40%) did (3 to pre-extensively resistant and 1 to extensively resistant tuberculosis). The new treatment regimens included a combination of Linezolid with Bedaquiline and/or Delamanid as new regimen backbone. One patient was early lost-to-follow-up. Of the 11 remaining patients, 73% and 90% showed culture conversion at 2 and 6 months respectively after treatment initiation. One patient died after one year of treatment and serious adherence issues.

Conclusions: A SCR with conventional second line drugs and regimens with new and re-purposed anti-TB drugs are complementary new therapeutic strategies to fight MDR-TB. Countries need ensure there is access to both SCR and to both novel drugs bedaquiline and delamanid to achieve optimal treatment outcomes for all persons with MDR-TB.

PS21-627-26 Initiation of patient enrollment in treatment with new drugs: developing a patient selection and monitoring model

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Background and challenges to implementation: As of March 2018, Bedaquiline (BDQ) is not registered in Ukraine and, therefore, has not been included in the national guidelines. Clinical management policies on the new and repurposed TB drugs are not developed, and providers have no experience.

Intervention or response: BDQ introduction launched in Ukraine in July 2017, by the National Institute for TB and Lung Diseases (TB Institute), under the USAID-funded Challenge TB Project implemented by PATH. A patient selection and monitoring system was devel-

oped, and International Advisory Council (IAC) was established, comprising TB Institute, KNCV, PATH, and Ukraine's NTP to ensure efficient patient selection and determine optimal treatment regimens using BDQ and repurposed drugs. Each patient potentially eligible for a new drug regimen is first vetted by an oblast Advisory Council; if found eligible, the patient's case is reviewed by IAC to recommend the final treatment plan.

Results and lessons learnt: As of March 2018, 148 patients were reviewed and 100 were enrolled in the program. The average review time lasted three days and enrollment decisions were based on IAC member consensus.

Main reasons for rejection were high level resistance, limited or no access to clofazimine and meropenem, and high risk of interrupting treatment. Treatment regimen determination was the most difficult for those who had been previously treated with second-line drugs, especially who received repurposed drugs with new mechanisms of action (e.g., linezolid) with no effect.

Conclusions and key recommendations: The creation of the IAC to guide patient selection proved to be highly efficient and effective for ensuring the quality of case management and in the learning process of providers on the new and repurposed drugs proper use. The results suggest that previous treatment history should be considered along with the resistance profile for estimating the proportion of patients requiring new or repurposed drugs for appropriate program management.

PS21-628-26 Effect of decentralization on MDR-TB treatment in Ayeyarwaddy Region, Myanmar

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Background: Ayeyarwaddy Region is the third highest MDR-TB burden region in Myanmar. In 2014, 2-year MDR-TB treatment under DOT was introduced but confined to 7 townships where physicians were available. In 2017, patients from other 19 townships were allowed to continue the treatment at their home townships despite of lacking the physicians. The objective of this study is to assess the coverage of treatment initiation and time to treatment (TTT) among diagnosed MDR-TB patients over these 4 years period.

Methods: The study was a retrospective cohort analysis. Data were retrieved from TB Control Office of Ayeyarwaddy Region.

Results: Among 754 diagnosed MDR TB patients during this period, 99.7% were adult cases Male and female ratio was 1.8:1. From Table 1, the number of diagnosed MDR TB patients was steadily increased. Likewise, the number of patients put on treatment was also progressively increased. The proportion of patients on treatment among diagnosed ones was increased from 43% in 2014 to 89% in 2017. On the other hand, the median time to treatment (TTT) of these patients was declining from about five months in 2014 to less than a month in 2017.

Conclusions: The program has made good progress in case detection, treatment and delay time reduction but there is still 14% of detected cases are left untreated and treatment outcomes need to be assessed.

Year	Townships with DOT treatment provided Project vs non-project townships (n)	Number of patients diagnosed with MDR-TB/treatment initiated (%)	Median and IQR of TTT (days)
2014	3 vs 0	66/152 (43)	150 (63-239)
2015	7 vs 0	108/171(63)	41 (21-85)
2016	7 vs 0	134/185(72)	26 (15-44)
2017	7 vs 19	115/137(84) vs 97/109 (89)	17 (10-25) vs 20 (11-30)

[Table 1. Coverage of treatment initiation and time to treatment in project vs non-project townships in Ayeyarwaddy Region, Myanmar (2014-2017)]

PS22 Treating TB-HIV patients under programmatic conditions

PS22-629-26 Missed opportunity for HIV testing among TB clinic attendees in Malawi: results from the Malawi population-based HIV impact assessment, 2015

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Background: HIV testing at tuberculosis (TB) clinics is an important entry point into the HIV treatment cascade. We analyzed data from the 2015-16 Malawi Population-based HIV Impact Assessment (MPHIA), a nationally representative household survey, to estimate HIV testing and treatment outcomes associated with prior TB diagnosis.

Methods: Adults aged 15-64 years were interviewed and tested for HIV status, antiretroviral (ARV) use and viral load. Self-reported TB data were analyzed using weight-

ed percentages and 95% confidence intervals (CI), accounting for complex survey design.

Results: Of 19,652 MPHIA participants, 4.7% (95% CI: 4.3-5.1) reported visiting a TB clinic. Prior TB diagnosis was reported by 1.6% (95% CI: 1.4-1.8) of adults (8.5% (95% CI: 7.1-9.9) of HIV-positive and 0.8% (95% CI: 0.6-1.0) of HIV-negative adults).

Of 1,119 adults reporting visiting a TB clinic, 48.0% (95% CI: 44.3-51.7) were HIV tested at the TB clinic and 42.9% (95% CI: 39.1-46.7) were not; 9.0% (95% CI: 7.1-11.0) were aware of their HIV-positive status at the time of the TB clinic visit. Percent of TB clinic attendees not tested for HIV was greater among non-TB cases (57.3%; 95% CI: 52.4-62.3) compared to TB cases (28.8%; 95% CI: 22.9-34.6).

Viral suppression (< 1000 HIV RNA copies/mL) among HIV-positive adults, awareness of HIV-positive status and ARV use among those aware of their HIV-positive status, were significantly greater in TB cases and non-TB cases (who visited a TB clinic) compared to those who never visited a TB clinic (Table).

Conclusions: Low HIV testing at TB clinics represent a missed opportunity for identification of HIV-positive individuals. HIV testing among TB clinic attendees was significantly lower in non-TB cases versus TB cases. Among HIV-positive individuals, prior visit to TB clinic, with or without TB diagnosis, may have been an entry point into HIV testing and treatment cascade and is associated with higher viral suppression.

Characteristics	Percent visited TB clinic, diagnosed with TB (N=221)		Percent visited TB clinic, but not diagnosed with TB (N=234)		Percent with no visit to TB clinic (N = 1,759)	
	95% CI	95% CI	95% CI	95% CI	95% CI	95% CI
Aware of HIV-positive status	98.7	96.8 - 100.0	89.0	83.1 - 95.0	73.2	70.6 - 75.7
On ARV (self-report or detectable ARVs among those aware of HIV-positive status)	98.3	96.4 - 100.0	94.1	90.4 - 97.8	90.0	88.1 - 92.0
Viral suppression (among those on self-report on detectable ARVs)	89.8	84.3 - 95.4	92.3	88.1 - 96.4	91.4	89.2 - 93.7
Virally suppressed (among all HIV+, irrespective of awareness and ARV status)	87.6	82.0 - 93.3	78.5	71.6 - 85.4	64.9	62.1 - 67.7

[Awareness of HIV-positive status, treatment and viral suppression among HIV-positive adults, 15-64 years, by prior TB diagnosis status, MPHIA 2015-16]

PS22-630-26 Early initiation of ART in HIV-positive patients reduces the risk of acquiring tuberculosis

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Background: University of Nairobi/ Manitoba clinic a HIV/STI research center started in early 1980s in Nairobi. It enrolled general population for HIV/STI care and treatment services. In 2009 it was noted many clients had TB hence, a TB center was opened. Over a period of time number of clients diagnosed with TB reduced significantly.

This study evaluates the trend of TB infection among clients at the clinic in the back-drop of changes to guidelines surrounding the recommended CD4 count at ART initiation.

Methods: Retrospective cohort study was used. Data for all active HIV positive patients screened for TB using ICF tool since 2015 - 2009 was extracted. TB Presumptive clients had sputum microscopy and x-ray done. The proportion of TB-positive tests was calculated annually and the trend compared with the level of CD4 when patients were initiated on ART. The Kenya Ministry of Health directed cut off CD4 counts for initiating a patient on ART; 2011 patients were started ART when CD4s were 250 copies and below, 2012 to 2013 patients were started on ART with CD4 of 350 copies and below, 2014 to 2015 CD4 count of 500 copies and below, in 2016 everyone who tested positive was put on same day ARVs irrespective of CD4 count.

Results: In 2010 TB incidence was 8.4% (263/3128), 2011 8.1% (277/3416), in 2012 TB incidence was 4.8% (178/3700). In 2013 it reduced to 2.8% (118/4221). In late 2014, it reduced further to 1.1% (49/4447). Relative Risk showed that clients with a CD4 of 250 and below were at 70% risk of acquiring TB, while those with a CD4 350 and below had a 33% risk of acquiring TB.

Conclusions: Earlier ART initiation improves quality of life and reduced TB incidence.

PS22-631-26 Barriers to tuberculosis drug adherence during community treatment among HIV-TB patients in Southwest China

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Background: Yunnan reports the highest cumulative number of HIV cases of any province in China. Yunnan AIDS Care Center (YACC) is the provincial reference hospital for patients living with HIV (PLHIV). Under the USAID Control and Prevention of Tuberculosis

project, YACC conducted a qualitative study to identify barriers for tuberculosis (TB) drug treatment adherence during community-based HIV-TB treatment.

Methods: YACC conducted in-depth interviews in 2017 used a semi-structured guide with 23 participants: 17 HIV-TB patients, one HIV-TB patient's family member, four doctors and one HIV peer educator. Surveyors tape-recorded face-to-face, individual interviews in a private counselling room, and then analyzed verbatim interview transcriptions using Nvivo 11 software to organize, code, and analyze identified themes. The surveyors also provided supplemental notes.

Results: Three main barriers affected TB drug adherence. First, most HIV-TB patients believed that antiretroviral therapy (ART) is more important than TB drugs. To avoid drug interactions, ART is prioritized over TB treatment. Second, referral networks are weak both between designated hospitals and the public health dispensaries, and between HIV and TB health care providers. For example, HIV-TB patients referred from the provincial-level YACC to the local prefecture-level HIV designated hospitals were sometimes poorly supported due to the lack of coordination with prefecture-level TB staff, thus affecting TB treatment in patients' home communities. Third, some elderly HIV-TB patients and patients who experienced severe adverse reactions to TB drugs believed Chinese traditional medicine best treats TB.

Conclusions: These findings identify major points that should be addressed to improve TB drug adherence in HIV-TB patients. First, counseling and education are needed to correct misperceptions and beliefs about TB medicines. Second, referral networks should be strengthened between provincial and prefecture levels; and between TB and HIV facilities. Finally, HIV-TB providers should improve management of adverse drug reactions for better TB treatment adherence.

PS22-632-26 Integration of services at a TB DOT Point improve access and treatment outcomes: the Kuvukiland story

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Background and challenges to implementation: Namibia is a high TB burden country in southern Africa with significant economic disparities. Of the 701 TB patients notified in Tsumeb District from 2014-2016, 53% came from Kuvukiland informal settlement. Kuvukiland has a population of over 10 000 people but does not have municipal services and lacks formal health services. TB patients often interrupted treatment due to lack of transport money to visit the clinic.

Frequent interruption of TB treatment resulted in poor treatment outcomes.

Intervention or response: A two-phased plan was implemented with the aim to reduce the LTFU rate by bringing TB and HIV integrated services to the community. In July 2016, one prefabricated structure was provided to Kuvukiland where a community health worker provided daily DOT, contact tracing and collection of follow up sputum. In July 2017, two additional prefabricated structures were provided. Two nurses trained in ART initiation and two health assistants were recruited and trained in TB screening, investigation and management resulting in provision of the full package of TB and HIV prevention and treatment services at the DOT points.

Results and lessons learnt: By December 2017, 106 TB patients had accessed treatment at this DOT point and 79 patients were successfully treated. LTFU reduced to 8% from 20% before the intervention. In addition, 25% of the community (2528) were tested for HIV within 6 months of establishing the PITC service, of whom 51 (2%) were HIV positive. All were linked to care and initiated on ART, 34 (67%) were put on Isoniazid preventive therapy while 11 additional at-risk clients were provided with HIV pre-exposure prophylaxis.

Conclusions and key recommendations: A TB DOT point can be used as a gateway to access TB and HIV services for hard-to reach communities resulting in improved adherence and better treatment outcomes. Replicating a similar project in other communities is highly recommended.

PS22-633-26 High prevalence, incidence and mortality of tuberculosis among people with advanced HIV disease, Viet Nam, 2015-2017

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Background: Vietnam has rapidly scaled up HIV care and treatment for people living with HIV (PLHIV). We assessed tuberculosis (TB) prevalence, incidence and mortality among PLHIV with advanced disease enrolled in the Vietnam Cryptococcal Retention in Care study.

Methods: ART-naïve PLHIV aged ≥ 18 years, with CD4 count ≤ 100 cells/mm³ and no history of cryptococcal meningitis or recent antifungal treatment were enrolled at 22 regionally representative HIV outpatient clinics in 10 provinces from 8/2015-4/2017. Baseline demographic and clinical characteristics, including past or current TB, were abstracted from clinical visit records. Prevalent and incident TB were defined as TB documented within the first month of enrollment or during follow-up beyond the first month, respectively. Multivariable logistic regression was used to identify factors associated with prevalent TB accounting for sampling design.

Results: Among 1,177 PLHIV enrolled, 495 (42%) had prevalent TB (median age, 34 years [Interquartile range (IQR): 30-40]; median CD4 count, 27, IQR: 11-51 cells/mm³). Prevalent TB was associated with male sex (adjusted odds ratio (aOR): 1.6, 95% confidence interval (CI): 1.1-2.2), less than a high school education (aOR: 1.4, 95% CI: 1.0-2.0), unemployment (aOR: 1.6, 95% CI: 1.1-2.3), body-mass index < 18.5 (aOR: 1.6, 95% CI: 1.1-2.4), and hemoglobin < 110 g/L (aOR: 2.0, 95% CI: 1.4-3.0). The median follow-up time was 354 (IQR: 190-372) days. There were 143 deaths yielding a mortality rate of 156/1000 person-years of follow-up (py); 43 deaths (30%) were attributed to TB. There were eight cases of incident TB equating to 15/1,000 py (95% CI: 8-30).

Conclusions: TB prevalence, incidence and mortality among PLHIV with advanced disease in Vietnam is substantial, suggesting the importance of early TB screening, diagnosis, and preventive therapy, along with enhanced education and social support among PLHIV who are male, have less than a high school education, are unemployed or have anemia.

PS22-634-26 Interim results in HIV patients treated for multidrug-resistant tuberculosis with bedaquiline and delamanid in Belarus

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Background: The M/XDR-TB epidemic in Belarus is further complicated by high rates of HIV co-infection. Poor treatment outcomes of M/XDR-TB HIV-infected patients started treatment in 2013 (treatment success - 41.8%, death rates 17.0%) continue to further deteriorate in those started treatment in 2015: treatment success - 38.9%, death rate - 24.8%. Introduction of new drug containing regimens is vitally needed.

Methods: We performed an interim analysis of cohort of M/XDR-TB HIV co-infected patients treated with bedaquiline (BDQ) or delamanid (DLM) containing regimens.

Results: We performed an interim analysis of cohort of MDR-TB HIV co-infected patients treated with bedaquiline (BDQ) or delamanid (DLM) containing regimens.

Results: Of 25 patients enrolled between June 2015 and July 2017 (with follow-up until February 2018), 18 were with XDR-TB, 4 with pre-XDR-TB (Fq), 2 with pre-XDR-TB (SLI), 1 with MDR-TB; 19 were previously treated, 6 - new cases. 12 patients started BDQ and 13 - DLM containing regimens. All patients were

on antiretroviral therapy (ART) at initiation of the regimens. Of the 25 patients, 24 (96%) had completed 24 weeks of BDQ/DLM, 1 had died due to XDR-TB progression with CNS involvement. Of the 24 patients with 6-month follow-up, 20 (83%) had sputum culture conversion. All patients developed adverse events (AEs) during 6 months of BDQ/DLM treatment. The most common AEs were: electrolytes (K⁺, Mg⁺⁺) disturbances, uric acid increase, hepatic or renal impairment, anemia, thrombocytopenia, oral candidiasis, seizures, polyneuropathy, headache, insomnia, QTcF interval prolongation. All AEs resolved spontaneously or with supportive treatment without regimen stop.

Conclusions: Interim safety and culture conversion results for MDR-TB HIV co-infected patients on ART treated with BDQ or DLM in Belarus suggest that new TB drugs may be both efficacious and safe.

PS22-635-26 Second-line anti-tuberculosis treatment outcomes among HIV-seropositive patients with multidrug-resistant tuberculosis in the country of Georgia

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Background: Drug resistant tuberculosis (DR-TB) and HIV co-infection is a global challenge. The aim of this study was to analyze risk factors for poor treatment outcomes with the second line anti-TB drugs (SLDs) among HIV-positive patients in Georgia.

Methods: A retrospective medical chart review was conducted of adult (>18 years of age) HIV-positive patients with bacteriologically confirmed Rifampicin resistant TB (RR-TB), who initiated treatment with the SLDs at the National Center for TB and Lung Disease, Tbilisi, Georgia between 1 January 2009 and 31 December 2014.

Results: ≤ There are 174 HIV-positive patients who initiated TB treatment with SLDs during our study period in Georgia. Out of 50 patients' charts reviewed until now 48 (96%) were male with mean age 41 years (range: 39 years), 9 (18%) patients we co-infected with Hepatitis C. Mean CD4 count at TB was 211 cells/cml. Only RR-TB was found in 3 (6%) patients, MDR-TB - in 21 (42%), additional resistance to fluoroquinolones or injectable agents (PreXDR-TB) - in 19 (38%), and Extensive Drug Resistant TB (XDR-TB) were found in 7 (14%) patients. Eleven patients (22%) was cured, 13 (26%) completed treatment, 2 (4%) died, 13 (26%) were lost-to-follow-up, and 11 (22%) were treatment failure. CD4 count <200 cells/cml (adjusted odds ratio (aOR) 18.7, *P* value <0.001) and age ≤41 years (aOR 5.8, *P* value <0.041) were significantly associated with poor treatment outcome.

Conclusions: Preliminary findings highlight that lower CD4 count and younger age at TB diagnosis predictors of poor DR-TB treatment outcomes among HIV-positive patients in Georgia. We plan to continue our research to assess association of CD4 count trends during the treatment, adherence to antiretroviral treatment, and demographic and socio-economic status with poor treatment outcomes among HIV-positive individuals in the country of Georgia.

PS22-636-26 Early presumptive TB treatment in South African HIV-positive hospital in-patients

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Background: HIV-associated tuberculosis (TB) remains a common cause of admission to hospital in HIV-endemic African settings, with high mortality risk. Current diagnostic strategies are suboptimal and have led to frequent presumptive TB treatment in HIV-positive inpatients.

However, rapid initiation of TB treatment prior to TB testing could undermine the impact of newer, more accurate TB diagnostics.

Methods: We aimed to characterise early presumptive TB treatment in HIV-positive adult admissions in Edendale Hospital, South Africa, through a retrospective cohort nested within the STAMP TB screening trial. We enrolled patients excluded from the trial due to starting TB treatment between admission and screening, and extracted data on clinical characteristics, reasons for starting TB treatment, TB diagnostic modalities and inpatient outcomes.

Results: Between January 2016 and September 2017, data was available for 113/126 (89.7%) admissions starting early presumptive TB treatment. Patients showed evidence of advanced immunosuppression- median CD4 cell count was 97 cells/ μ L, 54.6% were currently taking antiretroviral therapy (ART) and 38.1% had at least one WHO danger sign at presentation.

TB treatment was started rapidly, median time to treatment was 15 hours and 72% started within 24 hours. 44.2% of patients started treatment based on clinical grounds, 44.2% on radiological findings, and only 11.5% based on positive microbiology (half of which were from a prior healthcare attendance). 62% of patients had further TB investigations, and by hospital discharge or death, only 20 (17.7%) patients had microbiologically confirmed TB disease.

In-patient mortality was 25.6% (95% CI 18.4 to 34.6)-substantially higher than the overall mortality among HIV-positive medical inpatients (9.9%, 95% CI 8.4% to 11.7%).

Conclusions: Early presumptive TB treatment is common in HIV-positive in-patients. Most patients were started without microbiological evidence of TB, and outcomes were poor. This population would likely benefit from more extensive TB investigation, including rapid urine-based TB diagnostics.

PS22-638-26 Fungal profile of lower respiratory tract infections and drug susceptibility patterns among people living with HIV in Addis Ababa, Ethiopia

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Background: Lower respiratory tract fungal infections are the most common cause of clinical manifestations among People Living with HIV (PLWHIV). However, there is little information regarding the profile and drug susceptibility pattern of these pathogens.

This study aimed to determine the profile of lower respiratory tract fungal pathogens and their drug susceptibility pattern among PLWHIV in Addis Ababa, Ethiopia.

Methods: A cross-sectional study was conducted in St Paul's Hospital Millennium Medical College, Addis Ababa. We enrolled a total of 142 adult PLWHIV, with symptoms of lower respiratory tract infections consecutively. We used a structured questionnaire to collect socio-demographic variables and clinical data of the participants. One early morning sputum was collected for fungal culture and antimicrobial susceptibility testing. Four milliliter whole blood was also collected for CD4+ T cell count. Data was analyzed by SPSS version 22.0. We used descriptive statistics to describe the data, and multiple logistic regression model was employed to determine factors associated with fungal infections.

Results: Of total participants 62% were females and the average age was 39.8 (+10.35) years with age range 16 to 75 years. The overall fungal pathogens isolated were 32.4%, and *Aspergillus* species were the most frequently (11.3%) isolated pathogen. CD4+ T cell count (AOR = 1.02; 95% CI, (1.01 - 1.03)) and WHO HIV clinical stages (AOR = 6.1; 95% CI, (5.9 - 8.01)) were significantly associated with fungal infection. Only *Candida krusei* was resistant to Fluconazole.

Conclusions: The overall magnitudes of fungal pathogens isolated were considerable. *Aspergillus* species was the most frequently isolated fungal pathogen. Fungal pathogen screening among PLWHIV with symptoms of

lower respiratory tract infections is crucial, while targeting individuals with low CD4+ T cell count and at advanced WHO HIV clinical stages.

PS22-639-26 Clinical, microbiological and molecular profiles of HIV-associated tuberculous meningitis patients in Myanmar

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Background: Tuberculosis (TB) and HIV are major public health problems in Myanmar. Tuberculous meningitis (TBM) is a devastating manifestation of TB and TBM in HIV-infected patients leads to diagnostic and therapeutic challenges. This study was carried out to describe the clinical profile, anti-TB drug susceptibility and genotypic characteristics HIV-associated TBM patients in Myanmar.

Methods: Cerebrospinal fluid (CSF) samples were collected from HIV patients with clinical signs and symptoms of TBM in three HIV care hospitals in Yangon during 2017-2018. TBM diagnosis was confirmed by CSF Xpert MTB/RIF assay and *Mycobacterium tuberculosis* complex (MTB) culture. Drug susceptibility of MTB isolates was determined by phenotypic anti-TB drug susceptibility testing. Sanger DNA sequencing and 24 loci MIRU-VNTR typing was applied to detect drug resistance-associated gene mutations and genotypic characteristics.

Results: Of 174 clinically presumptive HIV-associated TBM cases, laboratory-confirmed cases were 21 (12.1%). The mean age was 42.5±10.1 years and 15 (71.4%) were male patients. The most common clinical manifestations were headache and neck stiffness. Median CD4 count was 73 cells/mm³. Of 21 MTB isolates, 12 (57.1%) were resistant to at least one of first line anti-TB drugs. Multidrug-resistant (MDR) and MDR plus were detected in 9 (42.9%) and there is no extensively drug-resistant isolate. Patients with CD4 count of > 100 cells/mm³ and previously treated TB were significantly associated with any anti-TB drug resistance (P< 0.05). Mortality was found in 11 cases and 7 were MDR-TB patients. Most frequent mutation in *rpoB* gene conferring rifampicin resistance was S531L and that in *katG*

gene conferring isoniazid resistance was S315T. Genotype distribution was diverse and most prevalent strains were Beijing (33.3%) and East-African-Indian (23.9%).

Conclusions: This study highlights the magnitude of HIV-associated TBM in Myanmar. The findings pointed out disease characteristics and high anti-TB drug resistance situation among these patients and support the need for elaborative management strategies.

PS22-640-26 Frequency and significance of hyponatremia in tuberculous meningitis: a prospective cohort and causal survival model

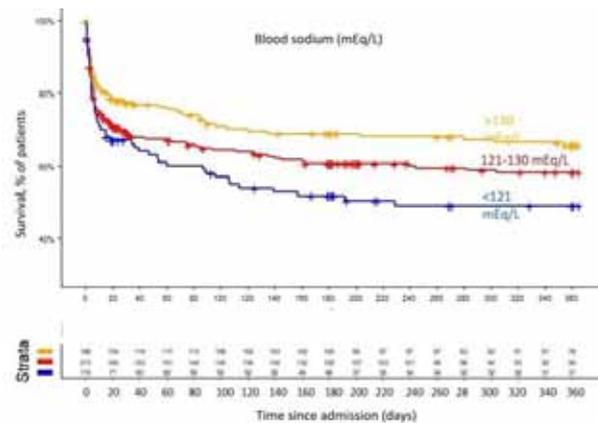
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Background: Hyponatremia is commonly seen in patients with tuberculous meningitis (TBM), but its relation with disease severity and outcome is largely unknown.

Methods: We examined the prevalence and significance of hyponatremia in a prospective cohort of adult TBM patients in Indonesia. Besides Cox regression, we used causal modeling to determine relationships between hyponatremia and other clinical and routine inflammatory markers, and identify what factors contribute to patient mortality.

Results: Among 678 TBM patients (median age 29 years, 61.2% male, 16% HIV-infected), 83% had hyponatremia, including 17.8% with severe hyponatremia (< 120 mEq/L). Patients with severe hyponatremia more often had concomitant pulmonary TB infection, culture-confirmed TBM, a lower Glasgow Coma Scale (GCS), higher Cerebrospinal Fluid (CSF) inflammatory markers and higher blood neutrophils counts (p < 0.05). One-year mortality was 44.6% (95% CI, 41%-48.5%) and strongly associated with HIV infection, decreased consciousness, motor deficits, fever, male and older age (all P values < 0.05). Severe hyponatremia was associated with higher mortality in univariate Cox regression (hazard ratio 1.68, 95% CI 1.16-2.44, p=0.006) but only in HIV-negative patients and not in multivariate analysis. In causal modeling, the most stable predictors of mortality was HIV infection, but not hyponatremia.

Conclusions: Hyponatremia is common in patients with TBM and associated with clinical severity, CSF inflammation, and death. However, hyponatremia does not seem to contribute to increased mortality, and correction of hyponatremia is unlikely to significantly improve prognosis.



[Kaplan-Meier curves with tables for numbers at risk for hyponatremia]

PS22-641-26 HIV disclosure by partnership status among PLHIV initiating IPT in Dire Dawa and Harar, Ethiopia

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Background: Disclosure of HIV status is an important initial step in building support for treatment adherence and preventing transmission to sexual partners. Prior to “Test and Treat”, people living with HIV (PLHIV) were offered disclosure counseling during preparatory sessions. We examined the prevalence and correlates of disclosure among PLHIV initiating isoniazid preventive therapy (IPT) who enrolled in the Enhance Initiation and Retention in IPT Care for HIV (ENRICH) Study.

Methods: ENRICH was cluster-randomized trial in 10 health facilities in Ethiopia, evaluating a combination intervention package to improve IPT initiation and completion among PLHIV. Interviewer-administered baseline questionnaires (collected 07/2013-05/2015) were analyzed to describe HIV disclosure among participants with and without sex partners. Correlates of disclosure were assessed with generalized linear mixed models with a random intercept to account for site clustering.

Results: Among 316 participants, median age was 30 years (IQR 26.0-38.5); 63.3% were female; and 41.1% were married/cohabiting. Overall 74.7% had disclosed their HIV status to ≥1 person. Those with sex partners (n=176) were more likely to disclose versus those without a partner (n=140) (92.1% vs. 52.9%; p< 0.001). Among participants with partners, those who were male or married/cohabiting were more likely to disclose to their partners, while those aged ≥25 were less likely to disclose (Table). Among participants without partners, those who were Orthodox, on ART at IPT initiation, lived with other PLHIV, or had a one-person social network were more likely to disclose (Table).

Conclusions: Prevalence and correlates of HIV status disclosure among PLHIV initiating IPT varied by partnership status. In order to use disclosure as a tool to reduce HIV transmission and improve treatment outcomes in the era of “Test and Treat”, it is imperative that disclosure interventions tailored to meet the needs of PLHIV with and without partners are provided as a key component of the HIV care package.

Correlates	aRR [95% CI] *
Disclosure to any partner among participants with partner (N=176)	
Male vs. Female	1.18 [1.04 - 1.34]
Age	
25-29 vs 18-24	0.78 [0.62 - 0.92]
30-34 vs 18-24	0.70 [0.58 - 0.85]
35-39 vs 18-24	0.70 [0.50 - 0.98]
40-44 vs 18-24	0.85 [0.71 - 1.02]
>=45 vs 18-24	0.60 [0.41 - 0.87]
Married/cohabiting vs. divorced/widowed	2.10 [1.54 - 2.86]
Disclosure to anyone among participants without a partner (N=140)	
Orthodox religion vs. Others	1.52 [1.02 - 2.28]
On ART at IPT initiation vs. not on ART	1.63 [1.02 - 2.60]
Other PLHIV at home vs. None	1.46 [1.08 - 1.99]
Size of social network 1 vs. >=2 or None	1.62 [1.09 - 2.42]

*Adjusted for health facility

[Table: Correlates of disclosure by partnership status among PLHIV initiating IPT]

PS23 The human right to health

PS23-642-26 A qualitative exploration of disclosure of MDR-TB status in South Africa

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Background: In South Africa, it is estimated that 3.5% of new cases of tuberculosis (TB) have rifampicin or multidrug resistance (MDR). Recent research has shown that failure to disclose TB status is a predictor of future diagnosis with MDR-TB and that limited perceived social support is an important risk factor for non-adherence to treatment.

Methods: To explore the broader personal impacts of MDR-TB for a project directed at enhancing economic evaluation with social justice, in-depth interviews were conducted with people being treated for MDR-TB (n = 35) and healthcare providers (HCP) (n=38), in Cape Town and Klerksdorp, South Africa between 2015 and 2017. Interview guides included prompts related to how the patient came to know their diagnosis, their experience with treatment for MDR-TB (compared to previous treatment for TB if relevant), and how having MDR-TB has affected their relationships, employment and future life planning.

Results: Disclosure was discussed in all patient interviews but one. The majority of patients indicated support from families after disclosing status. A few indicated that disclosure or knowledge of diagnosis led to negative responses from family members. Fear of infection was noted as the primary reason for negative responses. Two respondents mentioned that disclosure to their employer led to loss of their job. Most patients (n=24) either perceived, or had direct experience of rejection and stigmatization by some in the community based on their status. Of the 14 interviews with HCP in which disclosure was discussed, twelve believed stigma most frequently came from the community or other healthcare providers, compared to patients' internal circles. Most HCP attributed stigma as a response to underlying fears of infection/contagion, lack of education, or misinformation about the disease.

Conclusions: It is important to consider consequences of disclosure from multiple perspectives to identify strategies to address stigma among people with MDR-TB.

PS23-643-26 Factors associated with stigmatizing attitude towards tuberculosis patients in the general population of Ethiopia

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Background and challenges to implementation: Health-seeking behavior of TB patients seeking care is shaped by geographic and economic accessibility and the capacity to overcome barriers within the makeup of the society. People with TB often face social barriers that prohibit them from seeking care. These scientifically unfounded beliefs can add to their suffering more than the disease itself. Here, we assessed factors associated with stigmatizing attitudes in the general population of Ethiopia.

Intervention or response: This is a cross-sectional study conducted from October 25 to November 18, 2017 in all 11 regions of Ethiopia. A multistage sampling technique was used to select study participants. Semi-structured pre-tested questionnaires were used to obtain information about TB related stigma in the general population. Electronic data was collected by CSPro and analysed using SPSS Version 20. The study participants were grouped by high and low stigma score using the mean stigma score as a cut-off point.

Results and lessons learnt: The mean stigma score was 18.6 (range: 9 - 45). 38.7% had a high stigma score. A high stigma score was inversely correlated with wealth, educational status, and knowing TB as preventable and

curable. A high stigma score was 43% less likely among respondents with an education level above secondary than it was among those who could not read and write, and was 48% more likely in the second wealth quintile than in the highest wealth quintile. A high stigma score was 65% and 99% more likely for those who did not know that TB is preventable and curable respectively, compared to those who did.

Conclusions and key recommendations: This study shows that stigma exists in the general population, the main reasons being knowledge about the disease, wealth, and educational status. Therefore, improving TB-related knowledge is important to improve health-seeking behavior and to reach missed cases in the community.

PS23-644-26 Assessing and overcoming human rights-related barriers to TB in 11 countries

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Background and challenges to implementation: Tuberculosis (TB) disproportionately affects economically and socially marginalized people and people living with HIV, who continue to face a range of human rights challenges. TB's roots in poverty and discrimination are often assumed but rarely documented or addressed. A pioneering initiative of the Global Fund to Fight AIDS, TB and Malaria and its partners is assessing human rights barriers to TB services and supporting the scale-up of programs to reduce or remove these barriers over a five-year period.

Intervention or response: An extensive consultation identified 11 countries for inclusion in this effort - Cameroon, Côte d'Ivoire, DR Congo, Indonesia, Kyrgyzstan, Mozambique, Philippines, Sierra Leone, South Africa, Uganda and Ukraine - as part of a larger 20-country project that includes HIV and malaria. In each country, research teams assessed existing barriers to TB services and the effectiveness of programs to address them, and proposed costed comprehensive programmatic responses.

Results and lessons learnt: Findings clearly demonstrate that human rights barriers impede access to TB services in all the countries. Few effective programs are being funded to address these barriers, representing a serious gap in the TB response and undermining the achievement of global goals. In particular, TB-related stigma

remains a substantial barrier to services, independent of HIV-related stigma. Though the TB burden is generally greater for men than for women, harmful gender norms limit women's ability to independently seek TB services, to limit household TB exposure from their male partners, and to care for other family members, especially very young TB-infected children.

Conclusions and key recommendations: Multi-stakeholder consultations in the 11 countries are finalizing comprehensive five-year plans, including evaluation strategies and needed investments, to substantially scale up programs to reduce human rights barriers to TB services. This initiative will provide unprecedented, well evaluated and soundly costed models for removing human rights barriers to accessing TB services.

PS23-645-26 Discriminatory experiences of TB patients across 30 districts in India

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Background: Tuberculosis patients often experience stigmatizing and discriminating behavior from community members, friends or even close family members. In a country like India with diverse cultural beliefs and low literacy rates, this is even more. However, as the national TB program and various stakeholders' awareness programs efforts to reduce these discriminating behavior is increasing and we hope to see a positive change in this situation. We compare the findings from two KAP surveys conducted in 2012-13 and 2017.

Methods: As part of Project Axshya, Knowledge Attitude and Practice (KAP) surveys were conducted at the beginning, midterm and end of the project over a seven year period. The surveys were conducted across 30 districts in randomly selected primary sampling units. The rural: urban ratio was as per the Census 2011. TB patients were identified through household line-listing process and interviewed after obtaining consent. In midline 496 and in endline 323 patients were interviewed.

Results: Most of the TB patients shared about their disease status with their families/households in endline (93%) and midline (95%) and experienced supportive behavior from their families. About 60% informed their disease status their friends in both midline and endline of which average 23% experienced discriminatory practices. Of those who were married, 10% in endline and 15% in midline experienced discriminatory behavior from their partners. In endline 29% shared disease status with their employers where as in midline only 17% shared. 25% in endline and 34% in midline had to change their work due to TB.

Conclusions: The experiences of TB patients did not much change over the years. Family seems to be the most consistent support. Though there seem to be few gains

in community acceptance or employer behavior, over five years they seem insignificant. We need radical strategies to improve the quality of social life of TB patients.

	Midline N=496 Year - 2013		Endline N=323 Year - 2017	
	N	%	N	%
Informed disease status to household/family	469	95	299	93
Were they supportive?	453	96	287	96
Informed disease status to your friends?	298	60	203	63
Did you experience any discrimination from them?	72	24	44	22
Discriminatory change in the relationship with your spouse	57	15	28	10
Did you share your disease status with your employer?	86	17	95	29
Did you have to change your employment because of your disease status?	29	34	24	25

[Table 1. Discriminatory behaviors experienced by TB patients across 30 districts in India]

PS23-646-26 The right to complete TB treatment in the Netherlands

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Background and challenges to implementation: As of 1996 the Immigration Act allows undocumented migrants with tuberculosis (TB) to complete TB treatment in the Netherlands, the now called Article 64 arrangement. A temporary postponement of eviction is arranged until TB-treatment is completed. During this period costs for living, housing and (health)-insurance are also covered.

TB nurses of the Public Health Services provide treatment support to all notified patients, as well as psycho-social and socio-economic support if needed. For undocumented patients, the TB nurse will initiate the application for Article 64 arrangement, in consultation with the patient.

Intervention or response: Two surveys in 1996/1997 and 2002/2003 showed the Article 64 arrangement has a positive effect on treatment results of undocumented migrants. However, the arrangement was underused in eligible undocumented patients, and structural monitoring and evaluation was recommended. Since 2014, the use of Article 64 arrangement in case of undocumented patients is recorded in the National TB Register

Results and lessons learnt: In the period 2014-2016 41 of 66 undocumented TB patients (62%) applied for the Article 64 arrangement. The application was granted for all

patients who applied. 36 of these 41 TB patients (88%) completed treatment, compared to 17 of 25 (68%) in the TB patients without Article 64 arrangement.

Conclusions and key recommendations: The Article 64 arrangement enables TB patients to complete TB treatment, but is used for only 2 thirds of the undocumented migrants with TB. Since the absolute number of undocumented migrants is low individual TB nurses may not be aware of the possibilities and inexperienced with the complicated administrative procedure of the application. KNCV Tuberculosis Foundation offers support to TB nurses with a roadmap and helpdesk and intends to maintain awareness among TB nurses to make use of the Article 64 arrangement through professional training.

	2014		2015		2016		Total	
	N	%	N	%	N	%	N	%
Total undocumented migrants with TB	21		15		30		66	100%
Undocumented TB patients, no Article 64 arrangement	6	29%	7	47%	12	40%	25	38%
Undocumented TB patients with Article 64 arrangement	15	71%	8	53%	18	60%	41	62%
Treatment completion TB patients, no Article 64 arrangement	3	50%	6	86%	8	67%	17	68%
Treatment completion TB patients with Article 64 arrangement	15	100%	7	88%	14	78%	36	88%

[Percentage of treatment completion in undocumented migrants, 2014-2016]

PS23-647-26 Humanizing TB: let's talk about people, not numbers

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Background and challenges to implementation: Stigmatization and discrimination is associated with interruption of treatment (see table). Lack of understanding and/or interest by funders and physicians also means that new drugs and treatments do not always reach drug-resistant tuberculosis (DR-TB) patients in time to save them.

Intervention or response: In order to lift these obstacles in Kyrgyzstan, KNCV through the Challenge TB (CTB) Project reinforced its communication strategy by telling about the people affected by DR-TB. CTB regularly published personal, detailed stories of patients and health workers, gave them a voice at all events and encouraged them to express themselves through a country-wide contest. Patients started participating in the fight against stigma, including some who were ashamed of

their disease initially. CTB enhanced every clinical training, presentation and report with these stories to remind its audiences that they help save lives.

Results and lessons learnt: Making DR-TB personal proved efficient to convince authorities to allow new drugs and regimens into the country, doctors to prescribe them, patients to adhere to treatment, the community to support patients, and donors to continue funding. Facebook posts with a human story reached up to 30 times more people than other types of posts. Six months after the page was created, the highest post reach was 1,448 people for a short story on a 2-year-old cured from DR-TB (lowest post reach:39). These stories were shared by partner organizations and in the WHO Childhood TB Roadmap. Our strategy was adopted in other CTB countries. When talking about TB, we talk about parents grieving their child and children left orphaned, about question marks set on tomorrows, about fates still unknown.

Conclusions and key recommendations: Strong, positive and human-centered advocacy can help decrease stigma, create a more supportive environment for patients and motivate authorities and medical workers. Adopting a humanizing communication strategy will increase commitments to end TB.

Have you ever interrupted treatment?	Answered yes to "Have you ever been discriminated or felt ashamed due to your TB?"	Answered no to "Have you ever been discriminated or felt ashamed due to your TB?"	Total
Yes	29 (54%)	22 (39%)	51 (46%)
No	25 (46%)	34 (61%)	59 (54%)
Total	54	56	110

[Stigma and adherence to treatment in Kyrgyzstan according to a survey among drug-resistant tuberculosis patients, February-March 2018 (n=110)]

PS23-648-26 Challenging stigmatizing language in TB research and practice: achievements and lesson learned from the community research advisors group experience

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Background and challenges to implementation: Stigma remains a major barrier to health equity for persons affected by tuberculosis (TB). One source of stigma is stigmatizing language, which perpetuates harms and normalizes negative beliefs about people with TB, especially when used by health care providers or in scien-

tific communications. By engaging local, national, and global stakeholders, the Community Research Advisors Group (CRAG) advocated to end stigmatizing language in TB care and research. Here we reflect on lessons learned and suggest further areas for action.

Intervention or response: To initiate this campaign, CRAG wrote letters to global professional societies and research networks calling for retiring stigmatizing language from the global discourse. CRAG subsequently provided input to Stop TB Partnership's draft TB Terminology Guide to shape the development of patient-centered language and published a call to action in *BMJ*. Locally and nationally, CRAG members launched campaigns to obtain commitments from TB programs to avoid stigmatizing language, most notably in the United States and South Africa.

Results and lessons learnt: As a result of CRAG-led advocacy, Stop TB Partnership finalized its terminology guide and the Union announced its commitment to respecting people affected by TB in its communications (conferences and scientific journals). The Stop the Stigma campaign launched by the Heartland National TB Center in Texas resulted in commitments from the U.S. National Society of TB Clinicians and National Tuberculosis Controllers Association to use person-centered terminology, and the Unmask Stigma campaign led by TB Proof in South Africa galvanized healthcare workers. Several TB research networks committed to avoiding stigmatizing terms in scientific discourse.

Conclusions and key recommendations: There is now increased awareness about the harms of stigmatizing language and an emerging normative consensus that such language is incompatible with commitments to compassion and equity in TB care. This new norm must be nurtured; the challenge now is to move from commitment and acknowledgment to actual realization of stigma-free discourse.

PS23-649-26 Understanding gender differences and barriers that exist for men and women in accessing TB services for improved TB case notification in Pakistan

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Background and challenges to implementation: Pakistan ranks 5th among thirty high-burden TB countries.^[1] Mercy Corps (MC) is implementing the country's largest Public Private Mix (PPM) initiative in 75 districts. To date, the program has not paid much attention to understand the barriers and factors that affect women's and men's access to TB care services. A gender assessment was carried out in four districts with diverse geographical and cultural contexts.

[1] Global TB Report 2017, World health organization

Intervention or response: Through analysis of sex and age disaggregated data of two and a half years, districts were identified where more men were accessing TB services than women and vice versa. Gender assessment using Gender Analysis Framework^[1] was carried out, including focus group discussions with communities, key informant interviews with PPM General Practitioners and TB patients. This was followed by data analysis and a workshop to devise strategies to address these gender differences.

[1] A tool developed by Mercy Corps to help teams identify the gender specific information needed to design and deliver smart, targeted program activities that meet the needs of men, women, boys and girls in their context.

Results and lessons learnt: The key barriers for women are limited financial control, lack of knowledge, restricted geographical accessibility, restricted mobility, limited decision making power, less attention to women's health and stigma. For men, the key findings included treatment cost, stigma and quacks as first point of contact. The analysis provided recommendations for addressing these barriers by implementing interventions such as women only chest camps, engagement of Lady Health Workers, GPs training on gender, economic opportunities for TB patients, women specific activities, incentives for male TB patients for bringing female family members to health facility, awareness raising activities, vouchers schemes, more female GPs, engaging informal providers, and increased outreach.

Conclusions and key recommendations: Gender responsive TB programming can help reduce the inequalities in TB notification and outcome.

PS23-650-26 A new political framework for stimulating TB drug R&D incorporating concepts from bioethics and human rights

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Background: Medical advancements have improved the lives of millions, yet investments in research and development (R&D) leave many health issues unaddressed, and many individuals struggle to access health services. The United Nations has recognized health innovation and access to medicines as essential development goals. Both are important for tuberculosis (TB), where patients suffer from a lack of R&D and face difficulties in accessing new tools. There is a need for new approaches to R&D that can resolve this separation between research and access.

Methods: Dominant approaches to innovation treat research and development as separate from dissemination and diffusion of outcomes. As an alternative, we propose a contemporary framework for TB R&D that integrates bioethical principles and human rights, focusing

on the right to enjoy the benefits of scientific progress and its applications. Ethical concepts such as distributive justice, dignity, non-discrimination, reciprocity, and participation are central to the right to science and help to bridge development and diffusion. The goal of the framework is to create state accountability for investing in R&D in ways that connect TB affected communities to the benefits of science.

Results: The framework contains three main components: development, diffusion and accountability. Development concerns encouraging public investment in science, and diffusion refers to the equitable dissemination of knowledge derived from science. Under this framework, development and diffusion become obligations on the same plane of concern for governments. Accountability ensures the complexities of these processes translate into policies aimed at equitable distribution of goods without discrimination.

Conclusions: If put into practice, such a framework could help to ensure more equitable outcomes for the populations most in need of innovation and access to new TB technologies. Elucidating the connections between bioethics and human rights helps to establish that research policy is human rights policy, and that human rights are central to the scientific endeavor.

PS23-651-26 Perceptions of family members of tuberculosis patients about TB-associated stigma in Ethiopia

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Background and challenges to implementation: The effectiveness of TB prevention and control effort is determined by its capacity to reduce barriers to seeking care. Within a society the role of families of TB patients is instrumental in providing necessary support to the patient during and after illness. Therefore, understanding the perception of close families have of the disease is important. Hence, this study aimed to assess the perception of the families of TB patients about TB in Ethiopia.

Intervention or response: We conducted a cross-sectional survey from October 25 to November 18, 2017 in all 11 regions of Ethiopia. A multistage sampling technique was used to select study participants. Semi-structured pre-tested questionnaires were used to obtain information about TB-related stigma. Electronic data was collected by CSPro and analysed using SPSS Version 20. The study participants were grouped by high and low stigma score using the mean stigma score as a cut-off point.

Results and lessons learnt: We included 836 participants, of whom 84.0% would want to consult medical personnel if they had TB. However, less than a quarter of them would want to disclose to family members or close friends. 25.2% and 21.6% indicated that the community avoids or rejects a person with TB, respectively. Also, 18.6% and 16% of respondents reported that people would avoid them and think less of them if they had TB, respectively. The mean stigma score was 20.46 (rang, 10-46) and 38.0% had high stigma score. High stigma score was associated with educational status, wealth, residence and knowledge about TB as curable disease.

Conclusions and key recommendations: Family members of TB patients reported the existence of stigmatizing perception in their households. This indicates that health care workers are missing the opportunity to provide proper health information to households of TB patients. Therefore, focused health education should be provided to improve the support TB patients receive in their families and communities.

PS23-652-26 Lawyers' knowledge about tuberculosis patient's rights in India

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Background and challenges to implementation: The Constitution of India guarantees right to life under Article 21 and the recent National Health Bill 2009 upholds "health" as a fundamental right. The results from analysis of judgement cases of Tuberculosis filed in National Consumer Disputes Redressal Commission highlighted the dilemma of diagnosis, treatment and insurance claims. In this regard it is important to know how lawyers who represent clients understand about the "rights" of Tuberculosis patients and their perception about ensuring TB services.

Intervention or response: A total of 21 lawyers were interviewed using a snowballing method in Chandigarh, India. The questionnaire was categorised into (a) knowledge - about TB infection, diagnosis and treatment (b) practice -knowing the rights of TB patients under "Right to Information (RTI)" and "public interest litigation (PIL)" (c) opinion about TB services - approaches government need to follow.

Results and lessons learnt: Overall 76% of lawyers had basic knowledge about tuberculosis. Nearly 20% and 28%, said TB is hereditary and not to marry a person who is on treatment/previously treated respectively. Only 28% of them believed TB patients are protected under "Article 21" of the constitution. None had applied to RTI or PIL to know the rights or to uphold the rights of TB patients. In their opinion, government to take steps - to include TB in healthcare bill (66%), free medication (71%), and health insurance (38%). Legal-

ly, 62% of lawyers supported the idea of filing petition in consumer court if patients were not treated as per guideline.

Conclusions and key recommendations: Knowledge about Tuberculosis among lawyers is better; however need to be strengthened through a series of training programme. Most importantly, awareness about Rights of TB patients are abysmally low and need immediate attention if lawyers are willing to support TB patients in filing petition in consumer courts.

PS23-653-26 Factors affecting uptake of TB services in the communities: findings from a TB knowledge, attitude and practice survey in Nigeria

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Background: Knowledge about the cause and symptoms of TB plays a vital role in the uptake of TB services among persons with the symptoms of TB. Also important is the understanding of the people about TB treatment services being offered, which can inform programme managers about the likely factors that could impede early TB case diagnosis and treatment.

Methods: Data used was from the Knowledge, Attitude and Practice (KAP) survey conducted for National TB and Leprosy Control Program (NTBLCP) in Nigeria, in December 2017. Study coverage entails 240 Enumeration Areas, 48 Local Government Areas with equal representation of urban and rural areas across 12 states. Two states represented each of the six Geo-political zones in Nigeria. A cross sectional approach, with mixed research methodologies was adopted.

Results: A total of 10,079 persons were interviewed among the general population; male: 54% and female 46%; 8,605 (85%) have heard of TB, while 457 (5%) have been diagnosed of TB. Barriers associated with uptake of TB treatment among those who have had TB were; ignorance about TB- 49% ($p < 0.0001$), ignorance about where TB services are located; 37% ($p < 0.0001$). Stigma and discrimination; 39% ($p < 0.0001$). Non availability of TB services in the local health facility; 23% ($p < 0.0001$) and TB treatment centres being too far; 23% ($p < 0.01$).

At multivariate analysis, those who had TB are 44 times more likely to know how TB can be transmitted than those who do not have the disease (OR=1.44, CI: 1,152 - 1,809 $p < 0.001$). Similarly, they are 6.93 times more likely to demonstrate good health seeking behavior than those with no TB (OR=7.93, CI: 6,335 - 9,948 $p < 0.0001$).

Conclusions: TB programme managers must address these barriers to increase access to TB services through demand creation strategies, and expand TB services to more health facilities in the communities.

PS24 Tuberculosis infection: diagnostics and immunology

PS24-654-26 Adenosine deaminase and CCL1 discriminate between active and latent tuberculosis

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Background: There is an urgent medical need to differentiate active (ATB) from latent tuberculosis (LTBI), but this remains a complicated and time-consuming process. The aim of this study is to identify novel biomarker profiles to aid in the differentiation between ATB and LTBI.

Methods: Sera from 80 adult participants were analyzed for 40 cytokines/chemokines and activity of adenosine deaminase (ADA) isozymes. The population was classified into four groups: ATB (n=20), LTBI after completion of prophylaxis (LTBI+; n=20), LTBI without prophylaxis (LTBI-; n=20) and healthy controls (HC; n=20). Logistic regression analysis was used to design a prediction model combining significant biomarkers in differentiating ATB from LTBI-.

Results: Sparse Partial Least Squares regression analyses identified VEGF, CCL1, CRP and CXCL10 as potential biomarkers to differentiate ATB from LTBI-. These markers and the ADA (ADA2) activity were significantly increased in ATB compared to LTBI-, ($p \leq 0.007$). CCL1 and the activity of ADA (ADA2) were the only biomarkers to be significant predictors and additions to the prediction model. Combining these biomarkers yielded a sensitivity and specificity of 100% and 80% respectively in differentiating ATB from LTBI- subgroup.

Conclusions: CCL1 and ADA activity in serum are promising biomarkers in differentiating ATB from LTBI. These biomarkers need validation in a prospective clinical trial.

PS24-655-26 Immunomodulation in latent tuberculosis infection with isoniazid prophylactic therapy in view of invariant natural killer T (iNKT) cells

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Background: The mechanism underlying the effects of isoniazid prophylaxis therapy (IPT) in preventing conversion of latent tuberculosis infection (LTBI) into active pulmonary tuberculosis (PTB) is unknown. Therefore, this study aimed to evaluate whether treatment of LTBI with IPT resulted in modulation of innate immunity via invariant natural killer T (iNKT) cellular function in the host.

Methods: Overall, 20 newly diagnosed PTB patients, 30 LTBI patients, and 23 healthy controls (HC) without malignancy or autoimmune disorders were prospectively enrolled. Patients were followed for at least 3 months if they received conventional anti-TB chemotherapy or IPT for PTB or LTBI, respectively. Th17, Treg, and iNKT cell proliferation index (PI) and extracellular cytokine levels in peripheral blood samples were evaluated by flow cytometry and ELISA.

Results: iNKT cell PI was higher in the LTBI and HC groups than in the PTB group, and an increased Th17/Treg PI ratio was observed after iNKT cell stimulation with α -galactosylceramide (α -GalCer)+IL-2 in the LTBI group. In LTBI patients receiving IPT, iNKT cell proliferation, extracellular cytokine (IFN- γ and IL-23), and pro-inflammation cytokine (IL-17) expression was increased, but secretion of IL-4 was decreased; these observations were not noted in PTB patients with conventional anti-TB chemotherapy. However, the Treg response after α -GalCer+IL-2 stimulation was predominant in treatment-naïve PTB patients.

Conclusions: IPT may have immunomodulating effects in LTBI through enhancement of iNKT cellular function, Th17 response, and downstream pro-inflammatory cytokine expression.

PS24-656-26 Quantiferon-TB gold plus is a more sensitive screening tool than quantiferon-TB gold in-tube for latent tuberculosis infection among older adults in long-term care facility

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Background: We investigated the prevalence of latent tuberculosis infection (LTBI) among the elderly in long-term care facilities (LTCFs), and the performance of QuantiFERON-TB Gold In-Tube (QFT-GIT) and the new QuantiFERON-TB Gold plus (QFT-Plus).

Methods: We assessed the diagnostic performance against a composite reference standard of any reproducible positive result of QFTs within one month. Subjects (n=246; median age, 80) in seven LTCFs in Taiwan were enrolled; 72 (29.3%), 12 (4.9%), and 162 (65.9%) subjects were classified as definite, possible and not LTBI, respectively.

Results: Seventy-three (29.7%) and 80 (32.5%) subjects had positive results of QFT-GIT and QFT-Plus, respectively, and 231 (93.9%) subjects showed agreement results. For definite LTBI, the sensitivity, specificity, positive predictive value, and negative predictive value of QFT-GIT were 90.3%, 95.4%, 89.0%, and 96.0%, respectively, and those for QFT-Plus were 98.6%, 94.8%, 88.8%, and 99.4%. The sensitivity of QFT-GIT decreased gradually with age, whereas QFT-Plus displayed significantly higher sensitivity (100.0% vs. 81.8%, $P=0.036$) and similar specificity (98.2% vs. 98.2%) among subjects aged ≥ 75 years.

Conclusions: A high prevalence (29.3%) of LTBI was found among elders in LTCFs, and the new QFT-Plus test demonstrated a higher sensitivity than QFT-GIT in older adults.

PS24-657-26 Early tuberculosis infections assessed by serial QuantiFERON-TB Gold Plus testing in a prospective cohort of household contacts

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Background: The accurate discrimination of newly from previously acquired latent tuberculosis (TB) is important as recent infections have a higher risk of progressing to active TB. The new QuantiFERON-TB Gold

Plus assay (QFT-Plus) contains an extra antigen tube which, according to the manufacturer, additionally elicits a CD8⁺ T-cell response above the CD4⁺ T- response. It has been suggested that a stronger interferon- (IFN-) response in this new antigen tube is associated with recent infection. We aimed to assess the characteristics of CD4 (TB1) and CD4/CD8 (TB2) tube response in subjects with newly acquired latent TB infection.

Methods: We prospectively followed-up household contacts (>14 years-old) of pulmonary TB cases at primary health care clinics in Santiago, Chile. Enrolled contacts had symptoms screening, chest X-ray and QFT-Plus testing at baseline and 12-week follow-up. QFT-Plus read-out was categorized according to the conventional cut-off (0.35 IU/ml) for both antigen formulations. The difference (TB2 minus TB1) between IFN- response in the two antigen tubes was determined.

Results: From 87 contacts enrolled, 42 (48%) had a positive QFT-Plus at baseline. Of 23 negative contacts at baseline that completed the 12-week follow-up, 8 (35%) converted to a positive test. Overall, there was a strong agreement between TB1 and TB2 with concordant positive results in all new conversions. IFN- levels were not different in recent converters compared to baseline positive (TB1: 2.94 vs. 1.69 IU/ml; $p=0.52$, TB2: 2.71 vs. 1.83 IU/ml, $p=0.7$, respectively). Median IFN- difference (TB2 -TB1) was -0.01 UI/ml (IQR: -0.51-0.29) in recent converters and 0.04 UI/ml (IQR: -0.16 -0.33) in subjects positive at enrolment ($p=0.47$).

Conclusions: The IFN- response in the new QFT-Plus test was not different in the CD4/CD8 versus the CD4 tube in contacts with newly acquired latent TB infection. All subjects with QFT-Plus conversion had a strong and concordant IFN- response in both tubes.

PS24-659-26 The TEKO trial: implementation of the QuantiFERON®-TB Gold In-Tube test at CD4 blood draw for diagnosing latent tuberculosis among newly diagnosed HIV-infected adults in South Africa

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Background: Tuberculosis (TB) remains the leading cause of death in HIV-infected individuals in South Africa. Implementation of preventive treatment (PT) against TB is suboptimal. *QuantiFERON®-TB Gold In-Tube* (QGIT) and tuberculin skin test (TST) are recommended to identify patients who would benefit from PT.

Methods: We conducted a cluster-randomized trial to compare two methods of targeting those with latent TB infection (LTBI): blood draw for QGIT at the time of first CD4 blood draw in newly diagnosed HIV-infected

patients, and then-current standard of care TST. Fourteen public clinics in North West Province were randomized to either QGIT or TST. Consenting HIV-infected adults were interviewed after HIV diagnosis and followed for two years via medical record abstractions to compare proportions who initiated IPT.

Results: Enrollment began November 2014 and follow-up ends May 2018. 3,235 newly diagnosed HIV-infected patients were enrolled; 2,925 with no prior TB diagnosis were eligible to receive a test for LTBI. Median age was 31 (IQR 26-39), 69% were women and median CD4 count was 330 cells/mm³ (IQR 178-515). In QGIT clinics, 1131/1630 (69%) were QGIT tested; 453 (40%) were positive, 585 (52%) negative and 93 (8%) indeterminate. In TST clinics, 70/1295 (5.4%) had a TST placed; 30 (43%) were negative, 10 (14%) positive and 30 (43%) not read. Average clinic IPT initiation was 44% in QGIT clinics and 27% in TST clinics; adjusted difference: 17% (95% CI: 2-36%; $p=0.08$).

Though the QGIT arm increased IPT initiation, the QGIT *result* appeared not to impact initiation, as 36%, 42%, 38% started IPT among those whose QGIT result was positive, negative, and indeterminate, respectively.

Conclusions: QGIT implemented at CD4 blood draw markedly increased testing for LTBI, and increased IPT initiation, albeit indirectly. TST use has declined markedly in South Africa and while the QGIT at CD4 blood draw strategy clearly increased testing, if it is to be useful in directing IPT initiation, QGIT results must be acted on appropriately.

PS24-660-26 Utility of QGIT as an adjunct to TST for screening of latent tuberculosis infection among Indian health care workers

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Background: Health care workers (HCWs), are at particularly high risk for acquiring tuberculosis (TB) in India. Use of QuantiFERON® TB Gold Test (QGIT), in addition to Tuberculin Skin Test (TST), for LTBI screening of HCWs in high prevalent settings is unclear and needs to be assessed.

Methods: A prospective longitudinal cohort study of medical and nursing trainees in a public tertiary care teaching hospital in Pune, India was conducted be-

tween May 2016 and December 2017. They underwent TST and QGIT at study entry. QGIT was repeated at 1 month and every 3 months thereafter for a year; TST was repeated at annual follow up. LTBI was defined as TST ≥ 10 mm and/or QGIT 0.35 IU/ml. Test positivity at baseline was analyzed by frequency rate. Agreement was assessed by coefficient of kappa value at baseline. All analyses were performed using STATA V 13.1.

Results: Of the 200 HCWs enrolled, 90 (45%) were nurses and 110 (55%) were residents with a mean age of 25 years (IQR 19 - 27 years) with 113 (57%) female. With a standard cutoff of TST at ≥ 10 mm and QGIT at 0.35 IU/ml, test agreement was 87% with kappa 0.58 (Correlation coefficient: 0.68), indicating fair agreement. Adding QGIT to TST testing for LTBI screening increased the positivity by 18 (9%). Test discordance was noted in 11% (TST-, QGIT+) and in 8% (TST+, QGIT-). Test concordance was noted in 86% (TST-, QGIT-) and in 76% (TST+, QGIT+). During follow up of one year, 1 developed active TB in the discordance group and 5 developed active TB in concordance group.

Conclusions: QGIT as an adjunct to TST for LTBI screening increases the positivity rate. There is a fair agreement between the two tests. Concordance between the tests is a useful predictor for active TB on follow up, however discordance should not be neglected.

PS24-661-26 Differential protein expression in peripheral blood CD4⁺ T cells between latent and active tuberculosis patients

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Background: Tuberculosis (TB) is a prominent global health threat because of the enormous reservoir of sub-clinical latent tuberculosis infection (LTBI). Identifying a more robust signature for LTBI is important for TB prevention and elimination. However, there are not gold standard methods to diagnose LTBI at present. CD4⁺ T cells play an important role in host defense against mycobacterium tuberculosis. To screen potential biomarkers between active TB and LTBI, we established label-free profiles with high resolution and reproducibility of the protein in CD4⁺ T cells from individuals with TB and LTBI.

Methods: CD4⁺ T cells were purified by negative selection using magnetic microbeads from active TB, LTBI and healthy controls (HC). The total proteins were analyzed by label-free quantitative proteomic technology. Finally, the differential protein expression was analyzed by using Gene ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway analysis software. Student's t test was applied in analysis of the differential expression between two groups.

Results: The basic frames of proteomic distribution in these two types of CD4⁺ T cells were very similar, but each had different protein spots. 53 differential protein spots were identified between TB and LTBI group. Among these 53 protein spots, 5 spots were poorly expressed and 48 highly expressed in TB.

Conclusions: The label-free profiles with high resolution and reproducibility of CD4⁺ T cells of TB and LTBI are established. There are 53 proteins expressed differently exist between these two types of CD4⁺ T cells, which have a potential role to become biomarkers between TB and LTBI.

PS24-662-26 Target-responsive liposome facilitated by catalyzed hairpin assembly enables highly sensitive detection of tuberculosis-related cytokine

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Background: Tuberculosis (TB) seriously threatens human health and is the leading cause of death all over the world. In recent years, interferon-gamma (IFN- γ) as the most well-known TB-related cytokine has attracted increasing attention in view of its potential as diagnostic biomarker of TB.

Methods: Herein, we propose a new fluorescent method that enables highly sensitive detection of IFN- γ with the adoption of target-responsive liposome facilitated by catalyzed hairpin assembly. The core concept of the method is a scheduled cycle of DNA hairpin assembly which is operated upon the presence of target IFN- γ and designed to recruit peptide probes that disrupt membranes of fluorescein (FAM)-encapsulated liposomes, facilitating the release of fluorescent compounds for signal responses. The method combines a DNA self-assembly based amplification process with a liposome-based amplification process, therefore offering very high sensitivity.

Results: Under optimized conditions, the method allows absolute detection of IFN- γ down to 0.047 pM, showing superior sensitivity as compared to previous aptamer-based methods. Moreover, the method can exhibit high specificity and good reproducibility and can be directly used in serum samples.

Conclusions: The method may have great potential for improve tuberculosis diagnosis.

PS24-663-26 Utility of the T-SPOT.TB test to differentiate active TB from LTBI in patients from Cape Town, South Africa

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Background: IGRAs are considered to lack the ability to distinguish between latent infection and active TB disease. This study investigated the potential utility of applying the ratio between TB antigen (TBAg)-induced spot counts and PHA-induced spot count changes in an ELISPOT assay to distinguish stage of disease.

Methods: This study retrospectively evaluated differences in TBAg/PHA ratio using T-SPOT.TB assay (Oxford Immunotec, Milton Park, UK) in 56 active TB patients and 18 LTBI individuals from South Africa. Active TB cases were identified as culture positive and/or geneXpert positive. LTBI was determined as geneXpert negative/ culture negative individuals but with a positive T-SPOT.TB test. The numbers of ESAT-6, CFP-10 and PHA spot forming cells (sfc) were counted using CTL analyzers, and the larger value of ESAT-6 or CFP-10 spot counts were used in the TBAg/PHA ratio for each patient.

Results: There was an increase in the average antigen spot count in active disease patients versus LTBI (176.3 vs. 62.8) with a concomitant average decrease in PHA induced spot counts (372.0 vs. 540.8); however, the increase in spot counts was variable and therefore the TBAg/PHA ratio was calculated to further distinguish the two groups. This ratio in active TB had a mean value of 0.7413 ± 0.22 compared to 0.1292 ± 0.04 for LTBI (p value < 0.0001). Using 0.25 as a cut-off ratio the sensitivity, specificity, positive predictive value (PPV) and likelihood ratio for this approach was 57.1%, 94.4% 97.0% and 10.29 respectively. A ROC analysis indicated an AUC of 0.7937.

Conclusions: Our results are consistent with results from previous studies in that the TBAg/PHA T-SPOT.TB test ratio differentiates active TB from LTBI and might be a useful adjunct in identifying individuals at increased risk for active TB disease.

PS24-664-26 Immune responses among adult household contacts resistant to Mycobacterium tuberculosis

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Background: Identifying protective mechanisms that prevent and eliminate transient infection with *Mycobacterium tuberculosis* (*Mtb*) in individuals that remain persistently TB uninfected is important for the development of efficacious TB vaccines and/or therapeutic strategies to prevent TB infection.

Methods: We measured *Mtb*-specific T cell responses among HIV uninfected adult household contacts of persons with active TB, Rustenburg, South Africa. PBMC were stimulated *in vitro* with *Mtb* whole lysate for 18 hours, and the proportion of CD4+, CD8+, T cells expressing IFN γ , TNF γ , granulysin and granzyme A were measured by flow cytometry. We compared immune responses between 13 household contacts who tested Tuberculin Skin Test (TST) and Quantiferon Gold In-tube (QFT) positive (TST+QFT+) and 10 household contacts who tested TST-QFT- over 6 months. Statistical comparisons were determined by a Mann-Whitney U nonparametric t-test.

Results: TST-QFT- status was characterized by high proportions of CD4+ T cells compared to TST+QFT+ (p<0.05). There was a trend towards decreased proportions of CD8+ T cells among TST-QFT- household contacts (p=0.06). We observed no significant differences in the proportion of T cells between the study groups. TST-QFT- household contacts had significantly lower proportions of IFN γ + and TNF γ + CD4+ T cells compared to TST+QFT+ (p<0.05). There were no significant differences in the proportion of IFN γ +, TNF γ +, granulysin+ and granzyme A+ subsets of T cells between the study groups.

Conclusions: Elevated proportions of IFN γ + and TNF γ + CD4+ T cells among TST+QFT+ indicate adaptive responses reflecting sensitization due to TB infection. Although no significant differences were observed in T cell responses, evidence of *Mtb*-specific T cells among TST-QFT- household contacts could suggest prior antigen exposure and/or clearance by innate or adaptive mechanisms. Alternatively, because *Mtb* lysate contains both TB-specific and nonspecific T cell stimulatory

antigens, the detection of TB-nonspecific responses could prevent the detection of differential TB specific responses.

PS25 Tulips and tuberculosis: emerging themes for children

PS25-665-26 Increasing childhood TB diagnosis through symptom screening in pediatric outpatient departments of key hospitals in Karachi

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Background: Pakistan, ranked the 5th highest TB burden country worldwide, reported 34,000 children with TB in 2015. Modelling data show that we are missing at least 2/3 of the actual TB load in children. In 2016, The Indus Health Network launched a Childhood TB program as part of the Zero TB initiative in Karachi to screen for TB in children in busy outpatient departments (OPD) at eight hospitals.

Methods: A trained nurse screens children at pediatric OPDs using structured questions on symptoms and other risk factors. Presumptive children are evaluated by a trained medical officer dedicated to the program. After a history and physical exam, further tests are done as needed (including chest X-ray, Xpert MTB/RIF assay). Children diagnosed with TB are linked to treatment and followed up during the course of treatment.

Results: Screening identified 1,095 children with TB between July 2016 and December 2017 with the majority of the TB cases identified in the 5-9 years group (n=465, 42.5%) (10-14 years: n= 325, 29.7 %, 1-4 years: n=303, 27.7%, and < 1: n=2,0.2%). Diagnosed patients were notified to the National TB Program (NTP). The number of children with TB reported from our Childhood TB sites increased from 1,333 in 2016 to 1,974 in 2017, resulting in a 48% increase in notifications. Overall in Karachi a 52% pediatric TB notification increase was seen in 2017 (n=2,955) compared to 2016 (n=1,948). Pediatric notification as a proportion of all forms TB cases notified by the city increased from 9% (1,948 of 20,560 all-forms TB cases) in 2016 to 11% (2,955 of 25,064 AFTB cases) in 2017.

Conclusions: Screening at busy hospitals can help identify children with TB who may otherwise be missed or present late to the health system. Strengthening of health systems with trained health personnel and diagnostic capacity is essential.

PS25-666-26 Assessment of the IPT cascade for under five childhood contacts of smear-positive TB

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Background: In Kenya, 6 months of isoniazid preventive therapy (IPT) is recommended for children under the age of five years who are close contacts of smear positive TB after exclusion of active disease. Despite proven effectiveness of IPT for reducing the risk of developing TB, initiation and completion of IPT is low in many countries. We sought to evaluate the programmatic performance of the IPT cascade among child contacts in western Kenya.

Methods: We conducted a retrospective cohort analysis of data abstracted from IPT registers from health facilities in Kisumu County. The study included all children aged under five years enrolled on IPT in 2013 through 2015 because they were TB contacts; children who initiated IPT as part of the management of HIV were excluded. Data on smear positive TB notifications was obtained from the electronic TB register (TIBU).

Results: From 2013 through 2015, 4125 smear positive TB cases were reported in Kisumu; 109 were children and 4016 were adults. In the same period 114 children aged under five years who were contacts of smear positive TB were enrolled on IPT, for an average of 1 child enrolled on IPT per 36 smear-positive cases. Of the childhood contacts on IPT 54% (n=61) were female. HIV testing was recorded for 83% (n=95) children, of whom 4% (n=3) were HIV-infected. A total of 60 (n=68%) children completed the 6-month course of IPT. Evaluation results for 6- and 12-month follow-up visits were recorded for 27% (n=31) and 3% (n=3) children, respectively.

Conclusions: Very few children were enrolled on IPT compared to the number of patients treated for smear-positive TB. There was a high rate of non-completion of six months of IPT, with poor follow-up. We recommend intensified identification of child contacts of smear positive cases and closer adherence monitoring.

PS25-667-26 Alarming child TB under-reporting in Pakistan: need to strengthen child TB surveillance

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Background: Every day, up to 200 children lose their lives to tuberculosis, which is a preventable and curable disease. TB in children is often missed or overlooked due to non-specific symptoms and difficulties in diagnosis.

This has made it difficult to assess the actual magnitude of the childhood TB epidemic, which may be higher than currently estimated. Most patients in Pakistan visit at least 4-5 healthcare providers before receiving TB diagnosis, resulting in long treatment delays. In Pakistan, 27% of TB cases were not notified to NTP and under-reporting was 2.5 times higher in age group < 15 years.

Methods: The present study aimed to quantify the level of under-reporting to the national surveillance system, among diagnosed childhood TB cases. A surveillance system was established among all non-NTP providers in randomly selected 12 districts across Pakistan from April to June 2016. Record linkage was done to measure the under reporting.

Results: Across those facilities, 8,056 children were enumerated in total of which 7,125 were considered to be presumptive TB cases. Of the presumptive TB cases, 623 (9%) were bacteriologically-confirmed, 4,626 (65%) clinically-diagnosed, 786 (11%) not a TB case, 834 (12%) still under investigation. Of the 5,249 TB cases diagnosed from the health facilities participating in the study during the study period only 153 were notified to the NTP. During the same period and across the same districts participating in the study an additional 1,283 children were diagnosed with TB and notified to official NTP data. This corresponds to a crude, national level of TB under-reporting among children of 78% which is huge.

Conclusions: The study estimated that the proportion of cases notified to the NTP was very low. TB surveillance should be strengthened to reduce under-reporting in children and special attention must be given to GP's and private child TB specialist.

PS25-668-26 Xpert MTB/RIF assay to diagnose suspected pediatric tuberculosis: a retrospective cohort study in Shanghai, China

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Background: As the majority of childhood tuberculosis (TB) is bacteriologically unconfirmed and just clinically diagnosed, diagnosis of childhood TB remains a challenge in China. WHO recommends that Xpert MTB/RIF assay (Xpert) can be used as the initial test in children with suspected TB instead of attempting to detect Mycobacteria through smear and culture, but little data about Xpert in the diagnosis of pediatric TB in China has been reported. We aim to evaluate the diagnostic performance of the Xpert in suspected pediatric TB according a retrospective cohort study.

Methods: Retrospective review of children evaluated for presumptive pulmonary TB in Shanghai Public Health Clinical Center in China, from January 2014 to Decem-

ber 2017. All children were tested by smear microscopy, solid or liquid culture, and Xpert. Sensitivity and specificity were calculated to assess the performance of Xpert. Kappa statistics were calculated to assess agreement between Xpert and culture.

Results: We enrolled 173 children for sputum sampling. 25 children were excluded, and 145 children were analysed. Using culture as a reference standard, Xpert Sensitivity among culture-positive samples were 66.7% (32/48, 95% CI 51.5-79.2), 76.7% (23/30, 95% CI 57.3-89.4) for smear-positive and 50% (9/18, 95% CI 26.8-73.2) for smear-negative TB, respectively, specificity of Xpert was 87.6% (85/97, 95% CI 79.0-93.2).

There were 12 culture-negative but Xpert-positive children and 16 Xpert-negative but culture-positive children were eventually diagnosed as pulmonary tuberculosis during the follow-up.

The agreement between the Xpert and the culture was 81% (kappa=0.56). Xpert and culture detected 10 and 11 cases of rifampicin resistance TB, respectively, these two methods performed similarly in detecting rifampicin resistance.

Conclusions: Xpert is an efficient diagnostic tool in childhood tuberculosis, however, using xpert or culture alone can lead to missed diagnosis of childhood tuberculosis. The combined use of culture and Xpert is superior to use culture or Xpert alone.

PS25-669-26 Improving pediatric TB diagnosis in North Kivu, DR Congo, by targeted GeneXpert on gastric aspirates

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Background: According to WHO estimates, the incidence of tuberculosis (TB) in the Democratic Republic of Congo (DRC) is 323/100,000. A context of civil conflict, displaced populations and mining activities suggests a higher regional incidence in North Kivu. Médecins Sans Frontières (MSF) supports the General Reference Hospital of Masisi, North Kivu, covering a population of 520,000, including a high number of malnourished children. Twenty-five percent of the current TB cohort in Masisi are children. HIV prevalence is less than 1%. In the summer of 2017, Gene X-pert on gastric aspirates (GA) were introduced and utilisation of the MSF pediatric TB diagnostic algorithm was reinforced.

Methods: We performed a retrospective review of TB diagnosis and treatment in children admitted to pediatrics and the inpatient therapeutic feeding centre (ITFC). We compared the last 6 months of 2016 and 2017. Targeted GA was performed respecting the MSF pediatric TB diagnostic algorithm in 2017.

Results: In 2017, 94 GAs were performed, compared to 0 in 2016. Twelve percent (11/94) of samples were Gene Xpert positive. Sixty-eight children (3,1% of total admissions) started TB treatment in the second half of 2017, compared to 19 (1,5% of total admissions) in 2016 ($p < 0.05$). Patients with a negative Gene X-pert result, but a clearly positive result of the TB diagnostic algorithm, started treatment based on clinical criteria.

Conclusions: After the introduction of Gene X-pert for GA samples and the reinforcement of the MSF pediatric TB diagnostic algorithm, more than 3 times the children started on TB treatment than previously observed, mostly on clinical grounds. Increased awareness of clinicians, due to the frequency of positive pediatric sample results, likely played a role in increasing TB diagnosis.

PS25-670-26 Implementation of systematic investigation and preventive therapy in children under 5 years living with smear-positive pulmonary tuberculosis in four French-speaking African countries: preliminary results

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Background and challenges to implementation: To demonstrate the feasibility of systematic investigation and preventive therapy for contact children within the National Tuberculosis Program (NTP) framework and to document the effectiveness of this intervention.

Intervention or response: The study has been implemented in 4 countries: Benin, Burkina Faso, Cameroon, Central African Republic. Children under 5 years, close contacts of smear-positive pulmonary tuberculosis (SS+PTB) patients recruited in 13 participating Basic Management Units are enrolled. Children are evaluated during home and clinic visits using standardized questionnaire, clinical examination, tuberculin skin test and chest X-Ray. Children free of active TB received preventive therapy using 6-month isoniazid in Benin or 3-month rifampicin-isoniazid (RH75/50) regimen in other countries. Children are followed-up every month during their treatment, and every three months during 12 months after the end of their treatment.

Results and lessons learnt: Within 18 months of implementation, 4 314 patients notified with SS+PTB were interviewed and 1 162 were eligible, of which 1 065 (92%) gave consent and were visited at home. A total of 1 943 children were included, of whom 99 (5%) were diag-

nosed with active TB and 1 753 (90%) started preventive therapy. Wide inter-country differences were observed in rates of X-rays abnormalities and in prevalence of TB diagnosed at inclusion. No serious adverse event was reported and very few TB cases were diagnosed during the course of preventive therapy. Standardized tools were developed and distributed.

Conclusions and key recommendations: These results indicate that preventive treatment is feasible within NTP framework provided appropriate staff training, friendly information to patient's families and transportation fees for home and clinic visits. The 3 RH regimen appears well accepted with no evidence of lesser effectiveness. Results reinforce the need to generalize contact tracing and preventive therapy among children.

PS25-671-26 Enhancing laboratory diagnosis of Mycobacterium tuberculosis in samples from children in The Gambia

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Background: Routine laboratory diagnostic methods for *M. tuberculosis* complex (MTBC) in induced sputum samples such as smear microscopy, GeneXpert and liquid Mycobacteria growth indicator tube (MGIT) culture are often negative due to the paucibacillary nature of childhood tuberculosis. We hypothesise that prolonged incubation beyond routine culture time could potentially improve MTBC detection in specimens.

Methods: Out of over 1000 induced sputum samples collected during our childhood TB contact tracing research program, we randomly selected 102 MTBC-negative MGIT cultures that had either been reported

as contaminated (n=35) or negative (n=67) and further incubated these at 37°C for the duration of one month. Ziehl-Neelsen microscopy, MPT64 Antigen secretion and GeneXpert tests were repeated on all samples to detect MTBC. Bacterial DNA was extracted by CTAB method and genotyped using Spoligotyping analysis.

Results: Of the 1160 routinely collected induced sputum samples 12 (1%) were smear positives; 41 (3.5%) Xpert positives and 51 (4.4%) MGIT culture MTBC positives. The remaining MGIT cultures were flagged as contaminated 393 (33.9%) or MTBC negative 644 (55.5%). After prolonged incubation and retesting of the randomly selected ones, 26/102 (25.5%) were now microscopy positive, 2/55 (3.64%) were GeneXpert positive, 8/102 (7.8%) MPT64-Antigen positive, and 38/102 (37.2%) had readable Spoligotyping patterns. The predominant lineages were *Mtb*-Euro-American 16 (42.1%), *Mtb*-Indo-Oceanic 11 (28.9%) and *M. africanum* West African type-2 8 (21%).

Conclusions: Prolonged incubation of routinely MTBC-negative induced sputum cultures yielded positive results upon retest, highlighting the low sensitivity of routine diagnosis tools on pauci-bacillary paediatric samples. Spoligotyping was more sensitive to detect MTBC compared to GeneXpert. However, prolong incubation will cause diagnostic delays and thus better strategies are needed to improve timely childhood TB diagnosis.

PS25-672-26 Scaling up childhood TB diagnosis in Malawi through capacity building and active contact investigation

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Background and challenges to implementation: The diagnosis of tuberculosis (TB) in children is a challenge globally. In Malawi, where only 54% of all TB cases are identified, an even larger gap likely exists in identifying children with TB. This gap is exacerbated by challenges intrinsic to the manifestation of TB in children, as well as limited resources available for investment in clinical capacity building and follow up for children known to be exposed to TB.

Intervention or response: The National TB Control Programme (NTP) in Malawi, working with the Clinton Health Access Initiative and the USAID-funded Challenge TB project, carried out an assessment on the knowledge and practice of managers and frontline clinicians on the subject of TB diagnosis and management in pediatric populations; the findings were used to guide the development and scale up of a Childhood TB diagnosis training for clinicians as well as standard operating

procedures for conducting TB contact investigations. Facilities within high-burden districts were classified as high, medium, and low volume based on historical TB burden and catchment size. Beginning with high-volume facilities, clinicians from each facility received a focused, two-day Pediatric TB Clinical Essentials training, including the provisioning of Childhood TB Diagnostic job aides. The training was then scaled to medium and low volume facilities in the target districts. Strengthening of TB Contact Investigation occurred concurrently in the same districts.

Results and lessons learnt: The number of children diagnosed with TB annually in the target districts increased by 20.65%, from 1,312 children diagnosed in 2016 prior to the training to 1,583 children diagnosed in 2017 during and following the training.

Conclusions and key recommendations: Diagnosis of childhood TB requires skilled staff that receive active mentorship. These models demonstrate an effective means of improving the capacity of clinical staff to diagnose TB in children, as well as contacts of known TB patients.

Notified TB cases all forms	2016	2017
0-4 years old	504	642
5-14 years old	808	941
Total Childhood Notifications (0-14 years)	1312	1583

[Childhood TB Notifications]

PS25-673-26 Baseline characteristics and clinical presentation of African and Indian children with smear-negative non-severe (minimal) TB in the SHINE trial

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Background: The appropriate treatment period for TB in children, in particular minimal TB, has never been subjected to a randomised trial. We describe baseline characteristics and the clinical presentation of children enrolled in the SHINE trial.

Methods: SHINE is a phase III, treatment shortening (4 vs. 6 months) randomised trial of first line treatment, using standard recommended doses and novel WHO pre-qualified paediatric fixed-dose combination (FDC) dispersible tablets. 1200 HIV-infected and uninfected children, < 16 years, with smear-negative TB (pulmo-

nary or peripheral lymph node disease) are being enrolled from 5 sites in South Africa, Zambia, Uganda and India (Chennai and Pune).

Results: 880 children (53% male, 13% HIV-infected, median age 3.3 years (IQR 1.4, 6.8)) were enrolled up to March 2018. Children in India were older compared to Africa (median age 7.6 (IQR 5, 10.5) and 2.8 (IQR 1.3, 5.9) years, respectively); most HIV-infected children were enrolled in Zambia (30%). Most commonly reported symptoms were weight loss/poor weight gain (64%), cough (82%) and fever (54%) with 320 (36%) reporting all three. Most children (64%) had cough \geq 2 weeks; 444 (50%) had a known TB contact in the last year. Overall, 94% (n=827) had abnormal chest X-ray. Of 643 children tested, 59% had positive Mantoux. 13% of 719 had culture-confirmed TB.

Conclusions: Despite known challenges of TB diagnosis and respiratory sample collection in children, SHINE is on track for completing enrolment and 18 months follow-up by end 2019 with results expected in 2020. Most children presented with cough and weight loss. Compared to Africa, children enrolled in India are older and more commonly present with lymph node enlargement and fewer respiratory symptoms. Nested SHINE sub-studies are investigating the pharmacokinetics (plasma and hair) and acceptability of the new FDCs in Indian and African children. Samples are being stored for diagnostic and biomarker studies.

Clinical presentation	India n=104 (%)	South Africa n=224 (%)	Uganda n=280 (%)	Zambia n=272 (%)	Total n=880 (%)
Cough +/- other symptoms	55 (53)	182 (81)	264 (94)	223 (82)	724 (82)
Enlarged peripheral lymph node(s) with no cough	38 (37)	19 (8)	9 (3)	9 (3)	75 (9)
TB Contact in the last year	45 (43)	148 (66)	147 (53)	104 (38)	444 (50)
Other clinical presentation (e.g. fever, weight loss/poor weight gain, night sweats)	11 (11)	23 (10)	7 (3)	40 (15)	81 (9)

[Baseline Clinical Presentation in children by Country in the SHINE TB treatment shortening trial (n=880)]

PS25-674-26 Use of chest radiographs in a Phase 3 randomised controlled efficacy trial for treatment shortening of non-severe drug-susceptible TB in children: the SHINE Trial

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Background: Chest x-ray (CXR) is an important diagnostic tool for paediatric pulmonary tuberculosis (PTB). SHINE is a randomised open-label multicentre non-inferiority trial comparing 4 versus 6 months of standard first-line TB treatment in 1200 children with non-severe PTB and/or peripheral TB lymphadenitis. Eligibility depends on local site clinicians' assessment of TB disease status and severity. We describe clinician assessment of baseline CXR features across countries.

Methods: Children < 16 years, with non-severe TB, were enrolled at 5 sites in Zambia, South Africa, Uganda and India. Workup included symptom screen, TB contact history, CXR, clinical assessment, HIV testing and bacteriology (smear, Xpert MTB/Rif and culture). Children with smear+ PTB or clinical or radiological features of severe TB were ineligible (and not described here). Clinicians were trained on reading CXRs and completed standard CXR reporting forms; CXRs were classified as 'typical' or 'not typical' of TB and by severity of radiological features.

Results: Baseline CXR data were analysed for 881 children enrolled: 47% female; median age 3.3 years (IQR 1.4, 6.8); HIV prevalence was 13%. Overall, 90/719 (13%) children had culture-confirmation of *Mycobacterium tuberculosis*. 351/881 (40%) of CXRs were classified as 'not typical of TB' (Table). The commonest radiological pattern in the 'typical TB' spectrum was 'uncomplicated lymph node disease' (511/530, 97%) and in the 'not typical TB' was perihilar infiltrates (231/351, 66%). Variability in CXR reporting across countries was minimal.

Conclusions: Despite challenges in interpreting CXRs for PTB in young children, acceptable quality CXRs were reported from all sites. Appropriate training, standard reporting forms and well-defined approaches for classifying radiological abnormalities were essential. 40% of children with non-severe PTB had CXRs reported as 'not typical' of TB. Independent retrospective blinded expert reading of CXRs is ongoing, and will provide information to an independent committee adjudicating TB disease status and trial endpoints.

	India (2 sites) N (%)	South Africa N (%)	Uganda N (%)	Zambia N (%)	Total N (%)
Number with CXR	103 (12)	224 (25)	280 (32)	274 (31)	881 (100)
CXR classified as acceptable quality	99 (96)	189 (84)	275 (98)	260 (95)	823 (93)
CXR classified as 'typical of TB'	49 (48)	131 (58)	184 (66)	166 (61)	530 (60)
CXR classified as 'not typical of TB' (includes 'normal')	54 (52)	93 (42)	96 (34)	108 (39)	351 (40)

[Baseline chest radiographs (CXR) in children (n=881) enrolled in the SHINE TB treatment shortening trial by country, reported by site clinicians]

PS25-675-26 Active case finding at tertiary care hospitals to increase pediatric tuberculosis case notification in Bangladesh

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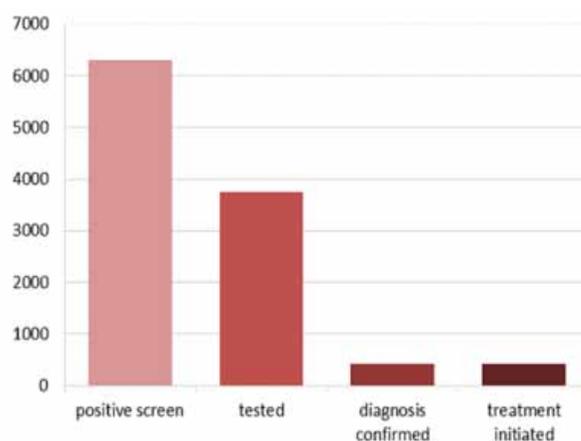
Background and challenges to implementation: Every year, nearly one million children develop tuberculosis (TB) worldwide, and 400 die from TB every day. In 2016, the majority of cases were missed; only 9,266 (26%) of the estimated 36,000 pediatric TB cases in Bangladesh were notified. Active case finding (ACF) can be an effective intervention to increase case notification in children to address this gap.

Intervention or response: Between March and December 2017, children were verbally screened at the paediatric outpatient departments (OPDs) of six tertiary hospitals. At each of the hospital, two health workers (HWs) screened all pediatric OPD patients using an electronic decision support screening tool (on Android's smart phone platform) to identify suspected TB cases. All suspected TB cases were referred for clinical evaluation and diagnostic test (Smear microscopy, GeneXpert, Chest X-ray, Histopathology etc.) to a hospital physician and, if diagnosed, were initiated on treatment according to the national child TB guidelines.

Results and lessons learnt: During this ten-month period a total of 240,564 children were screened. Among them, 6,295 (2.6%) were identified as suspected TB cases and, of these, 3,753 (60%) were tested. Among those tested, 409 (11%) children were diagnosed with TB and initiated on treatment. The mean age of those diagnosed was 7.6 years, and 214 (52%) of the sample were female. Of all diagnosed, 156 cases (38%) were pulmonary and 253 (62%) extrapulmonary. One out of every 588 children screened, were positive for TB. ACF resulted in an in-

crease in child TB detection in participating hospitals of 139 (34%) as compared to the corresponding period in 2016.

Conclusions and key recommendations: Data indicates that ACF at paediatric OPDs of big hospitals has increased child TB detection. Scale-up of ACF could supplement current strategies to find missing child TB cases, lead to early diagnosis, and better treatment for children in Bangladesh.



[Detection of Pediatric Tuberculosis through OPDs (March - December 2017)]

PS25-676-26 Immune reconstitution syndrome in hospitalized HIV-infected children starting ART

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Background: Children diagnosed with HIV during hospitalization often begin ART in the setting of TB co-infection, which may pose risk for immune reconstitution inflammatory syndrome (IRIS). Few prospective studies have evaluated incidence and determinants of IRIS in children with suspected TB.

Methods: ART-naïve HIV-infected hospitalized children were enrolled in a clinical trial on timing of ART initiation (< 48 hours vs. 7-10 days). Children were routinely followed for clinical evaluation at 1 and 2 weeks after ART initiation, and monthly thereafter for 6 months. Children were evaluated prospectively for symptoms or signs of IRIS, and suspected IRIS cases were classified by an external adjudication committee. At enrollment, children underwent intensified TB screening, including microbiologic confirmation of respiratory and stool

samples with Xpert/culture, CXR and TST. Children with suspected TB received TB treatment according to Kenyan national guidelines. HIV-1 viral load (VL) and CD4 count were obtained at enrollment. Chi2 tests and Cox regression were used to evaluate clinical associations with IRIS.

Results: Of 181 children starting ART, 22 (12%) had IRIS and median time to IRIS was 22 days (IQR 8, 47); 17 of 22 (77%) children with IRIS had suspected TB and received TB treatment. Clinical features associated with IRIS included finger clubbing ($p=.04$), Ghon focus ($p=.004$) or cavitory lesion on CXR ($p=.01$). Children with confirmed TB had increased risk for IRIS compared to children with unlikely TB [HR 8.8, 95% CI 2.7-29), $p<0.0001$]. Number of days on TB treatment prior to ART was associated with decreased risk for IRIS [HR .98 (95% CI 0.97-0.99), $p=.001$]. Higher baseline HIV log₁₀ VL was associated with increased risk for IRIS [HR 2.2 (95% CI 1.3-3.5), $p=.001$].

Conclusions: TB co-infection was a strong risk factor for IRIS among HIV-infected hospitalized children starting ART; clinical features associated with development IRIS may reflect TB bacillary burden.

PS26 Improving case finding and reducing diagnostic delays

PS26-677-26 Pre-treatment loss to follow-up from regional referral hospitals in Uganda: implications for optimizing the patient centered care model

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Background and challenges to implementation: The 2014/15 National TB prevalence survey established that the prevalence and incidence were 1.5 times higher than previous WHO estimates at 253 and 234 per 100,000 respectively. During 2017,40% of the expected annual incident TB cases were missed due to system and patient related factors affecting the cough to cure pathway including loss to follow up (LTFU). Accordingly, finding the missed TB cases and treating them to cure is the priority for the National TB control efforts. The USAID Defeat TB project is a five-year technical assistance mechanism for TB control that is aimed at increasing TB case detection and treatment outcomes using the

health systems strengthening approach. We assessed the linkage of newly diagnosed bacteriologically confirmed (BC) TB patients to treatment at selected hospitals in Uganda.

Intervention or response: We assessed the linkage of newly diagnosed bacteriologically confirmed (BC) TB patients to treatment by tracking diagnosed TB patients from the laboratory and presumptive TB registers to the treatment register at 9 hospitals. The TB cases that could not be traced through to the treatment register were notified as part of the activity and efforts were initiated to trace them from their communities to start treatment.

Results and lessons learnt: Of the 468 DS-TB cases diagnosed over 3 months, only 282 (60%) were duly initiated on treatment. Pre-treatment LTFU ranged between 4% and 47% at the different hospitals. The care teams were unaware of the gaps and did not utilize routine patient data for monitoring the diagnostic/treatment cascades, and designing client-centred care with proactive tracking and optimum linkages throughout the care pathway.

Conclusions and key recommendations: Strengthening the capacity of health facility TB care teams to routinely monitor and improve the TB diagnostic/treatment cascade will reduce the missed cases and optimize TB control efforts. Patient centered mechanisms for tracking linkage, retention and early treatment initiation will be essential to achieve this.

PS26-678-26 Tuberculosis intervention model targeting mobile population of truckers in Delhi, India

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Background and challenges to implementation: The mobile population of truckers is at considerable risk of Tuberculosis (TB) due to their work environment and lifestyle habits which make access to health care services a challenge under programmatic conditions. An intervention study was conceptualized for provision of quick diagnosis and treatment to the truck drivers while on route from transport hub in Delhi.

Intervention or response: The study targeted 100,000 mobile truckers population in the year 2016 with the objectives to demonstrate an effective model of TB intervention and to formulate specific strategies for implementing TB services in them. Para medical workers conducted TB advocacy campaigns with surround and

engage technique. TB diagnostic protocol and treatment services were modified and structured based on the need of truckers (within the framework of Revised National TB Control Program). McNemar test was deployed to measure the impact of the intervention on uptake of program services. An effective model of TB intervention in the mobile group of truckers was framed for State wide replication.

Results and lessons learnt: During the study period, 833 advocacy sessions were held and 16088 truck drivers sensitized. Knowledge on TB diagnosis and management showed significant increase after sensitization ($p < 0.01$) and 327 presumptive TB got tested. Majority of truckers had Clinical TB diagnosed based on Chest X-ray and clinical consultation from the program Chest Clinic. The modified diagnostic and treatment strategy reduced turnaround time for TB diagnosis (with upfront CB-NAAT) and treatment initiation. Continuation of care was ensured through reminder messages to assistants of truck drivers while on route.

Conclusions and key recommendations: TB Intervention model aligned within the network of ongoing activities at transport hubs is beneficial to improve access to program services in truck driver's population. The study shows that strong policy inducement promoting replication of the TB intervention model is essential to improve health service access among mobile population groups in high burden settings.

PS26-679-26 A novel community-based tuberculosis case finding mentorship intervention to find missing cases in Southern Nations Nationalities and Peoples Region, Ethiopia

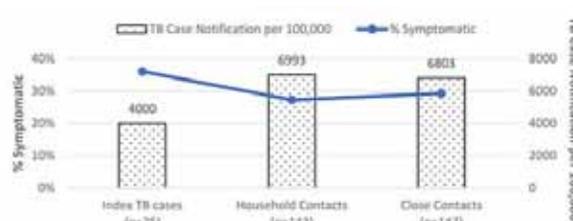
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Background and challenges to implementation: Tuberculosis (TB) case notification (CN) has been stagnant in SNNPR, Ethiopia for several years. A community based TB case finding (CF) mentorship intervention was designed to identify missing TB cases at community level.

Intervention or response: In SNNPR, USAID/Challenge TB (CTB) project adopted an intervention to improve CF via community based mentorship. In this intervention, TB CF was demonstrated at household level. TB screening was jointly conducted with TB focal persons, and health extension workers in households of index TB cases (ITBC) and their close contacts (CCs). Sputum samples were collected on the spot whenever presumptive cases were identified. This was done in catchment areas of 12 health facilities (HFs) located in Wolaita,

Dawro, and Konta zones. For demonstration purposes, the team visited a minimum of two households of ITBC per HF and a minimum of one neighboring household per ITBC.

Results and lessons learnt: The team visited 35 households of ITBC and 28 neighboring households (HHs) during October to November 2017. 36% (9/25) ITBC who completed treatment, 27% (39/143) household contacts and 29% (43/147) CCs were found to be symptomatic and investigated for TB which identified one relapse, 10 new TB cases each from household and CCs. Corresponding CN were 4000, 6993, and 6803 per 100,000 respectively. Following this demonstration, health care workers conducted contact investigation in households of ITBC (from the past five years) and four neighboring households per index case. This identified 135 new TB cases in December 2017, bringing total number of cases notified to 223 for the quarter, including 67 detected by passive CF. CN increased to 172/100,000, 3x from baseline notification and reaching national TB prevalence of 177/100,000.



[Tuberculosis Case Finding Demonstration by USAID/Challenge TB Team, Oct-Nov 2017]

Conclusions and key recommendations: CTB team contributed to 9% (21/223) of CN in intervention HFs during Oct-Dec 2017. CF using contact investigation by targeting household and CCs was effectively scaled-up at community level in identifying missing cases.

PS26-680-26 Targeted intervention to improve contact tracing and case finding in a complex case in a low-incidence country

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Background and challenges to implementation: Smear positive cavitory lung and intestinal tuberculosis was diagnosed in a young boy with Down syndrome after a doctor's delay of six months.

Contact investigation in the Netherlands is organized according to the stone-in-the-pond approach. The challenge for the public health was to conduct source and contact investigation within a group of mentally and physically disabled people.

Intervention or response: After initial risk assessment, close contacts were prioritized according to contact ring and vulnerability and invited for evaluation. For this

special target group we expected challenges in participation, no show, start and completion of treatment.

We chose a patient centered approach to enhance participation: all health education was adapted to the intelligence grade of this group. The investigation and necessary medical consultations were organized in the home environment of this group.

Results and lessons learnt: 94% of eligible contacts were evaluated, this is higher than the national average (87%). The percentage of contacts with active Tuberculosis (TB) or Latent tuberculosis infection (LTBI) was 22 % overall, indicating an extremely high level of infectiousness of the index patient, likely due to bad cough hygiene combined with a long diagnostic delay.

The number of contacts in the first ring was very high (70). The percentage who already developed TB or LTBI in the first ring was much higher than the national average of 1.8 % TB or 18.6% LTBI (2015).

Conclusions and key recommendations: The medical and nursing interventions, adapted to the intelligence grade of this group, proved efficient and effective, both for emergence and effective treatment of TB infections. In a low-incidence country the awareness of TB among General Practitioners and medical specialists is low, which could cause long delay. Awareness raising of TB is an important task for public health in low incidence countries.

Ring	Invited	Examined	Infected	Percentage	Active TB	Percentage
First	70	70	39	55.7%	4	5.7%
Second	166	152	15	9.9%	3	2.0%
Third	106	98	7	7.1%	2	2.0%
Total	342	320	61	19.0%	9	2.8%

[Results of the contact tracing and case finding]

PS26-681-26 Accessibility of health care facilities contributes to reducing pre-treatment delay among tuberculosis patients in Central India

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Background: A critical component of the End TB strategy is engagement of all care providers to ensure access to high-quality diagnosis and patient-centric care. In India, TB-symptomatics often begin health consultation from informal private sector, then seek care from qualified practitioners, and eventually end up in the public sector. There is a delay of nearly 2-months in diagnosing TB; patients are seen on average, by three different providers before diagnosis (Sreeramareddy et al, 2014).

Methods: A cross-sectional study was undertaken to measure the patterns of pre-treatment delays amongst microbiologically confirmed pulmonary TB (PTB) pa-

tients and reasons thereof. Data was collected from 8 districts of Madhya Pradesh (MP) amongst PTB patients registered in public sector and analyzed using SPSS for Windows version-23.

Results: A total of 163 new-smear positive PTB patients were interviewed, 63.8% males and 36.2% females. Median delay from onset of symptoms to first visit to any healthcare provider is 15-days; longest delay reported is 180-days. About 76.1% TB patients consulted healthcare provider within 30-days of onset of symptoms. Awareness about TB also influenced them (41.7%) in seeking early medical care (OR: 1.15; 95%CI: 0.56-2.37). Patients living within accessible distance from government healthcare facility reported earlier (OR: 2.84; p<0.005). TB patients who first visited a government healthcare provider were significantly associated with decreased overall delay in treatment initiation (OR: 1.65, 95%CI: 0.84-3.22). Accessibility to diagnostic healthcare facility is a factor for healthcare seeking behaviour (seeking care in public-sector), which further contributed to a decreased overall delay in TB treatment initiation (aOR: 0.82, 95%CI: 0.12-5.77).

Conclusions: Considering magnitude of pre-treatment delay, it is imperative to improve access to diagnostic and treatment facilities. Besides, strengthening partnership between public and private health sectors, improving access at periphery and educating community on symptoms and treatment of TB should be given due emphasis.

PS26-682-26 Experiences of household tuberculosis contacts with SMS results and instructions and influences on intention to seek care

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Background: WHO recommends household tuberculosis (TB) contact investigation in high-burden countries, but many patients who complete screening and evaluation for TB never receive test results. Use of automated short-messaging services (SMS) to deliver results could improve awareness of TB status and linkage to care. We sought to explore the experience of contacts with receiving test results and follow-up instructions by SMS, and the influence of these experiences on follow-up intentions.

Methods: Semi-structured interviews were conducted with household contacts of index TB patients. Participants had TB symptoms and provided sputum for TB testing. We asked the contacts how they felt about receiving their results via SMS and the actions that they took based on the SMS results. We organized emergent themes using the theory of planned behaviour (TPB), analyzing respondents' intentions to act on a request to respond by SMS if their symptoms persisted or worsened (for negative results) or follow-up at a clinic (for positive results).

Results: We interviewed ten contacts. They reported relief upon confirming their TB status via SMS, but also said they lacked confidence in results delivered by SMS. Until they spoke to a community health worker (CHW), some worried that their negative result was an error. Contacts said their intentions to request help via SMS or seek care were influenced by their beliefs about the curability of TB; expectations of support from CHWs; consequences of disregarding CHW instructions; and barriers to treatment.

Conclusions: Household contacts experienced relief when they received negative TB results by SMS. However, they were less confident about results delivered via SMS than results delivered by CHWs. Delivery of results by SMS should complement continued interaction with CHWs, not replace it.

PS26-683-26 Late presentation hampers successful TB treatment in the era of TB-HIV integrated care in Uganda

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Background: TB-HIV integration has been shown to improve TB treatment outcomes, but there is limited data on the sustainability over longer time periods. We aimed to assess TB treatment outcomes of HIV-positive patients enrolled on TB treatment during 7 years of TB-HIV integrated model of care at the Infectious Diseases Institute (IDI) clinic, Uganda.

Methods: We included HIV-positive adult patients newly diagnosed and initiated on TB treatment between 2009 and 2015. We described patients' characteristics, and TB treatment outcomes, focusing on proportion of treatment success ("cured" or "completed" treatment), deaths, lost to follow up, and promptness of antiretroviral therapy (ART) start. We used ² trend analysis to examine trend in TB treatment outcomes over the 7 years of integration. Kaplan-Meier and Log-rank methods were used to compare mortality across factors.

Results: The analysis included 1,318 new TB cases; over 7 years, majority of patients were females (>50%), median age ranged from 34 to 36 years, and >60% were late presenters (CD4 count < 200 -cells/ μ L at TB diag-

nosis), median CD4 cell count at TB treatment start ranged from 100 to 146 cells/ μ L. TB treatment success was sustained over the 7 years of TB-HIV integration ranging from 67% to 76%. Loss to follow-up (LTFU) systematically declined, from 7% in 2010 to 3.4% in 2015 (trend P value < 0.01). ART start during intensive phase improved from 47% in 2009 to 97% in 2015 (trend P value < 0.01). Nonetheless, deaths remained stable (>15%) overtime, and the probability of death at month 2 of TB treatment was 52% higher among late presenters compared to non-late presenters (13% vs. 6%, P value < 0.01).

Conclusions: Positive initial gains from TB-HIV integration can be sustained overtime with a complete integration model in a resource limited setting, however treatment success can be compromised by late presenters.

PS26-684-26 Assessment of health facility based active case finding intervention effect in increasing TB case notification among the elderly

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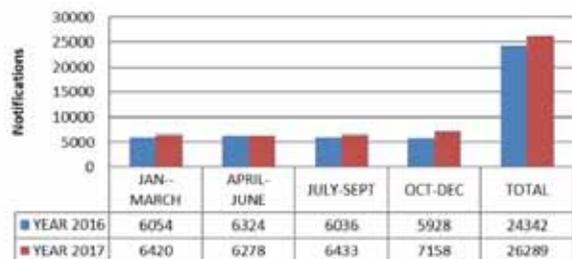
Background and challenges to implementation: According to 2017 WHO TB Global Report, Tanzania misses 108,429 TB cases annually. CTB in collaboration with National Tuberculosis Program (NTP) is implementing health facility based active case finding (HFB-ACF) aiming at increasing case detection. The Global report also states a high TB prevalence among the elderly suggesting a 2 folds higher rate than the rest of the population.

Intervention or response: ACF implementation among elderly was scaled up from 20 to 32 Health Facilities in CTB supported regions by December 2017. Targeted TB screening was conducted among all elderly aged 55 years and above who attended geriatrics clinics. The National Quality Improvement (QI) Toolkit for TB case detection with presumptive TB registers as key tools, were used to conduct and document ACF. Formal orientation, focused mentoring and health care workers sensitization facilitated incorporation of ACF agenda in the facility QI plans. QI focal persons were appointed as custodians of ACF in those HFs.

Results and lessons learnt: We observed an increasing trend of quarterly TB case notified among elderly aged 55 years and above, during the intervention period of April -December 2017, as compared to the similar period before the intervention in 2016, Figure 1. TB notification among elderly in the same HFs also reveals 19.7% contribution to annual notification increase in 2017.

Conclusions and key recommendations: Since the intervention demonstrates increasing yield of TB cases among elderly at HFs, it calls for the need to strengthen TB screening in elderly in existing clinics and beyond.

Scaling up of geriatrics clinics is therefore recommended as potential sites for increasing TB case detection. ACF focused mentorship visits were the catalyst for the intervention.



[Comparative TB Case notification among elderly pre and post HFB-ACF intervention]

PS26-685-26 Increasing TB case finding through implementation of Leadership Development Program action plans in selected Nigerian states

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Background and challenges to implementation: Low tuberculosis (TB) case finding remains a huge challenge in Nigeria. Despite all efforts, the National TB and Leprosy Control Program (NTP) was only able to notify 15% (90,584) of the estimated 586,000 cases in 2015 and 25% (100,433) of the estimated 407,000 cases in 2016. This represents a huge gap in case finding.

Lack of motivation, resources, and leadership abilities have had detrimental effects on the attitude and commitment of health workers and this has been identified as the reason for low case finding.

The goal of this intervention was to use the Leadership Development Program (LDP) to foster leadership and management skills in health workers for performance improvement.

Intervention or response: The LDP training was conducted for the State, Local Government TB team and selected health workers in Rivers and Akwa Ibom states on the 6th-9th September 2016 and 8th-11th November 2016 respectively. Action plans to increase case finding within six months were made after the training, which focused on the following skills:

- Good service delivery
- Timeliness
- Information dissemination
- Professionalism
- Teamwork & motivation

Emotional Intelligence: self-awareness, social-awareness, self-management, and relationship-management.

Results and lessons learnt: Analysis of pre & post-LDP case finding trends from 2016-2017 in the states shows that:

- 22% (822) and 9% (735) increases in Q1&Q2 2017 compared to pre-LDP Q4 2016 (673) in Akwa-Ibom.
 - 17% (724) and 23% (759) increases Q4 2016 & Q1 2017 compared to pre-LDP Q3 2016 (617) in Rivers.
- These rates continued to be marginally higher than pre-LDP periods throughout the year

Conclusions and key recommendations: The steady increase in case finding can be attributed to the gains of the LDP; its impact has helped to increase the commitment of health workers and improve professionalism, thereby strengthening the health system.



[Comparing the case finding trend of Challenge TB (pre & post LDP) and non-Challenge TB States]

PS26-686-26 How does the community contribute to increased TB case finding?

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Background: Indonesia continues to face challenges in TB control. Based on the 2014 prevalence survey, the TB prevalence in Indonesia was 647 per 100,000 population with 1,020,000 incident cases annually. Active tuberculosis case finding (ACF) is considered an effective approach to improve the case detection rate and requires engagement at the community level. Since 2013, Lembaga Kesehatan Nahdlatul Ulama (LKNU) has built the experience to implement ACF at the community level in Indonesia through the engagement of volunteer cadres. **Methods:** LKNU covered 35 - 50% of Public Health Center (Puskesmas) sub-districts in 10 ten districts. 359 trained and active volunteer cadres conducted home visit to do verbal screening to close household contacts, including neighbors and family members of the patients. People identified with TB symptoms would be referred by the voluntary cadres to the Puskesmas for diagnosis. Diagnostic results were collected routinely and analyzed

by LKNU data officer, with subsequent comparison of these results to the trends of achievement within the last 5 years of project cycle in the districts.

Results: LKNU support showed an impressive increase in smear positive findings at the *Puskesmas*. Percentage of contribution attributable to CEPAT-LKNU in this overall increase in smear positive findings varies, ranging from 6 - 37%. The highest contribution was in Kediri district in East Java province (37%).

Conclusions: The role LKNU with voluntary cadres showed the impressive impact of ACF at the community level as implemented through volunteer workers in increasing TB case finding in districts. Continued support from government and other stakeholders is needed for future success, especially for capacity building logistical considerations like transportation costs and rewards to motivate the volunteer cadres.

PS26-687-26 Effectiveness of an upfront sputum sample collection and transportation strategy to reach missed TB cases: a study of 62 districts in India

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Background and challenges to implementation: India tops the list of the countries with highest missed tuberculosis (TB) cases. One of the major challenges to reach missed TB cases is to ensure all presumptive TB patients (PTBP) get diagnostic test for TB. Through project Axshya SC&T offered to identified PTBPs during implementation period of Phase II (April'13 - September'15) and Phase III (October'15 - December'17) in 62 districts of 7 states (Haryana, Delhi, Rajasthan, Bihar, Uttar Pradesh, Chhattisgarh and Maharashtra) in India.

Intervention or response: In 62 districts project Axshya was implemented for community mobilization. This study based only Phase II and Phase III of this project. In Phase II emphasis was given on identified PTBPs get tested on their own through referral, if they didn't reached to designated microscopy centre (DMC) for smear sputum test then only SC&T offered to them. In phase III, upfront SC&T was offered to all PTBPs along with referral. Information were collected using questionnaire, verified with DMC laboratory register and data analysed using SPSS software.

Results and lessons learnt: In Phase II 56% of identified 227966 PTBP offered for 'Referral' and 44% for 'SC&T', whereas in Phase III it is 36% 'Referral' and 64% 'SC&T' out of 141591 PTBP. Using upfront SC&T strategy chances of getting test done at DMC increase from 57% in Phase II to 72% in Phase III among total identified PTBP. This strategy also enhances chance of TB patient (TBP) identification among total identified PTBPs from 5% in Phase II (11075 TBP out of 227966 PTBP) to 8% in Phase III (11134 TBP out of 141591 PTBP), 1.6 times higher than Phase II.

Conclusions and key recommendations: Results of our intervention suggest that offer of upfront SC&T to all PTBP can potentially prevent sizeable number of TB cases getting missed. We recommend replicating this on a larger scale to reach missing millions.

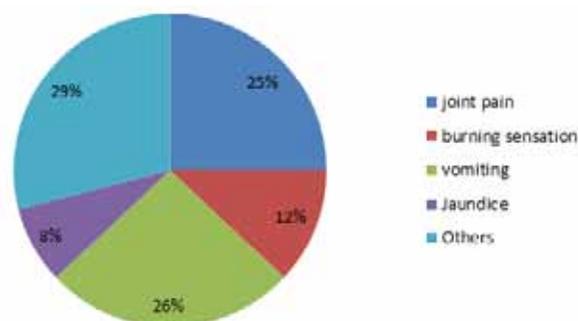
PS26-688-26 Monitoring DOTS in patients with multidrug-resistant tuberculosis in Bangladesh using mHealth platform

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Background and challenges to implementation: Bangladesh is a high tuberculosis (TB) burden country with an estimated 5,300 multi drug resistance TB (MDR-TB) cases. Community-based programmatic management of DR-TB was introduced in 2012. Currently, trained directly observed treatment, short-course (DOTS) providers use mobile phones with an application to monitor activities and improve patient management through an MDR-TB DOT monitoring system. While visiting patients, the DOTS provider submits data about medications, side effects and symptomatic contacts which enables real-time monitoring of DOTS provider's performance and other supportive tasks.

Intervention or response: During each DOTS session, an mHealth application guides the provider through the treatment protocol while recording the patient's treatment data. The GPS function of the mobile phone verifies exactly where each DOTS session was held and recorded. We analyzed and demonstrated how the mHealth platform was used for monitoring and supervising DOTS services for MDR-TB patients and improving treatment adherence.

Results and lessons learnt: Between June 2013 and January 2018, the mHealth app monitored 1,657 MDR-TB patients' treatment and their DOTS providers' activities. Currently, 453 DOT providers in 42 districts are being supervised and monitored using the smart phone application.



[Most common side effects reported by patient (January 2017-January 2018)]

Data indicates that using mHealth platform over 93% DOTS for MDR-TB patients were ensured that resulted in increased treatment compliance. From January 2017-January 2018, the built-in adverse events monitoring system successfully referred 99% of 172 patients who experienced side effects to nearest doctors/facilities for treatment.

Conclusions and key recommendations: The mHealth application provides real-time information regarding DOTS and side effects and ensures patients are receiving daily treatment in the community. It also demonstrated the potentials of enhancing the quality of care for MDR-TB patients and can serve as a vital component of patient-centered TB care in Bangladesh.

PS27 Xpert for all: optimistic or realistic?

PS27-689-26 Decentralization of Xpert MTB-Rif in to hospitals: the impact on MDR case finding. Jogjakarta, Indonesia

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Background: In the 2017, the Jogjakarta Provincial Health Office (PHO) expanded eight Xpert MTB/RIF machines in eight hospitals in five districts. Pre-decentralization, there was one Xpert MTB/RIF machine in laboratory A and one MDR referral hospital. All health facilities had to refer presumptive MDR TB to the MDR referral hospital, which were examined in laboratory A. Post-decentralization, eight hospitals now can receive presumptive MDR TB from community health centers (Puskesmas) and other hospitals. Only RR cases will be referred to the MDR referral hospital. With this decentralized approach, the expectation is to increase case findings and case detections.

The objective of the study was to evaluate any difference in case findings and case detections of MDR TB pre-and post-decentralization.

Methods: Data were collected from PHO and hospital Xpert MTB/RIF reports (TB 04). All presumptive MDR TB included without inclusive and exclusive criteria. We compared data from August until December 2016 (pre-decentralization) with data from August until December 2017 (post decentralization). Descriptive analysis used SPSS and t-tests to determine any significant differences between the two conditions.

Results: The increased number of test between pre- and post-decentralization periods (312 cases to 992 cases) was significant (P value < 0.05, with $p=0.004$). There

was also an increased number of presumptive MDR TB tested /case findings from 312 to 443 cases, which was significant (P value < 0.05, with $p=0.021$), although the increased RR case detection from 7 to 14 cases was not significant (P value > 0.05, with $p=1.000$). The referral cases from Puskesmas decreased from 29% (91) to 3.6% (23) of cases which were referred to Xpert MTB/RIF in the hospitals.

Conclusions: Post-decentralization, there was almost three-fold increase of Xpert MTB/RIF test, and double the number of case detections. To proportionally increase case findings and case detections, the Xpert MTB/RIF expansion must be in line with the strengthening of the referral networking.

PS27-690-26 Xpert MTB/RIF assay for detection of rifampicin-resistant *M. tuberculosis* from presumptive drug resistance tuberculosis patients in Ethiopia

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Background: Rifampicin is a potent first line drug for treatment of *M. tuberculosis* and acts by inhibiting bacterial DNA-dependent RNA polymerase, encoded by the RNA polymerase gene (*rpoB*). Resistance to rifampicin has mainly been associated with mutations in the *rpoB* gene. Xpert® MTB/RIF (Cepheid, Sunnyvale, CA, USA) is real-time PCR technology that uses molecular beacons to detect rifampicin resistance in the *rpoB* gene. In the current study, we aimed to assess the accuracy of Xpert MTB/RIF for detection of rifampicin-resistance *M. tuberculosis* in pulmonary tuberculosis (TB) patients in Ethiopia.

Methods: A cross-sectional study was carried out at Mycobacteriology Research Center of Jimma University in Southwest Ethiopia. A total of 67 smear-positive sputum specimens collected from pulmonary TB patients with increased suspicion of drug resistance were tested by GenoType MTBDR^{plus} line probe assay and Xpert MTB/RIF tests.

Results: Of 67 pulmonary TB patients, 21 (31.3%) were multidrug resistant TB (MDR-TB) (resistant to both rifampicin and isoniazide). Xpert MTB/RIF detected rifampicin-resistance in 23 (34.3%) pulmonary TB patients, of these 22 were also confirmed to be rifampicin-resistant by line probe assay. In addition, 21 (91%) Xpert MTB/RIF-rifampicin-resistant cases were confirmed as MDR-TB cases, making rifampicin-resistance a good surrogate marker of MDR-TB in Southwest Ethiopia. Probe E related mutations (codon 447-452) was the most common *rpoB* genetic mutation observed in 87% of rifampicin-resistant strains, suggesting successful transmission of these strains in Ethiopia. Compared to line

probe assay, Xpert MTB/RIF detected all rifampicin-resistance cases correctly with 100% sensitivity and 97.8% specificity.

Conclusions: The high sensitivity and specificity of Xpert MTB/RIF for rifampicin-resistance detection support its use as an initial diagnostic test for drug resistance TB. Implementation of Xpert MTB/RIF for direct diagnosis of rifampicin-resistance would be of great benefit in adapting treatment regimens and limiting transmission of drug resistant strains.

PS27-691-26 GeneXpert positivity rate among smear negative TB patients in Mombasa County, Kenya in 2017

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Background: Mombasa Island has a population of 1.2 million people and is one of the 47 counties with high TB burden. The number of TB patients has been declining over the years from 5,000 in 2009 to 3,900 in 2017. The first post independent prevalence survey done in 2015 showed that country over 40,000 cases of TB are missed during the diagnosis. The County embraced Gene Xpert as first line of test early in 2017 to identifying these missing cases. There are seven machines in the County each serving an average population of 171,000 people. Lab networking system established through collaboration with partners to transport sputum sample from the peripheral facilities to Gene Xpert sites.

Methods: This is a cross sectional study involving a sample size of 431 who were tested by smear microscopy and were found to be negative and retested by Gene Xpert in the 2017. The Gene expert lab register was review for the study period for all the 7 testing sites.

Results: The participants were 62% (n=268) male and 38% (n=163) female with an age ranging from 2 years to 95 years old. Out of 431 samples retested by gene expert 25% (n=106) were found to be positive for MTB with 0.7% (n=3) rifampicin resistant.

Conclusions: This study showed that despite the test being negative for smear microscopy it cannot be ruled out as negative unless the same has been retested with gene expert.

PS27-692-26 Role of Xpert MTB/ RIF in diagnosis of tuberculous meningitis: genotypic, phenotypic and clinical evaluation

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Background: Tuberculous Meningitis (TBM) is one of the severe forms of Tuberculosis. Microbiological confirmation is difficult and treatment is often delayed which increases mortality and morbidity. The Xpert test was evaluated in a large cohort of patients with suspected tuberculous meningitis.

Methods: Five hundred eighty two cerebrospinal fluid (CSF) specimens from patients with clinical suspicion of tubercular meningitis received at accredited Intermediate Reference Laboratory (IRL) of an apex tertiary care centre in North India from April 2017 to December 2017 were subjected to ZN- microscopy, Xpert MTB/RIF assay and Liquid culture and Drug susceptibility testing by MGIT 960. Line probe assay (LPA) was done on culture positive isolates. Gene sequencing was performed on Rifampicin-resistance (RR)/MDR-TB isolates.

Results: Comparison of Xpert with culture, demonstrated sensitivity of 67.9% and specificity of 98.7% while comparison with Composite reference standards (CRS) showed sensitivity and specificity of 63.9% and 98.1% respectively. There was 100% concordance between the results of genotypic (Xpert, LPA and Sequencing) as well as phenotypic tests for rifampicin resistance.

Conclusions: In conclusion, the Xpert MTB/RIF test is able to rapidly identify a case of TBM with good sensitivity and specificity. The Xpert MTB/RIF gives a significant advantage in the early diagnosis and treatment initiation of this devastating condition.

PS27-693-26 Clinical utility of Xpert MTB/RIF assay for the diagnosis of extrapulmonary tuberculosis in Ethiopia

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Background: The diagnosis of extrapulmonary tuberculosis (EPTB) is often made on clinical suspicion alone, and many people receive the wrong diagnosis leading to unnecessary TB treatment or poor outcomes from untreated EPTB. In this study, we evaluated the

clinical utility of the Xpert MTB/RIF for detection of *M.tuberculosis* on routinely collected extra-pulmonary specimens in Ethiopia.

Methods: This study was carried out at Jimma University Specialized Hospital, Southwest Ethiopia from September 2015 to June 2017. Extra-pulmonary specimens were collected from 572 patients clinically suspected of suffering from EPTB. All specimens were tested for TB by smear-microscopy, culture and Xpert MTB/RIF. The diagnostic accuracy of Xpert MTB/RIF was calculated compared to a composite reference standard (CRS), composed of liquid culture and anti-TB treatment response.

Results: In total, 572 extra-pulmonary specimens (279 lymph node, 159 pleural, 80 peritoneal, 45 cerebrospinal and 9 pericardial fluids) were tested. The pooled sensitivity and specificity of Xpert MTB/RIF were calculated to be 91% and 90.6% respectively when compared to culture. The pooled sensitivity of Xpert MTB/RIF was decreased to 75% and the specificity was improved to 98% when Xpert MTB/RIF was compared to the CRS. The sensitivities among the specimen types differed markedly. The highest sensitivity was documented for lymph node (90%), moderate sensitivity for cerebrospinal (53%), while the sensitivity was lowest for pleural (30%) and peritoneal (32%) fluids. Xpert MTB/RIF in addition detected rifampicin resistance in 13 patients in perfect agreement with line probe assay.

Conclusions: Our study showed that Xpert MTB/RIF is likely to be of greatest utility when testing lymph node specimens. A negative Xpert MTB/RIF result on fluid specimens does not exclude the diagnosis of EPTB and patients with a high clinical probability of EPTB should be started on anti-TB treatment.

PS27-694-26 Valeur ajoutée du GeneXpert pour le dépistage de la tuberculose chez les usagers de drogue à Abidjan : comparaison d'algorithmes de diagnostic en vie réelle

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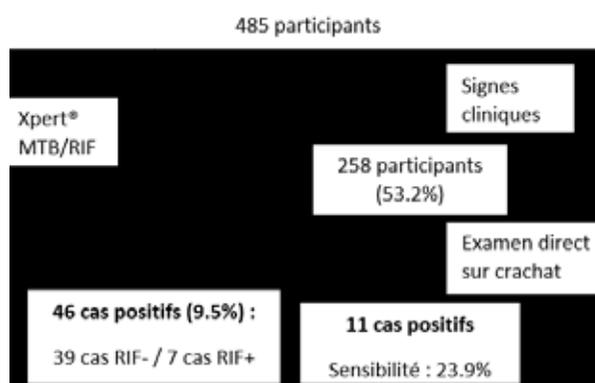
Background: L'usage de drogues (cocaïne/crack et héroïne) à Abidjan - Côte d'Ivoire - se fait principalement par inhalation dans des scènes ouvertes, appelées fumoirs, par 6.000 à 10.000 usagers de drogues (UD). Ce type de consommation favorise la transmission de maladies infectieuses respiratoires comme la tuberculose (TB). Les algorithmes de diagnostic de la TB basés sur l'examen direct sont peu sensibles, particulièrement

chez les populations immunodéprimées et malnutries comme les UD. A partir de données issues d'une étude de prévalence TB auprès des UD, l'objectif de cette analyse est de comparer plusieurs algorithmes de diagnostic de la TB pulmonaire.

Methods: Une étude transversale a été réalisée dans deux principaux fumoirs d'Abidjan. Les examens suivants ont été réalisés pour le dépistage de la TB : recherche de signes cliniques (SC), examen direct sur crachat (ED), Xpert® MTB/RIF, et radiologie pulmonaire (RP). Les participants Xpert® positifs ont été considérés comme ayant une TB pulmonaire confirmée. Seuls ceux ayant des résultats complets pour les différents examens ont été inclus dans cette analyse.

Results: Parmi les 532 participants de l'étude, 485 ont été inclus dans l'analyse, parmi lesquels 46 cas (9.5%) Xpert® positifs dont 7 cas (15.2%) résistants à la rifampicine. L'algorithme national de dépistage (SC puis ED) aurait dépisté 11 cas (sensibilité de 23,9%). D'autres algorithmes incluant les différents examens donnent une sensibilité comprise entre 13.0% (SC puis RP puis ED) et 71.7% (SC puis Xpert®). Ainsi, 76% des UD TB+ n'auraient pas été dépistés par l'algorithme national.

Conclusions: En Côte d'Ivoire, les UD sont particulièrement à risque de TB pulmonaire et doivent être considérés comme une population-clé dans les politiques de lutte contre la TB. Dans un objectif de santé publique, l'algorithme national devrait être révisé et inclure les UD comme population pouvant bénéficier du diagnostic par le Xpert®.



[Comparaison d'un algorithme Xpert® MTB/RIF et l'algorithme national de Côte d'Ivoire]

PS27-695-26 Challenges with implementation of Xpert MTB/RIF testing for tuberculosis using a hub-and-spoke model in Uganda. A health system perspective

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Background: Many high burden countries are scaling-up Xpert[®] MTB/RIF (Xpert) testing for tuberculosis (TB) using a hub-and-spoke model. Our objective was to assess variation in and challenges with Xpert implementation across a representative sample of health centers (spokes) linked to Xpert testing sites (hubs) in Uganda.

Methods: We conducted a mixed methods study at 23 community health centers linked to one of 15 Xpert testing sites between Nov 2016 and May 2017. Data sources included a standardized site assessment survey, routine TB notification data, and field notes from site visits.

Results: Of the 23 health centers, 14 were rural, 21 had stable electricity and 13 had a refrigerator for sample storage. Motorcycle riders transported sputum to Xpert sites and returned with test results once a week, 2x/week or 3x/week at 10 (43%), 9 (39%) and 4 (17%) health centers, respectively. Staff recorded Xpert results in the TB laboratory register at only one health center and called patients with positive results at only 2 health centers. Of the 15 Xpert testing sites, 5 (33%) had at least one non-functioning module. The median number of tests per day was 3.57 (IQR 2.06-4.54), and 10 (67%) sites had error/invalid rates >5%. Challenges with Xpert implementation occurred at every step of the diagnostic evaluation process (Table 1), leading to low overall uptake. 596 of 3044 (19.6%) patients were referred for Xpert testing. Of those, 57 (9.6%) were Xpert confirmed positive, and there was a substantial pre-treatment loss to follow-up (24 [42.1%]).

Conclusions: Although Xpert devices are now widely distributed throughout Uganda, health system factors across the continuum from test referral to results reporting and treatment initiation preclude effective implementation of Xpert testing for patients presenting to peripheral health centers.

Screening and referral	§ Staff awareness and use of TB case finding forms § Inconsistent use of presumptive TB registers § Lack of awareness among clinicians regarding which patients should be referred for Xpert testing
Sputum collection	§ Shortage of sputum containers (8 of 23, 35% health centers) § Lack of electricity and/or refrigerator to store sputum samples until transport (10 of 23, 43% health centers) § Failure of patients to return on anticipated sputum transport day (if sputum could not be stored) at all health centers
Sputum transport to Xpert testing site	§ Irregular sputum transport (range 1-3 times/week) § Improper packaging of the sputum samples before they are sent to Xpert sites in over half of the health centers. § Large number of health centers assigned to each hub rider (4-8 sites/day per hub rider) § Last-minute delays or absence by boda-boda riders limiting sputum transport at multiple health centers. § Impassable roads especially during the rainy season
Diagnostics testing with Xpert	§ Malfunctioning modules (5 of 15, 33% testing sites) § Testing not done for at least 30 days of the year due to lack of power back-up (2 of 15, 13% testing sites) § Recommended daily maintenance not performed (7 of 15, 47% testing sites) § Error/invalid rates >5% (10 of 15, 66% testing sites) § Ineffective supply-chain logistics to address gaps in Xpert cartridge inventory at all Xpert referral sites.
Return of results and treatment	§ Delayed notification of Xpert results (up to two weeks from sputum collection when notified at all) § Failure of patients to return to collect Xpert results and initiate treatment § Inconsistent recording of Xpert results in Lab Register § Lack of system to notify patients with positive results (21 of 23, 91% health centers)

[Table 1: Challenges with implementation of Xpert testing based on qualitative and quantitative site assessment.]

PS27-696-26 Results of a repeat GeneXpert MTB/RIF test among rifampicin resistant patients in a low MDR-TB prevalence setting, Uganda

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Background: The WHO 2014 GeneXpert MTB/RIF (Xpert) assay implementation guidelines recommend a repeat rifampicin resistant (RR) Xpert test only in low MDR-TB risk groups.

Methods: Ongoing cross-sectional study of all RR-TB patients referred to the MDR-TB ward at Mulago national referral hospital from peripheral health facilities for treatment initiation. Sputum samples were collected for smear microscopy, Xpert test, first-line Hain line probe assay (LPA) and liquid culture. We compared preliminary results of 36 RR-TB patients in the background of their treatment history and duration since the last RR-Xpert test

Results: Of the 36 RR-TB patients to-date, nine (25%) were negative, 21 (58.3%) were RR and 6 (16.7%) were rifampicin susceptible (RS) on repeat Xpert. Only 5/36 patients had started MDR-TB treatment (5, 7, 13, 14 and 25) days prior to collection of sputum for the second Xpert test. LPA testing results were: 3 (8.3%) indeterminate, 4 (11.1%) were negative for TB, 18 (50.0%) were RR, 10 (27.8%) were RS and 1 (2.8%) not done on LPA.

Among the ten RS patients on LPA, 2 (20%) were negative, 2 (20%) were RR and 6 (60%) were RS on repeat Xpert. Of the 6 RS patients on both LPA and repeat Xpert, one patient was 1+, three were 2+, one was 3+ and one was smear negative. Xpert grade were; one with high, three were medium and two were low. For the six RS patients, the median (interquartile range; IR) liquid culture time-to-positivity was 8 days (4 -11) and median time (IR) since the last Xpert was 26 days (5 - 35). Four of the six RS patients were new and two were previously treated for TB.

Conclusions: Our preliminary results show that a repeat RR-Xpert test on a second sputum sample would exclude 16% of the TB patients from MDR-TB treatment initiation.

PS27-697-26 Improved diagnostic accuracy with a single GeneXpert MTB/RIF® performed on two combined sputa versus smear microscopy of three separate sputum samples

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Background: The diagnostic performance of GeneXpert MTB/RIF® on combined sputum samples has not been systematically assessed in patients hospitalised with presumptive *Mycobacterium tuberculosis* (MTB). We aim to assess the diagnostic accuracy of a single GeneXpert MTB/RIF® test performed on two combined sputa versus smear microscopy performed on three (separate) sputum samples, using sputum culture as the reference standard.

Methods: We assessed all adult patients admitted to Blacktown Hospital between July 2017 and January 2018 with presumptive pulmonary TB. The presence of acid fast bacilli (AFB) in expectorated sputum samples, collected on three separate days, was assessed using standard auramine staining and light microscopy. For GeneXpert MTB/RIF® testing we combined 0.5mL from each of the first two sputa. The same Sputa were also cultured in liquid medium (MGIT; Becton-Dickinson) for 8 weeks. The diagnostic accuracy, time in isolation, duration of hospital admission and final diagnosis were recorded.

Results: Forty patients met the inclusion criteria and 37 (92.5%) consented to study participation; 7 were excluded due to insufficient samples. Of 30 eligible patients, 4 (13.3%) had culture-confirmed pulmonary TB. GeneXpert MTB/RIF® detected 3/4 cases with 100% specificity, while smear microscopy was positive in only 2/4 cases with 95.5% specificity. Of the non-tuberculosis patients; 13 had pneumonia, 3 had non-tuberculous mycobacterium, 2 had pleural MTB, 2 had non-pulmonary MTB and 6 had other pathology. The average time in respiratory isolation was 10.9 days and the average length of hospital stay was 12.5 days.

Conclusions: Performing a single GeneXpert MTB/RIF® test on a pooled sputum specimen had negative and positive predictive values of 96% and 100%, respectively, with improved diagnostic yield and accuracy compared to standard smear microscopy performed on three separate sputum samples.

PS27-698-26 Improving MDR TB diagnosis through Xpert MTB/Rif testing for high risk TB patients in Kampala

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Background and challenges to implementation: The TB prevalence in Kampala, Uganda is 504 cases per 100,000 population (2014/2015 Uganda population based TB prevalence survey). The MDR-TB burden is estimated at 1.4% among all new and 12.1% among previously treated TB cases. Of the 44,592 cases reported nationally, Kampala contributes to one fifth of all forms of TB. 10% of these are previously treated TB cases. In January to March 2016, Kampala health facilities tested only 65% of the previously treated cases with GeneXpert and notified only 2 Rifampicin resistant (“RR”) cases. To improve the DR-TB case finding, Kampala Capital City Authority (KCCA) with support of the USAID funded TRACK TB project implemented continuous quality improvement (CQI) interventions to raise the proportion of previously treated TB patients tested with GeneXpert to increase DR-TB diagnosis.

Intervention or response: We introduced quality improvement interventions in 45 facilities from between Jan 2016 - March 2017. Interventions included ‘mentoring 470 health workers on patient eligibility for Xpert MTB/Rif test, and diagnostic algorithm; provided printed algorithm for diagnosis of TB using Xpert MTB/Rif at all facilities; displayed hub riders’[1] schedule at 45

health facilities and conducted regular coordination meetings between hub riders, laboratory staff and TB clinic teams and monitored results documentation for re-treatment patients tested by Xpert MTB/Rif.

[1] Hub riders use motorcycles to support laboratory hub sample transportation within the hub network

Variables	Jan-Mar 2016	Apr-Jun 2016	Jul-Sep 2016	Oct-Dec 2016	Jan-Mar 2017
TB re-treatment cases	107	135	113	85	86
% tested by GeneXpert	65%	76%	81%	82%	79%
Rif resistant cases	2	7	20	18	20

[Table 1: GeneXpert results for previously treated TB patients]

Results and lessons learnt: The proportion of re-treatment TB patients who got Xpert MTB/Rif test improved from 65% in the first quarter of 2016 to 79% one year later. The number of RR TB cases notified increased from 2 cases to 20 cases during the same period.

Conclusions and key recommendations: Facility QI interventions have been successful in increasing the use of GeneXpert/Rif testing to improve DR TB diagnosis and notification.

PS27-699-26 7 years of implementing GeneXpert MTB/RIF diagnostic assay-lessons learnt from Nigeria

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Background: Nigeria is among the high TB burden countries that adapted GeneXpert MTB/RIF diagnostic assay in 2011, initially used among high-risk group to identify Rif Resistant TB(RR-TB) cases but eventually scaled-up in 2016 as the primary diagnostic-tool for TB. The number of GeneXpert MTB/RIF machines increased from 7 in 2011 to 390 by 2017. This study aimed at documenting lessons learnt in the roll-out of GeneXpert MTB/RIF technology to guide future expansion

Methods: Retrospective review of Programme reports and data from all levels including end-user's interviews.

Results: Skewed distribution driven by partners support which ranges from 1 XpertMTB/RIF machine/ 1 million populations in Borno to 8 machines/ 1 million population in FCT, placement of machines in facility not on need resulted in low utilization rate; functionality of the machines goes beyond installing the machines to include factors such as: regular alternate energy source; adequate human resources(HR); effective sputum transportation system; sensitization of all possible end-users and effective/responsive maintenance-system. The GX-

Alert-system enhances monitoring machines functionality and reduce time for DR-TB-treatment initiation, absence of unique identifier allows for double counting. The optimization strategy from March 2016 increased the number of tests conducted from 166,618 tests in 2016 to 373,126 tests in 2017(120% increased), Average utilization-rate of machines increased from 15% in March 2016 to 20% by end of 2016 and to 34% in 2017. Machines with utilization-rate above 100% have additional HR and alternate-power, The number of RR-TB cases diagnosed increased as the number of tests conducted increased by 35% from 1,686 in 2016 to 2,286 in 2017. 5% increased in DS-TB cases observed within the same period.

Conclusions: Optimal use of GeneXpert MTB/RIF machines increased DS-TB and DR-TB notification. Coordination, need-based distribution and prompt maintenance is key to enhancing utilization. electricity-independent point of care tests needed in the programme especially for hard-to-reach-areas

PS27-700-26 What causes the most unsuccessful results in GeneXpert: experience from Indonesia

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Background: Indonesia is in the process of rapidly expanding molecular diagnostic capacity for TB and DRTB diagnosis. The purpose of this study was to find out the cause(s) of unsuccessful tests over time.

Methods: A retrospective data was analysed from monthly reports over 4 years period from 2014-2017. All the GeneXpert sites submit monthly reports to NTP per standard format capturing total number of tests performed, results including number of unsuccessful tests, invalid and errors. Data was crossed checked and verified through national information system (SITT and e-TB Manager).

Results: A total of 227,416 tests were performed during the period of Jan 2014 to Dec 2017 from presumptive cases of TB and MDRTB. Out of total 227,416, MTB positive, Rifampicin resistant and unsuccessful test were 78,130 (34.3%), 12,280 (5.4%) and 10,855 (4.8%) respectively. Data regarding errors was available only for 67,455 tests and 2,470 (3.7%) tests run showed error as a result. Deep analysis of 2,470 errors showed that maximum number of errors i.e. 994 (40%) were linked to improper specimen processing, followed by 451 (18%) with cartridge quality and 142 (5.7%) with inferior quality of specimen. Errors related with module malfunction, voltage surge and module not detected were 3%, 3% and 2% respectively.

Conclusions: Most of the unsuccessful results were obtained either due to improper specimen processing or cartridge problem that could have been prevented by adhering with the SOPs and better supply chain management of cartridges. Our error rate is below 4% as reported from other parts of the world, however, further analysis is required to correlate the unsuccessful results with the type of specimens, training and geographical conditions.

PS28 How to make active tuberculosis case finding more active?

PS28-701-26 Prediction model of active TB in HIV-negative/unknown individuals: development, validation and cost-effectiveness analysis

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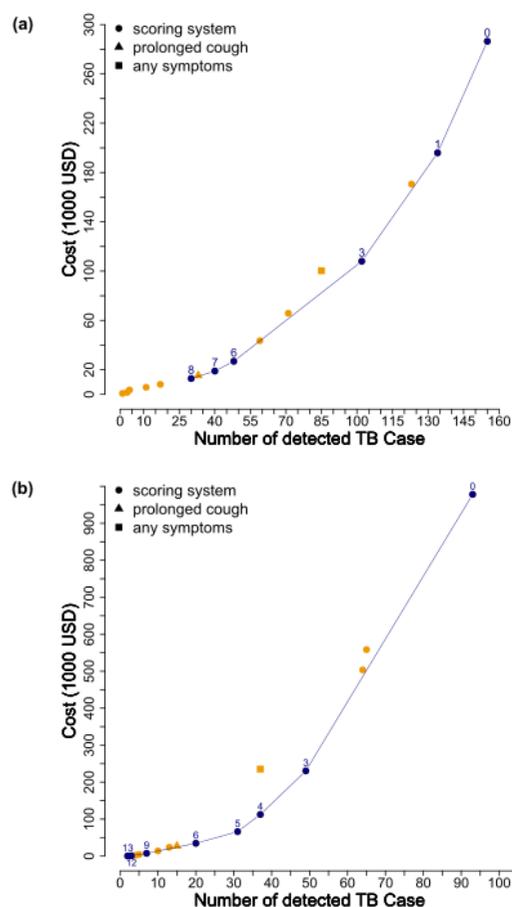
Background: Strategies to systematically screen for tuberculosis (TB) in resource-limited settings use prolonged cough or any TB symptom as criteria, which have suboptimal sensitivity and specificity. A prediction model of prevalent TB was developed to improve the use of relevant clinical information and assist decision-making when screening.

Methods: Cross-sectional data from the Zambia South Africa Tuberculosis and HIV/AIDS Reduction trial were used. All participants received sputum culture for TB detection. Potential predictors including conventional TB symptoms and known TB risk factors were considered. A multivariable logistic regression model using a South African (SA) training dataset was converted into a scoring system and evaluated in SA and Zambian validation datasets. Cost-effectiveness analyses compared the scoring system against conventional strategies.

Results: The number of culture-positive TB was 355 in the SA training dataset and 176 and 107 in the SA and Zambian validation datasets. The area under curve (AUC) of the new scoring system was 0.68 (95%CI 0.64-0.72) in the SA validation set, compared to prolonged cough (0.58, 0.54-0.62) and any symptoms (0.6, 0.56-0.64). In the Zambian dataset the AUC of the scoring system was 0.66 (0.60-0.72). In the cost-effectiveness analysis, the scoring system dominated the conventional strategies using TB symptoms (Figure 1). Under various

cutoff values of the scoring system, the cost per TB case detected ranged from 800 to 1,848USD in the SA validation set, and from 171 to 10,518USD in the Zambian dataset.

Conclusions: The prediction model had better discriminatory performance and cost-effectiveness than conventional strategies. It could provide flexible options for screening programs under budget constraints.



[Figure 1. Cost-effectiveness analysis in South African validation dataset using the algorithm with GeneXpert as the confirmatory tool (a). Cost-effectiveness analysis in Zambian dataset using the algorithm with smear plus GeneXpert as the confirmatory tool (b). Orange dots indicated the dominated plans.]

PS28-702-26 Prevalence of pulmonary tuberculosis among pregnant women in southern Mozambique (PREG-TB)

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Background: Tuberculosis (TB) is one of the leading causes of death among women of childbearing age. TB in pregnant women can increase both maternal and infant morbidity and mortality. The aim of this study was to estimate the burden of TB among pregnant women in a rural area of Southern Mozambique.

Methods: Cross sectional TB prevalence study among consecutive pregnant women attending the first antenatal care (ANC) clinic visit at the Manhica Health Care Center from September 2016 to January 2017. All women with compatible TB symptoms, those with a close TB contact and all HIV positive, regardless of symptoms were asked to provide a spot plus an early morning sputum sample. Samples were tested using Xpert MTB/RIF and liquid culture. Symptomatic patients were followed up within a month of their initial evaluation for verifying symptom resolution or the need for further diagnostic work-up.

Results: A total of 1980 pregnant women were enrolled. Of these, 678 were asked to provide a sample of sputum: 470 were HIV positive without TB symptoms, 151 HIV positive with TB symptoms and 57 were HIV negative with TB symptoms. A total of 10 TB cases (all HIV positive) were diagnosed: 5/151 (3%) and 5/470 (1.1%) among women with and without TB compatible symptoms. Half (5) were microbiologically confirmed. The overall prevalence of TB among pregnant women was 505 per 100,000 (95% CI: 242-926) and 1610 per 100,000 (95% CI: 775-2941) among HIV positive ones. Two newborns born to mothers with TB in pregnancy died in the neonatal period.

Conclusions: The overall prevalence of tuberculosis among pregnant women is compatible with the overall prevalence estimated for Mozambique. Active case finding strategies are useful in order to find TB cases in pregnant women, especially among HIV positive ones.

PS28-703-26 Active massive tuberculosis case finding in East Jakarta, 2016-2017: the role of Ketuk Pintu Layani Dengan Hati and Juru Pemantau Batuk cadre programs

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Background and challenges to implementation: Indonesia has the 2nd highest number of incidents of tuberculosis (TB). It accounts for 1.020.000 new cases per year, only 30% of which has been reported. To find the lost 70%, a massive active case finding was conducted through two programs: Ketuk Pintu Layani Dengan Hati (KPLDH) and Kader Juru Pemantau Batuk (Jumantuk cadres), who also plays a role in child TB screening.

Intervention or response: Methods: Data was collected and analyzed through Tuberculosis Integrated Online System from 2014 to 2017 involving 152 DOTS facility with 87 primary health centers in East Jakarta.

Results and lessons learnt: East Jakarta consists of 2.900.722 people. KPLDH program started in February 2016 consisting of 84 teams (310 people). Jumantuk cadres was formed 4 months later (218 people). The number of new TB cases in East Jakarta (primary health center) from 2014 to September 2017 respectively is as follows: 6.499 (2.637), 7.438 (2.651), 8.948 (3.211), 9.444 (2.826). Meanwhile, the percentage of child TB case discovery in primary health center was 8,5%, 9,8%, 12,1% from 2014 to 2016 respectively. In 2017, child TB case discovery was 12,5% for the 1st quartal, 19,5% for 2nd and 3rd quartal. Treatment of Isoniazide Prophylactic Therapy (IPT) is also increased in 2017.

Discussion: Increased TB incidence rate from 2014 to 2017 was 14,4%, 20,3%, and 27,4% respectively in East Jakarta, and 0,5%, 21,1%, and 14% in primary health center. This reveals the positive role of KPLDH and Jumantuk in TB detection and reporting. Likewise, these programs were responsible for the increase in child TB case finding, especially in the first 3 months of 2017 (Ketuk Pintu TB Day program) and the next 3 months (active child TB screening).

Conclusions and key recommendations: KPLDH and Jumantuk are actively involved in increasing TB case finding in both adults and children.

Keywords: Tuberculosis, case finding program, primary health center

PS28-704-26 Yield of active tuberculosis case finding in a high-burden district of South Africa

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Background: Household contacts of infectious TB patients should be systematically and actively investigated for TB as they are at high risk for infection. This facilitates early detection and initiation of TB treatment towards improved health outcomes and community-level reduction in TB transmission. In high prevalence settings like South Africa, self-presentation of symptomatic individuals on its own is insufficient to eliminate TB. The yield of TB among household contacts of various infectious index cases is described to inform active case finding scale-up efforts in a high burden resource-restricted district.

Methods: A pilot study was conducted among household contacts of purposively-selected TB patients — children < 5 years, HIV co-infected pulmonary TB (PTB) cases, HIV-negative PTB cases, and multidrug-resistant TB (MDR-TB) attending primary health care facilities in Mangaung Metropolitan district. The contacts were screened for TB symptoms and symptomatic individuals and children < 5 years were referred for clinical evaluation. The yield of TB among contacts of each type of index case is described.

Results: Out of 259 contacts screened, 102 (39.4%) were referred for clinical evaluation, of whom 48 (47.1%) complied. Seventeen contacts were newly diagnosed with TB. Fifteen contacts needed to be screened to diagnose a new TB case and three needed to be clinically evaluated to detect one new TB case. The proportion of newly diagnosed TB cases was highest among contacts of HIV-negative patients (47.9%) compared to the other three index case groups (HIV-positive ≥5 years: 41.2%; children < 5 years: 11.8% and MDR-TB: 0%).

Conclusions: Results showed variation in the yield of TB across the different types of index case groups with most new TB cases among contacts of HIV-negative patients. Systematic household contact investigation to improve case finding among household contacts of all four types of TB index cases should be maximised in this and similar high-burden settings.

PS28-705-26 Risk of tuberculosis transmission in Cali, Colombia, 2009-2013

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Background and challenges to implementation: According to Global Tuberculosis (TB) Report 2017, TB incidence is decreasing. However, the current decreasing rate will not allow to reach the goals for epidemiological impact by 2050. Other strategies are required, particularly those that involve the study of the geographical distribution of risk and the identification of populations at higher risk, in order to implement cost-effective interventions for prevention and control in high transmission settings.

Intervention or response: This is an exploratory ecological study to identify the spatial and temporal distribution and to determine the risk of TB transmission in urban areas of Cali, Colombia, during 2009-2013. Information of 5172 confirmed TB cases registered in the local TB control programme database was analyzed through the use of GIS.

Results and lessons learnt: Five significant clusters ($p \leq 0.05$) were identified over time, using interpolation strategy, hot-spots and average nearest neighbor index. Clusters were in areas characterized by overcrowding, drug dependence, malnutrition, poverty and alcoholism. Those characteristics represent a greater risk of getting TB and are related to structural and proximity factors. One of the clusters was found in a population considered not vulnerable.

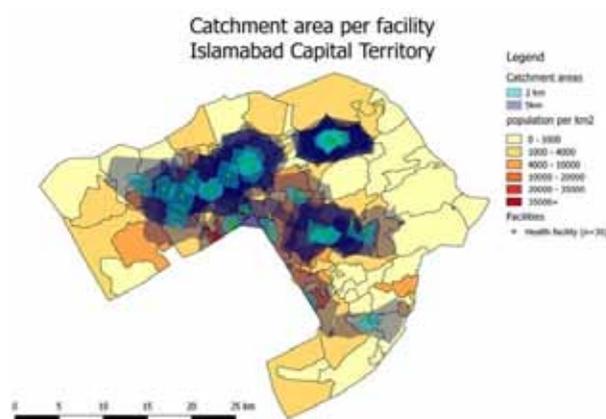
Conclusions and key recommendations: Spatial and temporal analysis is a useful tools to understand the behavior of TB risk as well to identify vulnerable geographic areas where TB transmission is more active, therefore provides substantial evidence for TB prevention and control.

PS28-706-26 Access to TB services in urban environments and its relationship to district-level TB case notification rates in Islamabad and Khairpur districts in Pakistan

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Background: Limited access to TB diagnostic and treatment facilities services due to physical distance poses a challenge to utilization of TB services. Using spatial data to measure accessibility to health facilities identi-

fies inequity in service provision in terms of geographic distribution. Combined with other data, it can identify areas with high probability of containing missed people with TB. This study assesses geographical distribution of and physical accessibility to TB health facilities and their relationship with TB case notifications in Pakistan. **Methods:** A service availability assessment was conducted among all 72 public and private TB health facilities in



[Islamabad TB Facility Catchment Areas (2 and 5 km)]

Islamabad and Khairpur districts in 2017, capturing elements of treatment, referral, and diagnostic services, staff capacity, reporting practices, and GPS locations. Road network data and network analysis were used to estimate catchment populations within 2 and 5 kilometer travel distances from all facilities. Poisson regression was run to determine influence of catchment populations and selected survey elements (service availability and utilization) on facility level TB case notifications. Results of the poisson model were used to predict and map availability and access to TB care services, in which health facilities were stratified by variables found to be significant in the regression.

Results: Results presented focus on the relationship between geographical distribution and physical accessibility to facilities and case notifications in Islamabad and Khairpur. There are more private than public facilities in both districts (28:8 in Islamabad; 35:11 in Khairpur), public facilities notified many more TB patients in 2016. Health facility coverage is substantially better in Islamabad compared to Khairpur. Factors associated with health facility case notifications will be presented.

Conclusions: Results of the poisson regression and spatial analyses will inform recommendations on improved services for each facility to increase case notifications. These may relate to diagnostic or treatment services or human resources, or geo-locations of new health facilities.

PS28-707-26 Geospatial hotspots in the spatial spread of tuberculosis in Ethiopia

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Background: Geospatial tuberculosis hotspots are hubs of TB transmission both within and across community groups. We aimed to quantify the extent to which these hotspots account for the spatial spread of TB in a high-burden setting.

Methods: We developed spatially coupled models to quantify the spread of TB from geographic hotspots to distant regions in rural Ethiopia. The population was divided into three 'patches' based on their proximity to transmission hotspots, namely hotspots, adjacent regions and remote regions. The models were fitted to five-year notification data aggregated by the metapopulation structure. Model fitting was achieved with a Metropolis-Hastings algorithm using a Poisson likelihood to compare model-estimated notification rate with observed notification rates.

Results: A cross-coupled metapopulation model with assortative mixing by region closely fit notification data as assessed by the Deviance Information Criterion. We estimated 45 hotspot-to-adjacent regions transmission events and 2 hotspot-to-remote regions transmission events for every 1000 hotspot-to-hotspot transmission events. Although the degree of spatial coupling is weak, the proportion of infections in the adjacent region due to mixing with hotspots was high due to the high prevalence of TB cases in a hotspot region, with approximately 75% of infections attributable to hotspot contact.

Conclusions: Our results suggest that the role of hotspots in the geospatial spread of TB in rural Ethiopia is limited, implying that TB transmission is primarily locally driven.

PS28-708-26 Prevalence of pulmonary tuberculosis in an urban city with increasing internal migration in China

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Background: Internal migration mainly from rural areas to urban cities has become a major challenge to tuberculosis (TB) control in China. We aimed to investigate the prevalence of both drug-susceptible and drug-resistant tuberculosis among local residents and urban migrants in a populous city.

Methods: We conducted a retrospective analysis of 55 857 TB cases from 2009 to 2016 in Shanghai, China. We collected and linked the epidemiological and laboratory data from the local disease surveillance system and estimated the prevalence of both drug-susceptible and drug-resistant tuberculosis. We also used geographic data to address the spatial distribution patterns of disease among migrants and residents.

Results: During the 8-year study period, migrant contributed to 44.4% (n=24802) of the notified pulmonary TB cases. Nearly half of the TB patients (48%) were more than 55 years old among residents, in contrast, two thirds of the TB cases were young individuals under 35 years old among migrants. Of 14 612 culture-confirmed TB cases, 891 (6.1%) were MDR-TB. The rates of MDR-TB were similar among new migrant (4.2%) and new resident (4.7%) patients, however, the rate was significant higher among retreated migrant (27.1%) than that among retreated resident patients (17.6%, $p < 0.0001$). We observed a heterogeneous spatial distribution patterns of overall TB patients and drug-resistant patients; while migrants had multiple hotspots related to local context in each districts in Shanghai. The detection of spatial aggregation of many MDR-TB patients suggested the spread of MDR *M tuberculosis* strains in local community.

Conclusions: The influx of rural-to-urban migrants, as well as local aging population, have contributed substantially to the tuberculosis disease burden in Shanghai. Richer local data including spatial information are crucial to address the complex epidemics of tuberculosis in urban areas with massive migration.

PS28-709-26 Prevalence of and risk factors for active tuberculosis among school children in Mongolia

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Background: A 2015 prevalence survey in Mongolia showed that TB prevalence in adults was three times higher than previously estimated. Expanding and improving active case-finding efforts will be critical to closing the case detection gap. We conducted an investigation to determine the prevalence of, and risk factors for, active tuberculosis among school children in Mongolia being screened for eligibility to participate in a clinical trial.

Methods: A total of 9,814 children aged 6-13 years attending 17 schools in Ulaanbaatar, Mongolia were screened for TB infection using an interferon-gamma release assay (QuantiFERON TB-Gold, QFT-G). QFT-G-positive children were referred for further diagnostic evaluation including history and examination performed by a pediatrician and chest X-ray. Children diagnosed with active TB were referred for TB treatment.

Results: 946/ 9,814 children were QFT-G-positive. Further diagnostic evaluation was completed in 938 children, of whom 129 (13.8%) were diagnosed with active TB disease. Risk factors for active TB were history of household TB contact (adjusted relative risk [aRR] 2.43, 95% CI 1.77 to 3.33), enrolment in March-May or December to February vs. June to November (aRR ≥ 2.72 , 95% CI 1.32 to 5.60) and active smoking (aRR 5.26, 95% CI 2.43 to 11.37).

Conclusions: We observed a high yield of school children with active TB through active screening. This suggests that active case finding, not only among TB contacts, but also among school children, may be useful for closing the case detection gap in Mongolia.

PS28-710-26 Tuberculosis disease outbreak in a secondary school in Mukono District, Central Uganda, October 2017

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Background: In October 2017, the Uganda National TB and Leprosy Program (NTLP) was notified of four students with confirmed Tuberculosis (TB) during the past year in a large boarding secondary school (1400 students and 82 staff) in Central Uganda. The spread of TB in congregate settings like schools can be rapid. We evaluated the burden and associated risk factors for TB disease in this setting.

Methods: We conducted a cross-sectional study between October and November, 2017 in which 1387 participants were enrolled. We investigated for TB disease by clinical evaluation, Chest X-ray and Xpert MTB/RIF®. We defined a presumptive TB case as onset of ≥ 1 of fever, night sweats, cough, chest pain, fatigue or weight loss, probable case as chest X-ray abnormality suggestive of TB, Clinically Diagnosed (CD) TB if Xpert MTB/RIF®

but CXR suggested TB. Bacteriologically Confirmed (BC) TB if Xpert MTB/RIF® detected TB. We evaluated dormitory crowding and ventilation.

Results: We identified 35 TB case-patients (13 BC and 22 CD) among 1387 screened; overall attack rate (AR) was 2.5%. TB cases occurred among year 11 (23/145, AR=16%), year 12 students (7/79, AR=8.9%), year 13 students 1.7% (3/172) and among staff 4.3% (2/47). Males (AR=3.8%) were more affected than females (AR=1.4%). Among close contacts (dormitory and class mates) of the initial TB case-patients with chest X-rays performed, 13% (25/191) were suggestive of TB. In dormitories, average per-student living space was 3.1m² and the window-to-living-space area ratio was 4.5% (Ministry of Health recommended: 20%). We isolated and treated the case-patients and distributed TB prevention information.

Conclusions: TB burden was high in this school with males more affected. Congestion and inadequate ventilation might have facilitated TB transmission. We recommend strengthening TB surveillance in the school health program, improving dormitory ventilation and residential space for students.

PS28-711-26 Are classrooms and dormitories equally dangerous for tuberculosis transmission among adolescent students in Guangxi, China?

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Background: In China, adolescent TB outbreaks often occur in boarding schools. We aimed to compare the risk of TB transmission in classrooms and in dorm rooms.

Methods: A series of adolescent TB contact tracing was conducted in classrooms and dorm rooms in Guangxi, China. A similar survey was conducted in a control class randomly selected from a matched control school in the same county during November 2016 to October 2017. Contacts of both groups were investigated for active TB using chest radiograph, sputum smear and culture. Genotype of *M. tuberculosis* isolates were analyzed using 15-locus based MIRU-VNTR typing. Latent TB infection (LTBI) was detected by tuberculin skin test and QuantiFERON TB Gold In-Tube.

Results: 6263 classmates of 112 index TB and 6130 classmates of 112 controls were investigated. 1140 dorm mates of 104 index cases were also investigated (8 index cases were ambulatory students). 23 and 2 new active TB cases were detected among the classmates of index cases and of the controls, respectively. The corresponding numbers of LTBI detected were 69 and 26.

Two classroom contacts and no dorm room contact had the same genotype of *M. tuberculosis* with that of their index case. Compared with contacts of the control students, odds ratio (95% CI) and population attributable fraction (PAF) for acquiring TB from exposure to an index case in the same classroom was 6.54 (1.43-29.94) and 77.9%. The respective values for TB exposure in the same dorm room was 4.69 (1.93 - 11.4) and 34.6%. For LTBI, the values for exposure TB in the classroom were (OR=1.88, 95% CI: 1.1 - 3.19), PAF=34.1%. Dorm room TB exposure was not significantly associated with increased LTBI.

Conclusions: All available data from this study suggests the need to emphasize improvement of TB prevention in the classroom although the dorm room should not be neglected.

PS28-712-26 High yield of tuberculosis case finding by mobile chest X-ray screening in Ho Chi Minh City, Viet Nam

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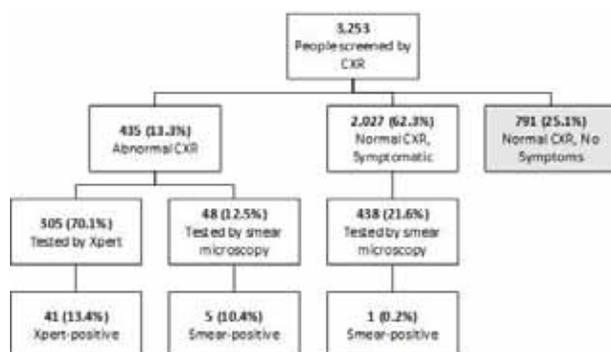
Background and challenges to implementation: Chest X-ray (CXR) are a highly-sensitive triage tool for prioritizing the use of expensive molecular assays for diagnostic testing. Yet, in many low-income countries, people face access barriers which prevent them from visiting facility-based X-ray services.

Intervention or response: One-off, mobile CXR screening camps were organized across 5 districts of Ho Chi Minh City over 6 days in Dec 2017. Household contacts and community members were invited in advance by gov't health facility staff and community health workers. All people attending the camps were screened by CXR and for TB symptoms. CXR images were interpreted by an on-site radiologist. Sputum from people with abnormal CXRs was tested with the Xpert MTB/RIF assay, while sputum from symptomatic people with normal CXRs was tested by AFB smear microscopy. All samples were transported to gov't laboratories for testing and anyone with lab-confirmed TB was linked to appropriate treatment at gov't health facilities.

Results and lessons learnt: 3,253 people were screened at the mobile camps and 435 people (13.4%) had abnormal CXR images. 305 of these people (70.1%) were tested on Xpert, resulting in the detection of 41 people with TB (13.4%). An additional 48 people with abnormal CXRs (12.5%) were tested by only AFB smear microscopy and 5 (10.4%) were smear-positive. 438 people with normal CXR images were tested by AFB smear microscopy, resulting in the detection of just one smear-

positive person (0.2%). The number needed to screen (NNS) to find one person with TB at these camps was just 69. Being male (aOR=1.5) and having productive cough (aOR=1.4), weight loss (aOR=1.4) and prior history of TB (aOR=1.9) were factors associated with lab-confirmed TB.

Conclusions and key recommendations: This mobile case finding approach achieved a high yield by eliminating individual and institutional barriers for accessing care. CXR screening effectively prioritized the use of Xpert MTB/RIF tests to maximize yields.



[Tree chart of mobile CXR screening results in Ho Chi Minh City, Viet Nam]

PS29 Active case finding

PS29-713-26 Yield of retrospective vs. prospective tuberculosis contact investigations: survey findings in four Ethiopian towns

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Background and challenges to implementation: The risk of developing TB is higher in the two years after TB infection. Since the existing prospective approach of monitoring patients for up to two years following completion of treatment is time consuming and expensive, we designed and implemented a retrospective approach to assess the comparative yield of retrospective contact investigation and its associated factors in four towns of Ethiopia.

Intervention or response: We conducted this study in four Ethiopian towns between August 2017 and January 2018. The sites were selected because of their routinely reported high TB burdens. First, we trained TB focal persons to carry out retrospective contact investigation

in 14 health facilities. They listed fully treated TB cases from the past two years, then traced and screened their contacts using symptom checklists. We calculated the yield stratified by basic socio-demographic data and compared it to the yield from routine contact investigations for the period June 2016-July 2017. We did a multivariable logistic regression analysis to determine factors associated with TB diagnosis in the retrospective group.

Results and lessons learnt: The retrospective screening included 1136 contacts of 534 index cases. Women constituted 47.1% of those screened, their median (interquartile range) age was 30 (0-85), and 75.7% were contacts of bacteriologically confirmed TB cases. We identified 65 (5.7%) TB cases in the retrospective, significantly higher than the 0.8% yield in the routine system. Contacts of bacteriologically confirmed cases (AOR=0.04; 95%: 0.04-0.75), older aged index cases, (AOR=0.96; 95% CI:0.94-0.98) and workplace contacts (AOR=3.69; 95% CI: 1.28-10.66) were associated with TB diagnosis in the retrospective contact investigation.

Conclusions and key recommendations: The yield of TB in the retrospective approach was seven times higher than that of the prospective approach. Retrospective contact investigation should be included as part of the routine TB case finding strategy especially in settings where the prospective approach is not routinely practiced.

Variables	Retrospective	Routine/prospective
Number of index cases	534	24,043
Contacts traced and screened	1136	63,703
Number (%) of presumptive TB cases among the screened contacts	369 (32.5)	1409 (2.2)
Number (%) of TB cases among the screened contacts	65 (5.7)	507 (0.8)

[TB yield comparison of prospective versus retrospective contact investigation in four towns of Ethiopia.]

PS29-714-26 Ending the TB epidemic: role of active TB case finding using mobile units for early diagnosis of tuberculosis in Nigeria

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Background and challenges to implementation: Delayed TB diagnosis contributes to transmission of TB infection and TB mortality. In 2016, 300,000 Nigerians were not diagnosed or diagnosed but not notified. Ending the TB epidemic, entails early diagnosis and treatment

of missing TB patients. We explored the role of mobile diagnostic units in finding and treating missing persons with TB early.

Intervention or response: Two trucks, each equipped with a digital x-ray and 8-module GeneXpert capacity machines were used to actively screen and diagnose TB among targeted populations. Sputum samples from presumptive TB clients identified by a combination of symptomatic (cough) and chest x-ray screening were tested with GeneXpert. Mycobacterial load in sputum samples was estimated by the grade of GeneXpert test positivity. The grades were used as biomarkers for the stage of TB disease; very low and low as early TB disease, while medium and high as late TB disease. The grades of TB patients diagnosed with the mobile GeneXpert machines were compared with those diagnosed with another two 4-module GeneXpert machines in selected health facilities over a four-month period starting from October-November 2017. The facility-based machines test routine samples, diagnosed similar number of TB patients and are located in the same states as the trucks.

Results and lessons learnt: The two trucks diagnosed 200 TB patients of which 91 (46%) had early TB disease, compared to 46 (22%) of the 209 TB patients diagnosed with the health facility-based GeneXpert machines ($P < 0.001$). In both situations, the majority (54% vs. 78%) had late TB disease. This shows that most of the patients are diagnosed late and that early diagnosis is more likely with active case finding.

Conclusions and key recommendations: Active TB case finding using mobile units detects TB patients earlier than passive case finding. It is fundamental to halt TB transmission and reduce TB incidence in a high disease burden country as Nigeria.

PS29-715-26 Active TB case finding among seniors in rural China: findings from a pilot project

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Background: China continues to experience a substantial tuberculosis (TB) disease burden and an aging population. Compared to other age groups, the senior population (aged 65 and over) is particularly at risk for TB. This project was designed to explore feasible methods of active case finding (ACF) among seniors.

Methods: We incorporated TB examinations into the annual physical check-up of basic public health service to pilot ACF among seniors in Bayi community, Sichuan Province from March to June 2017. Participating seniors were screened for TB symptoms and had health records reviewed for risk factors. Seniors with TB symptoms or at least one risk factor were offered a follow-up chest x-ray.

Seniors with abnormal chest x-ray or clinical symptoms were asked to provide sputum samples for laboratory diagnosis using smear and culture. In-depth individual interviews and focus groups were held with health workers and seniors to evaluate the acceptability and feasibility.

Results: Of the 2,393 seniors residing in Bayi, 2,049 (85.6%) participated in the TB screening project. Three participants were confirmed with active TB, including one smear-positive and culture-positive case and two clinically diagnosed cases. The overall detection rate was 146/100,000. Most staff and workers provided positive feedback about the aims of the project. At the same time, workers voiced concerns about the time required for home visits, chest x-ray and sputum tests. The majority of participants supported implementation of the project on a regular basis if more resources (or staff) could be provided.

Conclusions: Our pilot ACF project demonstrated feasibility and high acceptance among seniors. The detection rate found in this project was three times greater compared to the general population in Jiangyou County, highlighting the need for additional interventions for the elderly. Integrating TB screening with the annual check-up platform was beneficial for health care staff and seniors.

PS29-716-26 Does mobile screening for tuberculosis identify cases earlier among vulnerable populations? Community-based active case finding in Palawan, the Philippines

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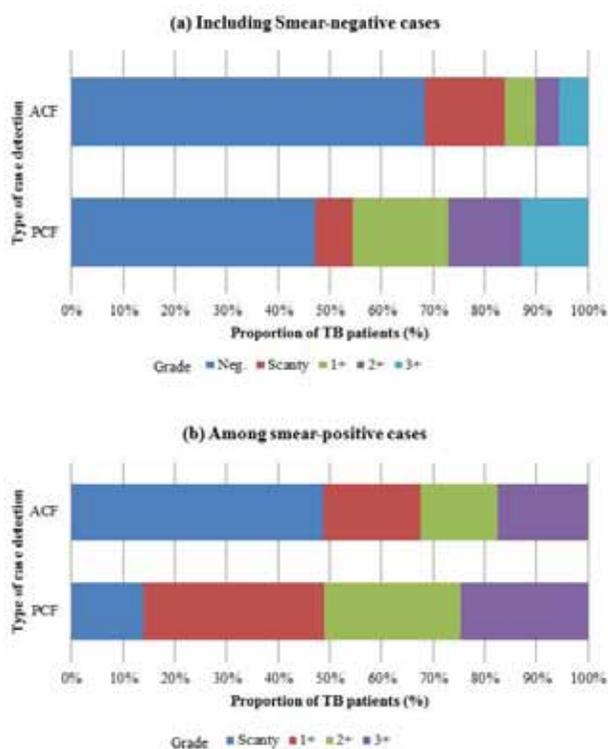
Background: Tuberculosis (TB) case-finding project (DetectTB) using mobile unit equipped with digital X-ray machine, Light Emitting Diode Fluorescence Microscope (LED-FM) and GeneXpert machine has been implemented in Palawan, the Philippines since 2012. The project organized the systematic screening for TB among vulnerable populations.

This study aimed to compare the earliness of TB case detection between active case finding (ACF) group and passive case finding (PCF) group.

Methods: We established an intervention group consisting of those detected by the project and a control group consisting of those detected by the routine system in the project sites between 2013 and 2014. The data were collected from the DetectTB database and medical records. We compared results of smear microscopy and duration of diagnosis and treatment delay between ACF and PCF groups.

Results: A total of 776 participants were enrolled comprising 242 from ACF group and 534 from PCF group. Smear positive rate of pulmonary TB was significantly lower in ACF group (31.6%) than in PCF group (54.1%) ($p < 0.001$). Smear grades among smear positive cases were also lower in ACF group than in PCF group ($p < 0.001$). Total diagnosis and treatment delay was significantly shorter in ACF group than in PCF group ($p = 0.007$) where not only patient delay was shorter in ACF group than in PCF group ($p = 0.082$) but also health system delay was shorter in ACF group than in PCF group ($p < 0.001$).

Conclusions: The TB patients detected by the mobile screening had less serious status of the disease and a shorter diagnosis and treatment delay compared with those detected by the routine system. Mobile screening may be an alternative to enhance early case detection of TB thus reducing transmission of the disease among hard-to-reach populations.



[Distribution of smear grades by case finding method]

PS29-717-26 Motivating private physicians to notify TB cases: a case study from rural India

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Background and challenges to implementation: Notifications of TB patients from the private sector in India continue to significantly lag the large number of cases diagnosed in the sector. In the state of Bihar (population 110M, 88% rural) rural areas reported fewer than

12/100,000 private cases compared with 54/100,000 public cases (2016). An intervention aimed at improving private notifications in rural Bihar was supported by the India Health Fund (an initiative led by the Tata Trusts, in collaboration with the Global Fund).

Intervention or response: The intervention targeted the Dalsinghsarai block of the Samastipur district in rural Bihar. The block has a high concentration of accredited physicians (13). All 9 physicians contacted in the pilot agreed to refer their TB cases. Every week, program staff visited participating clinics to collect details of diagnosed patients (name, phone number and address). Patients were counseled in-person or telephonically every 3 weeks after seeking their consent. Counseling focused on infection control and adherence. Cases were notified to the NTP via the web-based Nikshay system.

Results and lessons learnt: From April 2017 to March 2018, 387 referrals were received from participating physicians, of which 367 (95%) have been notified to the NTP thus far (incomplete data and operational delays account for the as-yet-unnotified cases). In comparison, a total of 145 private patients (none from our catchment) were notified from the entire district in the preceding year (2016). The intervention block notification rate was 45/100,000 compared with the district's rate of 3/100,000 (2016). Of 387 referrals, 328 (85%) were traceable, and 314 consented to counselling.

Conclusions and key recommendations: Providing a clear incentive to private physicians (tracking and counselling their TB patients over the duration of treatment) has the potential to dramatically increase notifications.

PS29-718-26 Diagnostic delays and barriers to tuberculosis service delivery in hard-to-reach riverine areas of the Niger Delta, Nigeria

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Background: Nigeria is one of the high tuberculosis (TB) burden countries. However, only 24% of estimated TB cases were notified in 2016. Riverine populations of the Niger Delta are some of the most hard-to-reach, and vulnerable to poor medical care. This TB REACH intervention explored TB-related knowledge, attitudes, perceptions (KAP) and healthcare seeking pathways to address regional challenges to diagnosis and notification.

Methods: An exploratory operational research study was conducted in 6 communities of Bayelsa and Delta States in 2017, involving pilot-tested KAP surveys, focus group discussions (FGD), and key informant interviews.

Data were analysed using Epi Info 3.4.1 and thematic content analysis.

Results: The survey was completed by 597 community members (51.6% female) and 51 TB patients (56.9% female); 65 community members and 15 HCWs participated in FGDs and interviews respectively. Community members' mean [SD] knowledge and attitudinal scores were 6.1/10 [2.2] and 4.8/12 [1.9] respectively. Older age (>40y) ($p=0.04$) and regular income ($p<0.001$) were independent predictors of TB knowledge. Good TB knowledge and formal education were associated with positive TB attitudes. Patients' TB knowledge was similar at 6.8/8 [1.5]. Most patients (72.6%) were scared or depressed by their diagnosis, 41.2% felt discriminated. Most (98.8%) respondents took >1 hour to access the nearest diagnostic centre. Mean patient-related and health system-related diagnostic delays were 16.3 and 3.7 weeks respectively. Belief in faith healing and herbal remedies, transport barriers, and negative HCW attitudes were prominent themes in FGDs. Problems transporting sputum samples and tracing mobile communities were primary HCW complaints.

Conclusions: This mixed-methods study helps quantify and explain diagnostic delay in this remote region. Individual and structural challenges to TB service access and delivery may be alleviated through community outreach, awareness-building, and engagement with informal providers.

PS29-719-26 Effects of active household contact screening on TB case detection in Afghanistan

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Background and challenges to implementation: National TB Program (NTP) in Afghanistan implemented active household contact screening of all bacteriologically confirmed index TB cases since 2014. However, the implementation was poor and all areas were not covered. NTP identified barriers/ challenges, like lack of inappropriate management structure and screening tools, weak human resources, low community awareness, and poor adherence of INH Preventive Therapy (IPT).

Intervention or response: NTP implemented active contact screening with assistance from Challenge TB (CTB) and Global Fund (GF) countrywide, which included door-to-door screening of TB index case contacts and referred contacts to the health facilities for testing. Health workers received trainings and mentorship on contact investigation practices. The supervisors checked 20% of the screened contacts to confirm the practice.

Results and lessons learnt: In 2017, the NPT notified 47,406 all form TB cases and 21,316 were bacteriologically confirmed TB cases in Afghanistan. Also, in 2017, household contacts to 19,634 index TB cases visited. This figure was 11,325 in 2016. In total, 129,738 household contacts registered and symptomatic screened for TB. That is 6.6 contacts per index case. Of those screened, health care staffs identified 16,017 (12.3%) as presumptive TB patients and, 3,071 (19%) were diagnosed as all forms of TB. The yield of TB case notification is 2,367 in 100,000 household contacts. Active contact screening contributed 7.1% in TB case detection countrywide in 2017. About 30,821 children under 5 were put on Isoniazid Preventive Therapy (IPT), 21,651 of them completed their IPT and the rest is under IPT (Table 1).

Conclusions and key recommendations: Active household contact screening had remarkable contribution in TB cases detection and provision of IPT for children. TB among household contacts is 12 times higher than WHO estimated incidence of 189 in 100,000 populations. We recommend implementation of active contact screening nationwide.

Indicator	2016	2017	P-Value
Number of Bacteriologically Confirmed TB Cases evaluated	11325	19364	NA
Number of Household contact diagnosed as all form TB patients	1654	3071	0.01
Number of children under 5 years of age	18377	33148	0.00001
Number of children put on INH preventive therapy	16712	30821	0.00001

[Table 1, Effects of active household contact screening to TB case detection in Afghanistan]

PS29-720-26 Narrowing the gap of missing cases in Myanmar: active TB case finding in hard-to-reach and poor urban areas

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Background and challenges to implementation: Myanmar is one of the 30 TB high burden countries, with an estimated incidence of 361 new TB cases per 100,000 population. In 2016, only 72% of the estimated total number of new TB cases were notified, and case notification rates were as low as 55% in certain parts of the country (WHO Global TB Report, 2017). Thus, the National TB Program (NTP) 2016-2020 National Strategic Plan includes an aggressive strategy for Active Case Finding (ACF).

Intervention or response: In collaboration with the NTP, the Challenge TB (CTB) project and partners supported two ACF strategies: 1) a private-public mix (PPM), engaging TB educated/trained drug sellers from 15 poor urban towns; and 2) working with community volun-

teers from 22 hard-to-reach townships. The project worked with drug sellers and community volunteers to extend TB screening, sputum collection and transport, and community-based active case management for local and ethnic communities. CTB analyzed the yield of notified cases and number needed to test (NNT) for both strategies from July to December 2017.

Results and lessons learnt: CTB's ACF activities contributed to 15% of total notified cases across 37 townships between July and December 2017. The yield of patients diagnosed with TB through PPM and through community volunteers was 20% and 6% respectively. The NNT was only five through PPM, compared to 17 people through the community volunteer approach.

Conclusions and key recommendations: Both ACF activities can help close the gap of missing TB cases in poor urban and hard-to-reach settings. The yield of TB cases identified by PPM was higher than through community volunteers. The contribution of both approaches to overall ACF was similar (47% vs. 53%). Criteria for prioritizing ACF interventions should include the expected yield of various approaches.

	Presumptive TB Case (N)	Notified TB Case (N)	Contribution to Total Notified TB Case (%)	Yield (%)	NNT (N)
PPM (Drug Seller)	1985	396	10	20	5
Hard-to-Reach (Community Volunteer)	7664	455	23	6	17
Total	9649	851	15	9	11

[Table 1]

PS29-721-26 Integrating TB screening in HIV testing outreaches targeting key HIV populations improves TB case detection in Bugiri district, Uganda

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Background and challenges to implementation: The burden of TB in Sub-Saharan Africa remains high despite efforts to improve case detection and reduction in HIV incidence. In Sub-Saharan Africa countries, almost one-third of TB cases are attributable to HIV. However, TB screening is not routinely integrated in HIV testing services (HTS). The USAID Regional Health Integration to Enhance Health Services in East Central Uganda (RHITES-EC) project sought to determine whether integration of TB screening in HTS targeting key-populations in HIV hotspots is effective in identifying TB cases. **Intervention or response:** From November through December 2017, RHITES-EC trained health workers in the use of intensified case finding tool, sputum collection from presumptive cases. Sputum from presump-

tive cases was referred to the nearest health facilities for GeneXpert examination. Clients who tested positive for TB were tracked by phone call or physically by village health teams. Serial outreaches to key-populations in HIV hotspots were conducted with integrated HIV-TB screening. Program data was analyzed retrospectively to determine the proportions of patients screened, tested and proportions of patients diagnosed with TB. The numbers of contacts needed to screen (NNS) and the number of contacts needed to test (NNT) to identify a TB cases were also calculated.

Results and lessons learnt: Overall, six TB-HIV testing outreaches targeting key-populations were conducted in November 2017, during which 403 patients were screened, 37 (9.18%) of whom were presumptive cases. All the 37 presumptive cases provided sputum, 4 were diagnosed with sputum-positive TB and were all initiated on TB treatment. NNS and NNT were 100.75 and 9.25 respectively. The prevalence of TB in the screened patients was 992.55 per 100,000 while the TB positivity rate in the presumptive cases was 10.81%.

Conclusions and key recommendations: Integrating TB-screening in HTS outreaches targeting key-populations in HIV hotspots improved TB case detection. HIV programs should integrate TB-screening in HTS services targeting key-populations in HIV hotspots.

PS29-722-26 Role of intensified tuberculosis case finding among drug users in Afghanistan

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Background and challenges to implementation: Afghanistan is home for 940 thousand drug users. The co-morbidity between TB and drug users resulted in increased risk of developing TB disease and also it worsening TB treatment outcomes and they will remain source of TB infection spread it in the community. The aim was to estimate the yield of pulmonary TB among this vulnerable population

Intervention or response: The USAID funded Challenge TB (CTB) project assisted national TB program (NTP) to screen drug users for TB. Study team developed questionnaire, trained field workers and supervisors. All drug users in community and those attending DDRCs were screened for TB. They identified and collected sputum samples of those had cough for more than two weeks and taken their chest X-ray, sputum sample tested by GeneXpert.

Results and lessons learnt: In total, 9,519 drug users attended study, 7,925 (83%) male and 1,594 (17%) female. Mean age was 35.8 year. 10% of study participants were

HIV positive and 7.5% were infected by HBS/HCV. 66% of study participants were illiterate, 18% had completed primary school, 11% secondary school and 1% was faculty graduate. 4,737 (50%) were married, 2365(39%) single, 315(3%) widow, and 65(0.6%) divorced. Mean weight was 60.4 Kilogram and height of 162.6 centimeter. 224 (2.4%) had had TB during their life time. 80 (0.8%) were still under TB treatment. Also, 1,335 (14%) had cough more than two weeks who tested for TB and 101 (1.1%) of them diagnosed as all forms TB. The yield of TB turned to be 1,061 in 100,000 drug addicts (Table 1).

Conclusions and key recommendations: The study discovered that yield to TB among drug users is 5.6 times higher than WHO estimated incidence (189/100,000) for Afghan population. We suggest extension of DOTS to DDRC centers and active case finding among drug users and facilitating six month stay for co-morbid TB individuals at DDRC.

Variables	Value , (%)	
Total study population	9,519	
Presumptive TB Patients (Cough+Sputum)	1,335 (14%)	
All forms of TB Cases	101 (1.1%)	P-value: 0.0001 OR: 5.6
Yield of TB in 100,000 population	1,061	

[Table 1. Characteristics of study population]

PS29-723-26 Role of pharmacy in TB active case finding: a case in St Mary's Hospital Mumias

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Background: Kenya prevalence survey (2016) show that we are missing 50% of TB cases annually. About ¾ of patients with TB come to hospital but are missed. The program has piloted ACF in 13 County hospital which has contributed to 12% increase in case finding country-wide. ACF is concentrated in all patients' entry points and the pharmacy which is the end point is not targeted. The study aimed in finding cases at the exit point to determine the gap in ACF.

Methods: The study was done at St. Mary's Hospital, in Mumias. The pharmacists were sensitized on ACF and provided with a presumptive TB register. No patient was to be issued with any drug/antibiotic before being screened for TB. Patients who had missed TB screening in other departments were screened, entered into presumptive register and referred back to the clinicians for further evaluation using Genexpert testing and/or X-ray. Those with TB were linked to TB treatment and care.

Results: For the period July - December 2017, 38,000 patients were screened from all departments of which 7% (2571) were screened at the pharmacy. Presumptive cases

all departments 1249. presumptive from pharmacy 435. Total TB cases 210. TB cases from pharmacy 22/210 (10%) identified through active case finding.

Conclusions: Pharmacy greatly contributed to Active case finding. Pharmacy should therefore be involved in active case finding. More efforts should be made to sensitize all clinicians through training and mentorship on ACF. Suggest that no antibiotics/ drugs to patients before getting screened for TB.

PS29-724-26 Active case finding among people living with the human immunodeficiency virus in Rwanda using chest radiography

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Background and challenges to implementation: Routine Rwanda National TB Program (NTP) surveillance data shows that the routine screening among people living with Human Immunodeficiency Virus (PLHIV) using symptoms might not be detecting all TB cases. In Rwanda, 30% of all TB cases reported are from Kigali city, the capital of Rwanda. By introducing screening using x-ray, the NTP hopes that the strategy can detect TB cases missed by the routinely used symptoms screening.

Intervention or response: Active case finding among PLHIV using digital chest radiography was conducted in 9 selected health facilities (HFs) in Kigali city. All PLHIV registered in anti-retroviral treatment (ART) services (except those on anti TB treatment) were expected to be screened for TB using chest radiography. All PLHIV with abnormal chest x-ray images were expected to give a sputum sample for Xpert MTB/RIF examination.

Results and lessons learnt: The screening was conducted in 9 selected HFs. 15,775 (92%) out of 17,124 PLHIV were screened for TB, 2276 (14%) of those screened had an abnormal chest x-ray image and were therefore classified as presumptive TB. 139 new TB cases were diagnosed during the active case finding in 9 HFs in Kigali city. 6 (4%) of 139 new TB cases had Rifampicin resistance.

Conclusions and key recommendations: Active case finding among PLHIV using chest radiography detects TB presumptive people, and in combination with Xpert MTB/RIF, diagnoses TB cases missed by routine symptoms screening. This strategy should be adopted in PLHIV.

PS30 How do programmes find tuberculosis cases: lessons from the field

PS30-725-26 Does mobile screening for tuberculosis alleviate the financial burden of patients among vulnerable populations? Community-based active case finding in Palawan, the Philippines

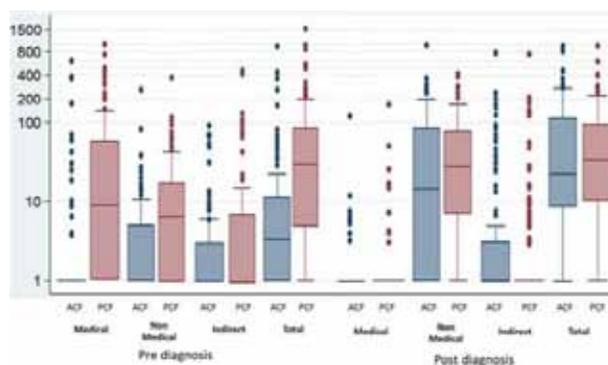
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Background: Tuberculosis (TB) case-finding project (DetecTB) using mobile unit equipped with digital X-ray machine, Light Emitting Diode Fluorescence Microscope (LED-FM) and GeneXpert machine has been implemented in Palawan, the Philippines since 2012. The project organized the systematic screening for TB among vulnerable populations. This study aimed to compare the financial burden of TB patients between active case finding (ACF) group and passive case finding (PCF) group.

Methods: We established an intervention group consisting of those detected by the project and a control group consisting of those detected by the routine system in the project sites between 2017. We collected direct medical costs, direct non-medical costs, indirect costs and household income through face-to-face interviews. We compared patient costs, proportion of TB-affected household facing catastrophic costs and proportion of dissaving between ACF and PCF groups.

Results: A total of 235 participants were enrolled comprising 107 from ACF group and 128 from PCF group. The median total costs were lower in ACF group (USD 46.2) than in PCF group (USD 96.5) ($p=0.002$) where the median costs before diagnosis were significantly lower in ACF group (USD 3.3) than in PCF group (USD 28.9) ($p<0.001$) while the median costs after diagnosis were not significantly different between ACF group (USD 22.8) and PCF group (USD 33.5) ($p=0.643$). Proportion of TB-affected household facing catastrophic costs was 17.7% in ACF group and 23.7% in PCF group ($p=0.276$). Proportion of dissaving was significantly lower in ACF group (26.2%) than in PCF group (41.4%) ($p=0.014$).

Conclusions: The TB patients detected by the mobile screening incurred lower costs and a lower proportion of their household faced catastrophic costs compared with those detected by the routine system. Mobile screening may be an alternative to reduce TB patient costs among hard-to-reach populations.



[Distribution of patient costs by case finding method]

PS30-726-26 Public-private partnership to enhance access of key populations to public sector health facilities for diagnosis and treatment of tuberculosis

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Background and challenges to implementation: Key populations including Transgender (TGs) and Male Sex Workers (MSWs) have limited access to health care services particularly in public sector due to stigma and discrimination which often results in delay in diagnosis and treatment of TB. Through Public Private Partnership (PPP) the access of TGs and MSWs to public sector diagnosis and treatment TB centers could be enhanced.

Intervention or response: From May 2017 to March 2018 we implemented public private partnership program supported through TB REACH grant in Karachi (the most populated city of Pakistan) and five other major cities of Sindh Province.

TGs and MSWs were approached for verbal screening for TB by trained outreach workers through gurus (for TGs) and focal persons (for MSWs) at their residence / workplace. Presumptive TB cases were identified and sputum specimens collected and specimens were sent for testing with Xpert MTB/RIF at public sector Basic Medical Units (BMUs). Diagnosed TB cases were registered at public sectors BMUs for treatment and were followed up by gurus / focal persons working as treatment supporters. BMUs staff including doctor, lab technicians and paramedics were trained and sensitized to understand cultural and social sensitivities of key populations.

Results and lessons learnt: The attitude of health care providers towards TGs and MSWs became friendly and nonjudgmental after trainings. Nonjudgmental and friendly attitude of health care providers mitigated fears and misconceptions of TGs and MSWs about public sector health facilities. Active involvement of gurus and focal persons resulted increased motivation of TGs & MSWs and improved their health care seeking behaviors.

Conclusions and key recommendations: Through PPP model we were able to increase the access of TGs and MSWs to public sector health care facilities and total 587 TGs and MSWs were diagnosed TB and successfully treated through trained and gender sensitized staff at public sector health care facilities.

PS30-727-26 Leveraging rapid molecular tests for TB detection in a key population, India

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Background and challenges to implementation: Revised National TB Control Programme (RNTCP) has aligned its diagnostic and treatment policies to End TB epidemic by 2025, ahead of global targets. Presumptive TB among key population viz., PLHIV, children and extra pulmonary symptoms are prioritized to offer upfront rapid molecular diagnostic test for TB detection since 2014-15. Till 2015, 128 Cartridge Based Nucleic Acid Amplification Test (CBNAAT) testing facilities were available with inadequate linkages for specimen transportation from the catering area.

Intervention or response: In 2016, 500 new machines were procured and CBNAAT network was expanded to 628 labs that lead to nationwide expansion of upfront CBNAAT testing for key populations. Till 2016, specimen collection system from the peripheral health facility to CBNAAT labs was fairly established across the country especially from 521 Anti Retroviral Treatment (ART) Center and 436 Medical Colleges, which are specialized health facilities to collect specimen including extra pulmonary sites.

Results and lessons learnt: During 2017, 107963 specimen of presumptive pediatric TB patients were subjected to CBNAAT, among whom, 9025 (8.4%) had M.TB detected including 1096 (1.0%) Rif resistant (RR) TB. Also, 190218 specimen of PLHIV were subjected to CBNAAT, among whom, 20591 (10.8%) PLHIV had M.TB detected including 1351 (0.7%) RR-TB. In addition, 125746 extra pulmonary specimen were subjected to CBNAAT, among whom, 35147 (28%) patients had M.TB detected including 5687 (4.5%) RR-TB. Increment of 13% pediatric TB case detection observed (2016- 76475, 2017- 86139).

Conclusions and key recommendations: Offering rapid molecular test for the TB detection helps in enhancing early detection, microbiological confirmation and TB notification. Quality screening and specimen collection and transportation system are the essential prerequisites to leverage with rapid molecular tests.

PS30-728-26 A successful model of TB contact investigation in Ukraine

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Background and challenges to implementation: Finding missing tuberculosis (TB) patients is a significant challenge for many countries. The Stop TB Partnership estimates that Ukraine, with the second highest TB burden in the European region, has approximately 10,500 sensitive missing TB patients TB contact investigation has not been effectively undertaken in many years due to health system challenges and lack of clear definitions of patient indexes, contact prioritization, and standardized procedures. A new system of TB contact investigation was, therefore, needed.

Intervention or response: In 2015, the USAID-funded Challenge TB Project initiated the development of a model that sought to identify and standardize an algorithm for tracing and screening well-defined circles of contacts of index patients. The process of developing, gaining approval, and implementing the model in Ukraine has involved primary health care providers, TB specialists, and epidemiologists. Active contact-tracing was initiated as a pilot in two regions of Poltava City in 2016.

Results and lessons learnt: In 2015, before initiation of active contact investigation, one index patient yielded, on average, just 1.3 new contacts, or a total of 879 contacts within 12 months. By 2017, the number had increased nearly 10-fold, to 12.6 new contacts per one index patient, or 7,033 contacts within 12 months. Of these, 91% were evaluated and 42 new TB cases were identified, compared to just 8 in 2015. Poltava's TB notification rate among contacts also increased from 6.7 cases per 1,000 contacts in 2015 to 10.1 cases per 1,000 contacts. Based on these promising results, this active contact investigation model will be introduced in other project regions in Ukraine.

Conclusions and key recommendations: The active contact investigation model implemented in Poltava, Ukraine, proved highly effective in identifying new TB cases. Close collaboration among various health services is critical. The process of developing and implementing this model is useful for other regions within and outside of Ukraine.

PS30-729-26 Expansion of tuberculosis services across the world's largest humanitarian crisis

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Background and challenges to implementation: Since August 2017, 671500 nationals from Rakhine State of Myanmar were forcibly displaced and have resided in Cox Bazar, Bangladesh. They are faced with adversity due to limited supplies of food and shelter along with poor access to health care services. BRAC, a non-government organization in collaboration with Government of Bangladesh, UN, and other national and international partner (IOM, MSF, Red Cross etc.) organizations has been expanding their services including TB management across 13 makeshift camps.

Intervention or response: BRAC intervened by establishing 10 diagnostic laboratories and deployed TB Screeners who visit every household and are on the lookout for presumptive TB cases. The laboratories act as the focal point to receive sputum and smears from the screeners, multiple outreach centers, and miscellaneous sources, such as UN and other partner organization's clinics and primary healthcare centers. Upon diagnosis of a case, Field Staff (PO) ensure DOTS through local leaders called 'Majhi' or a person nominated by the 'Majhi', based on location of the patient, as per advice of graduated physicians following NTP guidelines. If required, further evaluation (X-ray, FNAC) are executed in the nearby facilities after valid permission from the security agencies.

Results and lessons learnt: In a span of seven months, from September 2017 to March 2018, 27,604 presumptive cases (Male 47%, Female 53%) were tested. A total of 310 people were confirmed with TB of which 270 cases were bacteriologically confirmed and 07 clinically confirmed. Results also included 7 extra pulmonary, 7 relapse cases, and 01 case of Drug Resistant TB.

Conclusions and key recommendations: Intervening influx population with vigilant health services such as TB can forestall public health epidemic, improve quality of life, and support to thrive in a fragile environment. Strong monitoring and supervision may enhance case findings.

PS30-730-26 Geospatial mapping of current and former mineworkers in a high incidence TB setting: Zambia

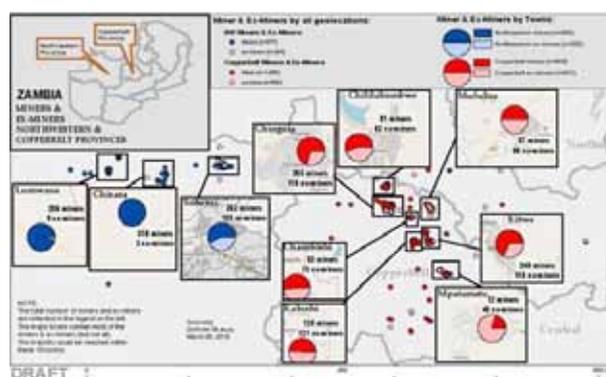
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Background: Mineworkers and ex-mineworkers in sub-Saharan Africa have been shown to have a profound impact on the spread of tuberculosis (TB). Despite several well-designed studies highlighting the association between mining and TB, little epidemiologic work has focused on the geographic distribution of current and former mineworkers' residences and their relation to mines and healthcare facilities; such work may facilitate targeted prevention and treatment programs.

The aim of this study is to overlay survey data with geospatial mapping of current and former mineworkers in the Northwest and Copperbelt Province of Zambia.

Methods: All current and former (ex-) mineworkers in each region were eligible for this cross-sectional survey. Convenience sampling identified eligible participants in mining communities, in partnership with the mines, community leaders, and health facilities. Structured knowledge, attitudes, and practices (KAP) surveys were administered and GPS coordinates were captured at the residences of enrolled participants.

Results: A total of 2792 mineworkers (1956 current and 836 ex-) were enrolled. Ex-mineworkers were more likely to have a history of TB (12% vs. 3.0%; $p < 0.001$). Among ex-mineworkers with a history of TB, one-fourth (25%) were diagnosed within the previous six months and one in five (22%) found it difficult to go to a clinic when sick. Striking differences exist in the geographic distribution of mineworkers and ex-mineworkers by province (Figure 1).



[Figure 1: Geospatial distribution of former and current mineworkers, Zambia]

In the Northwest province, while current mineworkers were relatively evenly distributed throughout three towns, almost all of former mineworkers (92%) in this

study resided in one town. This is in contrast to the Copperbelt province, where comparable proportions of mineworkers/ex-mineworkers were similarly distributed across 7 towns.

Conclusions: Mineworkers are a critical bridge population in TB transmission. Understanding differences in the geospatial distribution and perceptions of these populations provides insight into public health programs aiming to reduce TB transmission in Zambia.

PS30-731-26 Tuberculosis health services for mineworkers in Zambia: policies vs. practices

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Background: The Copperbelt Province in Zambia, where most mineworkers and ex-mineworkers reside, has the highest national rates of tuberculosis (TB) and HIV and the greatest gap between estimated TB burden and notifications. Mineworkers in both the Copperbelt and North-Western Provinces access both private mining and public health facilities for care. We assessed current practices in the TB cascade of care - from symptom screening through treatment initiation and completion - in these health facilities.

Methods: All mine-operated health facilities and public health facilities in mining communities on the Copperbelt and North-Western provinces of Zambia were targeted for inclusion. The TB cascade of care was assessed through key informant interviews and objective assessments of practices using standardized tools. We compared each step in the TB Cascade of Care to National Guidelines for TB Management. The proportion of facilities consistent with guidelines was calculated, and discrepancies were noted.

Results: Of the 21 facilities assessed, two were referral centers; we analyzed 19 facilities providing TB diagnostic and care services. Twelve (63%) health facilities were following guidelines for TB symptom screening; others used a limited number of symptoms (e.g., cough only) or included restrictions of duration to indicate presumptive TB. GeneXpert MTB/RIF was underutilized, with six facilities not sending any specimens for testing (32%) and three limiting Xpert use to HIV-positive persons. One facility was using Xpert according to guidelines. Deficient specimen courier systems and inconsistent turnaround times were noted.

All facilities were following guidelines for treatment and treatment monitoring. The majority were using the national TB register (87%) and patient treatment card (100%).

Conclusions: Methods for TB screening and testing varied and were often inconsistent with national guidelines. These findings highlight the need to provide ongoing mentorship and supervisory support to health facilities to ensure standards for TB screening, testing and treatment in Zambia.

PS30-732-26 Active tuberculosis case finding in health care settings: feasibility and promise of case detection and treatment initiation

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Background: Cambodia recently achieved the reduction of Tuberculosis (TB) prevalence. But missing case of around 40% is still a national major concern. Active case finding (ACF) aims to diagnose and treat TB among people who do not seek care for TB symptoms. Many approaches of ACF had been conducted through communities. We assess the feasibility of ACF among individuals come to seek care in hospital.

Methods: A cross-sectional study using program data collected during TB ACF activities. All individuals who seek care in hospital were voluntarily invited to screen for TB. Those present with one of the four symptoms or those age over 50 years old (regardless symptom) were undergo CXR and sputum smear at the same time. When CXR abnormal and first smear negative, then Xpert test done. Two smears were done if CXR normal.

Results: Between 1 September 2015 and 30 March 2016, 2,074 individuals were screened for TB, 62% (1,285/2,074) were female, median age 55 (IQR 41-65) and 63% (1,315/2,074) from province. Of all, 13% (275/2,074) TB cases were diagnosed in which 51% (141/275) bacteriological positive, 45% (123/275) bacteriological negative and 4% (11/275) extrapulmonary TB. The majority 68% (187/275) of TB cases were diagnosed using CXR. Overall, 7.5 and 14.7 clients had to be tested to diagnose one TB patient and bacteriological confirmed respectively. Of bacteriological positive, 30% (43/141) smear-/Xpert-MTB+. 7% (43/595) Xpert-MTB+ with CXR abnormal not consistent with TB. Same-day treatment initiation was more frequent when CXR was interpreted on the day (IQR: 0-6).

Conclusions: ACF in health care setting is feasible and promising in case detection and treatment initiation. Combining CXR and Xpert testing in high risk groups is probably the most effective approach. If access to Xpert testing is restrained, Xpert testing could be preserved for those with a negative CXR and sputum smear microscopy.

PS30-733-26 To study the complications and sequelae in patients with pulmonary and pleural tuberculosis at a tertiary care hospital in Pakistan

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Background: To study the post TB sequelae in patients treated for TB in a tertiary care hospital of a high TB burden country.

Methods: An observational study on patients treated for TB at outpatient pulmonology clinics of Aga Khan University Hospital, Karachi, Pakistan from Jan 2015 to Dec 2016. Clinic records and Chest x-rays were reviewed for post TB sequelae.

Results: A total of 315 patients were treated. 59% were male and 41% were females. 208 (66%) patients were treated as pulmonary tuberculosis (PTB), 93 (29.5%) were treated as pleural tuberculosis and 14 (4.4%) patients were treated as both. 93.3% were new cases. 111 (35.23%) patients were AFB culture positive. The cure rate was 80.3%. Post-treatment chest x-ray was available in 192 (60.95%) patients during the period of one year. Only 24 (12.5%) patients had complete resolution of radiological abnormalities. 168 (87.5%) patients developed post-treatment parenchymal and pleural sequelae. The sequelae were unilateral fibrosis with loss of lung volume 35.71%, unilateral pleural thickening 13.09%, unilateral pleural thickening with fibrosis 13.09%, bilateral fibrosis with volume loss 9.52%, unilateral bronchiectasis 6.54%, unilateral bronchiectasis with fibrosis 5.35%, bilateral bronchiectasis with fibrosis 4.16%, bilateral pleural thickening with fibrosis 4.16%, unilateral loss of lung volume 1.78%, bilateral loss of lung volume 1.78%, unilateral pleural thickening with bronchiectasis 1.78%, bilateral bronchiectasis 1.19% and bilateral pleural thickening 0.59%.

Conclusions: The post TB sequelae are alarmingly high in our group of study and were a cause of persistent respiratory symptoms. Treating tuberculosis is not the end but the debilitating complications post-treatment has more deleterious psychosocial and financial impact. It is of utmost importance to be aware of the full spectrum of these disorders to facilitate early diagnosis and treatment.

PS30-734-26 The yield of tuberculosis mass screening among refugees in Western Ethiopia

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Background and challenges to implementation: Ethiopia, being the host for the second largest population of refugees in Africa, prioritized refugees as key population groups for TB care. We implemented and assessed the yield of mass screening as TB case finding strategy in Ethiopia.

Intervention or response: We organized a mass screening campaign from January to February 2018 in four refugee camps in Benishangul Gumuz region of Ethiopia. We used a symptom-based checklist as screening tool to identify all patients with two or more weeks of cough. About 4-5 ml of spot and morning sputum sample was collected for AFB microscopy and GeneXpert. AFB microscopy was first done for all presumptive TB (PTB) patients and AFB negative sputum was confirmed by GeneXpert. Data was analyzed using SPSS software package version 20.0.

Results and lessons learnt: Of 47,000 refugees screened, 56.4% and 99.4% were men and Sudanese by sex and citizen, respectively; and 179 (0.4%) were presumptive TB cases. Among 179 presumptive TB patients evaluated, five TB patients were confirmed to have TB including one newly diagnosed and four already on treatment. All patients were detected among contacts sharing same cell within camps. The point prevalence of PTB was 11 per 100,000 population. About 57.5% and 58.1% of presumptive TB patients were underweight and illiterate, respectively. All of the four TB patients on treatment were confirmed to have TB by both AFB microscopy and GeneXpert at the time of treatment. The newly diagnosed TB case was negative by AFB microscopy but was confirmed to have TB by GeneXpert.

Conclusions and key recommendations: The yield of mass screening was low among refugees in Western Ethiopia. The existing system had already identified 80% of the patients. Strengthening the local health system and implementing targeted screening among contacts of index TB patients are more feasible strategies.

Indicators	Number (%)
Total screened	47,000
Presumptive TB identified	179 (0.4)
Confirmed TB	5
Linked to treatment	5

[Yield of Mass TB Screening among Refugees in Western Ethiopia]

PS30-735-26 Active case finding using mobile units in urban slums, Ulaanbaatar, Mongolia

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Background: Mongolia is one of high tuberculosis (TB) burdened countries among Western Pacific Region. Because of the gap between notification data and prevalence survey, more efforts to find TB cases using systematic screening strategy should be required. The study aims to examine the impact of active case finding (ACF) using Mobile unit in urban slum including homeless, Ulaanbaatar, 2016-2017.

Methods: The study team operated a mobile unit equipped X-ray machine to screen TB among urban slum. If the screening identified a case who had TB presumptive signs on Chest X-ray, sputum smear and molecular test using Anyplex™ II MTB/MDR/XDR Detection was followed to confirm TB. We evaluated the performance of the ACF and identified predictors of active TB.

Results: Totally, 17,774 participants were screened by chest X-ray (CXR) and identified 2,445 cases with TB presumptive signs. Sputum collection was done at 96.7% of participants having TB signs on CXR and identified 129 active TB cases. The final diagnosis included 50 SM+/PCR+, 1 SM+/PCR-, 56 SM-/PCR+ and 22 clinically diagnosed cases. 122 (94.6%) cases were enrolled on treatment. TB prevalence within this study was higher (726/100,000) than the recent National Prevalence survey (560/100,000). In multivariate analysis, we identified risk factors of active TB that included male, cough symptom (duration), sputum, weight loss, chest pain, previous TB history and TB contact history.

Conclusions: The case detection strategy using mobile unit with CXR and rapid diagnosis was feasible and presented high yield in urban slum setting, Mongolia.

PS30-736-26 Active case finding for tuberculosis among people attending the general out-patient department at Bungoma Hospital, 2017

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Background: World Health Organisation launched the End TB Strategy in 2015 with the ambitious goal of ending the global tuberculosis (TB) epidemic by 2035; this

requires a dramatic improvement in current case-detection strategies. A reliance on passive case finding has resulted consistently, in over three million TB cases missed per year, leading to ongoing transmission of infection. Active case finding is likely to lead to an improved early diagnosis of TB, early initiation of treatment, reduced morbidity and mortality, reduced community transmission, and reduced incidence/prevalence of TB. TB case detection is low in Bungoma only 40% of TB cases are detected each year. We aim to screen the entire patients attending general outpatient in Bungoma hospital.

Methods: In 2017 Bungoma hospital conducted screening of all patients attending general outpatient. Trained Cough monitors performed TB health education, symptom screening, and collection of sputum and facilitated specimen transport to the laboratories. For those mycobacterium TB detected were put on TB treatment.

Results: A total of 82,418 patients were screened with 7,683 (9.3%) of them being presumptive TB cases. Among them 5,648 (74%) submitted sputum sample for Genexpert, and 476(8.4%) had bacteriologically TB. In addition 196 were diagnosis with other forms of TB using X-ray and clinical evaluation giving a total 672.

Conclusions: Using a sensitive symptom screening followed by Genexpert testing, contributed to improved case detection of TB, shortening of diagnostic delay and successful putting patients on treatment.

PS31 Scaling up diagnosis: the way forward

PS31-737-26 Sputum smear slide referral by non-laboratory professionals as an interim solution in remote areas, Amhara Region, Ethiopia

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Background and challenges to implementation: Direct sputum smear microscopy remains the most common method for diagnosis of pulmonary tuberculosis in resource-poor countries. Shortages of medical laboratory professionals have reduced the capacity of health centers (HCs) to provide tuberculosis (TB) microscopy services. In October 2017, 359 (40.0%) HCs did not provide TB diagnostic services.

Intervention or response: To overcome the shortage of laboratory professionals, HC TB focal persons were trained in the preparation of sputum smears and their

transportation to the nearest diagnostic health facility. This innovative short-term solution was started in one zone, then scaled up to all zones. There has been support from USAID funded projects HEAL TB and Challenge TB since April 2016 in the form of: training health care workers, supportive supervision, job aid provisions (SOP), review meetings, and one-on-one reviews. Routine sputum smear slide referral data from 2015 to 2017 were analyzed. We assessed the yield of TB among sputum smear referral from non-diagnostic HCs in Amhara region.

Results and lessons learnt: From January 2015 to September 2017, 63,459 slides were collected from 26,488 presumptive TB cases. 62,972 (99.2%) of these were processed, 591 (0.94%) tested positive, and 268 (1.0%) SS+ TB cases were detected and referred for treatment. During the same period, the annual number of presumptive TB cases giving sputum samples increased from 7,605 to 12,775, with the number of cases detected increasing from 85 to 111 correspondingly. The challenge is that under half of HCs have been making referrals - during April-June and July-September 2017, only 166 (49.4%) and 118 (33.1%) HCs did so respectively.

Conclusions and key recommendations: Significant numbers of TB cases have been detected using sputum smear slide referral from non-diagnostic HCs. Sputum slide referral should be strengthened to address the shortage of laboratory professionals in remote health facilities.

Indicators	Number
# of presumptive TBs whose sputum sample referred to diagnostic HF	26,488
# sputum slides referred to diagnostic HFs	63,459
#(%) of TB positive slides	591(0.9)

[Performance of presumptive TB sputum slides referral to diagnostic Health facilities, 2015-17]

PS31-738-26 Are we adequately utilising available diagnostic resources for DR-TB in India? Assessment of annual status report

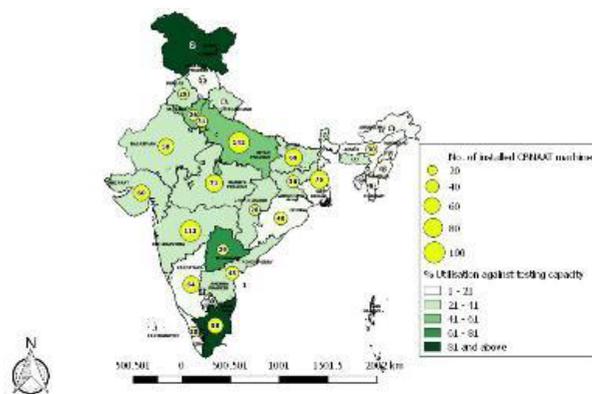
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Background and challenges to implementation: In India, tuberculosis remains a major public health challenge with an incident of 147,000 MDR-TB cases. According to Global TB report, India accounts for 25% of global MDR-TB burden. PMDT services were introduced in 2007. Management of multi-drug resistant tuberculosis (MDR-TB) is challenging especially in countries with limited resources. NSP aims to achieve, universal testing for all DR-TB cases and rapid scale-up of short-course regimens for drug-resistant TB and DST guided treat-

ment approaches. For decentralized diagnosis of TB and Rifampicin resistance, 1135 CBNAAT machines have been provided at district levels. This paper aims to assess the potential utilisation of these CBNAAT machines.

Intervention or response: CBNAAT facilities have been established at District levels for decentralised molecular testing for TB and simultaneous detection of Rifampicin resistance. CBNAAT and Line Probe Assay introduced in 2009 and scaled up from 2012 onwards, have ensured that rapid molecular diagnostics are available throughout the country. In 2017, 734,247 Presumptive DR-TB patient patients have been tested using these methods and 38,854 Rifampicin resistant /MDR-TB patients have been diagnosed.

Results and lessons learnt: An analysis was carried out to assess the potential use of CBNAAT machines established and the number of Presumptive DR-TB patient subjected to DST/DRT during the year 2017. Compared to the potential capacity of the CBNAAT machines, sub-optimal utilisation was found in north-east states, HP, Odisha etc. 40-60% utilisation found in Maharashtra, UP, Chandigarh and Telengana. States like TN and J&K utilised to the maximum capacity. The detailed information is shown in the below map:



[Statewise patterns of % utilisation of CBNAAT machines against testing capacity-India (2017)]

Conclusions and key recommendations: In order to diagnose the emerging TB/DR-TB cases, optimum utilisation of CBNAAT labs, it is very essential that the diagnostic resources are effectively utilised. The data implies that the deployment of machines needs to be carefully installed in strategic locations and establish proper sampling collection linkages and ensure adequate testing of samples through the machines.

PS31-739-26 TB one stop services, a diagnostic hub offering one stop services: an innovative approach to increase bacteriologically positive TB case detection in the private sector

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Background and challenges to implementation: The Private Sector(PS) accounts more than 70% of outpatient healthcare in India Reasons for non-involvement of PS are -perceived threat to their business, no faith in public facilities, lack of awareness of STCI, scarcity of endorsed diagnostics in PS, lack of support systems for effective referrals and linkages and lack of a socio-business model.

Intervention or response: TB One Stop Services Project (Supported-by-STOP-TB-Partnership) and implemented by TB-Alert-India is initiated from September 2017 in 2 Districts of Andhra Pradesh State, India.

After mapping of Private Facilities, established 5 Private TB Diagnostic Hubs at Private-Diagnostic-Centres. Ensured each Diagnostic Hub offering similar services of a NTP Tuberculosis Unit (TU):

Pre-Diagnostic-Services: Sensitize PPs on STCI , Active Screening among PP Out Patients, Assisted Referral to Diagnostic Hub

Diagnostic-Services-at-Project-Established-Diagnostic-Hub: Follow NTP Diagnostic Algorithm Sputum Microscopy (Free), X Ray (Subsidised) and GeneXpert-CB-NAAT test (Subsidised-IPAQT) (FREE-test-for-ONE-in-4-Test-Socio-Business-Model), Digital Communication of Results

Post-Diagnostic-Services: NTP Notification, Public Health Action , Patient Counselling, Monthly Follow up

Results and lessons learnt: During October 2017 to March 2018, Project facilitated 4535 Presumptive TB Cases of Private Provider Outpatients get tested in Project Established 5 Private TB Diagnostic Hubs. Among them 1343 TB Patients identified (973 (73%) are Bac+ (AFB/XPert) and 370 (27%) Clinically Diagnosed)

Project-Additionality-to-NTP-October-2017-to-March-2018- Project-Coverage-Area: 2499 cases Notified by NTP for Private Sector, Among them 1343(54%) cases facilitated by TOSS and among them 973 (73%) are Bac+.

Evaluation-Population-&-Control-Population-4Q2017
Evaluation-Population:1202-TB-Cases-Notified-and-307-Bac+

Control-Population:952-TB-Cases-Notified-and-30-Bac+

State-&-TOSS-Project-Contribution-October-2017-to-March-2018

Total-9845-Cases-Notified State level among them 1343 (14%) Cases are notified by TOSS project

Conclusions and key recommendations: WIN -WIN -WIN-Patient-PS-NTP

WIN- Patient

Quality Assured Diagnosis - Early, Accurate & Affordable, One stop services

Benefits of subsidy / IPAQT passed on to patient

WIN - PS

Patient Loyalty is retained

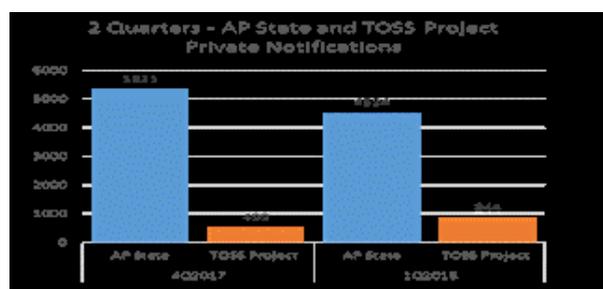
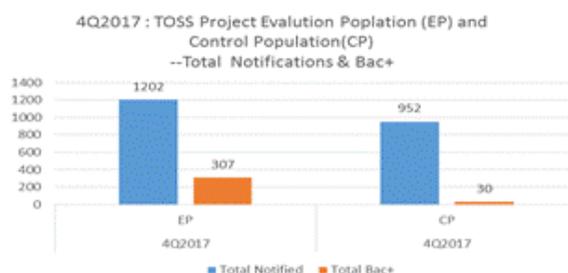
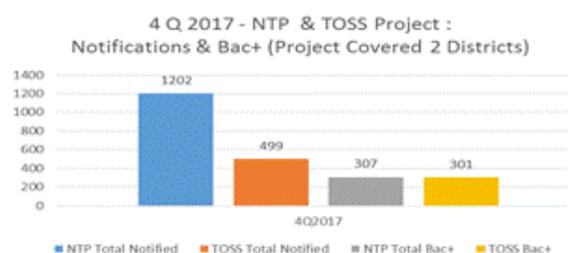
Socio-Business-model-protecting-their-interests

Follow up services for better outcomes and adds to their reputation

WIN - NTP

Greater Bac+ TB Notifications from PS

STCI-followed-by-PS



[TOSS GraphV6]

PS31-740-26 Use of motorcyclists for specimen referral: phased implementation in Tanzania specimen referral network

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Background and challenges to implementation: Strengthening specimen transport and referral has been identified as a strategic priority of the Global Laboratory Initiative (GLI) in 2017 to ensure universal access to rapid tests and DST under The End TB Strategy. Access to quality TB laboratory services in developing countries is limited mainly due to infrastructural and human resource challenges. In Tanzania, there are three systems for delivery of specimens to laboratories: referral of patients, referral of slides (fixed sputum smears) prepared by community sputum fixers and referral of sputum specimens.

Intervention or response: In 2016 Challenge TB introduced the use of motorcyclists for transportation of sputum specimens from non-GeneXpert sites to GeneXpert sites. A pilot study in four CTB supported districts of Ilala 1, Kinondoni and Kwimba, thereafter in Oct-Dec 2017 Rombo and Sengerema District was added based on burden of TB and HIV. Specimen collection tools, transportation manual, training materials, sample referral register, reporting and recording forms were developed. Sensitization meetings were conducted to the regional and district Laboratory and TB coordinators and health management teams. 5 motorcyclists were hired to transport collect specimens from 40 facilities.

Results and lessons learnt: A total of 4,186 specimens were collected and transported to GeneXpert facilities for testing from October 2016 to December 2017; out of them 410 (9.8%) were diagnosed with TB and 11 (0.3%) were rifampicin resistant. All the patients were initiated on TB treatment. 50% of the patients were from the HIV care and treatment clinics.

Conclusions and key recommendations: Use of local means of transportation has a role to play on improving utilization of GeneXpert technology. The country needs to find a sustainable way to roll out and sustain this initiative of the use of motorcyclist as efforts to increase the GeneXpert utilization countrywide.

There is a great need of developing and standardize a robust specimen referral system.



[Trend of specimen transportation using motorcycles from October 2016 to December 2017]

PS31-741-26 Ineffective implementation of interventions: the largest road block to the end TB strategy

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Background and challenges to implementation: Accurate diagnostic technologies and anti-TB therapy are available and yet new cases continue to rise and more die of tuberculosis (TB) every year.

Intervention or response: A multi-national operational study was conducted in three African countries using implementation of TB molecular diagnostics to investigate the underlying causes why TB control tools haven't reached those who most need them.

Results and lessons learnt: Views obtained from 1119 participants including District/County health officers, healthcare practitioners, TB patients, survivors, and carers, community leaders, and policymakers. TB control is the least considered in domestic budget allocation resulting in limited coverage and underutilization of diagnostic technologies. Persons to test ratio was 557,996:1 XpertMTB/RIF, 18,750,000:1 Line-Probe-Assay (LPA), and 15,000,000:1 culture. XpertMTB/RIF was fully utilized in < 10% of the healthcare facilities and < 1% for LPA. Surprisingly, we found that knowledge and awareness of TB is low both among healthcare practitioners and community leading to low suspicion index at the clinic and high stigma against TB patients. In some sections of community, TB is still regarded as a spiritual curse rather than a bacterial infection. Community and individual poverty meant unfordability of pretreatment diagnosis since free TB care is only available after TB confirmation. Poverty increased risk of self-medication with either herbs or cheap ineffective antibiotics obtained over-the-counter. Low appreciation of the magnitude of the TB problem and donor mentality at policymaker level meant that without external funding, the national TB control policies would never see the light of implementation.

Conclusions and key recommendations: Based on findings, ending TB requires bottom-up approach that effectively rallies policymakers at country level to commit adequate resources to universally implement interventions; sustained sensitization of the public and practitioners to eliminate stigma and increase case detection. Early interaction between diagnostic/therapy developers and target users to ensure compatible products, and deliberate investment in socioeconomic empowerment programmes are critical to the end TB strategy.

PS31-742-26 Reaching vulnerable communities in hard-to-reach areas of Myanmar: increasing access to TB diagnosis through sputum collection centers

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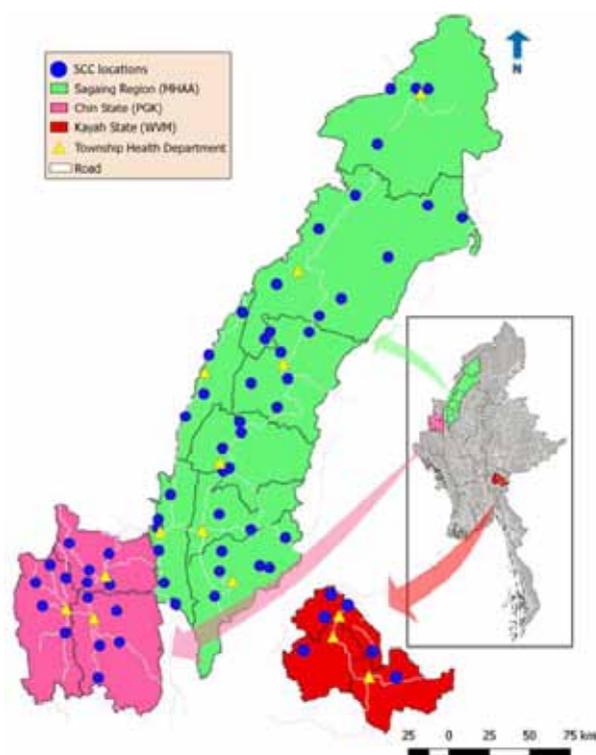
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Background and challenges to implementation: In Myanmar, approximately 27% of the estimated incident TB cases went undetected in 2016 (Global TB Report 2017, WHO). Missing cases are estimated to be higher in some states and regions, where the transportation infrastructure challenges limit access to health care services, including TB diagnosis and treatment.

Intervention or response: The USAID Challenge TB project and partners established a sputum transport system by establishing sputum collection centers (SCCs) in hard-to-reach areas in the northwestern and southeastern parts of Myanmar. The Project trained volunteers, provided required materials, transportation costs and supportive supervision. Community volunteers or basic health staff at each SCC received sputum samples from surrounding villages and sent them to the township diagnostic center. Following testing, SCCs delivered results back to the community members to promote early diagnosis and treatment.



[Sputum Collection Center Location Map, USAID Challenge TB Project, Myanmar]

Results and lessons learnt: Since August 2017, 63 SCCs were established in 14 townships of Chin, Kayah, and Sagaing; 61 of the 63 centers were active as of February

2018. Between August 2017 and February 2018, sputum samples from 1,444 presumptive TB patients were received at SCCs and transported to respective township diagnostic facilities for testing. Individual SCCs received an average of 24 samples (range: 1- 85). Fifteen of the 61 active SCCs (25%) identified sputum positive cases. Approximately 17% of all patients with bacteria confirmed TB notified by the Project across the 14 remote townships were identified through the SCCs.

Conclusions and key recommendations: Sputum transport by SCCs expanded access to early TB diagnosis and treatment services to hard-to-reach communities in Myanmar. The sputum transport system supports the National TB Program's efforts to reduce the gap of missing TB cases in Myanmar, and expansion to other states and townships would further improve access to TB services.

PS31-743-26 Pre-evaluation of pyrazinamide resistance among MDR-TB isolates: a study from an apex tertiary care center in India

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Background: Inclusion of Pyrazinamide (PZA) in Tuberculosis (TB) chemotherapy has significantly shortened the treatment duration. This is the only drug which is used in the treatment of both drug sensitive as well as Multi Drug Resistant (MDR) form of Tuberculosis. Although resistance to PZA is associated with poor treatment outcome Drug Susceptibility testing (DST) of PZA is not routinely performed due to technical difficulties in public health laboratories in India.

Methods: A prospective study was undertaken on 117 MDR-TB patients' sputum specimens confirmed by LPA. Following this, all samples were cultured on solid media and PZA DST was performed.

Results: A total of 117 MDR-TB suspects were tested for PZA DST using LJ media and almost 50% of the MDR isolates showed phenotypic resistance to PZA. In addition to this *pncA* gene was sequenced and results were found to be 100% concordant for both the methods phenotypically and genotypically.

Conclusions: This kind of pre-classification of PZA DST among MDR-TB patient will help the clinicians in forecasting patient treatment outcomes. Therefore, in future more clinical studies are required to take this forward.

PS31-744-26 Detecting drug-resistant tuberculosis in patients with history of prolonged stay in high-burden countries, Taiwan

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Background and challenges to implementation: Line probe assay (LPA), one of rapid molecular diagnostics, will improve the timeliness of drug-resistant tuberculosis (DR-TB) diagnosis. In Taiwan, universal drug susceptibility testing has already been applied, which revealed 1% and 6-8% of MDR-TB among new and previously treated patients. LPA has been used in smear-positive notified patients with history of prolonged stay in high burden countries since 2013, but the completeness of testing remained low at the beginning of this program.

Intervention or response: Public health nurses were educated to collect and record patients' history of cumulative one month or longer stay within one year in high burden countries in TB registry. We identified eligible patients in TB registry from April 1, 2013 to December 31, 2016 and estimated the proportion of LPA performed and yield rate of DR-TB. We defined timeliness of LPA as collecting sputum for LPA within 7 days after the first date of sputum collection for TB diagnosis. We used ² trend test to evaluate the programmatic progress.

Results and lessons learnt: There were 777 eligible smear-positive TB patients identified. The proportion of LPA performed increased from 27 to 78.8% from 2013-2016 ($p < 0.001$). The proportion of timely LPA performed in 2016 increased by 41.5% compared to that in 2013. The overall proportion of isoniazid-resistance, rifampin-resistance, and MDR was 2.4%, 1.6%, and 3.8%, respectively. The yield rate of MDR-TB was highest in patients who had prolonged stay in China, which was 6.9%, and the following was 4.0% among those who stayed in the Philippines and 2.9% in Viet Nam, respectively.

Year	No. of smear-positive patients No. of LPA performed (%)	Isoniazid-Resistance (%)	Rifampin-Resistance (%)	MDR (%)
2013	40 (27.0%)	3 (7.5%)	2 (5.0%)	3 (7.5%)
2014	48 (24.7%)	3 (6.3%)	1 (2.1%)	2 (4.2%)
2015	121 (52.2%)	3 (2.5%)	2 (1.7%)	4 (3.3%)
2016	160 (78.8%)	0 (0%)	1 (0.6%)	5 (3.1%)

[Number and proportion of line probe assay performed in smear-positive patients with history of prolonged stay in high burden countries]

Conclusions and key recommendations: The completeness and timeliness of LPA performed in patients who had prolonged stay in high burden countries improved year by year. Automatic and systematic alert should be established to further enhance the completeness. The

yield rate of MDR-TB is high in this population that should be prioritized for detecting DR-TB.

PS31-745-26 A qualitative approach to determine dynamics behind low GeneXpert utilization in Jinja Health region, Uganda

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Background: In 2010, World Health Organization endorsed the use of Xpert MTB/RIF assay for diagnosis of Tuberculosis (TB) and Uganda started GeneXpert implementation in 2011 in two health facilities. Through support from partners, this increased to 112, across the country by June 2017. Currently, the Uganda National TB and Leprosy Program (NTLP) encourage facilities with GeneXpert machine to use it as initial diagnostic test for all presumptive TB patients while those without GeneXpert on site are to refer high risk groups (HIV +ve, children < 15years, health workers, contacts of drug resistant Tuberculosis (DR TB) patients, through the sample transportation system. Despite the increased number of GeneXpert machines and more inclusive eligibility criteria for Xpert MTB/RIF assay, utilization of GeneXpert testing is still low. By June 2017, average utilization stood at 5 tests/day (31%) countrywide and 2 tests/day (12.5%) in Jinja health region. Our survey aimed to determine the dynamics behind low utilization of GeneXpert in Jinja region.

Methods: Twenty two health facilities (1 hospital, 9 HC IV and 12 HC III) these are two high volume diagnostic units in 11 districts were surveyed. Records reviews of outpatient registers, presumptive and laboratory registers were done. Focus group discussions were held with the Facility staff .

Results: Out of 3574 presumptive TB patients only 846 (24%) were sent to laboratory for sputum examination and 195 (5.5%) were tested using GeneXpert. Of the facilities that participated (n=22), knowledge gap on eligibility criteria (19/22), lack of sputum mugs (17/22), poor staff attitude towards TB patients and samples (16/22), low suspicion index (13/22), lack of masks (11/22), lack of incentive (4/22) and high workload (3/22), contributed to the low utilization.

Conclusions: Refresher training, mentorship, Continuous medical education, and incentive should be provided by Government, donors, partners, and all stakeholders to increase Gene Xpert utilization.

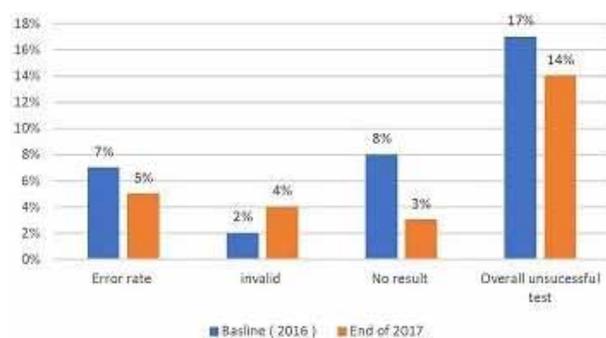
PS31-746-26 Improved GeneXpert utilization through capacity building activities in Southern Nations Nationalities and Peoples Region, Ethiopia

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Background and challenges to implementation: In Ethiopia, since 2016, all presumptive TB cases are being tested by GeneXpert at sites which had a GeneXpert machine. There are currently 23 GeneXpert machines in South Nations Nationalities and Peoples Region (SNNPR). However implementation of GeneXpert testing faces many challenges. To strengthen the implementation of GeneXpert testing services, supportive interventions are required.

Intervention or response: Baseline assessment was conducted by the SNNPR Regional Public Health Laboratory, with financial support from the USAID funded Challenge TB (CTB) project. Power interruption, training gaps and a weak sample referral system were key challenges identified that affected the GeneXpert testing. CTB provided logistical and technical support including training, supervision and routine mentorship. Routine quarterly data was collected and analyzed to document the effect of the interventions on the GeneXpert testing in the region.

Results and lessons learnt: A total of 6,675 and 16,502 tests were conducted in 2016 and 2017 respectively. The average test uptake per machine was 333 and 717 in 2016 and 2017 respectively. After implementation of the different interventions, test uptake has increased in 2017 as compared to baseline. But it was not in the acceptable range of 2640 tests per machine per year. Of the 15,615 successful tests conducted in 2017, 2,129 (13.6%) of them were positive for TB. The number of RIF cases detected were 56 and 72 in 2016 and 2017 respectively. Bar “invalid result”, both “no result” and “error” rates reduced in 2017 as compared to the baseline (Fig 1), but they still remain above the acceptable range.



[Fig1. GeneXpert unsuccessful test in 2016 and 2017 in SNNPR]

Conclusions and key recommendations: The interventions improved the level of utilization and quality of the GeneXpert testing in the region. Future interventions should focus on strengthening the sample transportation, strong mentorship and improving the power interruption to enhance the test uptake and further improve the quality of testing services.

PS31-747-26 Barriers to uptake of GeneXpert testing where recommended: insights from a district hospital in Sierra Leone

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Background and challenges to implementation: In December 2010, the World Health Organization (WHO) recommended the use of the Xpert MTB/RIF assay for the diagnosis of Multi-Drug resistant Tuberculosis (MDR TB) and is preferred as the approach for diagnosis of Tuberculosis in special populations such as children and People Living With HIV/AIDS (PLWHA). However, access to GeneXpert testing in resource limited settings has been impeded by prohibitive costs to logistics needs and implementation resulting in slow and/or poor uptake. Sierra Leone is one of 30 countries with the highest burden of the disease in the world and has a national HIV prevalence of 1.7%.

Intervention or response: The Ministry of Health and Sanitation (MOHS) of Sierra Leone scaled up public sector GeneXpert testing to 8 public sector hospitals. The Xpert MTB/RIF platform was introduced to Port Loko District Hospital, a district with high HIV prevalence, in March 2017. Key to this was the centralized training of technical and administrative personnel from the district and hospital level, and the supply of logistical needs and leveraging of the existing National Specimen and Result Transport Network (NSRTN) to enable expedited access to central level support.

Results and lessons learnt: A total of 193 TB cases were registered between April 2018 and March 2017, out of which 28 (14.5%) were HIV positive and 14 (7.2%) were Childhood TB cases. 13 out of the 75 (17.3%) sputum smear positive cases were HIV-TB co-infected. Only 21/193 (10.8%) of these patients were ever linked to the laboratory for GeneXpert test though eligible by the National TB diagnosis guidelines. Significant gaps existed in the timely linkage and documentation of patients eligible for GeneXpert between the hospital service providers.

Conclusions and key recommendations: Sustained decentralized capacity building to facilitate front line service provider compliance with the new guidelines is warranted to support uptake of GeneXpert testing at peripheral facilities such as Port Loko District Hospital.

PS31-748-26 Increased mortality during rifampicin-resistant TB treatment associated with inadequate laboratory testing

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Background: Treatment success for rifampicin-resistant tuberculosis (RR-TB) in Botswana is relatively good (75%); however, mortality remains high (17%). Previous analysis identified HIV positivity with low CD4 as a risk factor for mortality. We examined additional risk factors, including access to drug susceptibility testing (DST). While WHO recommends DST to detect and manage RR-TB, only 41% of TB patients globally in 2016 received first-line DST, and of those initiating RR-TB treatment, only 39% received second-line DST.

Methods: All 704 patients enrolled on treatment through the Botswana national RR-TB program from 2006-2014 were included. Demographic, clinical and laboratory data were retrospectively collated from registers and patient charts. Adjusted hazard ratios (aHR) with 95% confidence intervals (CI) for time to mortality were calculated using multivariate Cox regression, controlling for gender, age, HIV, smear, radiology, treatment facility and resistance pattern.

Results: Mortality during treatment among RR-TB patients was 17% (122/704). Increased mortality was associated with Pre-XDR or XDR-TB diagnosis and with presumptive cases missing both first- and second-line DST (Table).

Resistance pattern	Total	Deceased n (%)	Reference / % deceased, n/N (%)	aHR	CI	p-value	
Confirmed RR-TB, 2nd line DST missing	360	58 (16%)	Confirmed RR and 2nd-line susceptibility	14/129 (11%)	1.71	0.94-3.12	.078
Presumptive RR-TB, 1st and 2nd-line DST missing	105	31 (30%)	Confirmed RR and 2nd-line susceptibility	14/129 (11%)	3.33	1.72-6.44	.000
Confirmed Pre-XDR/XDR	59	15 (25%)	Confirmed RR and 2nd-line susceptibility	14/129 (11%)	2.85	1.35-5.99	.006
Confirmed Rifampicin mono-resistance	51	4 (8%)	Confirmed RR and 2nd-line susceptibility	14/129 (11%)	0.89	0.28-2.79	.836

[Table: Risk of mortality by resistance pattern and availability of DST results]

Having first-line DST confirming RR but no second-line DST also suggested increased risk (not statistically significant) (Table). Additional statistically significant factors associated with increased mortality include HIV+ not on ART (aHR 3.70, CI 1.63-8.39), HIV status unknown (aHR 19.04, CI 5.07-71.54), baseline smear positivity (aHR 2.67, CI 1.55-4.60), missing baseline radiology (aHR 1.90, CI 1.17-3.09) and treatment through two of the five treatment facilities (aHR 2.59, CI 1.49-4.51 and aHR 2.67, CI 1.36-5.22). Also statistically significant, age ≤ 18 years was associated with lower risk of mortality (aHR 0.24 CI 0.07-0.81).

Conclusions: Missing both first- and second-line DST was associated with three-fold higher mortality, similar to patients with Pre-XDR or XDR-TB. Findings highlight the importance of access to DST to properly diagnose and to detect treatment failure. Further investigation of all risk factors is needed.

PS32 Tobacco control programmes: are they key to sustainable tobacco control?

PS32-749-26 Compliance with tobacco control law in public places: a survey in Dhaka City

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Background: Bangladesh enacted a tobacco control law in 2005 with some of the provisions of the WHO Framework Convention on Tobacco Control and amended in 2013. Some newspaper reports and observation by the researchers in Bangladesh found violations of the tobacco control law in public places in the country. Hence, this study aimed to investigate compliance with the current tobacco control law in selected public places in Dhaka City Corporation area.

Methods: A total of 588 respondents drawn from 28 selected spots of 7 different categories of public places of study area for face-to-face interview from 3 categories of people including visitors, dwellers and authority with a combination of both smokers and non-smokers as part of this mixed method study. Moreover, an observation protocol was used to triangulate the findings.

Results: The study found that most of the visitors and dwellers did not see any smoke-free signage in public places. Over one-fifth of respondents observed smoking in public places during the study period. In case of smokers, most (96.0%) mentioned they have never been punished for smoking in public places. Similarly no authority was fined for negligence of their duty to imple-

ment the law. The study also found tobacco buying/selling activities in certain places including by/to minors, which is non-compliant with the law. Violation of the Law took place mostly in cinema halls, public transportation stations and shopping malls in different places. Lack of punishment and inadequate monitoring was found to be the main cause for violating the law.

Conclusions: The study recommended regular monitoring activities, reasonable punishment for violating the Law, proper training for the implementing authorities and increased awareness among the general public to ensure compliance with the current tobacco control law. In addition, future tobacco control policy should consider comprehensive smoke free public places with no exemptions and provisions for ventilation.

PS32-750-26 Innovative financing of tobacco control yielding desired outcomes in low income settings: experience from the state of Himachal Pradesh, India

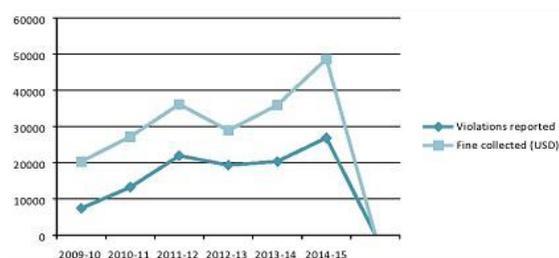
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Background and challenges to implementation: Indian tobacco control law (COTPA) was enacted in 2003 and National Tobacco Control Program (NTCP) was started as pilot in selected districts in the year 2006. Out of 29 states, Himachal Pradesh with a population of 7 million was not covered under NTCP till 2015 in spite of the fact that as per GATS (2010) report, the smoking prevalence among males (33.4%) was quite high and more than the national average (24.3%). 82.5% adults were exposed to tobacco smoke at homes. There was no financial support from the Central or the state Government for tobacco control till 2015.

Intervention or response: The strategic partnership between the State Health Department and a local NGO HPVHA achieved Smoke free Shimla City in 2010. The next plan was to make the entire state smoke free and to implement MPOWER policies. This required huge funding for capacity building, awareness generation and sustainability. Keeping in view the rampant violations of the COTPA, the law enforcers were empowered to utilise the funds collected as fine for financing tobacco control activities.

Results and lessons learnt: Empowerment of the law enforcers motivated them for effective implementation of the tobacco control policies and the entire state achieved Smoke State status in July 2013 (Figure 1). The funds collected as fine were utilised for awareness generation, capacity building and enforcement. As per the GATS - 2 report the prevalence of tobacco use reduced from 21.2 to 16.1 % in the state. The passive smoking exposure at home declined to 32.9%. There is a visible progress in implementation of the MPOWER policies

Conclusions and key recommendations: Funding for tobacco control will remain a challenge in low income settings. Utilising the funds collected as fine is the way forward for sustaining tobacco control



[Figure 1. Year wise violations reported and funds collected for financing tobacco control in Himachal Pradesh]

PS32-751-26 Emergent Issues in Philippine tobacco control and priority reform recommendations from the Department of Health's Omnibus Policy Project

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Background and challenges to implementation: Although tobacco control (TC) in the Philippines has advanced much with the ratification of the WHO FCTC in 2005, the prevailing TC policy regime remains rooted to a pre-FCTC institutional, legal, and regulatory structure that fails to address the contemporary and changing epidemiology of tobacco-related diseases and emerging trend of electronic (non-) nicotine delivery system use. This paucity leaves the youth particularly vulnerable to nicotine dependence, as shown by a 4.7% increase in youth smoking prevalence (GYTS 2011-2015).

Intervention or response: The study initiated the most recent, comprehensive, and exhaustive review of national TC policies through the project, *Technical Assistance for the Development of an Omnibus Department of Health (DOH) Policy for Tobacco and Smoking*, funded by the Department of Science and Technology. All statutes, DOH TC-related administrative orders (AOs), and other quasi-legislative issuances were reviewed for enforceability using technical issue-, process-oriented, and legal analyses through statutory construction techniques.

Results and lessons learnt: DOH AOs contain regulatory measure provisions which are redundant, based on outdated evidence, or obsolete. Substantial regulatory gaps exist due to the pre-FCTC framework established in the 2003 Tobacco Regulation Act, which institutionalized a problematic primary jurisdiction recourse that renders violation and prosecutorial measures ineffective.

Similarly, DOH-regulation is effectively narrowed to advocacy, health literacy, or healthcare service-linked TC such as smoking cessation. Regulation of E(N)NDS is currently inoperative at the national level. Overall, Philippine national TC policy is not compliant with many FCTC standards.

Conclusions and key recommendations: The national tobacco control law must be amended to genuinely centralize regulations under the DOH. Substantial national legislative amendments are necessary to incorporate FCTC norms and protect public health. Current efforts have gained momentum but tobacco industry interference in Congress is manifest, potentially derailing critical reforms. Advocacy must consider supplementing national advocacy with local government-level TC ordinance development, where FCTC Article 8-compliance has proven significant.

PS32-752-26 Coordination and collaboration of national tobacco control activities: lessons from Bangladesh

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Background and challenges to implementation: National Tobacco Control Cell (NTCC) was established under the Ministry of Health and Family Welfare to coordinate all tobacco control activities and boost-up government tobacco control initiative. NTCC is central organ of the Government of Bangladesh lacking financial and human resources. So NTCC sought financial resources to mobilize its operation and fortunately gained support from Bloomberg Initiative to reduce tobacco use, facilitated/managed by The Union.

Intervention or response: NTCC organizes bi-monthly tobacco control coordination meetings with central level GO-NGOs to ensure proper utilization of resources and to support their activities. NTCC is coordinating different ministries through National Taskforce meetings and provide guidance's to all District and Sub-district Taskforces to ensure implementation of tobacco control law at their jurisdiction. NTCC guided Non Communicable Diseases Control program, Directorate General of Health Services to ensure proper implementation of tobacco control activities under its five years operational plan. NTCC linked between Bangladesh Bureau of Statistics, CDC-USA, WHO-Bangladesh, institutions/universities and concerned GO-NGOs to conduct nationwide surveys (i.e.; GATS, GYTS, health/economic cost study etc.).

Results and lessons learnt: This GO-NGO collaboration have gained tremendous successes that includes an amendment of tobacco control law and new rules, imposed 1% Health Development Surcharge on all tobacco products and a policy approved at the cabinet to utilize surcharge as sustainable funding for tobacco control, two national policies (tobacco control and tobacco cultivation control) are now at hand for final approval and Prime Minister declared the country to be tobacco free by 2040. Amended law ensured 50% graphical health warnings for all tobacco products packets, various public places became 100% smoke free including schools-hospitals-children parks, tobacco selling and buying to and by below 18 years are banned, tobacco advertisements-promotions-sponsorships are banned and financial punishments for law violation is increased.

Conclusions and key recommendations: Every country should coordinate all tobacco control efforts by GO-NGOs to make more success within limited resources.

PS32-753-26 Institutionalization of the tobacco control programme is key to sustained results: a case study from the challenge-ridden state of Bihar in India

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Background: Bihar is the 3rd highest populated state (99 million) and amongst the poor in health and socio-economic indicators in India. Tobacco use was very high (53.5%) in comparison to national average (34.6%) as per GATS 2010. A number of initiatives were undertaken over the last five years which resulted in dramatic decrease in tobacco use (25.9%) in GATS 2017 survey, which is not only lesser than national average, but also the largest decrease amongst all states of the country.

Methods: Bihar has started Tobacco control journey since 2010 when National Tobacco Control Program (NTCP) was launched in merely 02 out of 38 districts. In the midst of apathy towards the cause, SEEDS started sensitizing government and other stakeholders in 19 districts for policy developments. Several effective strategic interventions were undertaken. Institutional framework was developed through four pronged strategies i.e. intense advocacy, capacity building & follow up with government officials, effective monitoring at state and district level and consistent media mobilization without losing out to capture even a smaller event related to tobacco control issues. With continuous efforts and series of capacity building programme, tobacco control was institutionalized and State and District Tobacco Control Coordination Committees meets regularly to review the progress of tobacco control.

Results: Tobacco control is being reviewed periodically by officials at state and district level. 13 out of 19 focused districts have achieved high compliance for Smokefree rules. Two districts have also been declared TAPS-free at point of sale, huge media coverage (more than 1200 clippings) on tobacco control issues.

Conclusions: Sensitization of policy makers, capacity building and regular follow up are instrumental in prioritizing tobacco control in governments' agenda. NGOs and media played very important role and must be considered as key partner for reducing tobacco prevalence in high tobacco burden states.

PS32-754-26 Critical analysis of tobacco control program implementation at state and district level in India

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Background and challenges to implementation: Tobacco control program implementation has always remained a tough task for state and district administration in India as it involves lot of stakeholders and also in India the priority of states is still focused on maternal, infant mortality, family planning and TB and AIDS control Program. The study is done in order to understand the loopholes in tobacco control program implementation at state and district level and suggest new ways for improvement.

Intervention or response: The study is done in Madhya Pradesh state of India by conducting SWOT, analysis PESTEL analysis through systematic literature review related to state level tobacco control program implementation, observation, monitoring of media reports related to tobacco control at state level.

Results and lessons learnt: Tobacco is still considered as medical problem and health department focuses more on awareness generation rather than enforcement and stakeholder coordination. Regular meetings of state level and district level committee does not happen. Nodal officers for tobacco control are not full time dedicated to tobacco control and they have to manage 3 to 4 programs and tobacco remains at last priority for them. Coordination between health, police and administration needs to be improved. Very few or no dedicated staff available at state level for tobacco control. Monitoring system is also not proper. GATS data is not utilized in program planning and implementation at state level. Most of the time top down approach is followed. Grass-root level health workers involvement is lacking. Administrative official are more effective in tobacco control than health officials.

Conclusions and key recommendations: The role of District collector in program implementation needs to be increased as wherever District Collector takes lead good results are seen. Tobacco control can not remain as responsibility of health department and there is need

for more involvement of district administration and police department in act implementation. Media has a supportive role and its use can be made in more constructive manner.

PS32-755-26 Countering tobacco industry tactics to recruit youth tobacco users: where are we in India after a decade of tobacco control programme and legislation enforcement?

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Background and challenges to implementation: Reducing youth exposure and initiation to tobacco products is an important strategy for offsetting future prevalence of tobacco use. India's Tobacco legislation mandates the ban of smoking at public places, ban on sale to & by minors, sale of tobacco products within a 100 yard of educational institution, prohibits TAPS and mandates display of pictorial warning on all tobacco products. Interventions and legislation enforcement made to reduce access since 2007 has made variable progress although high compliance exists in three states in India where baseline and end line studies were conducted.

Intervention or response: Compliance surveys to measure enforcement of provisions which protect minors (Section 6 of COTPA) was done in three large states (Karnataka, Bihar, Himachal Pradesh,) covering 44 districts (population 60 million) where stringent legislation enforcement activities were conducted between 2015-17. The compliance survey methodology used was developed jointly by The Union in consultation with its partners.

Results and lessons learnt: All districts where compliance studies were repeated showed an increase in level of compliance from 40% in the baseline to 76% in the end line survey. Global Adult Tobacco Survey (2017) data suggests that youth age of initiation of tobacco use has increased in these states between GATS 1 and 2 i.e. Bihar from 18.8 to 18.9 years Karnataka from 17.7 to 19.8 years and the prevalence of tobacco use among minor at the age of 15-17 is decreased marginally from 1 to 3 % in all three states.

Conclusions and key recommendations: Tobacco companies continue to advertise heavily at retail outlets near schools and playgrounds to target youth since they are more receptive of tobacco use. Hence youth prevention strategies although mired with tobacco industry interference are a proven tobacco control strategy and should be implemented aggressively.

PS32-756-26 Journey toward local enforcement of tobacco control in metropolitan Manila, Philippines

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Background and challenges to implementation: Local enforcement is critical in the success of tobacco control implementation. The Metropolitan Manila Development Authority supported by a grant from Bloomberg Philanthropies through The Union, initiated enforcement of the smoke free environment policy. To patch the gaps and legal conflicts, MMDA advocated for the passage of WHO - FCTC compliant ordinances among the region's legislative councils. Six of these have passed and approved ordinances based largely on the WHO - FCTC in 2017.

Intervention or response: To determine the process of having laws passed at the local level, desk review and focus group discussion were conducted with key informants from the six local legislative councils. Discussion focused on the events that occurred from introduction of the ordinance until approval in its final form.

Results and lessons learnt: The process of passing ordinances involves various steps: first reading when title is read on the floor and draft is assigned to appropriate committee; limitless hearings; second reading when legislators debate and vote on the draft which may indefinitely be laid on the table until all issues are resolved; third reading when title is again read on the floor and legislators sign the approved ordinance and last, mayor's approval and signature. There are no prescribed timelines in between each step. One city passed its ordinance in two months while another took a year. In every step of the way, the tobacco industry may step in and cause delays in the process.

Conclusions and key recommendations: The passage of tobacco control ordinances needs close monitoring. Local legislators must be updated on tobacco control issues and their capacity to counter tobacco industry interference strengthened. Interpersonal relationships must be nurtured at the local level. Advocating for tobacco control does not stop with the passage of the ordinance. It must continue to ensure local enforcement, a critical component of successful tobacco control implementation.

PS32-757-26 Strengthening of Article 11 and 14 of FCTC: efficacy of pictorial warnings on tobacco products in promoting cessation

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Background: The use of pictorial warnings on smoked tobacco products is effective in inducing thoughts about quitting and enhancing motivation to quit. The objective of the study was to determine the quit behaviour among current adult smokers after noticing warnings on tobacco products.

Methods: This cross sectional study was conducted in the period of December 2015 till March 2016. A three stage sampling technique was used for collecting data from three randomly selected districts representing three major regions of Punjab, India. A sample size of 510 individuals was divided equally into urban and rural area with proportionate sampling on basis of subsets of age groups and gender. The questionnaire based on Tobacco Questions for Survey (TQS), a subset of key questions from Global Adult Tobacco Survey was used.

Results: Among all respondents 15.2 percent of males were smokers and no female smokers were identified. The hand rolled cigarettes (bidis) contributed 64.1 percent as compared to that of manufactured cigarettes (35.8 percent). Among the current smokers 97.4 noticed health warning on the product packs while 63.1 percent of these thought about quitting because of warning label. The health warning was noticed more by respondents in age group 25-44 years (48.7 percent), rural locality (56.4 percent) and self employed category (53.8 percent).

Conclusions: The pictorial warnings are a reliable strategy to control the global tobacco epidemic and effective in promoting smoking cessation in resource constraint settings. Policymakers and implementers should integrate the pictorial warning strategy along with other MPOWER strategy in order to strengthen Article 11 of Framework Convention on Tobacco Control.

PS32-758-26 Qualitative analysis of stakeholders' perspectives of the Ekiti State tobacco control law prohibiting smoking in public places

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Background: Smoking in public places is still prevalent in the developing countries including Nigeria. Tobacco control law was enacted in 2012 in Ekiti State, Southwest Nigeria but not a lot has changed. The enforcement of the law across the state has been

absent. There is therefore a need to assess stakeholders' views of the tobacco control law. This study was conducted to assess perception of the state tobacco control law prohibiting smoking in public places among stakeholders in Ekiti State, Southwest Nigeria using qualitative approach.

Methods: A descriptive cross-sectional study was conducted using qualitative approach. The qualitative survey employed key informant interviews (KIIs) using KII guide. Ten respondents who were Permanent Secretaries, Directors and Focal Persons from the 20 eligible MDAs, Parastatals, and Non-Governmental Organizations in the State were selected for the KIIs. The themes identified include awareness, attitudes, perceptions, willingness to create awareness and factors associated with compliance/adherence to effective implementation of the law. Qualitative data were analyzed using thematic approach.

Results: Awareness was low and attitude towards tobacco prohibition is still low with little or no collaborative efforts among stakeholders in the State. Most of the stakeholders have not participated in awareness creation, public enlightenment and enforcement of the law. All the KII participants reported that nobody has been prosecuted or sanctioned for violating the law. Nine of the 10 stakeholders believed that communication gap between law makers and stakeholders has negatively influenced the implementation of the law and continue to breed unhealthy attitude. Factors reported for non-compliance to the law prohibiting smoking were political constraints and addiction to smoking.

Conclusions: There is a need for concerted efforts for more advocacy and public enlightenment on the concepts of tobacco control law/smoking to the public. Those violating the law prohibiting smoking in the public should be sanctioned.

PS32-759-26 Methods used to control tobacco consumption in post-war Sri Lanka

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Background: In fact, we have the bitter experience of the ethnic conflict in north and east of Sri Lanka for three decades. During this period the public was not educated at all about the adverse effect of the tobacco consumption. The normalcy returned in the life of the general public when the war was ended in 2009. The trade organization and multi-national companies attracted the people of north and east towards tobacco in this period. Even though the sponsorships ban in Sri Lanka, Ceylon tobacco company has build two police stations, given loan grants to famers for tobacco cultivation and encourage shop owners to sell cigarettes and some other similar strategies in 2010 and 2011.

Objective was to empowering the government bodies to free people from tobacco consumption and disclosed the company strategies.

Methods: We were trained public health officers, social and economic development officers and youth teams to expand tobacco prevention at grass root level. We have carried out social marketing campaigns and awareness programs to educate people through media to abolish the myths and about tobacco among the public. Our intervention carried out among the community as well as authorized officials to formulate law and regulation at the same time.

Results: As results, 600 shop owners were stopped cigarette selling and it's promotions. according to the research of Alcohol and Drug Information Centre, 2011 to 2014 smoking has been reduced by 20% in Jaffna District Northern province. And available skillful resource persons located in north and east provinces and they integrated best prevention activities.

Conclusions: It is useful strategy to prepare existing structures to prevent tobacco industry interferences at whatever level in their community.

PS32-760-26 SmokeFree caravan: popularizing the national executive order on smoke free implementation and tobacco control in selected key cities in the Philippines

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Background and challenges to implementation: The President of the Philippines signed Executive Order (EO) 26 entitled *Providing for the Establishment of Smoke-Free Environments in Public and Enclosed Places* on 16 May 2017. This EO imposes a nationwide ban on smoking in all public places in the Philippines, and took effect on 23 July 2017, 60 days after its publication in a newspaper.

3 months after its effectivity, implementation in majority of the cities remains to be seen. There seem to be an inertia among Local Chief Executives in implementation, not knowing how to do it effectively.

Intervention or response: Local Government Units (LGUs) who have passed Smokefree Ordinances even before the signing of the SmokeFree Executive Order, have shown the way in implementation by banning smoking in public places, banning tobacco advertising, providing smoking cessation counselling services, etc., and in fact received the Red Orchid Awards given by the Department of Health, a recognition given to LGUs that have been consistent in promoting a "100-percent tobacco-free" environment.

To help popularize EO 26, Smokefree Philippines, a group of advocates against smoking, conceptualized SmokeFree Caravan campaign, a travelling roadshow to highlight the successful Smokefree implementation around the country. It also promoted the adoption of local smokefree ordinances to other LGUs.

Results and lessons learnt: 5 LGUs have passed their own Smokefree Ordinances as a result of the Smokefree Caravan campaign. Furthermore, more than 10 LGUs signified their intention to pass their own local policy, and have started the legislative process to adopt EO 26. The Smokefree Caravan worked in convincing LGUs to adopt and implement the EO 26.

Conclusions and key recommendations: Banning smoking in public places is a tried and tested measure to protect the lives of the public from the effects of second-hand smoke. The SmokeFree Caravan campaign is a good way to convince the Mayors and the LGUs to adopt and implement the EO 26.

PS33 Activism or evidence: what drives tobacco control?

PS33-761-26 Role of mass media in tobacco control: a study of the Indian context

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Background: Media plays a key role in disseminating knowledge related to tobacco; it shapes opinions, attitudes, and behaviour among individuals and within communities. Advertisements and other campaigns promoting tobacco products leads to initiation at younger age, higher consumption and lesser likelihood of quitting. India has strict rules for banning direct and indirect advertisement of tobacco products. In spite of the strict laws the presence of tobacco advertisement and promotion is quite high in India. under this background the paper tries to examine the role of mass media in tobacco control in India.

Methods: The study is based on Global Adult Tobacco Survey India (GATS-India) 2016-17 data. Suitable bivariate and multivariate techniques have been used.

Results: Nineteen percent of adults noticed smoking tobacco advertisement and 18.3% of adults noticed smokeless tobacco advertisement. 5.3% and 5.4% of adults noticed cigarette and *bidi* promotion respectively while 6% adults noticed smokeless tobacco promotion. Overall, 22.3 percent adults had noticed some form of marketing (advertisement or promotion) of smoking tobacco. Analysed by current smoking status, 30.0 percent current smokers and 21.3 percent current non-smokers noticed some form or the other of marketing of tobacco products. On a brighter note 68.0% of adults noticed anti-smoking tobacco information on television or radio and 59.3% of adults noticed anti-smokeless tobacco information on television or radio. 61.9 percent of cigarette smokers, 53.8 percent of *bidi* smokers and 46.2 percent of smokeless tobacco users noticed health warnings on packages and thought of quitting tobacco use because of the warning label.

Conclusions: In order to bring down the tobacco use in India Government should place emphasis on increasing the anti-tobacco mass media messages and limiting the tobacco advertisements and promotions.

PS33-762-26 Exposure to second-hand smoke and risk of TB in children: what do Challenge TB Project's active case finding data tell us?

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Background: Widespread tobacco consumption is an important public health hazard in Bangladesh. Evidence suggests that both direct and second-hand smoke (SHS) pose significant health hazards to women, babies, and young children. Using data of 240,564 children who were actively screened for tuberculosis (TB) this paper examined the association between SHS exposure and TB among children in urban settings in Bangladesh.

Methods: Data was extracted from the electronic database of the Challenge TB (CTB) project's active case finding (ACF) intervention. ACF among sick children was conducted by health workers (HWs), who collected data from from parents in paediatric outpatient departments (OPDs) and patients admitted to six big tertiary hospitals between March and December 2017. HWs screened children visiting the OPDs using an Android smartphone-based screening tool and identified presumptive child TB cases. Additionally, SHS exposure history at home was collected from parent interviews. Data was analysed statistically using SPSS. Multiple logistic regressions were used to investigate associations between SHS and active TB.

Results: Among 240,564 children screened, 53% children had historical exposure to SHS. Among the 409 children with active TB, SHS exposure history was 68% (n=278). Active TB positive status and significant SHS exposure-response relationships were observed among children over 5 (OR 1.6; 95% CI 1.1-2.5; p 0.05), females (OR 2.3; 95% CI 1.4-3.8; p< 0.01), children exposed to SHS through parents (OR 3.6; 95% CI 2.1-5.3; p< 0.01), and children living in slum-settings under crowded household conditions (OR 2.8; 95% CI 1.6-4.7; p< 0.05).

Conclusions: Echoing the results of other studies, our findings suggest that SHS exposure is associated with an increased risk of TB among children living in slum settings. Further research in this area may have important implications for TB and tobacco control programs, especially among vulnerable children in urban slum settings with high SHS exposure and TB burden.

PS33-763-26 What is the prevalence of e-cigarette use among current smokers and users of tobacco in India? A multicultural cross-sectional study

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Background and challenges to implementation: Electronic nicotine delivery systems (ENDS) have entered the Indian market and prevalence of use (occasional versus regular) is not known. ENDS like all tobacco are poorly monitored in terms of volumes of sales, revenues and consumption. Manufacturers of ENDS advertise as “safe alternative to cigarette” and “a cessation” aid. The safety of ENDS has not been scientifically demonstrated. This illusive ‘safety’ of ENDS can be deceptive to consumers. Tobacco control advocates contend that ENDS could undermine the implementation of WHO Framework Convention on Tobacco Control Article 12 (denormalisation of tobacco use); could also hamper the implementation of Article 8 (protection from exposure to tobacco smoke). Ultimately, it will impede implementation of India’s National Tobacco Control Program and enforcement of tobacco legislation. Globally countries several countries (Brazil, Norway, Indonesia, Bhutan and Singapore) have taken various measures to regulate ENDS. In India, Central Government is still debating the use of ENDS.

Intervention or response: We conducted an unobtrusive cross sectional survey conducted across the country. The data has been collected from 220 randomly but geographically representative points of sales. A questionnaire was pretested and administered on 2500 consumers of tobacco products and data was double entered using OpenEpi. The questionnaire aimed to estimate the frequency of current use of ENDS, concurrent use, age and geographic dispersion, source of purchase and price paid, and perception of safety of ENDS with respect to other tobacco products. (Union Ethical Approval number: 2013.)

Results and lessons learnt: The results are being analysed and will be presented at the World Lung Conference 2018

Conclusions and key recommendations: Early topline results indicate a surprising trend of current smokers graduating to use ENDS and the penetration of ENDS into new markets. The result of this study will help to policymakers to understand the magnitude of the problem of both conventional and emerging forms of smoking products, which will establish effective tobacco control.

PS33-764-26 Diffusion of metals in the liquids of electronic cigarettes

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Background: Some few works report the presence of metals in the vapors of electronic cigarettes. These metals come from the heating device of the electronic cigarettes after their dissolution in the e-liquids. This work determines the impact of the liquid composition on the diffusion of metals in the liquids.

Methods: 20ml of a liquid (100% Propylene Glycol (PG), 100% Glycerin (G), 50/50% PG/G, 33/33/33% PG/G/H₂O) are heated to boiling point with 2 commercial heating filaments for 1 hour in a distillation device. The liquids contain 0, 0.4 or 0.8% v/v nicotine. Three air flows in the liquid are used: 0, 0.5, 1.0 L/min. The metals are analyzed with X-Ray Fluorescence.

Results: The heating devices have an impact on the diffusion of 4 metals: Fe, Ni, Cu, Zn, Pb (found in concentrations of 0.07-55, 0.08-24, 0.001-8.3, 0.02-22 and 0.04-5.8 mg/L respectively). Cr, Ca, K, Sr, Ti, Co, Cl and Br are also found in the liquids, but the heating devices have no impact on their concentration.

The diffusion of metals increases 3-8 times with air flow and 4-40 times with nicotine. Water increases doubles the diffusion of Fe and decreases the diffusion of the other metals (0.3-0.9 times). Glycerin increases the diffusion of metals 5-160 times comparing to PG.

Distillation temperature has a very strong effect on the diffusion of metals and higher the distillation temperature higher the diffusion rate.

Conclusions: The composition of the liquids, the content of nicotine, air flow, water content and temperature have a strong effect on the diffusion of metals from the heating devices to the liquid of electronic cigarettes.

PS33-765-26 Can stigma work in the fight against the tobacco industry?

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Background and challenges to implementation: Sri Lanka is known to effectively use community-based actions to counteract tobacco industry activities and demand

for policies and control measures. Ceylon Tobacco Company PLC (CTC), the subsidiary of British American Tobacco, has the monopoly of cigarette sales in Sri Lanka. CTC is identified as a politically ‘powerful’ entity, due to the political affiliations formed via personal and professional connections of the management and the investors.

Intervention or response: We aimed to explore the feasibility of using stigma to strengthen community actions against the tobacco industry, using the CTC’s Annual General Meeting (AGM) as the trigger. Stakeholder meetings were held to decide themes of actions. The theme, collectively formulated, was “Ceylon Tobacco are Murderers”, based on the country’s 20,000 annual death toll due to tobacco. First action was to send a letter to shareholders of CTC, containing the death toll due to tobacco and requesting them to discontinue their contribution for the deaths due to tobacco. Second step was a community-led poster campaign targeting the CTC headquarters and the residence of CTC management and major investors. Finally, at the day of the AGM, a public demonstration near the headquarters was held in the form of a traditional funeral service, to commemorate the Sri Lankans who died because of CTC.



[Community actions against the Annual General Meeting (AGM), CTC]

Results and lessons learnt: The process improved the enthusiasm and participation of the community stakeholders. They came up with innovative actions and tools to highlight the death toll due to tobacco and the company’s contribution to it. The final demonstration had

a participation of more than 500 participants, including religious leaders representing main religions in the country. The demonstration received wide media coverage.

Conclusions and key recommendations: ‘Stigma’ is an effective theme in mobilizing communities against tobacco industry activities.

PS33-766-26 Impact of electronic cigarette aerosol in chick lung development

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Background: Tobacco smoking constitutes a major public health issue associated with high mortality rates. Currently, new nicotine delivery systems, electronic cigarettes (e-cig), have been developed aiming to overcome the well-known toxic effects of conventional cigarettes (c-cigs). E-cigs vaporize a liquid creating an aerosol that reaches the lung. Several studies have shown that c-cigs and nicotine exposure impairs lung development, however, the effect of e-cig aerosol in lung development is not known so far. In this sense, the goal of this work is to determine the impact of e-cigs aerosols in lung development since they are becoming increasingly popular among pregnant women.

Methods: For this purpose, *in vitro* embryonic chick lung explants were cultured in culture medium exposed to either c-cig smoke or e-cig aerosol, for 48h. Nicotine levels in the medium were quantified by GC-MS. Control explants were incubated with the smoke/aerosol-free medium. Explants were photographed at D0 (0h) and D2 (48h) and morphometrically analyzed by assessing total, epithelial, mesenchymal area and perimeter, in both time points. Morphometric results were expressed as D2/D0 ratio and groups compared for statistical differences, by One-way ANOVA.

Results: C-cig treated explants presented a decrease in all morphometric parameters analyzed when compared to controls (31.4% total area; 28% epithelial area; 28.6% mesenchymal area; 19.7% mesenchymal perimeter and 16.3% epithelial perimeter) indicating that lung growth is impaired.

On the other hand, e-cig treated explants displayed a statistically significant decrease in lung’s total area (9.6%) and mesenchymal perimeter (9.9%), which account for an overall decrease in lung size. Additionally, there was a

statistically significant difference in all the morphometric parameters between e-cig and c-cig treated explants.
Conclusions: This study shows, for the first time, that e-cig aerosol effect in lung development is approximately 70% less severe than c-cig.

PS33-767-26 High yield of earned media in a month-long Tobacco Free Punjab campaign in Punjab, India

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Background and challenges to implementation: Tobacco is an established preventable risk factor for NCDs. WHO has laid down MPOWER strategy to tackle the menace of Tobacco use. 'W' or warn is an important component of the strategy to sensitize general public about the harms of tobacco use. The objective of the study is to analyze the amount of earned print media focused on harms of tobacco use in a month long Tobacco Free Punjab campaign.

Intervention or response: Punjab State conducted a one month long Tobacco Free Punjab campaign in May 2017 to create awareness about the menace of Tobacco. Audio-Visual Awareness Van was specially prepared for this purpose. This van visited all the Major towns of State and Government/Government aided schools were also covered to sensitize children and youth about the ill effects of tobacco through Posters, Audio and Video clips. The cost description of the hypothetical value of the earned media was carried out. The area of the news item in cm sq. was multiplied by the average charges for display advertisement in that particular newspaper.

Results and lessons learnt: There were total 1377 News items published in various Newspapers during the month of May 2017. The hypothetical value of all earned print news items related to the campaign was US\$ 402507.60 (Rupees 26.1 Million), which is five times more than the funds spent on all programme activities in the whole year.

Conclusions and key recommendations: In the absence of adequate funding for IEC activities, the campaign strategically used earned media to promote tobacco control policies and to create awareness regarding the ill effects of tobacco in the state. This earned print media reduced the financial burden in implementing various programme objectives and activities.

PS33-768-26 Understanding Corporate Social Responsibility strategies adopted by tobacco companies in India

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Background: Companies Act 2013 of India mandates all corporate to spend at least 2 percent of net profit on CSR activities. Tobacco companies including cigarette makers, bidi makers and smokeless tobacco manufacturers are using CSR as a tool to showcase themselves as socially responsible companies. The study was done in order to understand the CSR initiatives by tobacco companies.

Methods: It is an exploratory study done through secondary research. A total of 15 leading tobacco companies were analysed including 5 bidi, 5 smokeless tobacco and 5 leading cigarette manufacturing companies. The study was done by analysing the contents of websites, annual report, directors report, media reports related to CSR activities.

Results: Most of CSR activities focused in companies operational area. Projects are implemented directly or in collaboration with government or NGOs. Some companies provide priority to CSR beneficiaries to become vendors and employees. Companies also show responsibilities towards stakeholders and respect for human rights.

CSR activities are done in more aggressive way by Cigarette and Smokeless tobacco companies and less aggressive way by Bidi companies. Major activities are mainly focused in rural areas. Activities include infrastructure development by building education institutions, temple, hospitals. Curing barns for safe storage of crops, taking care physically and mentally challenged, relief during disaster, riots, donating medical equipments, medical treatment, and old age homes.

CSR also focuses on safeguarding interests of farmers, helping women to enhance livelihood, model village development, water and soil conservation, farmer development societies, eliminating child labour improving conditions of women working in tobacco industry, self help group formation. Integrated community development, adoption of river banks for clean river, restoring heritage, livelihood, sponsoring sports events, sanitation, and skill building.

Conclusions: Tobacco companies through CSR activities try to gain social respect and changing and improving their image. Companies present themselves as partners for sustainable development and improving community development. It is important that public should be informed about true purpose of CSR by tobacco companies. Government department should also not participate in such activities.

PS33-769-26 Tobacco use among rickshaw pullers of Dhaka City: behavior, awareness and prevention

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Background: Tobacco smoking and other forms of tobacco use impose large and growing public health burden globally and in Bangladesh. Overall tobacco consumption has been rising in Bangladesh in recent years, where the low-income groups are identified as a major group who consume excessive amounts of tobacco and face considerable health and economic consequences.

Objective: The objective of the study was to understand the tobacco use or consumption pattern of rickshaw pullers, and to assess their knowledge, perception and behavioral aspects towards tobacco consumption.

Methods: A sample survey method was used for collection of data. Total of 400 rickshaw pullers living in Dhaka city were selected as respondents. Ten spots were selected randomly and from each spot 40 rickshaw pullers were interviewed using a semi-structured questionnaire. Focus group discussions were also used. The processed data was interpreted by using descriptive, as well as bi-variate analyses.

Results: The results showed that majority of respondents used smoking tobacco with a few of them using the smokeless form of tobacco. Majority of the respondents noticed the dangers of tobacco use from the posters, watching television and listening to the radio. When asked about anti-tobacco activities, majority of the respondents believed the activities could raise awareness among people and reduce tobacco consumption significantly. Findings also showed that more than half of the respondents started smoking between the age of 13 and 24 years. Almost all of the respondents were aware about the harmful effect of tobacco use- smoking and smokeless. About half of the respondents had low perception about the adverse effects of tobacco use.

Conclusions: The results of the study suggest that there is a need to provide stronger support for tobacco control in Bangladesh. It is recommended that tailored interventions be developed to increase awareness among socially and economically disadvantaged groups such as rickshaw pullers.

PS33-770-26 Implementing a tobacco control law in Bangladesh: challenges and way forward

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Background: Bangladesh enacted the Tobacco Control Law back in 2005 and amended it in March 2013. Government finalized necessary rules of the Law in March 2015. Despite of the law, rules; Bangladesh is ranked among top tobacco consuming countries. Therefore, the law and its proper enforcement are essential from the point of view of public health.

The main objective of the study was to identify the challenges in enforcing the law and identifying existing gaps between the Tobacco Control Law and its effective implementation to reduce tobacco consumption in Bangladesh.

Methods: This was a cross-sectional study and exploratory in nature. Mix methods approach was used which included a sample survey and key informant interviews. A total of 771 survey respondents who were tobacco consumers were interviewed using semi-structured questionnaire covering all divisions of Bangladesh. Key informants included members of tobacco control law implementing agencies, government officials, tobacco activists, members of academia, public health specialists and representatives of civil societies.

Results: The results found that 22% respondents were aware of the Tobacco Control Law. Among the respondents who knew about the law, only 12% perceived that the law was being implemented effectively. About 58% respondents indicated that implementing agencies were not fully aware of the role they needed to play. About 23% of the respondents supported the idea of total ban of the tobacco industry. Key informants thought that law implementation was weak due to lack of specific focus on tobacco control by local level task force committees.

Conclusions: This study concluded that lack of knowledge on Tobacco Control Law among citizens as well as law implementer is undermining the importance of reducing tobacco consumption. A comprehensive program with multi-stakeholders involvement is necessary to control tobacco consumption in Bangladesh.

PS33-771-26 Tobacco control measures: focus group discussions in Georgia

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Background: As part of *The Bloomberg Initiative To Reduce Tobacco Use* project "Supporting endorsement and enforcement of strengthened legislation on tobacco demand reduction in Georgia in order to meet WHO

FCTC requirements”, qualitative survey was conducted. The aim of the survey was to identify the knowledge and attitudes towards tobacco control measures.

Methods: 4 separate focus groups were conducted:

I - smoker women,

II - non-smoker women,

III - smoker men,

IV - non-smoker men.

Results: Focus group discussion revealed social influence as a major factor to the smoking initiation. No difference between older and younger generations; only difference in social acceptance of smoking. Common opinion was expressed that it is important how acceptable/unacceptable youth perceives smoking. Regarding price and tax measures as a mean to reduce smoking, opinions were split between those who strongly agree that high prices have a significant influence and those who think that only price is not enough and also there have to be some other measures. Existing health warnings on tobacco packs are ineffective and more convincing images to be introduced.

Conclusions: Stigma around unacceptability of women smoking is diminishing; smoking is perceived as “normal” with only exception of pregnant women. Smoking ban in public places can have a greater impact on reducing smoking rates than increasing price on cigarettes, but if prices are increased at least other measures such as banning of advertisement and depiction of smoking in movies, banning of smoking in public places, pictorial health warnings, strong and understandable evidence based anti-tobacco messages, ban of selling tobacco to minors should be introduced as well. Clearly more efforts should be focused on awareness raising campaigns.

PS34 Drug safety and efficacy in Europe

PS34-772-26 Case study: applying a comprehensive care model to improve MDR-TB treatment success and reduce mortality in Mykolayivska Oblast, Ukraine

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Background and challenges to implementation: Ukraine has the second highest multidrug resistant TB (MDR-TB) burden in the European region. National cohort 2014 data suggest that success rates for MDR-TB cases remain well below WHO targets, at 46%. In Mykolayivska Oblast in southern Ukraine, the treatment success rate for the 2012 cohort of MDR-TB was 37% and the

mortality was 33%. Patients with MDR-TB faced long hospitalizations, poor treatment regimens, fragmented health services, and little to no support from social services or primary health care providers to care for them.

Intervention or response: The USAID-funded Challenge TB Project initiated work in Mykolayivska Oblast in 2014. It focused on building cooperative, multidisciplinary teams among TB specialists, primary health care, Red Cross visiting nurses, social workers, psychologists, and community-based organizations.

Significant attention was also given to capacity building of TB and primary health care providers, establishing supportive supervision systems for quality diagnostic, treatment and advocacy with regional health authorities to support an ambulatory care approach for MDR-TB.

In early 2015, patients began receiving a tailored service packages for their specific needs, including psychosocial support, legal services, alcohol and drug treatment, nutrition, transportation vouchers, phone time, and other.

Results and lessons learnt: Between cohorts 2012 and 2014, MDR-TB treatment success rates in Mykolayivska oblast rose from 36% to 59%, now the highest in Ukraine. The mortality rate dropped from 33% to 13%. The key to this success was the patient centered approach to care based on ambulatory treatment and proper programmatic management of drug resistant TB (PMDT).

Conclusions and key recommendations: Implementing a comprehensive patient-centered care model that is tailored to MDR-TB patient needs along with capacity building and supervision of providers has resulted in a profound reduction of human suffering and deaths due to MDR-TB, as evidenced by improvements in key indicators. This model of care was recommended to be scaled up nationally and regionally.

PS34-773-26 From compassionate use to programmatic use of delamanid and bedaquiline: safety data from Armenia

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Background: Delamanid (Dlm) and bedaquiline (Bdq) were quickly integrated into the National Tuberculosis Control Program in Armenia, following early access through compassionate use. We present programmatic data from the endTB project and beyond.

Methods: Patient data was entered into an electronic medical record. Using automatic standard reports for programmatic management for patients that started

Bdq or Dlm between April 2015 and March 2018, we describe patient characteristics and safety: pre-defined adverse events of interest (AEIs) in the first 6 months of Bdq or Dlm and all serious adverse events (SAEs).

Results: A total of 155 patients started Dlm or Bdq in the reporting period, 24 of which had both, either simultaneously or sequentially. The majority were men (130/155, 83.9%), median age was 42 years and comorbidities HIV, hepatitis C serology positive and diabetes were present in 11.2% (17/151), 25.1% (39/155) and 11.0% (17/155) respectively.

A total of 162 AEIs during the first 6 months of Bdq and Dlm were reported, with 45.6% (36/79) of patients experiencing at least one. Most frequently reported were prolonged QT interval (41/162, 29.3%), hearing loss (32/162, 19.8%), raised hepatic enzymes (25/162, 15.4%) and peripheral neuropathy (20/162, 12.3%). A total of 55 SAEs were reported in the same period. Criteria of seriousness were: 21.8% (12/55) death, 52.7% (29/55) medically significant (full treatment interruption), 18.1% (10/55), hospitalisation, 5.4% (3/55) disability/incapacity and 1.8% (1/55) life threatening. Most common were raised liver enzymes (10/55, 18.1%), extensive TB disease (5/55, 9.0%) and anaemia (4/55, 7.2%).

Conclusions: In Armenia, the programmatic use of bedaquiline and delamanid with active drug safety monitoring is properly implemented. The system in place allows adequate reporting and management of adverse events. As part of the endTB project, a subset of this cohort will be additionally analysed.

PS34-774-26 Eligibility for shorter treatment of multidrug-resistant tuberculosis in Kyrgyzstan

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Background: The shortened MDR-TB regimen has good results in various settings. WHO recommends its use for patients who are not resistant to fluoroquinolones or injectable second-line anti-TB drugs. There is little evidence on how widely this regimen can be used in MDR-TB high burden countries of Eastern Europe and Central Asia.

The objective of this study is to assess the number and proportion of MDR-TB patients eligible for the WHO shortened regimen in Kyrgyzstan.

Methods: We performed a retrospective analysis of routinely collected data of patients treated for MDR-TB in Kara-Suu, Kyrgyzstan from 2012 to 2017. We assessed the proportion resistant to at least one injectable drug or one fluoroquinolone and those with presence of InHA

mutation on Hain test identified. Patients eligible for the WHO shortened regimen were those with none of these resistances.

Results: A total of 364 Rifampicin-resistant patients were included. Full DST on second-line drugs was available for 130/364 (35.7%) patients. Resistance to at least one injectable drug was found in 33/364 (24.6%) patients and 21/364 (5.8%) were resistant to fluoroquinolones. Taken together, a total of 92/364 (25.3%) patients were sensitive to fluoroquinolones and to injectable drugs. Among them, 1 was diagnosed as Isoniazid-resistant based on Hain test. Finally, 91/364 (25.0%) patients would have been eligible for the WHO shortened regimen and for 234 (64.3%) it was not possible to decide due to lack of second-line DST results.

Conclusions: A low proportion of Rifampicin-resistant patients would be eligible for the shorter regimen in this context and for a high proportion it is not possible to determine the eligibility. These findings stress the need of rapid tests for second-line DST before introducing the shorter regimen. In addition, it is urgent to find shorter MDR-TB regimen, potentially with new drugs, that can be used in all MDR-TB patients including injectables- and fluoroquinolones-resistant.

PS34-775-26 Interim treatment outcomes of multidrug-resistant tuberculosis patients in individualized treatment regimens with new drugs in Tajikistan

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Background: Tajikistan belongs to the 30 countries with the highest burden of MDR-TB in the world. According to the last drug resistance survey (2017), 30% of detected MDR-TB patients had resistance to fluoroquinolones (FQ), second-injectables (SLI), or both. With support of USAID's Challenge TB project (CTB) implemented by KNCV, treatment with individualized treatment regimens (ITR) containing bedaquiline (Bdq) and repurposed drugs was started in December 2016.

Methods: MDR-TB patients not eligible to receive the shorter treatment regimen (STR) were enrolled on ITR containing Bdq and repurposed drugs. We analyzed adverse events (AEs) and interim conversion rates at 6 months for DR-TB patients enrolled in 7 CTB pilot sites (Dushanbe city and 6 districts) from mid-December 2016 to end of December 2017.

Results: Of 64 patients enrolled on ITR, 23 (36%) were new, and 41 (64%) were previously treated for TB, of which for 40 the previous MDR TB treatment had failed. Nineteen (30%) patients showed resistance to FQ, 12

(19%) to SLI, and 33 (30%) to both. One patient was HIV positive. The majority of patients on ITR (72%) started treatment as inpatients. Five (8%) serious adverse events (AEs) (3 fatalities (5%) and 2 (3%) hospitalizations) were reported and were probably related with advanced TB disease rather than the treatment.

Thirteen AEs of special interest (e.g., QT prolongation, myelosuppression, peripheral neuropathy) have been recorded thus far. Of the 35 patients enrolled between December 2016 and June 2017, 29 (83%) had reached sputum and culture conversion within six months of treatment.

Conclusions: Despite the fact that all patients showed resistance to SLI and/or FQ, the preliminary results are promising in terms of ITR safety and efficacy, which will facilitate expansion of these new regimens in the country.

PS34-776-26 Program implementation of bedaquiline in Ukraine: challenges and achievements

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Background and challenges to implementation: Ukraine's 2015 national tuberculosis (TB) drug resistance survey revealed an alarmingly high proportion of multidrug-resistant TB (MDR-TB) cases (24.1% among new and 58.1% among previously treated cases). In 2016, 1,195 of 7,778 registered MDR-TB cases were confirmed as extensively drug resistant (XDR-TB), making Ukraine a clear candidate for new, more effective drugs against MDR-TB. As of March 2018, bedaquiline (BDQ) was not registered in Ukraine and BDQ-based regimens had yet to be included in national guidelines; thus, the National Institute of TB and Lung Disease of the National Academy of Medical Sciences initiated BDQ pilot introduction in 2017 with the support from USAID Challenge TB project.

Intervention or response: To ensure health system readiness for BDQ introduction and proper clinical use, significant effort was expended in three areas: (1) establishing and closely supervising implementation of new protocols, algorithms, and standard operating procedures; (2) ensuring good clinical practices, including engagement with an international advisory board for patient selection, clinician training and support, laboratory readiness (use of molecular diagnostics), and proper drug management (dosing, quantification, and storage); and (3) patient-centered care and informed consent for optimal patient enrollment and adherence based on actual needs (e.g., in-person directly observed therapy

[DOT] versus video DOT) and potential drug side effects (using active TB drug-safety monitoring and management aDSM).

Results and lessons learnt: A minimum of six months was needed to adequately prepare each field site for new drug introduction to ensure health system and clinician/laboratory readiness. Close supervision continues to be required. As of March 2018, 100 people with X/MDR-TB were enrolled in care.

Conclusions and key recommendations: Ukraine's BDQ pilot introduction has generated critical evidence for national implementation and regional expansion. Key elements include standardized algorithms and tools to maximize the effectiveness of BDQ introduction, well-defined site and patient selection criteria, and strong supervisory and oversight systems.

PS34-777-26 Use of bedaquiline to treat TB-HIV co-infected individuals in Ukraine

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Background and challenges to implementation: Ukraine has the second largest HIV epidemic in Eastern Europe and Central Asia and second highest tuberculosis (TB) burden in the European region. In 2016, 9,000 TB cases were reported among HIV-positive people. About 21% of confirmed TB cases in Ukraine were HIV positive (2016); of these estimated 29% had multidrug and extensively drug resistant TB (MDR/XDR-TB). Current global recommendations propose delamanid for treatment of MDR/XDR-TB in HIV-positive people on antiretroviral therapy (ART), to avoid negative drug interactions with anti-HIV medications. In Ukraine, however, delamanid is not available, so alternative treatment approaches for TB-HIV co-infected people are required. **Intervention or response:** Pilot implementation of bedaquiline (BDQ) started in Ukraine in July 2017 with the National Institute of TB and Lung Disease under the USAID-funded Challenge TB Project. The project gathered advice from global experts and organizations with implementation experience to develop recommendations regarding how and when to use BDQ in co-infected patients, which were endorsed and added to the BDQ introduction protocol. Medical providers from the TB and HIV services closely collaborate to quickly assess patients' eligibility for treatment initiation by looking at current ART regimens, TB resistance profiles, and other illness characteristics. Together, they monitor all patients for treatment response and side effects.

Results and lessons learnt: Since November 2017, 13 patients with TB-HIV co-infection who met the criteria have been enrolled in the BDQ introduction pilot. As of

March 2018 (four months since enrollment), no side effects have been reported; all patients are responding positively to treatment as evidenced by sputum conversion.

Conclusions and key recommendations: BDQ can be used in TB-HIV co-infected patients in the absence of delamanid after patient assessments have been conducted and the ART regimens adjusted appropriately. A key requirement for success is close and efficient collaboration between TB and HIV services; any delays in treatment initiation for co-infected patients may be lethal.

PS34-778-26 Use of delamanid and bedaquiline in Georgia: description and results from the end TB cohort programmatic data

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Background: We present country level programmatic data from the endTB observational study in Georgia, an early implementer of delamanid and bedaquiline.

Methods: Country level data entered into the custom made electronic medical record was analysed with standard reports at country level. For patients in the the endTB study, we describe characteristics of patients starting delamanid or bedaquiline as part of MDR-TB treatment between April 2015 and April 2017 and clinician assigned end of treatment outcomes as per national program definitions for patients starting delamanid or bedaquiline between April 2015 and December 2015. Culture conversion is defined as 2 negative cultures, at least one treatment month apart.

Results: From April 2015 - April 2017, 298 patients started bedaquiline (215/298, 72%) or delamanid (83/298, 28%) as part of MDRTB treatment. Among them, 65 (22%) received both bedaquiline and delamanid sequentially (not concomitantly). Most (250/298, 84%) started a MDRTB regimen containing new drugs, and 48 (16%) had new drugs added to an ongoing regimen. The majority were men (81%), median age was 37, including 5 adolescent cases aged 14 to 17 years old. Comorbidities present at baseline included: hepatitis C serology positive (71/297, 24%), diabetes mellitus (31/294, 10%), HIV (17/296, 6%), and hepatitis B serology positive (12/297, 4%). The majority had pulmonary TB (292/298, 98%), previous history of second line TB treatment (208/298, 70%) and bilateral disease (158/267, 60%). Extensively drug resistant TB was present in 41% (121/298).

Culture conversion rate at 6 months for patient's culture positive at baseline was 88% (220/250).

End of treatment outcomes for 2015 cohort were: 75% (91/121) success, 4% (5/121) death, 7% (9/121) failure, 12% (15/121) lost to follow-up.

Conclusions: In Georgia, MDRTB regimens including bedaquiline and delamanid show good effectiveness in patients with difficult to treat forms of MDRTB. Additional multi-centric analysis will be performed in the future.

PS34-779-26 Genomic context of drug resistance among *Mycobacterium tuberculosis* in Moldova

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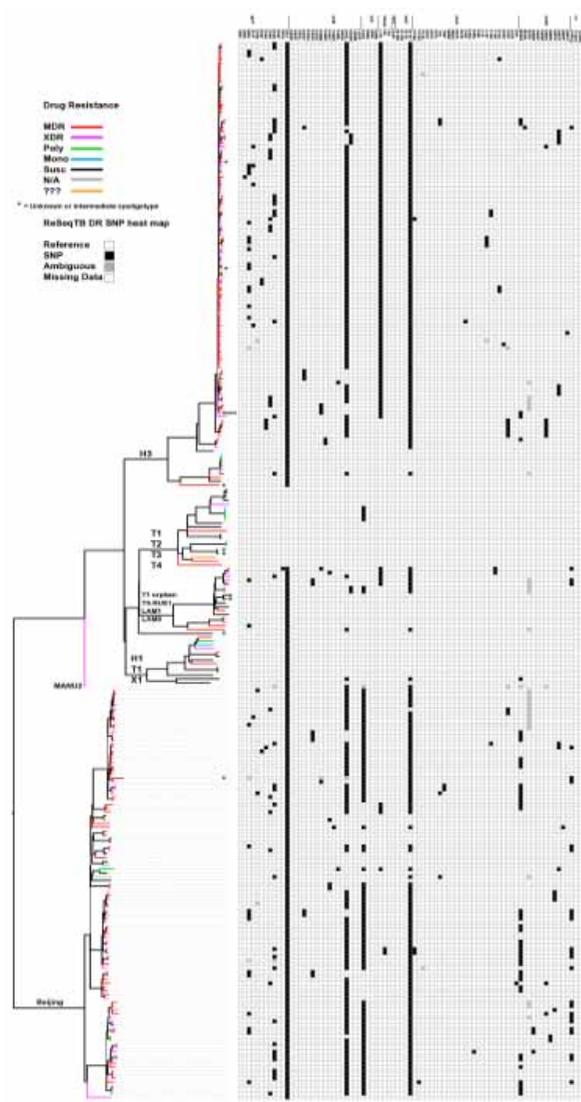
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Background: Drug-resistant tuberculosis (DR-TB) is a major health issue with global impact. DR-TB incidence and relapse rates are alarmingly high in Eastern Europe and countries of the former Soviet Union. As part of a larger genomic analysis of DR-TB in the region, we sequenced and analyzed the genomes from 287 isolates collected from 190 patients in the Republic of Moldova.

Methods: Clinical sputum samples were collected from patients of the Chisinau Phthisiopneumology Institute TB clinic. Samples of drug-resistant and drug-susceptible tuberculosis cases, including relapse cases were selected for the study. Drug susceptibility testing (DST) and whole genome sequencing of *Mycobacterium tuberculosis* (*M.tb*) was performed. Sequences were mapped to the *M.tb* reference genome followed by variant calling and annotation. Digital spoligotypes and drug resistance predictions were computed. A phylogenetic tree with DST and DR SNP annotations was constructed using 13,321 genomic SNPs.

Results: Genomic analysis revealed that the majority of the isolates were equally split between the H3 and Beijing lineages (41% and 38%, respectively). Phylogenomic analysis demonstrated that DR-TB, including multi- and extensively drug resistant (MDR and XDR), was being transmitted from person-to-person rather than evolving *de novo* from susceptible isolates (48% of samples). Analysis of relapse case isolates from 87 patients found that two-thirds of the infections exhibited little change over time (58 cases, 67%), though a third of the patients demonstrated reinfection by divergent lineages (29 cases, 33%).

Conclusions: We found that the majority of MDR and XDR TB cases in this study were the result of direct transmission of DR bacteria. Another important result suggests that in many cases of TB relapse, the pathogen was not fully eradicated when the patient was treated for the initial infection. These findings may support stricter control measures in hospitals both during treatment and upon patient release.



[Phylogeny and drug resistance diversity among *M. tuberculosis* isolated from patients in Moldova.]

PS34-780-26 What needs to be done to sustain progress achieved in TB control in EECA region before critical decisions are made

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Background: The Global Fund (TGF) is the single largest Tuberculosis (TB) financing authority, whose contribution to external assistance on TB amounted to 55.5% globally in 2016. In the era of recent global economic crisis donors started decreasing commitments, including for TB. In response to this dynamic TGF introduced new Sustainability, Transition and Co-Financing (STC) policy and started gradually reducing allocations for countries planned for transition over coming years. Eastern Europe

and Central Asia (EECA) region is primarily bearing the impact of STC policy where nine of the world's 30 high M/XDR-TB burden countries are located with the highest proportion of new and retreated cases with MDR-TB, 18.4 and 46.2% in 2016, respectively.

Methods: A multi-country research study was designed to investigate the impact of STC policy on access to quality TB drugs and commodities covering 2014-2017 in TGF TB grant recipients only in EECA region (12 countries). Research, narrowly examining domains of health systems for TB drugs and commodity, implied systematic collection of qualitative and quantitative data from published documents, public databases and through in-depth interviews.

Results: TGF requirement requesting increased government contribution in national TB strategic plans resulted in optimized budgeting of the National TB programs since 2014 and increased a role of the domestic funding sources. Significant decline in the average treatment cost per patient was also observed between 2014-2017 due to positive market dynamics reducing cost of drugs. Although, lack of adequate attention to national drugs policy/regulations was outlined, affecting import/procurement of externally produced quality assured drugs and commodities. Diversity in public procurement practices and delays in timely supply of drugs/commodities were also revealed.

Conclusions: The study identified significant challenges at different domains posing risks to maintaining the public health gains achieved on TB programs after transition unless effective policy is in place - recognizing performance problems have multiple causes.

PS34-781-26 Introduction of active drug safety monitoring and management in Tajikistan

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Background and challenges to implementation: World Health Organization (WHO) recommends active drug safety monitoring and management (aDSM) to ensure safe introduction of new drug-resistant tuberculosis (DR-TB) treatments (shorter and individualized regimens). aDSM was not established in Tajikistan prior to introduction of new regimens. Patients had to pay for clinical tests of doubtful quality which could not be used for clinical decision-making. With the introduction of new regimens in 2015, the USAID Challenge TB project (CTB) led by KNCV in Tajikistan implemented activities to establish aDSM.

Intervention or response: CTB established the WHO-recommended aDSM system to manage adverse events (AEs) and report serious AEs (SAEs). The intermediate

aDSM package was selected, an aDSM Thematic Working Group was established with a causality assessment subgroup, aDSM guide and reporting/ recording forms were developed and approved by MoH, TB clinicians from CTB pilots were trained on aDSM recording and reporting, and equipment for clinical monitoring (audiometers, ECG, ultrasonic scanning) was procured and installed. For patients' clinical monitoring a private laboratory was contracted for conducting regular clinical-biochemical investigations.

Results and lessons learnt: From December 2016 to December 2017, in total 139 DR-TB patients were enrolled on treatment with new regimens: 75 on the shorter treatment regimen and 64 on regimens containing Bedaquiline (Bdq). Five SAEs were registered for patients on regimens with Bdq, of which 3 were fatal and 2 required hospitalization. All these SAEs were judged to be unlikely related to Bdq. Thirteen AEs of special interest (e.g. QT prolongation, myelosuppression, peripheral neuropathy, etc.), were also registered during the treatment of DR-TB patients on new regimens. No SAEs were reported for patients enrolled on the shorter treatment regimen.

Conclusions and key recommendations: CTB interventions allowed to establish an aDSM system in Tajikistan. The national policies are developed, and the practice established in pilot sites will be expanded to new sites introducing new DR-TB treatment regimens.

PS34-782-26 Is the shorter multidrug-resistant tuberculosis regimen suitable for Eastern Europe? The example of Armenia

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Background: A standardised shorter MDR-TB regimen is recommended by WHO for certain MDR-TB patients. Due to its limited use in Eastern Europe, we explore eligibility and implications of implementation in Armenia.

Methods: We retrospectively analysed routinely collected programmatic data from the Armenian National Tuberculosis Control Centre for MDR-TB patients treated September 2005 to April 2015. We estimated the proportion of patients eligible for shorter MDR-TB regimen based on WHO eligibility criteria: no resistance to second line drugs (SLDs), no previous treatment with SLDs, no resistance to drugs in the regimen. We estimated 5% of patients would require regimen change on the shorter regimen due to injectable toxicity.

Results: Of 996 MDR-TB patients, 517 (51.9%) did not have all the necessary results available to estimate eligibility. No results were available for fluoroquinolone (Fq) for 333 (33.4%), amikacin or kanamycin (Am/Km) for 341 (34.2%) and capreomycin (Cm) for 348 (34.9%). Resistance to pyrazinamide was documented in 494 (49.6%) and was missing for 174 (17.5%).

There was documented resistance in 186 (18.7%) for Fq, 173 (17.4%) for amikacin or kanamycin (Am/Km) and 138 (13.9%) for capreomycin (Cm). Resistance to at least one injectable and both injectables was seen in 174 (174/996, 17.4%) and 125 (125/996, 12.55%) respectively. Nearly one third, 316 (31.7%) were previously treated with SLD

As per WHO recommendations, 14.6% (146/996) of patients had documented eligibility for the shorter MDR-TB regimen. An estimated further 7 (5%) patients would subsequently withdraw due to ototoxicity related to injectable drugs.

Conclusions: In settings of high second-line resistance, a limited number of patients are eligible for the shorter regimen as recommended by WHO, reduced further by injectable drug ototoxicity. Results are required to all drugs in the shorter regimen to better estimate the exact number of patients eligible, likely to be substantially lower than found in our limited evaluation.

ABSTRACT PRESENTATIONS SATURDAY 27 OCTOBER 2018

ORAL ABSTRACT SESSIONS

OA19 Building workforce capacity through education and training

OA19-314-27 Scaling up TB workforce development around the globe: the ECHO experience

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Background and challenges to implementation: According to the WHO, approximately one third of the world's population is infected with tuberculosis (October 2017). Both high and low-burden countries have a need to adapt and scale up evidence-based strategies to combat TB in their local contexts. Common to all of these settings is a scarcity of well-trained TB health workers.

Intervention or response: The ECHO [Extension for Community Healthcare Outcomes] tele-mentoring model—based on a combination of videoconferencing, case-based learning, sharing of best practices, and monitoring of outcomes—is an innovative evidence-based education and training intervention designed to strengthen the knowledge and practice of clinical and programmatic teams in underserved communities. The model supports development of communities of practice and learning that link national and international experts with site level TB practitioners for workforce development and collaborative problem solving to improve quality of and access to care.

Results and lessons learnt: In the span of three years, the ECHO model has been adapted and implemented to strengthen TB programs in 10 countries in Asia, Africa, and the Americas: in Viet Nam, India, Georgia, Kenya, Mozambique, Tanzania, Uganda, Guatemala, Mexico,

and the United States. The programs have focused on DR-TB, Pediatric TB, TB Infection, and TB in low-incidence settings in the U.S., as well as TB along the US-Mexico border. In India, the ECHO model is now incorporated in the national guidelines for programmatic management of DR-TB and is under consideration by the Government of India for expansion from five to all 29 states, and to implementation of a new TB-HIV ECHO program with the National AIDS Control Organization.

Conclusions and key recommendations: Uptake of the ECHO tele-mentoring model of education and training by a diverse array of National TB Programs around the world highlights its usefulness as a tool for TB programs to strengthen workforce development and quality of care which will be critical to achieving the End TB Strategy.

OA19-315-27 Is knowledge retained by healthcare provider after training? A pragmatic evaluation of drug-resistant tuberculosis management in China

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Background: Providing quality and standardized health services particularly by healthcare providers (HCPs) in rural areas is critical to address the growing burden of drug-resistant tuberculosis (TB) in China. In light of the importance and lack of evidence on the impact of training interventions, this study evaluates whether lecture-based training improves knowledge about management of multidrug-resistant tuberculosis (MDR-TB) in the short and long term.

Methods: The study involved 91 HCPs, including doctors and nurses managing TB at provincial CDC and hospitals providing TB services in Liaoning and Jiangxi province in China. HCP's knowledge about standardized management of MDR-TB was assessed at three points: pre-training, immediately post-training (through a paper-based test) and one year after training (through a phone-based assessment using questions from the paper-based test). The proportion of correct responses in the phone-based assessment was compared with the pre- and immediate post-training tests using a ² test. Regression analysis was conducted to identify factors that influence participants' long-term knowledge retention.

Results: Knowledge of definitions of drug-resistant TB, standardized MDR-TB case detection protocols and laboratory diagnosis was improved one year after the training by 14.5% ($P = 0.037$), 32.4% ($P < 0.001$) and

31% ($P < 0.001$). However, compared to immediately after the training, the knowledge on the three topics decreased by 13.2% ($P = 0.043$), 14.8% ($P = 0.009$) and 15.6% ($P = 0.037$) respectively. We found that obtaining a higher score in the long-term knowledge assessment was associated with more years of clinical experience (coefficient = 0.51; 95%CI 0.02 to 0.99; $P = 0.041$) and attending training in Liaoning province (coefficient = 0.50; 95%CI 0.14 to 0.85; $P = 0.007$).

Conclusions: Our results suggest an overall positive long-term impact of lecture-style group training on participants' MDR-TB knowledge. To reduce knowledge declines, follow-up training can be provided, particularly targeting HCPs with less working experience.

OA19-316-27 Competence-based training of frontline health workers in paediatric TB management to increase paediatric TB case identification in Rwenzori region, Uganda

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Background and challenges to implementation: Paediatric TB case identification lags behind that for adults with paediatric TB case finding at 7.2% in Uganda compared to estimated 15-20%; being mostly diagnosed at hospital level. We evaluated the effect of competence-based training of frontline health workers in paediatric TB management on paediatric TB case detection in seven districts within south western Uganda.

Intervention or response: In the period Jan-June 2016, more than 800 health workers of various cadres underwent competence-based training in paediatric TB management. This involved a 5-day regional training of trainers, and 3-day facility-based trainings for health workers within TB diagnostic and treatment units (DTUs) at health centre (HC) levels III, IV and district level hospital. Data was extracted from the national district health information system (DHIS2) for the period before training (2015) and period during and after training (2016 and 2017). TB indicators analysed included; new and relapse bacteriologically-confirmed pulmonary TB (PBC) cases (< 15years, ≥15years), new and relapse clinically-diagnosed pulmonary (PCD) TB cases (< 15years, ≥15years). Descriptive analysis was done.

Results and lessons learnt: The number of new and relapse paediatric TB cases increased by almost four times from 36 (3.5%) in 2015 to 137(6.6%) in 2016 and tripled in 2017 (121, 5.6%). There was also >100% increase in total number of new and relapse TB cases from 994 in 2015 to 2103 (2016) and 2130 (2017). Number of TB-

HIV co-infected persons also doubled from 363 cases in 2015 to 882 cases in 2017. Facility-based trainings yielded more trained health workers, seemed more affordable, and may be a more sustainable model for competence-based training in resource-limited settings. Health workers' capacity building complements TB diagnostics to improve paediatric TB case finding.

Conclusions and key recommendations: Decentralizing TB diagnosis to lower healthcare levels through facility-based training greatly improves paediatric TB case finding in resource-limited settings. National TB programs can consider using this approach.

OA19-317-27 Impact of Fogarty HIV-TB training program on 'institutional research capacity building' at the Byramjee Jeejeebhoy Government Medical College, Pune, India

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Background: In August 2013, a five-year Fogarty Training grant was awarded to Johns Hopkins University (JHU) in partnership with the Byramjee Jeejeebhoy Government Medical College (BJGMC). In India, public teaching hospitals are focused on clinical practices and patient care, with few resources and encouragement for research. Fogarty training program was designed to develop institutional research capacity. We undertook evaluations at the beginning of the training program and at the end to understand if our designed programme activities had the intended impact.

Methods: This study used mixed methodology to analyse 32 web based surveys and 26 in-depth interviews of TB research experts, BJGMC leadership and Fogarty scholars. The study endpoint looked at perception shift of the participants related to research capacity building at BJGMC; number of publications, basic research knowledge and linkages with other TB researchers.

Results: Twenty-one mid-level teaching BJ faculties were trained for conducting HIV TB research. Scholars had 22 HIV-TB research publications after enrolment into the programme. Of the 20 respondents at baseline, 10 (49%) felt the need to upgrade basic research knowledge, 11 (55%) specified up-gradation in scientific output. A shift in perception was revealed during the final evaluation with only 1 (3%) and 7 (24%) feeling the same need respectively. At baseline, 5% had reported very poor linkages with other TB researcher, whereas 18% reported improvement in the same at end evalua-

tion. Programmes thrust on ability to design a perfect research question was a success indicator, whereas lack of dedicated research time was a major obstacle for the scholars that prevented them from achieving the programme goals.

Conclusions: A well designed Fogarty Training program had a significant impact for institutional research capacity building. However, for future sustenance of this impact at the institutional level highlights the need for dedicated research time as perceived by the scholars.

OA19-318-27 Using innovative digital tools to measure physicians' diagnostic behaviour

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Background: Digital tools are increasingly being used to drive behavior change among healthcare providers in low- and middle- income countries. These tools provide extensive reach at a relatively low cost and time. However, due to the high cost associated with conducting randomized trials, evaluation of digital tools remains a challenge in low-resource settings.

Methods: We created an e-game to simulate the classic Tuberculosis (TB) symptoms that a patient would present to a treating physician. The game allows the physician to do all the things s/he might do in clinic—ask questions, conduct a review of systems, order lab tests, view test results, call patients for follow-up visits or start treatment. Physicians are scored based on how closely their decision algorithm matches Standard of TB Care guidelines.

Results: With a development time of seven days, the game was made live to private TB treating providers through a physician engagement application, Curofy. The game collected data from 1,059 physicians over a period of 44 days. 22% physicians came to a confirmed diagnosis before the patient dropped-off due to excessive follow-up visits. The total cost of creating the game was ~US\$7,160 resulting in a cost per participant of US\$6.76. In contrast, the cost per contact of conducting a standardized patient (SP) trial, that lasts for ~120 days (including recruitment and training of SPs) to reach ~100 physicians, ranges between US\$100-150 plus physician consultation fee.

Conclusions: Compared to traditional trial methods such as SP, online trials not only reach larger numbers of participants in a relatively short period at significantly lower costs, but also ensure follow-up visits and participant anonymity and reduce ethical barriers. Next, we will be analyzing the results from this game to compare differences in scores of physicians who attended a 10-month digital engagement campaign on TB (conducted by CHAI) with comparable physicians who did not.

OA19-319-27 The experience of using video-conferencing technology to improve access to life-saving services for TB patients in remote parts of Ethiopia

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Background and challenges to implementation: For many years, the Ethiopian TB program relied on off-site workshop style trainings to meet human resource training needs in its national TB program. However, staffing shortages and frequent staff turnover are critical barriers to expanding access to TB services in settings with a high TB burden. We aimed to illustrate the use of digital technology to improve health workforce efficiency and service accessibility in TB care in Ethiopia.

Intervention or response: Since 2014, with support from USAID-funded projects, we established a video-conferencing facility at ALERT hospital that was used to organize blended learning approaches for health workers and to facilitate clinical consultation between consultants working at tertiary hospitals and those based in primary health facilities. We used the facility to organize international and local trainings and live consultations in support of the introduction of new MDR-TB drugs. A live video-conference, instructor-led interactive training session was held from Toronto, Canada Shoebox supplier. Local consultant physicians provided teleconsultation services from a tertiary facility in Addis Ababa to clinicians based in remote regions of Ethiopia. We decentralized the video-conferencing facility to four additional centers.

Results and lessons learnt: Using the blended approach, it was possible to address 50 to 60 participants at a time, compared with the traditional class room capacity of 15 to 20. An average of three working days of displacement was minimized with this innovative approach. Further, the cost of training was 50% less. Forty MDR-TB clinicians from all over the country received training on the use of smartphone-based audiometry for monitoring the side effects of MDR-TB drugs.

Conclusions and key recommendations: The use of digital technology in knowledge transfer to remote areas needs to be considered as an option to address the scarcity of local expertise and reach a large number of participant without removing them from their work places.

OA19-320-27 South African National Department of Health and CDC partnered with John Hopkins School of Nursing MDR-TB Short Course Training of Clinicians, 2017-2018

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Background: Correct treatment for Multi-Drug Resistant Tuberculosis (MDR-TB) is critical for successful patient management. The National Department of Health (NDoH) accelerated the rollout of 9-month MDR-TB short course regimen increased opportunity for non-adherence. Training curriculum was developed to address clinical needs for providers as new short course guidelines were not readily available.

Methods: Johns Hopkins School of Nursing and the NDoH partnered to create and deliver a format to expand the new information across the country in a timely fashion. Clinical decision support training was structured as a 4-day program which included didactic course work, case studies and small group breakout with report back sessions. Eleven training events for nurses, doctors, and public health scientists (n=512) were held throughout South Africa from January 2017 through March 2018.

Results: Matched Pre-Test and Post-Test were received from 470 (91.8%) didactic training participants. Pre- and Post-Test average test score were 64% (Range 7-24) and 84% (Range 14-25), respectively. Understanding between Pre- and Post-test (n=448) scores improved (p<0.0000). Course evaluations addressed strengths and weaknesses of MDR-TB training, as well as perceived needs of additional training. Feedback after the pilot, reduced the didactics from 5 days to 4. Nurses iterated that more attention was needed for designing regimens adding more time for case studies and practical work, i.e. HIV+ patients, symptom management, and drug side effects/interactions.

Conclusions: Trainings were well-received with attendees wishing to attend more courses of a technical nature for patient management. Common themes from evaluations and feedback were that more trainings are needed to capacitate colleagues who require better understanding MDR-TB, and additional decision support for regimens to address drug side effects. Didactic training with clinical case studies, followed by a guided clinical training appears to be a successful model to increase the number of well-trained clinicians but additional follow up of time is recommended.

OA19-321-27 TB/MDR-TB education and training for nurses improving the quality of TB services in Malawi

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Background: TB remains a leading cause of mortality in Malawi. Capacity building initiatives to nurses as frontline caregivers in the management of TB can significantly improve delivery of services and ultimately reduce mortality rate. However, nurses are not actively involved in TB activities at all levels. This has negatively affected quality of TB services resulting in patients not receiving proper care.

Methods: Since 2006 National Organisation of Nurses and Midwives of Malawi (NONM) in collaboration with International Council of Nurses (ICN) have been conducting targeted education and training to nurses working in TB settings as trainer of trainers across Malawi. The training sessions were co-facilitated by Ministry of Health through NTP. Periodic review meetings were conducted where nurses shared progress reports and challenges experienced, way forward discussed. We compared data for one year before instituting this education and training program and one year after.

Results: Thirty nurses were trained in 2016 and the mean pre-test TB knowledge score was 64% correct; this increased to 88% on the post-test. One-year post training, 21 nurses completed an evaluation and reported having initiated various interventions which significantly improved TB service delivery in their facilities. Twenty (95.2%) nurses reported making changes to sputum collection and 100% reported these changes resulted in a decrease in the turnaround time for results from the lab. All 21 reported that they made changes to improve treatment adherence; 20 (95.2%) improved emotional and psychosocial support for patients and 95.2% reported improving education to patients and families. Nurses also made changes to infection control; 71.4% reported now screening all patients for TB, improved ventilation, and improved access to N95 respirators respectively.

Conclusions: Training nurses and increasing their knowledge of TB/MDR-TB is important in stimulating an increase in quality patient-centered TB care service delivery to patients.

OA20 A potpourri of tuberculosis: subclinical disease to dirty money

OA20-322-27 Prevalent pulmonary tuberculosis diagnosed in participants, stratified by transcriptomic correlate of risk, in a clinical trial of targeted preventive therapy

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Background: The South African Tuberculosis Vaccine Initiative (SATVI) is recruiting participants in Worcester, Western Cape, South Africa (TB incidence \pm 1%), into CORTIS-01, a randomised, partially-blinded clinical trial of Isoniazid and Rifapentine therapy to prevent pulmonary tuberculosis (PTB) in high risk individuals, identified by a transcriptomic correlate of risk (COR). COR positive prevalence is estimated as 15% in this community's young adults.

Methods: Volunteers are enrolled based on screening status of a host blood-based COR signature. Per protocol, study population is 47% COR+. (enrolment ongoing, data remain blinded). Other inclusion criteria include HIV-negative, 18- 60 years, and no TB or known household multidrug resistant TB contact in last 3 years. At enrolment two sputum samples are collected for Xpert-MTB/RIF assay. If a single sample is XpertMTB/RIF positive, the second is cultured and an additional sputum collected for XpertMTB/RIF and MGIT culture.

Results: Between September 2016 and March 2018 SATVI consented 5098 volunteers, screened 4792, and enrolled 720 into CORTIS-01. PTB was diagnosed on enrolment sputa in 29 (4.0%) participants. Of these, 25/29 (86.2%) were XpertMTB/RIF positive on 2 sputum samples, 2/29 (6.9%) were single Xpert positive and MGIT positive, and 2/29 (6.9%) were single sample XpertMTB/RIF positive. Rifampicin resistance was detected in 2/29 (6.9%). None of these participants had reported symptoms suggestive of TB at screening. PTB had previously been diagnosed in 10/29 (34.5%), all more than 5 years prior, and 3 (10.3%) had co-habited with a TB patient on treatment in the last 3 years. There was a smoking history in 28/29 (96.5%). All were referred to the local clinic for treatment.

Conclusions: Through active screening of a population enriched for TB risk on the basis of mRNA biomarker status, *Mycobacterium tuberculosis* was found in the sputum of a surprisingly large proportion of symptom-free, apparently healthy adults, consistent with subclinical, infectious pulmonary TB disease.

OA20-323-27 Final tuberculosis treatment outcomes of patients receiving a socio-economic support intervention: long-term follow-up from a randomized controlled trial in Peru

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Background: The WHO End TB Strategy recommends economic support for tuberculosis-affected households. We previously reported increased tuberculosis treatment success in patients receiving an integrated socioeconomic intervention in Peru. However, follow-up was short-term (6 months), causing outcome data to be preliminary for one-fifth of participants. Through long-term follow-up, we aimed to evaluate the final treatment outcomes of patients receiving a socioeconomic intervention for tuberculosis-affected households.

Methods:

Design - A household-randomized controlled trial. *Setting* - 32 shantytowns, Callao, Peru.

Participants - All consenting patients with TB treated by the Peruvian TB Program.

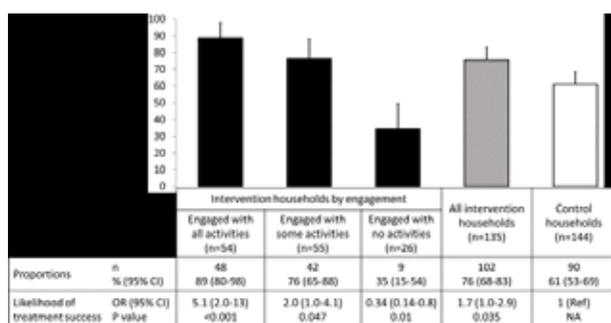
Randomisation - Patient households were randomly assigned 1:1 to control households that received Peruvian TB program standard of care or intervention households that additionally received the socioeconomic intervention.

Intervention consisted of socioeconomic support throughout TB treatment. Economic support constituted conditional cash transfers averaging US\$183 (8% of average TB-affected household annual-income) to mitigate TB-related costs, incentivise and enable care. Integrated social support constituted household-visits and TB club community meetings aiming to inform and empower, reduce stigma, and facilitate mutual-support. *Follow-up* - Participants were recruited from February-August 2015 and were followed up until November 2017. *Outcomes* - TB treatment success in patients from intervention versus control households, stratified by engagement with the intervention.

Results: Final outcome data was available for 132/135 (98%) intervention and 132/144 (92%) control patients. TB treatment success was more likely in intervention than control patients (76% versus 61%, OR=1.7 [95%CI=1.0-2.9], p=0.035), especially with full

engagement in intervention activities (89%, OR=5.1 [95% CI=2.0-13], $p < 0.001$, Figure). Being poorer (OR=10 [95% CI=2.2-44], $p=0.003$) or previously incarcerated (OR 3.1 [95% CI=1.1-9.0], $p=0.04$) were independently associated with not engaging with intervention activities.

Conclusions: Long-term participant follow-up showed that a socioeconomic intervention improved rates of TB treatment success in an impoverished setting, but engagement was limited by social determinants. The intervention has been refined to improve its equity in the Community Randomized Evaluation of a Socioeconomic Intervention to Prevent TB (CRESIPT).



[Treatment success of patients with TB from intervention ($n=135$) versus control ($n=144$) households]

OA20-324-27 Contribution of multi-sectoral approach of Public-Private-Mix in new cities of Afghanistan: urban DOTS experiences

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Background and challenges to implementation: Afghanistan National Tuberculosis Program (NTP), with support from the USAID-funded Challenge TB (CTB) project, implemented PPM and urban Directly Observed Treatment, Short Course (DOTS) in Kabul in 2009; Kandahar, Herat, Jalalabad and Mazar-i-Sharif in 2015 and Pulikhomri in 2017. The approaches look to strengthen coordination mechanisms and establish partnerships between the NTP, and public and private health sectors. The NTP assessed the implementation outcome to understand the impact of DOTS on case finding in public and private health facilities (HFs).

Intervention or response: NTP and CTB trained health-care staff on TB service delivery, distributed anti-TB drugs, laboratory consumable and DOTS packages, which included educational materials, sputum sample transferring materials and medication boxes with pa-

tients' entire treatment regimens. NTP and CTB conducted regular supervision and monitoring to urban DOTS health facilities. Patients received free diagnosis and treatment in public and private HFs. NTP and CTB technical teams evaluated the role of PPM and urban DOTS on TB case notification and outcomes, and reviewed TB data from the 2016 and 2017 and compared it with national TB surveillance data.

Results and lessons learnt: DOTS coverage reached 58% (106 out of 183 health facilities) in 2017 compared to 32% (49 out of 153) in 2015 and 8,147 cases were notified in 2017 compared to 6,492 in 2015 (P value < 0.00001). Of the 8,147 cases diagnosed, 2,715 (1,748 in 2015) were bacteriologically confirmed TB (See Table 1). Among 8,147 TB cases diagnosed in 2016, 2,030 (25%) were detected by the private health sector.

The treatment success rate increased by 2% to 83% at the end of 2016 (81% in 2015).

Conclusions and key recommendations: PPM and urban DOTS approaches contributed to significant improvements in case notification. The private health sector's contribution to case notification is significant. We recommend the scale-up of both approaches in other cities in Afghanistan, and in similar settings globally.

Indicators/Years	2015	2016	2017
# and % of HFs covered by DOTS	49 (32%)	84 (50%)	106 (58%)
# of all form TB cases registered	4,727	6,492	8,147
# of bacteriologically confirmed TB patients	1,748	2,397	2,715
# of all form TB cases identified by private sector	276	1,166	2,030

[Table 1, Effects of engaging public and private health facilities in TB case finding in Afghanistan]

OA20-325-27 Strengthening leadership pays: a look at TB program indicators after a leadership development program in Cote d'Ivoire

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Background and challenges to implementation: In early January 2017, Cote d'Ivoire MOH leadership requested GFATM assistance to improve leadership at the district level of Sud-Comoé. That region had high TB prevalence and low success in detection and referral. They sought similar good results to what had been produced by stronger leadership program for HIV programs in two other regions.

Intervention or response: Between January and December 2017, staff from district hospitals and TB centers in Sud-Comoé participated in the hands-on leadership program (LDP+). During the LDP+, run entirely by

local facilitators, teams attended four 3 to 4 day workshops, spaced about 2 to 3 months apart. They developed skills to improve results of the TB program, looked closely at data, identified root causes of challenges, and aligned key players

in order to come up with feasible strategies to take action together and inspire each other by producing intended results. In between the sessions local coaches visited the teams to encourage them and help with problem solving.

Results and lessons learnt: Leadership success was measured in two ways:

(1) metrics on progress towards targets that were linked directly to national indicators including # of cases detected, # of patients lost to follow up, # of patients cured, and

(2) self-report by LDP+ participants asking about their knowledge, attitudes and behavior before and after the intervention.

Over various periods of time, ranging between 2 and 9 months, 7 hospitals set themselves specific targets related to the metrics listed above: 2 hospitals focused on increasing detection rates, 2 focused on notification and referral, 2 hospitals focused on reducing people lost to follow up and 1 on increasing the number of diagnostic exams. All but one reached or surpassed their target.

Conclusions and key recommendations: The implementation of the LDP+ in Sud-Comoé has improved the TB indicators.

It would be desirable to implement LDP+ approach in all the regions.

OA20-326-27 Risk-benefit analyses using novel methods in the A5279 latent TB clinical trial

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Background: In most clinical trials, efficacy and safety are analyzed separately. This approach may not capture each patient’s overall clinical experience, limiting its utility for clinical decision-making. Risk-benefit analysis is a systematic approach to examine safety and efficacy jointly, which has been advocated in antibiotic and cardiovascular disease trials; however, it has not been applied to TB trials.

Methods: A5279/BRIEF-TB (NCT01404312) was a TB prevention trial comparing the efficacy of 1 month of rifapentine and isoniazid (1HP) with 9 months of isoniazid (9H) in HIV-infected adults and adolescents, which

demonstrated 1HP had non-inferior efficacy to 9H. A post-hoc risk-benefit analysis was applied by:

(1) creating nine ordinal categories based on desirability considering sequential prioritization of survival, TB diagnosis, and AE severity,

(2) assigning scores/ranks to categories based on survey results from 18 clinicians,

(3) assigning participants to a category, and

(4) conducting a superiority test to compare between arms using the Wilcoxon rank-sum test.

Results: The rank-based risk-benefit analysis confirmed that 1HP is the preferred regimen, with the difference between arms driven by fewer deaths and targeted AEs in the 1HP arm (p=0.03). Ranking can be subjective, and the survey showed differences of opinion (e.g., TB & < Grade 2 AE is better than No TB & Grade 4 AE); however, most ranked categories similarly.

Category	No TB & <G2 AE	No TB & G2 AE	No TB & G3 AE	No TB & G4 AE	TB & <G2 AE	TB & G2 AE	TB & G3 AE	TB & G4 AE	Death
Median Survey Score	100	85	72.5	50	30	25	20	10	0
Rank	1	2	3	4	5	6	7	8	9
1HP n (%)	1269 (85%)	90 (6%)	62 (4%)	22 (1%)	20 (1%)	1 (<1%)	1 (<1%)	2 (<1%)	21 (1%)
9H n (%)	1234 (82%)	113 (8%)	69 (5%)	31 (2%)	17 (1%)	3 (<1%)	2 (<1%)	1 (<1%)	28 (2%)

[Table 1: A ranked risk-benefit outcome with 9 categories, with frequency by arm]

Conclusions: We showed 1HP to be superior to 9H in A5279/BRIEF-TB using a risk-benefit approach that examined efficacy and safety simultaneously. If well-designed, this approach allows researchers to conduct a superiority rather than a non-inferiority comparison for TB trials, and may better capture stakeholder preferences. Additional factors such as tolerability, quality of life, or number of AEs may be incorporated into scoring, providing additional power in TB trials with low event rates.

OA20-327-27 Neural network analysis as a tool to develop screening algorithm for tuberculosis

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Background: World Health Organization established the goal of tuberculosis (TB) elimination by 2050. To achieve that it is necessary to develop TB screening algorithms to identify those at higher risk to have TB. Neural network is a modeling analysis that assigns different weight to each variable to understand the relationship

between independent variables and the outcome measuring the contribution of each variable. The aim was to compare two statistical modeling techniques to predict the risk of having TB.

Methods: To create the predictive models we used the data of a cohort of 1305 prisoners with respiratory symptoms. Each prisoner was studied with auramine-rhodamine stain and three cultures to discard the TB, and sociodemographic and clinical characteristics were collected. We performed a logistic regression model and neural networks to predict the presence or absence of TB. The database was divided in two: 70% of patients were used to create the model, and the other 30% was used for validation. In total 18 variables (weight, history of prior TB, diabetes, hemoptysis, HIV, sweating, contact with a TB case, subsidized or contributive health insurance, chronic obstructive pulmonary disease, dyspnea, age, fever, sex, expectoration, pleuritic chest pain, cough) were included and coded as 0 and 1.

Results: Comparison of the models showed that neural network has an area under the curve (AUC) of 99%, while the logistic model has an AUC of 73%. The sensitivity (82.6% vs. 2.2%), specificity (98.1% vs. 100%), positive predictive value (70.4% vs. 100%) and negative predictive value (99.1% vs. 95%) of neural network were better compared to logistic regression.

Conclusions: Neural network is useful to develop screening algorithms for TB due to accuracy in assessing the attribution of each variable and its high sensitivity. The next step is to validate the algorithm in external cohorts.

OA20-328-27 A quantitative assessment of general wellbeing in TB-affected people

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Background: Tuberculosis (TB) is an infectious disease strongly associated with poverty and stigma. Most wellbeing tools used to assess TB-affected people focus on physical health, and/or are cumbersome to apply. The WHO-EUROHIS quality of life tool (WHO-EUROHIS-QOL) assesses physical and non-physical wellbeing whilst only containing 8 items.

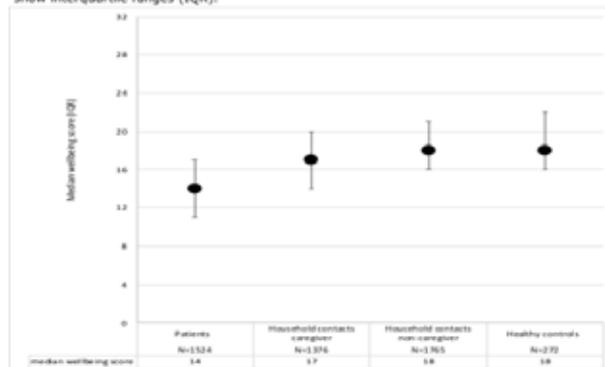
Objective: To evaluate the WHO-EUROHIS-QOL to assess general wellbeing in TB-affected people in resource-constrained settings.

Methods: Participants were recruited in Callao, Peru from 13/7/2016-24/2/2018. Inclusion criteria were age ≥ 15 years and informed written consent from: patients newly diagnosed with TB disease ($n=1,545$); 'contacts' who reported being in any patient household for ≥ 6 hours/week ($n=3,141$); and community controls randomly-selected from maps ($n=277$). A questionnaire was used to record: wellbeing (WHO-EUROHIS-QOL); negative affect (Beck depression inventory, BDI-II); perceived TB-related stigma (adapted EMIC); the World Bank adapted social capital assessment tool (SASCAT); and locally validated assessment of TB-related knowledge, symptoms and demographic data. Ill-being was defined as WHO-EUROHIS-QOL in the lowest quartile ($\leq 11/32$).

Results: The WHO-EUROHIS-QOL was successfully completed by 99% of participants (4938/5002). Patient ill-being was associated with: female gender (adjusted odds ratio, aOR=1.4, 95% confidence interval, 95% CI=1.1-1.9, $P=0.02$); stigma (aOR=1.02, 95% CI=1.01-1.04, $P=0.004$); lower SASCAT-assessed emotional support (aOR=0.86, 95% CI=0.75-0.99, $P=0.03$); and lower BDI-II assessed affect (aOR=1.1, 95% CI=1.1-1.2, $P<0.0001$). Patients experienced lower wellbeing than controls ($p<0.0001$, Figure) predominately in physical health and self-satisfaction. Contacts who were caregivers to the patient experienced lower wellbeing compared to: non-caregiving contacts, or to healthy controls (both $P<0.001$). Ill-being in contacts was associated with: being female (aOR=2.0, 95% CI=1.5-2.8, $P<0.0001$); being a care-giver (aOR=1.5, 95% CI=1.1-2.1, $P=0.01$); and if the patient was also experiencing ill-being (aOR=2.2, 95% CI=1.6-3.0, $P<0.0001$).

Conclusions: Wellbeing in TB-affected people can be meaningfully assessed by the WHO-EUROHIS-QOL 8-item tool. This study highlights the psychosocial and economic impact of TB, which transmits to care-giving members of their household.

Graph comparing the median wellbeing scores between patients, household contacts who are caregivers, household contacts who are non-caregivers and healthy controls. Note, error bars show interquartile ranges (IQR).



[Figure]

OA20-329-27 Screening currency notes for *M. tuberculosis* using loop-mediated isothermal amplification

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Background: The most common form of currency that is used worldwide is in form of paper currency notes. Paper currency notes are most commonly exchanged fomites which can be contaminated and their potential to transmit pathogenic organisms causing skin infections and gastrointestinal problems has been well recognized. They may also pose public health problem in control of tuberculosis. Hence, the aim of this study was to investigate the contamination of Indian paper currency notes with *Mycobacterium tuberculosis*.

Methods: A total sample size of 1000 ten rupee notes was collected from individuals in North Delhi. The notes were collected in sterile plastic bags. Fresh currency notes obtained from bank were also screened in addition to collected notes. The notes were washed with sterile solution and total genomic DNA was extracted using Chelex-100 resin. Loop mediated isothermal amplification assay was carried out to detect presence of *Mycobacterium tuberculosis*.

Results: The currency notes were classified according to condition, appearance and degree of dirtiness as new, moderate and torn. Fresh currency notes obtained from bank tested negative. Out of 1000 samples, 213 were positive for presence of *Mycobacterium tuberculosis*. The correlation between condition of note and positive status was also determined.

Conclusions: The findings of the this novel study highlighted that currency notes show presence of *M. tuberculosis* which represents risks and public health issues to the community and individuals handling currency notes. The technique used is simple, rapid and reliable for detection of causative micro-organism which is difficult to culture. This study has potential implications in control of this deadly infectious disease and may also be applied for screening for drug resistance in future.

OA21 Multidrug-resistant tuberculosis: more pearls and wisdom

OA21-330-27 Interim cohort analysis of drug-resistant TB patients on bedaquiline-containing regimens in Viet Nam

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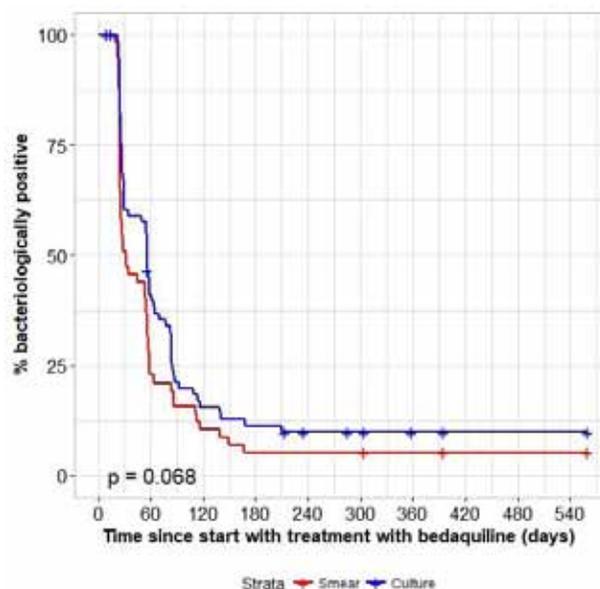
Background: Vietnam is a high multidrug-resistant TB (MDR-TB) burden country with high fluoroquinolone (Fq)- and second-line injectable (SLI)-resistance. New and repurposed drugs are urgently needed for 900 patients estimated annually to have pre-extensively drug-resistant (XDR) and XDR-TB, and a significant number manifesting intolerance to standardized MDR-TB treatment. Bedaquiline was introduced as a cohort study in 2015.

Methods: An observational interim cohort analysis assessed safety and effectiveness of Bedaquiline- (Bdq) containing regimens for pre-XDR-/XDR-TB and MDR-TB patients intolerant to second-line drug regimens from December 2015 to March 2017.

Results: Of 99 patients enrolled in Bdq-containing treatment, 34 (34%) were XDR-TB, 42 (42%) pre-XDR-TB with Fq-resistance and 23 (23%) pre-XDR with SLI-resistance. Bdq was given for six months in three-fourths of the cohort, 23 patients (23.2%) receiving prolonged Bdq for maximum 32 weeks. Culture conversion at 6 months (180 days) of treatment was achieved in 65 of 75 (87%) patients being culture-positive at baseline; 58 (77%) within 90 days of treatment. By December 2017, 53 still underwent treatment; 27 patients had successfully completed, 11 lost-to-follow-up, 1 failed and 7 died; causality assessment showed a likely association with Bdq-containing regimen in 02 of the deaths.

All 99 patients encountered at least one adverse event (AE), 26% serious. The most common AEs were hypocalcemia (73%), hypokalemia (72%), hyperglycemia (62%) and hyperuricemia (51%). QTcF prolongation > 500ms occurred in 14% of patients, only 4 requiring suspected drug withdrawal, 2 of whom requiring permanent Bdq discontinuation.

Conclusions: Interim outcomes of patients on Bdq-containing regimens in Vietnam showed impressive culture-conversion results at three and six months of treatment. However, more vigilance is needed to address the high loss-to-follow-up and death rates over the treatment course. Active drug safety monitoring and management (aDSM) is likewise essential, particularly clinical monitoring of electrolytes and QT prolongation, and their proper management.



[Time to smear and culture conversion]

OA21-331-27 Provision of guideline-based care for drug-resistant tuberculosis in South Africa: individual and health system characteristics affecting guideline adherence

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Background: The objective of this study was to address the knowledge gaps pertaining to prescription of guideline-based treatment for DR-TB at treatment initiation and examine the influence of individual and health system factors on the prescribed treatment for youth and adults with DR-TB in South Africa.

Methods: This study, nested within an ongoing cluster-randomized trial, took place at ten DR-TB treatment sites in Eastern Cape and KwaZulu Natal provinces, South Africa. Participants included 337 patients treated for DR-TB. Medication, dosage, and frequency at treatment initiation, were compared against South African treatment guidelines to determine adherence. Logistic regression was used to identify individual and health system characteristics related to adherence to South African guideline-based treatment regimen that included four oral and one injectable medications.

Results: The sample included 19% youth (15-24 years), overall mean age 34.8 years, 53% male, 73% HIV coinfected (of whom 86% were on ART), and 51% with pri-

or history of TB disease. Guideline-based selection of medication was correctly prescribed for 88%, however, complete guideline adherence to medications, doses, and frequency was achieved for 30% of patients. The prescription of correct medications were significantly influenced by younger age, HIV coinfection, rural treatment setting, and KwaZulu Natal province. The adjusted odds ratios (with 95% confidence intervals) are as follow: younger age (0.97, 0.94-0.99), HIV coinfection (2.089, 1.02-4.30), rural treatment setting (0.24, 0.109-0.53), and KwaZulu Natal province (0.24, 0.109-0.529).
Conclusions: Many DR-TB patients in South Africa are initiated on the correct combination of medications; however, few patients receive the correct combination of medications, doses, and frequency, which may lead to increased resistance. Further study is needed to examine the root causes for treatment guideline deviations and opportunities for improvement.

OA21-332-27 An observational study documenting treatment and pregnancy outcomes in women exposed to MDR/RR-TB treatment during pregnancy

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Background: Data on safety and efficacy of second-line drug treatment for MDR/RR-TB in pregnant women are severely limited due to exclusion from clinical trials and expanded access programmes for new drugs. Safe and successful treatment of MDR/RR-TB increases the mother's chance of survival and reduces infectious risk to the foetus/infant, but may also improve pregnancy outcomes and early development of the infant. Bedaquiline has been shown to improve outcomes in South African patients with MDR/RR-TB, but evidence in pregnant women is limited.

Methods: In this cohort study pregnant women were enrolled for treatment of MDR/RR-TB at King Dinuzulu Hospital in Durban, KwaZulu-Natal from 1st January 2013 - 31st December 2017. From retrospective record review and prospective clinical assessment we describe the treatment course and treatment and pregnancy outcomes.

Results: Of 90 pregnant women, 71 (79%) were HIV-infected. Seventy (77%) had MDR/RR-TB with no further resistance and 20 (23%) strains with additional

resistance to fluoroquinolones and/or injectable agents. Seventy five (83%) were pregnant before starting MDR/RR-TB treatment. Forty four women were treated with an injectable agent, 32 with bedaquiline and 14 with neither drug group; 9 (10%) women received the shorter 9-12 month regimen. Five women were still pregnant at the time of reporting but of the 85 women to have delivered, 77 (91%) have delivered healthy babies, while there have been 5 still births, 2 miscarriages and one early neonatal death. Forty three women are still on treatment and of the 47 who have completed treatment, 26 (55%) have had successful outcomes. Most women who received bedaquiline have not yet completed treatment so it is not yet possible to compare outcomes and toxicity (to the mother or baby) between treatment groups.

Conclusions: In pregnant women with MDR/RR-TB treatment outcomes are comparable to non-pregnant adults. The majority of women delivered healthy babies.

OA21-333-27 Mathematical modelling of the epidemiological impact, cost-effectiveness and budget impact of novel tuberculosis vaccines on multidrug-resistant tuberculosis

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Background: The role of vaccines in anti-tuberculosis drug resistance is an emergent but under explored area. Given increasing MDR/XDR-TB incidence and costs, and constraints surrounding resource allocation to new TB control efforts, this area warranted further investigation. We aimed to estimate the potential impact of novel TB vaccines on MDR-TB burden and identify those vaccine characteristics that will contribute most effectively to achieving the 2030 UN SDG and 2050 WHO End TB targets for tuberculosis control.

Methods: We constructed a compartmental age-stratified dynamic transmission model of tuberculosis, which includes treatment history and drug resistance strata. Baseline (no new vaccine) scenarios fitted historic country-specific epidemiological and demographic data and projected (MDR-) TB epidemiology over the model time horizon (until 2050) for India and China.

Into these scenarios, we simulated the impact of potential prophylactic TB vaccine candidates, with varying characteristics (duration of protection, efficacy, and host infection status required for efficacy).

New TB vaccines were introduced in 2027, with routine vaccination delivered to 9 year olds, and 10-yearly mass vaccination campaigns for ≥ 10 year olds. We estimated economic costs from a health service perspective.

Results: The results demonstrate the numbers of avertable cases, reductions in incidence rates achieved, cost-effectiveness, and TB programme budget saved by im-

plementing new TB vaccines. Using this we demonstrate the value of vaccines in future TB control, including alongside scale up of other MDR-TB interventions.

Conclusions: Understanding the epidemiologic and budget implications of new TB vaccines with a focus on MDR-TB highlights the importance of TB vaccines in the fight to end TB by 2030 and eliminate TB by 2050. This is the first TB vaccine model to include MDR-TB. Such data are important to inform decisions for investment in vaccine research, strategic decisions in development of new vaccines, and policy and resource allocation decisions.

OA21-334-27 Six-month culture conversion among a MDR-TB cohort with high HIV co-infection treated with delamanid or bedaquiline in Lesotho

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Background: Lesotho has the second highest TB incidence in the world and 7% of incident cases are estimated to be multidrug resistant or rifampicin-resistant (MDR/RR). HIV co-infection is present in 73% of TB cases. Partners In Health has supported use of bedaquiline or delamanid in the Ministry of Health MDR TB program since October 2015 through its Unitaids-funded Expand New Drug Markets for TB project. We describe six-month sputum culture conversion among a prospectively enrolled observational cohort of MDR/RR TB patients treated with bedaquiline or delamanid between 1 October 2015-28 February 2017.

Methods: Study participants had confirmed RR TB and were eligible to receive bedaquiline or delamanid based on World Health Organization guidance. Sputum cultures were performed monthly. Culture conversion six months after initiation of bedaquiline or delamanid was assessed among patients with positive baseline culture at initiation. Univariate analyses were conducted to identify factors associated with culture conversion.

Results: Of 73 participants enrolled, 30 (41%) had a positive baseline culture. Twenty-two participants (73%) were HIV co-infected and 5 (17%) had extensively drug resistant TB (XDR TB). Sputum culture conversion occurred by six months in 23 (77%). None of the variables examined (HIV-positivity, smear positivity, presence of XDR TB and baseline body mass index < 18.5 kg/m²) was significantly associated with sputum culture conversion (Table 1); however, HIV-seropositivity was borderline positively associated with conversion ($p=0.06$).

Conclusions: Sputum culture conversion after 6 months of therapy with a bedaquiline- or delamanid-containing regimen was high. These findings support use of bedaquiline and delamanid as recommended in WHO

guidelines, at least among those at high risk for poor treatment outcomes. In light of the large proportion of patients with negative cultures at bedaquiline or delamanid initiation, likely reflecting drug toxicity as the indication for their initiation, standardized methods are necessary for evaluating interim response in this important subpopulation.

	Total (N=30) n (%)	Culture converted at 6 months (N=23, 77%)	Culture not converted at 6 months (N=7, 23%)	p-value
HIV serostatus				
Positive	22 (73%)	19 (86%)	3 (14%)	0.06
Negative	8 (27%)	4 (50%)	4 (50%)	
Baseline smear				
Positive	15 (50%)	11 (73%)	4 (27%)	1.00
Negative	15 (50%)	12 (80%)	3 (20%)	
XDR TB (N=29)				
XDR Positive	5 (17%)	3 (60%)	2 (40%)	0.27
XDR Negative	24 (83%)	20 (83%)	4 (17%)	
Baseline BMI (N=28)				
<18.5 kg/m ²	15 (54%)	9 (60%)	6 (40%)	0.08
≥18.5 kg/m ²	13 (46%)	12 (92%)	1 (8%)	

[Univariate analysis of factors associated with culture conversion in patients receiving bedaquiline and or delamanid In Lesotho (Oct 2015-Feb 2017)]

OA21-335-27 Safety of regimens containing bedaquiline and delamanid among cohort of drug-resistant tuberculosis patients in Ethiopia

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Background: Bedaquiline and delamanid were introduced in Ethiopia under programmatic conditions. The safety data of regimens containing these new drugs is being systematically collected. The objective of this study is to estimate the frequency of adverse events of special interest (AEIs) and serious adverse events (SAEs) among a prospective cohort of DR-TB patients treated with regimens containing these drugs.

Methods: We describe all SAEs and non-serious AEI during the first 6-months of treatment among study patients enrolled in Ethiopia. SAEs were defined as any

untoward medical occurrence that is: fatal, life-threatening, requiring hospitalization or prolongation of hospitalization, resulting in significant disability, congenital anomaly, or otherwise medically important. AEIs were defined as all adverse events pertaining to Peripheral neuropathy, Myelosuppression, Prolonged QT interval, Optic neuritis, Hepatitis, Ototoxicity, Nephrotoxicity, Hypokalemia, and Hypothyroidism. These were reported in real-time and SAEs were graded according to the MSF Severity Scale.

Results: 27 DR-TB patients initiated regimens containing bedaquiline or delamanid between July 2, 2016 and July 31, 2017; 15 received bedaquiline, 10 delamanid and 2 both. Median age was 36 (IQR 28-46) years. Nearly 60% (16) were male. BMI was < 18.5 in 19 (70%) and 11 (41%) were co-infected with HIV. SAEs (2) were reported in 1 (3.7%) participant within 6-months of starting a regimen containing bedaquiline or delamanid. Peripheral neuropathy and hearing loss occurred as SAE each once. AEIs (27) occurred in 15 (55.9%) participants within the first 6-months of treatment. Toxicities related to injectables (ototoxicity, hypokalemia, nephrotoxicity) accounted for 17 (63.0%) of the AEIs. Linezolid-related toxicities also occurred frequently (7, 25.9%). QTc prolongation reaching the AEI threshold occurred once (3.7%).

Conclusions: SAEs and AEIs occurring during the first 6-months of treatment in Ethiopian cohorts were disproportionately related to second-line injectable drugs and linezolid, rather than bedaquiline or delamanid.

OA21-336-27 Development of a multi-variable prediction model for poor outcome of tuberculosis treatment in drug-resistant tuberculosis patients: a nationwide database study from The Netherlands

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Background: Tuberculosis drug resistance is associated with poor clinical outcome. Although the incidence of drug resistant tuberculosis (DR-TB) in The Netherlands is low, identification of high-risk patients for a poor out-

come may allow efficient targeting of such patient for close monitoring and additional care. The objective of study was to develop a multi-variable prediction model for poor outcome of TB treatment among adult DR-TB patients.

Methods: We conducted a retrospective cohort study using The Netherlands Tuberculosis Registry (NTR) database. Adult patients identified as DR-TB patients with microbiological confirmation during 2005-2015 were included. Patients who had unknown clinical outcome were excluded. Potential predictors were identified in an earlier systematic review that examined five categories, i.e. socio-demographics, current TB diagnosis, history of TB disease and treatment, risk groups, and comorbidities. The poor outcome was defined as combination of defaulted, failed treatment and death due to TB disease. We conducted multi-variable logistic regression analysis with Hosmer-Lemeshow and area under the receiver operating curve (AUC) tests to examine calibration and discrimination of the prediction model.

Results: The study showed that incidence of poor outcome of TB treatment was 31 of 545 DR-TB patients. Homelessness, drug addiction and MDR/XDR-TB patients were associated with defaulted and failed treatment, while miliary and central nervous system TB were associated with mortality. The final risk model included homelessness (OR 5.36; 95% CI 1.47-19.58), drug addiction (5.01; 1.38-18.20), MDR/XDR TB (2.66; 1.14-6.20) and combination of pulmonary and extra-pulmonary TB (5.55; 1.35-22.91). The calibration and discrimination was good (*P* value 0.30 and ROC AUC-curve 0.77; 95% CI 0.65-0.87).

Conclusions: Our preliminary analysis showed that a good prediction model for poor outcome of TB treatment in DR-TB can be developed. Internal and external validation will be the next steps to further improve the validity of the model.

the drug. We therefore investigated whether resistance to isoniazid and/or pyrazinamide is associated with unfavourable treatment outcome.

Methods: Ninety MDR-TB patients from Bangladesh who were treated with the short MDR-TB regimen including high-dose gatifloxacin and whose baseline isolates had high-level fluoroquinolone resistance (gatifloxacin MIC \geq 2 mg/L) were included in the study. Isoniazid MIC was determined on LJ medium (1.6, 3.2, 6.4, 12.8, 19.2 and 25.6 mg/L) and classified as susceptible (MIC \leq 0.2 mg/L), low-level (0.8 \leq MIC \leq 1.6 mg/L), moderate-level (3.2 \leq MIC \leq 12.8 mg/L) or high-level resistant (MIC \geq 19.2 mg/L). Genotypic resistance was determined using line probe assays, Sanger sequencing or whole genome sequencing.

Results: Of 90 patients (15 with high-level isoniazid resistance, 72 moderate-level, and 3 low-level) 40 experienced unfavourable treatment outcome, including 28 failure or relapse. High-level isoniazid resistance was associated with failure/relapse in 9 (60%) patients, compared with 19 (31.7%) patients with moderate-level isoniazid resistance (*p*=0.042). Six of 8 patients (75.0%) with high-level isoniazid resistance in combination with pyrazinamide resistance experienced failure/relapse, versus 11 of 32 (34.4%) with moderate-level isoniazid resistance and pyrazinamide resistance (*p*=0.038).

Conclusions: Among patients with high-level fluoroquinolone resistance, especially patients whose isolate had an isoniazid MIC \geq 19.2 mg/L in combination with pyrazinamide resistance faced a high failure/relapse rate on the short MDR-TB regimen containing high-dose gatifloxacin. Irrespective of pyrazinamide resistance, patients with isoniazid MICs between 3.2 and 12.8 were less likely to experience failure/relapse, suggesting that high-dose isoniazid continues to contribute to treatment success in the majority of MDR-TB patients.

OA21-337-27 High-dose isoniazid continues to contribute to treatment success in the majority of MDR-TB patients

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Background: It is unclear whether isoniazid and pyrazinamide contribute to the short MDR-TB treatment regimen even in case of resistance to these drugs. Most isoniazid resistance occurs at minimum inhibitory concentrations (MICs) smaller than the serum peak of around 15 mg/L upon the WHO recommended high dose of 15-20 mg/kg, suggesting remaining activity of

OA22 Global approaches to child tuberculosis

OA22-338-27 Improving TB case detection in children aged < 15 years: experiences from Kampala, Uganda

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Background and challenges to implementation: Children are a high risk group for TB because diagnosis is problematic and is often delayed by exclusion of differential diagnosis. The true burden of TB in children is unknown mainly due to under diagnosis and under reporting. Despite improvements in the sensitivity of national pediatric TB screening and diagnostics, TB notification in children has remained low in Kampala, Uganda. In 2011/2012, the proportion of pediatric TB cases notified was only 5% of total notification.

Intervention or response: The Mulago National Referral Hospital Pediatric Unit, with support from TRACK TB, conducted monthly targeted Continuing Medical Education (CMEs) and mentorship on pediatric TB diagnosis for clinicians in high TB volume facilities from 2012/13 to 2016/17. They selected 480 staff to train from high TB risk facility areas, primarily, nutrition units, pediatric outpatient clinics, in-patient wards, and OPD/assessment centers. Trainings focused on using the MOH intensified case finding (ICF) tool, the pediatric TB diagnostic algorithm, and learning how to obtain sputum by induction. TRACK TB provided sputum induction equipment and sample collection tools. TB samples were tested using GeneXpert.

Results and lessons learnt: Overall, there was an increase in the proportion of children < 15 years initiated on treatment from 2011/2012 (5%) to 2017/2018 (12%).

Age category	Baseline-2011/12	2012/13	2013/14	2014/15	2015/16	2016/17	2017/18
Children (0-14Yrs)	384 (5%)	385 (5%)	365 (5%)	453 (6%)	485 (7%)	687 (10%)	174 (12%)

[Table 1: TB case detection by age]

Conclusions and key recommendations: Regular practical training of clinicians from high risk areas on detection of TB in children and using sensitive tools, coupled with the provision of key equipment improves TB diagnosis in children. This intervention may be a useful to other high volume facilities with similar diagnostic challenges.

OA22-339-27 Virologic outcomes among Kenyan children receiving cART and TB therapy

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Background: HIV-infected children initiating combination ART (cART) frequently have TB co-infection requiring concurrent TB treatment. Few studies have evaluated the impact of TB treatment and type of ART regimen on virologic treatment outcomes in young children.

Methods: HIV-infected hospitalized children were enrolled in the Pediatric Start of HAART (PUSH) clinical trial on timing of ART initiation (< 48 hours vs. 7-10 days) (NCT02063880). HIV-1 viral load (VL) was measured at enrollment and 6 months after ART initiation. Children underwent intensified TB screening, including evaluation of clinical symptoms, TB contact history, tuberculin skin test, chest x-ray, respiratory cultures/Xpert and stool Xpert testing. TB treatment was started per Kenya National TB guidelines with a cART backbone of super-boosted LPV/r for children < 3 years and EFV-based ART for children >3 years on TB treatment. Cofactors of viral suppression in cART-treated children with and without TB treatment were assessed by chi2 tests and multivariable logistic regression.

Results: Of 121 HIV-infected children with median age 2.3 years (IQR 1.2, 6.3) and VL data 6 months after ART initiation, 45 (37%) achieved viral suppression < 40 copies/mL. Higher baseline Log₁₀VL and younger age were independently associated with decreased odds of viral suppression [OR 0.60 (95% CI 0.39-0.94) and 0.88 (0.78-0.99), respectively]. The proportion of children achieving viral suppression was similar among children with and without TB treatment (42% vs 32%; p=0.30). Among TB-treated children, EFV-based therapy was associated with higher odds of viral suppression compared to PI-based therapy [OR 10.6 (95% CI 1.03-111.1)] after adjusting for age and baseline viral load.

Conclusions: HIV-infected children receiving TB treatment were more likely to achieve viral suppression if treated with EFV-based therapy compared to PI-based therapy. Alternate cART regimens for young HIV-infected children receiving TB treatment are needed.

OA22-340-27 Rifampicin and pyrazinamide exposures in children with DS-TB on WHO-recommended FDCs in the SHINE trial

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Background: Rifampicin and pyrazinamide drive sterilizing activity of the current standard WHO-recommended regimen for drug-susceptible tuberculosis. The development of 50/75/150mg isoniazid/rifampicin/pyrazinamide and 50/75mg isoniazid/rifampicin dispersible fixed-dose-paediatric combinations (FDCs) has facilitated uptake of WHO 2010 dosing guidelines for childhood tuberculosis.

Methods: We evaluated rifampicin and pyrazinamide pharmacokinetics in 39 South African and Ugandan children receiving WHO-recommended doses in the SHINE shortening trial. Children 4-7.9, 8-11.9, 12-15.9 and 16-24.9 kg, respectively, received 1, 2, 3 and 4 paediatric FDCs (Macleods Pharmaceuticals Ltd) per dose. Children ≥ 25 kg received adult doses, using 75/150/400/275 FDCs of rifampicin/isoniazid/pyrazinamide/ethambutol (2 tablets, for children 25-36.9 kg). Plasma rifampicin and pyrazinamide concentrations were measured in samples drawn pre-dose and at 1, 2, 4, 6, 8 and 12 hours after an observed dose, after at least 2 weeks of treatment. Noncompartmental analysis was used to compute the pharmacokinetic measures.

Results: Interim analysis includes 33 children sampled during the intensive phase and 6 during the continuation phase of treatment. Median (IQR) peak concentrations (C_{max}) and 0-24 hour area-under-the-curve (AUC) were 7.5 (4.9,11.8) mg/L and 26.6 (17.8,41.8) mg.h/L for rifampicin (n=39), and 39.4 (29.3,46.4) mg/L and 322.3 (263.4, 454.4) mg.h/L for pyrazinamide(n=33), respectively. Exposures differed by weight band in those receiving 1 (n=7), 2 (n=11), 3 (n=9), 4 (n=8) paediatric FDCs and adult doses (n=4), respectively: median AUC 17.8, 26.8, 38.8, 40.2, and 15.5 mg.h/L for rifampicin (p=0.011); 244.3, 322.3, 385.2, 434.2 and 302.6 mg.h/L, for pyrazinamide (p=0.015).

Conclusions: While median rifampicin and pyrazinamide exposures were similar to adults for children 12-24.9 kg, for rifampicin they remain substantially below recommended exposures. Children in the lowest 2 weight bands and those over 25 kg on adult doses had the lowest values. While the findings need confirmation with further data, current weight band-based doses may need adjustment.

OA22-341-27 Reaching zero TB deaths among children: strengthening health systems to accelerate detection and prevention of pediatric TB in Viet Nam

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Background and challenges to implementation: In Viet Nam, approximately 90% of childhood tuberculosis (TB) cases go undetected. Isoniazid preventive therapy (IPT) coverage is below 50%. *Breath for Life (B4L)* is a National Tuberculosis Program (NTP), PATH, and Johnson & Johnson initiative that aims to accelerate case detection, treatment and prevention to achieve zero childhood TB deaths.

Intervention or response: B4L addresses health system challenges contributing to low childhood TB detection and prevention in four of 21 districts in Nghe An province. Between 2016 and 2017, three key strategies were applied: engaging non-NTP public and private health facilities in childhood TB management; strengthening systematic symptom-based screening of child TB contacts and enrolling eligible children in IPT; and decentralizing childhood TB management within the public health care system. Outcomes were measured by comparing numbers of childhood TB cases diagnosed and enrolled on treatment and numbers of eligible children initiated on IPT from 2015 to 2016/2017 with between pilot and non-pilot districts.

Results and lessons learnt: Annual average of new childhood TB cases detected in the pilot districts increased 1.6 times from 74 in 2015 to 118 in 2016 and 2017; an annual average of 30 new childhood TB cases were detected in each pilot district, compared to 24 in non-pilot districts. Notably, the proportion of new childhood TB cases identified in the four districts from the total childhood TB cases of the entire province increased significantly, from 29% in 2015 to 35% in 2016 and 40% in 2017. The number and proportion of eligible children on IPT in the four districts also increased from 77% (49/64) in 2015 to 92% in 2016 and 2017 (189/205 and 271/294 respectively).

Conclusions and key recommendations: B4L demonstrated that health system strengthening can accelerate detection and prevention of childhood TB. NTP recognizes B4L as a best practice and is committed to its replication in other provinces.

OA22-342-27 Tuberculosis contact investigation in Mozambique improves case detection and preventive therapy initiation

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Background: Contact investigation (CI) for tuberculosis (TB) patients is a targeted, effective approach to find undiagnosed prevalent TB cases and children under 5 years of age eligible for Isoniazid preventive therapy (IPT). However, to date CI has not been implemented systematically in Mozambique, a high-burden country (incidence of 551 per 100,000). We evaluated a programmatic implementation of home-based CI in Beira Ciudad, in central Mozambique.

Methods: We began with a week-long training for community health workers (called "Activists") in conducting CI for newly diagnosed TB patients, including: screening household contacts for active TB, referring symptomatic contacts for evaluation, and initiating eligible children on IPT. We assessed the impact of CI on TB case detection and IPT initiation, comparing six months of data before and after implementation.

Results: Starting in July 2017 we trained 27 activists, working in 8 health centers throughout Beira. From July through December 2017: CI was conducted for 1801 TB patients; 6128 contacts were screened, including 1011 children under 5; and 43 contacts were diagnosed with TB and started on treatment. Compared to the first six months of 2017, after CI initiation the average number of contacts screened per TB patient increased from 2.0 to 3.4, the proportion of screened contacts diagnosed with TB increased from 0.11% to 0.70%, and the number of children under 5 started on IPT increased 67% from 509 to 848 ($p < .001$).

Conclusions: This initial evaluation of home-based CI suggests it is feasible and effective at increasing TB detection and IPT initiation among children under 5 in Beira, Mozambique. Based on these results, the activity will soon be scaled up in Sofala Province and then nationally. Further evaluation will show the potential impact of the intervention at scale to contribute to national case detection and IPT targets.

OA22-343-27 Good treatment outcomes in children with extensively drug-resistant tuberculosis: a systematic review and individual patient meta-analysis

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Background: Extensively drug-resistant (XDR) tuberculosis (TB), caused by *Mycobacterium tuberculosis* resistant to rifampicin, isoniazid, a fluoroquinolone and second-line injectable drug, is associated with extremely poor treatment outcomes in adults. Although >1000 paediatric XDR-TB cases are estimated annually worldwide, there are limited data on paediatric XDR-TB treatment.

Methods: As part of a global systematic review and individual patient data meta-analysis of children with multidrug-resistant TB, commissioned by the World Health Organization, we reviewed the presentation, treatment and outcome of children aged < 15 years with XDR-TB. Published and unpublished data were included from prospective and retrospective cohorts between 1999 and 2013.

Results: We identified 37 children with a median age of 11 years (interquartile range [IQR]: 6-13.1). All cases were bacteriologically confirmed. Thirty-two (87%) children had pulmonary TB and 20/31 (65%) had severe TB on chest radiograph. Among the 29 with known HIV status, seven (24%) were HIV-infected. The median treatment duration for children who completed treatment was 7.0 months (IQR: 6.0-8.2) for the intensive, and 12.2 months (IQR: 10.0-16.2) for the continuation phase. The most commonly used drugs were a second-line injectable, fluoroquinolone, cycloserine/terizidone, ethionamide/prothionamide and para-amino salicylic acid. No children received bedaquiline or delamanid, as the study preceded their availability. Thirty (81%) children had favourable treatment outcomes. Four (11%) children died, one (3%) failed treatment and 2 (5%) were lost to follow-up during treatment.

Conclusions: We describe the first globally aggregated cohort of children with XDR-TB, recognising this is a selected group of confirmed XDR-TB with limited data on some parameters. We demonstrate a high proportion of favourable treatment outcomes prior to the use of novel TB drugs, with mortality markedly lower than in adults. Regimens and the duration of treatment varied considerably. Improved reporting of XDR-TB along with an evaluation of shorter, effective and safe new regimens in children is required.

OA22-344-27 Tuberculosis contact investigation and its yield in children aged under 5 over a five-year period in Amhara Region, Ethiopia, 2013-2017

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Background and challenges to implementation: Investigation of contacts of patients with tuberculosis (TB) is increasingly being considered as a priority case finding strategy in resource-limited settings. It also has the added value of serving as an entry point for TB prevention and treatment in children. The aim of the study was to assess the trends in childhood TB detection rate among under-five children in a routine TB contact investigation program in Amhara Region.

Intervention or response: Contact investigation was introduced by the Regional Health Bureau with support from USAID-funded projects in 2013. During the first year, only contacts of smear positive pulmonary TB index cases (SS+) were screened, but all forms of TB were added in subsequent years. Project support included training of health care workers, supportive supervision, provision of job aids, review meetings, and one-on-one review of progress. We analyzed routine data for the period 2013-2017.

Results and lessons learnt: Of the 3,412 under-five child contacts among 17,999 SS+ index cases registered, nearly all (3,342, or 97.9%) were screened. Of those screened, 226 (6.8%) were symptomatically screen positive and 66 (29.2%) TB cases were detected, accounting for 4.0% of all under-five child TB cases reported in this period. The TB CNR was 1,975 per 100,000 under-five children, which was nearly nine times the estimate for the general population. The yield, however, declined from 2.6% at baseline to 0.9% in 2017.

Conclusions and key recommendations: Routine implementation of contact investigation was a high-yield strategy to identify missed children with TB. Diversifying the screening approach, including the use of digital x-rays, could be considered to further improve the yield.

Indicator	2013	2014 - 2015	2016 - 2017	Total
SS+ TB index cases (Number of under five children registered)	1360 (235)	10,815 (2,154)	5824 (1023)	17,999 (3412)
Number of under five children screened (Number of presumptive cases identified)	235 (32)	2104 (125)	1003 (69)	3342 (226)
Number of TB cases identified out of presumptive cases (%)	6 (18.8%)	48 (38.4%)	12 (17.4%)	66 (29.2%)
Yield of contact screening	2.60%	2.30%	1.20%	2.00%

[Contact investigation of under-five children who were household contacts of SS+ TB cases, Amhara Region, Ethiopia, 2013 - 2017]

OA22-345-27 Performance of MPT64 antigen detection test compared to Xpert MTB/RIF assay and culture for diagnosis of extra-pulmonary tuberculosis in children in Tanzania

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Background: Diagnosis of extrapulmonary tuberculosis (EPTB) in children suffers from lack of better diagnostic tools. The Xpert MTB/RIF assay (Xpert) endorsed by the WHO for diagnosing EPTB in children, has shown varying sensitivity. We have developed a better and robust diagnostic test based on detection of *Mycobacterium tuberculosis* complex specific antigen MPT64, by immunohistochemistry, from biopsies, biological fluids, and fine needle aspirates. The objective of this study was to validate the MPT64 antigen detection test for diagnosis of EPTB among children and compare it with the Xpert, and other routine diagnostic tests in a high TB burden setting.

Methods: Sixty three presumptive pediatric (≤ 18 years old) EPTB cases in Mbeya Zonal Referral Hospital (MZRH), Tanzania, were prospectively enrolled between April 2016 and July 2017. The patients were followed up from diagnosis to completion of treatment. Samples including fluids, aspirates and biopsies from any suspected EPTB sites were taken. The MPT64 test was implemented in the routine EPTB diagnostic setting. All the samples were subjected to the routine diagnostic work up; AFB microscopy, culture, histopathology and Xpert. The MPT64 test was read by the pathologists in MZRH and quality control was done by TM, and LS. Composite Reference Standard (CRS) including Xpert, Culture, AFB microscopy, radiology, Histology/Cytology findings and response to anti-tuberculous therapy was used to define TB cases.

Results: Of the 63 patients, 29 were defined as having EPTB; 12 TB adenitis, 9 peritonitis, 5 meningitis, 3 pleuritis. Of these, 10 were positive for culture, 1 for acid fast staining, 9 for Xpert, and 24 for MPT64. Pooled sensitivity for MPT64 was 92%, Xpert 32%, and culture 37%. The specificity was 77%, 97% and 100%, respectively.

Conclusions: MPT64 antigen detection test is far better than routine tests, including Xpert, for diagnosing EPTB in children.

OA23 Reaching the hard-to-reach populations in high tuberculosis burden countries

OA23-346-27 Impact of active case finding of tuberculosis among prisoners using the WOW truck in North Central Nigeria

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Background: In Nigeria, TB (Tuberculosis) screening and diagnosis among prisoners remains very poor as a result of inadequate TB surveillance systems among this key population.

The objective of this study is to measure the impact of WoW (Wellness on Wheel) truck on TB screening and diagnosis in this population.

Methods: The study utilized a mobile truck fitted with an X-ray machine aided by a CAD4TB (Computer aided diagnosis for TB) software and 2 four module GeneXpert machines. Cough history of ≥ 2 weeks as well as mass radiography was used to generate a list of presumptive TB cases tested using GeneXpert. All participants screened by cough were also screened by X-ray generating a score after every exposure. A score of ≥ 60 was used as inclusion criteria for presumptive TB cases.

Results: 4 prisons were visited with a total of 1123 prisoners (M- 1095; F- 28) screened, 149 (13.2%) presumptive TB cases identified, 26 (17.4%) MTB cases detected including 5 (19.2%) with rifampicin resistant.

Of the 26 TB cases identified, 15 (57.7%) had a history of cough > 2 weeks and an abnormal CAD4TB score (>60), 8 (30.7%) had abnormal CAD4TB score but no history of cough >2 weeks. 3 (11.7%) had a history of cough >2 weeks but had normal CAD4TB scores with the lowest score being 52. From this study, the yield of tuberculosis in the screened population was 2.3%. This implies a TB prevalence rate of 2300 per 100,000 prisoners and DR-TB prevalence rate of 445 per 100,000 prisoners.

Conclusions: TB screening and diagnosis remains a major challenge for prisons in Nigeria. The Wellness on Wheel (WoW) intervention can contribute immensely to closing this gap and providing support for TB surveillance systems in Nigerian prisons, while advocating for fortifying the prison health system itself.

OA23-347-27 Genomic evidence of tuberculosis spillover from prisons to the community in Mato Grosso do Sul, Brazil

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Background: Globally, rates of tuberculosis in prisons are >30 times higher than they are in the general population. In Brazil, a country with the third largest incarcerated population, 8% of TB occurs in prisoners, who represent $< 0.3\%$ of the population. However, the role of prisons as institutional amplifiers - propagating TB epidemics through spillover into the general population - is unknown.

Methods: We conducted population-based TB surveillance in Mato Grosso do Sul, a state with a high TB incidence in prisons (1760 per 100,000) and the highest incarceration rate in Brazil. We collected detailed incarceration and contact histories and sequenced whole *Mtb* genomes from 616 cultured isolates from 186 prisoners, 19 ex-prisoners, and 411 community members, representing $>90\%$ of the state's culture-confirmed cases (2010-2017). We inferred evolutionary relatedness between *Mtb* isolates with maximum likelihood and Bayesian phylogenies and multivariate genetic clustering.

Results: A maximum likelihood phylogeny inferred from 14,298 single nucleotide polymorphisms revealed that prison and community TB epidemics are closely interrelated. *Mtb* isolates from prisoners and community members cluster together throughout the phylogeny and in each of 15 predicted ancestral clusters. A recently emerged clade (most recent common ancestor: 45 years ago, 95% CI: 28-65 years ago) includes isolates from 44 prisoners, 3 ex-prisoners, and 50 community members. 44% (22 of 50) isolates from community members in the emerging clade are most genetically similar to isolates from prisoners or ex-prisoners, suggestive of transmission spillover.

Conclusions: We find genomic evidence of a recently emerged, widespread clonal TB outbreak spanning prisons and the community, indicating that prisons act as institutional amplifiers of the broader TB epidemic in Mato Grosso do Sul, Brazil, with transmission from ex-prisoners driving community incidence. To achieve TB control in the general population, the epidemic of TB in prisons must be prioritized and effectively addressed.

OA23-348-27 Active case finding among vulnerable populations reduces catastrophic costs due to tuberculosis diagnosis

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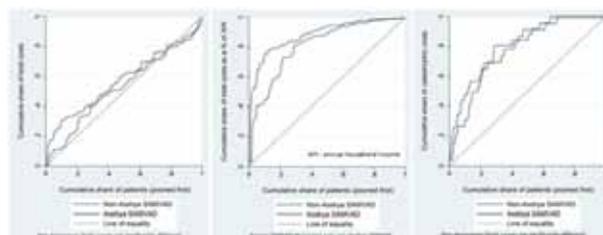
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Background: There is limited evidence on whether active case finding (ACF) among marginalised/vulnerable populations mitigates the financial burden during TB diagnosis. We determined the effect of ACF among marginalised/vulnerable populations on prevalence and inequity of catastrophic costs due to TB diagnosis among TB-affected households when compared to passive case finding (PCF).

Methods: This was an observational analytic study. In 18 randomly sampled ACF districts in India, during March 2016-February 2017, we enrolled all new sputum positive TB patients (registered for treatment under programme) detected through ACF and an equal number of randomly selected patients detected through PCF. Direct (medical/non-medical) and indirect costs due to TB diagnosis were collected through patient interviews. We defined catastrophic costs due to TB diagnosis as 'total costs (direct and indirect) due to TB diagnosis more than 20% of annual pre-TB household income'. We used concentration curves/indices to assess the extent of inequity.

Results: We included 234 ACF and 231 PCF patients. When compared to PCF, ACF cases had incurred lower median direct medical (US\$ 3.3 versus 15.7, $p < 0.001$), direct non-medical (US\$ 0.31 versus 1.89, $p < 0.001$), indirect (US\$ 0.09 versus 0.63, $p < 0.001$) and total costs (US\$ 4.6 and 20.4, $p < 0.001$). The prevalence of catastrophic costs in ACF and PCF was 10.3% and 11.5% respectively. After adjusting for potential confounders, patients detected through ACF had 32% lower prevalence of catastrophic costs when compared to PCF [aPR(0.95 CI):0.68(0.69,0.97)]. The concentration indices (0.95 CI) for total costs in both ACF [-0.15(-0.32,0.11)] and PCF [-0.06(-0.20,0.08)] were not significantly different from the line of equality and each other. The concentration indices (0.95 CI) for catastrophic costs in both ACF [-0.60(-0.81,-0.39)] and PCF [-0.58(-0.78,-0.38)] were not significantly different from each other: however, both the curves had a significant pro-poor distribution.

Conclusions: ACF among marginalised/vulnerable populations reduced prevalence of catastrophic costs due to TB diagnosis, but could not address inequity.



[Figure. Concentration curves, stratified by Axshya SAMVAD and non-Axshya SAMVAD groups]

OA23-349-27 Household contact investigation by community health workers improves TB case detection in Uganda

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Background and challenges to implementation: Despite WHO recommending household contact investigation for sputum-positive patients, the recommendation has not been fully implemented in many Sub-Saharan countries due to system barriers like limited health workforce. In Uganda, there is no policy guideline on conducting TB contact investigation, it is only rarely conducted by health workers based at health facilities. The USAID's RHITES-EC project sought to determine whether community health workers (CHWs) can effectively implement contact investigation in program settings.

Intervention or response: From October 2017 through March 2018, CHWs in nine districts of East-Central Uganda were trained to conduct contact investigation. Household contacts of index TB cases were then physically tracked in their homes by CHWs and screened using the standard WHO intensified case finding tool. Sputum was collected from presumptive TB household contacts and referred to the nearest TB diagnostic facilities for microscopic or GeneXpert examination. Identified TB cases were initiated on TB treatment. The proportions of contacts screened, tested and diagnosed with TB were determined. The numbers of contacts needed to screen (NNS) and the number of contacts needed to test (NNT) to identify a TB cases were also calculated.

Results and lessons learnt: During the study period, 7096 contacts of 617 index sputum-positive TB cases were tracked and screened of whom 2269 (32%; 95% CI, 30.9%-33.1%) were presumptive cases out of whom 2117 (93.3%) provided sputum for testing, yielding 171 sputum-positive TB and 166 (97%) were started on treatment. NNS was 41.5 while the NNT was 12.4. The prevalence of TB household contacts was 2,410 per 100,000 and a positivity rate of 8.1% among the presumptive contacts.

This led to an overall 30% increase in the case notification rate for the region.

Conclusions and key recommendations: The prevalence of TB among household contacts is high in East-Central Uganda. CHWs can effectively implement household contact investigation in resource limited settings.

OA23-350-27 Household contact tracing for families of Mozambican mineworkers

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Background and challenges to implementation: Screening of household (HH) contacts of persons with TB is a critical component of TB control. We conducted screening and testing for TB among HH contacts of Mozambican mineworkers and ex-mineworkers, as part of a cross-border program aiming to improve access to TB services for mineworkers and their families.

Intervention or response: Mineworkers and ex-mineworkers with TB disease were identified through review of TB registers from January 2017-February 2018, and through a targeted case finding campaign in December 2017. Index cases were contacted to obtain their residential locations in Mozambique and South Africa and a listing of persons living in each household. All adult HH contacts were screened for TB and offered HIV counseling and testing. Children (< 15) were referred to the health facility for TB evaluation and isoniazid preventive therapy (IPT), if indicated. Sputum specimens were obtained from adults with ≥ 1 symptom and transported to the nearest laboratory for testing according to national guidelines.

Results and lessons learnt: A total of 277 mineworkers and 308 ex-mineworkers were identified with TB. One thousand five hundred and sixteen (n=1516) HH contacts were identified (923 adults and 593 children). Of the 645 adult HH members in Mozambique screened for TB to date (ongoing; screening in South Africa starting April 2018), 199 had ≥ 1 symptom and were tested for TB; 26 (4.0%) were diagnosed with TB and linked to care. Three hundred and nine children aged < 15 were referred to the nearest health facility; 119 were initiated on IPT.

Conclusions and key recommendations: Screening of household contacts of mineworkers in Mozambique identified several persons with TB disease. Efforts are ongoing to screen HH contacts of migrant mineworkers both in Mozambique and South Africa. Screening families and additional close contacts of mineworkers, who have multiple residences, may be a key strategy for early case detection in labor sending and mining communities.

OA23-351-27 Community-based active TB case finding to improve coverage of NTP services in Viet Nam

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Background and challenges to implementation: Despite existing NTP services covering an estimated 83% of Viet Nam's TB burden, many people with TB are still missed and those who are treated in routine settings often present with significant delays. Community TB case finding activities were established as an extension of the National TB Program in 6 districts across Ho Chi Minh City to increase TB treatment rates and promote early case finding.

Intervention or response: A cadre of gov't-managed community health workers visited index patient homes to verbally screen family contacts and conducted targeted screening in high-risk populations, such as the elderly, economic migrants and urban poor. Screening activities were supported by a custom-built mHealth app loaded on 4G enabled tablets which is bi-directionally linked to Viet Nam's TB notification system. Symptomatic individuals were referred to gov't X-ray services. People with an abnormal chest X-ray were then tested with the Xpert MTB/RIF assay, while those with a normal CXR were tested by AFB smear microscopy. All patients detected by the project were initiated on treatment within existing gov't health services.

Results and lessons learnt: Over a period of 6 months, 179 community health workers verbally screened 83,740 individuals and successfully referred over 7,000 symptomatic people for CXR screening. 2,261 people were tested by either AFB smear microscopy and/or Xpert, resulting in the detection of 175 people with lab-confirmed TB (7.7%). These community case finding efforts led to a +13.9% increase in TB notification rates in project areas compared with baseline quarters a year prior.

Indicators	Yields
People verbally screened for TB symptoms	83,740
People with one or more TB symptoms	7,051 (8.4%)
People screened by CXR	7,019 (99.5%)
People tested by Xpert and/or AFB smear microscopy	2,261 (32.2%)
People with Bac(+) TB	175 (7.7%)
All Bac(+) notifications	
Baseline period (16-Q4 & 17-Q1)	1,342
Intervention period (17-Q4 & 18-Q1)	1,528
Additional Bac(+) notifications	186 (+13.9%)

[Yield and impact of community-based active TB case finding in Ho Chi Minh City, Viet Nam]

Conclusions and key recommendations: In a setting with high treatment coverage rates, expanding NTP services into the community resulted in further increases in TB treatment rates. The full integration of these TB case finding activities within existing NTP services enables a level of sustainability rarely achieved by community-based initiatives.

OA23-352-27 Systematic TB symptom screening increases the yield of TB case finding in hospital settings: lessons from Cambodia

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Background and challenges to implementation: TB incidence in Cambodia is estimated at approximately 55,200 cases. In 2016, 33,736 were notified and 29% (24,164) of TB cases were missed. Most hospitals lack both systematic TB symptom screening at triage and within in-patient departments, and comprehensive tracking of referrals within and between hospitals and health centers. This is a missed opportunity for TB case finding in the country.

Intervention or response: To improve TB case detection via screening of presumptive TB patients at triage and in-patient wards, a baseline assessment of TB case management practices was conducted, assessing the number of TB cases detected, health care workers' knowledge on TB and flow of patients in the hospital. Monthly meetings were organized to build the capacity of health care providers, track the performance and identify solutions. Four key TB symptoms were included in both triage and in-patient medical record forms to remind physicians to identify presumptive TB patients. Cough triage and the "FAST" approach were introduced in the triage area. A referral process was identified and strengthened to ensure that diagnosed patients continued treatment after discharge.

Results and lessons learnt: From June 2015 to Mar 2018, 5 government hospitals screened 447,867 clients for TB, identified 31,917 (7%) as presumptive TB and diagnosed 7,963 (1.8%) TB cases. Approximate one quarter of clients with presumptive TB were diagnosed with TB. Both the number of patients screened for TB and TB case notifications increased yearly. The Government adopted this approach and is scaling it up with support from the Global Fund.

Conclusions and key recommendations: Introduction of systematic TB symptom screening in out-patient and inpatient departments increases TB case finding. Inclusion of four TB symptoms in patient record forms, introduction of TB cough triage, and strengthening of referral systems have improved yield of TB case notification in the hospital. The approach is operationally feasible and replicated.

Year	Number of consultation cases	Number of presumptive patients	Number of TB diagnosed
2015	127,294	6,695	1,705
2016	151,452	12,290	3,040
2017	169,121	12,932	3,218

[Table: Results of systematic TB screening in health facilities]

OA23-353-27 Finding the 'missing TB cases' in South Africa

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Background and challenges to implementation: Every year, 450,000 people get sick with TB in South Africa, but more worrying, 29.3 percent (WHO, 2017) of these individuals do not even receive care - they are "missed" by the health systems at diagnosis, treatment or reporting. Many of this "missing" individuals will die or continue to be sick and transmit the disease or, if treated with improper drugs, contribute to the growing menace of drug resistance. Finding missing cases which is aligned to the Sustainable Development Goals and Universal Health Coverage agenda is key to the attainment of the End TB strategy.

Intervention or response: In January 2018, the USAID TB South Africa Project in collaboration with the National Department of Health launched a "comprehensive package" of services aimed at finding additional 15,200 of the 154,000 missing TB cases. Implementation of the package targeted undetected TB cases along the continuum from community through all levels of the public and private health facilities. Based on the heterogeneity of SA TB profile across provinces and districts, the package varied and was adapted to each locality. The package was complemented by a continuous quality improvement approach to address gaps in the TB care cascade.

Results and lessons learnt: Early results within two months from the launch of the package, a total of 887 additional TB cases were found; of which 369 were from the community and 518 at the various health facilities. The closer engagement from the community through the public and private sector with the comprehensive package of services facilitated identification of the TB cases who otherwise would have been missed.

Conclusions and key recommendations: Finding the missing cases and ending TB is critically important for South Africa; Implementation of a multipronged and comprehensive strategy to identify missing cases is recommended to interrupt TB transmission, save lives and improve the health of affected communities nationally and globally.

SHORT ORAL ABSTRACT SESSIONS

SOA17 From low to high drug-resistant tuberculosis

SOA17-1168-27 Geospatial characterization of extensively drug-resistant tuberculosis transmission areas using varying location types in Durban, South Africa

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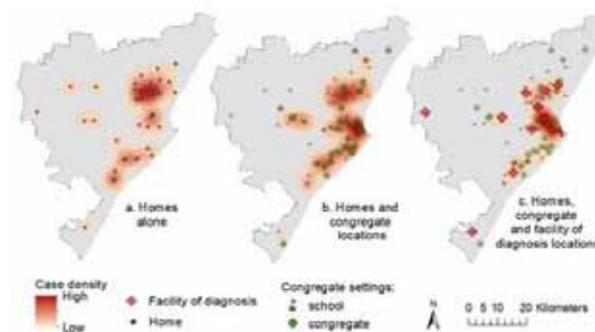
Background: Extensively drug-resistant tuberculosis (XDR-TB) treatment outcomes remain poor with 30% success globally. In South Africa, recent data suggests transmission is driving XDR-TB incidence rather than inadequate treatment. Geospatial analysis can help inform where to target interventions to potentially halt transmission; however, results may vary depending on whether cases are geolocated using home, hospital, or other locations. We examined spatial patterns using multiple location types for XDR-TB patients in Durban (eThekweni district), South Africa.

Methods: We enrolled XDR-TB patients diagnosed from 2011-2014 and collected GPS coordinates for their home and diagnosing facility. Those with residing within eThekweni district were included in this analysis. Participants were interviewed about congregate settings where they regularly spent two or more hours per week; these locations were geocoded using Google Earth. We used ArcGIS to map locations, calculate distances between them and create kernel density surfaces that included progressively more location types.

Results: Among 132 participants, 75 (57%) were female and 87 (66%) lived in urban or suburban locations. Coordinates for home and diagnosing facility were available for all (100%). Congregate locations were successfully geocoded for 43 (33%); these included 40 places of work, two schools, and nine miscellaneous locations (e.g., church, casino, prison). Using home location, a northeast area of the district showed the highest case density (Figure 1a).

Addition of congregate settings and diagnosing facilities shifted results to highlight another high-density area in the Durban metro (Figure 1b-c). Median home-work and home-facility distances were 10.4 and 10.3 kilometers, respectively.

Conclusions: Congregate locations and diagnosing facilities for XDR-TB patients were often far from their home; accounting for these locations produces new geospatial patterns of disease. As spatial analysis is increasingly used in public health, recognizing human movement by using multiple locations where persons spend time can yield a more comprehensive understanding of disease hotspots for targeting interventions.



[Figure 1. Extensively drug-resistant tuberculosis case density with home, congregate, and facility of diagnosis locations in Durban, South Africa]

SOA17-1169-27 Transmission drives the increase of multidrug-resistant tuberculosis in Rwanda

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Background: The first cases of multidrug-resistant tuberculosis (MDR-TB) in Rwanda were diagnosed in 1991, while the programmatic management of MDR-TB (including initiation of standardized MDR-TB regimen) started 15 years later (2006). The prevalence of MDR-TB among new TB patients rose from 1.3% in 1993 to 3.9% in 2005. We hypothesize that most new MDR-TB patients resulted from ongoing transmission.

Methods: In this retrospective analysis (1991-2010), phenotypically rifampicin resistant isolates from drug resistance surveys and routine samples in Rwanda were whole genome sequenced and subsequently analysed for *rpoB* gene mutation diversity, lineage classification and transmission patterns.

Results: Of the 233 isolates analysed, 229 (98%) were lineage 4, predominantly within the Uganda sub-lineage (91%). Using a 12- single nucleotide polymorphisms cut-off, 195 (84%) of isolates formed transmission clusters with at least one other isolate. Within these clustered isolates, 151 (77%) were found to belong to one large cluster, spanning 19 years (1991-2010), with a Ser450Leu mutation in *rpoB*. Four (1.7%) isolates had rifampicin resistance due to a Val170Phe mutation, including two clustered isolates.

Conclusions: MDR-TB in Rwanda appears to have been mostly driven by high transmission of one dominant circulating type representing most of the MDR-TB population structure. Further prospective MDR-TB transmission analysis including epidemiological links is highly needed for guiding programmatic control measures. Finally, the occurrence of resistance due to Val-170Phe, which is located outside of the 81bp rifampicin resistance determining region in *rpoB* that is covered by commercial molecular resistance tests, highlights the need to supplement rifampicin resistance testing with phenotypic drug susceptibility test, particularly in high risk groups.

SOA17-1170-27 Genetic diversity of multidrug-resistant *Mycobacterium tuberculosis* isolates in Bangladesh

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Background: Despite the fact that multidrug-resistant (MDR) tuberculosis (TB) is high, a major gap exists in our understanding of molecular characteristics and transmission dynamics of MDR isolates circulating in Bangladesh. This study aims to characterize and classify the MDR-TB isolates circulating all over Bangladesh and to investigate the mode of transmission.

Methods: MDR *M. tuberculosis* isolates obtained from pulmonary TB patients were genotyped by using TbD1 deletion analysis, spoligotyping and 15-loci mycobacterial interspersed repetitive unit-variable number tandem repeat typing (MIRU-VNTR). These isolates were obtained from a nationwide drug resistance TB surveillance study between the periods of 2011 to 2015 which included 14 hospitals covering all seven geographic divisions of Bangladesh.

Results: A total of 390 culture confirmed MDR *M. tuberculosis* isolates were included for genotyping. Deletion analysis showed that 313 (80.3%) isolates were the modern type (TbD1⁺) while 77 (19.7%) were the ancestral type (TbD1⁻). By spoligotyping, 323 (82.8%) isolates were grouped into 26 clusters; the largest comprised 134 (34.4%) isolates of Beijing genotype (ST1), followed by 35 (8.9%) & 28 (7.2%) isolates of LAM9 (ST42) and CAS1-Delhi (ST26) genotypes, respectively.

There were 48 (12.3%) isolates from unknown spoligotype (Orphan). Although not significant, the proportion of Beijing genotype in the retreated cases (34.9%) was higher compared to the primary cases (26.5%) ($p = 0.35$). MIRU-VNTR analysis revealed that 211 (54.1%) isolates exhibited unique patterns; whereas 179 (45.9%) isolates grouped into 34 clusters.

The largest cluster comprised 19 strains of Beijing and LAM9 genotypes each. The rate of recent transmission was estimated to be 37.2%.

Conclusions: Our results demonstrate that MDR *M. tuberculosis* isolates circulating in Bangladesh are mostly the modern virulent type. Among genetically diverse MDR-TB isolates, Beijing genotype was the predominant one.

We recommend scaling up of sensitive and rapid MDR TB diagnostics throughout the country to control the high rate of transmission.

SOA17-1171-27 Increasing drug resistance in National Survey of Susceptibility to Anti-Tuberculosis Drugs in Peru

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Background: Peru is the only Latin American country with a high burden of MDR-TB. Currently, only 50% of patients diagnosed with tuberculosis are tested, for drug-susceptibility, so periodic surveys are still necessary for estimating the real burden of drug resistance. Here, we report the results of the fourth national survey on drug resistance of tuberculosis.

Methods: A two-stage stratified cluster sample design was used, proportionally to the number of smear-positive patients reported in 2013. Demographic and treatment history data were recorded. Two sputum samples were collected and transported to the National Mycobacteria Laboratory/INS. Drug susceptibility was determined through the standard agar-plate proportions

method for isoniazid, rifampin, ethambutol, pyrazinamide, kanamycin, ciprofloxacin, levofloxacin, and capreomycin.

Results: From September 2014 to March 2015, 2897 patients were included. 721 (24.9%) samples were excluded due to contamination or non-growth. 2176 samples were included for analysis, 1904 (87.5%) were patients with no previous treatment (“new”) and 272 (12.5%) were previously treated. 56.5% of patients were less than 35 years and 63% were male. 57.7% were from Lima. 70.6% of isolates tested were susceptible to isoniazid and rifampin, 8.5% were MDR-TB and 0.3% were XDR-TB. Of the 6 patients with XDR-TB pattern, 5 were “new”. In the bivariate analysis, only previous treatment (OR 2.8, 95% CI 1.9-3.9) and provincial residence (OR 0.39, 95% CI 0.27-0.57) differed in patients with a susceptible pattern from those with MDR-TB.

Conclusions: The MDR-TB proportion in “new” cases increased from 5.3% in the previous national survey (2006) to 7.4%, while it decreased from 23.2% to 16.2% in previously treated. Most XDR-TB patients are “new”. This raises concern about the resistance of the strains currently circulating in the community. More efforts should be directed towards rapid drug-susceptibility testing and contact tracing.

SOA17-1172-27 Molecular epidemiology of pulmonary tuberculosis in Southern Ethiopia

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Background: Understanding the epidemiology of tuberculosis (TB) and the development and spread of drug resistant TB is limited by scarce molecular epidemiologic data in Africa. We sought to characterize the drug susceptibility testing (DST) patterns and genetic diversity of *M. tuberculosis* isolates circulating in Southern Ethiopia.

Methods: A cross-sectional study was conducted among new smear positive tuberculosis (SPTB) patients visiting nine TB facilities in Southern Ethiopia from June 2015 to June 2016. Three consecutive sputum samples (spot-morning-spot) per patient were examined using AFB smear microscopy and positive samples cultured. Isolates were tested for DST using indirect proportion method and typed with RD9 deletion and spoligotyping and assigned to Lineages and families using SpolDB4 and ‘Spotclust’.

Results: Among 250 new SPTB patients enrolled, 132 (53%) were male and 132 (53%) from urban areas. TB-

HIV co-infection was 11 (4%). All 214 isolates tested were *M. tuberculosis*; with 60 spoligotype patterns, of which 23% (49/214) were new: 179 (84%) belonged to Euro-American lineage, 25 (12%) to East-African-Indian and 8 (4%) to Lineage 7 (Ethiopian lineage). The most dominant shared types were SIT149 and SIT53. Strains fell into 22 clusters and clustering of strains by geographic locations was observed. DST found that 14% of isolates tested were resistant to ≥ 1 first line anti-TB drugs and 9% to INH. SIT 149 was dominant among drug resistant isolates.

Conclusions: The presence of several clusters and of new strains of *M. tuberculosis* in the study area, suggesting recent transmission, including of drug resistant TB, calls for wider monitoring of DST and improved control responses.

SOA17-1173-27 A case control study to identify community venues associated with genetically clustered multidrug-resistant tuberculosis disease in Lima, Peru

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Background: The majority of tuberculosis transmission occurs in community settings. The primary aim of this study was to assess the association between exposure to community venues and multidrug-resistant tuberculosis (MDR-TB) disease. The secondary aim was to describe the social networks of MDR-TB cases and controls.

Methods: This case-control study was conducted in Lima, Peru. We recruited lab-confirmed MDR-TB cases and community controls matched on age and sex. Whole-genome sequencing was used to identify genetically-clustered cases. Venue-tracing interviews were conducted to enumerate community venues frequented by participants. Logistic regression was used to assess the association between person-time spent in community venues and MDR-TB disease. A “venue-affiliation” network was constructed with respondents connected if they reported frequenting the same venue. An exponential random graph model (ERGM) was fitted to model the venue-affiliation network.

Results: We enrolled 59 cases and 65 controls. Participants reported 729 unique venues. Mean number of venues reported was similar in both groups ($P=0.92$). Cases reported spending more person-time (hours) in healthcare and transportation venues than controls ($P<0.05$). Person-time in healthcare (Odds Ratio (OR))=1.67,

$P=0.01$), education ($OR=1.53$, $P<0.01$), and transportation venues ($OR=1.25$, $P=0.03$) was associated with MDR-TB disease. Healthcare, market, and transportation venues were commonly shared among clustered cases. Case networks more densely connected than controls. The final ERGM indicated significant community segregation between cases and controls.

Conclusions: In this population, exposure to healthcare, education and transportation venues was associated with increased odds of MDR-TB disease. Social network analysis revealed significant community segregation between cases and controls. Combining whole genome sequencing with social network analysis in this way can identify places for MDR-TB infection control interventions.

SOA17-1174-27 Emergence of tuberculosis drug resistance by different patient-matching strategies using laboratory data

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Background: To identify emergence of drug resistance, tuberculosis care sites and laboratories must link multiple laboratory results to a single patient's records. We determined the proportion of patients with multidrug-resistant tuberculosis (MDR-TB; resistance to at least isoniazid and rifampicin) who developed resistance to fluoroquinolones (critical for successful MDR-TB treatment) using four matching strategies.

Methods: Data from the South African Western Cape Province National Health Laboratory Service (NHLS) from January 2008 through June 2015 identified MDR-TB patients who developed fluoroquinolone resistance after having fluoroquinolone-susceptible tuberculosis.

We used four methods to match results belonging to unique patients: A) exact match on NHLS patient number based on referring facility folder number; B) exact match on surname, first name, date of birth; C) custom algorithm using approximate matches for patient identifying variables developed at Stellenbosch University; and D) custom approach using iterative assessments of approximate matches on patient identifying variables developed for this study. We manually reviewed differences in unique patients identified by each method.

Results: We focused on 30,381 laboratory results for which ofloxacin drug susceptibility test results were available. Estimates of ofloxacin resistance development were 4% for methods A and B, and up to 8% for methods C and D (Table). Multiple folder numbers per patient and variation in name spelling resulted in duplicate patient identification in exact approaches. Manual review determined 598 correct matches of 688 total matches identified by all methods; method D had the highest percent of correct matches (98%).

Conclusions: The customized approach for this study maximized correct and minimized incorrect matches, and estimated that 8% of patients with MDR-TB developed fluoroquinolone resistance (twice as high as exact matching methods) in the Western Cape Province of South Africa from 2008-2015. Our findings underscore the importance of reliable patient identification methods at the time of patient or laboratory specimen registration.

	A) Exact Match NHLS Patient Number	B) Exact Match Surname, First name, DOB	C) Custom Match Stellenbosch University	D) Custom Match This Study
Uniquely identified patients (n)	20,492	21,079	17,028	16,802
Uniquely identified MDR-TB patients (n)	10,225	10,188	8,178	7,949
Patients with ofloxacin sensitivity, then resistance (n)	449	453	627	603
% MDR-TB that developed ofloxacin resistance (95% CI)	4.4 (4.0-4.8)	4.4 (4.1-4.9)	7.7 (7.1-8.3)	7.6 (7.0-8.2)

[Comparison of unique patient identification approaches to determine ofloxacin-resistant tuberculosis development]

SOA17-1176-27 The national prevalence of drug resistance tuberculosis in Morocco, 2014

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Background: Drug-resistant tuberculosis (DR-TB) is a serious problem to fight against tuberculosis worldwide. Globally in 2016, the estimated multidrug resistant TB

(MDR-TB) prevalence were 4.1% for new TB cases and 19% for cases previously treated. In Morocco, Drug Resistance Survey in 2004 showed MDR-TB prevalence to be 0.5% in new cases and 12.2% in previously treated cases. This study aimed to estimate the national prevalence of DR-TB in order to observe its trends and factors associated with DR-TB.

Methods: A cross-sectional prospective study was conducted from December 2013 to October 2014. The study population was selected by cluster sampling method using WHO guidelines. Sampling included 30 clusters from 28 provinces of Morocco and each cluster included at least 37 new pulmonary tuberculosis cases bacteriologically diagnosed. All TB patients previously treated were included during the study period. Sputum specimens were processed for culture and drug susceptibility testing for first-line drugs by the proportion method using Löwenstein-Jensen medium. Association between DR-TB and socio-demographic and clinical variables was explored by logistic regression.

Results: 1309 TB patients included, among them 85.1% were new cases and 14.9% were previously treated for TB. The prevalence of resistance to at least one anti-TB drug was 5.2% among new cases and 16.4% among previously treated cases. The prevalence of MDR-TB was 1% in new cases and 8.7% in previously treated cases. The prevalence of isoniazid resistance was highest. The prevalence of resistance to at least one anti-TB and MDR-TB increased significantly with number of previous TB treatment. Gender and history of contact with active TB patients were significantly associated with MDR-TB.

Conclusions: The prevalence of MDR-TB remains Low in Morocco. This suggests that TB drugs were well managed although they have been introduced in Morocco for several decades. Associations between DR-TB and demographic and clinical variables should be evaluated in future studies.

SOA18 How expert is Xpert?

SOA18-1177-27 Is Xpert MTB/RIF as an initial test adequate for patient management in high HIV-TB settings?

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Background: The spread of *Mycobacterium tuberculosis* (MTB) strains resistant to both isoniazid and rifampicin (RIF), multidrug-resistant (MDR) tuberculosis (TB) is a major public health problem posing formidable challenges due to its complex diagnostic and treatment requirements. The study aimed to determine the frequency of probes for different *rpoB* gene mutations using Xpert[®] MTB/RIF assay in the (RRDR).

Methods: A total of 75 MTB positive participants with rifampicin resistance tested by Xpert MTB/RIF platform from the 2nd national anti-tuberculosis drug resistance survey of Swaziland were analyzed. Gx Alert, a remote laboratory monitoring system was used to collect the data. Culture and drug susceptibility testing (DST) were performed for RIF-resistant cases that had no missing probes.

Results: The proportion of various probes among RIF-resistant strains was observed as: probe A, 5% (4/75); B, 5% (4/75); E, 47% (35/75); D, 26% (19/75); and no RIF-resistance was observed with probe C. The probe E&D mutation combination was found in only 1% (1/75). In 12/75 (16%) RIF-resistant cases had none of the 5 probes but had C_T Max > 3.5. The 12/75 with C_T Max > 3.5 were: 50% (6/12) MTB+, 42% (5/12) did not grow, 8% (1/12) non *Mycobacterium tuberculosis*. From FL MGIT DST and LPA on the 6/12 MTB+ isolates were as follows: 3/6 (50%) cases were RIF-susceptible on both LPA and MGIT DST, 33% (2/6) MGIT FLDST cases was concordant with Xpert while one of these was susceptible and 17% (1/6) unsuccessful on LPA, 17% (1/6) case was RIF-susceptible on LPA while it could not be further tested for MGIT DST.

Probe	Hhohho N (%)	Lubombo N (%)	Manzini N (%)	Shiselweni N (%)	Total
ΔCT Max > 3.5	2 (16)	5 (42)	1 (8)	4 (33)	12
Probe D (523-529)	3 (16)	3 (16)	11 (58)	2 (11)	19
Probe E(529-533)	3 (9)	5 (14)	17 (49)	10 (29)	35

[Molecular epidemiology of common *rpoB* gene mutations in the 81 bp RIF resistance determining region in Swaziland]

Conclusions: The RIF-resistant cases that had none of the probes may underscore the occurrence of infection with multiple strains in HIV-TB high burden settings. Current diagnostic platforms seem inadequate for diagnosis of hetero-resistance and mixed infection in high TB-HIV settings.

SOA18-1178-27 Real-life impact of the implementation of Xpert MTB/RIF on patient management, time to treatment initiation and mortality among people diagnosed with rifampicin resistant TB

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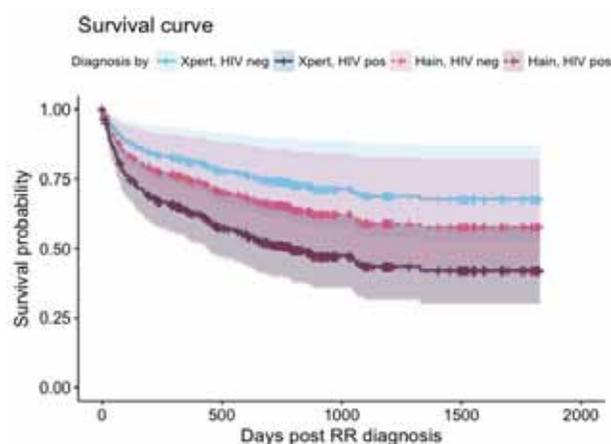
Background: The Xpert MTB/RIF (Xpert) assay is recommended by the World Health Organisation for simultaneous detection of *Mycobacterium tuberculosis* and rifampicin-resistance (RR). We investigated the impact of the phased implementation of Xpert in South Africa on management, time to treatment initiation and mortality of patients diagnosed with RR-TB.

Methods: The EXIT-RIF prospective cohort of patients diagnosed with RR-TB (Jan-2012—Dec-2013) during the phased implementation of Xpert in Gauteng, Free State and Eastern Cape, provided the opportunity to investigate Xpert's impact on time to treatment initiation and patient mortality.

Results: Overall, 749 patients were enrolled, of which 504 were diagnosed with RR-TB by Xpert (67.3%), and 245 by the GenoType MTBDR^{plus}-version1 (Hain) (32.7%). Socio-demographic characteristics were similar between the two groups. Similar proportions of patients were HIV-positive (77.2% Xpert vs. 78.3 Hain) and on ART at the time of RR-TB diagnosis (33.9% Xpert vs. 31.8% Hain). Patients diagnosed by Hain were more likely to be retreatment cases (60.4% Hain vs. 48.0% Xpert), have other risk factors for drug resistant TB (21.2% Hain vs. 16.0% Xpert), and be smear-positive (58.6% Hain vs. 41.3% Xpert). Time to RR diagnosis decreased from 27 days (IQR 15-42) by Hain to 1 day (IQR 0-1) by Xpert. Similar proportions started any TB treatment (87.3% Hain vs. 91.9% Xpert) after a median of 8 days after the first clinic-visit (9 days Hain vs. 7 days Xpert). Patients diagnosed by Hain were more like-

ly to only receive first-line treatment (OR 1.89 95% CI 1.16-3.07). Xpert increased the probability of receiving second-line drugs (OR 2.90 95% CI 1.95-4.35). Overall, mortality between those diagnosed by Hain and Xpert was similar (aHR 0.71 95% CI 0.32-1.57), but modified by HIV-status (Interaction-term aHR 2.22 95% CI 1.24-3.98).

Conclusions: While Xpert improved time to RR-TB diagnosis and second-line treatment initiation, it did not affect overall survival.



[Survival Curve for patients diagnosed by Xpert or Hain by HIV-status]

SOA18-1179-27 Xpert Ultra can unambiguously discriminate among rifampicin resistance-conferring mutations

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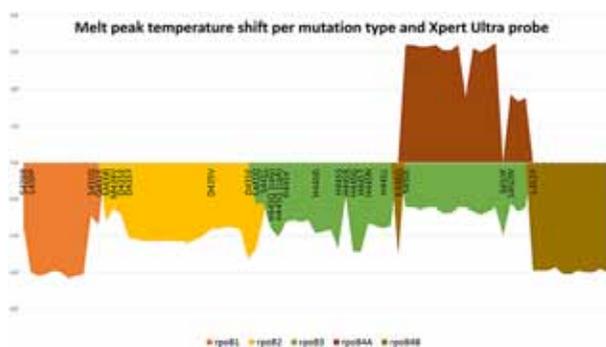
Background: The deluge of data generated by Xpert-MTB/RIF (Cepheid) provides opportunities for molecular epidemiological surveillance to improve global rifampicin-resistant tuberculosis (RR-TB) control strategies. Recently, a new, more sensitive version of the test (hereinafter called Ultra) was released. Determining the relationship between RR-conferring *rpoB* mutations, Ultra probes, and melting temperature shifts (T_m) - the difference of mutant and wildtype melting temperatures - allows Ultra results to be fully utilized for rapid detection of RR-TB strains and specific underlying mutations, which benefits surveillance studies.

Methods: To validate the usefulness of Ultra results for predicting specific mutations, we analyzed 10 RS-TB and 107 RR-TB strains harboring 36 unique RR-conferring mutations determined by *rpoB* sequencing.

Results: Overall, the Ultra assay correctly identified

31/32 (97%) mutations inside the Rifampicin Resistance Determining Region (RRDR). Mutation His445Arg gave an indeterminate result among 3/4 strains tested that may be caused by its $|T_m|=1.8^\circ\text{C}$ compared with $|T_m|$ typically exceeding 2°C for other mutations. We observed negative T_m for all probes and mutations except probe *rpoB4A* and mutations in codon 450 (Figure 1). Distinct combinations of probe and $|T_m|$ differentiated mutations in codons 428, 430, 431, 432, 434, 435, 441, 445, 446, and 452, including disputed mutations commonly missed in rapid phenotypic DST namely Leu430Pro, Asp435Tyr, and Leu452Pro. Contrastingly, codon 450 mutations were not distinguished due to overlapping $|T_m|$.

Conclusions: Our findings confirm the ability of Ultra to unambiguously identify specific *rpoB* mutations on a larger variety of *rpoB* mutants than previously tested. With the unprecedented roll-out of XpertMTB/RIF and associated connectivity solutions, Ultra results may rule-out transmission between RR-TB patients in a specific setting, distinguish relapse from reinfection, and resolve discordance between an RR Ultra result and a low-level RS phenotypic result due to a disputed mutation. For such applications, it is key that the T_m is included in the exported results.



[Figure 1. Melt peak temperature shift per mutation type and Xpert Ultra probe]

SOA18-1180-27 The experience of innovative specimen transportation and GeneXpert expansion in Ethiopia

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Background and challenges to implementation: GeneXpert MTB/RIF has been rolled out in Ethiopia to improve TB diagnosis and ensure universal drug susceptibility testing. Utilization of GeneXpert as the primary diagnostic test was piloted in 4 urban areas from Janu-

ary to June 2017, which was followed by roll out to 11 regions of the country starting from July 2017. Before the Xpert for all implementation the utilization of GeneXpert system and bacteriologically confirmed cases were very low.

Intervention or response: The USAID-funded Challenge TB project's regional and zonal cluster laboratory teams and eight specimen referral vans were strategically positioned and provide regular mentorship and specimen transportation for the implementation of Xpert for all initiative. A total of 122 of the GeneXpert machines were connected to TB GxAlert which led to improved data reporting, including: summary reports available to the national programme, enabling rapid analysis of data at various levels; and monitoring of the performance of GeneXpert machines in real-time.

Results and lessons learnt: GeneXpert service utilization increased from 28% to 75% while number of machines increased from 97 to 156, from 2015 to 2017 (Table 1). Improved bacteriologically confirmed TB cases from 36% in 2015 to 55% in 2017. Using a van courier transport system, TB specimens were transported from the 62% of MDR-TB treatment initiation centres to Regional Reference laboratories. The laboratory results were delivered through eSpecimen software system in selected sites resulting in a turnaround time reduction from 5 days to 1 day.

Conclusions and key recommendations: GeneXpert expansion has contributed to increased bacteriologically diagnosed TB case finding. Expansion of an integrated specimen transport using van system, eSpecimen and GxAlert across the country is highly desirable.

Year	Total Test (#, %)	# of MTB Detected	# of RR (% RR among MTB)	# of Unsuccessful Tests
Jan-June, 2016	29,960 (28%)	3661(12%)	338(8%)	2827(9%)
July-Dec, 2016	39,500(34%)	5301(13%)	346(6%)	5080(13%)
Jan-June, 2017	59,747(61%)	6720(11%)	454(6%)	7330(12%)
July-Dec, 2017	124,225(75%)	11,884(10%)	451(4%)	8,783(7%)

[Trend in Xpert utilization, RR and MTB case finding, and unsuccessful tests, 2016-17]

SOA18-1181-27 Factors associated with negative MTB culture results among GeneXpert-positive MTB patients

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Background: Patients with previous history of tuberculosis may have residual DNA in sputum that confounds nucleic acid amplification tests such as Xpert MTB/RIF. However this becomes a cause for concern for clinicians when observed among new TB patients (with no history of previous TB treatment). There is inadequate literature quantifying factors associated with Xpert positive but culture-negative MTB results among TB patients in Swaziland. To determine factors associated with negative TB culture results among patients (new and previously treated) who were diagnosed MTB positive by Xpert.

Methods: We studied respiratory and non-respiratory samples collected from 1299 patients diagnosed by gene Xpert between April 2017 to December 2018 and had MGIT Culture results. Logistic regression was used to measure the factors associated with false MTB positive results, and 95% confidence interval for all statistical tests.

Results: From a total of 1299 cases with both Xpert and Culture results of which 757/1299 (58%) were males while 542/1299 (42%) were females. Among the cases who were MTB Positive by Xpert but MTB negative by MGIT culture, 128/180 (71%) were new cases while 52/180 (29%) were retreatment cases. In the multivariate logistic regression the study found that the following factors were more likely to have false positive result: retreatment cases Adjusted Odd Ratio 2.5 (95% CI: 1.7, 3.6); Extra pulmonary 2.2 (95 CI: 1.9, 4.9), age and residence were not significantly associated with false positive results.

Conclusions: After controlling for confounding variables the study found that retreatment cases and extra pulmonary cases were associated with false positive. It is important that the national TB program considers strengthening the diagnostic and treatment algorithm for all TB patients and invest in the use of advanced differential TB diagnostic techniques for better clinical management of TB patients.

SOA18-1182-27 Feasibility of ultra-deep high fidelity amplicon sequencing (SMOR) on genomic DNA from used Xpert MTB/RIF (G4 and Ultra) cartridges for full genotypic drug susceptibility testing

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Background: Drug-resistant tuberculosis (DR-TB) is a public health crisis. Key barriers to drug susceptibility testing (DST) are test rapidity, sensitivity, and completeness (i.e., full DST). We have shown that mycobacterial genomic DNA from used Xpert MTB/RIF G4 (Xpert) cartridges can be used for MTBDRs/ DST and that single molecule overlapping reads (SMOR), a targeted next-generation sequencing approach, improves sequencing error and read depth in a highly multiplexed manner, thereby allowing the detection of cryptic micro-heteroresistance to first and second-line drugs. We evaluated whether SMOR could be done using the cartridge extract (CE) from Xpert and Xpert MTB/RIF Ultra (Ultra).

Methods: Xpert-positive RIF-susceptible (n=24), Xpert-positive RIF-resistant (n=7), and Ultra-positive RIF-susceptible (n=20) cartridges were collected and CE used for SMOR. Paired cultures were collected for Xpert-positive RIF-resistant 3/7(43%), and Ultra-positive RIF-susceptible 16/20(80%) where possible and phenotypic DST (pDST) was done (rifampicin, isoniazid, ofloxacin, amikacin, kanamycin, pyrazinamide).

Results: Ultra CE displayed a trend towards less actionable reads (i.e., presence of >10 total-reads and, if resistant, >0.1% reads indicating resistance) compared with Xpert CE [8/20(40%) vs. 14/24(58%);p=0.22], and more likely to have non-actionable results at a higher mycobacterial load [median C_{Tmin} (IQR)] compared to Xpert (Ultra 18.3[17.1-23.1] vs. Xpert 27.3[22.7-9.9];p=0.007). Therefore, SMOR on Ultra CE will require further optimisation for paucibacillary specimens. C_{Tmin} at which SMOR yielded actionable results were 23.15 and 16.75 for Xpert and Ultra, respectively. At these thresholds, Ultra had a specificity of 90% and Xpert had a sensitivity and specificity of 100% and 75%, respectively. pDST results showed concordance with SMOR on Ultra actionable results for all drugs but rifampicin.

Conclusions: This proof-of-concept study shows that SMOR is feasible on CE and could lead to fast and effective elaboration of second-line drug resistance. Further

optimisation will be done to improve SMOR on Ultra CE and confirm the sensitivity of SMOR on CE for resistance.

SOA18-1183-27 How does Xpert Ultra compare to Xpert MTB/RIF in patients with TB symptoms in a mixed ancestry and African population in Cape Town, South Africa?

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Background: Tuberculosis (TB) is a widespread disease that is responsible for the most South African deaths annually and is the single biggest killer of people with HIV/AIDS. Rapid point of care TB tests such as Xpert MTB/RIF (Xpert) have been successfully implemented in clinics for this research study, however, the benefit or next generation Xpert Ultra (Ultra) compared to Xpert in such a setting has not been determined. The aim of the study is a head-to-head evaluation of the diagnostic accuracy of Xpert vs. Ultra.

Methods: Mixed ancestry and African study participants with TB symptoms were screened using Xpert MTB/RIF and liquid culture tested on induced sputa as part of the participant's routine care (n=303). An additional induced sputum was collected and biobanked for later Ultra testing. Head-to-head comparison data analysis was only performed on patients with matching specimens and actionable results (n=237).

Results: The HIV prevalence was 20% and 39% of patients had a history of previous TB. Overall, the sensitivity of Xpert is 82% (confidence interval (CI) 72-91) compared to Ultra's 87% (CI 76-94; p=0.495) and a significantly different specificity of 99% (CI 95-100) for Xpert vs. a 90% (CI 84-94; p<0.001) for Ultra. If "MTB trace detected" Ultra results (n=13, six of these patients have a history of previous TB) are reclassified as "MTB not detected", then the sensitivity of Ultra decreases to 81% (CI 70-89; 0.831) and the specificity increases to 95% (CI 90-98; p=0.078). If trace results are excluded from the analysis, then the sensitivity of Xpert is 83% (CI 72-91) compared to Ultra's improved 86% (CI 75-93; p=0.641) and the specificity of Xpert is 99% (CI 96-100) compared to a significantly decreased Ultra of 95 (90-98; p=0.031).

Conclusions: Ultra has improved sensitivity compared to Xpert, but Ultra is offset by significantly decreased specificity even if trace results are excluded.

SOA18-1184-27 Comparison of Xpert MTB/RIF and Xpert MTB/RIF Ultra for detection of tuberculosis

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Background: Xpert MTB/RIF, a diagnostic tool with higher sensitivity and specificity for tuberculosis (TB), is a World Health Organization (WHO) endorsed point of care (POC) test in effect from 2010, but a successor technology introduced in 2017, the Xpert MTB/RIF Ultra, is said to have increased detection using the same test hardware. The objective of our study was to determine the agreement between Xpert MTB/RIF and Xpert MTB/RIF Ultra in detecting TB.

Methods: Presumptive TB patients from private sector coming to three icddr,b TB Screening and Treatment Centres (TBSTCs) of Dhaka for chest X-ray and Xpert MTB/RIF were enrolled for further testing by Xpert Ultra with the sample remaining from Xpert MTB/RIF. Their demographic and clinical data were collected using a semi-structured questionnaire and analyzed to see the agreement between the two tests.

Results: From 8th January to 15th February 2018, 493 Xpert negative but X-ray suggestive TB patients and 100 Xpert positive TB patients were tested with Xpert Ultra. All Xpert positive patients were positive in Xpert Ultra. Of the Xpert negative patients, 13 were Xpert Ultra positive, 436 were negative and results of 44 patients were either trace detected or invalid or error. Among these 44 patients, 13 patients were retested with Xpert Ultra (one was positive, five were again trace detected indicating positivity, seven were negative) and the remaining patients couldn't be retested due to patient non-compliance. Thus 19 cases were additionally detected (3.99%) by Xpert Ultra while 443 patients (89.86%) showed negative concurrence. The agreement between these tests was 96.62% with kappa 0.8924.

Conclusions: The analysis showed that Xpert Ultra had a higher detection than Xpert MTB/RIF although this is an underestimation of the actual scenario due to use of leftover sample from Xpert MTB/RIF.

SOA18-1185-27 Evaluation of the GeneXpert MTB/RIF Assay on cultured samples from the sanatoria in North Korea

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Background: In Democratic People's Republic of Korea (North Korea), the incidence of tuberculosis is very high (513 per 100,000), and the rate of multi drug-resistant tuberculosis among drug-resistant patients is 16% in re-treatment cases. There is a continuing need for rapid drug-resistant diagnose in accordance with the increasing trend of global multidrug-resistant tuberculosis. This study applied South Korean's pulmonary specimens to Xpert, and compared the rpoB mutations from South and North Korean's.

Methods: 104 cultured isolates from sanatoria in North Korea were applied for this study. North Korean's sputum samples were collected from 17 sanatoria and transferred to the MNTH than *M.tberculosis* were isolated from 2007 to 2009. Phenotypic Drug susceptibility Test (pDST) was performed using the absolute concentration methods in L-J medium. The critical Rifampicin concentration were set 40.0 µg/mL following the WHO guideline. GeneXpert MTB/RIF was performed according to manufacturer's manual. Rifampicin Resistance Determine Region (RRDR) of the samples with inconsistent results was amplified by PCR. Sanger sequencing of PCR products were performed to find the cause of the discrepancies.

Results: As result of applying 103 cultured specimens to Xpert, the sensitivity and specificity were 87.8 and 76.2 %. Through the sequencing we found that the 15 mismatched samples, 6 samples are considered to have mutations outside the RRDR region.

Conclusions: Mutations in I527F (ATC/TTC) occurred in two of the mismatched specimens and both S522Q (TCG/CAG) and V547V (GTC/GTT) silent mutation occurred in one of the mismatched specimens. The I527F and S522Q mutations have been reported in previous articles, but the V547V mutation is a new mutation that has never been reported. Although a small number, there are some regional differences of drug resistant mutations in clinical TB isolates.

SOA18-1186-27 Performance of the Zimbabwe mycobacterial culture and drug susceptibility testing system among retreatment tuberculosis patients during the scale-up of Xpert MTB/RIF

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Background: In Zimbabwe, while Xpert MTB/RIF is being used for diagnosing tuberculosis and rifampicin-resistance. Retreatment TB patients are still expected to have culture and drug sensitivity (CDST) performed at national reference laboratories for confirmation. The aim was to document Xpert MTB/RIF scale-up and assess how the CDST system functioned for retreatment TB patients.

Methods: Ecologic study using national aggregate data. **Results:** Xpert MTB/RIF assays increased from 11829 to 68153 between 2012 and 2016. In general, Xpert assays worked well with successful tests >90%, tuberculosis detection rates at 15%-17%, and rifampicin-resistance <10%. During Xpert scale-up, the number of sputum specimens from retreatment TB patients reaching national reference laboratories for CDST increased from 12% to 51%. However, laboratory performance was marginal: culture contamination increased from 3%-17%, positive cultures from 13%-17% and successful CDST from 6%-14%: the proportion of CDST showing any resistance to rifampicin averaged 44%. From 2009-2016, of the notified retreatment TB cases, the proportion with successful CDST increased from <1% to 7%.

Conclusions: Zimbabwe's CDST system for retreatment TB patients has improved marginally during the scale up of Xpert MTB/RIF, but performance is still poor. The country must either invest in improving CDST performance or in advanced molecular diagnostic technology.

SOA18-1187-27 The utilisation of an Android-based application to increase access to quality GeneXpert test

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Background: In 2016, the Ministry of Health of Indonesia issued a regulation that specimen of presumptive Tuberculosis (TB) should be tested using GeneXpert. To achieve this, a mechanism of specimen transportation from health facilities that do not have GeneXpert to GeneXpert facilities should be developed well. SITRUST, an Android-based application system, was

developed to facilitate the specimen transportation to GeneXpert test in cooperation with the National Post Office. This study assessed the effectiveness of SITRUST to improve the utilisation of GeneXpert test and the benefits of using this application from the perspective of health workers.

Methods: We conducted pilot in 50 districts in 10 provinces across Indonesia that were purposively selected to implement SITRUST in specimen transportation to GeneXpert facilities. Data collection included audit of records from the application dashboard and the results of Yes-No questions survey to health workers.

Results: In total, 1,124 primary health care providers in this pilot study had been provided training on using SITRUST. During the period of September 2017 to March 2018, the participation of primary health care providers using SITRUST for specimen transportation was more than 40% and there were 1,926 specimen of presumptive drug resistance TB and 4,699 specimen of presumptive TB delivered to GeneXpert facilities. During March, this mechanism has contributed 39% to the utilisation of GeneXpert. Two hundreds health workers participated in the survey on the benefits of SITRUST. More than 90% participants stated that SITRUST is user friendly, accountable, clear referral system, and easy to track the delivery. However, internet is the most common issue in using SITRUST.

Conclusions: This pilot study demonstrated that SITRUST increased access to GeneXpert test and potentially contributes to improve the utilisation of GeneXpert. Therefore promoting SITRUST to other districts and integrating it into the national reporting system is considered to be important to improve TB notification report.

SOA19 Tobacco use in various populations: implications for policy and practice

SOA19-1188-27 Connaissances et attitudes des étudiants de la faculté des sciences de la santé de Niamey sur le tabagisme

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Background: Le tabagisme est un problème de Santé Publique. Le Niger, par sa position charnière entre l'Afrique subsaharienne et l'Afrique du nord constitue une zone de transit du tabac. Notre pays dispose d'une

loi anti tabac mais pas contre la chicha. Pendant ces 10 dernières années nous constatons une consommation grandissante du tabac notamment celle de la chicha par les jeunes Nigériens. Ceci nous a poussés à réaliser ce travail

Methods: C'était une étude prospective transversale du 1^{re} Janvier 2016 au 31 Aout 2017 chez 601 étudiants (1^{re} à 7^{me} année Médecine et 1^{re} à 3^{me} année Pharmacie) de la Faculté des Sciences de la Santé (FSS) de Niamey. Les données avaient été recueillies sur une fiche d'enquête après un entretien. Le fumeur était l'étudiant déclaré fumeur quotidien ou occasionnel au moment de l'enquête.

Results: Au total 601 étudiants de la FSS de Niamey avaient été colligés. La prévalence du tabagisme était de 10,64%. Le sexe masculin représentait 53,40% et l'âge moyen était de 22,55 ans. La chicha était le mode de consommation du tabac le plus fréquent et le plus fumé par les femmes avec 76,48%. Le coût moyen journalier du tabac était de 150 à 300 FCFA pour 66,66% des fumeurs. Selon le test de Fagerström, 10% des fumeurs quotidiens présentaient une forte dépendance. Pour 33,50% des étudiants fumer de la chicha n'était pas considéré comme du tabagisme, 55,30% ignoraient que la chicha est plus nocive que la cigarette. D'autres habitudes toxiques (alcool et ou cannabis) s'ajoutaient au tabagisme chez 65,70% des fumeurs actuels.

Conclusions: La prévalence du tabagisme est faible mais relativement élevée pour une population qui aura le rôle de protéger la société contre les méfaits du tabac. Cependant une attention particulière doit aussi être accordée à la consommation grandissante de la chicha dans notre société.

SOA19-1189-27 Does smoking have an impact on TB treatment outcomes? - A prospective cohort study from India

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Background: More than 20% of the global TB incidence may be attributable to smoking. India is the second largest consumer of tobacco products and has the highest burden of TB globally.

The impact of smoking on TB treatment outcomes as compared to non-smokers remains a question of significance in India.

Methods: This data is part of a multi-centric prospective observational cohort study among newly diagnosed adult Pulmonary Tuberculosis patients initiated on ATT and followed up for 6 months to assess the impact of smoking on smear conversion and treatment outcomes. This was measured as favorable (cured or completed) and unfavourable (failure, recurrence or death). Fisher's Exact and Kruskal-Wallis test were used to assess the factors associated with smoking status. The relationship between independent factors and treatment outcomes were examined by Poisson regression model.

Results: Of 404 enrolled, 130 had a history of smoking with 63 current smokers and the rest ex-smokers. We compared the profile and treatment outcomes of smokers vs. non-smokers.

Significant differences were seen among smokers with respect to older age group ($p < 0.001$), Alcohol use (89% vs. 24%: $P < 0.001$), BMI < 18.5 (64% vs. 43% ($P < 0.01$), smear (Positives 78% vs. 62% $P < 0.05$) and smear conversion < 2 months (73% vs. 80% $p < 0.05$) being significantly more among non-smokers.

It was also interesting that among those Ex-smokers who had unfavourable outcomes 75% were failures as compared to non-smokers. Being older (aIRR: 1.05, 95% CI: 1.02 - 1.09) being a smoker (aIRR: 9.70, 95% CI: 3.86 - 24.37) were found to have a higher incidence rate ratio of unfavorable outcome after adjusting for confounding factors.

Conclusions: The study calls for smoking cessation and alcohol intervention among smokers current and those with history of smoking with focus on improvement of nutrition to improve BMI for better treatment outcomes.

SOA19-1190-27 5 percentage points (21.2 to 16.1%) reduction in tobacco use in the state of Himachal Pradesh - a self enforcing and sustainable model in India

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Background and challenges to implementation: MPOWER is the evidence based toolkit for effective tobacco control under the WHO- Framework Convention on Tobacco Control (FCTC). Indian Tobacco Control Law (COTPA, 2003) and National Tobacco Control Program (NTCP, 2006) are not fully compliant to FCTC. So to implement MPOWER policies, new innovations are needed to bridge the policy gaps. Himachal Pradesh a northern hilly state in India with a population of 7 million was not included under NTCP till 2014 whereas as per Global Adult Tobacco Survey (GATS) 2009 -10 the prevalence of smoking among males (33.4%) was much higher than the National average (24.3%) with highest exposure of passive smoking (82.5%) at homes.

Intervention or response: The strategic partnership between the local NGO (HPVHA) and the State Health Department with the support of the International NGO

“The Union” helped in bridging the policy gaps through advocacy and capacity building. Sharing responsibilities among the key stakeholders and empowering them to utilize the funds collected as fine for financing tobacco control helped in policy implementation effectively.

Results and lessons learnt: GATS, 2016-17 shows a significant decline in tobacco use from 21.2 to 16.1% in Himachal Pradesh. The decline is 6th highest among all 31 states in India. The passive smoking at homes has declined from 82.5 to 32.9 % which are highest in the country. MPOWER has achieved substantial progress and monitoring tobacco is a regular feature (M). Himachal achieved Smoke Free status in July 2013 (P). The tobacco cessation facilities are expanding to sub district level (O). High compliance of specified pack warnings (W) is supported by effective ban on tobacco advertisement (E). There is a modest rise in tobacco taxes (R).

Conclusions and key recommendations: MPOWER is highly effective and easily implementable in low cost settings provided the strategic partnership between Government and NGOs is ensured.

SOA19-1191-27 Prevalence and associations of tobacco use among a men who have sex with men (MSM) in Lagos, Nigeria

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Background: Nothing is known about prevalence of tobacco smoking and associated factors among Men who have Sex with Men (MSM) in Nigeria. The objective of the study was to examine the prevalence and correlates of smoking among MSM in Lagos, Nigeria.

Methods: The study took place between December 2017 and January 2018 and was a cross-sectional study design of 167 MSM interviewed across hotspots across hotspots in Lagos. The participants were recruited through a respondent driven sampling (RDS) assessments. Questionnaire used for the study was adapted from University of San Francisco Center for Research among Key Population as part of the regional MSM survey across Lagos MSM hotspots. Data were captured on sociodemographics, tobacco use, alcohol and drug use and were entered into Microsoft Excel and later imported into SPSS version 21 for analysis.

Results: 71.4% of MSM currently smoke, 16.7% quit smoking while 11.7% either smokes sparingly or did not smoke at all. History of current cough was positive among 25% (41) while 75% (126) were not coughing. Among 41 MSM with current cough, 42.9% had lasted for 1 week, 28.6% for 1-2 weeks and 28.6% for more than 2 weeks. 16.7% (28) have had tuberculosis in the past while 85.3% (139) had no history of previous Tuberculosis. There was a significant association between tobacco

use and being enrolled as student. 90% of MSM who are current tobacco smokers were students or enrolled as a learner in an institution of learning ($p=0.018$).

Conclusions: The prevalence of tobacco smoking among MSM in Nigeria is higher than that among the general population. The current education materials are not targeting the younger educated student population enough. There is a need to further look into moderators of these relationships so as to develop targeted tobacco smoking interventions and tobacco control policy targeting young student MSM in Nigeria.

SOA19-1192-27 Socioeconomic inequalities in adult smoking within a weak tobacco control system: a cross-sectional study in Indonesia

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Background: Indonesia is the 4th largest cigarette consumer in the world and has suffered from growing tobacco-related mortality with more than 240,000 deaths annually. The Indonesian government has introduced tobacco control policies corresponding with MPOWER since 2007. However, little is known about the impact of these measures on trends of cigarette smoking behaviour among Indonesian adults. This study investigated the changes in smoking behaviour and identified socioeconomic inequalities associated with these trends in Indonesian adults.

Methods: A cross-sectional study was conducted to analyse Indonesian adults (aged 15 years and above) and household data from two waves of Indonesia Family Life Survey (IFLS) in 2007 ($n=13,535$ households; 44,103 individuals) and 2014 ($n=16,204$ households; 50,148 individuals). Regression analyses were performed to identify factors associated with cigarette consumption and spending. Relative Income Price (RIP) of cigarettes in 2007 and 2014 was calculated to evaluate the change in cigarette affordability in Indonesia.

Results: Cigarette smoking prevalence (31.9% vs. 30.8%; $p < 0.01$) and consumption, as well as cigarette spending were significantly increased in 2014 compared to 2007. Adults in 2014 were 11% (aOR 1.11; 1.06, 1.17) more likely to smoke compared to those in 2007. Males, youths and the poor had a higher likelihood of being smokers in both years. Cigarettes were more affordable as the RIP of cigarettes in 2014 was lower than that of 2007 (1.65% vs. 1.97%).

Conclusions: The implementation of tobacco control measures failed to reduce the cigarette use among adults in Indonesia between 2007 and 2014. Instead, socioeconomic inequalities in adult smoking were identified. It implies that tobacco control policy in Indonesia was ineffective and unequally affected subgroups of the population.

The government is urged to formulate tailored tobacco control interventions targeting the most socially and economically disadvantaged population.

SOA19-1193-27 Opportunities and threats for smoking cessation counseling of tuberculosis patients in Armenia

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Background: Tuberculosis (TB) and smoking are two colliding epidemics that together pose a significant public health concern. The urgency of implementing tobacco dependence treatment interventions among TB patients has been acknowledged by the global public health community. This study aimed to investigate the existing opportunities and threats for implementing smoking cessation interventions within TB control in Armenia, a country in transition with high smoking and TB burden.

Methods: A qualitative study was conducted among in-patient and out-patient TB physicians and experts in the field of TB and tobacco control. Overall, 26 TB physicians and experts were recruited from Yerevan (the capital city), and three regions of Armenia to participate in in-depth interviews ($n=4$) and focus group discussions ($n=5$). Semi-structured interview guides helped to moderate the data collection.

Results: We identified several opportunities for initiating smoking cessation interventions among TB patients. Firstly, the participants highlighted that the diagnosis of TB serves as a key teachable moment for discussing quitting with TB patients. Participants believed that continuous patient-provider encounters during TB treatment establish an environment of strong mutual trust, which can be used as an opportunity to engage TB patients in smoking cessation counselling. In the meantime, the study participants revealed several factors that can potentially threaten provision of smoking cessation counseling to TB patients such as patients' psychological distress upon discovering their diagnosis, anxiety because of the nature of TB treatment (long duration, fear of infecting others, isolation), withdrawal symptoms, and reluctance to accept pharmacological interventions along with TB medications.

Conclusions: There are various threats and opportunities for engaging TB patients into smoking cessation counseling in Armenia. The acknowledgement of these threats and opportunities may facilitate identification of the key, effective measures needed for joining TB and tobacco efforts to combat the deadly pairing of TB and tobacco epidemics.

SOA19-1194-27 How new economic policies (demonetization of higher currency notes and GST) impacted on sale of tobacco products in India. A comparative analysis

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Background: On November 8, 2016, the Government of India announced its decision to demonetise two denominations of Rs 500 and Rs 1,000. The new tax regime i.e. GST came into effect from July 1, 2017. This study measured the impact of the shortage of cash and higher tax on tobacco products on purchase and use of smoked tobacco in urban and rural settings in West Bengal, India - a high prevalent state.

Methods: The study was conducted in two districts i.e. Paschim Medinipur and Kolkata selected purposively. In Paschim Medinipur two Blocks were selected randomly as rural sites while. The most populated municipality was also selected as the urban study area. In Kolkata, the commonly regarded better-off place, areas dominated with offices and a slum were selected. In addition, regular tracking of prices of tobacco products has been done.

550 tobacco consumers were interviewed and for every 5 consumers one vendor (i.e. 110 in number) was selected by using the transect walk methodology. For better understanding of the impact and representation, the samples were distributed as per age groups. The study was conducted in February 2017 to March 2018.

Results: Demonetization has very little impact on bidi sale. The popular perception i.e. demonetization compelled the customers to focus their spending on essential items is not fully supported in this case. But for cigarette smokers the situation is different; reduced cigarette consumption was evident from the study results. The findings conform the newspaper reports that sale of cigarettes was hit by demonetization. On the other hand, the prices of Bidi and Cigarettes increases substantially after the introduction of GST.

Conclusions: The shortage of cash in hand leads to a decline in loose cigarette sale. If The loose cigarette sale could be stopped the consumption of number of cigarettes will be reduced drastically.

SOA19-1195-27 Tobacco retailers' association: the beginning of 'Front Groups' in Sri Lanka

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Background: Sri Lanka made remarkable progress in tobacco control during the past few decades. Despite numerous strategies employed by the tobacco industry, the concept of organised 'Front Groups' was alien in Sri Lanka, even though individuals were seen from time-to-time, representing interests of tobacco companies. Sri Lankan government announced two new tobacco legislations in 2016: ban of single stick sales and ban of tobacco sales within 100m radius of schools. Several media reports appeared with statements from 'Tobacco Retailers' Association' (TRA) protesting those legislations. This study aimed to explore the role of TRA as a front group in tobacco related issues.

Methods: Investigative research techniques were employed to obtain details about the TRA. The media reports, TRA press release and related incidents were reviewed using Newspaper articles, Television news and Website reports published on them. Telephone interviews were conducted with the respective journalists, media personnel that coordinated the publishing of that article, and the members of TRA. The data was analysed using thematic analysis.

Results: TRA was not a registered association in Sri Lanka. TRA's name publicly appeared in three occasions related to the issue: a meeting with the Prime Minister when a cabinet sub-committee was appointed when the legislation was first put through to the cabinet (May 2017); a meeting with the new Minister of Finance in the first month of his appointment (May 2017) and a press conference after the legislation got cabinet approval (May 2018). TRA statements, and the media reports based on them, were positive towards the cigarette industry in all three incidents. The interviews revealed that journalists did not use investigative research techniques in reporting the incidents but published the content they received via superior officers with minor modifications.

Conclusions: TRA should be identified as an entity that represents the interest of the cigarette industry in tobacco related issues.

SOA19-1196-27 A youth internship program to promote the image of the tobacco industry: a case study from Sri Lanka

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Background: Tobacco industry uses covert strategies to promote their organization and brands. In Sri Lanka, Ceylon Tobacco Company (CTC) holds a monopoly to manufacture and sell cigarettes. Sri Lanka implemented National Tobacco and Alcohol Authority (NATA) Act in year 2006 prohibiting advertisement and promotion of tobacco, generating an unfavorable condition for the tobacco industry. This study aimed to explore the use of a youth internship programme to build the image of CTC.

Methods: Fast Track 15 (FT15), the internship program for undergraduates from “diverse areas of business” was launched by CTC in 2010. The internship is provided to 15 selected interns in collaboration with different industrial partners and received media coverage in national print media. Paper articles, Websites, Social media posts and industrial reports were reviewed and content was analyzed to explore the use of words and images to promote the industry image.

Results: From its initiation FT15 was implemented for seven consecutive years. The stated aim of the CTC was to attract “the right talent and further positioning themselves as a great place to work”. Even though the selected is to be the ‘best 15’, the method of selection was not reported in any of the documents.

Two banks (Commercial and HSBC) and the largest conglomerate group in Sri Lanka (JKHoldings) partnered with the CTC for FT15, and all three had previous links/business partnerships with CTC. FT15 received a wide positive media coverage in national newspapers which used attractive words such as “unique, best talented, great opportunity, talent, Rewarding, young talented undergraduates”.

Conclusions: “Fast Track 15” was used to draw a wide media publicity and engage youth with potential to become corporate leaders in Sri Lanka. National level policy amendments are required to prevent industry influences of this nature if to control tobacco effectively.

SOA19-1197-27 Civil society organization’s involvement in advocating and supporting local governments of Indonesia in smoke-free laws

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Background and challenges to implementation: Even though Indonesia has not ratified the Frame Work Convention on Tobacco Control, it has Health Bill No. 30 Year 2009 which mandates the government to protect its people from the dangerous of tobacco smoke in public places. Local governments (415 districts and 93 cities in 34 provinces) should develop local regulation on Smoke-Free Laws (SFLs). Limited local capacity in understanding the comprehensiveness of SFLs was one of the big challenges besides tobacco industry interference in policy making. The Union worked together with Government of Indonesia at the local level through its partnership with civil society organizations (CSOs) in Jakarta, Central Java, West Java, Bali, and East Java with various backgrounds such as faith-based organization, universities and community-based organizations with a targeted population of 137 million people. Besides giving support, CSOs played their role in monitoring and criticizing the SFLs.

Intervention or response: The interventions improved local capacity with capacity building; bridged networks and partnerships between CSOs and the government; provided evidence through research, surveys and public opinions; policy advocacy worked; gave assistance in developing and monitoring the SFLs; and worked with media.

Results and lessons learnt:

1. Improved local capacity in planning, assisting, and developing strategies
2. Local governments gained support from CSOs in developing and monitoring SFLs; encountered opposition with evidence and data; gained public support through surveys/opinions polls conducted by CSOs.
3. Increased media involvement in spreading information and public education
4. A vast network and alliances from CSOs has made them able to advocate policy change.

Conclusions and key recommendations: CSOs have proven their significant role and involvement in SFLs policy advocacy. By maximizing their networks and expertise, they were able to assist, support and advocate local governments in SFLs, tobacco control and other health related issues in Indonesia. The Union has improved local capacity by providing CSOs with tools, comparative studies from other countries and technical assistance.

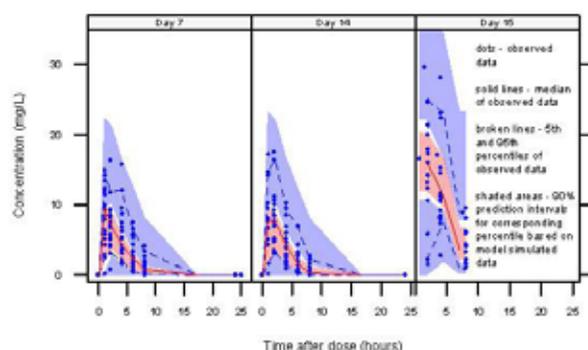
SOA20 The changing landscape of childhood tuberculosis

SOA20-1198-27 Pharmacokinetics of rifampicin in children from the OptiRIF study: dosing cohort 1

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Background: Higher rifampicin doses accelerate treatment response and may enable shortening of anti-tuberculosis therapy. While 35 mg/kg has been shown safe and effective in adults, no studies have been performed in children. The OptiRIF study aims to establish paediatric rifampicin doses that would match exposures observed in adults using a 35 mg/kg dose (AUC_{0-24h} 235 mg/L·h) and evaluate their safety/tolerability.

Methods: OptiRIF is a multicenter, open-label study in South African HIV-uninfected children 0-12 years with drug-sensitive tuberculosis. Cohorts of 20 children are sequentially enrolled, with dose escalation in steps, based on the exposure results of the preceding cohorts. In cohort 1 the standard WHO-recommended paediatric dose of rifampicin (20 mg/kg) was given for 14 days, followed by a single dose of 35 mg/kg on day 15. Pharmacokinetic sampling was conducted on day 7, 14, and 15 and plasma concentrations were determined by LC-MS. An existing paediatric population pharmacokinetic model with saturable hepatic extraction was updated with the observed data and used to derive AUC_{0-24h} and predict doses for cohort 2.



[Figure. Visual predictive check of rifampicin model fitted to OptiRIF cohort 1 data.]

Results: Median (range) age and weight were 2.9 (0.4-11.5) years and 10.8 (5.1-22.0) kg. All children had been on rifampicin-containing treatment 2 weeks before the first pharmacokinetic sampling, hence autoinduction was complete. Observed concentrations were well described by the existing model with pharmacokinetic parameters re-estimated on the new data (Figure).

The median (range) AUC_{0-24h} at day 7, 14 and 15 were 38.2 (15.8-71.0), 39.5 (11.7-76.1) and 81.8 (33.0-155) mg/L·h, respectively. A dose of 50 mg/kg was predicted to result in AUC_{0-24h} of ~215 mg/L·h. At day 15, no Grade 3/Grade 4 adverse event related to rifampicin was reported.

Conclusions: In cohort 2, children will receive 35 mg/kg on days 1-14 and a single dose of 50 mg/kg on day 15, with additional max-limits on doses for children <1 year.

SOA20-1199-27 Implementation of the childhood TB road map addressed the missed childhood TB cases in Addis Ababa

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Background and challenges to implementation: In Ethiopia, the proportion of childhood TB among notified TB cases was 11.2-13.6% during 2015-2017. The lowest proportion was recorded in Addis Ababa, 5.1% in 2016 and 4.7% in 2017. The atypical presentation of TB in children and the lack of capacity to diagnose TB among health care workers (HCW) were the main reasons. Hence, the national TB program (NTP) developed a childhood TB road map and a training manual. This study tried to determine TB screening and diagnosis among children after the implementation of the road map in Addis Ababa.

Intervention or response: Thirty out of 100 health centers were selected based on the annual case load of under-5 visits in 2016. Sensitization workshops for the heads of health facilities and family health and TB program officers were conducted. The 30 health centers (HCs) were involved in 3 phases, 10 HCs per round in 3 months interval after childhood TB trainings.

Baseline assessment on childhood TB screening, diagnosis and TB cases was carried out for 2016. Job aids, algorithms, revised registers and pediatric naso-gastric (NG) tubes were provided. A joint supportive supervision was performed by the NTP and the family health unit. On-site NG aspiration demonstration was also performed.

Results and lessons learnt: From September 2016–November 2017, 125,777 under-5 children visited under-5 clinics, where 97.4% were screened for TB, with the screening levels increasing from 28.3% to 97%. Identified presumptive TB cases increased from 0.06% to 0.4%. Sample collection using NG aspiration was done in 109 children and 50 TB cases were diagnosed. Ten (20.3%) of the cases were bacteriologically confirmed using Xpert MTB/RIF (Table).

Conclusions and key recommendations: The implementation of childhood TB road map demonstrated that TB disease in children can be diagnosed by trained HCWs at primary health care units. Integration of family health and the NTP should further be strengthened to find the missing TB cases.

Variables	Baseline (June-August 2016)	Sept-Nov 2016	Dec 2016-March 2017	April-July 2017	August-November 2017	Total (Sept 2016–November 2017)
Screened for TB from total children seen at integrated management of neonatal and child illness (IMNCI) clinic (%)	4812 (28.3)	16370 (96.3)	39611 (100)	34941 (98)	31590 (99.8)	122,512 (97.4)
Presumptive TB cases (% of screened)	3 (0.06)	48 (0.29)	130 (0.33)	66 (0.2)	257 (0.8)	501 (0.4)
Gastric Aspirate done and tested for AFB /Gene X-pert.	0	16	38	27	28	109
TB case (% of presumptive TB)	1(33.3)	6 (12.4)	14 (10.8)	18 (27.3)	12 (11)	50 (10)

[TB screening and diagnosis from in Addis Ababa health centers, September 2016–July 2017]

SOA20-1200-27 Ten years of routine paediatric TB surveillance data in South Africa: high disease burden and poor treatment outcomes

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Background: Improving surveillance data for children with tuberculosis (TB) is a key priority. Evaluation of routine surveillance data is important for programmatic monitoring and evaluation and to understand local epidemiology and the impact of program changes. We evaluated 10 years' routine paediatric TB treatment surveillance data.

Methods: Retrospective cohort analysis of all newly registered children (< 15 years of age) recorded in the routine South African National TB programme (SANTP) electronic TB register for drug-susceptible TB (ETR. Net) from 2004–2013. We report routinely collected demographic, clinical and treatment outcome data. Data was analysed in 4 age bands: 0-1, 2-4, 5-9, and 10-14 years.

Results: A total of 456,441 paediatric TB cases (232,059; 50.8% males) were identified, contributing 11-14% of the total TB caseload amongst newly registered TB patients annually. Children < 5 years comprised nearly two thirds (0-1 years: 140,758 [30.8%]; 2-4 years: 142,238 [31.2%]; 5-9: 113,520 [24.9%]; 10-14 years: 59,921 [13.3%]). The age distribution did not change over time. Documentation of HIV status improved over time (2004=0.3%, 2009=37.6%, 2013=82.6%). Annually since 2010, the proportion of children with HIV co-infection varied between 20 and 21%.

Pre-treatment bacteriological test results were recorded in only 76,401(16.7%) children, with bacteriological confirmation in 41,501(9.1%). Diagnostic confirmation increased with age: 0-5 years=3.0%; 5-9 years=9.5%; 10-14 years=37.1%. Only 294,453(64.5%) had favourable outcomes (cured/treatment completed). Unfavourable outcomes included 7,660 (1.7%) deaths, 114,388 (25.1%) moved/transferred out and 39,536 (8.7%) loss-to-follow-up/not evaluated.

Conclusions: Many children have been treated for TB and reported in ETR.net in South Africa. Although the proportion of children overall (11-13%), and proportion of these < 5 years of age (62%) are consistent with that expected in high burden TB settings, the proportion of children with confirmed disease is low (9%). Further analysis should explore age, TB disease spectrum, HIV co-infection and treatment and reasons for poor treatment outcomes in children.

SOA20-1201-27 High burden of undetected tuberculosis among children with no known contacts in The Gambia

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Background: Childhood tuberculosis (TB) is usually a sentinel event and mostly attributable to an adult infectious case in the household. However, many children with presumptive TB have no known TB contacts and present at child health centers rather than via National TB Program pathways. We evaluated for TB children referred to our dedicated child TB clinic from health centers in Gambian communities.

Methods: We evaluated symptomatic and/or Tuberculin skin test positive household child (< 15 yrs) contacts of adults with sputum smear positive TB identified

through contact tracing and symptomatic children referred via sensitized governmental health clinics without known contacts. Chest x-ray and sputum examination were performed for diagnosis of TB.

Results: Of 1531 children examined, 1353 (88.4%) were referred following contact tracing and 178 (11.6%) from sensitized health centers. 109 TB cases were diagnosed; 35 (32.1%) were bacteriologically confirmed. Children referred from health centers were significantly younger (median age 5.3 (2.4 - 8) vs. 7 (3.4 - 10)), had at least 3 times the odds of TB diagnosis (AOR 3.4 (95%CI 2.2 - 5.5) and 6 times the odds of bacteriologically confirmed TB (AOR 6.1 (95%CI 3.1 - 12.2) compared to those identified following contact tracing. Additionally, children referred from health centers were more likely to be 'underweight' (median WFA z-score - 1.75 vs. -.85; $p < 0.001$) and 'wasted' (median WFH z-score - 1.28 vs. -.62; $p < 0.001$) but these nutritional indices did not predict TB disease in these children or overall.

Conclusions: Unacceptably high numbers of children with TB disease are being missed in the routine health system in The Gambia. Absence of a known TB contact in an ill child should not exclude TB in an endemic setting. Dedicated childhood TB clinics could increase identification of children with TB who would otherwise be missed in the routine system.

SOA20-1202-27 Pharmacokinetics, safety and dosing of levofloxacin 100 mg dispersible tablets in children exposed to multidrug-resistant tuberculosis

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Background: A 100-mg scored dispersible levofloxacin formulation (Macleods Pharmaceuticals) is now WHO pre-qualified and expected to be available for routine paediatric multidrug-resistant (MDR)-TB care. Its pharmacokinetics and optimal paediatric dosing have not yet been characterized.

Methods: We completed an open-label lead-in pharmacokinetic study to TB-CHAMP, a phase III cluster randomised trial, comparing levofloxacin vs. placebo for prevention of TB in South African MDR-TB exposed children. Children aged < 5 years in households with an MDR-TB case were enrolled and received daily weight-banded doses of levofloxacin 15-20 mg/kg dispersed in 5-10 mL of water. After 7-21 days, children were sampled pre-dose and at 1, 2, 4, 6 and 8 hours post-dose. Levofloxacin concentrations were quantified with validated LC-MS/MS. Nonlinear mixed-effects modelling was used to analyse data, which was pooled with previously published levofloxacin data from 105 children

with MDR-TB receiving routinely available adult (250 mg) tablets. Weight-band dosing was optimised using simulations targeting the levofloxacin adult exposure achieved with 750 mg. Adverse events were recorded and assessed for severity and attribution to levofloxacin.

Results: 24 children, all HIV-uninfected, were enrolled, median (IQR) age 2.0 years (0.8 to 2.7). Levofloxacin pharmacokinetic parameters were similar to those of our previously published cohort, except for 70% higher bioavailability for the new dispersible tablets. The value of CL/F for a typical 2-year old, 12 kg child was 2.8 L/h, consistent with previously reported adult values, after adjusting for the effect of body size with allometric scaling. No children had any grade 3 or 4 adverse events, or any serious events. Optimised weight-banded dosing is shown in table 1.

Weight band (kg)	3-3.99	4-4.99	5-5.99	6-6.99	7-10.99	11-15.99	16-21.99	22-27.99	28-34.99
Number of 100 mg tablets	0.5	0.75	1	1.5	2	3	4	5	6
Daily dose (mg)	50	75	100	150	200	300	400	500	600
Daily dose (mg/kg)	14.3	16.7	18.2	23.1	22.2	22.2	21.1	20.0	19.1

[Optimal weight-banded doses of levofloxacin 100 mg dispersible tablets]

Conclusions: Exposures in children receiving the novel 100 mg dispersible levofloxacin tablets were much higher than previously observed due to higher bioavailability of the new formulation. The proposed weight-banded dosing can be used for this novel formulation.

SOA20-1203-27 Understanding TB treatment initiation delays among children in Lima, Peru: a qualitative study

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Background: Diagnosing TB and initiating appropriate treatment in children is a formidable challenge because reliable TB diagnostic tools for this population do not exist. However, even when a TB diagnosis is confirmed, delays in treatment initiation are common but for poorly understood reasons. We conducted a qualitative study among parents and caregivers of children with pulmonary TB in Lima, Peru for whom treatment initiation was not immediate following diagnosis to understand the reasons for delays.

Methods: We conducted semi-structured, in-depth interviews with caregivers of children aged 11mos-14 years who were diagnosed with pulmonary TB and experienced a delay of ≥ 5 days between diagnosis to the start of treatment. Using a narrative approach, participants

were asked to describe their experiences in the time-frame between their child’s TB diagnosis and treatment initiation. Interviews were recorded, transcribed verbatim and analyzed using systematic comparative and descriptive content analysis. Emergent themes regarding TB treatment initiation delays were mapped onto a conceptual framework.

Results: In-depth interviews were conducted among caregivers of 15 children diagnosed with TB (median age 3.1 years [IQR 2.3-7.7]). Median time in delay from diagnosis to treatment initiation was 18 days [range: 6-50]). The following themes emerged regarding treatment initiation delays: ineffective caregiver-provider interactions (apparent tentativeness by providers in making a clinical diagnosis, providers shaming parents); health-system challenges (staffing shortages, burdensome paperwork requirements, bureaucracy); and, parental/caregiver concern for child’s well-being (emotional responses to diagnosis; denial, fear, doubt). See figure.

Conclusions: Reasons for pediatric TB treatment delays were varied but clustered around parent/provider interactions and concern for their child’s health and health system inadequacies. Once diagnosed with pulmonary TB, treatment initiation should be swift to prevent further morbidity. Interventions that improve communication of TB-related information between parents and providers and provide support in navigating the TB treatment system in Peru are urgently needed.



[Figure 1. Conceptual framework for delays in treatment initiation]

SOA20-1204-27 A review of Mycobacterium tuberculosis culture yield from three daily gastric aspirate specimens versus multiple samples obtained in one day (2013-2017)

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Background and challenges to implementation: The Pediatric TB Service adopted an hourly (Q1H) gastric aspirate (GA) method to obtain secretions for tuberculosis (MTB) studies in 2016 - hoping to effect a change in practice to one that is less traumatic, one that can lead not only to earlier anti-TB medication treatment initiation but also shorter hospital stay and earlier return to the community.

Intervention or response: We compared MTB culture yield from GA specimen obtained once daily on three consecutive days (ODx3), to those taken from multiple samples in one day (MSx1), and those obtained from hourly sampling (Q1H).

Demographic, epidemiologic, clinical information, investigations - Q1H versus MSx1 versus ODx3 gastric aspirates and mycobacteriologic results, and chest x-ray (CXR) findings on patients seen by the Pediatric TB Service from January 2013 to December 2017 were reviewed, tabulated and described.

Results and lessons learnt: Fifty-eight patients (32 males: 26 females) were admitted for GA. Ages ranged from 3 to 94 months. CXRs results were: 26 adenopathy, 31 parenchymal opacity, 5 pleural effusion. Thirty-one had samples ODx3 (interval of ≥ 24hrs between samples), 6 had MSx1 sampling (interval of ≥ 2hrs between samples), 21 had Q1H X 3 sampling after being 6 Hrs NPO in the early morning. Six of the 31 ODx3 patients had positive MTB cultures, while 2 of the 6 MSx1 patients cultured positive and 9 of 21 Q1H patients cultured positive. Culture positivity was strongly associated with CXR parenchymal changes more than adenopathy.

Number	Daily (ODx3)	Multiple samples in a day (MSx1)	Hourly sampling (Q1H)	Total
Patients	31	6	21	58
Samples obtained	92	14	63	169
Culture (+) samples, %	11, 11.95%	4, 28.5%	19, 30.16%	34, 20.12%
Culture (+) patients, %	6, 19.35%	2, 33.3%	9, 42.85%	17, 29.31%

[Results of daily versus multiple versus hourly gastric aspirate sampling for tuberculosis]

Conclusions and key recommendations: Q1H GA sampling is a less traumatic, better yielding process to obtain specimen for MTB culture in young children compared to ODx3. It also offers earlier treatment start, and faster discharge home.

SOA20-1205-27 *Mycobacterium tuberculosis* detection from stool in young children using a novel centrifugation-free method with Xpert MTB/RIF

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Background: The microbiological confirmation of paediatric tuberculosis (TB) is challenging as it requires collection of relatively invasive specimens, which may not be feasible in many settings. *Mycobacterium tuberculosis* is detectable from the stool of children using molecular methods, but pre-test processing of stool specimens is currently resource-intensive.

Methods: A novel, simple, centrifugation-free processing method for use with the Xpert MTB/RIF (Xpert, Cepheid) platform, using two stool masses 1) 0.6g and 2) stool swab was evaluated. Children < 13 years of age with suspected intrathoracic TB were enrolled at two referral hospitals in Johannesburg and Cape Town, South Africa. A minimum of one and up to two stool specimens per child were collected and evaluated by both methods. A minimum of one and up to four respiratory specimens were collected per child and evaluated by smear microscopy, liquid culture and Xpert.

Results: 280 children were enrolled: median age 15.5 months; 35 HIV-infected (12.5%). Compared to a single respiratory Xpert, the sensitivity of stool Xpert using the 0.6g and swab protocols was 44.4% (95% confidence interval; CI: 13.7-78.8%) for both methods, with specificity >99%. In 249 (88.9%) children, a second stool was tested: the combined sensitivity of two stool tests vs. the first respiratory Xpert was 70.0% (95% CI: 34.8-93.3%) and 50.0% (95% CI: 18.7-81.3%) for the 0.6g and swab, respectively, while retaining high specificity (>98%). Re-testing stool specimens with initial non-determinate Xpert results improved non-determinate rates from 26/279 (9.3%) to 11/279 (3.9%), and from 24/279 (8.6%) to 12/279 (4.3%) for 0.6g and swab, respectively.

Conclusions: This stool processing method is well-suited for settings with limited capacity for respiratory specimen collection. Combined with more sensitive molecular assays, this simple method could in future improve access to diagnostic testing for children with suspected intrathoracic TB from resource-limited settings.

SOA20-1206-27 Advanced molecular detection of pediatric pulmonary tuberculosis on gastric aspiration and stool samples

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Background: The WHO endorsed the Xpert MTB/RIF assay (Xpert) for diagnosing pediatric pulmonary tuberculosis. Studies showed a sensitivity of 51%-81% on gastric lavage; 51%-73% on expectorated or induced sputum; 50% on stool samples (HIV-negative). The difficulty of collection of specimens and low diagnostic yield rendered Xpert still dissatisfactory for pediatric pulmonary tuberculosis. The Xpert MTB/RIF Ultra (Ultra) assay was developed to improve the diagnostic yield of Xpert.

Methods: A cohort study is under way in Shanghai Public Health Clinical Center in China from Jan 2018 to Dec 2018. All children admitted into this hospital with suspected pulmonary tuberculosis were consecutively screened and tested by routine microbiological tests, gastric aspiration Xpert & Ultra, and stool Ultra tests. The results were carefully analyzed to assess the diagnostic accuracy of Ultra for pediatric pulmonary tuberculosis. Children without a definitive diagnosis or with suspicion of gastrointestinal tuberculosis were excluded from analysis.

Results: Up to March 25th, 2018, 78 children with suspected pulmonary tuberculosis was screened, of which 29 children had a definitive diagnosis (22 were confirmed TB, 7 TB excluded), and 49 were under follow up. For definitive cases, the sensitivity of Xpert on gastric aspiration (GA), Ultra on GA and Ultra on stool were 86.36% (95% CI 0.65-0.97), 100.00% (95% CI 0.85-1.00) and 68.18% (95% CI 0.45-0.86), respectively. The specificity of Xpert on gastric aspiration (GA), Ultra on GA and Ultra on stool were 100.00% (95% CI 0.59-1.00), 100.00% (95% CI 0.59-1.00) and 85.71% (95% CI 0.45-0.86), respectively.

Conclusions: This mid-term result showed that the Xpert MTB/RIF Ultra assay provide better reliability and practicality for diagnosing pediatric pulmonary tuberculosis. Ultra assay on GA provides a higher sensitivity over Xpert assay on GA samples. Ultra assay on stool is potentially a non-invasive and efficient test for pediatric pulmonary tuberculosis, which may reduce 2/3 invasive gastric aspiration, especially for infant.

SOA20-1207-27 Comparison of two DNA extraction procedures for the detection of *Mycobacterium tuberculosis* in pediatric stool samples

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Background: *Mycobacterium tuberculosis* (MTB) DNA detection from stool is promising, however method optimization has been limited. We compared two methods for detecting MTB DNA from pediatric stool samples.

Methods: We collected clinical stool samples from two groups of symptomatic children in Lima, Peru: those with culture-confirmed pulmonary TB and those in whom tuberculosis was clinically ruled out. Samples were processed for detection of MTB-DNA by two procedures: (1) using 5 gr of stool, filtered with gauze, centrifuged, washed with PBS, then incubated at 56°C with Liquefaction Buffer (Kit TruPrep Akonni Biosystems); and (2) subjecting 0.3-0.5 gr of stool to magnetic forces in the MagVor instrument and incubating it at 56°C with Lysis Buffer F. DNA extraction for both procedures was performed using the TruPrep instrument (Akonni Biosystems) and MTB was detected by qPCR targeting the IS6110 insertion element. Sample positivity was determined by a Cp threshold < 37 with a fluorescence value ≥10. We compared Cp and fluorescence values using Wilcoxon signed-rank analyses.

Results: Among samples from eight children with culture-confirmed TB from sputum or gastric aspirate, method 1 yielded a sensitivity of 62.5% (5/8; 95% CI: 24% - 91%) while method 2 was 100% sensitive (8/8; 63% - 100%). Both methods showed 100% specificity (N=6). Among children with confirmed TB, the signal for DNA detection on qPCR for method 2 as compared to method 1 tended to be stronger, as indicated by a lower median Cp and a higher median fluorescence (30.6 vs. 31.6 and 34.7 vs. 29.0, respectively); however, these differences were not statistically significant.

Conclusions: Method 2 yielded a high sensitivity and specificity. This is the preferred processing method given that it does not require gauze filtering, uses a smaller sample volume, and has a shorter processing time. Larger sample sizes will facilitate better understanding of method 2 performance.

SOA21 Special populations, special needs, special care

SOA21-1208-27 Systematic monitoring and evaluation of TB contact evaluation practice

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Background and challenges to implementation: Tuberculosis (TB) contact investigation (CI) in the Netherlands is performed following a stone-in-the-pond approach: when there is evidence of transmission among close contacts (1st ring) CI is scaled up to casual contacts. Monitoring and evaluation of the cascade of care is essential for effective CI. The Netherlands TB register captures results on number of identified contacts, and coverage and yield of CI for each notified TB patient.

Intervention or response: CI results of TB patients notified from 2011-2015 were used. Data included patient characteristics, number of contacts identified, evaluated, and diagnosed with TB or latent TB infection (LTBI). CI coverage and the prevalence of TB and LTBI per contact ring and by infectiousness of the index patient were calculated.

	Close contacts (1st ring) n=6847	% of total TB/LTBI	Casual contacts (2d ring) n=4273	% of total TB/LTBI	Community contacts (3d ring) n=440	% of total TB/LTBI
Extrapulmonary or smear-negative pulmonary TB	Coverage - Median number examined (interquartile range) 88% - 3 (1-4)		83% - 4 (2-11)		97% - 2 (1-4)	
	TB / LTBI prevalence 0.60% / 9.7%	87% / 77%	0.14% / 4.1%	13% / 22%	0 / 3.1%	0% / 1%
Sputum-smear positive pulmonary TB	Coverage - Median number examined (interquartile range) 90% - 5 (2-10)		85% - 10 (4-25)		86% - 3 (1-10)	
	TB / LTBI prevalence 1.95% / 17.7%	80% / 55%	0.23% / 7.0%	17% / 34%	0.08% / 4.3%	3% / 10%

[Coverage and yield of contact investigation by infectiousness of the index patient and contact ring]

Results and lessons learnt: In total 4,441 index patients were notified, around whom 2886 (64%) CIs were initiated. Of the 51,761 contacts identified as eligible for screening, 44,602 (86%) were examined. The median number of contacts examined was 2 per index patient (interquartile range 0-8); 35% of the CIs performed were around smear-positive pulmonary TB patients and 74% of contacts screened were contacts of smear-positive patients. The prevalence of TB and LTBI among these contacts was 0.68% and 9.5%, respectively, compared to 0.41% and 7.4% among contacts of patients with smear-negative or extrapulmonary TB. The preva-

lence of TB and LTBI among 1st ring contacts of smear-positive pulmonary TB patients was 1.95% and 17.7% respectively. Prevalence was lower in 2nd and 3th ring than in the first ring, but the number needed to screen to detect one patient met the criterium for TB risk groups (NNS < 1:2000). Of contacts with LTBI, 81% started LTBI treatment and 86% completed LTBI treatment.

Conclusions and key recommendations: The stone-in-the-pond approach to CI is an effective method to identify TB contacts with a high likelihood of TB and LTBI, and provide (preventive) treatment.

SOA21-1209-27 Tuberculosis among older adults in Kenya: implications for an aging population

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Background: The tuberculosis (TB) epidemic in sub-Saharan Africa is largely among young adults. However, as life expectancy increases, TB among older adults will become increasingly important. We describe the epidemiology and TB treatment outcomes in older versus younger adults in Kenya.

Methods: We performed a cross-sectional retrospective analysis of adults (age ≥ 20 years) using TB surveillance data from 2012-2015. Younger adults were defined as aged (20-49 years) and older adults (≥ 50 years). De-identified data were obtained from the national electronic TB surveillance system and analyzed using Stata 12.1. Treatment outcomes based on 2013 WHO definitions were analyzed as a binary variable, favorable outcome if cure or treatment completion and unfavorable outcome if death, loss to follow-up, failure or unevaluated. Case fatality was the percentage of death among all patients. We described frequencies and odds ratios with 95% confidence interval (CI) and *P* values.

Results: We analyzed data for 362,680 TB patients, of whom 246,794 (68.0%) were young adults and 57,418 (15.8%) were older adults. Older adults were 64.0% male and median age 59 years (IQR: 53-66).

Compared with younger adults, older adults were more likely to have extra-pulmonary TB (19.0% v.16.2%), $p < 0.001$ and relapsed TB (10.7% v. 10.3%), $p = 0.002$ and less likely to be smear positive (34.0% v. 50.8%) $p < 0.001$ or HIV-positive (26.4% v. 39.6%), $p < 0.001$.

While they were more likely to be on antiretroviral therapy (ART) if HIV positive (91.0% v. 89.5%), $p < 0.001$, they were less likely to be treated successfully (aOR 0.83, 95% CI: 0.81-0.85).

Case fatality for older adults was 10.4% and increased compared to 2.3% for young adults. Proportions of case-fatality correlated with age quintiles are shown in Figure 1.

Conclusions: Despite lower HIV prevalence, older TB patients have significantly higher mortality than younger adults. Other causes of deaths among older adults should be explored and managed.

SOA21-1210-27 Identifying yield of pulmonary TB among mental disordered patients in Afghanistan: a cross-sectional study

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Background and challenges to implementation: Sixty percent of Afghans have mental disordered. WHO estimates 65,00 incidence number of TB cases for Afghanistan. The comorbidity could lead to delayed in diagnosis and treatment among mental disordered patients and could result in poor adherence to TB treatment. The estimated burden of TB was not known among mental disordered patients. The aim of this study was to estimate yield of pulmonary TB among mental disordered patients in five provinces of Afghanistan.

Intervention or response: This was a cross-sectional study, conducted in five cities: Kabul, Jalalabad, Kandahar, Herat and Mazar-e-Sharif. The field staffs selected study subjects from the existed mental health registers, including those attending private clinics and hospitals for care. All mental disordered patients with coughs were screened by Chest X-ray and sputum examination using GeneXpert technology

Results and lessons learnt: In total, 7,980 mental disordered patients attended the study. 2328(29.3%) were male and 5653 (70.8%) female. 803 (10%) suffered general Anxiety, 3,970(50%) depression, 207(2.6%) panic attack, 92(1.2%) post-traumatic stress disorder (PTSD), 299(3.7%) Schizophrenia and 2,609 (32.7%) of other mental disorders. Mean age of attendees was 33.5 year and mean disease duration was 4.5 year. 234(2.9%) were cigarette smokers. 42 (0.5%) of study participants had already had TB and two of them were under TB treatment. 208 (2.6%) of study participants had cough for more than two weeks and their chest X-ray taken and sputum tested by GeneXpert. The health care staffs diagnosed 47(0.6%) of study participants as pulmonary TB cases. All were put under standard treatment (tab 1). The yield of TB was 600 in 100,000 mental disordered patients, a three times higher than WHO estimate for all forms of TB.

Conclusions and key recommendations: The yield of pulmonary TB among mental disordered patients is significantly higher than WHO estimates for all forms TB for Afghanistan. Thus, we recommend integration of TB case finding in mental health facilities.

Variable	Value	Remark
Total study participants	7,980	
Presumptive TB patients among study participants	208 (2.6%)	
Pulmonary TB diagnosed	47 (0.6%)	
Yield of TB among study participants	600 in 100,000	p-value= 0.0001 OR=3.13

[Key study findings]

SOA21-1211-27 Predictors of failure to continue tuberculosis treatment after release from prison in Malaysia: a cohort study

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Background: Individuals with incomplete tuberculosis (TB) treatment may remain infectious, posing a significant risk to the general population. Prisoners face several challenges after release to the community and may fail to attend to their TB treatment requirements. A recent survey in a prison in Malaysia showed that 65% of prisoners with TB were released before completing treatment with no information about the outcome of treatment in the community.

Methods: A cohort study among due-to-be-released prisoners before completing TB treatment in five men prisons in Malaysia was conducted from January 2017 to January 2018. Consented participants were interviewed using a structure questionnaire that include demographic information, history of TB treatment and HIV infection. After release, contacts were made with the designated TB clinics, other nearby clinics, main hospitals, and the tertiary TB referral centre to ascertain treatment continuation (registration at a TB clinic within 30 days of release to the community). Logistic regression analyses were explored to investigate factors associated with non-continuation of TB treatment after release.

Results: The mean age of the 105 participants was 41.6 years (SD 10.2) and most had a secondary education or higher (77.1%), previously incarcerated (97%), pre-incarceration heroin users (74.8%) and not HIV-infected (70.5%). Forty six participants (43.8%) failed to continue treatment after release from prisons and this was independently associated with age (aOR 0.95 [95%CI 0.91-0.99]) and not having a stable housing before current incarceration (aOR 2.80 [95%CI 1.15-6.78])

Conclusions: Almost half of released prisoners with incomplete TB treatment failed to continue treatment in the community. Finding a stable housing is a major challenge to released prisoners and may influence the enrolment in community treatment programmes. There

is an urgent need to establish programmes to support prisoners in the immediate post-release period to ensure continuity of TB care.

SOA21-1212-27 Results of tuberculosis screening program among drug or alcohol depended individuals and cost-benefit analysis in Tel Aviv, Israel (2013-2016)

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Background: Most tuberculosis patients in Israel are migrants from countries with high prevalence of tuberculosis. However, additional vulnerable groups, such as drug or alcohol users (DAU) are also at risk for infection. Delays in diagnosis may lead to further spread of the *mycobacteria* to additional members of the DAU community. Tel-Aviv, which is the major metropolitan city in Israel, hosts the largest DAU community. This study aims to assess the prevalence of tuberculosis among DAU and evaluate to cost-benefit measures of the screening process.

Methods: All DAU who are referred to drug/alcohol rehabilitation and individuals who are in drug-substitutes programs perform annual chest radiography in the Tel-Aviv tuberculosis clinic to detect radiological signs suggestive of pulmonary tuberculosis.

Results: Between 2013 and 2016, 512 DAU performed 860 chest radiographies (1-4 films per individual). Four (0.8%) were infected with HIV and 3 (0.6%) were previously treated for tuberculosis. Of all DAU, 467 (91.2%) showed normal chest radiography and 38 (7.4%) demonstrated various pathologies. The radiography results of 7 (1.4%) individuals were not recorded. Of the pathological results, 9 (23.7%) displayed old ribs fractures, 2 (5.2%) had suggestive signs of healed tuberculosis, 1 (2.6%) showed pneumonia, 3 (7.9%) demonstrated obstructive airways disease and 19 (50.0%) presented radiographic signs suggestive of tuberculosis (pleural thickening, obstruction of the costo-phrenic angle, lung fields' calcifications and effusions). Of all suspected films, 3 (15.8%) were diagnosed with pulmonary tuberculosis.

The direct cost to identify a single tuberculosis patient in DAU screening was 4,600 Euro, while the cost to treat a single patient was 12,450 Euros.

Conclusions: During the 4-years of the screening program, including 512 DAU, 19 (3.7%) had pathological findings and 3 (0.6%) were diagnosed with pulmonary tuberculosis. Although the screening program showed positive cost-benefit ratio, cheaper technologies can be evaluated, such as tuberculosis-related symptoms questionnaire.

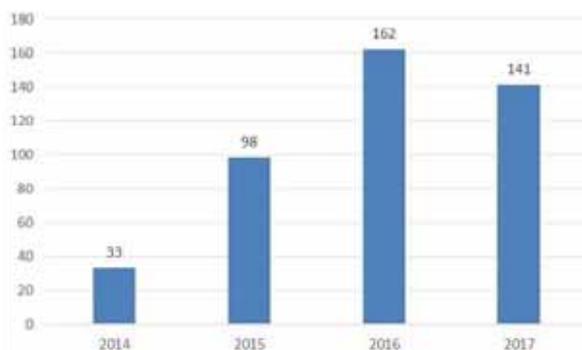
SOA21-1213-27 Experience of involvement NGOs in TB control among migrants in Kazakhstan

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Background and challenges to implementation: The growth of Kazakhstan's economy has become attractive for labor migration; however, increased trends of migration flows can pose challenges for TB prevention and control. Migrants are often isolated, live in cramped living conditions in close proximity with others, and lack of local language knowledge. These unique factors make it difficult for health workers to reach migrants and for migrants to access medical services, which lead to late TB diagnosis and treatment.

Intervention or response: Local non-governmental organizations (NGOs) participated in the implementation of the program "Addressing cross border TB, M/XDR-TB and TB-HIV among labor migrants" funded by GFATM. For the first time a network of NGOs was created to help control TB among migrants in Kazakhstan. A model of NGO involvement in TB control among migrants was developed and implemented in eight pilot territories. NGO staffs were trained, and program documents and background information materials were developed. The 6 local NGOs, with a staff of 85 outreach and social workers and 100 volunteers provided information, social, legal, and motivation support to TB patients. A network of 70 migrant-friendly medical facilities to TB diagnosis and treatment was established.

Results and lessons learnt: In the pilot territories, a network of NGOs with the capacity to work with migrants was established. In the 2.5 years of the program, nearly 145,000 migrants received TB information and education. More than 44,000 of them were screened for TB and 1,607 TB patients, (including 401 external migrants) were identified, treated and covered with motivation support. The notification of TB among external migrants increased greatly in 2016 and 2017 compared with the beginning of the program (Chart 1).



[Number of all TB cases among external migrants in pilot sites of Kazakhstan]

Conclusions and key recommendations: Involvement of NGOs to organize work among migrants in TB control contributed to TB detection and treatment by removing barriers to access medical services increased the effectiveness of interventions for TB control among migrants.

SOA21-1214-27 Primary isoniazid prophylaxis for prevention of tuberculosis infection: a randomized, placebo-controlled trial among high-risk prison inmates

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Background: While there is a large body of evidence demonstrating efficacy of isoniazid for treatment of latent tuberculosis to prevent disease, there is little known about whether isoniazid can prevent initial tuberculosis infection. Recent studies in 12 prisons in central-western Brazil demonstrated that <10% of inmates had latent tuberculosis at the time of incarceration, but that the annual risk of infection during incarceration was 26%, leading to TB incidence >1700 per 100,000. As the average prison sentence is 1-2 years, we aimed to test whether short-term provision of isoniazid could prevent infection in this high-risk setting.

Methods: We are conducting a randomized, double-blind, placebo-controlled study, which will recruit 728 Quantiferon-TB Gold Plus (QFT) negative male inmates aged <45 years, serving a 12-month sentence. Participants are allocated to two arms: 1) 900 mg of INH twice weekly; or 2) placebo twice weekly, with both arms directly observed for every dose for 52 weeks. The primary endpoints are QFT conversion at 26 and 52 weeks. A data safety monitoring board is evaluating outcomes and adverse events.

Results: Since September 2017, we screened 924 inmates for eligibility, of whom 409 (44%) were QFT positive and excluded. We have enrolled 417 QFT-negative participants, in whom HIV prevalence is 0.8%.

To date, 161 participants (38%) have withdrawn from the study due lack of continued interest (52,9%) or to transfer from the prison (28,5%), but no serious adverse events have occurred. The most common adverse events have been headache (14.6%), somnolence (14.2%), dizziness (11.8%), stomach pain (11.4%) and nausea (7.3%).

Conclusions: This study will be the first placebo-controlled trial to assess whether isoniazid can prevent tuberculosis infection. Interim efficacy evaluation will be performed in June 2018 and these results will be available for presentation at the Union meeting in October 2018.

SOA21-1215-27 Fear of job loss as a barrier to TB care among mine workers in Zambia: impact of TB-related policies

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Background: The 1999 Compensation Act in Zambia prohibits persons with a history of tuberculosis (TB) from working in the mines. We aimed to understand the influence of this policy on perceptions and health-seeking behavior among mineworkers in Zambia.

Methods: We conducted semi-structured knowledge, attitudes and practice (KAP) surveys among current and former mineworkers and healthcare workers (HCWs) at mine-operated and public health facilities in mining communities in the Copperbelt and North-Western Provinces.

Results: A total of 2,782 current (n=1,956) and former mineworkers (n=836) and 94 HCWs completed the KAP surveys. While only 41% of mineworkers knew of the formal policy, 71% of mineworkers knew they are prohibited from mine work after a TB diagnosis. A large majority (77%) of mineworkers indicated they would not disclose their TB status to their supervisor; in contrast, 73% indicated they would discuss their diagnosis with their spouse. HCWs mentioned mineworkers' fear of losing employment as a key barrier to providing TB care and often cited that this leads to late disease presentation and failure to provide accurate contact information. Only half (53%) of current mineworkers underwent annual TB screening while almost all (97%) were annually screened for silicosis.

Conclusions: The 1999 Compensation Act in Zambia results in mineworkers withholding their TB status from their employer for fear of losing employment and is a key barrier to TB care among mineworkers. Revision of the policy is underway but is only the first step in facilitating early TB diagnosis and treatment. Annual occupational health screenings for silicosis is a missed opportunity to screen mineworkers for TB. A formal partnership between mining companies and the public health sector, including advocacy, education and continued provision of TB services without fear of job loss, may be an effective approach to controlling TB transmission among mineworkers, ex-mineworkers, and their communities.

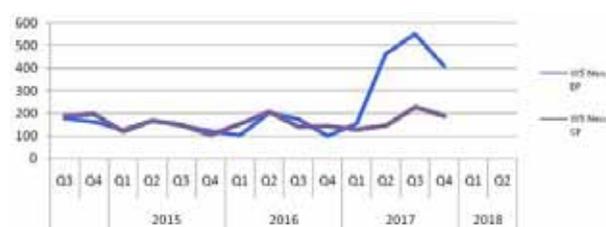
SOA21-1216-27 Finding and treating missed cases among key affected population - primitive tribal groups of central India

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Background: With an estimated TB burden over 10 times the general population estimate, the Sahariya tribe of central India is one of the most-at-risk groups in the country. Recent studies suggest a TB prevalence of 3294 per 100,000 population. Access to the health facilities is severely restricted by remote geography and extremely poor health seeking behaviours.

Methods: In 2017, a community based active case-finding (ACF) intervention was undertaken by locally trained Community Health Workers (CHW) to act as an extension of National TB Program. CHWs conducted verbal screening targeting households, identified presumptive TB cases, collection and transportation of sputum specimens to aid rapid diagnosis. Upon TB confirmation, patients were treated and counselled at their door step for the entire treatment duration thereby reaching the last mile of the TB care cascade. CHWs received a fixed honorarium, petrol allowance and incentives for identifying and initiating diagnosed patients on treatment.

Results: During the first three quarters of the intervention, CHWs verbally screened 146,929 people, with 9941 (7%) identified as presumptive TB cases, of which 9097 presumptive cases were tested for TB using smear microscopy (92%). Interventions yielded 1923 B+ (21%) and 2027 AF (22%) from ACF activities. All diagnosed patients were initiated on treatment with no pre-treatment loss to follow-up. Significant gains have been observed with an unadjusted additionality of 952 B+ and 839 AF; and with 200% and 112% departure from baseline notifications for B+ and AF respectively in the evaluation population.



[Three-year trend in B+ notifications among Evaluation and Control Population]

Conclusions: Identification of missing TB cases among the key population groups is crucial to saving lives and reducing TB incidence. ACF interventions engaging

CHWs targeting Sahariyas have resulted in significant notification gains, and helped to find and treat missing TB cases among these most-at-risk groups in Central India.

SOA22 The need for quality tuberculosis sciences

SOA22-1218-27 An assessment of socioeconomic factors, including gender, contributing to diagnostic delay and treatment non-adherence among tuberculosis patients in the Kyrgyz Republic

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Background: The Kyrgyz Republic is one of the 30 countries with a high burden of multidrug-resistant tuberculosis (MDR-TB). Circumstances outside of the health system, such as socioeconomic and cultural factors, contribute to care-seeking delays and adherence issues that can lead to the development of MDR-TB. This study aimed to explore how socioeconomic and cultural factors, including gender norms and stereotypes, stigma and discrimination, affect the behavior of TB patients, their families, and their communities.

Methods: The study used a combination of qualitative and quantitative methods: a survey among 320 TB patients; 36 semi-structured interviews with health workers, patients who interrupted their TB treatment and family members of TB patients; and 4 focus groups with former TB patients. The study was carried out in four locations in the Kyrgyz Republic: Bishkek and Jalal-Abad cities and Kemin and Bazar-Korgon districts.

Results: The study found that TB stigma is high and pervasive (30.9 out of 50 points according to the international standardized scale), impedes timely TB diagnosis and treatment compliance, strains relationships in families, and affects both genders but in different ways. For young men, tuberculosis is associated with a risk of losing the family breadwinner status. Women can face a risk of a ban on reproduction, domestic violence and neglect. Poor treatment adherence and lack of knowledge about TB treatment are also caused by limited trust in health care systems and widespread TB-related stigma and discrimination among health workers.

Conclusions: The study revealed that sociocultural norms, including those associated with gender, play a key role in shaping TB/MDR-TB patients' treatment

decisions. It is important to promote social and behavior change communication strategies aimed at reducing stigma and discrimination among the population. Building capacity of health workers in effective counselling helps to enhance TB case management and provide more supportive care to patients.

SOA22-1219-27 Articulating the state duty in human rights protection towards public health-oriented carceral reforms in the Philippines

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Background and challenges to implementation: The Philippines has one of the most congested penal systems in the world, with jail overcrowding reaching 511% nationally and as high as 961% in one administrative region, according to official government audits (2016). Deteriorating or substandard facilities, sanitation issues, lack of jail officer training, public stigmatization, and the government's prosecutorial drug control policy in its "War on Drugs" further aggravate these detention conditions, resulting to an increasing incidence of infectious diseases, especially tuberculosis. Without examining and addressing the normative regime that facilitates high incarceration rates, fundamental legal bases for penal or carceral reforms remain obscure, and the public health needs of this vulnerable, marginalized population cannot be addressed.

Intervention or response: This study presents the most comprehensive legal analysis of the human right to the presumption of innocence in Philippine constitutional law. Jurisprudential review of Philippine Supreme Court decisions and comparative law approaches were utilized, with focus on Anglo-American constitutional standards and international human rights principles as articulated in conventions, caselaw of international human rights tribunals, and "soft law" instruments.

Results and lessons learnt: The right to the presumption of innocence has been articulated as a core constitutional guaranty that compels legislative action towards urgent carceral reforms and, particularly, against prolonged pretrial detention. The interdependence of this right with due process, the right to the highest attainable standard of health, and the right against degrading treatment require substantial restructuring of State apparatuses related to bail, detention, and prosecution.

Conclusions and key recommendations: The interdependence of the right to health with civil, political, economic, social, and cultural rights, in relation to complex and dynamic social and environmental determinants, necessitates an integrated view of the criminal justice system, both with respect to analysis and reform. Available legal remedies must consider their links in order to fully protect, promote, and realize human dignity.

SOA22-1220-27 Providing guidance on a programmatic approach to reducing human rights- and gender-related barriers to TB services

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Background and challenges to implementation: TB remains the most important cause of death among people living with HIV in most countries. HIV-TB coinfection is a major public health problem. Many of human rights-related barriers to HIV services - including stigma, gender inequality and undue criminalization - also apply to TB, and the two diseases affect many of the same key populations. The project aimed to develop specific technical guidance on addressing human rights-related barriers to TB programs.

Intervention or response: The Global Fund to Fight AIDS, TB and Malaria (GFATM) and partners, including Stop TB Partnership and WHO, convened a working group to develop technical guidance on rights-based TB services. Based on identified, human rights-related barriers to TB services and Stop TB Key Populations series and other materials, it assessed the relevance of the UNAIDS 7-key human rights program to reduce stigma and discrimination and increase access to justice in the TB context.

Results and lessons learnt: The group concluded that all seven categories of programs to reduce rights-related barriers to HIV are also pertinent to TB. In addition, several TB-specific rights concerns were noted. The technical guidance includes 7-key programs as well as avoidance of involuntary isolation for the purpose of TB treatment, equal access to workplace protections (including for migrant workers) in high-risk occupations, and ensuring access to TB services for people in jails and prisons.

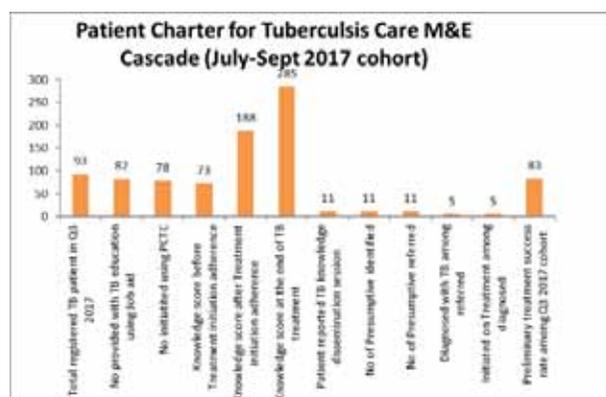
Conclusions and key recommendations: For many people, human rights-related barriers hinder access to and retention in TB services. In the absence of TB-specific guidance on a programmatic response there had previously been little investment in efforts to reduce these barriers. Since the technical guidance was published, it has informed the grant applications to the GFATM and resulted in an increasing investment on these programs. However, sustained efforts will be needed to ensure this trend continues and programs to reduce barriers are implemented at scale and evaluated.

SOA22-1221-27 A right-based approach for institutionalizing patient charter for tuberculosis care in Nigeria: implementation framework, results and lessons learned

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Background and challenges to implementation: The Patient Charter for Tuberculosis Care (PCTC) highlights the rights and responsibilities of TB patients. PCTC serves as the roadmap for achieving integrated patient centered service as part of the end TB strategy. Systematic and effective Implementation of the charter has been hampered due to lack of step-by-step guide and methodology for its roll-out. This abstract describes the use of a systematic approach to implement the PCTC framework and pilot results in 37 private health facilities in Nigeria.

Intervention or response: Between February and March 2017, medical directors of 37 private health facilities and their DOTS providers were visited to advocate for the introduction of the charter for TB patients, its benefits and expected results. Implementation tools (PCTC clinic card, TB health literacy desk guide, 10 M & E indicators and quarterly reporting template) were developed. By June 2017, DOTS providers of all clinics were invited for training on the PCTC implementation steps, cascade recording tools and measurement scales using participatory learning approaches.



{Patient Charter for Tuberculosis Care M&E Cascade (July-Sept 2017 cohort)}

Results and lessons learnt: 88 % (82) of the 93 patients registered between July-September 2018 received TB education using the health literacy tool; 84% (78) were

initiated and provided with adherence counseling using the TB Patient Charter. Average knowledge score of the 78 patients increased from 18.5% (73/395) before initiation to 72% (285/395) by the end of treatment. TB patients in this cohort identified and referred 11 presumptives from the community, all were tested for TB using Genexpert and 5 were confirmed and all initiated on TB treatment. Preliminary 6 months Treatment success rate was 83%.

Conclusions and key recommendations: Structured implementation of PCTC in Nigeria has demonstrated proven benefits not only on quality adherence counseling and treatment completion but also has shown the empowering effect on TB patients, still on treatment, contributing to case finding through peer-to-peer referrals of TB cases from the community.

SOA22-1222-27 Establishing community structures through the engagement of lay providers can improve TB contact screening: initial lessons from the USAID Defeat TB Project in Uganda

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Background and challenges to implementation: TB case finding efforts have largely been passive and health facility-based with minimal community involvement. Although contact tracing is a high yielding activity, it is not systematically done. Contact tracing involves invitation of contacts to the facility or facility health workers going into the community to screen contacts. The USAID Defeat TB project developed a community system strengthening strategy with a focus on use of community linkage facilitators (CLFs) to lead the community screening of contacts of index TB patients for active TB and link diagnosed cases to treatment initiation at the facilities.

Intervention or response: 50 CLFs were selected and deployed at 41 TB diagnostic and treatment facilities in Mukono, Kampala and Wakiso districts. These CLFs were trained using a standard curriculum, with emphasis on TB prevention and contact investigation processes, counselling and communications skills, recording and reporting of community work and their roles. Lists of TB patients whose contacts were not screened were generated by health facilities and shared with CLFs. Appropriate recording tools were availed and sputum sample collection supplies provided.

Results and lessons learnt: In one month, data received from 17/38 facilities showed 2,019 contacts of index TB patients were identified, 1,623 (80%) screened for TB, 433 (26.7%) presumptive TB cases identified, 60 (3.7%) TB cases diagnosed with TB and started on treatment.

234 presumptive TB contacts were tested for HIV and 28 tested HIV positive, and five were diagnosed with TB-HIV co-infection.

Conclusions and key recommendations: Engaging community structures such as CLFs, who are trained and equipped with the necessary skills and information, contributes to an effective system for contact investigation. CLFs also improve access to TB care by bringing services closer to communities and establishing a robust linkage and referral system between the community and health facility.

Integrating community volunteers is key in improving TB screening coverage and case finding.

SOA22-1223-27 Effective civil society and government partnership for improved TB case detection and treatment outcomes in Mulanje district, Malawi

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Background and challenges to implementation: In 2012, Mulanje District had a 78% TB cure rate and 16% lost-to-follow-up rate, with cases detected through passive case-finding. Case detection and treatment outcomes were hampered by various challenges: Low TB knowledge/awareness levels; associated stigmatisation of patients; limited diagnostic centres, equipment and trained staff; and overall limited support services for TB patients.

Intervention or response: From 2015-18, TB Alert implemented a cross-cutting project with the district health department. The project focus was to address stigma to increase demand for and uptake of TB services, and improve the quality and accessibility of TB diagnostic, treatment and adherence services for patients.

Community volunteers conducted door-to-door campaigns that improved TB awareness and facilitated community-based screening, sputum collection and/or referrals. This community network also provided treatment support to affected families. Local health infrastructure was improved via training of Microscopists and provision of microscopes to increase the number of diagnostic centres.

Results and lessons learnt: Over the duration of the project, TB Cure rate increased from 78% to 88%. Patients lost-to-follow-up declined from 16% to 1.5%. Seven new diagnostic centres were opened and testing of sputum samples subsequently doubled: From 255 per month (Year 1) to 528 per month (Year 3). A total of 24,005 samples were tested and 2057 new TB cases detected. 52.9% of cases were detected by community-based volunteers, demonstrating the success of active case-finding approaches. The partnership with government ensured effective collaboration and an increase in local capacity to address tuberculosis within the existing health system and wider community.

Conclusions and key recommendations: Active case-finding approaches work well but need effective and close collaboration between the implementing CSO(s) and the district health office. A combination of increased demand for and uptake of TB services; improved availability and quality of diagnostic services; and provision of effective support to TB patients ensures that improvements in case finding are matched by better treatment outcomes.

SOA22-1224-27 Finding the missing cases among the elderly - a hard-to-reach and vulnerable group

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Background and challenges to implementation: In 2016, the TB incidence and mortality rates in Cambodia were 345 and 20 per 100,000 population respectively. TB prevalence rate among the elderly (≥ 65 year old) was 3,046 per 100,000, four times greater than the general population than it cites. Approximately 80% of the Cambodian population is rural. Consistent with poor access to TB care, high costs associated with seeking healthcare and low awareness about TB. In Cambodia, the elderly have economic, physical, and structural barriers to accessing high-quality TB services.

Intervention or response: The USAID Challenge TB (CTB) project mobilized village health support groups (VHSG) and health center staff to implement comprehensive interventions to screen elderly clients who come to pagodas/mosques by involving religious laymen (Ajar) and imams as supporters in TB control. TB posters were displayed at pagodas to promote TB awareness and VHSG informed the community on TB screening services on certain days. Health center staff and VHSG set up discrete, private areas at pagodas/mosques for evaluating individuals with TB symptoms. Sputum were collected on-site from presumptive TB patients and sent to the nearest laboratory for GeneXpert testing. Presumptive TB cases with negative results were referred for x-ray and further investigation. Transportation support was provided.

Results and lessons learnt: Between July 2015 and December 2017, 23,547 elderly people were screened for TB. Of these, 13,241 (56%) had TB symptoms and submitted sputum for GeneXpert. Of the presumptive, 950 (4%) were found to have active TB, 100% of whom initiated TB treatment.

Conclusions and key recommendations: Active case finding in pagodas/mosques provides additional yield of TB case notification. HC staff and VHSG at community level have significant roles to find missing cases among the elderly who have difficulty in accessing health facilities. Adding chest X-ray for all presumptive with negative GeneXpert results may find even more additional cases.

SOA22-1225-27 The strategic collaboration between NTP Mozambique and civil society partners through USAID-supported project to enhance TB case finding in Nampula and Zambézia Provinces, Mozambique

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Background and challenges to implementation: TB case notification is a major challenge in Mozambique. The National TB Program (NTP) collaborated with the USAID Challenge TB (CTB) project and ADPP Mozambique, a premier NGO of the country to enhance notification in the highly populated provinces of Nampula and Zambézia.

Intervention or response: The NTP in Mozambique, is responsible for policy, coordination, and overall implementation of TB services. The USAID CTB project, led by FHI 360, provides strategic leadership and technical assistance to the NTP, including monitoring and supervision, in the implementation of TB activities in 4 provinces. With funding assistance of CTB, ADPP Mozambique implements community-based case-finding activities in 7 districts in Nampula and 10 districts in Zambézia. The activities include door-to-door active case finding, contact screening, sputum collection and transportation, household education and stigma reduction, HIV testing of new TB patients, capacity building of cough officers, engagement of TB activists, observance of community-level cough days, and community treatment support and mentoring.

Results and lessons learnt: TB case notifications increased in Nampula (12% increase in 2016; 40% in 2017) and in Zambézia (44% increase in 2016; 30% in 2017). These were the highest increases reported from all the provinces in Mozambique during 2016-17. The TB cases notified through CTB and with ADPP's implementation contributed to 55% of total additional cases notified in Nampula in 2016, and 51% in 2017. Similar contribution in Zambézia was 23% in 2016 and 64% in 2017. Overall, CTB & ADPP contributed to 12% of the total additional cases notified in the country in 2016 and 32% in 2017. During this time, the overall estimated national treatment coverage increased from 45% in 2016 to 54% in 2017.

Conclusions and key recommendations: Community-based interventions that engage civil-society partners can improve NTP performance and increase case finding. Similar interventions can be replicated in other low-performing provinces to meet national TB elimination goals.

SOA22-1226-27 Engagement of lady health workers to enhance tuberculosis case notification in rural Sindh, Pakistan

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Background and challenges to implementation: Pakistan is a high Tuberculosis (TB) burden country. The 2011 national prevalence survey shows that TB prevalence is higher in rural populations. The TB response remains focused on addressing quality of diagnosis and care with little emphasis on community engagement especially in the rural areas. Mercy Corps (MC) has engaged Lady Health Workers (LHWs) having deep reach especially in rural populations, in three districts of rural Sindh. Each LHW covers a population of 1,000-1,500 through Community Support Groups (CSGs), Village Health Committees (VHCs) and household visits focusing on maternal, neonatal and child health messages. Their potential in TB case notification had never been tapped and no coordination existed between the LHW and TB Control Programs.

Intervention or response: Key stakeholders were engaged through Provincial Inter-Program Coordination Committee for policy decisions, tools and material finalization and progress review. 805 LHWs were trained on identification of presumptive cases through verbal screening and their referral to nearest public and private health facilities. MC field staff supported in sputum transportation as well as in contact screening. They also provided supportive supervision during CSGs and VHCs for creating awareness on TB. Chest camps were also conducted. LHWs were provided incentives against each registered case.

Results and lessons learnt: Between October and December 2017, a total of 189,774 persons were screened by LHWs; of which 1,501 were identified as presumptive. Of these, 953 were tested and 233 (53% females) all form cases (111 bacteriologically positive) were registered. The LHWs screened 572 eligible contacts, of which 154 were identified as presumptive and 5 all forms TB cases were registered. A significant increase in presumptive referrals and TB case notification in public sector is observed.

Conclusions and key recommendations: Strong linkages between TB Control and LHW programs, and capacity building and supportive supervision of LHWs can help identify "missing" TB cases embedded in underserved communities.

SOA22-1227-27 Psychological and educational intervention to improve tuberculosis treatment adherence in Ethiopia based on health belief model: a cluster-randomized control trial

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Background: Treatment non-adherence results in treatment failure, prolonged transmission of disease and emergence of drug resistance. Although the problem widely investigated, there remains an information gap on the effectiveness of different methods to improve treatment adherence based on theoretical models. This study aimed to evaluate the impact of psychological counseling and educational intervention on tuberculosis (TB) treatment adherence based on Health Belief Model (HBM).

Methods: A cluster randomized control trial was conducted in Addis Ababa, Ethiopia. Patients were enrolled into study consecutively from 30 randomly selected Health Centers (HCs) (14 HCs intervention and 16 HCs control groups). A total of 698 TB patients, who were on treatment for one month to two months were enrolled. A structured questionnaire was administered to both groups of patients at baseline and endpoint of study. Control participants received routine directly-observed anti-TB therapy and the intervention group additionally received combined psychological counseling and adherence education. Treatment non-adherence level was the main outcome of the study, and multilevel logistic regression was employed to assess the effect of intervention on treatment adherence.

Results: At enrollment, the level of non-adherence among intervention (19.4%) and control (19.6%) groups was almost the same. However, after intervention, non-adherence level decreased among intervention group from 19.4 (at baseline) to 9.5% (at endpoint), while it increased among control group from 19.4% (baseline) to 25.4% (endpoint). Psychological counseling and educational interventions resulted in significant difference with regard to non-adherence level between intervention and control groups (AOR = 0.31, 95% CI (0.18-0.53).

Conclusions: Psychological counseling and educational interventions, which were guided by HBM, significantly decreased treatment non-adherence level among intervention group. Provision of psychological counseling and health education to TB patients who are on treatment is recommended. This could be best achieved if these interventions are guided by health behavior theories.

SOA23 Tuberculosis diagnosis + DST: getting from here to there

SOA23-1228-27 Diagnostic accuracy of smear microscopy, TB-LAMP, GeneXpert assay and solid media culture for the detection of pulmonary TB in Madagascar

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Background: Early and effective tools to detect *Mycobacterium tuberculosis* are necessary for an effective tuberculosis (TB) control. Loop-Mediated Amplification test for TB (TB-LAMP) has been successfully developed and should be evaluated as an alternative for sputum smear microscopy. The objective of this study was to evaluate the diagnostic performance of the TB-LAMP technology and to propose an algorithm for the diagnosis of pulmonary tuberculosis.

Methods: From 2013 to 2014, a prospective cross-sectional study was conducted in Antananarivo, Madagascar. Sputum samples from adults suspected pulmonary TB were assessed using TB-LAMP, GeneXpert MTB/RIF, acid-fast bacilloscopy (AFB) and solid culture. The sensitivity and specificity using solid culture as a standard reference were estimated and compared. Three algorithms for the detection of pulmonary TB were evaluated for TB diagnosis: the currently available method using smear microscopy, TB-LAMP as a replacement of smear microscopy, TB-lamp as an add-on test following a negative smear microscopy. Yield, sensitivity and specificity of each algorithm were calculated and compared.

Results: Data from 488 patients with all studied diagnostic tests results available upon the included 523 patients recruited were analyzed. The sensitivity of AFB (73.6% [95% CI: 67.0% to 79.6%]) was significantly different to TB-LAMP (84.6% [95% CI: 78.8% to 89.3%]) and GeneXpert (86.6% [95% CI: 81.1% to 91.0%]) sensitivities ($p < 0.001$ and $p < 0.001$ respectively). No significant difference were observed for the respective specificities of AFB (99.0% [95% CI: 97.2% to 99.8%]), TB-LAMP (98.4% [95% CI: 96.2%-99.5%]) and GeneXpert (97.4% [95% CI: 94.9% to 98.9%]). Using TB-LAMP following a negative smear microscopy increased the detection of MTB by 21.2% with a respective sensitivity and specificity of 88.1% (95% CI: 82.8% to 92.2%) 98.0% (95% CI [95.9%-99.2%]).

Conclusions: TB-LAMP as an add-on test of smear microscopy can be proposed as an early diagnostic tool to diagnose pulmonary TB.

SOA23-1229-27 Correlation between routine phenotypic drug susceptibility testing, MIC using Middlebrook 7H9 media and genotypic resistance in consecutive MDR-TB isolates from Sweden

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Background: Along with increasing multi- and extensively drug resistant tuberculosis (M/XDR-TB), it is essential that current drug susceptibility testing (DST) methods guide therapy correctly. Molecular methods identifying established resistance mutations are much faster than phenotypic (pDST) methods which are culture-dependent. Novel methods such as minimum inhibitory concentration (MIC) determination in Middlebrook 7H9 media (7H9) are promising and may give valuable clinical information on the level of resistance although DST breakpoints are yet to be defined. The aim of this project was to explore genotype-phenotype correlation using currently established methods and to investigate the additional value of MIC determination.

Methods: Consecutive MDR-TB isolates from 1994-2014 (n=153) were routinely subjected to pDST for first- and second line drugs at the supranational reference laboratory in Stockholm, Sweden. Next generation sequencing (NGS) data (Ion Torrent or Illumina) was analysed and a set of resistance genes were screened for pre-defined high-confidence mutations (gDST). Additionally, MIC determination (7H9) was performed and the reference strain H37Rv ATCC 27294 was included in each test round.

Results: The agreement between pDST and gDST was >95% (95-99%) for isoniazid (INH), rifampicin, ofloxacin, moxifloxacin (MOX), amikacin, kanamycin, capreomycin and linezolid, but lower for ethambutol (EMB; 66%) and ethionamide (76%). The MIC distribution for *inhA* C-15T was 0.2-1.6 mg/L (INH), 0.5-2 mg/L for *gyrA* A90V (MOX) and 4-16 mg/L for *embB* M306V (EMB) whereas it was 0.5-5 mg/L for EMB gDST and pDST wild-type isolates.

Conclusions: The correlation between routine pDST and gDST in MDR TB isolates was satisfactory for most first- and second line drugs. MIC determinations in 7H9

may be useful for personalised treatment of difficult cases, although variability needs to be monitored by strict quality control. For EMB, gDST may be more reliable than pDST using current breakpoints.

SOA23-1230-27 Correlation of *gyrA* mutations with minimum inhibitory concentrations of ofloxacin- and moxifloxacin-resistant isolates from India

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Background: WHO has recently recommended use of new generation Fluoroquinolones (FQs) instead of Ofloxacin (OFX) for treating multidrug MDR-TB. However, there is limited data on genetic mutations associated with *gyrA* gene and critical concentration of these drugs. Also there are no clear guidelines to distinguish between borderline, moderate-level and high-level phenotypic resistance for these drugs.

Methods: A total of 359 MDR-TB isolates (278 from PTB samples and 81 from EPTB samples) were screened for pre-XDR and XDR, using Genotype MTBDRsl/VER 1.0. Strains showing mutations in *gyrA* gene were further tested for minimum inhibitory concentration (MIC) using colorimetric redox indicator (CRI) assay. Resistance was defined, as MIC of ≥ 2.0 $\mu\text{g/ml}$ and ≥ 0.5 $\mu\text{g/ml}$ respectively for OFX and MOX, as per WHO guidelines.

Results: Of the 359 isolates, second line DST by MTBDRsl, 125 (34.8%) isolates revealed genetic mutations. Of these 108 (86.4%) had mutation in *gyrA* and 17 (13.6%) had mutations in both *gyrA* and *rrs* genes. Taking the cut-off of 2 $\mu\text{g/ml}$ for OFX the CRI assay showed 119 of 125 (95.2%) isolates were OFX^R and 6 (4.8%) were OFX^S. Similarly using the 0.5 $\mu\text{g/ml}$ cut-off value for MOX, 112 (89.6%) isolates were MOX^R and 13 (10.4%) were MOX^S. Only 14 MOX^S isolates had a cut-off value of 0.25-0.5 $\mu\text{g/ml}$. Isolates with D94G mutation were maximum [in 53 of 125 (40.3%)], indicating strongly association of this mutation with higher MIC (2.0-4.0 $\mu\text{g/ml}$) for OFX^R and (0.5-4.0) $\mu\text{g/ml}$ for MOX^R isolates followed by A90V 34 (25.7%) with variable MIC range (1.0-8.0) $\mu\text{g/ml}$ and (0.25-1) $\mu\text{g/ml}$ for OFX and MOX, respectively. MIC₅₀ and MIC₉₀ were 1 $\mu\text{g/ml}$ and 2 $\mu\text{g/ml}$ for MOX and 8 $\mu\text{g/ml}$ and 16 $\mu\text{g/ml}$ for OFX respectively.

Conclusions: There is an urgent need to revise the critical concentration for the fluoroquinolones and specially the Moxifloxacin, which is in use for treating the MDR TB.

SOA23-1231-27 Reduction of MDR-TB prevalence by 50% in Swaziland: results of the 2nd National Anti-Tuberculosis Drug Resistance Survey, 2017

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Background: In 2009, Swaziland conducted its first National Anti-TB Drug Resistance Survey (DRS) which provided exceptionally high estimates for Multi-Drug Resistant TB (MDR-TB) in the country at 7.7% among new cases and 33.9% in previously treated cases. Results from a repeat National anti-TB DRS conducted in 2017 show significantly lower estimates.

Methods: This cross-sectional national survey was undertaken from 01 April - 31 December 2017 and included 100% national sampling of all public health facilities that screen patients for TB. All peripheral laboratories that perform GeneXpert MTB/RIF testing as per the national diagnostic algorithm were included as enrolment centres of all newly diagnosed and previously treated patients diagnosed with pulmonary TB based on GeneXpert MTB/RIF during the study period and meeting the inclusion criteria (not currently on TB treatment). The study sample size was 1008 new bacteriologically confirmed TB cases with available culture results as all GeneXpert MTB positive cases were cultured and whole genome sequencing performed on all isolates. Data were analyzed using STATA.

Results: The new estimates for MDR-TB prevalence (by MGIT) among new cases in Swaziland is 3.7% (95% CI: 2.6- 5.2%) and 10.9% (95% CI: 6.2-17.3%) among previously treated TB cases. Discordance was noted between GeneXpert MTB/Rif and MGIT for rifampicin resistance among new cases at 5.5% (95% CI: 4.3-6.9%) and 4.3% (95% CI: 3.1-5.8%), respectively. Conversely, the prevalence of rifampicin resistance among retreatment cases was higher by MGIT than by GeneXpert MTB/RIF, 13% (95% CI: 7.9-19.8%) vs 11.6% (95% CI: 7.7-16.5%).

Conclusions: The current 2017 estimates of MDR-TB prevalence among new and retreatment TB cases in Swaziland are significantly lower than from the previous 2009 survey. This bodes well for TB control in the country. Results from whole genome sequencing will be used to investigate discordant results and associated mutations as well as the implications for TB control and laboratory diagnostics in the county.

SOA23-1232-27 Resistance of *M tuberculosis* to second line TB drugs in Tajikistan

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Background: Tajikistan is one of the 18 high priority tuberculosis (TB) countries in the WHO Euro region and among the 30 high-burden MDR-TB countries globally. According to WHO (WHO Global TB report, 2017), MDR-TB is estimated to be about 22% in new TB cases and 45% in previously treated cases, with no official estimates on XDR-TB levels.

Methods: In order to collect reliable information, required for accurate estimation of drugs and other needs for treatment and care of TB patients, the NTP of Tajikistan with GFATM funding, started a nationwide Drug Resistance Survey (DRS) to determine MDR- and XDR-TB prevalence. Technical assistance in DRS implementation was provided by the USAID TB Control Program.

Results: Second line drugs tests were done on 355 MDR-TB strains isolated during the DRS, including: Kanamycin (Km); Amikacin (Am); Capreomycin (Cm); and Ofloxacin (Ofx). Tests were performed by a phenotypic proportional method on solid LJ and MGIT media.

Proportion of resistant strains for individual drugs varies from 14.8% (Am) to 27.5% (Km) in new TB cases and from 18.1% (Am) to 32.4% (Ofx and Km) in previously treated cases. Among tested strains, XDR-TB was found in 12.2% (new) and 22.1% (previously treated).

Conclusions: High levels of resistance to second line drugs, resulting in high XDR-TB rates in both new and previously treated TB patients, is a serious threat for successful implementation of TB control activities in Tajikistan.

In order to prevent further spread of XDR-TB strains in the community, the NTP should identify priority actions to:

1. Strengthen capacity for rapid diagnosis of X/MDR-TB.
2. Rapidly start treatment regimens with new TB medicines with strict adherence to the TB diagnostic and clinical algorithms.

Implement effective measures for infection prevention and control to prevent transmission of infection with resistant strains.

Drug	tests- New cases	Resistant	%	tests- Treated	Resistant	%
Ofx	246	52	21.1%	105	34	32.4%
Km	247	68	27.5%	105	34	32.4%
Am	250	37	14.8%	105	19	18.1%
Cm	249	45	18.1%	104	27	25.9%

[Table. Resistance to second line drugs in Tajikistan revealed during the DRS 2016-2017]

SOA23-1233-27 Evaluation of the Omnigene reagent for long-term preservation of sputum for MGIT culture in Uganda

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Background: Mycobacteria Growth Indicator Tube (MGIT) culture is highly sensitive for isolation of TB from sputum and is mostly implemented in central or reference laboratories. To reach these facilities samples often require long transport time at room temperature (RT), resulting in increased contamination and loss of mycobacteria viability. Omnigene (OM) is a reagent to preserve sputum up to 8 days without cold chain but requires further evaluation.

Methods: Fifty smear-positive newly-diagnosed patients from Uganda submitted 2 to 3 sputum samples that were pooled to achieve 10ml final volume. Four aliquots were prepared and tested with microscopy to check for homogeneity. Two of the aliquots were inoculated in MGIT at date of collection (D0); one added with Omnigene and one after decontamination with 1% sodium hydroxide (NaOH). The remaining two aliquots were inoculated after 8 days (D8) of storage at room temperature, and treated as above; with Omnigene and 1% NaOH respectively. MTB culture yield and rate of contamination were compared between Omnigene and NaOH treated aliquots at each time point.

Results: Of 200 aliquots, 46% were $\geq 2+$ by microscopy: 24/50 (48%) and 21/49 (43%) among Omnigene treated aliquots at D0 and D8, and 24/50 (48%) and 23/50 (46%) among NaOH treated aliquots respectively. After exclusion of contaminated and NTM, Mycobacteria tuberculosis (MTB) was isolated in 21/50 (42%) and 21/49 (43%) Omnigene treated aliquots and 43/49 (88%) and 46/49 (94%) NaOH treated aliquots at D0 and D8 respectively. Only 1 (2%) contaminated and 1 (2%) NTM cultures were observed among NaOH treated aliquots at D0 and D8 respectively.

Conclusions: In this proof of concept study, we observed an important loss of MTB recovery by MGIT among the Omnigene treated aliquots. Optimization of the Omnigene reagent is needed before its use to preserve samples before MGIT culture.

SOA23-1234-27 Performance of microscopic observation drug susceptibility assay in the diagnosis of multidrug-resistant tuberculosis in regional laboratories of Peru, 2016

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Background: The microscopic observation drug susceptibility (MODS) is a rapid test used for the diagnosis of tuberculosis (TB) and multidrug-resistant tuberculosis (MDR-TB). In 2016, there were four regional reference laboratories (RRL) that performed this test: La Libertad, Arequipa, Lima Provincias and Callao. The objective of this research is to evaluate the performance of the MODS test in the four RRL in Peru, during 2016.

Methods: A total of 426 sputum samples were evaluated: 111 from La Libertad, 112 from Lima Provincias, 101 from Arequipa and 102 from Callao. Each RRL performed the culture by MODS assay and Lowenstein-Jensen to evaluate TB.

To determine the susceptibility to Isoniazid (INH) and Rifampicin (RIF), only the MODS assay was performed for each RRL, since the National Reference Laboratory for Mycobacteria (LRNM) perform the proportion method in Middlebrook 7H10. Sensitivity (S), specificity (E) and predictive values (PPV and NPV) were calculated for the detection of MTB and susceptibility to INH, RIF and MDR for each RRL

Results: Sensitivity, specificity, VPP and VPN for the detection of MTB was 100% for Arequipa and Callao LRR. The results of La Libertad and Lima Provincias LRR were 99%, 100%, 99%, 95%; and 85%, 96%, 98% 71%, respectively. The results of the evaluation for INH and RIF susceptibility and MDR-TB detection are described in Table 1.

RRL*	RIF [†] (%)	INH [‡] (%)		MDR-TB [§] (%)	
		0.2 ug/ml	1.0 ug/ml	0.2 ug/ml	1.0 ug/ml
La Libertad					
No. of samples (% Rt)	80(5)	80(21)	80(18)	80(5)	80(5)
Sensitivity %	100	88	100	100	100
Specificity %	100	100	98	100	100
PPV [¶] %	100	100	93	100	100
NPV [¶] %	100	97	100	100	100
Callao					
No. of samples (% Rt)	64(17)	65(15)	65(12)	66(12)	65(9)
Sensitivity %	91	80	100	75	100
Specificity %	100	100	100	100	100
PPV [¶] %	100	100	100	100	100
NPV [¶] %	98	96	100	97	100
Lima Provincias					
No. of samples (% Rt)	65(20)	65(25)	65(22)	65(19)	65(17)
Sensitivity %	92	87	100	92	100
Specificity %	100	100	100	100	100
PPV [¶] %	100	100	100	100	100
NPV [¶] %	98	96	100	98	100

*Regional Reference Laboratory; [†]Rifampicin; [‡]Isoniazid; [§]Multidrug resistant tuberculosis; [¶]Positive predictive value; [¶]Negative predictive value; [¶]resistant percentage

[Table 1: Performance of MODS assay for detecting isoniazid and/or rifampicin susceptibility in sputum samples by Regional Reference Laboratory in Peru, 2016]

The results for Arequipa LRR are not presented since no strains resistant to rifampicin were detected. Finally, the average time in days for the emission of results was 11 for all samples with smear-positive and 13 for samples with smear-negative

Conclusions: The results of the present study indicate that the MODS assay performed by LRR is a rapid and adequate test for the detection of TB and MDR TB. Likewise, the quality of the test depends on the experience of the laboratory professionals who perform it.

SOA23-1235-27 Implementation of Universal DST in a Tertiary care TB hospital in Sindh province

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Background and challenges to implementation: Pakistan is high TB and DR-TB country. Drug resistance survey was conducted in smear positive PTB cases in 2012-13 and proportion of Rifampicin Resistance (RR) was estimated at 4.2% in new and 18.0% in re-treatment PTB cases. National DRTB case load was estimated based on this estimates for all type of new PTB cases. With scale up of Xpert testing, algorithm was expanded to screen all notified TB cases at start of treatment.

Intervention or response: Universal DST started at the end of 2015 and implementation started from health facilities having onsite testing facility. In the very first year among new PTB cases, 96% of sm +ve PTB were screened compared to 19.3% of clinically diagnosed PTB which increased to 89. % next year. High number of re treatment cases were screened (93%,100%) in contrast to EPTB cases.

		TB Patient Notified	TB Patient screen for RR	TB patient - MTB+ve	RR TB patient detected
NEW Sm+ve PTB Cases	2016	1271	1224 (96.3%)	1218 (99.5%)	56 (4.6%)
	2017	1630	1629 (100%)	1629 (100%)	67 (4.1%)
New Sm-ve PTB Cases	2016	1068	206 (19.3%)	40 (19.4%)	1 (2.5%)
	2017	1315	1173 (89.2%)	76 (6.5%)	1 (1.3%)
New EPTB	2016	554	56 (10.3%)	8 (14.3%)	0 (0.0%)
	2017	501	60 (12.0%)	2 (3.3%)	0 (0.0%)
Re-treatment TB cases	2016	515	480 (93.2%)	477 (99.4%)	70 (14.7%)
	2017	813	813 (100%)	813 (100%)	72 (8.9%)

[Universal DST and prevalence of drug resistance in New and previously treated TB cases]

Results and lessons learnt: Among new PTB cases, proportion of RR in sm+ve PTB cases was 4.6% in 2016 and 4.1% in 2017. Among clinically diagnosed cases, proportion of MTB+ve was 19.4% and 6.5% of those tested and RR detected was 2.5%, 1.3% in 2016 and 2017. RR in re-treatment cases declined from 14.7% in 2016 to 8.9% in 2017. No drug resistance was detected in small proportion of EPTB cases tested.

Conclusions and key recommendations: Proportion of RR in new sm+ve cases is close to that reported in DRS. A decline noted in proportion of RR in re-treatment cases is most likely an impact of universal DST. Only a small number of clinically diagnosed were MTB positive on Xpert and proportion of RR was lower than in sm+ve cases. There is need to implement and scale up Universal DST and strengthen system for surveillance of drug resistance for true estimation of burden of drug resistance in all forms of TB.

SOA23-1236-27 Mumbai: a step ahead in implementing universal drug susceptibility testing

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Background and challenges to implementation: Universal Drug Susceptible testing has been implemented in India from 1st Jan 2018. UDST is important to devise optimal regimens for patients with Multi Drug Resistant. Mumbai with 28 CBNAAT Machines has already rolled out UDST to all the TB Patients from 2017 and providing upfront CBNNAT test to Key Population started from 2016.

Intervention or response: Mumbai implemented UDST in 2017 to all the TB diagnosed patients

Results and lessons learnt: There is a sharp increasing trend in the total CBNAAT Sample tested at Public sites of Mumbai. In 2014, 2015, 2016 and 2017, total 13243, 20513, 39303 and 72067 (444% increase as compared to 2012) CBNAAT samples were tested by public sector CBNAAT lab respectively. From 2015, CBNAAT sites are providing diagnostic services to the private sector patients also. In 2015, 2016 and 2017 total 226, 1784, 9438 samples were referred from private sector respectively. In 2018 Mumbai is expected to test more than 1.2 lakh samples on CBNAAT machines and among these 24000 are expected to be private sample referral.

In 2016, out of 39303 CBNAAT samples tested, 25717 samples were from MDR suspects whereas in 2017, Out of 72067 CBNAAT samples tested, 58133 (126% increase) samples were from MDR suspects. This increase in MDR suspect samples during 2017 is due to inclusion of New and Retreatment TB cases in MDR Suspects

Conclusions and key recommendations: Mumbai has already taken a lead in implementing UDST without additional human resources. To expand this services further and to maintain this expansion there is an urgent need for additional CBNNAT Machines or provide 16 module CBNAAT machines along with additional human manpower.

SOA23-1238-27 Slide fixing and referral improved access to diagnosis: experiences of Oromia Region in Ethiopia

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Background and challenges to implementation: Ethiopia is among high burden country missing 40% of cases. NTP has decentralized diagnostic units to 3,808 health facilities in Ethiopia. Oromia region accounts for 1,412 diagnostic health facilities. However, due to high staff turnover and lack of laboratory professionals about 25% facilities do not provide AFB services. Therefore, alternative mechanisms to increase case finding are crucially important. We present results from the experience of using community health extension workers in slide referral in remote and rural Oromia region.

Intervention or response: Oromia Regional Health Bureau in collaboration with Challenge TB Ethiopia has designed a strategy to improve the diagnostic coverage implementing slide referral in facilities where there is no lab professional. We trained health extension workers in the rural communities, two non-laboratory health workers from each facility about slide preparation and referral and linked them with referral site in the districts. Health extension workers identified presumptive cases, collected sputum and prepared slides. The slides were referred to diagnostic units for examination.

Results and lessons learnt: From January - December 2017, slide fixing and referral was implemented in three zones of Oromia region. Health extension workers identified 3,420 presumptive TB cases in the communities. Slide fixing was done by trained health workers and referred to referral sites. Of 3,420 presumptive cases, 138 were smear positive with smear positivity rate of 3.8%.

Quarters	Presumptive cases	total # slide collected and examined	# of smear positive cases	Smear Positivity Rate
Jan - June, 2017	410	817	38	9.2%
Jul - Dec, 2017	3010	5993	100	3.1%
Total	3,420	6,810	138	3.8%

[Bacteriologically smear positive TB cases identified through sputum smear fixing and referral in Ethiopia]

Conclusions and key recommendations: Slide fixing and referral is feasible option for health facilities that do not have laboratory professionals. This alternative is crucially important to reach missed people with TB and could be scaled up with minimal investment.

SOA23-1239-27 Comparison of one-month storage of sputum in CPC, ethanol and OMNIgene•SPUTUM for molecular analyses

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Background: In resource-limited countries, molecular analyses are not available in peripheral laboratories, and samples are shipped to remote reference laboratories. Logistic constraints can delay the time between specimen collection and analysis, negatively impacting the results. We aimed to compare cetyl-pyridinium chloride (CPC), ethanol and OMNIgene.SPUTUM (DNA Genotek) for storage of sputum at ambient temperature (RT) for one month, before molecular analyses for tuberculosis (TB).

Methods: Three smear-positive sputa were collected from each patient. Each of the three sputa were stored at RT for 28 days with an equal volume of either 1%-CPC, ethanol or OMNIgene. At day 28, the stored sputa were centrifuged at 3800 g and the pellet was resuspended with distilled water. Part of the sediment was used for GeneXpert MTB/RIF, while another part was used for *rpoB* nested PCR after DNA extraction using the semi-automated Maxwell tissue DNA purification kit (Promega). The *rpoB* nested-PCR consists of two runs of conventional PCR followed by electrophoresis of PCR products on 2%-agarose gel.

Results: RT ranged from 26.0 to 30.9°C (average 28.5°C). Among 60 patients, GeneXpert positivity was 96.7% (58) for ethanol-preservation, 98.3% (59) for CPC, and 98.3% (59) for OMNIgene ($p=1$). The bacterial burden among the 58 GeneXpert-positive samples was highest for ethanol, then CPC, and then OMNIgene; with respectively 65.5% (38), 55.2% (32), 53.4% (31) with a 'high' bacillary load according to GeneXpert classification (ethanol-CPC $p=0.21$, ethanol-OMNIgene $p=0.143$). Conversely, the *rpoB* PCR positivity was higher for OMNIgene preserved sputa (96.7% versus 90.0% for CPC ($p=0.125$) and 88.3% for ethanol ($p=0.063$)).

Conclusions: The performance of CPC, ethanol and OMNIgene for 28 days' storage of sputum is excellent, and not significantly different either for subsequent GeneXpert or conventional PCR. The performance of these solutions for preservation of paucibacillary (microscopy-negative) specimens should be further investigated.

E-POSTER SESSIONS

EP07 Innovations in capacity building and translating evidence to policy

EP07-161-27 Claiming the right to good health by children: Rose campaign for tobacco free educational institutions

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Background and challenges to implementation: Tobacco use is a major threat for children and acknowledged as a pediatric disease. As per Global Adult Tobacco Survey reports 2010 and 2017 (GATS), prevalence of tobacco use in Indian state of Karnataka has reduced from 28.2% to 22.8%. The mean age of tobacco use initiation has also increased from 17.7 yrs to 19.8 yrs. It shows increased level of awareness among the children about harms of tobacco use.

Further section 6(a) of Indian Tobacco Control Law (COTPA 2003) prohibits sale of tobacco to and by minors and section 6b prohibits the sale within radius of 100 yards of educational institutions.

Intervention or response: Udupi district administration along with department of health, public instruction and education, conducted unique outreach program (Rose Campaign) to sensitize tobacco sellers around all educational institutions by involving sensitized school children. In this campaign approx. 4500 students, teachers, government officials and local political leaders had visited over 500 shops. The children gave a rose to the tobacco seller with an appeal to stop tobacco sale to minors. IEC materials on harm effect of tobacco and the law's provisions were also handed over to sensitise them.

Subsequently, on the basis of third party scientific compliance survey entire districts has been declared high complaint to section 6 (a and b) of COTPA.

Results and lessons learnt: As per impact assessment study, 85.8% (n=343 shops) voluntarily stopped sale of tobacco products. In discussion, the sellers who continued sale of tobacco shared that demand for tobacco products also reduced drastically.

Conclusions and key recommendations: Involving students to eliminate tobacco sale in and around educational institutions has multiple benefits. In addition to their own sensitization, their emotional appeals to sellers have strong impact. It would give sustained result with regards to eliminating tobacco sale to youths and protecting public health in long term.

EP07-162-27 Possibilities to eliminate tobacco cultivation: a case study from Karnataka, India

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Background and challenges to implementation: Article 17 and 18 of WHO's Framework Convention on Tobacco Control mandates Parties to adopt strategies for alternative farming for tobacco growers. The Indian state of Karnataka has shown its commitment in tobacco control. However Karnataka is also the second largest tobacco growing state India. The registered tobacco growers in the state have more than doubled has grown by 222.59% (from 18751 to 41737) and the area under tobacco cultivation has increased by 269.72% (from 29852 hectares to 80516 hectares) from in 2001 and 2016.

Intervention or response: Since 2015, Karnataka has adopted supply reduction measures of tobacco crop in a phased manner. The Department of Agriculture and Horticulture in collaboration with The Tobacco Board has piloted a project to help shift tobacco growers to alternative crops and adopt new cropping patterns. It has undertaken sensitization of farmers to adopt alternative cropping, provided access to soft loans from banks, free soil testing, drip irrigation, subsidized fertilizer, among other incentives; and have linked them to Horticultural Producers' Co-operative Marketing and Processing Society Ltd. (HOPCOMS) to ensure market for grown products.

Results and lessons learnt: In Hunsur block of Mysore 1000 tobacco growers have voluntarily stopped tobacco farming and have adopted alternate crops. Given the early success of the pilot project, The Government has scaled up the intervention from current 250 hectares to 4500 hectares, covering other four blocks in three tobacco growing districts.

Conclusions and key recommendations: Tobacco farmers are ready to shift to other crops or cropping patterns but need guidance and support from Government. Farmers realize that there is limited future in tobacco cultivation due to variability in rain and declining fertility of soil which they attribute to monocropping of tobacco; and more importantly an increasing awareness among the public (and growers) on the harms of tobacco use.

EP07-163-27 Emotional, behavioral problems and cigarette smoking behavior: a survey among Bangladeshi adolescents

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Background: Adolescent is a stage of significant growth and potential and experiencing a time of great risk as well, as most adolescents are facing pressures to use alcohol, cigarettes or drugs. There is limited data from Bangladesh regarding emotional and behavioral problems among adolescent smokers. The general objective of the study was to examine the association between adolescents' cigarette smoking behavior and their emotional and behavior problems.

Methods: A survey was conducted among 724 students aged 10-19 from the districts of Dhaka and Comilla. Respondents were gathered using a questionnaire where the emotional and behavioral status of the respondent was assessed from the self-reported Bangla version of Strength and Difficulties Questionnaire (SDQ) developed by Goodman, Meltzer & Baily (1998). Data were analyzed through descriptive statistics in terms of frequency distribution, percent, mean, standard deviation and inferential statistics were used to conduct correlation and examine association.

Results: Among all the respondents 6.4% were found to be current smokers whereas 2.8% reported that they smoked irregularly. Males were more likely to smoke than female ($p < 0.001$). The current smoking status of smoking status of respondents was significantly associated with their parents' education, occupation and family members' smoking status ($p < 0.005$) Age, gender, father's smoking status and family awareness activities about bad effect of smoking and SDQ total difficulties score were independently associated with adolescents' smoking. Also, after adjustment for several selected covariates, scores on conduct problems were associated with greater likelihood for smoking (OR=1.51; 95% CI: 1.23-1.85).

Conclusions: Findings of present study support the association between emotional, behavioral problems and smoking behavior of adolescents. Addressing the adolescents' need regarding their mental health could be helpful in designing and implementing effective interventions in the school environment and elsewhere for preventing or combating adolescents' cigarette smoking during this critical period of life.

EP07-164-27 The need to improve smoking cessation services provided to pregnant smokers in Greece

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Background: There is a considerably high percentage of smokers in Greece during the reproductive age. Smoking and second hand smoke exposure during pregnancy leads to various unfavorable pregnancy outcomes.

Methods: The aim of our research was to study the smoking status of pregnant women in Greece and also their exposure to second hand smoke. The research incorporated a structured questionnaire which was filled out by 900 pregnant women. It was conducted between May 2016 and March 2018 in two public Maternity hospitals in Athens, Greece.

Results:

- Despite 54.9% of women undergoing a planned pregnancy, 45.1% of them reported having entered pregnancy as active smokers.
- Also, 16.8% of all women reported having continued to smoke during pregnancy.
- 76.6% of the pregnant smokers reported having considered quitting and 70.9% of them did in fact attempt to quit.
- 70.7% of them reporting being aware of the existence of smoking cessation clinics. Yet, 10.7% of them reported that they had actually wanted to visit such clinics.
- Moreover, only 4.2% of the pregnant smokers eventually did reach out to a health professional specially trained in smoking cessation.
- Only 24.1% reported having been actively supported by their partner and family in their attempt to quit smoking.
- 87.3% of pregnant women reported having been exposed to second hand smoke.
- 62.9% reported trying to refrain from visiting places where they were exposed to second hand smoke.

Conclusions: It is observed that a significant percentage of women actually entered a planned pregnancy being active smokers. Most of them also didn't manage to quit throughout their pregnancies. This is a result firstly of poor information and help received during family planning by health care professionals and secondly of lack of Smoking cessation clinics inside maternity hospitals in Greece.

EP07-166-27 Trend of illicit cigarette use in Tehran: an experience from third pack survey in Tehran, 2018

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Background: Iran and Iraq are the two main target markets for tobacco smuggling in the Eastern Mediterranean Region. Two cigarette pack surveys in Tehran, were done in 2009 and 2015 which were showed that illicit cigarettes used rate were 20.9% and 15.4% respectively. We designed this study to update trends in the illicit cigarette trade in Tehran.

Methods: A cross-sectional study of 2331 smokers aged 15 years and over was conducted in Tehran in January 2018. The sampling method was the same as previous studies. Smokers were asked to show the interviewers their current pack of cigarettes, which was categorised as either: (1) legal cigarettes: displaying governmental pictorial warning and hologram or (2) illegal cigarettes: with no governmental labeling. The packs were also categorised as either domestic (a Persian brand name) or foreign (a foreign brand name).

Results: The sample included 1827 males (78.3%) and had a mean age of 40.3±12.1 years. In total, 1427 smokers (61.2%) had foreign and 904 (38.8%) had domestic cigarettes; 2072 (88.9%) had legal cigarettes and 259 (11.1%) had smuggled cigarettes. There was a statistically significant difference in the use of smuggled cigarettes and foreign cigarette by younger smokers (36.8±3.1vs 42.9±5.3 years) ($p < 0.001$). Marlboro was the only smuggled cigarette brand (259 packs; 100%).

Conclusions: The lower prevalence of illicit cigarettes in Tehran in 2018 compared to previous studies may be due to the control and monitoring on legal cigarettes distribution. All other foreign cigarette brands except Marlboro were imported legally or had legal joint production.

EP07-167-27 Knowledge of Nigerian smokers on health effects of tobacco smoking and their quit attempts: evidence from Global Adult Tobacco Survey (GATS) 2012

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Background: Offering help to tobacco users to quit is one of the six MPOWER strategies for ending the tobacco epidemics. Young tobacco users have expressed desire to quit but the addictive nature of nicotine, peer influence and not knowing the adverse health effects of tobacco has made quitting tobacco difficult for smokers.

This study was conducted to determine the relationship between knowledge of the health effects of tobacco smoking and quit attempts among smokers in Nigeria.

Methods: Data from the 2012 GATS survey in Nigeria was analysed. The dataset examined tobacco use in a nationally representative sample of 9,765 non-institutionalized men and women 15 years and older. A subset of 429 current smokers aged 15-79 years was analysed for this study.

Logistic regression was used to determine association between knowledge of health effects of smoking (first hand and ETS) and smokers quit attempt.

Results: The prevalence of tobacco use was 4.4%. Mean age of tobacco users was 39.4 years (SD=13.7). Majority (95.4%) were males and literate (63.9%). About three quarter 76.5% initiated smoking at ≥18years and 75.7% smoked daily. In the last 12 months, 40.6% had attempted to quit smoking. Knowledge of health effects of smoking and ETS were found to be good in 16.6% and 30.1% respectively. Smokers with good knowledge on health effects of ETS had 2.5 higher odds (95% CI=1.4-4.7), those with good knowledge of health effects of first hand smoking had 2.7 higher odds (95% CI=0.9-8.0), and those with good knowledge of first hand smoking causing lung cancer had 3.2 higher odds (95% CI=1.6-6.2) of attempting to quit tobacco smoking.

Conclusions: Cessation counseling session should help improve knowledge on the health effects of smoking.

EP07-168-27 Quit attempts and cessation services utilization among tobacco smokers in Nigeria: analysis of Global Adult Tobacco Survey (GATS) 2012

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Background: World Health Organization (WHO) Framework Convention on Tobacco Control (FCTC) article 14 has advocated for provision of cessation services in treatment of nicotine dependence. Nigeria, a developing country however lacks structured cessation services within the health system. This study was therefore conducted to assess the utilization of the available unstructured services among smokers with quit attempts in Nigeria.

Methods: The 2012 GATS dataset was used for this study. A nationally representative sample of 9,765 non-institutionalized men and women 15 years and older were chosen using a multi-stage sampling. The GATS survey obtained information on respondents' use of tobacco. The current smokers who reported quit attempts were further analysed using SPSS version 23.

Results: The prevalence of tobacco use was 4.4%. Mean age of current tobacco users was 39.4 years (SD=13.7). Majority (71.8%) resides in the rural areas and 75.7% re-

ported daily smoking of tobacco. In the last 12 months, 40.6% had attempted to quit smoking. About 17.5% sought any appropriate form of cessation services while 57.6% did not seek any form of assistance. Services sought included counseling (14.7%), nicotine replacement therapy (2.7%), smokeless tobacco of smoking (1.6%) while use of quit helpline was not utilized any one. Traditional medicine was used by 5.4% of those who reported quit attempt.

Conclusions: Smokers with quit attempt are willing to utilize the skeletal and unstructured cessation services available in Nigeria. Hence efforts at making a wide variety of cessation services available in Nigeria should be intensified. The non-utilization of quit helpline could be due to the non-availability of the service. It could also be an indication for developing culturally sensitive services especially in the rural area where majority of current smokers reside.

EP07-169-27 Deglamorizing smoking among young people through social media

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Background and challenges to implementation: Social media has become popular among the youth all over the world. Majority of young people use social media such as Facebook, Instagram, WhatsApp, Twitter, Email to exchange information as a powerful method in communicating.

Tobacco industry also takes the advantage from the above fact in promoting their products through social media. This is the most powerful and cost effective way for them to promote their products among the young people. We used this strategy to address the youth against the industry promotions and spread the ideas of tobacco prevention. This is a new concept in the prevention work compared to the different approaches we used before. The aim of this study was to explore the myths disseminated by tobacco industry through the social media.

Intervention or response: The posts and videos which glamorize tobacco use among youth were observed and identified. We created the similar type posts and videos which deglamorize the tobacco use. Further we created prevention messages in accordance to the Facebook trends from time to time.

The same prevention messages were distributed to administrative persons of the youth targeted websites in Sri Lanka. Requests were made to publish them regularly. Special posts were created targeting special days such as Valentine's Day, fathers 'day, Fool's day, laborers' day to enhance youth.

Results and lessons learnt: The Facebook posts we created during the time period from 2016 - 2017 June has received 2000- 20000 reaches while it has resulted in de-

veloping an argument among social media users regarding tobacco control. Specially created posts were shared in Facebook groups, pages and the personal profiles. Our Facebook videos received a vast coverage even by the television channels by telecasting them for free of charge.

Conclusions and key recommendations: Social media campaign is an effective way of tobacco control.



[Facebook posts]

EP07-170-27 Evaluation of different strategies (pharmacologic intervention vs. enhanced motivation vs. standard motivation) for smoking cessation in TB patients under treatment in the RNTCP, India

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Background: In India TB burden is still high, and smoking prevalence among males has increased. It has been found that higher relapse, increased morbidity, mortality (4 times) in smokers with TB. Objective of the study was to compare the effectiveness of pharmacologic therapy (Bupropion SR) versus enhanced counseling package in smoking cessation among TB patients initiating treatment, under program settings in India.

Methods:

Study design: Cluster randomized effectiveness trial.

Study setting: Villupuram and Kancheepuram RNTCP centres; Study population were TB patients and current smokers, Total Sample size=600.

Study procedure: Thirty six Direct Microscopic Centres (DMC) from two districts - Villupuram and Kancheepuram were randomly selected (cluster randomization) to receive T1 -Bupropion SR along with Standard counseling, or T2 -Enhanced Counseling arm including provisions of Educative materials on smoking cessation, Flip charts presentation, posters display, Video presentation or C - Standard routine counseling/Control arm, so that each TB patient who are current smokers enrolled to the study receives the intervention allotted to that study centre. Smoking cessation was assessed by self reporting and confirmed by Carbon monoxide monitors. It was done at 0, 2 and 6th month/end of ATT. TB outcome recorded at 6th month/end of ATT for these patients from RNTCP registers.

Results: A total of 517 patients were enrolled to the study, all were males. Of the total n=383 subjects for whom the quit status is available, the proportion of patients who have quit smoking in Drug, Enhanced and Standard arm at the end of TB treatment was 67%, 83% and 51% ($P < 0.05$).

Conclusions: Study finding suggests enhanced counseling as well as drug therapy, namely Bupropion are effective strategies for smoking cessation for TB patients treated in TB program. We recommend both strategies to be implemented in the TB program for TB patients who are smokers.

Final Status of smoking habit	Patients randomised to treatment arm			Total n (%)
	Bupropion n (%)	Enhanced Counselling n (%)	Standard Counselling n (%)	
Quit smoking	81 (66.9)	96 (82.8)	75 (51.4)	252 (65.8)
Still smoking	40 (33.1)	20 (17.2)	71 (48.6)	131 (34.2)
Total	121 (100)	116 (100)	146 (100)	383 (100)

[Table 1. Quit status among the TB patients given different strategies for smoking cessation at RNTCP centres in Villupuram and Kancheepuram districts,]

EP08 Innovations in tuberculosis—across the care cascade

EP08-171-27 Quantitative culture results predict treatment response and guide infection control during the first 14 days of therapy

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Background: Monitoring tuberculosis (TB) treatment response is important to confirm adequate therapy, identify those at risk of adverse outcomes, and to inform infection control.

Objective: To assess the utility of available tools during early treatment for pulmonary TB in Callao, Peru.

Methods: Between 2014-2015, before and after the first 14-days of DOTS treatment (D14), patients were weighed, interviewed and were requested to provide sputum for the number of acid-fast bacilli (AFB) in microscopy, colony-forming units (CFU) and time to positivity (TTP) in culture and GeneXpert PCR cycle times (CT). Patients (N=355) and their household contacts (N=1646) were followed for 2 years to determine clinical outcome and secondary TB disease.

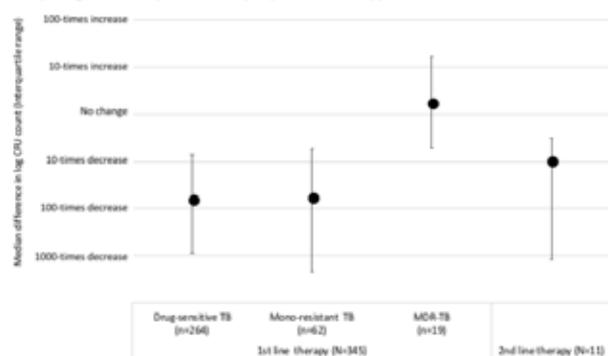
Results: Sputum culture from patients taking first-line therapy with drug-susceptible TB demonstrated that CFU counts decreased by median 63-times and TTP increased by median 14-days (n=264, both $p < 0.0001$), whereas AFB and CT had minor changes by D14. Changes in culture were similar between these patients versus those later found to have mono-resistance to isoniazid/rifampicin (n=62, $p=0.9$, Figure). However, no change was seen in culture results for those taking first-line therapy but later found to have multi-drug resistance (n=19, $p>0.3$). In patients with drug-susceptible TB, 2.3% (6/264) died, treatment failed or had disease recurrence, which was associated with appetite loss ($p=0.03$) or debilitating cough ($p=0.01$) at D14.

Microbiologically-confirmed secondary TB was diagnosed in 43 (2.6%) contacts. At D14, microscopy positivity did not predict secondary TB (odds ratio, OR=1.9, 95% confidence interval, 95% CI=0.9-3.8, $P=0.1$), and nor did GeneXpert (OR=1.1, 95% CI=0.5-2.5, $P=0.9$). However, contacts of patients who did

not have >10-times decrease in CFU at D14 were more likely to develop TB disease in analysis adjusted for pre-treatment AFB count, adherence and chemoprophylaxis (OR=2.3, 95CI=1.1-4.7, P=0.03).

Conclusions: If taking correct therapy, during the first 14-days culture results and clinical symptoms predicted patient outcome and infection control, whereas conventional sputum microscopy and GeneXpert results did not.

Graph showing changes in sputum mycobacterial concentration over the first 14-days therapy, calculated as the reduction in tuberculosis colony-forming units (CFU) cultured from sputum after 14 days therapy minus the corresponding result for that patient on the day they commenced therapy.



[Figure]

EP08-172-27 Sampling strategies for therapeutic drug monitoring of moxifloxacin with and without rifampicin in tuberculosis patients

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Background: Therapeutic drug monitoring (TDM) of moxifloxacin has been recommended to increase treatment outcomes, since moxifloxacin exposure shows large interindividual variability and is influenced by a clinically relevant drug-drug interaction with rifampicin. To reduce the burden of TDM, drug exposure can be adequately estimated using a small number of appropriately timed samples. This study aimed to develop sampling strategies for moxifloxacin alone (MOX) and together with rifampicin (MOX+RIF) in TB patients using a Bayesian approach as well as multiple linear regression.

Methods: Three datasets of moxifloxacin pharmacokinetic curves in TB patients were included in this study (n=101). A population pharmacokinetic model and sampling strategies using a Bayesian approach were de-

veloped for MOX (n=77) and MOX+RIF (n=24). Sampling strategies using multiple linear regression were developed as well for MOX and MOX+RIF. Jack-knife analyses were used for validation. Only clinically suitable sampling strategies (1-3 samples) were tested.

Results: Moxifloxacin exposure was non-clinically relevant underestimated in the models of MOX (-5.1%, SE 0.8%) and MOX+RIF (-10.2, SE 2.5%). Moxifloxacin exposure was adequately estimated with the Bayesian approach using 0 and 5 h post-dose samples for MOX (-0.4%, SE 1.3%) and t=0 and 6 h samples for MOX+RIF (-5.5%, SE 3.1%). The sampling strategies using multiple linear regression used 0 and 4 h post-dose samples for MOX (n=66) and t=1 and 6 h samples for MOX+RIF (n=14), showing a mean underestimation of -0.2%, SE 1.3% and mean overestimation of 0.9%, SE 2.1%, respectively.

Conclusions: In this study, we successfully developed four sampling strategies, i.e. Bayesian approach (MOX t=0 and 5 h, MOX+RIF t=0 and 6 h), and with multiple linear regression (MOX t=0 and 4 h, MOX+RIF t=1 and 6 h). All described sampling strategies are suitable to be implemented in clinical practice to facilitate TDM of moxifloxacin in TB patients.

EP08-173-27 Safety of recombinant fusion protein CFP10-ESAT6 (RP22) as a skin test reagent for tuberculosis diagnosis: a randomised, double-blind, single-centre Phase I clinical trial

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Background: This phase clinical trial was conducted to explore the safety dose of recombinant fusion protein CFP10-ESAT6(RP22) as a skin test reagent for the diagnosis of *Mycobacterium tuberculosis* infection.

Methods: We use randomized, double blindness, placebo control design, 72 healthy adult volunteers with negative chest X-ray results were recruited and randomized into six groups (groups A to F), all of them received QuantiFERON-TB Gold(QFT) test.

There were 12 subjects in each group, 8 cases of each group received the experimental drug, and 4 cases received placebo (both the ratio of male to female were 1:1). experimental drug was RP22, placebo was normal saline. the concentration of RP22 in the six experimental groups increased gradually, which were 0.1ug, 0.25ug, 0.5ug, 1ug, 2ug and 5ug respectively.

All subjects in each dose group received an intradermal injection of reagent (0.1 ml) via the Mantoux technique, the vital signs of all subjects were monitored then, and

skin reactions around injection sites and adverse events were recorded at different detection time points after the skin test.

Results: There were ten subjects had positive QFT results, of the ten subjects, eight had flush larger than 30mm, other two subjects had no skin reactions. Only one subject had flush larger than 30mm in the 62 negative QFT subjects. No serious adverse events were observed in all the groups, except one subject had a slight accident 72 hours after skin test, which had no correlation with the skin test.

Eight subjects in group F had unexpected flush after the skin test, all the red spots disappeared 30min after the skin test, we considered it related to the high concentration of drug.

Conclusions: A single dose of 0.1ug, 0.2ug, 0.5ug, 1ug, 2ug/ml of RP22 as a skin test reagent for *M. tuberculosis* infection diagnosis is well tolerated and safe in China.

EP08-174-27 Genetic diversity of MDR *Mycobacterium tuberculosis* isolates circulating in Cuba, 1995-2014

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Background: Cuba is one of the countries with lowest tuberculosis (TB) incidence rates in the world and the multidrug-resistance (MDR) is rare. However, limited information about the genetic variability of MDR *Mycobacterium tuberculosis* isolates circulating in this archipelago is available.

The objective of this study was to know the genetic diversity of MDR *M. tuberculosis* isolates obtained in Cuba in the time period 1995-2014.

Methods: Spacer oligonucleotide typing (Spoligotyping) was applied to 54 MDR *M. tuberculosis* isolates (representing 65.47% of total isolates) from the period 1995-2014. Classification into spoligotypes was carried out according to the international databases SpolDB4 and SITVIT2. Results were additionally analyzed with the online tool MIRU-VNTR^{plus} and also compared with the *M. tuberculosis* genetic patterns found in Cuba (1993-2014).

Results: Nineteen different spoligo patterns were observed, and two (3.7%) were absent in SpolDB4-SITVIT2. The three most common sub-lineages were Beijing (29.6%), LAM (26.0%), and T (20.3%), representing 76% of the studied isolates. The most frequent types (SIT) were SIT1(Beijing), SIT42 (LAM9) and SIT53 (T). Higher genetic diversity was seen in the years with larger quantity of isolates (period 2008-2014). Havana, Havana City and Guantanamo were the provinces with higher number of isolates and sub-lineages.

Conclusions: High genetic diversity was observed among the MDR *M. tuberculosis* isolates circulating in Cuba in the time period 1995-2014, indicating the MDR-TB transmission is a rare phenomenon in this country and giving some elements of the success of the TB program. The most prevalent sub-lineages found here have been previously associated to MDR-TB isolates in other regions, suggesting some facilitating factors of these sub-lineages. The increase of MDR-TB isolates in the period 2008-2014, may be an alert of some failures of the TB program in Cuba.

EP08-175-27 Chronic respiratory symptoms and lung abnormalities among people with a history of TB in Uganda: a national cross-sectional analysis

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Background: People with pulmonary tuberculosis (TB) are at higher risk of developing chronic respiratory disorders due to lung damage. However, the scope of the problem in high burden TB countries is relatively unknown.

Methods: Chronic respiratory symptoms (defined as cough and phlegm >2 weeks) and radiological lung abnormalities were compared between adults with and without a history of TB in 70 villages of Uganda. Data came from the national TB prevalence survey conducted in 2014-2015 and excluded people with active TB disease. Multivariable regression models were used to estimate odds ratios with adjustment for age, gender, smoking, education, setting and region. Random effects models accounted for clustering effect within villages. Population attributable risk fractions were calculated using standard formulas.

Results: Among 45,089 surveyed participants, 4,140 (9%) were excluded due to missing data. A total of 798 out of 40,949 (2%) people had a history of TB and among them, 16% had chronic respiratory symptoms, 41% had radiological lung abnormalities and 9% had both. Lung abnormalities and respiratory symptoms

were highly correlated ($p < 0.0001$). Adjusted odds ratios showed strong evidence for individuals with a history of TB having increased risk of respiratory symptoms (OR=4.02, 95% CI:3.25-4.96) and lung abnormalities (OR=17.52, 95% CI:14.76-20.79). Other risk factors were older age and smoking for both outcomes, and male gender for lung abnormalities. A history of TB attributed an estimated 6% and 24% of the population risk of respiratory symptoms and lung abnormalities, respectively.

Conclusions: In Uganda, a history of TB was a strong predictor of chronic respiratory symptoms and lung abnormalities, even before older age and smoking. Eliminating TB disease could reduce the prevalence of chronic respiratory symptoms as much as eliminating smoking. Future studies could assess what proportion of people with post-TB respiratory symptoms and lung abnormalities have or go on to develop chronic ventilatory impairment.

EP08-176-27 The results are in: survey on MDR-TB treatment preference

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Background: Clinical trials have yet to define optimal rifampicin-resistant TB (RR-TB) treatment. Thought leaders have questioned the use of injectables given limited evidence for their efficacy, and abundant data on harms (Reuter et al., IJTLD, 2017). To identify the preferred treatment for rifampicin-resistant tuberculosis (TB), we conducted an online survey.

Methods: After an impartial webinar sharing recent RR-TB trial results, we circulated an online survey (January-February 2018) to all webinar participants and through listservs for people working in TB or affected by TB. Participants selected one of four options:

- i) the WHO-recommended 18-24 months of 5 drugs, including an injectable;
- ii) 18-24 months of 5 drugs, with bedaquiline instead of an injectable;
- iii) WHO-recommended shorter standardized 9-12 months regimen of 7 drugs including an injectable; or
- iv) the standardized 9-12 months regimen, with bedaquiline instead of an injectable.

Respondents indicated reasons for their preference and what they would want to know before choosing.

Results: Preliminary analysis shows the majority of 115 respondents (88%) preferred a bedaquiline-containing regimen. The most common preference (49%) was regimen iv, followed by regimen ii (39%). When choosing a regimen, respondents valued: fewer/less severe side

effects, avoiding the pain of the injectable, treatment duration, clinical trial evidence on efficacy/safety, use of bedaquiline, cost, and in-country drug availability. Before choosing a regimen, respondents would want to know: drug susceptibility results; chance of cure/reinfection; safety in pregnant women; safety for people with co-morbidities; patient cost; and individual risk factors for side effects (e.g. QT prolongation, liver function).

Conclusions: Patients and providers in our sample preferred shorter, bedaquiline-containing, injectable-sparing regimens. As WHO is developing RR-TB guidelines, it is crucial to consider along with clinical trial evidence patient and provider preferences.

EP08-177-27 Body mass index and hyperglycemia interact among south Indian tuberculosis cases and household contacts

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Background: Diabetes and obesity are global co-epidemics and risk factors for tuberculosis (TB). We estimated the interaction effect of body mass index (BMI) and hyperglycemia on TB in a south Indian cohort.

Methods: We enrolled new pulmonary TB cases diagnosed by the Revised National TB Control Programme in Puducherry and Tamil Nadu along with their eligible household contacts into the Regional Prospective Observational Research for Tuberculosis-India collaboration. At baseline, we collected demographic information, measured body mass index (BMI), and checked random blood glucose (RBG). We fit adjusted generalized linear regression models with a Poisson distribution to estimate the TB prevalence difference (PD) by hyperglycemia (≥ 200 mg/dL) and BMI categories (< 18.5 kg/m² underweight, 18.5-24.9 normal, ≥ 25 overweight/obese). Unexposed were classified as having no history of diabetes, RBG < 200 mg/dL, and normal BMI.

Results: We enrolled 725 TB cases and 579 of their TB-negative household contacts. Among TB cases and contacts, respectively, 3.7% and 33.9% were overweight/obese and 62.6% and 17.1% were underweight. Mean RBG was higher among index cases compared to household contacts (174.8 versus 131.8 mg/dL, $p < 0.001$). Underweight participants with and without hypergly-

cemia or known diabetes had TB prevalences 0.63 and 0.47 higher, respectively (P values < 0.001), than the unexposed. Compared to the unexposed group, 21 fewer TB cases per 100 participants were observed among the obese without hyperglycemia ($p < 0.001$), but no difference was observed among those with obesity and hyperglycemia (PD=0.04; $p=0.527$). Overall, diabetes muted the effect of BMI ($p < 0.001$).

	BMI<18.5		BMI 18.5-24.9		BMI≥25	
	N cases/ total	PD (95% CI)	N cases/ total	PD (95% CI)	N cases/ total	PD (95% CI)
Random blood glucose <200 mg/dL	377/475	0.47 (0.41, 0.53); $p < 0.001$	97/354	Reference	2/150	-0.21 (-0.26, -0.15); $p < 0.001$
Random blood glucose ≥200 mg/dL or known diabetes	77/78	0.63 (0.55, 0.72); $p < 0.001$	147/174	0.45 (0.36, 0.54); $p < 0.001$	25/73	0.04 (-0.08, 0.16); $p = 0.527$
PD (95% CI) by BMI strata		0.14 (0.02, 0.26); $p = 0.027$		0.45 (0.36, 0.54); $p < 0.001$		0.32 (0.21, 0.42); $p < 0.001$

[Modification of tuberculosis prevalence difference (PD) by body mass index (BMI) category and hyperglycemia.]

Conclusions: As expected, the highest burden of TB was observed among participants with hyperglycemia and low BMI, a possible surrogate for low socio-economic status. Being overweight/obese appears to protect against TB, except in the presence of hyperglycemia or diabetes. These findings further support the integration of diabetes and TB screening, regardless of BMI.

EP08-178-27 HIV testing for all TB patients in Jember District, Indonesia: mission possible

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Background and challenges to implementation: Indonesia aims to accelerate the uptake of HIV testing among TB patients. In 2013, Jember District tested only 0.2% (6/3300) of TB patients for HIV and only 1.4% (44/3104) in 2014. Lack of decentralized HIV testing at TB treatment sites, a weak referral system, and problems with recording test results contribute to low uptake. In 2015, USAID/CHALLENGE TB (CTB), working closely with the DHO, began providing technical assistance and capacity building to Jember District.

Intervention or response: In 2016, with capacity building support from CTB and co-funding from the Global Fund, the DHO expanded HIV testing to all 58 health facilities providing TB treatment (50 health centers, 5 public and 3 private hospitals). During the expansion, TB staff from health facilities without HIV testing capacity collected blood specimens for HIV in nearby fa-

cilities. CTB worked with the DHO to provide targeted technical assistance to under-performing health facilities along with regular workshops to ensure complete and accurate data. TB-HIV testing is now included in routine DHO monitoring and supervision.

Results and lessons learnt: In 2017, Jember District achieved 100% coverage of HIV testing at TB sites. The number of TB patients tested rapidly increased, from 1% in 2014 to 74% in 2017 (see graph), while TB-HIV diagnosis also increased. However, a gap in HIV testing persists. Reporting HIV treatment results to TB sites is still incomplete and TB staff do not routinely offer HIV testing to pediatric TB patients, leaving HIV testing uptake in this group low (48% in 2017).



[Graph 1. TB Patients with known HIV Status in Jember District, 2013-2017]

Conclusions and key recommendations: Universal HIV testing in TB clinics is feasible and high HIV testing rates are possible in Indonesia once HIV laboratory services are available. However, there still is a need to strengthen the capacity of TB staff to offer HIV testing, especially for pediatric TB patients, and to further support TB recording and reporting systems.

EP08-179-27 The role of systematic TB contact investigation in an urban setting; experiences from Kampala Uganda

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Background and challenges to implementation: Kampala city with over 3 million people during the day has a TB prevalence of 504 cases per 100,000 population. Annually, the city notifies about 7,500 of all forms of TB cases. However, based on the TB prevalence survey, the city misses about 50% of TB cases. In addition, Kampala has a burden of TB and TB-HIV co-infection rates estimated at 53%.

Intervention or response: To increase TB case notification, the Kampala Capital City Authority (KCCA) with the support of the TRACK TB project through use of community linkage facilitators (CLFs) conducted con-

tact tracing among contacts of index pulmonary bacteriologically confirmed (PBC) TB patients to increase notification of TB cases from January 2015 to June 2016 in Kampala.

Results and lessons learnt: Among the 8,973 index PBC TB patients, we identified 27,371 close contacts whom we screened for TB symptoms. Of these close contacts, 4,550 presumptive TB cases (PTP) were identified, and 11.9% tested positive for TB. This represents a TB prevalence of 1,980 cases per 100,000 that is four times the known prevalence of any urban area in Uganda. The 8,973 contacts of index TB patients were educated about TB.

Indicators	Jan-Mar 2015	Apr-Jun 2015	Jul-Sep 2015	Oct-Dec 2015	Jan-Mar 2016	Apr-Jun 2016	Total
# of PBC patients	1,464	1,560	1,708	1,484	1,435	1,322	8,973
# of contacts identified and screened for TB	3,845	4,066	3,530	4,768	5,666	5,496	27,371
# of PTPs identified	670	556	497	1,086	970	771	4,550
# of TB cases detected (%)	31 (5%)	99 (18%)	53 (11%)	100 (9%)	153 (16%)	106 (14%)	542 (12%)

[Table 1: Results from contact investigation January 2015 to June 2016]

Conclusions and key recommendations: TB contact investigations helped to identify 542 new TB cases, which would have been otherwise missed. The resulting TB prevalence of 1,980 cases per 100,000 is four times the known prevalence of any urban area in Uganda of 504/100,000. Integrating TB contact investigation and the support of CLFs into routine TB care increases early TB case notification.

EP08-180-27 Evaluation of FAST strategy in the National Center for Tuberculosis and Lung Diseases (NCTLD) of Georgia

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Background and challenges to implementation: FAST Strategy represents a complex of interventions aiming at decreasing the Tuberculosis transmission within a medical facility and aims at identifying patients with TB symptoms and signs. The purpose of the intervention is to isolate patients referring the NCTLD with cough at admission and conduct the GeneXpert MTB/RIF testing.

Intervention or response: The implementation of the FAST strategy started since August 2017 in NCTLD. A cough officer identifies the self reporting patients with productive cough and isolates them in separate waiting room. The cough officer informs patients regarding

the importance of the GeneXpert testing and in case of consent refers them to the microbiology laboratory for testing. The GeneXpert test result reaches the cough officer within 24 hours since sputum submission. Patients who test positive undergo in-depth investigation for TB within the state TB program. The MTB+ patients are further followed by the NCTLD epidemiologists who inform the relevant TB facility about the patients test results and treatment regimen.

Results and lessons learnt: From September 2017 through March 2018 total of 1330 patients have been tested with FAST strategy, 1162 of which were MTB negative, 44 patients could not provide adequate quantity of sputum and 124(9.3%) were diagnosed with active TB. Out of the diagnosed cases, 101 were Rifampicin sensitive, 23 were Rifampicin Resistant (R/R) and in two patients resistance was not evaluated.

Conclusions and key recommendations: Patients who do not know they have TB and do not receive treatment represent the biggest risk group for transmission. The FAST strategy ensures that patients with presumptive TB are actively evaluated, separated and in case of diagnosis the treatment is timely initiated.

EP09 The importance of health workers and civil society organisations in finding tuberculosis in communities

EP09-181-27 Improving TB case notification through engagement of community volunteers: experience from Challenge TB supported districts in Tanzania

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Background: TB is a major public health problem in Tanzania with an estimated annual incidence of 287/100,000 population and notification rate of 40%, leaving a large proportion undiagnosed living in the community (*WHO 2017*). Community-level challenges to increase case notification include inadequate community awareness and delayed health-seeking.

Methods: From January to December 2017, 250 community volunteers and 32 sputum fixers were engaged to implement community TB activities using TB screening forms, community registers, and referral forms. Community volunteers were oriented and engaged to conduct contact investigation (CI), active case finding (ACF), and transportation of sputum specimens. Monthly follow-up visits were carried out to monitor and evaluate the performance.

Results: Contact investigation was conducted among 31,572 close contacts of 7,516 index patients. Consequently, 1,436 individuals were diagnosed with TB (18% via GeneXpert®, 64% via smear microscopy, and the remaining via chest x-ray and pediatric score charts), and 1,425 (99.2%) of those diagnosed with TB were initiated on anti-TB medication.

ACF among key populations identified 9,595 people with presumptive TB, of whom 8,869 (97.3%) were tested for TB. Of those tested, 812 (9.2%) were diagnosed with TB (30% via GeneXpert® and 44.1% via smear microscopy), and 807 (99.4%) of those diagnosed with TB were started on anti-TB medication.

Sputum fixers transported 3,055 specimen samples from non-diagnostic health facilities to diagnostic health facilities for testing; out of them 351 (11.5%) were found to have TB (21.4% via GeneXpert® and 78.6% via smear microscopy), and 349 patients (99.4%) were initiated on TB treatment.

Conclusions: Engagement of community volunteers in TB control can facilitate early diagnosis and treatment. More innovations on engaging the community are needed to maximize the service of community volunteers.

EP09-182-27 Leaders wanted for a TB free world: exploring prospects of community influencers for TB case finding in low reporting districts in Akwa Ibom State, Nigeria

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Background and challenges to implementation: Poor health seeking behavior is a major contributor to low TB case notification despite significant investments in facility-based TB control interventions. Community influencers can significantly shape decisions and health seeking behavior of community members. With strategic engagement, this resource can be deployed to increase community demand for TB services.

Intervention or response: Thirty community influencers consisting of community leaders, youth leaders, women leaders, church leaders, patent medicine vendors, a traditional healer and a sanitary chairman from 6 priority low-reporting districts were selected for pilot engagement (between April-September, 2017) in tuberculosis control activities in Akwa Ibom State by Challenge TB. They received orientation on awareness creation, identification of presumptive TB cases, referral to TB quality-assured laboratories and appropriate documentation. A linkage to district TB-service providers was also established during orientation to strengthen referrals.

Results and lessons learnt: Between April-September 2016 and April-September 2017, the number of presumptive TB cases tested in the 6 priority districts

increased by >100% following the engagement of community influencers (see table). Comparing the same period, the number of TB cases notified increased by 50%. Community influencers' activities accounted for 67% of the increase in presumptive TB cases and 80% of the increase in TB cases notified, comparing the baseline to the intervention period.

Conclusions and key recommendations: Community influencers can help improve TB case finding in areas with low TB case notification. This intervention should be explored for scale up.

Period	Total number of presumptive TB cases reported	# (%) of presumptive TB cases referred by community influencers	Total number of TB cases reported	# (%) of TB cases from community influencers
April-September 2016 (Baseline)	426	0	82	0
April-September 2017 (Intervention)	965	361 (37%)	126	35 (28%)
Increase between baseline and intervention periods	539	361 (67%)	44	35 (80%)

[Community influencers intervention results (April-September 2017) compared to baseline (April-September 2016).]

EP09-183-27 Pharmacists and rural health care providers and peer motivation strategy: experiences of piloting peer motivation strategy from PRATAM project, India

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Background and challenges to implementation: TB Alert India with an objective to engage Pharmacists and Rural Health Care Providers (RHCPs) in TB care and control implemented a project in Telangana state, India. United Way Worldwide on behalf of Lilly MDR TB Partnership supported project from 2012 to 2017. Pharmacists and RHCPs were referred as community based health care providers (CBHCP). CBHCP's were expected to refer people coming to them for cough treatment for TB testing. In third year of implementation project noticed, a gradual decrease in number of referrals from enrolled CBHCPs. A quick analysis revealed lack of constant follow up was the key reason for drop out of CBHCPs. Project adopted Peer Motivator Strategy and implemented for two years, till Oct' 2017.

Intervention or response: Project selected and trained 207 active CBHCPs as Peer Motivators (PM). PMs were trained on soft skills, TB basics and project required documentation. PM was expected to motivate fellow CBHCPs to remain linked with the project, refer presumptive TB cases (PTCs) for testing, and act as DOT

providers. One PM followed up around five CBHCPs in nearby area. Project had taken up a mixed method study interviewing 160 CBHCPs, to understand the effectiveness of the strategy.

Results and lessons learnt: Almost 92% of the CBHCPs gave credit to their PM for the increase in referrals and increase in their engagement with project. Project reported 10-18% increase in referrals in year 4 & 5 respectively. Around 37% of the CBHCPs who stopped referring started referring PTCs for testing. Around 86% of CBHCPs stated maintaining counterfoil of the referral slip issued for follow up. Around 36% of the CBHCPs interviewed started collecting information about testing either phone or contacting project coordinators.

Conclusions and key recommendations: Pharmacists/RHCPs are real assets who are widely spread at community level. Peer Motivators strategy can lead to their sustained engagement.

EP09-184-27 Sputum collection and transportation initiatives by local community volunteers under NGO-PP scheme in hard-to-reach-areas among vulnerable-populations increased sputum examination and TB notification in Bastar district, Chhattisgarh

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Background and challenges to implementation: TB is a major-public-health-problem in India. While the-routine-TB-services are essential-for case-management, it has proved-inadequate to-address the-estimated 3-million incidence-cases among the-high-risk-poor and vulnerable-populations where TB often-concentrates. Government-of-India devised National-Strategic-Plan in-line-with the-Global-Technical-Strategy-for-TB-prevention-and-care to reduce the-missing-million-cases. Chhattisgarh is one among the high-TB-burden-states in India (216 TB patients/100,000-populations). ≥40% of the sputum-microscopy-centres running under the public-health-facilities are categorised-as “*Difficult-to-Reach*” where sputum-examination for TB-diagnosis is a-difficult-task for the-local-community known as the “*Vulnerable-&-Deprived*”.

Intervention or response: Considering quality-assured-sputum-smear-microscopy as the-backbone-of-tuberculosis-diagnosis under the-National-TB-Control-Programme (NTP), NGO-PP supported Sputum-Collection-&-Transportation (SCT) activities have-been-intensified in Bastar-District to improve the-reach-and-access of TB-diagnostic-services in the-hard-to-reach-areas among vulnerable-populations during

2017-18. Trained on TB-basics; (the signs-&-symptoms, diagnosis-&-treatment, referrals-and-SCT), the-Community-Volunteers (CV) visited the-unreached-villages, interacted-with community-members, inform them about the-disease, its prevention-&-care and demonstrated cough-expectoration-procedures. CVs collected specimens in the-robust-sterile-clear-screw capped-transparent-and leak-proof plastic-sputum-containers and transported-thru certified-sputum-container-bags ensuring-that sputum-samples are labelled/placed properly and collected before-initiation-of-chemotherapy. Few Presumptive-TB-Patients (PTB) were given these-sputum-cups for early-morning-collection by self.

SCT service was provided to all PTBs identified-during-the-process besides few being-offered the-choice-of-referral-services. Sputum-transportation-standards were maintained as per NTP-and-ISTC-norm. CVs were guided and supervised by the NGO/NTP-staff and Lab-Technicians to ensure that biohazard/infection-control issues are addressed.

Results and lessons learnt: SCT for 2,949 cases was done during-the-period (Oct2016-Mar2018). With 100% sputum-examination done-for-all 2,949 SCT-cases, 411 patients (279Sm+ve-and-32 Sm-ve) were-diagnosed in 23 of 39 outreach-designated-microscopy-facilities (DMC) running in-the-tribal-dominated-district. SCT added 51% Sm+ve patients in-to-the-fold with 12% increase-in New-Adult-OPD vs. referral/microscopy-activities. Quality-smear-examination was ensured in around 26% of the DMCs where lab services were either casual or halted over-the-years due-to least/no sputum-samples available-under the-voluntary-referral-process. The 67% referrals reported-during the-six-quarter-period would-have-yielded more-cases if SCT would-have done for-the-neediest-most.

Conclusions and key recommendations: The intervention highlights the need-and-urgency for establishment-of-SCT services in hard-to-reach areas among-the-deprived. In the-absence-of-these-services, 411 patients would-have sought care from various/alternate-service-providers and not notified in-to-the-system contributing-to-the “*Missing-Million-Cases*”. This strategy would benefit the NTP, but needs-to-prioritize-appropriate areas and create a-network-of-willing-&-dedicated *TB-Supporters/CVs* to offer quality-SCT-services in such-locations in India-and-elsewhere.

EP09-185-27 The crucial role of community health workers, Shasthya Shebikas, for programmatic management of TB in Bangladesh: experience from BRAC

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Background and challenges to implementation: BRAC has been implementing community based TB control programme in Bangladesh since 1984. Currently BRAC and NTP jointly expanded this model to 45 districts covering 321 upazillas and 11 city corporations and blanket a 101 million population. Female community health volunteers (Shasthya Shebikas) are playing an important role in TB control activities at community level.

Intervention or response: SS are individuals who are appointed from within the local communities with the objective to play a dual role in TB management at the grass roots level. Following selection, the health workers undergo monthly basic and refresher training. SS play a key role in diagnosis and treatment of patients. Their task involves them visiting households to disseminate TB messages individually, identifying presumptive, and referring them to the nearest NTP laboratory. When presumptive begins treatment after being examined by a graduate physician, the SS ensure DOT and sputum follow-up test. The SS receive an incentive of BDT 600 for every patient that successfully completes treatment.

Results and lessons learnt: In areas where BRAC provides TB management, 162554 patients were diagnosed with TB in 2017; nearly half of whom (81502) were referred by SS. These areas exhibited a treatment success rate of 94% in 2016. Currently more than 67,000 SS are working across Bangladesh.

Conclusions and key recommendations: SS are evidently an effective component of the national TB management programme and the model serves as an effective tool to raise awareness, identify patients and ensure complete treatment adherence.

EP09-186-27 Bringing communities and civil society to the front line for tackling TB in England

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Background: In England, 74% of notified TB cases in 2016 were reported in people born abroad (mostly in high TB burden countries), therefore, a novel intervention within the Collaborative TB Strategy for England 2015-2020 is an evidence-based systematic programme for LTBI testing and treatment for new entrant migrants from high incidence countries. However, the rates of LTBI testing, treatment acceptance and completion are suboptimal and must be increased.

This study aimed to get insights from the community, community-based organisations (CBOs), statutory and academic stakeholders on interventions to improve uptake and therefore to maximize programme effectiveness.

Methods: A mapping and networking exercise was performed over six months, to gain insights on local resources, individuals and organisations with interest or experience in migrant health in the high TB incidence London boroughs of Redbridge, Tower Hamlets, Newham and Brent. Three stakeholder meetings and five focus group discussions were then held using an inductive thematic saturation methodology to gain new theoretical insights from the participants' perspectives.

Results: Three main themes emerged: access, priorities and stigma.

(1) The different skill sets of each sector should be harnessed to improve access to eligible populations, while reconciling their different priorities to maximize programme effectiveness.

(2) Stigma, in particular, could be reduced by making LTBI testing routine and through provisioning within CBO's own spaces.

(3) Community members could act as champions for health promotion raising awareness on LTBI testing, and providing a bridge between communities and primary care services.

Conclusions: LTBI testing services have to be taken out into the communities and commissioners should lead the early involvement of community members and CBOs in planning community-based services. Statutory service providers, community members and CBOs must

be brought together into a community-based model to support primary care delivery of testing for LTBI and other communicable and non-communicable diseases.

EP09-187-27 Effect of community engagement on TB case finding and treatment in Nangarhar province, Afghanistan

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Background and challenges to implementation: Not all people presumptive to have tuberculosis (TB) come to health facilities (HFs) for diagnosis and treatment. This delay, increases the risk of TB transmission in the community. A data review of National TB Program (NTP) surveillance was conducted to investigate the effectiveness of engaging communities in the promotion of case finding in rural areas. The purpose of this study was to explore the effects of community engagement on TB case finding in rural areas of Afghanistan's Nangerhar province.

Intervention or response: In late 2015, a total of 1600 community health workers (CHWs) were trained on community-based directly observed treatment, short-course (CB DOTS). In 2016-2017, the project oriented CHWs to execute awareness raising events, identify and refer presumptive TB patients (PTB) and provide TB treatment. 483 TB awareness events were held for 16,900 community members; TB awareness by local radio, in-kind gifts provided to 48 best performed CHWs. Also cured TB patient shura (CPS) meetings were conducted quarterly for 150 members. Data from NTP surveillance for the year 2016 - 2017 reviewed for comparison.

Results and lessons learnt: In 2016, 24,723 PTBs attended health facilities (HFs) and of them 1,095 were bacteriologically confirmed (BC) in Nangerhar province. CHWs and CPS referred 5,028 (20%) PTB, of them, 363 were BC that is 33% of all notified BC in Nangerhar province. However, in 2017, 28,895 PTBs attended HFs and of them 1,139 were BC. CHWs and CPS referred 6,906 (24%) PTB and 436 BC that is 38% of all notified BC. In 2016-2017, 2,234 TB patients treated in Nangerhar, of them, 634 (28%) received treatment from CHWs and CPS.

Conclusions and key recommendations: We conclude that engagement of the community in TB case finding in rural areas increased the TB case detection rate. We strongly recommended expansion of community-based DOTS to rural areas of other provinces.

Year	Presumptive TB patients notified in province	Presumptive TB cases referred by community and CHW	Bacteriologically confirmed TB cases notified in province	Bacteriologically confirmed TB cases referred by community and CHWs	TB patients who were treated by community and CHWs
2016	24,723	5,028 (20%)	1,095	363 (33%)	331 (30%)
2017	28,895	6,906 (24%)	1,139	436 (38%)	303 (27%)
Total	53,618	11,934 (22%)	2,234	799 (36%)	634 (28%)

[Table: Proportion of community on CB DOTS activities]

EP09-188-27 The case for active case finding in poor urban areas in Zambia

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Background and challenges to implementation: In 2016, Zambia was estimated to have 62,000 TB patients, of which, 21,000 (35%) went undiagnosed. The Copperbelt Province has the highest TB burden in Zambia (1,211/100,000). Ipusukilo compound is a densely populated slum in the Copperbelt, with a population of about 47,000. It is served by one clinic with only seven health workers. Historically, TB detection in Ipusukilo clinic has been passive; only 76 TB patients were notified in 2017.

Intervention or response: For 2018 World TB Day, the USAID Challenge TB (CTB) project conducted community activities in Ipusukilo to raise TB awareness and actively find TB cases. Over 10 days, working with clinic staff and community health workers, CTB set up mobile TB testing sites. To create demand, local radio programmes and drama performances were used to convey TB education messages.

Clients visiting testing sites were screened for TB and HIV; those screening positive for TB submitted sputum samples that were transported to Ipusukilo clinic and tested using GeneXpert. Onsite HIV testing was also offered to all clients.

Results and lessons learnt: A total of 770 clients were screened for TB and HIV, 212 submitted sputum samples, and 403 accepted HIV testing. Twenty-two (2.9%) had TB, 26 (3.4%) tested positive for HIV, and 5 were co-infected with TB and HIV. No-one tested positive for rifampicin-resistant TB.

Conclusions and key recommendations: There are significant numbers of undiagnosed TB cases in poor urban areas in Zambia. The 22 TB patients found translate into a point prevalence of 2,857/100,000, double that of the province. Targeted active case finding exercises in densely populated communities at high risk of TB can greatly contribute to finding missing TB patients. Studies to investigate reasons for the high proportion of presumptive TB patients in such communities can guide TB control.

EP09-190-27 Community volunteers help increase TB case detection among key affected populations: analysis from 16 designated microscopy centres across India

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Background and challenges to implementation: The government of India has taken robust measures to counter high burden of TB by increasing access to TB diagnostic services and treatment, including in the most remote regions. The large number of populations at risk of developing TB who are living in poverty and lack awareness of and access to TB services warranted alternate methods of early detection and treatment initiation of TB symptomatic patients. Community based Active Case Finding (ACF) is a strategy which is requiring systematic screening and clinical evaluation of KAP's.

Intervention or response: World Vision India and its 6 partners implemented project Axshya in 70 Districts from October 2015 to December 2017 supported by the Global Fund. The project trained community volunteers (CV) to conduct door-to-door TB screening using a four-symptom complex verbal screening tool. Symptomatic patients were either accompanied or their sputum samples transported by the CVs to the nearest DMC for testing. Keeping in-line with the National TB Program guidelines, additional chest X-ray was conducted in those individuals with presumptive TB with negative sputum tests. Patients were referred to about 800 DMC's across the project intervention area. Sixteen DMC's spread across four states in eight districts was randomly evaluated for contribution by community volunteers.

Results and lessons learnt: Total TB patients detected during 6 month period across these 16 DMC's were 1,458; out of which 563 (39%) patients were detected by 15 community volunteers. Community Volunteers therefore contributed to a 34% increase in TB case detection across 16 DMC's only through sputum testing with a sputum positivity rate of 9.1%. Addition of chest X-ray to the diagnostic algorithm contributed to 63% increase in TB cases detected at the DMC's.

Conclusions and key recommendations: Community Volunteers trained in identifying TB symptomatic patients can significantly contribute to early diagnosis and treatment initiation of TB in patients who may otherwise be missed or delay accessing TB services.

POSTER DISCUSSION SESSIONS

PS35 Programmatic and clinical management of drug-resistant tuberculosis

PS35-783-27 Performance and epidemiological impact of programmatic management of drug-resistant tuberculosis in Taiwan

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Background: Management of multidrug-resistant tuberculosis (MDR-TB) is challenging as it requires using toxic second-line drugs for a prolonged period of time. Globally, the proportion of MDR-TB patients registered in 2015 who had treatment success was 52%. To strengthen programmatic management of drug-resistant TB (PMDT), Taiwan MDR-TB Consortium (TMTC) was established in 2007 and has achieved more than 80% treatment success among MDR-TB patients. This study aimed to evaluate the performance and epidemiological impact of PMDT in Taiwan.

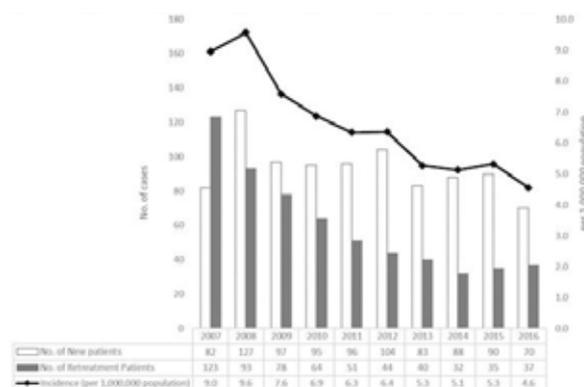
Methods: Incident MDR-TB patients diagnosed from 1 January 2007 to 31 December 2016 were analyzed. We assessed the enrollment of eligible patients (Taiwan citizens with pulmonary MDR-TB) into TMTC and the average interval between sputum collection to TMTC enrollment. We computed the prevalence and incidence of MDR-TB from 2007 to 2016. The Poisson regression model for trend test was used for analyzing the change of prevalence and incidence by year.

Results: There were 1,529 incident MDR-TB cases registered from 2007 to 2016, in which 1452 cases were eligible for TMTC care. The number of TMTC enrollment was 1197 patients (82.4%). Of the 255 cases not enrolled in TMTC, 106 (41.5%) died within 2 months of sputum collection. The average interval between sputum collection and enrollment was 5.3 months in 2007, which decreased to 2.2 months in 2016.

The incidence rate of MDR-TB in Taiwan was 9.0 case per million population in 2007, decreased to 4.6 cases per million population in 2016 (49% reduction) ($p < 0.0001$) (figure 1).

The prevalence of MDR-TB cases in Taiwan decreased from 19.5 cases per million population in 2007 to 8.4 cases per million population in 2016 ($p < 0.0001$).

Conclusions: The TMTC model of care has been efficient in the enrollment and effective in the treatment of MDR-TB patients, resulting in a significant declining trend of incidence and prevalence of MDR-TB in Taiwan.



[Figure 1. Number and incidence (per 100,000 population) of MDR-TB patients in Taiwan 2007-2016]

PS35-784-27 Time to treatment initiation of DR-TB patients in three South Western states of Nigeria: a retrospective study

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Background: Drug Resistant TB program in Nigeria aims to improve access to timely treatment. Delay in DR-TB treatment results in disease transmission, progression and poor treatment outcome. Significant delay in initiating treatment for DR TB patients exists as a result of patient and health system factors. This study assessed the time to treatment initiation of DR-TB patients in three south western states of Nigeria.

Methods: A retrospective review of DR-TB patients commenced on treatment in three south western states (Lagos, Ondo and Osun) between January 1 2015 to December 31 2017. The three states were purposefully selected being the three states KNCV TB Challenge project worked within the study period. Line listing of patients were done and Kaplan-Meier analysis using SPSS (version 22) was done to determine time to treatment initiation.

Results: Of the 760 DR-TB patients enrolled on treatment, 79.7%, 10.5% and 9.7% were from Lagos, Ondo and Osun respectively. Male: female ratio was 1.8:1 and

HIV co-infection rate was 10.5%. The median time to treatment initiation was 30 days (95%CI 27.4, 32.6 days). There was significant difference in time to treatment initiation between Lagos (29 days 95%CI 27.5, 30.5 days), Ondo (44 days 95%CI 35.6, 52.4 days) and Osun State (58 days 95%CI 33.7, 82.3 days) (Log Rank $p < 0.001$, Brestow $p < 0.001$, Tarone-ware $p < 0.001$). Females had a shorter median time to treatment initiation (29 days 95%CI 26.4, 31.6 days) than males (31 days, 95%CI 27.6, 34.4 days) (Log rank $p = 0.010$).

Conclusions: The median time to treatment initiation of DR-TB patients was high. Efforts should be made to identify the causes and find lasting solutions in order to avoid DR-TB epidemic in Nigeria.

PS35-785-27 Efficacy and safety of delamanid to replace the injectable agent in a rifampicin resistant tuberculosis cohort from Khayelitsha, South Africa

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Background: Injectable agents (IAs) - despite being ototoxic and nephrotoxic - remain a core component of standard rifampicin-resistant tuberculosis (RR-TB) treatment regimens. Delamanid is efficacious for the treatment of RR-TB; evidence is needed to evaluate if delamanid could be an alternative to the IA for RR-TB. **Methods:** A retrospective cohort study of patients with RR-TB susceptible to second line RR-TB drugs (IAs and fluoroquinolones), who started delamanid from November 2011 to December 2017 to substitute the IA because of contraindication or toxicity. We report on 2 and 6-month sputum culture conversion (SCC), 12-month treatment outcomes, and serious adverse events (SAEs).

Results: Sixty three patients were initiated on delamanid to substitute the IA within a median of 1.4 months (interquartile range [IQR], 0.7-2.3) from RR-TB treatment initiation. Median age was 34 years (IQR, 27-42), 37 (59%) were male, and 55 (87%) were HIV positive. Twenty five (49%) of the 51 culture positive patients at delamanid initiation had ≥ 6 months follow-up; SCC at months 2 and 6 were 77% and 91%, respectively. Thirty six (57%) of the 63 patients had 12-months of follow-up; 6% ($n=2/36$) had a successful treatment outcome, 67% ($n=24/36$) were culture negative, and doing well on treatment, 22% ($n=8/36$) were lost to follow up, 3% ($n=1/36$) died, 6% ($n=2/36$) reconverted to culture posi-

tive, 3% ($n=1/36$) was transferred out. In 14 patients, 28 SAEs were reported; 57% ($n=8/14$) of patients had SAEs assessed as possibly related to delamanid. The most commonly reported SAEs amongst all patients were: anaemia ($n=3/14$, 21%), drug induced liver injury ($n=2/14$, 14%), seizures ($n=2/14$, 14%), vomiting ($n=2/14$, 14%) and QtcF prolongation ($n=2/14$, 14%; one required permanent discontinuation of delamanid). **Conclusions:** Early treatment and safety outcomes from this programmatic setting suggest that delamanid may be a promising option to replace the IA within RR-TB regimens.

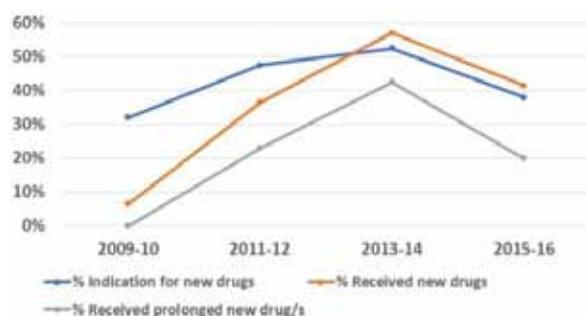
PS35-786-27 MDR-TB treatment: quantifying the need for new drugs

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Background: The WHO recommends the use of new drugs bedaquiline and delamanid for MDR-TB patients with additional resistance to fluoroquinolones or second-line injectables. It is estimated that globally one third of MDR-TB patients qualify for new drugs, while only 5% currently receive them. The objective of this study is to quantify the current routine use of new drugs in France as compared to the theoretical needs according to WHO guidelines.

Methods: A retrospective cohort study was performed including patients with proven MDR-TB whose treatment has been designed at the French MDR-TB Consilium from 01/01/2009 to 31/12/2016. The Consilium designs treatment regimens according to WHO guidelines. Prolonged bedaquiline/delamanid courses beyond 24 weeks are prescribed when stopping the new drugs would weaken the regimen. Indication for the new drugs was defined as resistance to any fluoroquinolone and/or second-line injectable. Trends were assessed using Cuzick's test. P values < 0.05 were considered as significant. **Results:** Overall, 337 MDR-TB patients were included. According to WHO criteria, 154 (46%) patients had indication for treatment with new drugs. Overall, 142 (42%) patients received new drugs: 130 bedaquiline, 4 delamanid, and 8 both in combination. 95 patients (28% of the total, 67% of those receiving new drugs) received prolonged treatment. While the rate of patients

with indication for the new drugs remained stable over time, there was a significant increasing trend in the rate of patients receiving new drugs in the analysed period ($p < 0,001$) (Figure).



[Patients with indication for new drugs, and those treated (standard and prolonged duration)]

Conclusions: In France, there was a progressive increase in the use of new drugs between 2009 and 2016, probably related to growing confidence by clinicians. New drugs were prescribed to 42% of MDR-TB patients, a significantly higher rate than what is estimated in current global projections. Up to two thirds of patients receiving new drugs may need prolonged treatment.

PS35-787-27 Decentralized multidrug-resistant tuberculosis care in south-eastern Ghana: assessment of implementation in 2015-2017

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Background: Multi-Drug Resistant TB poses major threat to Global TB control. Ghana adopted Decentralized model for MDR-TB care, yet there is limited data on the success of this model in our setting. This study assessed the implementation of the decentralized care model in the South-Eastern part of Ghana from 2015-2017 to determine treatment outcomes.

Methods: We conducted a cohort study of all MDRTB clients diagnosed in the Eastern Region of Ghana from 2015 - 2017.

Patients diagnosed with Rifampicin Resistance/MDR-TB were initiated on the 20-24 months treatment regimen and assigned to trained treatment supporters, Community Health Nurses who lived and worked in the clients' community. Treatment supporters ensured client adhered to daily DOTS.

Patients treatment progress were reviewed monthly on Out-Patient basis by trained MDRTB management team consisting of Doctors, Nurses, Pharmacist, Nutritionist,

Biomedical scientist, Psychologist and Social Workers at the Eastern Regional Hospital using National Treatment Protocol and MDR-TB treatment register updated.

Quarterly Supportive supervisory visits were conducted by district and regional TB teams to home of clients and treatment supporters. Treatment outcomes were declared based on WHO criteria. Treatment Outcome data were abstracted from treatment registers and analysed in Epi Info 7.

Results: The cumulative incidence of MDRTB was 14 cases per 1,000,000 population, with 63% males, 10% co-infected with HIV and 4.9% Case Fatality. Twenty nine percent have completed treatment with 83% success rate, 33.3 % cured rate and 8.3% loss to follow up. Of the 71% cases still in care, none was lost-to-follow-up however, 3.4% failed treatment and diagnosed Pre-Extensive-Drug Resistant-TB.

Conclusions: Undoubtedly, this study underscored a successful implementation of the decentralized model of care. It documented a high treatment success rate (83%) with minimal Loss-to-follow-up. However, it showed Pre-XDR/XDR-TB is an emerging concern that must be tackled by National Tuberculosis Program to achieve TB control targets.

PS35-788-27 Predicting aminoglycoside-induced ototoxicity among DR-TB-infected individuals in South Africa

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Background: Many individuals being treated for drug-resistant TB (DR-TB) in resource-limited environments experience permanent hearing loss due to the ototoxic effect of injectable aminoglycosides (AGs). Despite these known risks, there is no practical means to identify patients at highest risk for developing hearing loss. We therefore aimed to develop a prediction model of AG-induced ototoxicity among patients initiating DR-TB treatment in South Africa.

Methods: We evaluated a prospective cohort across 10 hospitals in the Eastern Cape and KwaZulu-Natal provinces of South Africa as part of an ongoing cluster-randomized trial investigating the effects of nurse case management in improving DR-TB treatment outcomes. All participants older than 13 years with confirmed DR-TB were included. Predictors were collected from clinical, audiological and laboratory evaluations conducted at the initiation of DR-TB treatment. The outcome of AG-induced ototoxicity was defined as AG regimen modification (i.e., discontinued or reduced AG

dose or frequency) due to ototoxicity. Multiple logistic regression was used to develop a parsimonious prediction model from data that would be readily available to treating clinicians.

Results: We used data from 600 participants to develop the model and from 299 separate participants to validate the model. The most parsimonious model with adequate discrimination included five factors: weekly AG dose, pre-existing hearing loss, AG type (amikacin or kanamycin), HIV status/CD4 count, and weight. This model demonstrated reasonable discrimination (area under ROC curve= 0.68) and calibration (Hosmer-Lemeshow $\chi^2(8)= 11.68$; $p= 0.17$). Using a cutoff of 40% predicted probability of AG-induced ototoxicity, the positive predictive value of this model was 58.7%, and the negative predictive value was 78.1%.

Conclusions: This prediction model using readily available clinical data may add value in identifying patients with DR-TB who are at high risk of developing ototoxicity during treatment.

PS35-789-27 Decentralization of audiology screening services for MDR-TB in Western Cape Province, South Africa

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Background and challenges to implementation: In South Africa, the standardized treatment regimen for MDR-TB includes an injectable aminoglycoside, which is strongly associated with ototoxicity. Previously, audiology screening for DR-TB was centralized at TB specialized hospitals. No alternative drugs were available for substitution in cases where ototoxicity occurred, until the introduction of Bedaquiline (BDQ) in 2015.

Intervention or response: With the decentralization of TB services in 2011, audiologists were appointed and audiology services were made available at district and sub-district levels. The National Department of Health (DoH) donated mobile audio-screening devices, namely Kuduwaves, to the Province, which can detect high frequency hearing loss. Additional Kuduwaves were purchased by the Provincial DOH to ensure all sub-districts had devices. Audiology training was commenced, and audiologists subsequently developed sub-district specific screening plans. This included audiology rosters and patient care pathways which were displayed in TB treatment areas.

Hearing tests became a policy requirement and were conducted at baseline, monthly and after discontinuation of aminoglycosides. In some sub-districts, with limited audiologists, Rehabilitation Care Workers were trained to do hearing tests under supervision. From 2015, if any hearing impairment, including vertigo or tinnitus, was detected, the patient could be referred for drug substitution with BDQ.

Results and lessons learnt: In 2016 and 2017, 38% (263/694) and 65% (711/1093) of patients had drug substitution with BDQ respectively. These patients all had some form of hearing impairment at baseline, or had developed ototoxicity on the aminoglycoside. Drug substitution was evident in the decline in number of hearing aids requested, from 343 in 2015 to 219 in 2016 and 82 in 2017.

Conclusions and key recommendations: The efficient implementation of decentralized audiology screening services has resulted in the timely access to a less ototoxic regimen for many MDR-TB patients, and will decrease the physical, social and economic impact of hearing loss on patients.

PS35-790-27 Site improvement monitoring system for programmatic management of drug resistant TB (SIMS for PMDT): experiences from Uganda

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Background: Site Improvement Monitoring System (SIMS) aims to increase the impact of PEPFAR programs on HIV epidemic through standardized monitoring of quality of care. The USAID Defeat TB project, a five-year technical assistance mechanism to the National TB and Leprosy Program (NTLP), adapted a standardized SIMS tool for the assessment of quality of Programmatic Management of Drug Resistant TB (PMDT). The tool assesses 18 standards, each containing 2-5 variables. The SIMS tool was used to determine the baseline quality of PMDT.

Methods: The Defeat TB project together with NTLP formed a supervisory team that piloted SIMS for PMDT assessments at 14 hospitals countrywide. The teams performed chart reviews, observed counseling and infection control practices, checked availability of standard operating procedures (SOPs), guidelines, policies and job aids. Each element was scored using a standardized scale and rated to create a dashboard. Feedback meetings were held and improvement actions collectively developed with the facility teams.

Results: The overall performance in 14 hospitals was 63% (figure 1), categorized as 'needs improvement'. Only 1 hospital scored above 80% (meets expectations), 6 hospitals scored below 60% (poor performance) and 7 scored between 61% and 79% (needs improvement) category. Of the 18 standards assessed, 9 were below expected standards, 7 needed improvement, 1 met expectations, while the other surpassed the expectation.

Description	1	2	3	4	5	6	7	8	9	10	11	12	13	14	Average
TB Diagnosis	85%	85%	85%	85%	85%	85%	85%	85%	85%	85%	85%	85%	85%	85%	85%
TB case holding	78%	78%	78%	78%	78%	78%	78%	78%	78%	78%	78%	78%	78%	78%	78%
Monitoring	72%	72%	72%	72%	72%	72%	72%	72%	72%	72%	72%	72%	72%	72%	72%
Surveillance	70%	70%	70%	70%	70%	70%	70%	70%	70%	70%	70%	70%	70%	70%	70%
Enrollment	68%	68%	68%	68%	68%	68%	68%	68%	68%	68%	68%	68%	68%	68%	68%
Baseline Culture	65%	65%	65%	65%	65%	65%	65%	65%	65%	65%	65%	65%	65%	65%	65%
Adherence	62%	62%	62%	62%	62%	62%	62%	62%	62%	62%	62%	62%	62%	62%	62%
Culture Monitoring	60%	60%	60%	60%	60%	60%	60%	60%	60%	60%	60%	60%	60%	60%	60%
Contact Tracing	58%	58%	58%	58%	58%	58%	58%	58%	58%	58%	58%	58%	58%	58%	58%
HIV Testing	55%	55%	55%	55%	55%	55%	55%	55%	55%	55%	55%	55%	55%	55%	55%
Enrollment on CTX	52%	52%	52%	52%	52%	52%	52%	52%	52%	52%	52%	52%	52%	52%	52%
Enrollment on ART	50%	50%	50%	50%	50%	50%	50%	50%	50%	50%	50%	50%	50%	50%	50%
MUAC	48%	48%	48%	48%	48%	48%	48%	48%	48%	48%	48%	48%	48%	48%	48%
AI's Screening	45%	45%	45%	45%	45%	45%	45%	45%	45%	45%	45%	45%	45%	45%	45%
Data systems	42%	42%	42%	42%	42%	42%	42%	42%	42%	42%	42%	42%	42%	42%	42%
Supply Chain	40%	40%	40%	40%	40%	40%	40%	40%	40%	40%	40%	40%	40%	40%	40%
Quality Improvement	38%	38%	38%	38%	38%	38%	38%	38%	38%	38%	38%	38%	38%	38%	38%
Infection Control	35%	35%	35%	35%	35%	35%	35%	35%	35%	35%	35%	35%	35%	35%	35%
Overall score	65%	65%	65%	65%	65%	65%	65%	65%	65%	65%	65%	65%	65%	65%	65%
Supplies	Meets expectations		Needs improvement				Poor performance								

[Figure 1: Jan-Mar 2018 SIMS Dashboard]

Conclusions: The SIMS tool provided the status of the quality of PMDT and will be useful for monitoring and prioritizing areas for improvement.

PS35-791-27 A quality improvement intervention for improving interim 6-month outcomes of patients initiated on DR-TB treatment in Swaziland

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Background and challenges to implementation: In the treatment of drug resistant TB(DR-TB), the monitoring of 6 months' outcomes at national level is crucial as recommended by WHO. At facility level, monthly cultures are done to monitor effectiveness of treatment and adherence of patients to treatment. It is expected that by 6 months, patients should have converted so that injectable could be stopped and continue with oral medication. In Swaziland, the NTCP however noticed a gap between national recommendations and its implementation in the facilities. These gaps were high cultures unknown and high lost to follow up (LTFU) rates.

Intervention or response: In 2016, Quality improvement projects(QIPs) were implemented in all DR-TB treatment sites in Swaziland, aiming at health worker led identification of implementation gaps, addressing them and improving six-month outcomes. To estimate the impact of this intervention, a before-after analysis of routine DRTB programme data was performed comparing six-month outcomes (culture conversion, culture positive, culture unknown, LTFU, deaths) of patients initiated on DR-TB treatment. Before was defined as the years 2014-2015 and after as the year 2017. Proportions were compared with equality of proportions tests using large-sample statistics.

Results and lessons learnt: A total of 1159 and 384 patients initiated DRTB treatment before and after the intervention. Of those, comparing before vs. after, culture conversion increased from 57.5% to 72.9% (p< 0.001), culture-positive status remained similar (8.8% vs. 6.5%, p=0.155) and culture unknown decreased from 17.9% to 12.0% (p=0.007). For the same time periods, LTFU decreased from 13.1% to 1.4% (p< 0.001) while deaths remained stable (8.4% vs. 7.8%, p=0.711). Quality improvement intervention created a platform for collaborative engagement of facility-based health workers and the NTCP for improving DRTB operations and patient outcomes.

Conclusions and key recommendations: Data driven interventions possibly have high impact. These results are encouraging for continued and collaborative engagement in quality improvement interventions and for monitoring progress towards improved outcomes for patients.

PS35-792-27 Bedaquiline use for drug-resistant TB treatment: interim result of its implementation in Indonesia

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Background and challenges to implementation: Until 2015, Indonesia did not have effective treatment options for patients with Pre- XDR (extensively drug resistant TB) or XDR TB. WHO published guidance in 2013 stipulating the use of Bedaquiline (BDQ) under research conditions and pharmacovigilance. Indonesia started the use of BDQ in September 2015. This paper describes the interim results of BDQ implementation study in Indonesia.

Intervention or response: The study populations are TB patients with resistance or intolerance to fluoroquinolone (FQ), resistance or intolerance to second line injection drugs (SLIDs), intolerance to ≥ 2 other second line drugs (Eto, Pto, Cs, PAS), and XDR TB. The inclusion criteria were patients aged 18-65 year-old, sign an informed consent form, and willing to come to hospital every day until treatment is completed. Patients who have abnormal QTc interval at the baseline, HIV, chronic liver or kidney disease, and patients who were pregnant or breastfed were excluded from the study. All patients' data were kept in manual form and entered into the national DR-TB electronic system.

Results and lessons learnt: A total of 120 patients (58% male) were enrolled between September 2015 to November 2017. The resistance pattern shows patients en-

rolled on BDQ are MDR (42%), pre-XDR (36%) and XDR (12%) TB. The majority of the patients (61.7%) achieved sputum culture conversion within 3 months and 5% within 6 months (5% culture negative at baseline, 10% not converted, 18.3% not yet converted). From the 29 patients who are past 20 months from the enrollment date, 69% cured, 6.9% lost-to-follow-up, 6.9% died, and 17.2% failed.

Conclusions and key recommendations: Before the availability of BDQ, patients with (pre-)XDR TB or intolerance to conventional second-line drugs had very limited treatment options and the majority was likely to die of the disease. The interim treatment results are encouraging, especially the early sputum conversion in the majority of patients.

PS35-793-27 What can we learn about drug-resistant TB patients' experiences of decentralised care from their routinely collected laboratory data? Visualising patients' journeys in South Africa

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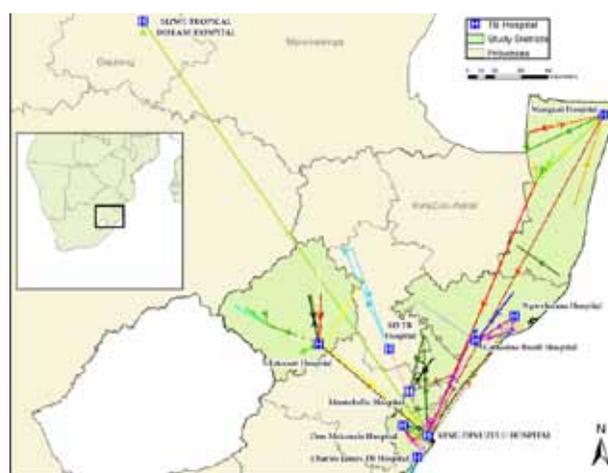
Background: Different implementations of decentralised care for drug-resistant TB (DR-TB) across South Africa have resulted in varying models of care. By visualising points of contact between patients and the health system over time and space, we aim to explore how routine data can be used to understand patients' health care journeys.

Methods: A random sample of 195 patients with a laboratory-confirmed diagnosis of DR-TB diagnosis across July-September 2016 was selected from urban and rural districts in three provinces, Eastern Cape (EC), KwaZulu-Natal (KZN) and Western Cape (WC). Patients with at least two laboratory results were included. For each patient, all laboratory records in the 270 days following DR-TB diagnosis were extracted. Laboratory records, GPS data and health facility information were combined for analysis and visualisation.

Results: Median cumulative distance travelled between facilities was greater among patients from rural districts (116km, IQR 50-290km) than those from urban districts (51km, 9-140km), and was lower in WC (36km, 2-172km) than in EC and KZN (76km, 19-266km, and 92km, 47-216km respectively). Patients spent a greater proportion of time at primary care facilities in WC and

EC (median 39%, IQR 16-91%, and 37%, 17-70% respectively) than in KZN (6%, 0-19%). Visualisation using maps and Gantt charts of time spent in different levels of care showed distinct patterns emerging from patients' journeys in different areas. Some reflected a semi-centralised model of care where patients were referred to regional hospitals; others had greater involvement of primary care.

Conclusions: Routine laboratory data can be used to explore patients' health care journeys. Quantitative results, maps and Gantt charts illustrate variation in terms of patient time and distances travelled by patients across provinces and between rural and urban areas. Programme managers focused on patient-centred care can use these methods to understand how variation in policy implementation impacts patients' journeys.



[Exemplar figure: map of health care journeys of DR-TB patients from study districts in KwaZulu-Natal]

PS35-794-27 Effectiveness of monthly interim cohort analysis (MICA) to improve enrollment and treatment adherence among drug-resistant TB patients in Indonesia

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Background and challenges to implementation: Indonesia is struggling with around 30% treatment gap: patients diagnosed but not accessing drug-resistant TB (DR-TB) treatment. In addition, 27% patients were lost to follow up during multi drug-resistant TB (MDR-TB) treatment (2014 MDR cohort). Monthly Interim Cohort Analysis (MICA) is a monthly activity led by the district TB program coordinator, together with patients' organizations and CSO's, aiming to increase treatment enrollment and adherence of all DR-TB patients residing

in the district. The monthly period means a patient can be missing appointments for not more than one month. This paper shows the effectiveness of MICA implementation in several Challenge TB districts in Indonesia.

Intervention or response: MICA is implemented in 13 CTB districts within 5 provinces. Data source for MICA is e-TB manager, the online electronic DR-TB recording and reporting system. All confirmed Rifampicin-resistant TB (RR-TB) patients are reviewed on whether they have initiated their MDR-TB treatment and patients on treatment in the last 2 years are discussed regarding their current treatment status. Patients confirmed with RR-TB who have not enrolled for treatment or patients missing appointment(s) are visited by primary health center (Puskesmas) staff, CSO cadres and/or patient's organization.

Results and lessons learnt: In the 13 districts where MICA is implemented, loss to follow up of MDR-TB patients reduce from 23% in 2016 to 13% in 2017. Patients' enrollment increased from 75% in 2016 to 78% in 2017. The main reasons of non-enrollment are patients' refusal due to their work and patients' cannot be traced (false address).

Conclusions and key recommendations: MICA allows district TB program coordinators to identify DR-TB patients in their area. Application of MICA contributed to the reduction of loss to follow up of MDR-TB patients and a slight increase in treatment initiation. Further efforts are needed to ensure actual decentralization of treatment and counseling of patients accordingly, and to ensure patients' addresses are correctly recorded.

PS36 Result of intensified case detection

PS36-795-27 APOPO's TB detection: results in 24h and patient tracking improve linkage to care, Tanzania, 2014-2017

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Background and challenges to implementation: Tuberculosis (TB) caused an estimated 10.4 million new TB cases worldwide in 2016, about 4.1 million remained undetected. APOPO does research into using TB detection rats (confirmed by WHO-endorsed methods) after conventional microscopy in 57 (2017) collaborating DOTS clinics in Tanzania to identify additional cases.

Enhanced case detection can only unfold public health value if patients are treated effectively. We aimed to assess whether faster result turnaround and patient tracking by community health workers (CHW) can reduce pre-treatment loss-to-follow-up.

Intervention or response: We used APOPO TB research data from Tanzania from 2014 to 2017, which comprise numbers of samples and patients evaluated, additional TB cases detected, and patients linked to care in the collaborating DOTS clinics (Ethical clearance ref. NIMR/HQ/R.8a/Vol. IX/366). We compared the percentage of patients linked to care before (2014-2016) and after (2017) the opening of our new central lab facility and a motorbike sample referral network in Dar es Salaam. In parallel collaboration with CHW from the patient organization MUKIKUTE, initiated in 2012, had been strengthened

Results and lessons learnt: From 2014-2017, a total 174,447 samples from 98,089 patients with presumptive TB were evaluated by APOPO and 4,971 (35%) TB cases detected in addition to 14,303 TB cases diagnosed at the DOTS centers. Over time, collaboration with two CHW per clinic has been achieved. The percentage of patients linked to care was 55% (777/1,412), 73% (870/1,198), and 71% (797/1,117) from 2014-2016, respectively, at a result turnaround time of 8-10 days. In 2017, after introduction of 24h result turnaround time in Dar, 81% (1,005/1,244) of patients were successfully linked to care, significantly more than before ($p < 0.05$).

Conclusions and key recommendations: Our results suggest that the combination fast diagnostic service and patient tracking are key in achieving higher treatment initiation rates among TB patients in Tanzania - a model which we aim to sustain and enhance.

PS36-796-27 Role of a contact center in TB control in Mumbai

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Background and challenges to implementation: The Private Provider Interface Agency (PPIA) in India strengthens the capacity of private practitioners serving people in slum areas to ensure early, accurate diagnosis of tuberculosis (TB), effective case management, and successful treatment. To cater to private-sector TB patients in Mumbai, in 2014 the PPIA leveraged an information and communications technology (ICT) platform that, coupled with a contact center, supports the generation of vouchers for free diagnostics, drug provision, and patient management.

Intervention or response: Beginning in April 2015, contact centers initiated the following simple steps for beneficiary management once a patient was enrolled.

Inbound calls:

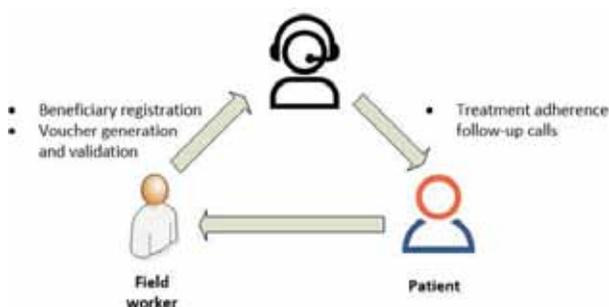
- Enroll presumptive TB cases with essential data points.
- Generate vouchers for screening and diagnostic services for patients: chest x-ray and CBNAAT (cartridge-based nucleic acid amplification test).
- Generate vouchers for prescriptions and drugs for patients initiated on treatment, in compliance with the list of approved TB drugs.
- Validate drug vouchers on calls from chemists.

Outbound calls:

- Call patients to cross-check drug intake in the previous week and mark adherence in the ICT application.
- Provide the monthly dashboard to the program team to share output.

Results and lessons learnt: From April 2015 through December 2017, 88,305 beneficiaries were provided services by the contact center on 93,393 inbound and 478,063 outbound calls.

Conclusions and key recommendations: For diseases like TB requiring lengthy treatment regimens, contact centers can provide convenient and accessible support for field workers to record and register multiple beneficiaries instantly. Considering their utility and benefits, the national TB control program has launched contact centers in two Indian states for various activities, including case notification, TB center information, disease information, and direct benefit transfer information to TB patients.



[Contact center process flow]

PS36-797-27 Facility-based active tuberculosis case finding in Nyeri County, Kenya: a feasible and effective strategy

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Background and challenges to implementation: According to 2016 tuberculosis (TB) prevalence survey, the TB prevalence in Kenya is 558 per 100,000 people and it is estimated that every year 138,105 people fall sick with TB. However, in 2015, 82,000 people were diagnosed with TB, meaning that 40% of TB cases remain undetected and untreated. This pool of missed cases continues to

fuel the spread of TB, considering that one undiagnosed and untreated individual can infect 10-15 people. In light of this Nyeri county initiated facility-based active TB case finding in public health facilities in the year 2017. We aimed to assess the feasibility of facility-based ACF for TB among patients seeking health services in Nyeri and determine its outcome on case detection.

Intervention or response: Between January to December 2017, public health facilities in Nyeri County conducted active TB screening to patients seeking health services. Health care workers performed symptom screening, collected sputum and facilitated specimen transport to the laboratories. GeneXpert was performed at tertiary levels and microscopy to lower levels. Mobile phone/short message system was used for same-day issuing of positive results. Data was captured using electronic medical records and analysed using excel.

Results and lessons learnt: During the time period, we diagnosed 1316 TB cases, an increase of 29% compared to the TB cases diagnosed in 12 months in 2016. Bacteriologically confirmed cases were 740, an increase of 11% compared to TB cases in 2016. Paediatric TB cases increased from 56 in 2016 to 117 cases in 2017. Facility-based TB ACF helps in early case identification and prevent TB transmission.

Conclusions and key recommendations: Our findings suggest that facility ACF for TB, using a sensitive symptom screening, followed by Gene Xpert and smear microscopy, contributes to improved case detection of TB, shortening the diagnostic delay, and successfully bringing patients into care. Health facilities to scale up TB ACF in all departments.

PS36-798-27 Cost analyses of active case finding programs in Cambodia and Tajikistan

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Background: With technological innovations, active case-finding (ACF) programs for tuberculosis (TB) have evolved as multi-dimensional programs. However, there is limited evidence and tools to systematically evaluate their costs, and existing studies lack transparency in their methodology and reporting.

Methods: The Cambodia program consisted of community-based symptom screening, followed by mobile diagnostic services (X-ray for all and Xpert MTB/RIF

[Xpert] for select patients). The Tajikistan program consisted of facility-based symptom screening (56 polyclinics, 1 pre-detention, and 1 diabetes center) using mobile-health tool, followed by Xpert for all presumptive TB patients. Primary cost and patient event data, obtained from program performance and financial reports and interviews with program managers, were organized in a matrix of key activity categories by relevant resource types. Costs were evaluated as economic costs, following the activity-based costing framework using top-down method and were expressed in 2015 USD.

Results: Over the two program years, each intervention screened tested 68,846 and 1,980,516 persons to test 4,589 and 19,764 presumptive TB patients with Xpert, resulting in 728 and 2,246 TB cases detection in Cambodia and Tajikistan. In Cambodia, additional 1425 cases were diagnosed using X-ray screening algorithm that included referral for smear at the clinic. Costs per TB case detected using Xpert MTB/RIF were \$479 and \$343 in Cambodia and Tajikistan respectively (Table).

Conclusions: X-pert test was the major cost drivers with high recurrent cost (esp. cartridge cost) in both countries; yet, larger Xpert testing volume resulting in lower cost per test and cost per case detection in Tajikistan suggests importance to achieve economies of scale and with non-selective Xpert testing and operational efficiencies. Our costing framework provides a systematic and comprehensive method for evaluating costs for the multi-dimensional ACF programs and can serve as important evidence for more in-depth economic research for better program management and policy making.

Program Location	Cambodia					Tajikistan				
	Total Personnel cost	Administrative	Staff training	Printing	Other	Total Personnel cost	Administrative	Staff training	Printing	Other
Personnel cost	150,000	120,000	20,000	5,000	5,000	1,500,000	1,200,000	200,000	5,000	5,000
Capital cost	100,000	100,000	0	0	0	1,000,000	1,000,000	0	0	0
Material cost	100,000	100,000	0	0	0	1,000,000	1,000,000	0	0	0
Other cost	100,000	100,000	0	0	0	1,000,000	1,000,000	0	0	0
Total activity costs	450,000	420,000	20,000	5,000	5,000	4,500,000	4,200,000	200,000	5,000	5,000
Total patients	68,846	68,846	68,846	68,846	68,846	1,980,516	1,980,516	1,980,516	1,980,516	1,980,516
Cost per patient	6.54	6.10	0.29	0.07	0.07	2.27	2.12	0.10	0.03	0.03
Cost per TB case	479	479	479	479	479	343	343	343	343	343

[Total program costs and unit costs in TB REACH projects in Cambodia and Tajikistan]

PS36-799-27 The impact of reactive (contact tracing) case finding versus proactive (door-to-door) case finding in the Shiselweni Region, Swaziland

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Background: Swaziland is burdened with tuberculosis (TB) and HIV. The coinfection rate is at 70%, HIV prevalence at 27% among 15-49 years and TB case detection was 59% in 2016 and currently 84%. The TB program envisioned finding TB cases beyond the facility and introduced a community-based case finding. The community case finding strategy is on visiting households, screening for TB, collecting sputum samples and linking TB positives for care, on the other hand trace contacts for index cases hence it is a two pronged strategy. The objective of this study is to understand the effectiveness of door to door screening versus contact tracing.

Methods: Different codes were used to[SJ1] delineate door to door identified cases from contact tracing cases in the paper based facility registers. A physical count of cases from October to December 2017 was conducted in 28 facilities in the Shiselweni region. A comparison of the two approaches was made to identify the proportion of clients diagnosed through door to door versus contact tracing. Data was analysed using descriptive statistics.

Results: The door to door approach screened 13689 people, 395 were presumptive and 8 were bacteriologically confirmed. The number needed to screen is 472. Yet contact tracing screened 436 people, 52 screened positive and 2 were bacteriologically confirmed. The number needed to screen for contact tracing is 148.

Conclusions: Door to door is more effective than contact tracing since 8 were diagnosed from door to door and the coverage was wider yet contact tracing diagnosed 2 and focusses on contacts of index cases. However, contact tracing is more cost effective considering the number needed to screen. Both approaches can be used complementary to find cases.

PS36-800-27 Increasing TB screening points in an urban district improved TB case identification: early results from Mukono district, Uganda

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Background and challenges to implementation: In Uganda each year, 46% of TB cases are missed and one missed case spreads TB to 10-15 people every year. The USAID Defeat TB project is working with the National TB and Leprosy Program (NtLP) to implement a five-year activity in three districts, the 15 regional referral Hospitals and two general Hospitals in Uganda with the aim of increasing TB case notification, case detection and treatment outcomes through health system strengthening, to contribute to ending the TB epidemic in Uganda.

Intervention or response: Methodology: An assessment of TB services at 15 health facilities in Mukono district revealed that inadequate TB screening was affecting TB case identification. Using quality improvement (QI) coaching sessions, facility teams were guided to develop changes, prioritize them and develop action plans to increase screening.

TB health education talks and screening were conducted in the out-patient department (OPD), the HIV clinic, the inpatient department (IPD) and the maternal, newborn and child health (MNCH) department to reach more patients and address misinformation related to TB disease. Strategies to increase TB screening involved adjusting the client flow to include TB screening using the intensified case finding (ICF) guide. Health workers agreed to use of TB presumptive register at all departments and assigned a focal person to oversee the screening process and make weekly reports.

Results and lessons learnt: The proportion of outpatient clients screened for TB in the 15 health facilities increased from 29,563/65,535 (45%) in Nov-Dec 2017 to 60,015/89,230 (67%) in Jan- Feb 2018; the number of patients diagnosed with TB increased from 112 to 144 in the same period. In the prisons, 231 prisoners were screened, 94 were presumed, 3 were confirmed TB cases by use of GeneXpert.

Conclusions and key recommendations: The improvement teams showed that by screening at multiple entry points they could reach more patients and increase TB case identification.

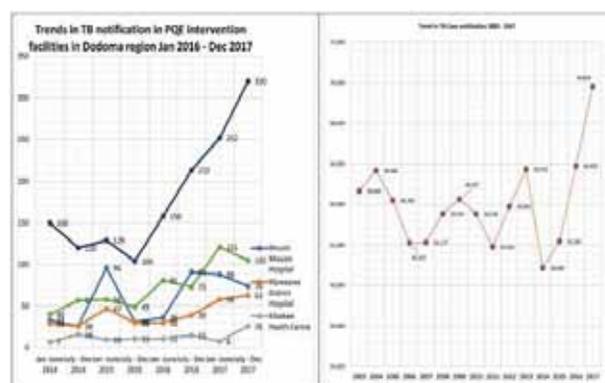
PS36-801-27 Successes in increasing TB case detection through quality improvement interventions in health facilities in Tanzania

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Background and challenges to implementation: The 1st TB prevalence survey conducted in 2013 revealed that TB prevalence was higher at 528/100,000 population and the country is missing over 100,000 TB cases annually. QI in TB case detection was introduced in June, 2016 with a focus on universal provider initiated TB screening at each entry point of health facility. The new innovative policy was initiated in 16 out of 31 regions.

Intervention or response: QI Toolkit, presumptive TB register and Job Aides including flip charts, booklets, posters developed. Providers in each unit oriented, champions trained and form district team of mentors. Facility selected TB QI focal person. Monthly consultative mentorship visits. Score cards were used to diagnose TB in children. Sputum samples sent to Lab and results sent to the requesting clinic. TB positives immediately treated and TB negatives re-evaluated using TB diagnostic algorithm.

Results and lessons learnt: Up to over 100% increase in TB case detection observed in intervention facilities. Notification of all cases increased by 12.4% from 62,180 in 2015 to 69,864 cases in 2017 after 18 months of implementation. Functional TB focal persons in place and QI in TB case detection became a permanent and key agenda of both clinical and coordination meetings and fully integrated into health facility QIT, WITS, and CME.



[Trend in TB case Notifications at National and Health Facilities levels]

Conclusions and key recommendations: Approaches and activities under QI proved to increase TB notification with minimum resources. Policy enforcement, inte-

grating QI TB into existing systems, close monitoring and on-site consultative mentorship are key in changing health workers practices towards improved notifications.

PS36-802-27 An attempt to identify actively practising private practitioners and their potential contribution to TB care in Bandung Municipality, Indonesia

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Background: Half of TB patients managed by private practitioners (PPs) and hospitals are not notified to the national TB program (TB prevalence survey, 2014-2015). Our INSTEP (INvestigation of Health Services for TB by External Private providers) study aimed to describe the behaviour of PP in relation to health care pathways taken by TB patients.

Methods: We randomly selected 30 (out of 73) community health centres (CHC) area in the Bandung Municipality covering a population of 1.4 million out of 2,5 million total. In this area, 5912 cases from Hospital and 1322 from CHC were reported in 2017 (total notification rate of 513/10⁵). We conducted a survey by visiting each PP in the CHC areas. Actively practicing PP were contacted and interviewed. Information gathered included their location, type of medical service provided, whether they provided general patient care, estimated number of TB patients diagnosed in the last 3 months and those under treatment. Data were presented using descriptive statistics.

Results: Of 1848 registered PPs, only 1047 (57%) were found. However, 856 PPs were actively practising, including general practitioners (71.1%), internists (3.9%), pulmonologist (0.1%) and other specialists (24.9%). Interviews were successful in 625 (73%), and showed that 567 (90.7%) PPs were providing care to patients. Among these, 243 (42.9%) PPs had cared for TB patients by providing diagnosis and/or treatment. In total, 1147 TB patients were diagnosed in the last three months and 464 were under treatment at the time of the interview by the PPs

Conclusions: There is great discrepancy between the PP register and PP actively practising. PPs can potentially contribute to a significant proportion of diagnosed and treated TB in the Bandung Municipality. Integrating PPs into routine TB diagnosis and treatment notification along with the CHC is a high priority.

PS36-803-27 Implementation of active case finding as a strategy to find tuberculosis cases in Kericho referral hospital, Kericho county, Kenya

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Background: Tuberculosis remains a global public health concern with high mortality rate despite being preventable and curable. According to the 2016 Kenya Tuberculosis prevalence survey 135,105 people were estimated to have Tuberculosis annually. 2015 data reports only 82,000 cases were notified to the national Tuberculosis programme through passive case finding resulting to 56,105 missed cases. Kericho county notified 1,429 cases in 2016 and Kericho hospital notified 227. This indicates that there are many cases that are missed out leading to persistence of Tuberculosis in the community. **Methods:** A cross sectional study was done from January to December 2017 at Kericho hospital. The hospital health care workers who included medical officers, clinical officers, nurses and laboratory technologists were sensitized about the prevalence survey and active case finding strategy. Presumptive registers, sputum request forms and falcon tubes were available at service delivery points. Active Case finding tool was used with questions on cough, night sweats, weight loss and history of contact with persons with Tuberculosis. Each patient who visited the facility was administered the tool by the clinicians. Screening questionnaires were incorporated into the electronic medical records. Facility health volunteers were identified to transport samples to the medical laboratory. Those with symptoms were registered in the presumptive register and subjected to gene X-pert test. The results were relayed back to the clinicians.

Results: Tuberculosis cases increased in the county from 1,429 in 2016 to 1,729 in 2017 and from 227 to 351 in Kericho referral hospital. 21% and 55% respectively following the active case finding.

Conclusions: Active case finding helps in identifying cases which could be missed compared to passive case finding.

Sensitization sessions for health care workers is key in the implementation of active case finding.

Active case finding should be rolled out in all health care facilities.

PS37 Air pollution: measurement, risk and impact

PS37-804-27 Empowering village administrative body for preventing air pollution vis-a-vis lung diseases through environmental amelioration

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Background: The Panchayati Raj Institutes through elected village administrative bodies- the Panchayats, have been playing a significant role in development of rural India. Air pollution emanating from various industrialization/ developmental activities in rural areas, leading to lung diseases, was perceived as a public health challenge by a village Panchayat of Solan district. Thereafter a study was conducted with this volunteer Panchayat for assessing resident's knowledge, identification of air pollution sources, disease burden estimation and environmental amelioration.

Methods: This study was based upon an administrative decision taken by Panchayat, on record, to own and lead for the cause. A team involving 4 Accredited Social Health Activists, Panchayat President and Vice President, trained by Environmental, Epidemiological and Health science experts, using a pilot tested semi-structured questionnaire, surveyed 1350 residents of 309 houses across 29 villages and 108 workers from six industries, falling under this Panchayat.

Results: Unscientific solid waste disposal, stubble burning, garbage burning, untreated industrial emissions/ effluents and road dust were identified as pollution sources. 62% residents endorsed the existence of ambient air pollution. Burning of stubble, garbage and biomass (cooking) was practiced by 73%, 82%, and 85% villagers respectively. 82% agreed on disease occurrence due to pollutants. 72% residents knew that some plants can ameliorate pollution. 8 treated and 3 on anti tubercular treatment, 44 with shortness of breath, 58 hypertensive and 18 allergic rhinitis cases were identified. 5 Sensitization camps were organized. Avoiding stubble burning, waste collection at source level, pollution control plantations, endorsing setting up waste recycle and treatment plant were the important steps undertaken.

Conclusions: The study inferred the existence of air pollution even in the rural areas and that the Panchayats can play a crucial role in eco friendly environmental management for a better health warranting further technical, administrative and financial support from the Government sector.

PS37-805-27 Wood fuel usage is associated with a higher leukocyte count in pulmonary tuberculosis patients

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Background: Toxic environmental exposures such as wood fuel and tobacco smoke have been associated with oxidative stress and neutrophilic inflammation and dysfunction. In tuberculosis disease, unchecked neutrophils are associated with ineffective mycobacterial killing, proinflammatory cytokines, and more extensive lung destruction. This study aims to look at the effect of wood fuel use on peripheral leukocyte counts in pulmonary tuberculosis (PTB) patients.

Methods: Data from new culture-confirmed, HIV-uninfected PTB cases enrolled in the Regional Prospective Observational Research for TB (RePORT) cohort in Puducherry and Tamil Nadu, India were analyzed. Demographic and socioeconomic data were obtained at enrollment; complete blood counts were measured. The outcomes of interest were total leukocytes (normal range: 4,500 - 11,000 cmm), absolute neutrophils (normal range: 2,000 - 7,500 cmm) and lymphocyte counts (normal range: 1,300 - 4,000 cmm). T-tests and Pearson's ² tests were used; Linear and logistic regression models adjusted for potential confounders.

Results: Of 346 PTB patients with household data, 263 (76%) were male and the median age was 44 years (range 14 - 77); 167/346 (48%) used wood fuel for cooking. Compared to non-wood fuel users, wood fuel users had a significantly higher leukocyte count (mean: 10,970 vs. 9995; $p = 0.01$) and this association remained significant after adjusting for potential confounders (mean difference: 815 ± 391 ; $p = 0.04$). Wood fuel users had a higher proportion of high (vs. normal) absolute neutrophil count (91% vs. 82%; $p = 0.02$) compared to non-wood fuel users and this association was borderline significant (aOR 1.96; 95% CI 0.97-3.97; $p = 0.06$) after adjustment.

Conclusions: Wood fuel use by PTB patients is associated with a significantly higher total leukocyte count and borderline significant higher absolute neutrophil count. Mechanistic studies should assess the effect of wood smoke exposure on TB pathogenesis.

PS37-806-27 Do fuel type and place of cooking matter for acute respiratory infections among Afghan children? Evidence from a cross-sectional survey

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Background: In Afghanistan, acute respiratory infections (ARI) is a leading cause of under-five years child's death. Many studies predicted the effects of types of cooking fuel on ARI merely which act as 'sources of origin' of smoke and ignored the effects of kitchen room and location of cooking place which act as 'place of origin' of smoke. This study mainly focused on estimating the effects of fuel types and place of cooking on ARI among children aged under-five years.

Methods: We performed descriptive statistics and multilevel binary logistic regression analyses on 30 304 children living in 955 communities and nested in 34 provinces, using data from the first round of Afghanistan Demographic and Health Survey 2015. Children suffered from cough with short, rapid breathing and accompanied by fever during the last two weeks prior to the survey are categorised as "1" for ARI symptoms and "0" other than that.

Results: Overall, 13% of the children suffered from ARI symptoms during the two weeks before survey in Afghanistan varying widely across the country. From multilevel analyses, we found that using clean cooking fuel in house without separate kitchen room has 32% lower risk [95% confidence interval (CI)=0.50-0.91] to have ARI; and with separate kitchen room has 16% lower risk in the same (95% CI=0.68-1.04); whereas, using polluting cooking fuel in house without kitchen has 11% higher risk to have ARI (95% CI=0.89-1.40) than households using clean cooking fuel in outsides. Rather, mother's education and occupational status, community poverty, ethnicity are the more influential factors of ARI.

Conclusions: For the sake of reducing child mortality, the government should encourage people to use clean fuels for cooking and provide LPG at a subsidised price; promote education, and spread awareness; introduce compulsory pneumococcal vaccination and special policy programs for specific communities.

PS37-807-27 Air pollution risk factors, wheeze and dry cough in young children living in an industrial area of Gauteng Province, South Africa

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Background: The National Department of Environmental Affairs declared three areas as air pollution hot spots. The Highveld Air Pollution Priority Area (HAPPA) is one of these areas. The objective of the study was to determine air pollution-related risk factors associated with mother-reported wheeze and dry cough in children (1-26 months old) living in Tembisa in the Ekurhuleni Metropolitan Municipality (EMM), South Africa. The EMM is also part of the HAPPA.

Methods: A cross-sectional epidemiology study was conducted during February-December 2016 in the Olifantsfontein and Clayville industrial areas of Tembisa. The mothers and their children were recruited either while attending Olifantsfontein clinic for immunization or at their homes. The International Study of Asthma and Allergies in Childhood questionnaire was applied, with additional questions concerning tobacco use, income, living conditions and educational status of the mothers. Data analysis included ² tests and logistic regression models. The study was conducted after ethical approval.

Results: Mothers of 493 children took part in the study. The prevalence of wheeze ever and dry cough ever was 16.4% and 37.7%, respectively. The mothers lived in the study area on average for 25.2 years (SD 9.7 years). After controlling for confounders, a significant association was observed between wheeze ever and the number of years the mothers had lived in the study area (OR 1.05; 95% CI: 1.01-1.08). Children who had trucks passing their homes frequently everyday were nearly four times more likely to have ever had dry cough compared to those with no truck passing their homes (OR 3.88; 95% CI: 2.29-6.57).

Conclusions: The duration the mothers had lived in this part of the HAPPA was identified as a risk factor for wheeze among their children. Truck traffic was identified as a risk factor for dry cough.

PS37-808-27 The Cooking and Pneumonia Study: exploring social determinants of lung health in a low-income setting using the participatory methodology Photovoice

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Background: The Cooking and Pneumonia Study (CAPS) was a village-level randomised controlled trial of an advanced cookstove intervention in Malawi. Air pollution through cooking on open fires or inefficient cookstoves using biomass fuels has been linked with impaired lung health and it is estimated that over 4 million premature deaths per annum are linked with this exposure. Access to clean energy as detailed in SDG 7 'Affordable and Clean Energy' is therefore important to deliver SDG3 'Good Health and Well-Being'.

Methods: In depth exploration of the social determinants of cookstove use was carried out using the participatory methodology Photovoice. Participants in 5 CAPS intervention villages were trained to use cameras and collected images about cooking over 5 days. These were then discussed in village-level focus groups. Interim analysis of this data was used to design in-depth interviews with 12 representative participants. A thematic content approach was used for data analysis.

Results: Fifty participants (mean age 31 and 80% women) were recruited between April 2016 and July 2016. Emerging themes were that health was not necessarily a priority for trial participants; cookstoves were not primarily considered interventions to improve health; misperceptions about mechanisms through which cookstoves could improve health were common; feeding families was a daily struggle; rumours and 'satanic beliefs' were frequent.

Conclusions: In a setting of poverty where food was scarce in rural Malawi, there was active engagement in CAPS and this participatory sub-study, that enabled us to elicit the priorities of CAPS participants. The development of future cookstove research and implementation programmes should take household and community priorities and beliefs into account to maximise their chances of success.

PS37-809-27 Cooking on open fires in the kitchen and TB in India

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Background: TB is air borne disease and hence air quality plays an important role to regulate the risk of the disease. Kitchen location and types cooking fuel plays an important role of household air quality specially in rural areas as mostly food is cooked with open area by

wood/cow dung etc. The paper examines effect of different cooking fuel and place of cooking on TB prevalence in India.

Methods: Cross sectional data of 2,748,327 usual residents from the DHS-4 (2015-16) in India is used for the analysis. Predicted probability is calculated on TB prevalence and type of cooking fuel and also location of the kitchen in the house. Other socio, economic and demographic factors were controlled for the analysis.

Results: High TB rate were reported from those household where cooking fuel as Straw/Shrubs/grass (604), Agricultural residue (541), kerosene (482), Dung cake (433) are used compared to electricity or LPG/natural gas/biogas (212). Further, highest TB rate found among who are having outdoor kitchen (440), or not having separate room for cooking (401) compared to who are cooking in separate room (239). People who are living in rural areas, with low wealth index and cooking other than electricity/ gas also reported significantly high rate of TB. Open fire cooking with solid fuel also significantly increases TB cases.

Conclusions: Higher use of electricity and gas for cooking may help to reduce TB incidence in the country. Prime minister's Ujwala Yojana (by surrendering subsidy in LPG by high income class to provide LPG gas connection to rural areas) may help to bring more household under clean cooking fuel. Utilization of safe cooking fuel and reduce TB incidence is the key to achieve SDG.

PS37-810-27 Association between air pollution and respiratory disease mortality in Cape Town, Durban and Johannesburg, South Africa: effect modification by apparent temperature

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Background: Climate and air quality are often treated as separate risk factors. Very few studies investigated effect modification by cold/warm days on the association between air pollution and human health in Africa.

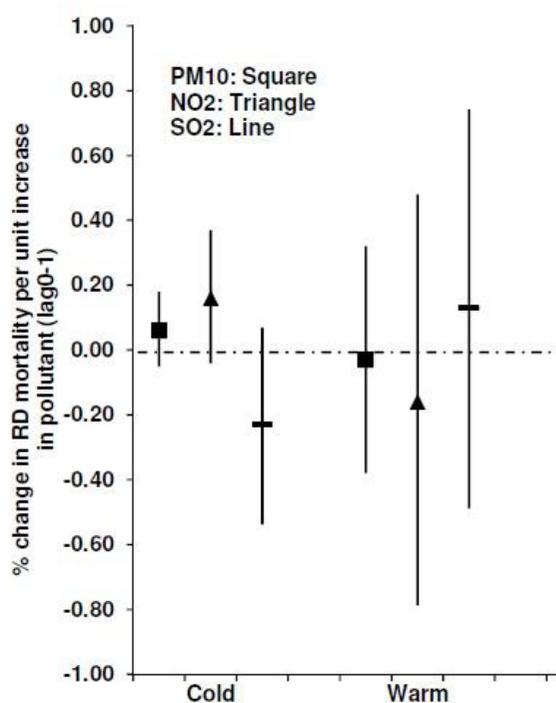
Methods: Individual level RD (ICD10: J00-J99) mortality data for 2006-2010 were obtained from Statistics South Africa, after ethics approval. NO₂, SO₂, PM₁₀, temperature and relative humidity data for 2006-2010 were obtained from the South African Weather Services. The time-series and case-crossover epidemiological study designs were applied. Lag0-1 was investigated, i.e. the average air pollutant level on the day and the day before death. Models were adjusted for confounders. Days with Tapp < 25th and >75th city-specific percentile were classified as cold and warm days, respectively. The effect estimates of the three cities were combined in a meta-analysis.

Results: A total of 10936, 17893 and 18847 RD deaths occurred in Cape Town, Durban and Johannesburg, respectively. The mean NO₂, SO₂ and PM₁₀ levels were

18.2, 10.5 and 32.7 $\mu\text{m}/\text{m}^3$, respectively in Cape Town. The mean levels were 34.2, 21.0 and 33.9 $\mu\text{m}/\text{m}^3$, respectively in Durban and 53.8, 18.5 and 59.5 $\mu\text{m}/\text{m}^3$, respectively in Johannesburg. Daily air pollutant levels regularly exceeded the WHO guidelines.

The association between PM_{10} or NO_2 and RD mortality were much stronger on cold days compared to warm days (Refer to the figure). The opposite was observed for SO_2 .

Conclusions: These results indicate that the risk of dying due to RD is different on cold and warm days in the three cities during 2006-2010. The observed results can be applied in risk assessments to estimate the impact of increased Tapp in South Africa due to projected climate change.



[Association between air pollution and respiratory disease mortality by cold and warm Tapp]

PS37-811-27 Comparison of atmospheric quality indexes: application in Athens

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Background: Air pollution is a global environmental problem that primarily affects the health of the urban population. The air quality index is an effective tool for providing the public with useful real time information on a daily basis as to the levels of air pollution. Many indexes are used all over the world using several

pollutants and calculation methods. The aim of this work is to compare the main indexes using the Athens air pollution.

Methods: 36 existing air quality indexes are used for this work. Athens air pollution measurements from 2007 up to 2016 are used as basis to compare the performances of these indexes. Then, the total daily mortality risk increase (RI_{total}, %) of Athens inhabitants is used to find out which index is better adapted to Athens air pollution.

Results: The indexes are compared between them by constructing a linear correlation table. Some of them are well correlated, other show a less well correlation and other are quite bad correlated.

Several indexes are well correlated to Athens pollution. The next step reveals that several indexes are also well correlated to the total daily mortality risk increase (RI_{total}, %) of Athens inhabitants. The best indexes are these used in Canada, Korea, Hong Kong and then the EU one. A modified EU index can better predict the total daily mortality risk increase.

Conclusions: Several indexes give similar results when used to a particular city, but other deviate significantly. Using the total daily mortality risk increase, the best indexes in Athens are these used in Canada, Korea, Hong Kong and then the EU one. Modified EU index can better predict the total daily mortality risk increase.

PS37-812-27 Deriving optimal mean indoor concentration threshold levels of PM2.5 and VOC for detecting respiratory symptoms among pregnant women in Zambia

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Background: Developing countries continue to carry the burden of air pollution-related morbidity and mortality due to poor environmental conditions fueled by limited air monitoring and lack of air quality standards at national level. The objective of the study is to determine an optimal mean indoor threshold concentration levels of $\text{PM}_{2.5}$ and VOC for detecting respiratory symptoms among pregnant women in Zambia.

Methods: Indoor $\text{PM}_{2.5}$ and VOC results and respiratory symptoms of 1170 participants were analysed. $\text{PM}_{2.5}$ and VOC were categorised according to cooking fuel types and respiratory symptoms. Mean differences using ttest were calculated to household air pollution (HAP) levels and maternal respiratory health (MRH) outcomes between rural and urban. ² to compare HAP and MRH. Multivariate analysis to determine association between HAP and MRH outcomes. A mean indoor $\text{PM}_{2.5}$ VOC concentration index developed and based on the principles of specificity and sensitivity we determined the optimal mean indoor concentration threshold for maternal respiratory symptoms.

Results: Compared to electricity users, biomass users recorded more respiratory symptoms with correspondingly higher indoor PM_{2.5} and VOC. PM_{2.5} was significantly associated with increased respiratory symptoms. HAP measurements were more than 10 times higher than WHO recommendations. An indoor PM_{2.5} mean concentration of 418 microgram per cubic metre and 372 micro gram per cubic metre in rural and urban respectively increases the risk of having at least one respiratory symptom among pregnant women.

Conclusions: HAP in Zambian houses is many times higher than WHO recommendation. Implementation of systematic PM_{2.5} and VOC data collection to enable air pollution-related respiratory health impact assessment is priority.

PS38 Windmills, clogs and healthy lungs

PS38-813-27 Pulmonary hypertension in a cohort of patients previously treated for Pulmonary Tuberculosis at Mulago Hospital in Kampala, Uganda

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Background: Despite microbiologic cure after TB treatment, Pulmonary TB survivors continue to experience respiratory symptoms as a result of residual pulmonary structural damage and pulmonary function abnormalities leading to gas exchange abnormalities and chronic hypoxia. Pulmonary hypertension may develop as a consequence but it is rarely assessed. We aimed to determine the burden of pulmonary hypertension in a cohort of patients previously treated for pulmonary tuberculosis at Mulago hospital in Kampala, Uganda.

Methods: This was a cross sectional study. We telephonically contacted a cohort of patients previously treated for PTB between January 2009 and May 2013 at Mulago hospital. All patients who responded were included in the study. We retrieved their clinical and TB diagnosis and treatment data from the database and measured their pulmonary artery systolic pressures (PASP) using 2-Dimensional Echocardiography. Participants were excluded if they had died or were unreachable by telephone. We constructed a multivariate analysis to identify factors associated with pulmonary hypertension.

Results: Among 720 participants eligible for the study, 196 responded and 102 came back for assessment and were enrolled. The median age of the participants was 34 years (inter-quartile range [IQR] 30 - 41), and 67/102 (66%) were women. We found a prevalence of post tu-

berculous pulmonary hypertension of 7.8% (95% CI 2.5 - 13.1). The PASP for post-TB PH participants ranged between 40 - 45 mmHg and all had an MRC breathlessness score of ≥ 2 . The pulmonary hypertension group had a higher proportion of participants treated >1 for PTB within a 5-year period compared to the group without pulmonary hypertension (38% vs. 6%, P value 0.003).

Conclusions: Pulmonary hypertension may occur in post-PTB patients who experience breathlessness on exertion. Our findings support early screening post-TB complications like pulmonary hypertension among TB survivors experiencing effort intolerance.

PS38-814-27 Respiratory disability assessment in treated cases of pulmonary TB: care beyond cure

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Background: Tuberculosis (TB), with an estimated 8.9 million new cases worldwide poses a significant challenge in today's healthcare scenario. Often pulmonary tuberculosis patients declared cured will have residual respiratory disability due to impaired pulmonary function that will have impact on their daily activities. With this background, we aimed to study pulmonary function impairment in treated pulmonary tuberculosis patients. **Methods:** A Hospital based cross-sectional study was conducted from June 2015 to December 2017 at India Gandhi Medical college Nagpur. Adult patients treated for sputum positive pulmonary tuberculosis were clinically evaluated followed by investigations including chest radiograph and spirometry.

Results: Males were 58(52.73%) and females were 52(47.27%) constituted the study population. Chest X-ray grading for residual lesions showed, Grade 1 in 19(17.27%), Grade 2 in 39(35.45%) & Grade 3 in 2(1.82%) .68 (61.81%) cases had impaired pulmonary function, of which obstructive pattern was the commonest 32(29.09%) followed by mixed pattern 19(17.27%) and restriction 17(15.45%). 42(38.18%) cases had normal spirometry. Of 68 cases with impaired lung function majority of the cases (48(70.59%)) did not have reversibility. Table no. 1 shows the distribution of spirometric abnormalities across the spectrum of radiological findings.

Spirometry	Normal Chest Xray	Grade 1 Chest Xray	Grade 2 Chest Xray	Grade 3 Chest Xray	Other Chest Xray abnormalities
Normal	35 (83.33%)	3 (7.14%)	0	0	4 (9.52%)
Obstruction	0	5 (15.62%)	21 (65.62%)	2 (6.25%)	4 (12.5%)
Restriction	1 (5.88%)	6 (35.29%)	6 (35.29%)	0	4 (23.52)
Mixed	1 (5.26%)	5 (26.31%)	12 (63.15%)	0	1 (5.26)

[Spirometry and chest radiographic findings in treated patients of pulmonary tuberculosis.]

Conclusions: A significant proportion of TB patients (61.82 %) even though cured develop post tuberculosis sequelae with impairment of their pulmonary functions. The study thus underlines the need for regular follow up assessment after anti TB treatment completion for evaluation and management of pulmonary impairment after tuberculosis.

PS38-815-27 Does bacteriological cure of MDR-TB patients also ensure good quality of life and preserved lung function?

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Background: Globally all national TB programmes target towards bacteriological cure of multi-drug resistant tuberculosis (MDR-TB) patients. However, whether bacteriological cure also ensures good quality of life (QOL) and preserved lung functions (LF) is largely unknown. This study was aimed to evaluate QOL and LF among bacteriologically cured MDR-TB patients under national programme in India.

Methods: 128 bacteriologically cured MDR-TB patients under national programme were prospectively enrolled in Delhi, India at completion of their 24-27 months of conventional treatment. They were evaluated clinically; radiologically by X-ray chest; Six Minute walk Distance (6MWD) and by complete pulmonary function tests (PFT) including spirometry, lung volume and diffusion capacity measurements. The quality of life (QOL) was evaluated by Seattle Obstructive Lung Disease Questionnaire (SOLDQ).

Results: 84.4% patients had some residual symptoms. 97.6% patients had residual radiological lesions on Chest X-ray. 121/128 (94.5%) could perform PFT; 96/121 (79.3%) patients were left with impaired pulmonary function. Mixed obstructive and restrictive pattern was most common abnormality observed in 55/96 (57.3%) patients. Diffusion capacity could be done in 106/128 (82%) patients; 91/106 (85.8%) patients had reduced diffusion capacity. 111/128 (86.7%) patients had low 6MWD. Patients had mean SOLDQ scores of: Physical function 66.2%, Emotional factor 62%, Coping skills 67.5% and Treatment satisfaction 52.1%.

Both, increasing severity of impairment of lung functions and worsening dyspnoea score were statistically significantly associated with decreasing QOL scores, especially in relation to physical function, emotional score and coping skills ($p < .05$).

Conclusions: Despite bacteriological cure and successful complete treatment of MDR-TB patients, significant number of patients have residual clinical symptoms, radiological lesions, and impaired lung functions leading

to poor QOL. In addition to achieving bacteriological cure, there is a need to add rehabilitation interventions under national TB programmes, focussing on management of post treatment sequelae and improving quality of life of the successfully treated MDR-TB patients.

PS38-816-27 Pulmonary outcomes in patients with tuberculosis: systematic review and meta-analysis

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Background: In the past few decades, treatment success in tuberculosis (TB) has been primarily defined as the eradication of active infection and patients successfully completing their anti-TB therapy are considered cured. However, accumulating literature suggests that lung impairment in TB patients is frequent and substantial. This systematic review is aiming at summarizing the scientific evidence on the association of active pulmonary TB infection and lung function impairment with a focus on spirometry outcomes.

Methods: PubMed was searched for records published before August 2017. Non-English articles, letters to the editor and conference abstracts were excluded. All included studies measured the lung outcome using spirometry, some with additional methods such as St. George Respiratory questionnaire, 6 minutes walking test, chest Xray or computer tomography. Where appropriate, we performed a meta-analysis, using only spirometry data. Methodological quality of the publications was assessed using the Newcastle-Ottawa Scale.

Results: Among 964 articles identified, 51 were included in this review representing all world regions. Spirometry data reporting differed between the studies, with some studies (21) reporting FVC and/or FEV₁ in liters; when others in % of predicted. Type of lung function impairment (obstruction, restriction, mixed or normal) was reported in 35 studies, while degree of impairment (mild to severe) was described in 14 studies. A meta-analysis of % of predicted FVC and FEV₁ from patients with sensitive and multi-drug resistant TB demonstrated that majority of results were below normal limit.

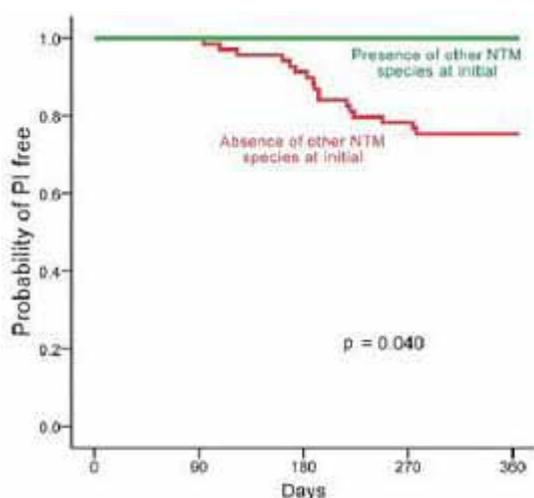
Conclusions: This systematic review demonstrated a heterogeneity in reporting the lung outcomes in TB patients and lack of reference standards. However, all studies described an impaired lung function in post TB patients. In order to address the diagnosis and therapy of TB sequelae in future TB guidelines, more scientific evidence is needed, e.g. on what the appropriate methodology and time points are for clinical pulmonary evaluation in TB patients.

PS38-817-27 The predictors of *Mycobacterium kansasii* pulmonary infection within 1 year for patients initially having a single MK isolate

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Background: *Mycobacterium kansasii* (MK) is one of the most virulent nontuberculosis mycobacteria (NTM) species, yet single MK isolate in multiple sputum samples is still unable to establish the diagnosis of pulmonary infection (PI) based on current guidelines. This study aimed to evaluate the predictors of developing MK-PI within 1 year for subjects with single MK isolate, with a special emphasis on concomitant presence of other NTM species in sputum.

Methods: Patients with a single MK isolate from at least three sputum samples collected within three months from 2008 to 2016 were retrieved from six hospitals in Taiwan. Those with ≥ 2 follow-up sputum samples and chest radiography in the subsequent nine months were included for final analysis. The primary outcome was development of MK-PI during follow-up. Independent outcome predictors were investigated by multivariate logistic regression analysis.



[Time to developing MK-PI, stratified by presence or absence of other NTM species at initial]

Results: A total of 84 episodes of single MK isolate at initial 3 months from 83 cases were analyzed. Within one year, 17 (20%) episodes progressed to MK-PI. Fifteen episodes had concomitant other NTM species and none of them developed MK-PI, whereas 15 (22%) of the remaining 69 episodes did ($p=0.034$). Among of them, three had high acid-fast smear (AFS) grade ($>=3$)

and all developed MK-PI, whereas 14 (21%) of the 66 episodes without high AFS grade did ($p=0.013$). Of the 66 episodes without high AFS grade, the independent predictors of developing MK-PI were elementary workers (OR 5.94 [1.15 - 30.742]; $p=0.034$) and high initial radiographic scores (>6) (OR 11.96 [1.98 - 72.08]; $p=0.007$). Diabetic mellitus was the protector of MK-PI (OR 0.12 [0.02 - 0.86]; $p=0.035$).

Conclusions: For patients with only one MK isolate from multiple sputum samples, early anti-MK treatment should be considered if no concomitant NTM species in sputum, high sputum AFS grade, radiographic scores >6 , and being an elementary worker.

PS38-818-27 Experience in developing a software visualization tool to increase the informative value of transbronchial biopsy in diffuse parenchymal lung disease

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Background: The urgency of the problem of diagnostics of DLPD is caused by a high proportion of diagnostic errors. A low-invasive method that allows the lowest risk of getting pulmonary tissue is TBB. The resulting material may be uninformative due to the small size of the biopsy and the "blind" sampling of the material. The objective of this project was to provide the user with a three-dimensional visualization and navigation model of the chest, as well as areas of the affected tissue. It should display, from where and to what distance it is necessary to push biopsy forceps. The program must perform all these operations automatically.

Methods: Developed software was intended to help the bronchologist at the stage of preparation for transbronchial lung biopsy and its use should lead to an increase in the informative value of TBB. The initial data for the program based on chest CT DICOM pack. Chest, lungs and elements of the affected tissue to be displayed in three-dimensional model. The program automatically determines the route and the distance to which you need to push the needle out of the endoscope, as well as the direction of movement of the biopsy cutters.

Results: It was not possible to obtain altered lung tissue in 16.7%. To compare the informative value of traditional TBB and TBB with 3D navigation was obtained in 83.3% of patients., biopsy samples of lung tissue obtained with traditional TBB in 56.3% of cases, in unchanged pulmonary tissue in 46.7% of cases.

Conclusions: The use of virtual navigation at the planning stage of TBBL increases the probability of obtaining altered pulmonary tissue by 1.56 times (from 53.3% to 83.3%).

PS38-819-27 Trends in epidemiology of asthma and chronic obstructive pulmonary disease from 2011 to 2016 in Northern India

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Background: Asthma and chronic obstructive pulmonary disease (COPD) are the most common chronic respiratory conditions in rural areas, contributing to heavy social and economic burden. responsible for pathogenesis. This study was conducted with objective to investigate trends in asthma and COPD at the population level in rural areas in Northern India over a period of six years - 2011-2016 to help understanding the relationships between disease prevalence, morbidity and mortality.

Methods: An ecological study was conducted in a secondary care hospital situated in a village catering the nearby rural areas in two states in Northern India. The hospital maintained a monthly record of total number of patients seen as per International Classification of Diseases -10 (ICD -10) system. Data was collected from the year 2011 to 2016 for total number of cases of asthma and COPD reported in the hospital over the same period. Data was analysed using SPSS software (version 17). Results were presented in mean (standard deviation), simple proportions and percentages.

Results: Data was extracted for 4.1 million patients reported in the hospital. There was little change over time in the incidence rate of COPD among females (8 per 1000 patients in 2011 to 7 per 100 patients in 2016). Among males, incidence rate of COPD changed from 9 per 1000 patients in 2011 to 12 per 100 patients in 2016. Asthma incidence rates were significantly different in males and females ($p < 0.05$) with increasing burden among males from 2011-2016 (2 per 1000 patients in 2011 to 5 per 100 patients in 2016). Potential risk factors may include poverty and environmental factors such as air pollution and smoking.

Conclusions: Very limited decrease in incidence rates despite policy efforts among the deprived groups of population is a cause for concern.

PS38-820-27 Global trends in lung cancer risk reduction among former smokers: an analysis from the Global Burden of Disease Study 2017

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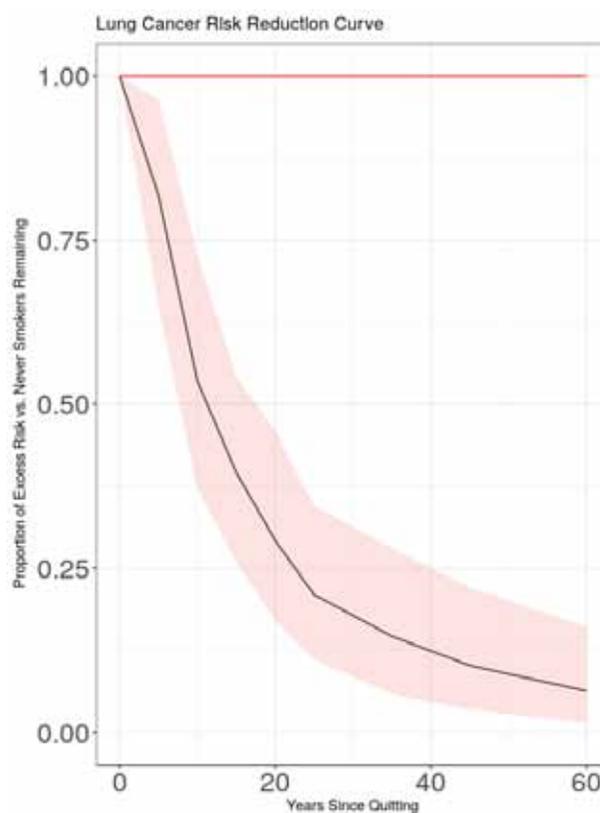
Background: Lung cancer risk increases with age and cumulative exposure to tobacco smoke and decreases with time since smoking cessation. Eligibility criteria and

modalities for screening vary worldwide. In the United States, the National Lung Screening Trial showed a mortality benefit in screening former heavy smokers between the ages of 55-74 years who quit within the prior 15 years.

Methods: We performed a Bayesian mixed-effects dose-response meta-regression to synthesize data from 25 prospective cohort and case-control studies examining the effects of former smoking on lung cancer risk, measured in years since quitting. Data were screened from PubMed and previous systematic reviews, dating between 1990 and 2013, and spanning 17 countries from North America, Europe, and East Asia.

Results: Excess risk relative to never smokers fell sharply within the first 20 years of quitting down to 30% [17%-46%] of its value at the time of cessation, before the slope of decline tapered (Figure 1). By 10-years post-cessation, the proportion of excess risk remaining was estimated to be 50% [37%-73%]; at 15-years post-cessation, 40% [26%-54%]. Lung cancer risk approximated that of never-smokers by 40 years post-cessation.

Conclusions: Consistent with prior landmark studies on the health benefits of smoking cessation, we found that global trends in lung cancer risk reduction conformed to expected patterns with increasing time post-cessation. The proportion of excess risk for lung cancer remains elevated above 20% for those individuals between 15-25 years post-cessation. Within the US context, these individuals would not currently be recommended for routine lung cancer screening, in spite of their elevated risk.



[Lung Cancer Risk Reduction Curve]

PS38-821-27 Connaissances et pratiques des médecins généralistes sur la BPCO à Niamey, Niger

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Background: Le médecin généraliste est en première ligne en matière de dépistage et de prise en charge de la BPCO. Il existe peu de données sur les connaissances et pratiques des médecins dans la prise en charge de la broncho-pneumopathie chronique obstructive. Au Niger il n'existe pas encore de guide national sur la prise en charge de la BPCO qui semble être sous estimée et mal connue. Ceci nous a poussés à réaliser ce travail. Le but de notre étude est de faire l'état des lieux des connaissances et pratiques des médecins généralistes sur la BPCO

Methods: C'était une étude prospective du 1^{er} Avril 2017 au 31 Décembre 2017 chez 144 médecins généralistes exerçant dans les services de Médecine interne, pneumologie, cardiologie et dans le secteur public et privé.

Results: Au total 144 médecins généralistes avaient été colligés, les hommes représentaient 62,5% et l'âge moyen était de 32,37 ans. La définition de la BPCO était connue par 37 médecins (25,7%), les entités appartenant à la BPCO étaient connues par 28 médecins (19,4%). Le tabac était cité comme facteur favorisant de la BPCO par 141 médecins (97,9%). Les principaux signes cliniques de la BPCO (Dyspnée, Toux et expectoration) étaient connus par 38 médecins généralistes (26,4%). La spirométrie était connue par 9,7% (14 cas) des médecins généralistes. Les diagnostics différentiels de la BPCO étaient connus par 26 médecins généralistes (18%). La thérapeutique utilisée était l'oxygénothérapie (77,1%), la Kinésithérapie (58,5%), les bronchodilatateurs longue durée d'action + corticoïde inhale (43,1 %), les bronchodilatateurs de longue durée d'action (41,7%), les bronchodilatateurs de courte durée d'action (35,4%).

Conclusions: La connaissance et la pratique des médecins généralistes sur la BPCO est insuffisante d'où la nécessité d'insister sur les enseignements post universitaire et la création d'un guide national sur la prise en charge de la BPCO.

PS38-822-27 Community-based screening for chronic obstructive pulmonary disease among the elderly in an urban area of South India

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Background: Underdiagnoses of chronic obstructive pulmonary disease (COPD) is common as this disease is often not recognised and diagnosed until it is moderately advanced. This study was an attempt to find the burden of COPD among elderly urban population.

Methods: This community based observational study was conducted among 1037 elderly people in urban areas of Puducherry in India. Participants were recruited using multistage random sampling technique. IPAG questionnaire [Cut off Score - 17 (Positive predictive value: 92%)] was administered among all study subjects. We compared quantitative parameters between COPD and non-COPD subjects using the student t-test and ² test was applied for qualitative variables.

Results: Among 1,037 subjects, 435 (41.9%) were male and the proportion of smokers among them was 16.5%. A positive IPAG questionnaire for COPD (≥ 17 points) was obtained in 342 (33.1%) subjects. Based on the responses by the probable COPD subjects, 69 (22.2%) had no cough, 215 (62.9%) reported sputum production in the absence of a cold, 186 (54.4%) cough up phlegm (sputum) in the morning, 162 (47.4%) had frequent or occasional wheezing and 113 (33 %) reported to have or had any allergies. Age and body weight found to be associated with positive IPAG questionnaire. Probable COPD was significantly higher among smokers (52.9%) as compared to non-smokers (31.7%) (P value < 0.01).

Conclusions: Proportion of subjects with possible COPD was high in community. IPAG questionnaire was an easy to administered tool for screening of COPD and little expertise is sufficient for its administration.

PS39 New agents, old ways: old agents, new ways

PS39-825-27 Treatment outcomes of delamanid for intractable TB patients in a National TB Hospital

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Background: Delamanid is a new anti-TB drug, but few data exist on its use outside clinical trials. This study was to investigate the clinical characteristics associated

with treatment outcome in drug-resistant tuberculosis patients after the treatment regimen containing delamanid.

Methods: Among the drug-resistant tuberculosis patients who were treated with a delamanid-containing regimen between November 2015 and March 2017 in Masan National Tuberculosis Hospital. We performed a retrospective cohort study among 26 patients with medical records who did respond to this regimen.

Results: A total of 26 patients with intractable TB, of which 7 (26.92%) were MDR-TB, 13 (50%) were pre-XDR-TB, 6 (23.07%) were XDR-TB, respectively. All completed 24 weeks of delamanid treatment from November 2015 to March 2017. Of 14 patients (53.85%) who had positive culture sputum at the initiation of delamanid treatment and 11 patients (42.31%) who had positive smear sputum respectively. The proportion of AFB smear conversion at 24 weeks was 34.61% (9 of 26). The proportion of culture conversion at 24 weeks was 38.46% (10 of 26) in solid medium. The median time to culture conversion was 97 days (range = 21-265). Of the 26 patients, there was no serious adverse event or death. Two patients developed a transient QTcF of > 500 ms.

Conclusions: The treatment of drug resistant tuberculosis including delamanid is effective, and the sputum culture conversion is similar to that of Phase II clinical trials conducted by pharmaceutical company.

PS39-826-27 A description of patients receiving bedaquiline and delamanid in Mozambique

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Background: Bedaquiline and delamanid have been recommended for treating MDR-TB patients with additional resistance to injectable drugs and fluoroquinolones and have shown higher success rate in this population. In 2015, these drugs were introduced in Mozambique.

Methods: We performed a retrospective analysis of the first MDR-TB patients receiving bedaquiline and/or delamanid at treatment initiation in Mozambique from 2015 to 2018. We described patients' characteristics and indications for receiving new TB drugs and reported the proportion of patients who received bedaquiline and/or delamanid for more than 6 months.

Results: A total of 35 MDR-TB patients received bedaquiline and/or delamanid at treatment initiation. They were mainly males (57.1%), median age of 32 years [IQR 24-40], median BMI of 17 kg/m² [IQR 15.6-19.2] and 45.7% HIV-positive. Among them, 25 (71.4%) received

bedaquiline only, 5 (14.3%) received delamanid only and 5 (14.3%) received concomitantly bedaquiline and delamanid. Indications for receiving these drugs were mainly based on second-line resistance: 27/35 (77.1%) were XDR and 6/35 (17.1%) were pre-XDR. All patients who received concomitantly bedaquiline and delamanid were XDR patients without any other choice of effective drugs due to long previous treatment with drugs from all other groups. Among patients who received bedaquiline and/or delamanid, 6 died in a median time of 2.1 months [IQR 0.4-3.6] after initiation, 3 cured, 1 was lost to follow-up and 25 were still alive and on treatment for a median time of 12.8 months [IQR 6.9-14.7]. The proportion of patients who received these drugs more than 6 months was: 17/30 (56.7%) for bedaquiline and 6/10 (60.0%) for delamanid.

Conclusions: Access to bedaquiline and delamanid is increasing in Mozambique for patients resistant to second-line drugs or, who failed, or are unable to tolerate MDR-TB treatment. An important proportion of patients received these drugs longer than recommended mainly due to the lack of other therapeutic options.

PS39-827-27 Treatment of drug-resistant tuberculosis with regimens containing bedaquiline and delamanid: description of patient eligibility criteria among Ethiopian cohorts

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Background: As part of endTB, Ethiopia introduced new TB drugs for DR-TB patients under programmatic conditions following the WHO guidance. This study is aimed at describing the indications for the use of these new TB drugs and assess delays between eligibility declaration and treatment start among the Ethiopian endTB cohort.

Methods: This is part of a prospective observational study on treatment of DR-TB with regimens containing bedaquiline or delamanid in Ethiopia. Eligibility for new drugs was based on the WHO Interim policy guidelines. We describe the distribution of indications for new TB drugs and the time delay between eligibility determination and actual treatment start with new-drug-containing regimens.

Results: 39 DR-TB patients received regimens containing bedaquiline or delamanid in the study-period. 21(54%) received bedaquiline, 13(33%) delamanid, 5 (13%) received both. 27 patients (69%) received bedaquiline or delamanid for likely compromised effectiveness of regimens lacking these drugs (Table). Intolerance of second-line drugs was the indication for 11 (29%) of patients. Bedaquiline or Delamanid was started at the beginning of the current TB treatment course in 29 (74%) of the patients, whereas 10 (26%) of the patients started on new drugs later in the course of treatment. The median delay between the date patients were declared eligible and actual treatment start date was 15-days with range of (1- 54) days.

Conclusions: The main indication for new TB drugs in the Ethiopian cohort of DR-TB patients was being unable to construct effective regimen due to resistance or failing from MDR-TB regimen, followed by intolerance to SLDs necessary for effective regimen. Very few patients with extensive disease or co-morbidities were received new-drug-containing regimens. Delays to treatment start with new drugs after eligibility determination were observed. Treatment initiation delays should be addressed to reduce risks of transmission and poor outcomes.

PS39-828-27 High cure rates with bedaquiline-based treatment of pre- and extensively drug-resistant tuberculosis in Niger

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Background: The treatment success rates for Pre and Extensively Drug Resistant (pre XDR/XDR) tuberculosis achieve suboptimal results worldwide barely exceeding 30% cure rate.

Methods: Ten patients were treated between 2012 and 2017 with a standardized regimen based on bedaquiline and linezolid (Lzd) as core drugs, supplemented by amikacin, clofazimine (Cfz), PAS, high dose of isoniazid and pyrazinamide (Z) as companion drugs. The intensive phase lasted 4 to 6 months and the total duration of the regimen was 20 months. Only sterilizing and companion drugs (Lzd, Cfz, Z and PAS) were maintained in the continuation phase.

Results: Among 10 patients, 1 had a strain resistant to all the fluoroquinolones, kanamycin and capreomycin (XDR), 1 had a pre-XDR strain resistant to kanamycin and capreomycin and 8 were pre-XDR with resistance to fluoroquinolones. All of them were males, HIV negative with a median age of 28 years and a median BMI of 17.2 kg/m².

All patients had smear and culture conversion (median: M2; range: M1 - M5).

Nine patients (90%) were cured and 1 died of stroke after 17 months of treatment. Eight patients assessed for follow-up 12 months after cure remained culture negative

The adverse events were mild hyperlipasemia (90%), hearing loss (80%) which was severe in 2 (20%) cases, mild hepatotoxicity (70%) and moderate peripheral neuropathy (60%). One patient had severe but reversible optic neuritis at M22 and linezolid was stopped. Another patient had severe myelosuppression, linezolid was stopped at M3 and reintroduced at a reduced dose. No patients had QTc prolongation according to Framingham formula at baseline (mean \pm SD: 374 \pm 21.7ms), day 7 (369 \pm 15.2ms), M1 (387 \pm 19ms), M3 (378 \pm 16.1ms) and M6 (377 \pm 15.5ms).

Conclusions: A standardized treatment based on bedaquiline, linezolid and clofazimine may achieve high cure rates if amikacin is still effective.

PS39-829-27 QTcF prolongation with bedaquiline: early experience from India

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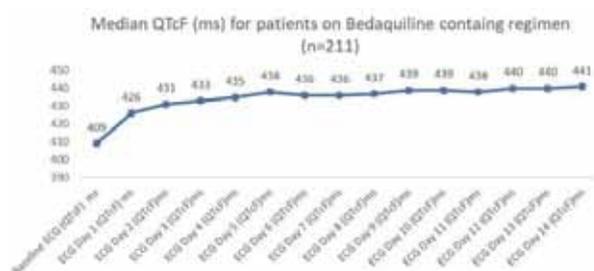
Background: India has introduced newer drug Bedaquiline under the Conditional Access Programme (CAP) during 2016. WHO has recommended use of this drug for the Multi drug resistant (MDR)/ Rifampicin Resistant (RR)-TB patients having addition second line drug resistance where the regimen could not be formed as per the standard WHO recommendation. Considering the potential cardiotoxic effects (QTc prolongation), Bedaquiline was introduced within national TB programme with strict monitoring protocol of active drug safety monitoring (aDSM).

Methods: Eligibility of MDR/RR-TB patients for newer drug containing regimen was assessed based on additional DST carried out for second line anti TB drug. All eligible and willing DR-TB patients were subjected to pre-treatment evaluation including baseline ECG. If QTcF is normal (< 500ms) along with other normal investigation are considered eligible for Bedaquiline. Drug was given 400 mg initially for 2 weeks and later to that it was given 3 times in a week. During follow up patient was evaluated with ECG daily till 14th days and after than weekly till the 3rd month of treatment. Than after ECG was done on monthly basis unless the any abnormal ECG finding reported.

Results: QTcF of initial 211 patients initiated on Bedaquiline containing regimen was analysed for initial 15days. Baseline median QTcF for enrolled patients was

409 ms with range of 318-488 ms. After introduction of Bedaquiline median QTcF value increased on first and second day were 11 ms and 21 second respectively. Median QTcF value for next 14 days is placed in image attached here.

Conclusions: Increase in median QtcF was observed during initial 14 days but this was within the safe range of (< 500ms). This suggests that the serious side effect of QTcF prolongation has not observed much frequently and patient is able to tolerate it well.



[Median QTcF of patient initiated on Bedaquiline containing regimen]

PS39-830-27 Poor quality of life in patients who experience adverse events while on treatment for drug-resistant TB

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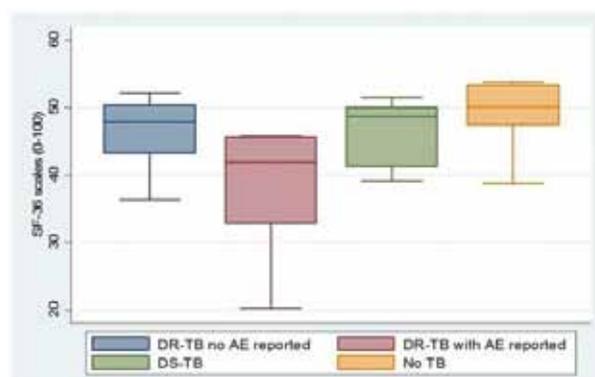
Background: Adverse events (AEs) are common during treatment of drug-resistant(DR-) TB. Little is known about the health-related quality of life (HRQoL) of patients receiving treatment for DR-TB or the effect of AEs on HRQoL

Methods: We conducted a cross-sectional study among adult patients with laboratory-confirmed rifampicin resistant TB who initiated treatment at a public-sector outpatient DR-TB clinic in Johannesburg, South Africa between 02/2015-01/2018. Data on HRQoL were collected by trained interviewers through face-to-face in-

terviews using the RAND 36-Item Short Form Health Survey (SF-36). We report averages for major domains (scales) and mental (MCS) and physical health (PCS) component summary scores, stratified by whether AEs were reported in the last four weeks. In a sub-analysis, we compared the scales of HIV-positive (+) patients with DR-TB to those of patients without TB or with drug-sensitive (DS) TB.

Results: We enrolled 149 patients (median age 36 years IQR 29-43, 45.0% female, 78% HIV-positive, 81% on ART, 40% on second-line TB treatment < 6 months). 42/149 (28%) patients reported a total of 48 AEs in the preceding 4 weeks: 15 hearing loss, 16 peripheral neuropathy, 10 vertigo, and 7 depression. Patients who reported an AE had significantly lower scales and were more likely to have a lower MCS and PCS than those who did not (Figure 1). HIV+ patients with DR-TB and AEs reported much poorer HRQoL than patients without TB and reported poorer emotional well-being than patients with DS TB.

Conclusions: Patients who reported an AE during DR-TB treatment reported poorer HRQoL, affecting both their mental and physical health, than those who did not. Patients require emotional support to deal with DR-TB and HIV and the potential overlapping toxicities which may be worsened by concurrent treatment. These findings are likely to have implications for patients' treatment adherence and outcomes as well as social well-being.



[Fig 1. SF-36 scales aggregated for DR-TB patients, stratified by whether adverse events were reported in the last four weeks, and compared to two comparison cohorts that were enrolled and interviewed (i.e. patients without TB or with drug-sensitive TB).

(DR-TB drug-resistant TB, DS-TB drug-sensitive TB, AE adverse event, SF-36 RAND 36-item Short Form Health Survey)]

PS39-831-27 Risk factors associated with acquiring drug-resistant tuberculosis as found at the Can Tho Tuberculosis and Lung Hospital, Vietnam

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Background: Drug-resistant tuberculosis (DR-TB) is currently the most challenging issue in the fight against TB. It has severely affected many countries, including Vietnam, a middle-income country with a high prevalence of tuberculosis. Vietnam has the 14th highest burden of DR-TB, with 6,421 DR-TB cases (2.7%) detected in 2014. DR-TB has both increased the economic burden for patients, as well as increased tuberculosis mortality. Our study aimed to understand the risk factors associated with acquiring DR-TB as found at the Can Tho Tuberculosis and Lung Hospital in Vietnam.

Methods: A cross-sectional study was done on 1,025 hospitalized TB patients at Can Tho TB and Lung hospital in 2016. Demographic and clinical data were collected from patients' medical records and interviews were conducted to assess potential risk factors for DR-TB. The association between the factors and DR-TB were determined by χ^2 or Fisher tests.

Results: The proportion of drug-resistant tuberculosis was 14% (144/1,025 patients). Most cases were multi-drug resistant (99.3%), and only a small number were extensively drug resistance (0.7%). For analysis, patients were grouped by age (15-29; 30-44; 45-59; ≥ 60). Statistically significant risk factors ($p < 0.05$) associated with DR-TB include: age (people less than 60 years old), occupation (merchant), type of housing (crowded and damp home), location of residence (urban) and history of contact with TB patients (household contact).

Conclusions: Our study can medical practitioners, health policy makers and the national TB program in Vietnam target screening activities to the most at-risk individuals. Communication and health education on DR-TB should be scaled-up nation-wide.

PS39-832-27 Short-course treatment regimens for multidrug-resistant tuberculosis

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Background: The need of the hour is to find out a robust, highly-efficacious, economically sustainable, and shorter duration treatment regimens for MDR TB that gives a good cure rate. We therefore conducted a systematic review of available evidence on treatment outcomes of short course MDRTB treatment regimens. We aimed to determine the cure rate, treatment completion, the incidence of adverse events and mortality.

Methods: Original studies were identified using the databases, till March 2017: Cochrane library, PubMed, Embase, International Journal of Tuberculosis and Lung Disease, abstracts in Union Conferences. Heterogeneity across studies was assessed using the Cochran's Q test and I² statistic. Pooled estimates of treatment outcomes were computed using the random effect model.

Results: The average study population (range) was 989. The age ranges from 16 to 76 years. The participants had previously received anti-tuberculous therapy. With the available data in 4 studies, most of them were males 509. The study period ranges from 1994 to 2011. The overall cure rate was 82.9% [95% CI 80.4%-85.2%] for the included studies whereas 5.9% (95% CI: 3.9-8.9%) defaulted from therapy, and 1.3% (95% CI: 0.6-2.7%) failed therapy and 1.9% (95% CI: 0.6-6.0%) relapsed.

Conclusions: This systematic review of MDR TB patients with no prior second line ATT drugs showed higher treatment cure rates with shorter regimens ranging from 9-12 months with very low relapse and failure rates. Treatment success was better with 12 month regimen compared to 9 months regimen and to surgical intervention. There has been no randomized study to address the comparative efficacy of chemotherapy versus surgery combined with chemotherapy in the management of MDR-TB. Prospective randomized controlled trials comparing different treatment strategies for MDR-TB will provide greater insight into the improvement of MDR-TB treatment protocols.

PS39-833-27 Efficacy and safety of the MDR-TB regimen containing clarithromycin

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Background: There have been disputes about shorter regimen and use of clarithromycin (Clr) since the “WHO treatment guideline for drug-resistant tuberculosis” was updated in 2016. We observed the efficacy and safety of the 18-month regimen containing Clr to provide evidence for rational treatment of MDR-TB.

Methods: 681 MDR-TB patients were enrolled from 20 hospitals 2009 -2015. Of them, 515 (observation group) were treated with the regimen 6Z-Am-Mfx-Clr+XY/12Z-Mfx-Clr+XY and 166 (control group) were treated with 6Z-Am-Mfx+XY/18Z-Mfx+XY. XY indicated two sensitive anti-tuberculosis drugs selected based on the individual drug susceptibility testing profile. Sputum conversion rate and the treatment outcome were used to evaluate the efficacy and the frequency of adverse reaction occurrence was used to evaluate the safety.

Results: Sputum culture conversion rate were 59%, 76% and 85% at the end of 3, 6, 18 month respectively in the observation group which were close to those in the control group ($P>0.05$). Moreover, the conversion rate at the end of treatment was slightly higher than the control one (85% vs. 79%, $P>0.05$). Compared to the control, higher treatment success rate (65% vs. 53%) and lower mortality rate (2% vs. 5%, $P<0.05$) achieved from the observation group while failure rate and loss rate were similar between the two groups ($P>0.05$). The total frequency of adverse reaction occurrence were 25% and 26% in the observation and control group ($P>0.05$) and the top three were drug-induced liver injury, nausea/vomiting and granulocytopenia in both groups ($P>0.05$).

Conclusions: The efficacy of the 18-month regimen with 6 drugs containing Clr was better than or equivalent to the regimen of standard 24-month regimen and didn't increase the adverse reaction occurrence. Therefore, it is worth for clinical application.

PS39-834-27 Isoniazid Mycobacterium tuberculosis resistance: genetic support and impact on patient treatment

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Background: Isoniazid resistance (INH-R) rate in Tunisia is estimated at 5.1% for new cases versus 15.5% for previously treated tuberculosis cases (TB-cases). The aim of this work is to study the genetic support of this resistance, and to evaluate the socio-demographic characteristics, treatment regimens and treatment outcomes according to the sensitivity's status and level of resistance to isoniazid.

Methods: Retrospective analytical cohort study including 42 cases of INH-R tuberculosis compared with 104 drug-susceptible cases isolated from 2013 to October 2016 in the NRL *Mycobacteria* - Pneumology Hospital A. Mami Tunisia. The INH-R strains are classified into a low ($n=15$) and a high ($n=27$) resistance levels according to gene mutations respectively *inhA* and/or *katG*.

Results: Patient characteristics of INH-R group were an average age of 34 years and sex-ratio of 2.5 versus 40.8 years and sex ratio of 4 in drug susceptible cases group. Previous TB treatment was significantly associated with INH-R (OR= 8.8; CI(95%)= [1.6-44]; ($p=0.007$)). Most cases of INH-R tuberculosis (52.4%) have received a standard 6-month regimen (2HRZE/4HR). INH-R tuberculosis was significantly associated with an unfavorable treatment outcome (OR=5.6; CI(95%)=[1.3-23.6]; $p=0,017$). These results are statistically more frequent in the group of patients already treated compared to new cases (33.3% vs. 5.6%; OR=8.5; CI(95%)= [1-78]). Progression to multidrug-resistant tuberculosis was observed in 4.8% of INH-R tuberculosis cases. Favorable treatment outcomes were similar between the two subgroups of low and high level of resistance to INH (93.3% vs. 81.5%; $p=1$).

Conclusions: This study suggests that a high priority should be given to the rapid and accurate detection of INH-R tuberculosis as well as the development of an effective strategy for the treatment of these patients and especially recommended for previously treated TB-cases.

PS39-835-27 Adoptive transfer of in vitro expanded autologous T cells enhances the efficacy of chemotherapy against MDR-TB

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Background: Currently, multidrug-resistant tuberculosis (MDR-TB) is still a difficult problem. The regimens of cytokine-induced killers (CIK), which are in vitro expanded autologous T cells, combined with chemotherapy have been reported to play a significant role in cancer treatment. However, it is unclear whether CIK could suppress *Mycobacterium tuberculosis* (Mtb) in MDR-TB patients.

Methods: Peripheral blood mononuclear cells (PBMC) from 9 participants were obtained. The T cells in PBMC were expanded in vitro following with recombinant human gamma-interferon (IFN- γ), anti-CD3 antibody, recombinant human interleukin (IL)-1 and recombinant human interleukin (IL)-2. Then these T cells were transfused to patients. The number of T cells infused was above 1×10^9 per patient and killing activity was more than 65%.

Results: After treatment for 1 month, the negative conversion rates of sputum and Mtb culture were both much higher in the group treated with CIK in combination with chemotherapy, both of which were both ratios of 8/9, compared to those of the group treated with chemotherapy, which were 0/9 and 2/9 respectively. After treatment for 3 months, the negative conversion rates of sputum and Mtb culture were also significantly higher in the group treated with CIK in combination with chemotherapy, which were 8/9 and 9/9 respectively, compared to those in the group treated with chemotherapy only, which were 2/9 and 5/9 respectively. The results of lung CT showed that in the group of CIK combined with chemotherapy, 5 of 9 cases (55.56%) were improved, 3 of 9 cases (33.33%) had no change and 1 of 9 cases (11.11%) were worsened, whereas in the group of chemotherapy only, 3 of 9 patients (33.33%) were deteriorated and 6 of 9 cases (66.67%) had no change.

Conclusions: CIK appeared to be an effective adjunct immune therapy for MDR-TB. The finding should be confirmed in further studies.

PS40 Public, private tuberculosis: separate and together

PS40-836-27 Contribution of the private health sector to TB case finding in Kabul, Afghanistan: document review

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Background and challenges to implementation: The USAID-funded TB project (TB CAP, TB CRE I and CTB) in Afghanistan has assisted the National TB Program (NTP) in implementing an Urban directly observed treatment, short-course (DOTS) approach in Kabul city, since 2009. Before 2009, private health facilities were not engaged to provide TB services. TB indicators were poor TB case detection rate was 37%. To address these challenges, USAID funded TB projects assisted NTP to engage private health sector in TB service delivery. This assessment aims to evaluate the contribution of private health facilities in TB case finding in Kabul city.

Intervention or response: In 2010, a baseline assessment was conducted, a memorandum of understanding with the private sector was signed, and medical staffs were trained in TB case management and TB recording and reporting formats. Supervision, monitoring, and feedback were provided to private clinics. NTP and CTB technical teams then reviewed and analyzed the TB surveillance data from 2010-2017 using standardized NTP recording and reporting tools.

Results and lessons learnt: In 2010, six private health facilities were engaged in TB. The number of all forms TB cases notified were 2,738 TB cases in Kabul city. Of them, 133 (5%) were diagnosed by the private sector and 30 (22.5%) were bacteriologically-confirmed (BC) TB cases that treated by the private sector. In 2017, of 6,702 total TB cases diagnosed in the Kabul province, the private sector notified 985 (14.7%), of which 239 (24.3%) were BC TB cases. In seven years, Kabul urban DOTS notified 35,650 TB cases of all forms, and private hospitals contributed 3,576 (10%) of these.

Conclusions and key recommendations: Engaging private hospitals in TB control activities increased notification of TB cases in Kabul. We recommend applying this practice in other private hospitals and involving them in TB activities.

	2010	2011	2012	2013	2014	2015	2016	2017
No of Private hospitals involved in TB	6	8	9	11	11	13	16	23
All cases identified by private hospitals	133	175	267	204	377	633	802	985
All Kabul TB cases identified	2738	2728	3215	3548	5007	5449	6089	6702
Contribution of private hospitals	4.85%	6.41%	8.3%	5.74%	7.52%	11.61%	13.17%	14.69%

[Trend of TB case finding in private hospitals in Kabul city]

PS40-837-27 Improve access to quality TB care through engagement of private clinics in Almaty city, Kazakhstan

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Background and challenges to implementation: TB care access in Kazakhstan was traditionally limited by being the designated responsibility of TB services and primary healthcare (PHC). Healthcare reforms commencing in 2014, expanded outpatient care through integration of TB service into PHC sector. Reforms allow for engagement of private clinics in provision of TB care through the state funded Guaranteed Volume of Free Medical Care (GVFMC). However, uptake of the new provisions and private healthcare sector integration into TB care service networks was hampered due to insufficient information and collaboration mechanism. One of the objectives of project "Improved TB-HIV prevention and care - Building models for the future"[1] was to support the engagement of the private sector in TB care. The project covers 16 private clinics in Almaty city.

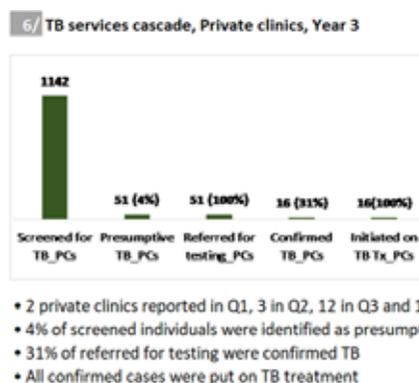
[1] Funded by the Dutch Government

Intervention or response: Initially a qualitative survey was conducted in Almaty city to gain insights about the current role of private clinics in TB care and their needs. Legal frameworks related to GVFMC and public-private partnership were analyzed. Results were used to formulate a public-private action plan. Activities included development of TB referral systems, integration of private sector into TB M&E systems, private doctors' capacity development in TB care provision.

Results and lessons learnt: The project solicited strong support from the healthcare department to engage the private sector in TB care. In 2017, 16 private clinics were enrolled to provide GVFMC funded TB care in Almaty city. They screened 1,142 people from key populations for TB, of which 51 were referred for TB diagnosis, TB was confirmed in 16 all of which commenced treatment.

Conclusions and key recommendations: Engagement of private sector increases healthcare system capacity in TB detection and treatment. Enhancing the private provider

capacity and adjusting the system including M&E are important to ensure access to quality TB care. Favorable legal environments and guaranteed state funding supports scale-up of public-private collaboration.



[TB services_private clinics_2017]

PS40-838-27 Nation-wide public-private mix for tuberculosis case holding in South Korea: a comparison of initial and expanded phases in 2009 and 2014

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Background: In Korea, a nation-wide PPM was initiated in 2009 and its purpose was to improve treatment outcome by the case holding activities in private sectors. The study aims to evaluate the achievement of the case holding activities between 2009 and 2014.

Methods: From the TB surveillance system, we constructed drug-susceptible (DS) and new TB cases cohort in 2009 and 2014, separately. Treatment outcome was categorized as treatment success and loss to follow-up (LTF) with excluding other outcomes such as failure and deaths. The study compared treatment outcome of public sectors with private sectors in 2009 and 2014. In addition, transfer history-stratified comparison was also conducted.

Results: Total number of DS and new TB cases was 33,596 and 32,791 in 2009 and 2014, respectively. Between 2009 and 2014, LTF rate was eventually decreased from 11.5% to 4.3% in public sectors and from 25.4% to 6.7% in private sectors. The gap of LTF rates between public and private was decreased from 2009 to 2014 (RR: 2.22, 95% CI: 2.06-2.38 in 2009; RR: 1.55, 95% CI: 1.30-1.86 in 2014). In the transfer history-stratified analysis there was no difference of LTF rates in cases who had at least 1 transfer history during treatment period between 2009 and 2014 cohort in public sectors. However, in private sectors LTF rate in cases who had transfer history was worsen in 2014 cohort.

Conclusions: PPM project in Korea was successfully reduced LTF rates in private sectors. The next plan should be focused on cases who had transfer history during treatment period.

PS40-839-27 Did prioritisation and strengthening of the law for public-private partnership in the RNTCP yield effective results in Central India?

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Background and challenges to implementation: To ensure proper TB diagnosis and its management and reduce transmission, it is essential to collect complete information of all TB patients. Hence, Government of India (GOI) mandated all healthcare providers to notify every TB patient diagnosed and/or treated, in 2012; yet maximum private providers fail to comply with the same.

Intervention or response: In the interest of public health, GOI evolved a scheme to incentivise private providers for TB patient notification, as part of National Strategic Plan (2017-25) keeping the vision of End-TB Strategy. In addition, GOI also introduced a Gazette Notification for all Clinical Establishments to mandatorily notify every TB patient to local Public Health Authority, failing which they might attract provisions of sections 269 and 270 of the Indian Penal Code. GOI issued instructions for Chemists/Druggists dispensing anti-TB drugs, to mandatorily record and report details of prescriber, patient, and name and quantity of anti-TB drugs sold. In Madhya Pradesh (MP), a series of sensitisation workshops were undertaken at state, district and sub-district levels for involvement of private sector with RNTCP and increasing TB notification. The same is being monitored through local public health authorities on regular basis.

Results and lessons learnt: Till 4Q2017, 4803 private health facilities (clinics/hospitals/laboratories) have been registered with RNTCP. During 2015-17, the total TB notification in MP increased by 22%, i.e. from 111,967 in 2015 to 136,166 in 2017. Contribution from public sector increased by 17%, while private sector contribution increased by 71%, i.e. from 9983 to 17110 over the last 3 years.

Conclusions and key recommendations: Despite excellent coverage by RNTCP, many TB patients still continue to seek healthcare from private sector. It is estimated that 34%-57% of TB cases are diagnosed and treated outside public sector (Satyanarayana et al, 2011). Thus realizing the importance of public-private partnership, apart from mandatory regulations, it can be achieved only through multi-strategical approach of regular sensitization meetings.

PS40-840-27 Accelerating tuberculosis case identification through public-private mix approaches: BRAC experience

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Background and challenges to implementation: Tuberculosis is the emerging public health crisis for Bangladesh. Although Bangladesh has been achieving significant improvement in terms of case detection still the country fails to detect 33% of the total disease burden. The recent prevalence survey demonstrates that prevalence of urban TB is higher than rural. To identify the missing cases in urban areas public private mix (PPM) approaches has been undertaken as pilot basis to see the TB case yield.

Intervention or response: BRAC selected four city corporations for this initiatives. Graduate private practitioners and pharmacy holders were listed and mapped. Seventy (70) graduate practitioners and 70 pharmacy holders from each area were selected for networking and to develop referral linkage. A half day information sharing session was held with them. They were provided the list of nearby NTP designated DOTS centers. When any TB presumptive/patients visited these providers, they sent them to the nearby DOTS centers and informed the assigned field staff through mobile SMS. Each pharmacy holder get USD 2 per month as mobile phone incentive. There was establishment of DOTS corner in five academic medical institutes to involve health professionals under NTP umbrella as they have the capacity to diagnose and treat all forms of TB.

Results and lessons learnt: This intervention took place from October, 2016 to December, 2017. Additional 2425 TB cases diagnosed and registered through this approach. Of them, 468 TB patients diagnosed from presumptive referred by pharmacy holder, 1,011 TB cases from graduate private practitioners and 946 TB cases from 5 DOTS corners.

Conclusions and key recommendations: Engaging these providers in TB control programme help to increase presumptive TB that leads to enhance TB case diagnosis in rapidly progressing urban areas of Bangladesh which ultimately aid to contribute for reaching missing TB cases.

PS40-841-27 The role of health system governance in strengthening the TB control programme in Nigeria

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Background: Although there have been several studies of the implementation of Nigeria's Tuberculosis (TB) control programme (NTP), studies examining the role of governance in designing and implementing TB control programme are scarce.

Methods: Published studies and policy documents describing or analysing the detailed processes of designing and implementing TB control in Nigeria published between 2000 and 2017 were obtained, analysed and synthesized. Data abstraction and synthesis of information were guided by Siddiqi and colleagues' framework for assessing health systems governance. Data were analysed using framework analysis in NVivo 11.

Results: The findings reveal many enabling governance practices and barriers. Factors enabling good governance include availability of strategic plans and policies for TB control; funding from development partners; stakeholder involvement in policy development and service delivery; needs-based drug distribution; effective data review meetings; and transition from paper to an electronic data management system that aligns with WHO recording and reporting standards and national health management information system. Barriers to good governance include insufficient or delayed government funding for TB control; poorly regulated private health sector; weak legal regimen for isolation of TB patients; inadequate integration of TB into general health services and the community; high transaction costs; absence of clear staff needs, frequent changes in leadership of the NTP and NTP's lack of authority to influence staff recruitment and distribution; poorly skilled, motivated and supervised TB service providers; dilapidated service delivery infrastructure; inadequate distribution system for TB drugs from state stores to health facilities; absence of social accountability mechanisms (complaint box, service charter and health facility committees); incomplete and delayed quarterly reporting; poor storage of surveillance data; and low ethical standards of care.

Conclusions: There is a need to strengthen specific practices in each governance domain to ensure attainment of the goal of eliminating TB in Nigeria and similar resource-constrained countries.

PS40-842-27 Self-notification through chemist: progenitor approach towards ending TB in Delhi

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Background and challenges to implementation: Engagement with Chemists and Drug Shop owners for TB Notification was conceptualized by Revised National TB Control Program (RNTCP) as part of the End TB mission in Delhi. With over 12000 Chemists registered in the capital to support patient's health needs, a study was undertaken to assess the feasibility of capturing data of TB patients coming to buy Anti-TB drugs at the Licensee level (Chemists and Drug Shop Owners) in Central Delhi.

Intervention or response: The prospective study was conducted from July 2017 to December 2017. TB Notification through Paper based system and through Self-Notification via online mode was the operational modality used for engagement with Chemists. A team of paramedical workers was deployed for data collection from those Chemists who chose to notify through paper mode. NIKSHAY web based reporting platform for the public sector under the RNTCP was used for Self-Notification from Chemists.

Results and lessons learnt: From the 330 Chemist sensitized, 807 TB Notifications were received during the study period. Of these, 564 (70%) were self-notified by Chemists themselves. For the remaining which was received on paper mode, 37 Chemists shops reported the data in the first visit of the health staff. The paramedical worker had to make an average of 4 visits to report any case in paper mode from the chemist shops. The annual TB case notification in Central Delhi showed two fold significant increase from 271 TB patients/100000 population to 758 TB patients/100000 population for the study period when compared with expected trends for the same period last year ($p < 0.05$)

Conclusions and key recommendations: Self-notification of TB engenders successful TB notifications from Chemists. This progenitor approach to TB notification in the capital emphasizes the need to categorize Chemists as an independent private care provider in the web based program reporting framework being used for TB notification across high burden setting.

PS40-843-27 Enforcement of Schedule H1 Provisions of Drugs and Cosmetics Act increased private TB notification by 95% in 11 districts of Jharkhand, India

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Background and challenges to implementation: India is home to 2.8 million TB cases with 1.8 million (64%) reported, missing the rest. In 2017, the notification system recorded 0.4million private TB cases against ~1.5million target. Pharmacies are the first point of contact for drugs by private patients. India's Drugs and Cosmetics Act 1940 amended till 31st Dec 2016 mandates all pharmacies to maintain records of all patients and practitioners for 46 drugs listed under Schedule H1 including all Anti TB Treatment(ATT) Drugs. Out of 850000 pharmacies, only 9% are engaged in TB programme by 2016. Jharkhand, an eastern tribal state of India reported 4211 private TB cases in 2016.

Intervention or response: RNTCP and Drug Directorate, Jharkhand started a joint pharmacy involvement initiative since July 2017 through enforcement of schedule H1. Quarterly district wise sale data of two C&F (Clearing and forwarding) agencies of major ATT drug manufacturers (Macleod and Lupin) were analysed and 11 high consumed districts and pharmacies therein were listed for intervention. 30 Drug Inspectors, 534 pharmacies were trained on Tuberculosis, Schedule H-1 provisions of Drugs and Cosmetics Law and TB patients reporting in a prescribed format during 2017-18.

Results and lessons learnt: Total Private TB notification(7701) increased by 83% in 2017 from 4211 in 2016, while that was 2% (36751 to 37219) in public sector. In 11 districts, it raised by 95% (3471 to 6768) with same 2% rise in public sector. During July-Dec' 2017, Pharmacies contributed 958(26%) cases out of 3705 pvt notification and it was up by 100% (1849 to 3705) in the state from 2016. Four districts(Deoghar, Giridih, Koderma and Ramgarh) who had reported only 20 cases in 2016 increased to 593 in 2017.

Conclusions and key recommendations: Pharmacies play a huge role in addressing mainstay of TB programme - identification, complete treatment with standard regiment and slice the infection chain. Pharmacies engagement cab bridge the gap of notification, counseling and universal access to TB care.

PS40-844-27 Programmatic preparations for TB patient triage approach

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Background and challenges to implementation: Treatment success rates among rifampicin-resistant tuberculosis (RR-TB) patients in Kyrgyzstan have been low: 56% for the 2014 RR--TB cohort.

Intervention or response: KNCV (within the framework of Challenge TB project (CTB) and in partnership with Global Fund, World Health Organization, Medicines Sans Frontiers) introduced patient triage approach utilizing introduction of second line probe assay (SL LPA) for early detection of second line drug (SLD) resistance RR-TB patients. CTB supported development and endorsement of regulatory and operational documents on RR-TB patient triage: 1) National implementation plan; 2) Clinical guidelines and standard operating procedures; 3) Importation waiver and permission for use of bedaquiline and delamanid. CTB support also included introduction of SL LPA, trainings and supervision for clinical and laboratory staff followed by on-the-job mentoring and regular supportive supervision.

Results and lessons learnt: In the period January 2017-January 2018, 336 RR-TB patients were enrolled in DR-TB treatment following patient triage approach in two pilot sites: 130 in shorter treatment regimen (STR); 206 in individualized treatment regimen (ITR): 131 containing bedaquilin, 5 containing delamanid and 70 containing repurposed drugs. During the first months of enrollment mainly patients with long history of unsuccessful DR-TB treatment were enrolled in ITR; gradually a higher proportion of patients were enrolled on STR. Preliminary treatment outcomes showed culture conversion for 75% of patients on ITR. Out of 64 patients enrolled in STR in the first half of 2017, 46 (74%) have already successfully completed treatment at the time of writing.

Conclusions and key recommendations: Comprehensive CTB support resulted access to the shortest possible and most effective RR-TB treatment regimen in Kyrgyzstan. Based on promising initial results from first pilot sites the access to STR and ITR is expanded to the whole country.

PS40-845-27 Effectiveness of public and private health sector engagement in TB services in Jalalabad city of Nangarhar

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Background and challenges to implementation: Afghanistan has 65,000 TB cases annually and in 2017 there were 47,436 TB cases notified. The private health sector is very strong in urban settings with almost 55% of clients seeking healthcare services, but TB engagement is very weak. The purpose of this study was to identify the role of the private sector in TB case finding and treatment in the Jalalabad, Nangarhar province of Afghanistan.

Intervention or response: Afghanistan National Tuberculosis Program (NTP) with support from Challenge TB (CTB), a USAID supported project, engaged the private health sector in TB services in September 2015 to implement various interventions including strengthening coordination between public and private sectors, training healthcare staffs, supplying anti-TB drugs, and lab consumable and DOTS packages of educational materials, sputum sample transferring materials and drug boxes with TB patients' entire treatment regimens. NTP and CTB technical staffs conducted supportive supervision, monitoring and provided on the job training to health facilities (HFs) staffs. Public and private HFs provided TB diagnosis and treatment free of charge and TB patients received a full course of treatment.

Technical teams from NTP and CTB evaluated the role of private sector on TB services and reviewed the data from 2016-2017.

Results and lessons learnt: DOTS coverage reached 65% (24 out of 37 HFs) in 2017 compared to 19% in 2015. There were 2,805 all form TB cases notified in 2017 compared to 1,404 in 2015 (P value < 0.0000001). Out of 2,805 cases, 566 were bacteriologically confirmed TB. Among 2,805 TB cases; 1,104 (39.3%) were detected by private health sector (See table 1).

Indicators/Years	2015	2016	2017
# and % of HFs covered by DOTS	7 (19%)	19 (51%)	24 (65%)
# of all form TB cases identified	1,404	1,899	2,805
# of all form TB cases identified by private health sector	80	382	1,104
% of treatment success rate	70%	77%	NA

[Table 1, Effectiveness of public and private health sector engagement in TB services in Jalalabad]

The treatment success rate increased by 7% in 2016 and reached 77% (70% in 2015).

Conclusions and key recommendations: Engaging the private health sector in TB services contributed significant improvements in case notification and treatment success. We recommend engaging the private sector in TB services in Afghanistan, and in similar settings globally.

PS40-846-27 TB reporting through DHIS2 in Bangladesh: road to digitalization

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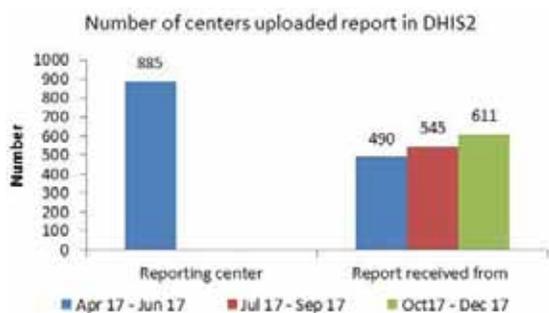
Background and challenges to implementation: District Health Information System v.2 (DHIS2) is open-source software for collection, analysis and presentation of aggregate and patient-based data. At the end of 2009, the Ministry of Health & Family Welfare of Bangladesh adopted DHIS2 to develop a common platform for collecting and visualizing data of all health programs.

The National Tuberculosis Control Program (NTP) manually and semi-electronically collected TB reporting data from 885 TB treatment centers for many years. Collecting, analyzing and compiling the data were a challenge because it takes more than a month to aggregate each quarter's reports. Unlike other health programs, TB reporting system was not integrated into DHIS2.

Intervention or response: Challenge TB (CTB) supported NTP to digitalize the TB reporting system to incorporate indicators into DHIS2, including three TB reporting formats (case finding, treatment results and sputum conversion).

Results and lessons learnt: CTB provided support to NTP for nationwide training on DHIS2 reporting for TB to all Upazilla Health Complexes (UHC) statisticians and other relevant government/NGO officials in rural and urban reporting centers. All 885 TB reporting centers are now connected with DHIS2. In June 2017, the NTP first received UHC's compiled TB reports through DHIS2. Currently, around 70% of the rural and urban reporting centers submit their quarterly TB reports within 15 days through this system. CTB is working with NTP to ensure regular and accurate online reporting from the entire country. Regular follow up is important from district and central NTP officials and NGOs to get quality reporting from all reporting centers within time particularly from urban areas.

Conclusions and key recommendations: The transition from manual to electronic reporting means that TB information is available within a few weeks, rather than two months while minimizing workload of health care workers. Policy makers from local to national level can use this data for program design and policy formulation.



[Fig. Number of reporting centers uploaded reports through DHIS2]

PS40-847-27 Optimizing community screening for TB: spatial analysis of localized case finding from door-to-door screening for tuberculosis in a district of Ho Chi Minh City, Viet Nam

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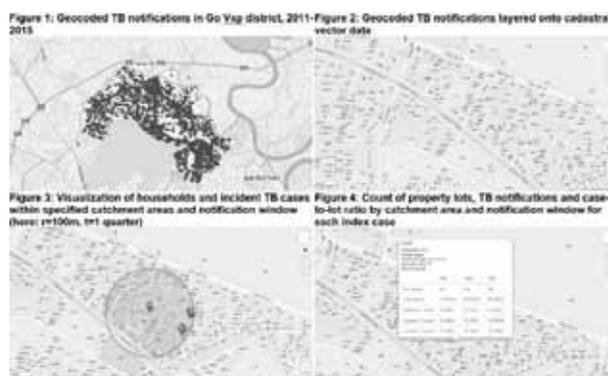
Background: Tuberculosis is the largest infectious disease killer globally. To reach ambitious global targets, early and increased TB case detection is essential. Many strategies find few cases or with long delays. New technologies and collaborations may improve screening to detect more cases.

Methods: This study used a cross-sectional, spatial analysis of routine TB surveillance and cadastral data in Go Vap district, Ho Chi Minh City. We mapped all people with TB to their household level with geocodes and calculated theoretical door-to-door screening yields to model community contact investigation in three concentric catchment areas (50m, 100m, 200m) and three notification windows (one, two and four quarters) for each index case. We compared these yields to reference values from literature and fit a GEE linear regression model with patient covariates onto the data.

Results: The sample included 3,046 TB patients over a 5 year period. Adjusted theoretical yields in 50m, 100m and 200m catchment areas in the two-quarter notification window scenario were 0.32% (95% CI: 0.27,0.37), 0.21% (95% CI: 0.14, 0.29) and 0.17% (95% CI: 0.09, 0.25), respectively. The 50m catchment area in all notification window scenarios and the other areas in the four-quarter scenario had significantly higher yields compared to a review of active case finding yields from lit-

erature. GEE regression evinced higher theoretical yield for treatment failure index cases ($\beta=0.12$, $p=0.001$) and short-term inter-province migrants ($\beta=0.006$, $p=0.022$), while greater distance to the DTU ($\beta=-0.02$, $p<0.001$) was associated with lower yield.

Conclusions: This study is an example of inter-departmental collaboration through the application of repurposed cadastral data to progress towards the end TB objectives. We showed that it may be possible optimize community screening via identifying and targeting catchment areas of index cases for spatially restricted community screening.



[Mapping of TB patients onto cadastral data]

PS41 Temporal trends, spatial distribution and modelling for human immunodeficiency virus and diabetes

PS41-848-27 Rapid, sustained scale-up of ART for HIV-positive TB patients in Mozambique, 2010-2017: successes and next steps

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Background: Mozambique has one of the highest rates of both TB (551 cases per 100,000 persons) and HIV (national prevalence: 13.2%) in the world and an estimated TB case detection rate of 54% in 2017. The WHO recommends that all TB patients are tested for HIV and all HIV-infected TB patients are started on antiretroviral therapy (ART). Mozambique adopted universal ART for TB-HIV patients in 2012 and began rapid scale-up of

ART. A *One Stop Model (OSM)* of service-provision, where HIV-infected TB patients receive ART and TB treatment in the same room, was adopted, reducing patient waiting time and frequency of clinic visits.

Methods: We analyzed the trend in routine Ministry of Health TB data collected from all health facilities in Mozambique from 2010-2017, including the number of TB patients notified, the number/percent tested for HIV, and the number/percent with HIV that started ART.

Results: The number of TB cases notified rose from 46,174 in 2010 to 86,515 in 2017 and HIV testing increased from 88% to 97%. The HIV co-infection rate decreased from 61% to 40% in the same period; of those co-infected, the proportion on ART increased from 25% in 2010 to 95% in 2017. TB treatment success rates are not disaggregated by HIV status, but overall increased nationally from 84.5% to 90% for the cohorts reported in 2010 and 2017 respectively.

Conclusions: There has been a notable improvement in the percent of TB of patients with known HIV status and percent of TB-HIV co-infected patients started on ART during the period of OSM expansion. Mozambique has maintained rates of ART uptake among identified TB-HIV patients that are above those reported globally (85% in 2017) since 2015. Further improvements in TB case detection are needed to close the gap between estimated and treated TB and TB-HIV patients.

PS41-849-27 A decline in the number of notified TB cases in the last 7 years could be ascribed to the decline in HIV infection rates in Ethiopia

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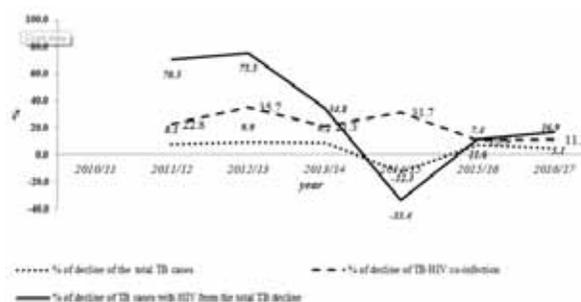
Background and challenges to implementation: In Ethiopia, the incidences of HIV and TB have declined by 90% and 50%, respectively, in the last two decades. However, the impact of the significant decline in the national HIV incidence rate on the number of notified TB cases has not been analyzed. We explored the relationship between the decline in the HIV infection rate and TB case notification rates in Ethiopia.

Intervention or response: We collated publicly available information on the annual number of notified TB cases, the TB-HIV co-infection rate and the linkage to antiretroviral therapy (ART) and isoniazid prophylaxis therapy (IPT) for eligible HIV-infected people (2010-2017). The trend of TB and TB-HIV co-infection was computed and the contribution of the annual TB decline in the TB-HIV co-infection rate to the decrease in total TB was

calculated and shown by the trend line. The nonparametric trend test across ordered group was used to test the significant decline in the trends.

Results and lessons learnt: The TB case load decreased from 159,017 in 2010/2011 to 118,059 in 2016/17, with a declining rate of 4.6% per year. During the same period, HIV testing for TB cases increased to 96%. ART coverage for TB-HIV co-infection increased from 42% to 61.5%, and IPT reached 54%. The TB-HIV co-infection rate declined from 25% to 7.1%. TB in the TB-HIV co-infection declined from 22.8% to 11.3% ($Z=2.19$ P value=0.029), with an annual decline rate of approximately 22.3%. The proportion of the decline in HIV-related TB to the total decline of total TB was 70% in 2010/2011 and 16.9% in 2016/2017 ($Z=2.17$ P value=0.03), with an annual declining rate of 29.3%.

Conclusions and key recommendations: The decline in HIV-associated TB should be taken into consideration when investigating the recent declining trend in the number of notified TB cases in Ethiopia.



[TB/HIV collaborative activities over seven years in Ethiopia, 2010/2011-2016/2017]

PS41-850-27 Temporal trends in tuberculosis notification rates following nine years of antiretroviral therapy scale-up in Uganda

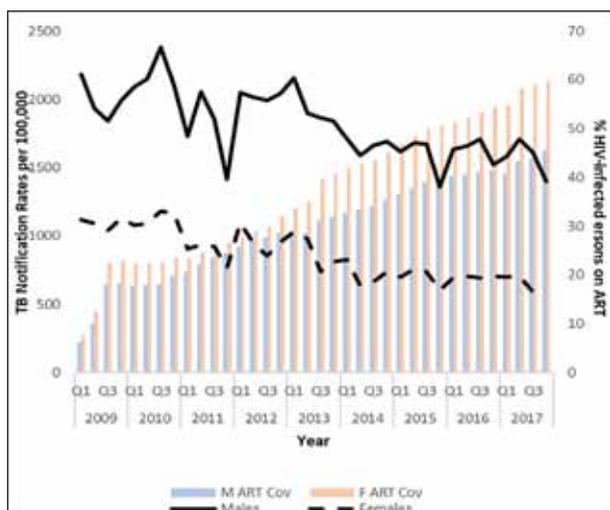
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Background: Antiretroviral Therapy (ART) is a key intervention for reducing the burden of tuberculosis (TB). ART significantly reduces individual risk for TB and has been associated with population-level decreases in TB notification rates. In Uganda, ART scale up started

in 2008 and since 2015, is offered to all HIV infected persons (“test-and-treat”). We aimed to assess the association between increasing ART availability and TB notification rates.

Methods: Annual TB notification rates per 100,000 population from Kampala and four surrounding districts were calculated using annual TB notifications as numerators and mid-year populations as denominators. The number of HIV-infected persons was calculated using HIV prevalence estimates from 2006, 2011 AIDS Indicator Surveys and 2015 district estimates. Numbers on ART from the AIDS Control Program annual reports were used to calculate ART coverage. TB notification rates overall and stratified by gender and HIV status were calculated for the period 2009-2017. Changes in TB notification rates were described in relation to ART coverage and introduction of integrated TB-HIV activities (2010) and Xpert MTB/RIF® testing (2012).

Results: From 2009 to 2017, HIV prevalence increased from 8.2% (95% CI 8.2 -8.3) to 9.4% (95% CI 9.3 -9.4). ART coverage increased from 15.1% (95% CI 15.0-15.2) to 58.0% (95% CI 57.9-58.1) among women and 13.2% (95% CI 13.1-13.3) to 43.4% (95% CI 43.3-43.5) among men. Overall, TB notification rates decreased by 3.3% (95% CI 2.7-3.9) per year. Among HIV-infected persons, TB notification rates increased slightly in 2010 and 2012 and then decreased steadily from 2013-2017 with a greater decrease among women 7.4% (95% CI 6.6-8.3) per year than men 4.7% (95% CI 4.3-5.2) per year (Figure 1).



[Figure 1: ART Coverage and TB Notification Rates among HIV positive persons stratified by gender]

Conclusions: The rapid scale up of ART has been followed by a steady decline in TBHIV notification rates particularly among women. Increasing ART coverage among men should be considered as a priority strategy to decrease the burden of TB in this population.

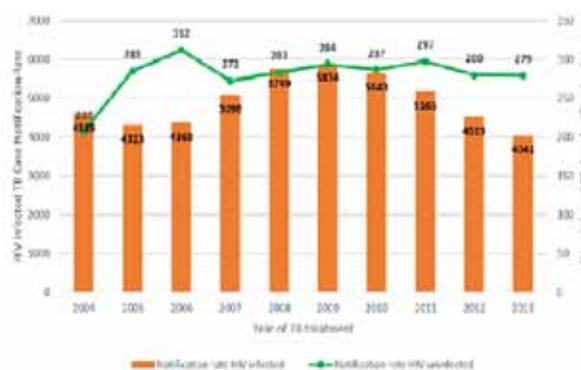
PS41-851-27 Trends in the South African tuberculosis epidemic with scale-up of TB-HIV integration services

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Background: South Africa (SA) remains the country with the highest incident tuberculosis (TB) globally including prevalence of HIV co-infection. Routine HIV testing among TB patients was implemented in SA from 2009. Introduction of the anti-retroviral therapy (ART) program in 2004 was initially slow and restricted by CD4 count thresholds and WHO HIV clinical staging. We describe trends in TB case notification rates in South Africa over a 10-year period, disaggregated by HIV status.

Methods: We conducted a retrospective cohort analysis of all patients routinely recorded in the SA electronic drug-susceptible TB register (ETR.Net) between 1 January 2004 and 31 December 2013. The proportion of TB cases tested for HIV was evaluated over time. Estimates of HIV co infection were made from those tested and TB cases were stratified based on these estimates. Census data and HIV prevalence estimates from Statistics South Africa were used to calculate the total HIV-infected and uninfected populations.

Results: During 2004-2013, 3,593,303 newly registered patients with TB were recorded across the 9 SA provinces. The TB case notification rate increased from 597/100,000 in 2004 to a peak of 824/100,000 population in 2009. The TB case notification rate among HIV-infected people peaked at 5,874/100,000 population in 2009 and remained 15 times greater than the TB case notification rate among HIV-uninfected people (Figure 1). In 2013, 90% of TB patients had an HIV test compared to 1% in 2004, 70% of co-infected TB patients had a CD4 count recorded and 72% were documented to be on ART during their TB treatment.



[South African TB case notification rates per 100,000 population stratified by HIV status, 2004-13]

Conclusions: HIV testing and ART coverage in SA have improved substantially over 10 years. The burden of TB amongst HIV-infected individuals is declining but remains substantially greater than among HIV uninfected. The overall declining trend in the TB epidemic appears less significant among the HIV-uninfected population.

PS41-852-27 TB-HIV coinfection: profile of cases and spatial distribution in the city of São Paulo, Brazil

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Background: Tuberculosis (TB) and the Acquired Immunodeficiency Syndrome (AIDS) have the highest mortality in the world. As the Human Immunodeficiency Virus (HIV) affects the immune system and facilitates the progress of TB, the TB-HIV coinfection is a potentially fatal association.

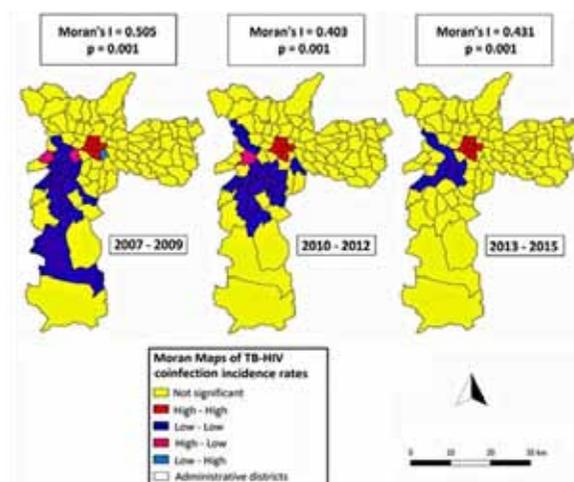
Methods: Descriptive study with data of all new cases of TB-HIV coinfection living in the city of São Paulo-Brazil reported from 2007 to 2015. Cases were described by sociodemographic, clinical and epidemiological characteristics, and temporal trend of incidence rates was analyzed. Cases with fixed address were spatially distributed, and the Global e Local Moran's I were used to identify spatial clusters.

Results: A total of 6,092 new cases of TB-HIV coinfection were reported in the period: 72.4% male, 39.4% white, 51.0% had 20 to 39 years of age, and 64.1% had 11 years or less of schooling. Around 65.4% of cases were diagnosed in secondary/tertiary health care services, 41.5% had extrapulmonary forms of TB, important portion report abuse of alcohol (11.2%) and drugs (11.5%), and 31.9% of cases had directly observed treatment.

Main outcomes of TB treatment were: cure (53.8%), death (22.5%), and default (20.7%). The incidence rates of TB-HIV coinfection had significant annual decrease of 3.6%, ranging from 7.0 cases (2007) to 5.3 cases (2015) per 100.000 habitants.

Cases with fixed address (91.8%) were used to calculate the incidence rates of TB-HIV coinfection, which presented positive and significant spatial autocorrelation and heterogeneous spatial pattern, with a high-risk cluster in the central region of São Paulo.

Conclusions: Decreasing trend of TB-HIV coinfection in São Paulo indicates important advance in TB and HIV/AIDS control from 2007 to 2015. Nevertheless, the poor treatment outcomes and the disproportionately impacted areas should be priorities for guiding policy formulation and health services organization, in order to improve prevention and control actions of TB-HIV coinfection.



[Moran Maps of TB-HIV coinfection incidence rates. City of São Paulo, Brazil, 2007-2015.]

PS41-853-27 Spatial analysis of the common risk of HIV and tuberculosis incidence in Kenya

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Background: A wealth of information exists concerning HIV and tuberculosis (TB) co-infection globally. The risk of developing TB is higher for people with HIV. However, little is known about how the risk of HIV and TB are geographically co-distributed at sub-national levels.

Methods: We obtained sub-national TB data from the National Leprosy, Tuberculosis and Lung Disease Program, aggregated for year 2012. HIV data was taken from the 2012 Kenya AIDS indicator Survey. We first conducted an exploratory spatial analysis using Moran's I statistics in GeoDa then fitted Bayesian joint spatial models using WinBUGS. The spatial variation in HIV and TB was separated into disease-specific and spatial shared components common to both diseases. Regions were then classified and ordered according to specific and shared risk of HIV and TB.

Results: TB and HIV incidence rates ranged from 50-1,250 and 200-25,600 cases per 100,000 population, respectively. Both HIV (Moran's I=0.41, p<0.001) and TB (Moran's I=0.35, p=0.001) exhibited significant spatial clustering. HIV was spatially associated with TB (Bivariate Moran's I=0.14, p=0.04). For TB, about 81% of the total variation in risk was captured by the shared HIV-TB risk component [Relative Risk ratio (RR)=0.81, 95% credible interval=0.72-0.89], while for HIV only 22% of

the total variation in risk was captured by the shared component. The shared component had a slightly stronger association with risk of TB than with risk of HIV.

Conclusions: Our findings show similarities in the spatial pattern of HIV and TB, with high risk in the Western parts of Kenya. Results suggest a need for comprehensive programming of HIV and TB interventions that reach sub-regions of spatially-concentrated risk of HIV and TB co-infection. Geospatial modeling presents an opportunity for identifying higher-risk sub-regions and generating hypotheses for further research aimed at targeted interventions for people living with HIV and at higher risk of TB co-infection.

PS41-854-27 Creating localized case-finding strategies by spatio-temporal analysis of LGA-level TB case notification data in South East and South West Nigeria

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Background: New strategies are needed to increase TB case detection rates in Nigeria, estimated at 25% in 2016. Case notification data are routinely collected at the local government area (LGA) level and used to inform country-level trends. However, these data also provide a potentially rich source of information on local TB epidemiology. In this study we investigated the use of LGA-level data to create localized case-finding strategies.

Methods: Case notification and DOTS facility data through 2016 were obtained for the 37 LGAs in Abia and Lagos States representing South East and South West Nigeria, respectively. TB burden was estimated via high-resolution data on known covariates including population density, male gender, poverty, and HIV prevalence. The combined spatio-temporal data set was analyzed for spatial autocorrelation (hotspots) and by multivariate regression with case notification rate as outcome, and the results used to parameterize an individual-based model of TB transmission to evaluate case-finding strategies.

Results: Both Abia and Lagos States exhibited geographical heterogeneity in case notification rates, with each containing one significant hotspot LGA ($p < 0.05$). Case notification rates correlated more strongly with DOTS coverage than with known covariates of TB burden. In Lagos State, DOTS lab coverage, adjusted for population density, explained 42% (CI: 8-72%) of the variance across LGAs, suggesting notifications were a proxy for healthcare access rather than burden. Males and younger adults were under-represented in the case notification data compared to estimated prevalence for the majority of LGAs. Based on these data, a mathematical model predicted that demographic-based intensified case-finding and density-based DOTS facility placement

would result in significantly greater reductions in TB burden than alternative strategies.

Conclusions: Case notification data at the LGA level in Nigeria, together with mathematical modeling, can be used to inform demographically and geographically localized case-finding strategies that may significantly impact TB burden.

PS41-855-27 Modelling the effect of HIV and diabetes co-epidemics on tuberculosis

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Background: Tuberculosis (TB) epidemics rarely evolve in isolation from other diseases. Depending on country context, co-epidemics including human immunodeficiency virus (HIV) and diabetes can have significant impact on TB progression and health management. We address the challenge of including co-affected populations within a TB-specific model without sacrificing its general applicability.

Methods: Optima TB, a compartmental model, was developed to depict progression through latent/active TB, associated care states, and drug sensitivity. The model was applied in Belarus, the Gauteng province of South Africa, and Peru. Populations were stratified by age, HIV co-infection in Belarus and Gauteng, and diabetes status in Peru. Transition rates, including those for disease progression and death, were varied across populations to represent co-epidemic impacts. Contracting HIV and/or developing diabetes was simulated by transitions between populations. Epidemic projections were investigated and allocative efficiency analyses performed.

Results: For these studies, data reflected integration of these additional diseases with TB control. Modelled trends of TB-HIV co-infection in Gauteng and Belarus aligned with other model estimates. In Gauteng, the increase in people living with HIV coincided with a rapid increase in TB until 2010, with a sharp decrease thereafter for both diseases coinciding with co-treatment scale-up. In Peru, modelled estimates of diabetic TB cases matched both reported TB notifications and Diabetes Atlas estimates.

Conclusions: Optimizing TB resource allocation, while considering those co-affected with HIV, diabetes or other diseases, will improve the representation of the TB epidemic. This will also draw attention to the unequal TB risk of co-affected populations. Model outputs underline the importance of considering the impact of these co-epidemics on TB incidence and deaths among co-affected populations. Findings also highlight the importance of integration of care and promise more effective improvements in health outcomes.

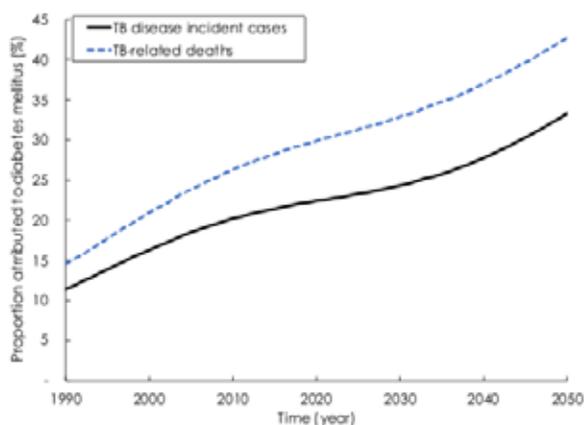
PS41-856-27 Forecasting the impact of diabetes mellitus on tuberculosis disease incidence and mortality in India

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Background: In context of rapidly expanding diabetes mellitus (DM) epidemic in India and slowly declining tuberculosis (TB) incidence, we aimed to estimate the past, current, and future impact of DM on TB epidemiology.

Methods: An age-structured TB-DM dynamical mathematical model was developed and analyzed to assess the DM-on-TB impact. The model was calibrated using a literature review and meta-analyses, and stratified the population by TB infection status and stage, TB disease form, TB treatment status, TB recovery status, and DM status. The DM-on-TB impact was analyzed using population attributable fraction metrics. Sensitivity analyses were conducted by accommodating less conservative effect sizes for the TB-DM interactions, by factoring the age-dependence of the TB-DM association, and by assuming different TB disease incidence rate trajectories.

Results: In 1990, 11.4% of new TB disease incident cases were attributed to DM (Figure). This proportion was estimated to increase to 21.9% in 2017, and 33.3% in 2050. Similarly, in 1990, 14.5% of TB-related deaths were attributed to DM. This proportion increased to 28.9% in 2017, and 42.8% in 2050. The largest impacts originated from the effects of DM on TB disease progression and infectiousness. Sensitivity analyses suggested that the impact could be even greater.



[The proportion of TB disease incidence and mortality cases attributed to diabetes in India]

Conclusions: The burgeoning DM epidemic is predicted to become a leading driver of TB disease incidence and mortality over the coming decades. By 2050, at least one-

third of TB incidence and almost half of TB mortality in India will be attributed to DM. This is likely generalizable to other Asian Pacific countries with similar TB-DM burdens. Targeting the impact of the increasing DM burden on TB control is critical to achieving the goal of TB elimination by 2050.

PS41-857-27 Characterizing the impact of diabetes mellitus on tuberculosis epidemiology: analytical insights

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Background: We aimed to develop a conceptual framework of diabetes mellitus (DM) effects on tuberculosis (TB) natural history and treatment outcomes, and to assess the impact of these effects on TB-transmission dynamics. The model was calibrated using TB data for India.

Methods: A conceptual framework was developed based on a literature review, and then translated into a mathematical model to assess the impact of the DM-on-TB effects. The impact was analyzed using TB-disease incidence hazard ratio (HR) and population attributable fraction (PAF) measures.

Results: Evidence was identified for 10 plausible DM-on-TB effects. Assuming a standardized effect size of 3.0 for each effect, the HR ranged between 1.0 (*Effect 9-Recovery*) and 2.7 (*Effect 2-Fast progression*); most effects did not have an impact on the HR (Table).

Table. The epidemiologic implications* of each of the plausible diabetes mellitus (DM) effects on tuberculosis (TB) natural history and treatment outcomes as measured by the "true" population attributable fraction (PAF_{true}) and incidence hazard ratio (HR).

Effect*	PAF _{true}	HR
Effect 2—Fast progression	34.5%	2.7
Effect 6—Disease infectiousness	29.9%	1.0
Effect 8—Treatment failure	14.8%	1.0
Effect 4—Latent reinfection	11.1%	1.4
Effect 1—Susceptibility	9.9%	1.4
Effect 3—Reactivation	8.2%	1.3
Effect 9—Recovery	3.8%	1.0
Effect 10—Cured reinfection	1.7%	1.1
Effect 5—Smear positivity	1.3%	1.0
Effect 7—TB mortality	-4.6%	1.0
If no effect of DM on TB	0.0%	1.0
Relevant reference measure	14.7% [§]	3.0 [¶]

*Effects are ordered from largest to lowest PAF. [§]PAF estimated using Levin's formula. [¶]Typical effect size using different, but closely-related statistical measures (such as hazard ratio, relative risk, rate ratio, and odds ratio) of the strength of the observed TB-DM association.

[†]We assumed a standard effect size of 3.0 for each mechanism with an expected effect size ≥1 and (an inverse) effect size of 1/3 for each mechanism with an effect size ≤1.

[Epidemiologic implications of each of the plausible diabetes effects on TB transmission dynamics]

Meanwhile, TB-disease incidence attributed directly and indirectly to each effect ranged between -4.6% (*Effect 7-TB mortality*) and 34.5% (*Effect 2-Fast progression*; Table). The second largest impact was for *Effect 6-Disease infectiousness* at 29.9% (Table).

Conclusions: DM can affect TB-transmission dynamics in multiple ways, most of which are poorly characterized and difficult to assess in epidemiologic studies. The indirect (e.g., onward transmission) impacts of some DM-on-TB effects are comparable in scale to the direct impacts. While the impact of several effects on the HR was limited, the impact on the *PAF* was substantial suggesting that the extent to which DM is impacting TB epidemiology may have been grossly underestimated.

PS42 Bicycles, cheese and canals: the changing face of paediatric tuberculosis

PS42-858-27 Tuberculosis among indigenous children and adolescents in Brazil: factors associated with death and loss to follow-up from treatment

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Background: The objective of this study was to describe clinical and sociodemographic characteristics, to estimate the incidence of the disease, and to analyze factors associated with default and death during the treatment of reported cases of TB among indigenous children and adolescents in Brazil between 2006-2016.

Methods: Historical incidence series was analyzed according to age and macroregion, and multinomial logistic regression was used to elucidate factors associated with default and death.

Results: Of the total of 2096 reported cases, 88.2% had a cure, 7.2% default treatment and 4.6% death. There was a predominance of cases in boys aged 15-19 years and a higher proportion of deaths (55.7%) in < 4 years. Considering the group of indigenous children and adolescents with TB in Brazil, the mean incidence was 49.1 / 100,000, varying from 42.4; 21.5; 84.5; 24.3 and 97.6 in the North, Northeast, Southeast, South and Central-West regions. Cases with insufficient and regular follow-up had a greater chance of default and death (OR = 11.1, CI: 5.2-24.8 / OR = 4.4, CI: 1.9-10.3, OR = 20,

3: CI: 4.9-84.9 / OR = 5.1, CI: 1.2-22.7, respectively). The cases in retreatment (OR = 2.4; CI: 2.08-8.55) and anti-HIV positive (OR = 8.2; CI: 2.2-30.9) were also associated with default. The extrapulmonary (OR = 1.8, CI: 1.1-3.3) and mixed forms (OR = 5.6, CI: 2.8-11.4) clinical forms, cases at < 4 years (OR = 2.8, CI: 1.1-7.1) and Central West (OR = 2.8, CI: 1.1-7.0) were associated with death.

Conclusions: We believe that TB control in indigenous children and adolescents can't be achieved without investments in research and development and without reducing social inequalities.

PS42-859-27 Risk factors for unsuccessful treatment outcomes in older adolescents with drug-susceptible tuberculosis in Lima, Peru

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Background: There are few reports about tuberculosis (TB) related treatment outcomes in adolescents. Individuals <15 years old are often grouped into pediatric cohorts, leaving older adolescents, aged 16-19, an underreported subgroup. We aim to identify risk factors for unsuccessful treatment outcomes in older adolescents with drug-susceptible (DS-) TB.

Methods: For a household contact cohort study conducted in Lima, Peru (2009-2012) individuals >15 years old with incident pulmonary TB were diagnosed at participating public health centers. These index TB patients were queried about demographics, clinical indicators, and comorbidities. We use logistic regression to identify risk factors for any unsuccessful treatment outcome (defined as death, failure, lost to follow-up/default). All tests are two-sided with an alpha of 0.05.

Results: We identified 357 older adolescents, aged 16-19, with pulmonary DS-TB in the cohort. The median age is 18 (IQR: 17-19) and 222 (62.2%) are male. Successful treatment outcomes were experienced by 319 (89.4%), while 23 (6.4%) experienced an unsuccessful treatment outcome, including 6.2% default and no deaths. Treatment outcome data were missing in 15 (4.2%). The only risk factor identified to have an association with experiencing an unsuccessful treatment outcome was self-reporting as a heavy drinker, as compared to no drinking or light drinking (OR: 5.7; 95% CI: 2.0-16.3; p: 0.001).

Conclusions: Heavy alcohol use in older adolescents is associated with unsuccessful treatment outcomes in older adolescents in this urban cohort in Peru's capital. A better understanding is needed about how to tailor interventions for older adolescents at risk of unsuccessful treatment outcomes.

PS42-860-27 Nutritional status in intra-thoracic tuberculosis disease and TB infection in children: an observational study from South India

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Background: Tuberculosis (TB) and malnutrition are overlapping and interacting public health problems in India. Data on prevalence of active TB and latent TB infection (LTBI) among children with varying nutritional status is limited. We studied the relationship between nutritional status and active TB and LTBI in children.

Methods: Children ≤ 14 years presenting to the outpatient clinic at five hospitals in Tamilnadu, South India with symptoms suggestive of pulmonary TB between 2013 and 2018 were included. Anthropometric measurements and demographic characteristics were collected, clinical examination was performed. Tuberculin skin test (TST) PPD 2 TU, chest X-ray and sputum/gastric aspirate smear/Xpert/culture for TB were performed. LTBI was defined with household TB contact in children <6 years and in >6 years with household TB contact and TST positive. Multivariate logistic regression was performed to evaluate the relationship between TB disease/LTBI status and nutritional status.

Results: Total of 1785 HIV negative children with median age of 5 years (range 3 months-14 years) were included. 59% were <6 years of age; 54.5% were males. 16% (285/1785) were diagnosed with TB [42.5% (121/285) bacteriologically confirmed], 31% (551/1785) had LTBI and 53% (949/1785) had no LTBI or TB. Overall 28.6% (510/1785) of children were wasted, 16.3% (292/1785) were stunted and 25% (446/1785) were underweight. Other findings are illustrated in Table 1.

Positive Mantoux test (TST +ve)	25% (439/1750)
Wasting (WHZ ≤ -2)	28.6% (510/1785)
Wasting in LTBI	27.2% (150/551)
Wasting in TB	33.7% (96/285)
Wasting in no LTBI no TB	27.8% (264/949)
Stunting (HAZ ≤ -2)	16.3% (292/1785)
Stunting in LTBI	15.8% (87/551)
Stunting in TB	20.4% (58/285)
Stunting in no LTBI no TB	15.5% (147/949)
Underweight (WAZ ≤ -2)	25% (446/1785)
Underweight in LTBI	28.9% (159/551)
Underweight in TB	26.3% (75/285)
Underweight in no LTBI no TB	22.3% (212/949)

[Table 1]

Wasted (aOR: 1.54; 95% CI: 1.08-2.17, $p=0.016$) and TST positive children (aOR: 20.24; 95% CI: 13.94-29.39, $p < 0.001$) had higher odds of TB disease. Children > 6 years (aOR: 2.17; 95% CI: 1.72-2.74, $p < 0.001$) had higher odds of LTBI.

Conclusions: Our study shows significant prevalence of malnutrition, active TB and LTBI. Malnutrition is a major risk factor for tuberculosis in India and further studies are needed to understand the relationship between them in order to reduce incidence.

PS42-861-27 Pattern of response to current short-course chemotherapy in children suffering from intrathoracic tuberculosis

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Background: Response of childhood tuberculosis (TB) to treatment is largely assessed on basis of clinical and radiological improvement. However, the pattern of response to modern day therapy is less clearly elucidated as most of current understanding comes from studies on older regimes. This study details clinical, microbiological and radiological course during intensive phase (IP) of standard chemotherapy among new paediatric cases with intrathoracic TB.

Methods: This hospital-based prospective observational study details symptom and radiological resolution among 84 newly-diagnosed (treatment-naïve, non-HIV coinfecting) patients under 18 years of age, with intrathoracic TB. Symptom resolution was monitored using a daily symptom diary, maintained by caregivers and by two-weekly clinical follow-up during IP. In addition, microbiological and imaging tests were done at 4 weekly intervals till end of IP.

Results: The study group had pulmonary TB (75% and isolated pleural effusion (25%). Bacteriological confirmation was possible in 61% (51/84) cases.

Constitutional symptoms like fever, appetite loss resolved ahead of cough, breathlessness and chest pain. Most symptoms abated in 90% children by end of 1 month of IP. Weight gain was highest in the first month of treatment. Of the 10 smear positive TB patients, all became smear-negative status at the end of IP. Radiological resolution lagged behind; as 10% patients showed significant (defined as $>50\%$ clearing of lesion radiological resolution) at end of 1 month, and about 37% cases at end of 2 months. Paradoxical upgrading reactions were identified in 13% cases. About 20% patients developed adverse reactions, mostly mild gastrointestinal disturbances and 2% patients developed drug induced liver injury.

Conclusions: This study provides a timeline of clinico-radiological recovery in children with intrathoracic TB with modern therapy. Symptom resolution happens in almost all by end of 1 month of therapy, while radiological response is more staggered and less complete.

PS42-862-27 Drug-resistant tuberculosis among children in Nigeria

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Background: Drug resistant tuberculosis (DR-TB) is better documented in adults than in children. As DR TB incidence is rising among adults, expectedly, there will also be an increasing number among children. TB in children represents a sentinel of disease in the community suggesting recent transmission from infectious adults. Data are scarce on DR-TB in children. The objective of the study was to evaluate drug resistant TB among Nigerian children in the national TB programme.

Methods: Information in the national electronic TB database was reviewed between 2011 and 2017 for notified DR-TB cases aged less than 15 years.

Results: Within the period reviewed, a total of 87 children were diagnosed with drug resistant TB by Xpert/MTB/Rif assay. The yearly trend of drug resistant TB in children showed that a total number, 61(70.1%) of the cases were notified within the last 2 years. The median age of the cases was 9 years with 27.6% among under-5years. Females accounted for 46 (52.9%). About 56% (49) of the child DR-TB cases notified were among previously treated TB cases. The type of drug resistance was either multidrug resistance (resistance to rifampicin and isoniazid) or mono-resistance with no case of extensively drug resistance seen. Only 2.7% (2) were co-infected with HIV. All the notified cases were enrolled on second line treatment. A mortality rate of 8/87 (8.1%) was recorded.

Conclusions: There is an increasing trend of TB drug resistance among children in Nigeria with low HIV co-infection rate. Drug resistance among previously treated cases was surprisingly high. There is need to intensify DR-TB among children in Nigeria.

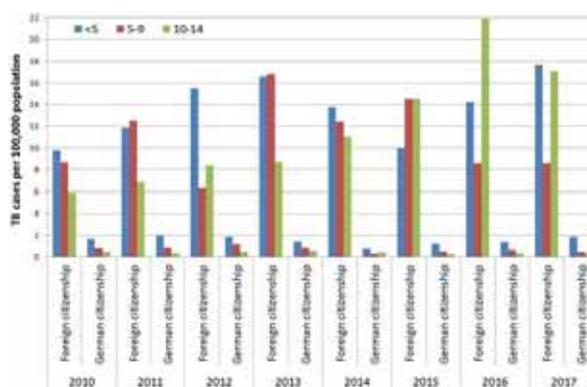
PS42-863-27 Recent trends in pediatric tuberculosis in Germany

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Background: The incidence of TB among children in Germany has started to increase once again. Since pediatric TB is a proxy for ongoing transmission, it is important to understand the underlying epidemiology for prevention and control measures.

Methods: All cases of active TB are reported to Robert Koch Institute's national TB surveillance database. A descriptive analysis of all pediatric cases (0-14 years) was conducted, focusing on 2016 and 2017.

Results: From 2015, more children became ill with TB compared to previous years (2014: 142 cases or 1.3 cases per 100,000; 2015: 192, 1.8/100,000; 2016: 228, 2.1/100,000; 2017: 238, 2.2/100,000). In 2017, 39.6% (89/225) of the notified cases had German citizenship, while 60.4% (136/225) had foreign citizenship, with TB-incidence among them being 10-42 times higher by age group compared to those with German citizenship (Figure 1). For 96 children with information on standard drug-susceptibility testing in 2017, 14 children (14.6%) had any resistance and 5 children (5.2%) had multi-drug resistant TB (2016: 19.1% and 2.2%). In 2017, 59.4% (101/170) of the cases were confirmed culture positive, 23 cases (45 with results) through sputum and 46 (93 with results) through gastric aspirate (2016: 52.4% culture positives). 15.0% (12/80) were sputum smear positive in 2017, an increase from the 6.6% in 2016. In 2017, more pediatric cases were discovered through active case-finding such as contact-tracing (101 cases; 2016: 76 cases) and screening of migrants (28 cases; 2016: 38 cases), rather than passive case-finding such as presenting with symptoms (79 cases; 2016: 93 cases).



[Figure 1: Incidence of pediatric TB in Germany by citizenship, 2010-2017]

Conclusions: Germany has a low incidence of pediatric TB; however, this has been increasing. Bacteriological culture results can be obtained from a high proportion

of children and should be sought for improved diagnosis and therapy. Active case-finding and preventive therapy of children with contact with adults with TB is an especially important control measure.

PS42-864-27 Innovation in pediatric MDR-TB treatment: a novel dose delivery system for MDR-TB medications

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Background and challenges to implementation: Pediatric MDR-TB treatment is a highly neglected area: there are no child-formulations of most MDR-TB drugs, deteriorating accuracy and making treatment highly complicated and time consuming. Few efforts have been initiated to solve this problem. As a result, children with MDR-TB are at risk for poor health outcomes and increased adverse events, and often remain hospitalized—with its attendant costs and consequences—so that medications can be properly prepared and administered.

Intervention or response: Health Advocacy Innovations has designed a device that will support treatment delivery by cutting and dispensing the correct amount of medication needed for a child, based on their weight range. The device removes literacy requirements, allows treatment to occur locally, and simplifies treatment to an easy two-motion operation. The device also removes dependency on pharma to prioritize child health and well-being globally, despite minimal profit motive.

Results and lessons learnt: The device was developed from concept to prototype through consultations with experts from TB Alliance, USAID, MSF, and others. HAI has partnered with TB Alliance for repeatability and reliability testing, and with Partners in Health and Harvard Medical School for pilot implementations in Peru and Pakistan. The device will be evaluated based on quantitative impact data on dose accuracy and treatment compliance, and qualitative feedback from health care workers and patient caregivers.

Conclusions and key recommendations: The device will significantly reduce the challenges of current pediatric MDR-TB treatment by increasing treatment efficiency and accuracy. The device can also be used in PK studies to determine more accurate dosage amounts for pediatric formulations.

PS42-865-27 Tuberculosis in children treated in primary health units and university centers in the metropolitan area of Rio de Janeiro, Brazil

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Background: Brazil is a high burden country for TB. Rio de Janeiro has the second highest incidence rate (63.5 cases/100,000) and the highest mortality rate (4.4 deaths/100,000). Children are more vulnerable to TB, especially in poor areas of metropolitan areas.

Methods: We performed a retrospective study based on chart review of pediatric TB cases from 2007 to 2016, aiming to evaluate TB characteristics of under 15 treated in four primary healthcare units (PHUs) in peripheral areas and three university centers (UCs) of Rio de Janeiro.

Results: 608 TB cases were evaluated; median age was 96 months (IQR 36-156), female/male ratio was 1.07 and pulmonary TB was the most frequent site (73%). 73% of children were treated in PHUs. TB diagnosis based on microbiological or molecular tests were offered to 55.9% of children, 70.2% were positive. HIV testing (92% vs. 71%, $p < 0.001$), HIV positivity (19.1% vs. 4.5%, $p < 0.0001$) and confirmed TB diagnosis (75.2% vs. 65.8%, $p=0.04$) were more frequent in children treated at UCs. In the logistic regression only pulmonary TB was independently associated with a positive microbiological result (OR= 6.0, CI 95% 2.1 - 17.0; $p=0.001$). Success of treatment was not significantly different between children treated at PHUs and UCs (89.7% vs. 84.9%, $p=0.08$). 8.9% were lost to follow up and 1.5% died. Only one case of MDR-TB (1/20, 5%) was identified.

Conclusions: Children with TB treated at PHUs had lower rates of HIV testing and microbiological confirmation. Diagnostic tests for TB should be more easily available to children at all levels of care. Although the success of treatment was high, lost to follow up and mortality rates are still higher than recommended.

The study is part of the European Respiratory Society-ERS/Latin-American Society of Respiratory Medicine and ERS/Brazilian Society of Pulmonology and Brazilian TB Research Network collaborative projects.

PS42-866-27 Estimating intervention impacts on pediatric tuberculosis mortality in India and Nigeria: a modeling study using MAP-IT, a user-friendly decision-support model for pediatric tuberculosis

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Background and challenges to implementation: Tuberculosis (TB) is a leading cause of pediatric morbidity and mortality in low income countries. Mathematical models, such as the Model for Assessment of Pediatric Interventions for TB (MAP-IT), a user-friendly, web-based, non-stochastic model, can be used to estimate the impact of TB interventions on pediatric TB-associated mortality.

Intervention or response: We used MAP-IT to model scenarios of improved availability and utilization of single and packaged TB preventive, diagnostic, and treatment interventions to estimate the impact on pediatric TB-associated mortality in India and Nigeria, two high-burden countries, from 2017-2021.

Results and lessons learnt: The current-care scenario estimated 276,800 and 82,500 TB-associated pediatric deaths from 2017-2021 in India and Nigeria, respectively. In India, interventions the greatest impact on pediatric mortality were improved pediatric fixed dose combination (FDC) regimens (15.2%); improved clinical diagnosis (12.6%); and, improved contract tracing (2%). In Nigeria, improved pediatric FDCs and clinical diagnosis had the greatest individual impact on pediatric mortality, with 8.7% and 8.6% reductions in pediatric mortality, respectively. Packaging TB interventions maximized the impact on pediatric TB mortality, with three-quarters of mortality prevented in both India and Nigeria.

Conclusions and key recommendations: Improved pediatric FDCs and clinical diagnosis had the greatest individual impact on pediatric TB mortality. However, packaged TB interventions have the greatest impact on the number of lives saved. Intervention strategies must address obstacles to implementation, including service access, financing, availability of interventions, and education. MAP-IT estimates indicate packaged interventions including improved diagnostics and child-friendly FDCs regimens had the greatest impact on pediatric TB mortality in two high-burden countries.

PS42-867-27 Delamanid with and without bedaquiline for adolescents and children with rifampicin-resistant tuberculosis

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Background: Data on the use of delamanid for the treatment of rifampicin-resistant tuberculosis (RR-TB) in patients <19 years is extremely limited. We describe early efficacy and safety of the use of delamanid with and without bedaquiline in <19 year olds from a high HIV-prevalence programmatic setting in South Africa.

Methods: This was a retrospective cohort study of patients, aged <19 years, initiating delamanid-containing RR-TB treatment regimens, with or without bedaquiline, between November 2016 and July 2017. We report on sputum culture conversion (SCC), interim treatment outcomes and safety at 6-months after delamanid initiation.

Results: Nine patients initiated delamanid for RR-TB; seven (78%) were male and the median age at delamanid initiation (baseline) was 15 years (interquartile range [IQR] 14 - 16). Four (44%) patients were HIV co-infected; median CD4 count was 194 cells/mm³ (IQR 170-283) and three (75%) had started antiretrovirals. Two (22%) patients had confirmed or presumed rifampicin-mono-resistant-TB, three (33%) had multi-drug resistant TB, and four (44%) had RR-TB with additional fluoroquinolone resistance. The indication for delamanid in six patients (75%) was drugs substitution for the injectable agent. The three patients with fluoroquinolone-resistance received both delamanid and bedaquiline.

Six (67%) patients had positive sputum culture results at baseline; 3 (50%) and 5 (83%) culture converted by 2 and 6-months and median time to SCC was 1.5 (IQR 0.4-2.4) months. Six-months after delamanid initiation, eight (89%) patients were still on treatment, clinically stable, with negative sputum cultures and one (12%) had treatment failure. Overall, five (66%) had delamanid extended ≥ 24 -weeks. None of the patients experienced serious adverse events; there was no QtcF prolongation >500ms; one patient experienced QtcF >60 ms from baseline at month-6.

Conclusions: Early efficacy and safety of delamanid is promising in children and adolescents; expanded access is needed.

PS42-868-27 Lessons learnt from integrating childhood TB case finding in a PEPFAR funded orphans and vulnerable children (OVC) program in Benue State, Nigeria

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Background and challenges to implementation: Nigeria has the second highest TB burden in Africa; with about half a million estimated new TB cases every year. Faced with poor health seeking behaviour among her populace, Nigeria requires innovative strategies to increase TB case finding among children. This abstract describes lessons learned from a pilot initiative which integrated TB case finding in a PEPFAR funded OVC program in Benue State Nigeria.

Intervention or response: Sustainable Mechanisms for Improved Livelihood and Household Empowerment (SMILE) is a USAID funded OVC activity implemented by Catholic Relief Services. At the request of USAID, SMILE integrated a community childhood TB case finding initiative to increase TB case finding among children in the project communities. A community based symptomatic screening checklist was used to identify presumptive TB cases, which were immediately referred and escorted by trained community case management officers and volunteers to health centers for TB diagnoses. Confirmed TB cases were supported to commence treatment at the DOTS centers.

Results and lessons learnt: Of the 11,125 children aged 0-17 years screened, 1,772 presumptive cases were referred to a health facility and 466 (421 (0-14years); 45 (15-17 years) childhood TB cases were confirmed. As at February 2018, a total of 431 children commenced TB treatment and 208 achieved successful treatment. In addition, 404 among the childhood TB cases were tested for HIV and 20 had TB-HIV co-infection. The 421 TB cases among children aged 0-14 years represent over 362% increase when compared with case notification for the state in 2015 (112) and 2016 (116).

Conclusions and key recommendations: Integration of a community based active case finding for childhood TB in SMILE OVC program using a multi-strategic approach recorded a dual benefit of significantly increased TB case detection in children and identifying children infected with HIV.

PS43 Tuberculosis and diabetes

PS43-869-27 Diabetes mellitus among pulmonary tuberculosis patients from four tuberculosis-endemic countries: the TANDEM cohort

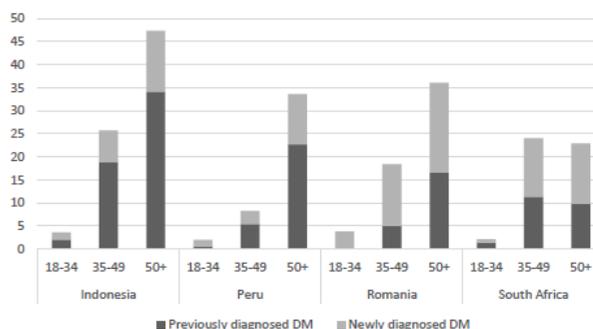
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Background: Diabetes mellitus (DM) is a risk factor for tuberculosis (TB). The TANDEM project examined age-adjusted DM prevalence, clinical characteristics and risk factors for DM amongst newly diagnosed TB patients.

Methods: Adult TB patients in four TB endemic countries (Indonesia, Peru, Romania and South Africa) were screened for DM using repeated HbA1c measured in accredited laboratories between 2014 and 2016. Diabetes was defined using repeated HbA1c or Fasting Plasma Glucose (FPG), pre-diabetes as a single measurement of lab HbA1c or FPG, and DM and TB characteristics were captured using uniform procedures and definitions.

Results: Among 2185 TB patients (median age 36.6 years, 61.2% male), 12.2% had DM, including 84 (3.8%) with newly diagnosed and 183 (8.4%) with previously known DM. Age-adjusted DM prevalence was in Indonesia 19.7%; 12.3% in Peru; 12.3% in Romania, and 9.2% in South Africa, with a median HbA1c among TB patients with DM of 11.3% for Indonesia, 10.6% for Peru, 7.4% for Romania, and 10.2% for South Africa.



[Figure. Diabetes prevalence amongst newly diagnosed TB patients]

Compared to those without DM, TB patients with DM were older (median age 52 years vs. 34 years), more often had a first episode of TB (17.2% vs. 25.7%), a higher bacterial load (80.2% vs. 72.9% smear positive), and a higher BMI (21.9 vs. 19.6; $p < 0.05$). Compared to TB patients with newly diagnosed DM, those with previously diagnosed DM had a higher BMI (22.6 kg/m² vs. 20.0), HbA1c (10.9 vs. 7.9), more frequent family history of DM (43.2% vs. 19.1%), comorbidity and greater loss of renal function.

Conclusions: Prevalence and characteristics of DM in TB patients vary considerably between countries, underlining the need for country and setting specific data. In all four countries, DM among TB patients is mostly previously diagnosed but poorly controlled, with significant comorbidity, indicating that TB-DM patients need additional interventions besides TB therapy.

PS43-870-27 Tuberculosis and associated transient hyperglycaemia in peri-urban South Africa: implications for diabetes screening in high tuberculosis/HIV-1 burden settings

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Background: Diabetes mellitus (DM) increases tuberculosis (TB) risk. TB may also cause transient hyperglycaemia that may normalise during or after TB treatment. This study determined and compared the prevalence of hyperglycaemia in TB patients at enrolment and at 2-3 months follow-up after initiating TB treatment; and determined the association between TB and hyperglycaemia.

Methods: Consecutive adult TB and non-TB participants presenting at a TB clinic in Cape Town were enrolled in a cross-sectional study with follow-up between 2013 and 2015. All participants were screened for diabetes by HbA1c and fasting plasma glucose. TB patients initiated treatment. After 2-3 months, study participants were followed up and screened for diabetes again. The association between TB and diabetes was assessed using logistic regression adjusting for potential confounders.

Results: Diabetes screening was performed in 850 participants (412 TB and 438 non-TB) at enrolment and in 638 (303 TB and 335 non-TB) at three-month follow-up. Among TB patients, diabetes prevalence was 11.89% (95% confidence interval (CI) 9.09 - 15.41%) at en-

rolment and 9.2% (95% CI, 6.37 - 11.71%) at follow-up. Among non-TB participants, diabetes prevalence was 10.04% (95% CI, 6.39 - 11.71%) at enrolment and 8.06% (95% CI, 6.67 - 11.05%) at follow-up. The association between TB and diabetes was positive and significant both at enrolment (adjusted odds ratio (OR) 2.41 (95% CI, 1.3 - 4.34)) and follow-up (adjusted OR 3.31 (95% CI, 1.5 - 7.25)).

Conclusions: Transient hyperglycaemia is frequent during tuberculosis. This suggests the need for diabetes confirmation during or after treatment. The association between TB and diabetes noted at enrolment persisted at 2-3 months highlighting the importance of diabetes control and prevention for TB control. Further research is required to investigate the impact of hyperglycaemia (transient or otherwise) on TB outcomes to ascertain the clinical significance of hyperglycaemia at enrolment.

PS43-871-27 The distribution of diabetes mellitus among TB patients in the State of Florida, USA

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Background: While TB has remained a global concern, there is a notable increase in the prevalence of Diabetes Mellitus (DM) in countries with a high burden of TB. There is a growing body of evidence that supports the association between TB and DM. This study aimed to examine the distribution of DM among TB patients and explore the risk of Drug resistant TB in Diabetics, using age as an effect modifier.

Methods: A retrospective cross-sectional descriptive case based study was conducted using secondary data (2009-2014) of patients diagnosed with pulmonary TB in the State of Florida, USA. A comparative analysis of TB cases with DM and cases without DM adjusted for age was conducted. The risk of Drug resistant TB associated with DM was estimated through logistic regression analysis and odds ratios of TB/DM comorbidity were calculated and adjusted for Age.

Results: A total of 3686 TB cases were analyzed of which 275 (7.4%) patients had drug resistant TB and the majority (87.3%) were resistant to Isoniazid. The majority of cases (65%) were males and likely unemployed (59.1%). The prevalence of DM was 12% but when adjusted for age the prevalence of DM was 3.9% amongst patients aged below 40 years and 16.7% in patients aged above 40 years. There was an observed pattern where Odds Ratios of TB and DM coinfection increased with age. Age category 70 years and above had an OR 8.59 (95% CI 5.93-12.44, $p < 0.0001$).

Conclusions: There is a positive correlation between high DM burden and increased TB prevalence. The risk of TB/DM coinfection increases with age. Therefore, it is recommended that prevention of DM, hyperglycemia and comprehensive management of DM be intensified to prevent TB and reduce the risk of drug resistant TB.

Age	Odds Ratio	95% CI	Pr > ChiSq
51-55	5.09	[3.40 - 7.62]	<.0001
56-60	6.36	[4.25 - 9.50]	<.0001
61-65	6.50	[4.22 - 10.02]	<.0001
66-70	6.85	[4.33 - 10.8]	<.0001

[Age adjusted Odds Ratios for TB cases with DM by age category, Florida, USA, 2009- 2014]

PS43-872-27 Gestational diabetes suppresses the inflammatory response to *M. tuberculosis* in pregnant women in Pune, India

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Background: The immunological changes of pregnancy increase TB risk. Pregnancy is also associated with an insulin resistance similar to diabetes-itself an independent TB risk factor. This study's objective was to determine if gestational diabetes (GDM) impacts the immune response to *M. tuberculosis* (MTB).

Methods: We are conducting a longitudinal cohort study of HIV-infected and HIV-uninfected pregnant women in Pune, India. Each woman is screened for latent TB with an interferon gamma release assay (IGRA) at entry and delivery. Women are also screened for GDM with an oral glucose tolerance test between 24 and 34 weeks gestation. We performed a nested case-control study of IGRA+ pregnant women with and without GDM. We matched cases to controls by gestational age, HIV status, and CD4 strata. Cytokines were measured from IGRA supernatant with multiplex ELISA using Luminex.

Results: Of 194 women, 17 (8.8%) had GDM. Prevalence was 15% in HIV-infected and 7% in HIV-uninfected women ($p=0.05$). Median CD4 for 51 HIV-infected women was 535 cells/mm³; all were on antiretroviral treatment. After MTB stimulation, those with GDM had significantly lower IFN- than those without GDM during pregnancy (4.55 vs. 7.89 IU/mL, $p=0.04$) and at delivery (0.15 vs. 1.96 IU/mL, $p=0.04$). The difference was greater in HIV-infected women (0.8 in GDM vs. 4.2 IU/mL without GDM, $p=0.04$) than in HIV-uninfected

women (6.4 vs. 7.2 IU/mL, $p=0.08$). Compared to women without GDM, women with GDM also trended towards lower IL-2 (62 vs. 86 pg/mL, $p=0.08$) with significantly more IL-10 (63 vs. 30 pg/mL, $p=0.05$).

Conclusions: Pregnant women with GDM have a decreased inflammatory response to MTB antigens compared to women without GDM. This may be related to increased IL-10, an anti-inflammatory cytokine. Antenatal clinics in TB-endemic countries should increase screening and treatment of GDM. Future studies will examine the impact of GDM treatment on the immune response to MTB.

PS43-873-27 Association between diabetes mellitus and multi-drug resistant tuberculosis: a systematic review and meta-analysis

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Background: Diabetes mellitus (DM) is an increasingly recognized comorbidity that can both accelerate TB disease and complicate its treatment. The aim of this review was to summarize available evidence on the association of DM and multi-drug resistant tuberculosis (MDR-TB) and to estimate a pooled effect measure.

Methods: All studies published in English prior to October 2017 and reported the association of DM and MDR-TB among TB patients were searched using comprehensive search strings. The quality of studies was checked using the Newcastle-Ottawa Scale for cohort and case-control studies and the Agency for Healthcare Research and Quality tool for cross-sectional studies. Potential sources of heterogeneity between the studies were examined by using the Cochrane statistic and I^2 . We checked potential publication bias by visual inspection of the funnel plot and Egger's regression test statistic. The random-effect model was fitted to estimate the summary effect (ORs) and 95% CIs across studies.

Results: We included a total of 21 studies published between 2001 and 2017 with a total sample of 13,273 participants with TB sampled from 15 different countries. The combined effect OR suggested that DM has a significant association with MDR-TB (Pooled OR=1.78, 95% CI =1.40-2.28, $I^2= 59.9%$, P for heterogeneity < 0.001). Moreover, a subgroup analysis showed even a stronger association for studies that reported OR at least adjusted for one co-variate (Pooled OR: 2.26; 95% CI: 1.86-2.74). There was no significant publication bias found either by the Egger's regression asymmetry test or by funnel plot inspection.

Conclusions: The result suggested that DM can significantly increase the odds of developing MDR-TB. Our results demonstrate that a more robust TB treatment and follow-up might be necessary for patients with DM. Efforts to control DM can have a substantial beneficial effect on TB outcomes, particularly in the case of MDR-TB.

PS43-874-27 Diabetes mellitus and latent tuberculosis infection in the Eastern China: a population-based, retrospective cohort study

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Background: Although the relationship between the diabetes mellitus (DM) and tuberculosis (TB) is clear, it is unclear if the correlation is due to the risk of latent tuberculosis infection (LTBI), progressing from LTBI to active TB or both.

Methods: We conducted a retrospective cohort study in rural Danyang County, Jiangsu Province. We compared LTBI in no DM, diagnosed DM and undiagnosed patients using a tuberculin skin test (TST) and an interferon- release assay (QuantiFERON [QFT]). 5-year follow-up was examined in this retrospective study to identify active TB patients.

Results: Between July 1 and 30 in 2013, a total of 5408 participants were actually eligible into our study, among whom, 1107 (20.5%) were QFT positive, whereas 2045 (37.8%) were TST positive. 817 (40%) of 2045 participants who were TST positive also had positive QFT tests. Overall agreement between the TST and the QFT test was moderate (71.93%; kappa coefficient 0.344, $P < 0.0001$). Factors significantly associated with LTBI were male sex, increasing age (≥ 20 years), smoking and undiagnosed DM patients (compared with no DM) for both TST and QFT tests. After nearly 5-year follow-up, a total of 15 (5-year TB incidence: 277.4/per 100 000) individuals progressed to active TB. 2 of 15 were DM patients with a 5-year TB incidence 655.7/per 100 000; 13 of 15 were no DM populations with a 5-year TB incidence 254.8/per 100 000 ($P=0.206$). Among 1107 QFT positive, 11 developed to active TB (5-year TB incidence: 993.7/per 100 000) ($P < 0.0001$); among 2045 TST positive, 9 developed to active TB (5-year TB incidence: 440.1/per 100 000) ($P=0.076$).

Conclusions: In conclusion, in a population-based retrospective cohort study, undiagnosed diabetes increased the risk of the latent infection tuberculosis, diabetes having hypoglycemic drugs modified this relationship, and the participants with QFT positivity were more likely to progress to be active TB.

PS43-875-27 Addressing diabetes and tuberculosis comorbidity: lessons from Bangladesh

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Background and challenges to implementation: The dual burden of tuberculosis (TB) and diabetes mellitus (DM) is a major public health concern in Bangladesh. Diabetes patients are two to three times more likely to become infected with TB than those without.

Intervention or response: In partnership with Bangladesh Diabetic Shomity (BADAS), the Challenge TB (CTB) project is implementing an intervention to increase access to TB services among DM patients in one tertiary level hospital and 95 affiliated facilities. This is intended to improve early case detection and management of TB among comorbid individuals. Intervention strategies include capacity building of staff, health promotion among DM patients and communities, and providing ambulatory services to strengthen TB care and prevention among DM patients.

Results and lessons learnt: In 2017, a total of 1,641,458 DM patients were screened, resulting in 12,634 (0.8%) presumptive TB cases identified and referred for smear microscopy. Among the total detected 1,374 (10.9%) TB cases - 983 (71.5%) were bacteriologically confirmed, 208 (15.2%) were clinically diagnosed, and 183 (13.3%) extra pulmonary TB. 21 of the cases detected were children. Per this data, the prevalence of TB among DM patients is 84/100,000 population, which is much lower than the national TB prevalence (260/100,000 population). There was a limitation in screening procedures, as some DM patients were screened multiple times which, by inflating the total number of screenings, makes the Case Notification Rate (CNR) among DM patients appear lower than it is.

Conclusions and key recommendations: Strong collaborative effort aimed at capacity building and awareness-raising activities could improve the health and wellbeing of patients with TB and DM comorbidity. The screening and recording processes should be strengthened to exclude double counting and to note exact prevalence of TB among DM patients. Further research is required to generate evidence on actual magnitude of DM and TB comorbidity in Bangladesh.

Indicator (January - December 2017)	Achievements
Number of DM cases screened for TB	1,641,458
Number of presumptive TB patients with DM tested for TB	12,634
Number of all forms TB notified among DM patients	1,374

[TB DM comorbidity identified from screening]

PS43-876-27 Scaling up diabetes mellitus screening in patients with pulmonary tuberculosis in Dhaka, Bangladesh, with a public-private model

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Background: Bangladesh is among the 22 high tuberculosis (TB) burden countries worldwide yet also accounts for a third of patients with diabetes mellitus (DM) living in the least developed countries. DM screening is recommended for adults ≥ 18 years with TB but is virtually absent in public facilities, and while DM screening is present in private facilities those settings may improperly screen and treat TB.

Methods: We sought to introduce DM screening in presumptive TB cases attending a public-private model setting in urban Dhaka- icddr, TB screening and treatment centers (STC)- by offering free glucometry tests along with current standard of computer-aided chest X-ray and sputum Xpert MTB/RIF to estimate factors associated with TB/DM and the number needed to screen (NNS) to diagnose one new case of DM. Presumptive TB cases with fasting blood glucose ≥ 7 mmol/L or random blood glucose ≥ 11.1 mmol/L were considered as DM. Clinical and laboratory findings were compared in TB patients with and without DM.

Results: From July 2014 to October 2017, 7,647 presumptive TB patients attending the STCs agreed to be screened for DM. Pulmonary TB was diagnosed in 16% (1,204) of those tested for diabetes. Among the TB patients, 252 (21%) were diagnosed as having DM with 47 (19%) newly diagnosed. The median age of TB patients with DM (45 years, IQR 39-55) were higher than TB patients without DM (35 years, IQR 25-50) ($p < 0.001$). Among presumptive TB, the NNS was 40 to diagnose 1 new case of DM, and among diagnosed TB, the NNS was 26.

Conclusions: Detection of DM was high among confirmed TB cases in this public-private setting in urban Dhaka. We recommend continued operational research of scale up strategies and linkage to DM care.

PS43-877-27 Bi-directional screening of TB and diabetes at private diagnostic and treatment centers, Karachi, Pakistan

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Background: In 2009, International Union Against Tuberculosis and Lung Disease (IUATLD) recommended bi-directional Tuberculosis (TB) and Diabetes (DM) screening and integrated management for both diseases in high burden countries. Pakistan ranks fifth among high tuberculosis (TB) burden countries and has the seventh highest burden for (DM).

Methods: Between July 2016 and March 2018, verbal screening was conducted at private health provider clinics and community screening camps. Individuals with presumptive TB were referred for Xpert MTB/RIF at private diagnostic centers. All patients with bacteriologically positive TB were tested for diabetes using HbA1c. Individuals with presumptive DM and known history of diabetes were tested for random blood sugar (RBS). All known and newly identified diabetics were tested for TB using Xpert.

Results: A total of 4,692 TB cases were screened for diabetes, out of which, 1,732 (36.9%) and 953 (20.2%) individuals were identified with pre-diabetes and diabetes respectively. The combined prevalence of pre-DM and DM identified among TB patients was 56.6% (NNT 4.9). This prevalence was lower among individuals aged >40 years (NNT 2.7) relative to patients aged < 40 years of age (NNT 7.2). A total of 3,825 DM patients were screened for TB, of which 2,934 (76%) were tested on Xpert MTB/RIF. A total of 281 cases tested positive for MTB on Xpert providing a yield of 9.4%. A total of 136 patients were diagnosed with TB on clinical history, examination and radiology findings.

Conclusions: A higher prevalence of DM was found among individuals with TB compared to the general population of Pakistan. Routine testing for diabetes is recommended among TB patients, particularly. Similarly, a high prevalence of TB was found among diabetics suggesting that this may be a suitable risk-group for screening for TB. Policies need to be developed to scale-up bi-directional screening with focus on engaging the private-sector.

	TB Cases Tested for DM	Pre-Diabetes	Newly Diagnosed DM cases	NNT
Total	4692	1732(36.9%)	953(20.2%)	4.9
Xpert Result				
MTB+	2116	901 (42.6%)	511(24.1%)	4.1
Clinically diagnosed	1831	831(45.4%)	442 (24.1%)	4.1

[Results of DM testing on cases identified with TB through screening in the private-sector in Karachi, Pakistan, from July 2016 to March 2018]

PS43-878-27 Improving integrated care of tuberculosis and diabetes comorbidities in South Africa

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Background and challenges to implementation: In most high burden of tuberculosis (TB) countries, including South Africa (SA), service delivery for diabetes (DM) and TB are vertical, and therefore patients at risk of or with both diseases do not receive integrated care. To address this gap and develop operational models for high-quality TB-DM services in SA, URC implemented a program for improved management of patients with TB-DM comorbidities, covering 22 high volume facilities in 4 provinces (KwaZulu Natal, Eastern and Western Cape, and Free State, n>350,000 patients) selected in cooperation with the NDOH.

Intervention or response: Over the course of the project, assessments via chart reviews, interviews, surveys and direct observations were conducted to determine needs and gaps in provider knowledge, and to measure patient understanding and experience of TB-DM care at the facility level. These informed the development and implementation of a series of educational, advocacy, and capacity-building interventions to improve the quality of integrated care at the facility level, and health seeking behaviors and awareness of DM and TB among the general population.

Results and lessons learnt: Chart reviews revealed an increase in screening for TB-DM: 78% of patients with TB screened for DM (n=8,603/11,047) and 64% of patients with DM screened for TB (n=14,026/21,792). A total of 536 healthcare professionals including community health workers were trained. Over 8,000 people were reached through advocacy and awareness campaigns. Patients reported improvements in exposure to screening, counselling, and health education on TB-DM comorbidities. However, surveys revealed large variation in these indicators across districts, suggesting a need for further harmonization of training, mentoring and other interventions.

Conclusions and key recommendations: Simple facility and community-level interventions can improve bi-directional screening of patients with TB-DM. To further strengthen integration of TB-DM, facility mentoring, redesigning data collection systems, and educational outreach are important areas for further research.

PS43-879-27 Active case finding and screening for HIV and diabetes as a potentially viable strategy for reduced transmission of tuberculosis in penitentiary institutions in India

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Background and challenges to implementation: Prevalence of TB among prisoners is higher compared to the general population. Overcrowding, inadequate ventilation and higher prevalence of common co-morbidities among prisoners increases the risk of developing active TB. The special ACF campaign conducted by the Government of India among high risk groups in 2017 discovered that the lowest number of persons needed to screen (NNS) to identify a TB case (489) was in prisons and other residential institutions.

Intervention or response: World Vision India and its six partners implemented project Axshya in 70 districts from October 2015 to December 2017 supported by the Global Fund with an aim to detect missing TB cases among key populations through ACF. In conjunction with district TB officials and the Prison Superintendent, 39 prisons across in 3 states were visited and all 15990 inmates present were verbally screened using a four-symptom complex verbal screening tool. Identified presumptive TB individuals were further tested either through Sputum Microscopy or Chest X-Ray (CXR). Sputum samples of those suggestive of TB were tested by GeneXpert. To ensure additional outcomes of screening whole blood testing for HIV and diabetes to anyone who consented was also offered.

Results and lessons learnt: From 15,990 prison inmates screened verbally, 4,803 TB presumptive cases were identified. Total of 4,803 CXR, 349 Sputum Microscopy and 771 GeneXpert tests were performed. As a result, 89 new TB patients were identified at the rate of one patient for every 180 persons screened; which includes one sputum positive, 48 clinically diagnosed, 38 Rif-Sensitive and 2 drug-resistant cases. 71 of the 6,044 persons tested for HIV were found reactive for HIV and 698 of 4,888 persons tested for diabetes were found to have random blood sugar >140 ml/dl.

Conclusions and key recommendations: ACF and screening for HIV and diabetes are important strategies for identifying and management of TB and can contribute to reduced transmission among penitentiary institutions.

PS44 Laboratory informatic system: where are we?

PS44-880-27 Connecting actions to connectivity: a case study

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Background and challenges to implementation: Deployments of connected diagnostic solutions to collect real-time test data from laboratories and clinical networks have been numerous. Yet this drive for real-time data collection has not consistently led to a commensurate rise in utilization of data to improve processes and patient care. This project identified blockers to data use, examined why these data have not translated to better management, and identified interventions to address the gap.

Intervention or response: Working with the Myanmar National TB program a comprehensive survey of data collection and review of usage by stakeholder groups was performed by FIND and CHAI in 2017. Key findings from the initial review concluded that data quality was reasonably complete, but there was limited use of the data and the advantage of what online data collection could provide: faster, more complete access, additional data collection was not being fully utilized.

Results and lessons learnt: Expected gains of the platform were limited to a narrow range of stakeholders whose main use was for patient tracing rather than realizing the broader set of benefits. Reasons for this gap included lack of training and knowledge of the connectivity systems across the variety of program roles. In addition, there can be challenges integrating a digital system into an established workflow, or changing an established workflow into an online system.

Conclusions and key recommendations: Current work to overcome these identified challenges include a collaboration with SystemOne, to create unique stakeholder-orientated action dashboards for regional clinical officers and laboratory staff, implemented to provide targeted data and suggestive actions on machine health, reagent health, connectivity and population testing targets in a single location. This is an intuitive icon driven approach that encourages effective actions.

PS44-881-27 Monitoring the quality of the National GeneXpert Program in Botswana against international benchmarks using a connectivity solution (GxAlert)

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Background and challenges to implementation: The GeneXpert has been installed in all 28 health districts in Botswana, and adopted as the initial diagnostic test for all presumptive TB cases. There were however, several challenges related to monitoring and evaluation of the instruments, as no data capturing mechanism was established and manual collection of data was not efficient. It could take weeks to months for data to reach the national level from peripheral labs, and was often incomplete, leading to inaccurate reporting and difficulty monitoring quality of the program.

Intervention or response: To address this, the USAID funded Challenge TB project supported the national implementation of GxAlert in 29/33 GeneXpert sites in Botswana. GxAlert, an open-source software, connects GeneXpert instruments via a secure network and allows automatic real-time reporting and fleet management. Through GxAlert, quality indicators such as 'no results', invalids, error rates and codes (categorised as 'unsuccessful' tests) were monitored against WHO/GLI acceptable/target thresholds.

Results and lessons learnt: Overall, a decrease was observed in unsuccessful tests reported from 2014 to 2017; from 11% to 7%. In 2017, Botswana reported a 1.8% 'no result' rate, above the acceptable threshold of < 1%; a 0.4% invalid rate, well within the acceptable threshold of < 1%. Error rates have steadily declined since 2015, from 10.2% down to an acceptable 5% in 2017. Two sites reported high 5006/5007 errors in 2017 (volume-related) and re-training on specimen processing was performed; three sites experienced power-related errors (non-functional UPS). A spike in assay-related errors was detected in November/December 2017 and tracked to a specific Xpert lot number.

Conclusions and key recommendations: These findings show the benefit of a connectivity platform for remote monitoring of quality indicators for the GeneXpert program and thus allows continuous quality improvement. The Botswana team also realized that for GxAlert to be used to its full potential, users need to be proactive with the system.

PS44-882-27 Predicting Xpert capacity targets based on annual notifications: using the WHO framework targets and indicators for laboratory strengthening capacity calculation tool

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Background: In 2016, WHO provided guidance for calculating laboratory targets to build diagnostic capacity. The capacity-calculation tool uses annual notifications to determine the number of MTB/RIF tests a country needs to effectively test all cases presumptive for TB/MDR-TB. From this estimate, the number of modules is determined to achieve testing and guide network expansion.

Methods: The WHO capacity-calculation tool was used to identify the module capacity required to test all cases presumptive for TB (initial test) and presumptive for MDR-TB (universal DST) for the 30 HB TB countries listed in the 2017 WHO TB Report. Testing was based on optimized module capacity at four tests/module/day over 240 workdays a year. Assumptions were used as recommended in the *Framework Targets and Indicators for Laboratory Strengthening* guidance document. Country profiles were constructed to illustrate scale-up needs with estimated costs.

Results: Results demonstrate that when testing is optimized 19/30 countries currently have enough modules to cover national notifications to “test all.” Only, 11 countries require more instruments. When reviewing national HBDC GeneXpert procurement data, only 2 countries are procuring cartridges to test at 50% of their existing capacity. The majority of countries are procuring (proxy for testing) at rates below 30% utilization. Reasons for low procurement volumes are hypothesized, but further exploration respective to country situation are needed. In addition, this exercise identified areas in the tool that need to be adapted or revised.

Conclusions: The WHO tool was useful to illustrate the level of expansion needed for each country to achieve optimal testing goals with universal testing for TB/MDR-TB. Further, the tool may guide costs related to expansion for better allocation of funds. Budget decisions will also need to include resources for network optimization by improving access and linkages to testing, expanding algorithm implementation for universal testing, and establishing work-efficiency and needed human resources at site-level.

PS44-883-27 Challenges and lesson learnt during implementation of GeneXpert GxAlert platform in connecting rapid tuberculosis diagnosis for better health outcomes in Tanzania

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Background and challenges to implementation: Effective TB care and prevention interventions require rapid identification of TB infected persons and proper treatment. Reporting of results in many low and middle-income countries takes couple of days to arrive at central level for compilation which may cause delays treatment initiation.

GxAlert is an electronic system designed to enhance rapid communication of Xpert MTB/RIF results through SMS and/or email among district, regional coordinators and national program managers. In Tanzania the first GxAlert was installed in 2013 with the aim of monitoring Xpert results and improving the rapid linkage of DR-TB patients to care. Before introduction of GxAlert, data were collected through telephone calls, email, EMS and physical visits from central to site which is very expensive.

GxAlert like other devices that use internet faces obstacles such as weak signals from local mobile network providers, interruption of internet connection due to frequent power cuts and lack of computer knowledge among laboratory personnel to perform minor troubleshooting.

Intervention or response: To overcome these challenges by the use of GeneXpert superusers, we revised the routine supervision to targeted supervision and mentoeship to sites with specific problem. The team could stay at site for some days conducting troubleshooting and mentorship to GeneXpert users.

Results and lessons learnt: After revising the routine supervision to targeted supervision and mentorship to sites with specific problem, the GxAlert connectivity increased from 38% in 2017 to 90% in Feb 2018. Experience learnt shows that when properly monitored, GxAlert connectivity is improved hence helping in remotely monitoring performance of machine, usage of cartridges and ensures all drug resistance TB (DR-TB) patients detected are put on treatment early.

Conclusions and key recommendations: Despite of the challenges, GxAlert health platform remains an important tool in enhancing rapid diagnosis and improving communication of DR-TB results within the health systems.

PS44-884-27 The utilisation of an Android-based application to increase access to quality GeneXpert testing

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Background and challenges to implementation: In 2016, the Ministry of Health of Indonesia issued a regulation that specimen of presumptive Tuberculosis (TB) should be tested using GeneXpert. To achieve this, a mechanism of specimen transportation from health facilities that do not have GeneXpert to GeneXpert facilities should be developed well. SITRUST, an Android-based application system, was developed to facilitate the specimen transportation to GeneXpert test in cooperation with the National Post Office. This study assessed the effectiveness of SITRUST to improve the utilisation of GeneXpert test and the benefits of using this application from the perspective of health workers.

Intervention or response: We conducted pilot in 50 districts in 10 provinces across Indonesia that were purposively selected to implement SITRUST in specimen transportation to GeneXpert facilities. Data collection included audit of records from the application dashboard and the results of Yes-No questions survey to health workers.

Results and lessons learnt: In total, 1,124 primary health care providers in this pilot study had been provided training on using SITRUST. During the period of September 2017 to March 2018, the participation of primary health care providers using SITRUST for specimen transportation was more than 40% and there were 1,926 specimen of presumptive drug resistance TB and 4,699 specimen of presumptive TB delivered to GeneXpert facilities. During March, this mechanism has contributed 39% to the utilisation of GeneXpert. Two hundreds health workers participated in the survey on the benefits of SITRUST. More than 90% participants stated that SITRUST is user friendly, accountable, clear referral system, and easy to track the delivery. However, internet is the most common issue in using SITRUST.

Conclusions and key recommendations: This pilot study demonstrated that SITRUST increased access to GeneXpert test and potentially contributes to improve the utilisation of GeneXpert. Therefore promoting SITRUST to other districts and integrating it into the national reporting system is considered to be important to improve TB notification report.

PS44-885-27 GxAlert field implementation: experience of Ethiopia

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Background and challenges to implementation: GxAlert implementation was started in the beginning of 2016 by Ethiopian Public Health Institute (EPHI) in partnership with USAID-funded Challenge TB (CTB) Project. GeneXpert machines performance monitoring using phone calls and manual data collection for quarterly report were very difficult, time taking and prone to transcriptional errors which challenges to use the information for decision making.

Intervention or response: Health facility based installation of GxConnect software in 129 (111 TB, 12 HIV-viral load and 5 HIV-1 Qual tests pages) GeneXpert machines were performed and configured for automatic reporting to the local server placed at national level. GxAlert training was provided, regional and end user level account created at each level to monitor the GeneXpert machine performance and provide data for program management.

Results and lessons learnt: The performance of 129 configured GeneXpert machines are well monitored with real time reporting of test results, service (machines maintenance issues), supply management and notification of Rifampicin Resistance (RR). A total of 274,996 test results were reported since the installation of GxAlert. Among the total tests 31,498 were positive for *Mycobacterium Tuberculosis* (MTB+), 3,120 RR positive, 813 indeterminate, 8729 invalid, 10,026 no result, 15,031 error results were reported. A total of 67 GeneXpert modules were replaced using information from GxAlert. The trend of GeneXpert machines utilization was analysed using the data obtained from GxAlert, and significant increase was noted from 28% in 2016 to 75% in 2018.

Conclusions and key recommendations: GeneXpert machines performance monitoring and patient centric real time data collection for programmatic management became easy due to GxAlert implementation in Ethiopia. Using multi test and multi device connectivity solution like GxAlert will ease TB program management at each level.

PS44-886-27 Innovation using 'line listing' with information communication technology for improving initiation of treatment in RR/MDR-TB patients: experience from Nigeria

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Background: The national policy on GeneXpert MTB/RIF as primary TB diagnostic test and rapid scale up of GeneXpert machines in 2016 increased the number of eligible patients who required initiation of RR/MDR-TB treatment in Nigeria from 1,279 in 2015 to 1,686 in 2016 and 2,286 in 2017. Sadly only 51% of eligible patients started MDR-TB treatment in 2015, which is below the global figure of >90%. Achieving the Global plan to End TB by 2020 is difficult if eligible patients diagnosed with RR/MDR-TB are not effectively documented and tracked to start treatment.

Objectives: This study aims to improve RR/MDR-TB diagnosis and treatment gap through the use of "line listing" with ICT.

Methods: A surveillance electronic dash board "line listing" was established to document and track all diagnosed Rifampicin Resistance (RR/MDR-TB) patients. This tool contains details of biometric data, date of Xpert MTB/RIF test, date of initiation of treatment (treatment center or community). The "line listing" tool is updated daily with information obtained from GxAlert installed on GeneXpert machines. The GxAlert was configured to automatically send out notification messages (SMS) once a RR/MDR-TB patient was diagnosed to mobile phones of state TB program managers, LGA TB supervisors and DOT health care workers who requested for the test. All diagnosed RR/MDR-TB patients are immediately contacted, traced and expectedly initiated on treatment. A retrospective review and impact of the line listing on enrollment has been conducted.

Results: The proportion of eligible RR/MDR-TB diagnosed patients who started treatment increased from 74% in 2016 to 78% in 2017. GeneXpert machines connected to GxAlert system also increased from 115/201 (77%) in 2015 to 370/390 (94%) in 2017.

Conclusions: "Line listing" as a surveillance tool with effective GxAlert notification system linked to mobile phones has a huge potential to increase RR/MDR-TB initiation of treatment.

PS44-887-27 Improving laboratory information management practices in tuberculosis laboratories: successful implementation of TBLIS® in tuberculosis laboratories in Africa

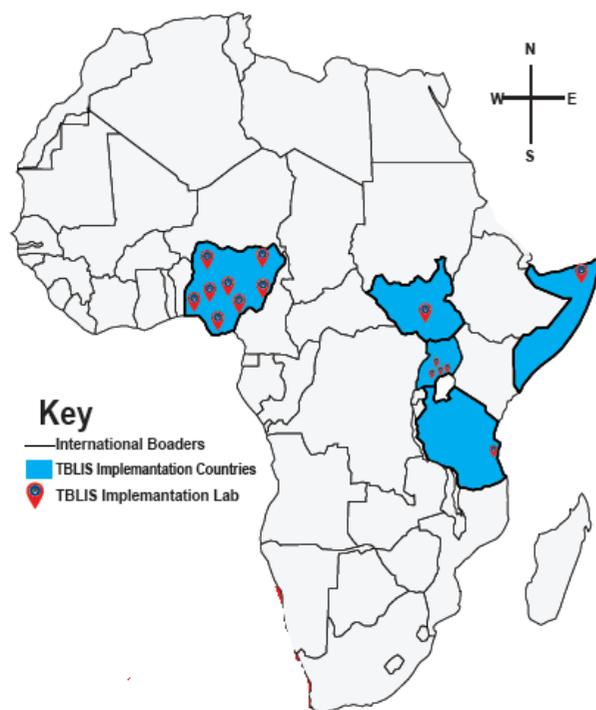
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Background and challenges to implementation: Timely and quality laboratory reporting of Tuberculosis (TB) is a necessity for prompt initiation of appropriate medical therapy for TB patients and rapid public health response. However, TB patients in resource-poor settings experience large delays in starting appropriate treatment and may not be monitored appropriately due to delays in communication of test results, and missing or error-prone laboratory data. Challengingly, most TB diagnostic laboratories in Africa implement paper-based information management systems while others implement electronic systems that do not meet the unique needs of a TB laboratory. They struggle with limitations in sample tracking, results reporting, monitoring of quality indicators and utilisation of information.

Intervention or response: With technical support from Landsat ICT Solutions since 2013, Uganda TB Supranational Reference Laboratory (SRL) implemented TBLIS® - an electronic laboratory information management system for tuberculosis laboratories to improve the quality of TB laboratory data, timeliness of results reporting, monitoring of laboratory quality indicators, patient treatment outcomes and effective patient care.

Results and lessons learnt: Uganda SRL successfully implemented TBLIS® in 2014. The system facilitated real-time monitoring of laboratory processes; supported monitoring of laboratory quality indicators and timely delivery of test results to clinicians; met information management requirements including the ISO 15189 standard; and was very useful in managing laboratory data for the Uganda TB Prevalence Survey 2014/15. TBLIS® has been scaled up for implementation in fourteen other TB laboratories in Uganda, Somalia, Tanzania, South Sudan and Nigeria in a period of three years. The fifteen laboratories where TBLIS® is implemented have achieved tremendous improvements in information management operations and audit scores.

Conclusions and key recommendations: TBLIS® is a novel model that supports unique needs of TB laboratory information management in resource-limited settings. The system is appropriate for both TB patient care and research laboratories, and can support laboratory accreditation. We propose TBLIS® as a tested option for information management in tuberculosis laboratories.



[Map of Africa Showing TBLIS Implementations]

PS44-888-27 Benefits of using technology-supported GxAlert in managing Genexpert high error rates in Nigeria

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Background and challenges to implementation: Nigeria is ranked one of the highest DR-TB burden country. The country relies on GeneXpert machine to often diagnosis DR-TB. However, testing for TB and reporting results is a lengthy process partly due to a reliance on paper records, overburdened labs, and slow data transit systems making it difficult for the Nigeria Tuberculosis Program to account for patients diagnosed for DR-TB, enroll for care and management decisions are not timely or focused on priority needs. High errors rates are recorded in most labs of the country leading to huge wastages and losses.

Intervention or response: GxAlert was developed by Systemone to automatically report test results for TB and MDRTB, Deliver real-time disease surveillance data to points of care for treatment initiation. Assessment of proportions of error tests from 2014 -2016 and to what extent these had changed between the two years for facilities in states using GxAlert. Linear regression was used to assess the relationship between year and number of errors and number of quality assurance tests. Data cleaning and analysis was done using Microsoft Excel and Stata 12 statistical software.

Results and lessons learnt: On average, states had 4.7% test errors in 2014 which decreased slightly to 4.1% in 2015, even with the addition of new facilities. The number of invalid tests increased from 1.4% to 4.6%. Twenty-four percent of tests were MTB positive in 2014, which decreased slightly to 23.1% in 2015.

Conclusions and key recommendations: The GxAlert system shows that there is management and disease monitoring benefits to a real-time database system that not only provides information on complete tests and cases, but also on test errors and quality assurance efforts. Based on these findings, a Refresher training or strengthened supervision may be needed on the use of the Genexpert equipment for facilities whose error rates have not improved.

PS45 Challenging diagnostics: hard to reach mycobacteria

PS45-889-27 Use of lateral flow urine lipoarabinomannan test to diagnose tuberculosis in critically ill people living with the human immunodeficiency virus in Uganda

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Background and challenges to implementation: In 2015, WHO recommended use of lateral flow urine lipoarabinomannan (LF-LAM) as a point of care test to assist in TB diagnosis among HIV positive patients symptomatic for TB with a CD4 count ≤ 100 cells/ μ L or seriously ill regardless of CD4 cell count. In 2016, Uganda piloted the use of LF-LAM in two National and fourteen Regional Referral Hospitals. 149 Health care workers were trained, use of LF LAM was incorporated in the National TB diagnostic algorithm and 5,000 kits donated from Alera supplied. We sought to determine the utilization of urine LF-LAM, adherence to guidelines and treatment outcomes of eligible TB LF-LAM positive patients.

Intervention or response: We retrospectively reviewed and analyzed data of hospitalized People Living with HIV (PLHIV) diagnosed with TB using TB LF-LAM from May 2016 to January 2017 at one National and seven Regional Referral Hospitals. These hospitals were supplied with 2,600 TB LAM test kits.

Results and lessons learnt: About half, 52% (1,352/2600), of the tests were utilized, 63% (852/1352) on PLHIV patients of which 22% (184/852) tested positive for TB. 87.5% (161/184) of these PLHIVs were new TB patients, 64% (117/184) had no smear done while 25% (46/184) had a negative smear result, only 31% (57/184) had a CD4 result with a mean count of 44.7 cell/ μ l, 79% (146/184) were on cotrimoxazole prophylaxis and 76% (140/184) were enrolled on ART. 20% (37/184) were treated successfully, 2% (3/184) failed treatment, 10% (19/184) died, 6% (10/184) were lost to follow up, 17% (32/184) were not evaluated and 45% (83/184) were not linked to care.

Conclusions and key recommendations: Utilization was average, guidelines were not fully adhered to and majority of patients had unfavorable treatment outcomes. We recommend strengthening compliance to policies and guidelines for TB and management of patients with advanced disease by health care workers to reduce on the death rate.

PS45-890-27 Comparison of Mueller Hinton and 7H9 broths for testing drug susceptibility of *Mycobacterium avium* complex using SLOMYCO Sensititre panel

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Background: The Clinical and Laboratory Standards Institute (CLSI) recommends the use of Mueller Hinton (MH) medium at pH 7.4 to test antimicrobial susceptibility of *M. avium* complex (MAC) by the microdilution method in replacement of the previously used pH 6.8 7H9 medium. There has been no study of the impact of medium on minimum inhibitory concentrations (MIC) measure of the antibiotics other than clarithromycin for MAC drug susceptibility testing. The study aimed at comparing the MICs obtained with these two media for susceptibility testing of MAC isolates.

Methods: The MICs of the main antimicrobial agents used in the treatment of MAC infections were measured for 158 clinical MAC isolates (80 *M. avium*, 40 *M. intracellulare*, 35 *M. chimaera*, 2 *M. yongonense*, 1 *M. timonense*) in MH broth and 7H9 broth using SLOMYCO panel.

Results: The concordance percentages for the MIC values between the 2 media evaluated are low to moderate: from 27% for clarithromycin to 60% for linezolid. These results are confirmed by the kappa test revealing a very weak agreement for clarithromycin, ethambutol, rifabutin and rifampicin ($0 < k \leq 0.2$), weak for moxifloxacin ($0.2 < k \leq 0.4$) and moderate for linezolid ($0.4 < k \leq 0.6$). When MICs were converted to sensitivity categories (SIR) according to the CLSI guidelines and Brown Elliott proposal, the kappa test showed a weak agreement for amikacin and moxifloxacin, a moderate agreement for linezolid and an excellent agreement for clarithromycin ($k > 0.8$) (attached table).

Conclusions: The main difference between the two media was the MIC results for clarithromycin due to the difference in pH (6.8 in 7H9 vs. 7.4 in MH). However, the existence of critical concentrations adapted to the medium allowed an excellent concordance for the SIR classification (98%). For the other antibiotics, the concordance was low or moderate. These differences question the clinical relevance of SIR categorization of antibiotics other than clarithromycin for MAC.

		Amikacin	Clarithromycin	Ethambutol	Linezolid	Moxifloxacin	Rifabutin	Rifampin
MIC values	% concordance (kappa score)	57 (0.39)	27 (0.18)	37 (0.18)	60 (0.43)	46 (0.24)	39 (0.17)	35 (0.09)
SIR classification	% concordance (kappa score)	87 (0.35)	98 (0.92)	Not applicable	73 (0.52)	59 (0.39)	Not applicable	Not applicable

[Concordance percentage and kappa score for MIC values and SIR classification of MICs obtained in both media for antibiotics tested by SLOMYCO panel]

PS45-891-27 Retrospective analysis of NTM in patients with suspected TB in the Moyen Ogooue Region of Gabon

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Background: The nontuberculous mycobacteria (NTM) are mycobacteria other than the *Mycobacterium tuberculosis* Complex (MTBC) that can cause diseases with similar symptoms of tuberculosis (TB). Diagnosis of NTM is a challenge in many countries with limited resources, thereby resulting in many NTM-infected patients being put on anti-TB regimens that are usually not very effective. To ensure effective treatment, it is important that the differential diagnosis between the

NTM and tuberculosis is performed. The purpose of this study was to determine the prevalence and different types of NTMs isolated from patients suspected of tuberculosis in the Moyen Ogooue Region of Gabon.

Methods: A retrospective analysis was conducted on sputum samples of presumptive TB cases processed at our TB Laboratory, in CERMEL, Lambaréné, Gabon from January 2014 to December 2017. The Capilia TB-Neo test was used to differentiate NTM isolates from MTBC isolates; while the Genotype Mycobacterium CM/AS was used to confirm and differentiate NTM isolates.

Results: Of 1513 samples analysed, 563 (37,2%) were positive by MGIT liquid culture, 471 (31,1%) were confirmed as MTBC, and 95 (6,3%) confirmed as NTM. Genotyping identified 11 different species as shown in Table 1, with most often isolated specie as *Mycobacterium intracellulare* 48 (3,1%), mixed infections MTBC/NTM were 4 (0,3%), and unknown species were 12 (0,7%).

<i>M. intracellulare complexe</i>	48(3,17)
<i>M. fortuitum</i>	16(1,05)
<i>M. stomatepieae</i>	2(0,13)
<i>M. mageritense</i>	1(0,06)
<i>M. celatum</i>	1(0,06)
<i>M. interjectum</i>	1(0,06)
<i>M. mucogenicum</i>	1(0,06)
<i>M. cosmeticum</i>	1(0,06)
<i>M. semiae</i>	1(0,06)
<i>M. bouchedurhonense</i>	1(0,06)
<i>M. avium complexe</i>	6(0,39)
<i>M. tuberculosis/M. fortuitum</i>	2(0,13)
<i>M. tuberculosis/M.intracellulare</i>	2(0,13)
Unknown species	12(0,79)

Table 1. Non-tuberculous *Mycobacteria* species in suspected TB patients in Gabon

Conclusions: With a prevalence of 6,3%, the infections caused by the NTM are becoming important in our setting. There is a need for prospective longitudinal studies for a better understanding of its epidemiology and clinical importance.

PS45-892-27 Accuracy of determine TB-LAM Ag to detect TB in HIV-infected patients in association with diagnostic methods used in Brazilian public health units

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Background: Determine® TB-LAM Ag (LAM) is a point of care test developed to diagnose tuberculosis (TB). The aim of this study was to evaluate the diagnostic performance of LAM using Brazilian public network algorithm for TB diagnosis.

Methods: Cross-sectional study, with consecutive inclusion of patients. Adults, HIV-infected with CD4 counts ≤ 200 cells/mm³ (in the Alere PIMA® CD4 assay at study screening), coughing for at least 2 weeks or presenting a chest radiography suggestive of TB were enrolled in two sites in Rio de Janeiro and two in São Paulo. LAM, combined with two sputa smear microscopy or one Xpert® MTB/RIF, was compared to *Mycobacterium tuberculosis* culture, as a reference standard.

Results: Two hundred patients were included. TB prevalence was 18.5%. Overall sensitivity of LAM was 0.479 and specificity was 0.908. The best performance of LAM was observed among patients with CD4 counts ≤ 50 cells/mm³ (sensitivity = 0.704 and specificity = 0.859). When smear is associated with LAM, this combination increased sensitivity by 26%. However, no improvement in TB diagnosis occurred when LAM was associated with Xpert® MTB/RIF. Overall, LAM's accuracy was 80.5% and the positive and negative predictive values were 62.2% and 84.7%, respectively. Among the 14 LAM false positive tests, Non Tuberculous Mycobacteria (NTM) were isolated in three cases, eight patients were treated for TB and other three cases were not defined as TB cases.

Conclusions: LAM is a real point of care test that increased TB diagnosis in immunosuppressed HIV-infected patients when associated with smear microscopy but not with Xpert® MTB/RIF in Brazilian public network sites. Some of the LAM false positive cases were considered true TB cases and a cross reaction with NTM was detected. The LAM test should be used in settings where immunosuppressed HIV patients need rapid TB diagnosis.

PS45-893-27 Clinical review of laboratory diagnostic techniques of tuberculous peritonitis

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Background: Tuberculous peritonitis accounts for up to 12% of extrapulmonary tuberculosis, common in the developing world. Analyzing available diagnostic techniques for tuberculous peritonitis are urgently needed because the disease is often associated with delayed health-care seeking, leading to serious consequences.

Methods: The clinical features and laboratory examination results (immunological tests and peritoneal effusion tests) were collected from 89 patients with tuberculous peritonitis who were hospitalized in Shenyang Chest Hospital in China from January 2015 to June 2017. The information were retrospectively analyzed.

Results: The main clinical manifestations in 89 patients were fever (64/89, 71.9%), abdominal pain and distension (78/89, 87.6%), fatigue and night sweating (54/89, 60.7%). Patients with abdominal pain accounted for 60.7% (54/89), with ascites 50.6% (45/89) and with classic “doughy” 36.0% (32/89). The Rivalta test of ascites was positive in all 89 cases, and the results of their protein quantitation were >25g/L, the proportion of their lymphocytes was 80.0~100.0%. The white cell counts of celiac effusion were >0.5×10⁹/L in 81 cases; 75 patients had increased adenosine deaminase (ADA) level with ascitic fluid (cutoff value 36U/L). The positive rate of MGIT 960 culture with ascitic fluid was 28.1% (25/89) and that of AFB smear was 0.0% (0/89); GeneXpert MTB/RIF assay was performed in 33 ascitic fluid samples and zero was positive. Blood T-SPOT.TB was positive in 82 cases. Among the 89 cases, 25 ascitic fluid samples were tested for T-SPOT.TB and the positive rate was 100.0% (25/25).

Conclusions: The diagnosis of tuberculous peritonitis requires a high clinical index of suspicion and should be considered in the differential of ascites with a lymphocyte predominance; the sensitivity of MGIT 960 culture in ascitic fluid was low and GeneXpert assay is not suitable for application in peritoneal effusion specimens. Nearly 70% of cases were clinically diagnosed without microbiology proof, indicating the need for the development of other biomarkers.

PS45-894-27 Current approaches to the diagnosis of tuberculous pleuritis

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Background: The etiological diagnosis of tuberculous pleuritis remains to be difficult. The aim of this study was to evaluate the intensity of production of IFN- after specific stimulation.

Methods: 93 subjects with pleural effusion were enrolled prospectively. The basic group included 30 patients with tuberculous pleuritis (TP) aged from 26 to 59. The control group included 44 patients with non-tuberculous pleuritis (Non-TP) aged from 44 to 70. Induction of the synthesis IFN- by immunocompetent cells in pleural exudate was carried out by the recombinant protein CFP10-ESAT6 produced by the genetically modified cultures of *Escherichia coli* BL21(DE3)/pCFP-ESAT, solved in the isotonic sterile phosphatic buffer. The levels of IFN-gamma were measured using commercially available ELISA-kits.

Results: The basic levels of pleural fluids IFN-gamma (without stimulation) were significantly higher in TP group (median (25% - 75%)) - 95.2 pg/ml (0.2 - 248.5) compared to the Non-TP group - 0.0 pg/ml (0.0 - 2.9) (p=0.0000006). The IFN- antigen induced levels in TP group were significantly higher compared to the control group (median (25% - 75%)): 234.2 pg/ml (28.1 - 2007.7) and 0.0 (0.0 - 6.1) respectively (p=0.0000001). The introduction of *M. tuberculosis* antigens into the pleural fluids samples of TP group caused a significant (p=0.0027) increase of the IFN- levels compared to basic level, which were not observed in the Non-TP group. **Conclusions:** An evaluation of the antigen-induced level of IFN-gamma is more promising for the diagnosis of tuberculous pleurisy than an assessment of its basal level.

PS45-895-27 Parallel tests using culture, Xpert MTB/RIF and SAT-TB in sputum plus bronchial alveolar lavage fluid significantly increase diagnostic performance of smear-negative pulmonary tuberculosis

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Background: At present, tuberculosis is still a serious threat to human health. The diagnosis of pulmonary tuberculosis is still difficult, and the prominent feature is the lack of a highly sensitive and specific method.

To explore the diagnostic value of parallel experiments by culture, Xpert MTB/RIF, and SAT-TB for detection of MTB in sputum samples and bronchial alveolar lavage fluid (BALF) in patients with smear-negative pulmonary tuberculosis (PTB).

Methods: This study prospectively included 258 patients with smear-negative PTB from May 2, 2015 to December 31, 2016. The sputum specimens and BALF of all patients were detected by culture, Xpert MTB/RIF, and SAT-TB respectively.

Results: Overall, the sensitivity of single test in culture, Xpert MTB/RIF, and SAT-TB are lower (range: 0.2403-0.4186), and the sensitivity rates in BALF are significantly higher than that in sputum samples. There are lower agreements in the detection results between sputum samples and BALF ($p < 0.05$). Parallel tests model using culture, Xpert MTB/RIF, plus SAT-TB, or culture plus Xpert or culture plus SAT achieves higher sensitivities compared with single test ($p < 0.05$). However, the joint detection using sputum and BALF can further increase the sensitivity ($p < 0.05$). A total of 221 cases of PTB (85.65%) were confirmed by parallel tests using sputum and BALF samples.

Conclusions: The parallel tests using culture, Xpert MTB/RIF and SAT-TB in sputum plus BALF significantly increase diagnostic performance of smear-negative pulmonary tuberculosis, and it is worthy of clinical application.

PS45-896-27 Differential diagnosis of prostate tuberculosis

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Background: Diagnosis of urogenital tuberculosis (TB), especially on its early stages, is very difficult. Clinical features are non-specific and similar ones in chronic prostatitis (CP). So the base for early diagnosis is identification of *Mycobacterium tuberculosis* (Mtb) and specific pathomorphology in prostate biopsies.

Methods: A total of 83 patients (age from 36 to 72 years) with prostate TB (n=45) and chronic prostatitis (n=38) were included in study. Standard 6-12 cores prostate biopsies were done for all of them.

Results: Among the patients with prostate TB 66.7% had active TB of another localizations, and 8.9% were cured from pulmonary TB. Among CP patients 7.9% had active pulmonary TB, and 15.7% were cured from pulmonary TB. In prostate TB patients Mtb was found in ejaculate in 35.5% and twice rarely - in expressed prostatic secretion. In CP patients Mtb was not found at all. Clinical features (pain, frequency, urgency, erectile dysfunction) were similar in both groups. Leukospermia was detected with the same frequency in both groups

(39.5% vs. 41.4%), but hemospermia was detected significantly more frequent in patients with prostate TB (22.2% vs. 7.8%; $p < 0.05$). Ultrasound investigation showed large calcifications (28.8% vs. 7.9%; $p < 0.02$), hyperechogenic fibrosis (71.1 vs 47.4%; $p < 0.05$) and seminal vesicles lesion (17.7% vs. 2.6%; $p < 0.05$) more frequently in prostate TB patient. Pathomorphology of prostate biopsy confirmed TB in 20% of patients in the group of prostate TB.

Conclusions: The diagnostic of prostate TB is difficult and based on Mtb detection, pathomorphology, radiological examination and patient history (TB in another localizations in present or past). But in the absence of specific symptoms indirect sign, such as large calcifications, hyperechogenic fibrosis in prostate, seminal vesicles lesion and hemospermia must be taken into account.

PS45-897-27 Rapid detection of circulating Mycobacterium tuberculosis DNA for the diagnosis of abdominal tuberculosis

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Background: Abdominal tuberculosis (ATB) continues to pose a major diagnostic challenge for clinicians due to its nonspecific clinical presentation, variable anatomical location and lack of sensitive diagnostic tools. ATB contributes to 3% of all extra-pulmonary TB cases. Conventional diagnostic assays like smear and culture yield low sensitivity and in spite of the development of various molecular assays, no single test is adequate for ATB diagnosis.

In this study, we for the first time report the detection of circulating *Mycobacterium tuberculosis* DNA in ascitic fluid using a newly developed probe-based qPCR assay targeting the *devR* gene.

Methods: Sixty seven ascitic fluid samples were included in the study and processed for cytological, biochemical, microbiological and molecular assays. A composite reference standard (CRS) was formulated to categorize the patients into 'Definite ATB' (*M. tuberculosis* culture positive n=2), 'Probable ATB' (n=15), 'Possible ATB' (n=13) and 'Non-TB' category (n=37). The molecular assays included the novel circulating *M. tuberculosis* DNA probe-based qPCR assay targeting *devR* gene and Xpert MTB/RIF assay (Xpert). The diagnostic accuracy of the molecular assays was assessed using CRS as reference standard.

Results: Loss of weight, fever, positive mantoux and alcoholism were found to be strongly associated with ATB disease ($p < 0.05$). The novel circulating *M. tuberculosis* DNA-based assay had a sensitivity of ~65% (95% CI:56, 91) with 95% specificity (95% CI:81, 99) in 'Definite ATB' and 'Probable ATB' category collectively. The sensitivity of the developed assay increased to 80% (95% CI:61, 92) on addition of 'Possible ATB' patients in the evaluation of the assay. Xpert had a poor sensitivity of ~7% (95% CI: 0.82,22) with a 100% specificity (95% CI: 90.5,100).

Conclusions: We conclude that the circulating *M. tuberculosis* DNA probe-based assay is a rapid and accurate molecular test which provides direct evidence of *M.tuberculosis* etiology and might pave the way for improving the diagnosis of ATB.

PS45-898-27 Evaluation of the yield of histology to diagnose lymph node tuberculosis in Morocco, 2016-2017

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Background: Extrapulmonary tuberculosis (EPTB) frequency has been increasing worldwide over the last two decades. In Morocco, There proportion is high, 46% among all TB cases reported. Lymph node tuberculosis is the most common form of EPTB (37%). The diagnosis is mainly based on clinical signs and histopathology evidence according to the national tuberculosis program guidelines. The bacteriological confirmation is rarely established. This study aimed to evaluate the yield of histopathology exam to diagnosis of lymph node tuberculosis to update the guideline for its diagnosis.

Methods: This is a cross sectional prospective survey including patients with cervical lymph node enrolled from November 2016 to May 2017 in three regions of Morocco. Sensitivity, specificity, Positive Predictive Value (PPV) and Negative Predictive Value (NPV) of histology were calculated for each histopathological entities in presence of: i) granuloma with or without caseous necrosis and ii) granuloma with caseous necrosis, using Gold standard, which included culture and Gene-Xpert MTB/RIF. ² test used to compare proportions with confidence interval at 95%.

Results: A total of 262 patients were included in this study. Histology was positive for 174 (66.4%) patients, among them 84.0% have granuloma with caseous necrosis. Gene-Xpert MTB/RIF test was positive for 123 (47.3%) patients and culture was positive for 27 (10.3%) patients. Sensitivity, specificity, PPV and NPV of histolo-

gy were respectively 95.6%, 66.9%, 74.1% and 93.2% in presence of granuloma with or without caseous necrosis. The sensitivity, specificity, PPV and NPV of histology were respectively 84.4%, 74.8%, 78.1% and 81.9% in presence of granuloma with caseous necrosis. The granuloma with caseous necrosis increased significantly the PPV and specificity of histology ($p < 0.001$).

Conclusions: The granuloma with caseous necrosis increased histology yield for lymph nodes tuberculosis diagnosis. The finding suggests to maintain histopathology exam to diagnosis lymph node tuberculosis and to explore other techniques to improve its diagnosis.

PS45-899-27 Bacteriological examination for the diagnosis of tuberculous lymphadenitis: is it sufficient?

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Background: Extra-pulmonary tuberculosis (EPTB) accounts for, 20% of all TB cases. In most resource constraint settings diagnosis of EPTB depends on histological examination of biopsied specimen with little emphasis on bacteriological confirmation. Xpert MTB/Rif assay endorsed by WHO for diagnosis EPTB with advantage of short turnaround time over culture. Prospective study is performed to compare bacteriological versus histological diagnosis and evaluate usefulness of both in the diagnosis of TB.

Methods: Presumptive TB patients with enlarged lymph nodes were included. Excision biopsy was performed in all and lymph node was divided into two part, one part was put in normal saline and processed for culture (LJ and MGIT) and Xpert testing and other was fixed in formalin for histology examination.

Bacteriological diagnosis was based on positive results for culture and/ or Xpert (composite standard). Histological diagnosis suggestive of TB (SOTB) was based on any one or combination of histological features including epithelioid cells, Langhertn typhs giant cells and caseous necrosis.

Results: Excision biopsy specimen from 413 patient were tested. Among all tested 178 were bacteriological confirmed TB cases (B+) and 198 had histology suggestive of TB. Among B+cases, 124(69.7%) were diagnosed on Xpert. Of 54 case which were positive on culture only, 45(83.3%) were registered as TB cases based on histology examination by time culture results were reported. Against reference standard of B+EPTB, estimated sensitivity, specificity, PPV and NPV of histological diagnosis suggestive of TB (SOTB) was 83.7%, 79.1%, 75.3%, 86.5%.

Final Bacteriology diagnosis	Xpert (MTB) Results	Culture Result	Total	Histology Suggestive of TB	Histology NOT suggestive of TB
B+ve	Not Detected	Positive	50	43	7
B+ve	Not Available	Positive	4	2	2
B+ve	Positive	Positive	82	78	4
B+ve	Positive	Negative	39	25	14
B+ve	Positive	NTM	3	1	2
B-ve	Not Detected	Negative	225	48	177
B-ve	Not Available	Negative	8	0	8
B-ve	Not Detected	NTM	2	1	1
TOTAL			413	198	215

[Bacteriological versus histological examination results of Lymph nodes]

Conclusions: Using Xpert MTB/RIF, 70% of the B+ TB Lymph node were diagnosed rapidly. Histological features suggestive of TB was reported in 83.7% of the B+TB lymphnode and can guide in the rapid clinical diagnosis of EPTB for cases not diagnosed or tested on Xpert or culture.

PS46 See, hear, speak: the use of the media for tuberculosis

PS46-901-27 Overcoming TB stigma through cultural health beliefs with the edutainment of TB disease in West Sumatera, Indonesia

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Background and challenges to implementation: TB control problems are associated with a low level of awareness and knowledge of TB, mainly due to the high level of TB stigma in the community. Stigma TB, is usually observed among isolated communities, population with low education and low socio-economic status, many of whom are not reached by the health care system. Selected District in West Sumatera are remote in the earthquake-prone area have lower Human Development Index and TB coverage detection rates are also the lowest. Given that health decision-making is often a communal rather than an individual process in many most low-income countries, including Indonesia, community health channel through cultural approaches seem warranted.

Intervention or response: We identified the famous singer or traditional musicians in the village in selected district Solok, Padang and Padang Pariaman, provided them the information about TB. The singer composed the song

to include TB information at which they will talk about TB to improve awareness of signs and symptoms of TB and knowledge about TB available services and to encourage health-seeking behavior. We conducted cultural approach: performed a story-telling and singing of Saluang, Indang and Rabab about TB, where traditional music included 2 edutainment sessions with free traditional music and ethnic theatricals by the singer.

Results and lessons learnt: Our findings had suggested areas of intersection between a patient's health care and their cultural beliefs that need unique health communication channel in population to reduce stigma. Traditional music from Minang tribe, Saluang, Rabab and Indang were effective channel to increase knowledge and awareness to in the TB program and reduced stigma. It improved awareness of symptoms and reduces stigma and access to TB testing and treatment. We increased the case detection rate from 47% to 85%.

Conclusions and key recommendations: It is thought that community health through cultural approaches may have greater impact on TB control.

PS46-902-27 Encouraging an evidence-based narrative

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Background and challenges to implementation: The media plays a pivotal role in raising awareness and bringing attention to matters of public importance. In 2011 when India awoke to a drug resistant TB epidemic, evidence-based information was the need of the hour. The country's proactive media had the potential to be more than just reporters; they could be educators and drive changes in policy. But to harness this potential, there was a need for nuanced evidence-based information and interactions with credible voices. Furthermore, in a country where political news was always priority, health reporting and particularly, TB needed sustained rather than sporadic space.

Intervention or response: Global Health Strategies (GHS) initiated its media advocacy and training efforts in 2012. To help them ask pertinent questions, explore challenges and focus on solutions, we provided health journalists access to simple data and evidence needed to understand the issues facing the TB epidemic from different perspectives. Along with sensitization workshops and interactions with government, technical and community voices alike, we helped bridge the gap between science and storytelling. We also worked to build buy-in with the editors to prioritize health and TB stories.

Results and lessons learnt: Reporting on TB today has evolved from being sensational to more nuanced and analytical. Journalists are now aware about the different facets of TB and equipped with the tools to translate data into engaging stories and drive policy change.

Whether through coverage of the methanol shortage in the 'dry' state of Bihar, or the need for social support, balanced and evidence based reporting has successfully resulted in positive government action.

Conclusions and key recommendations: A well informed and sensitized media can build awareness and drive positive policy change.

PS46-903-27 Social media, mass media and health advocacy: cross-promotion of tuberculosis information to increase TB diagnosis and adherence to treatment in South Africa

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Background and challenges to implementation: Challenges with TB diagnosis and patient adherence to treatment undermine South Africa's efforts to achieve the 90-90-90-90 TB targets by 2022. Using mass media to saturate audiences with TB information, and social media to support retention in care by linking patients to health advocates in their communities shows promise. The USAID Tuberculosis South Africa Project utilised community radio interviews to raise visibility of TB, along with social media initiatives to increase audience engagement with TB messages and content.

Intervention or response: Between January and December 2017, project staff gave 20 radio interviews.

The project engaged social media influencers to increase discussions about TB on these platforms. Influencers are South Africans - often celebrities - with large followings on social media and interest in health advocacy.

Media consumers infected and affected by TB made contact via project social media pages seeking assistance to access treatment, and support with communicating their needs to health facility staff.

Results and lessons learnt: Radio interviews reached approximately 17 million listeners.

In Mangaung District, Free State Province alone, 216,000 listeners were reached via community radio. Enhanced communication contributed to 13,243 more people being screened for TB in public healthcare facilities there in March 2017 (112,936) than in February (99,693).

In March 2017 alone, ten influencers with a combined reach of 6.1 million followers on Twitter and Facebook were engaged to raise visibility of TB. 10.6 million impressions were achieved on Twitter. Facebook reached 62,019 people, with 5,717 engaging with content.

Conclusions and key recommendations: Cross-promotion of TB messages on social and mass media, paired with pragmatic health service delivery and advocacy at community level, has potential to contribute to increased uptake of TB diagnostics services and retention

in care, particularly among younger age-groups, who are documented avid consumers of social and mass media content.

PS46-904-27 Using community radio to improve active case finding for TB in an indigenous community: a case study from West Bengal, India

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Background and challenges to implementation: Santal, an Indigenous community based in Purulia district of West Bengal accord high importance to TB and the stigma associated with it. A community radio station (CR) run and managed by community conducted series of programmes on TB between April and September 2017 and this was followed by a formative research to evaluate the effectiveness of the messaging and to plan for future CR based campaigns.

Intervention or response: A two-pronged strategy was adopted i.e. narrowcasting (pre-recorded audio played in the villages) and broadcasting programmes through the CR covering 200 thousand people. A video was also prepared on TB and CR for Santal People. The narrowcasting sessions were followed by group discussions to know the feedback from participants.

Pre-recorded programmes prepared by the community people themselves followed the edutainment approach while live-phone in programmes were participated by local and government experts. Action research method was followed and baseline and end-line surveys conducted.

Results and lessons learnt: End-line data showed that above 80% of the respondents have identified that cough, cough more than one week and cough with blood are the symptoms for TB while above 60% of the respondents have comprehended correctly that TB is air borne disease. Above 80% of the respondents came to know that malnutrition can lead to TB; above 40% of the respondents have admitted that the persons with unhealthy practices, having tobacco, living with the TB patients can have TB. Over 80% of the respondents have admitted that measures like covering mouth while coughing and eating nutritious food can reduce the prevalence of TB. Over 80% of respondents know about DOTS.

Conclusions and key recommendations: Community radio backed with interpersonal outreach is an effective medium for TB education and improves identification of symptom, early reporting and reducing stigma in remote and marginal populations which have little access to mainstream media.

PS46-905-27 Let's talk about TB on radio, a demand creation strategy for TB services: evidence from the evaluation of TB radio jingle in Nigeria

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Background: Demand creation for TB services in Nigeria is a major concern, necessitating the production and placement of TB radio jingles in English and major Nigerian languages on selected radio stations in 21 intervention states.

Methods: Data used was from the Evaluation of TB Radio Jingle conducted for National TB and Leprosy Control Program (NTBLCP) in Nigeria, in December 2017 covering 180 Enumeration Areas and 18 Local Government Areas across 9 states. A cross sectional approach, with mixed research methodologies was adopted.

Results: A total of 3,238 (male: 51% and female: 49% were interviewed; 1,917 (67%) had access to radio at home with 69% (2,251) access to radio information using a combination of other electronic devices aside radio. Those who have heard of TB was 88% (2,858) from different sources of information. Of these, 944 (29%) have been exposed to TB information on radio preceding the survey. Significant effect from exposure to TB messages on radio was observed. From bivariate level of analysis, 94% ($p < 0.0001$) of those exposed believed that TB is curable. They expressed non-discriminatory attitudes to persons with TB; 100% ($p < 0.0001$), had a relatively high risk perception of TB; 72% ($p < 0.0001$). Also, 75% ($p < 0.0001$) had encouraged someone with a prolonged cough to go to a hospital for treatment, while 49% ($p < 0.0001$) had told someone that TB test is free. About a third (32%), had told someone to take prolonged cough very seriously ($p < 0.0001$). At multivariate level of analysis, those exposed are 72 times more likely to demonstrate good health seeking behavior than those who were not exposed (OR=1.72, CI: 1,176 - 2,519 $p < 0.001$).

Conclusions: Dissemination of TB messages on radio, influences demand for TB services, with the Nigerian population access to radio, the TB programme in Nigeria should strengthen and support this effective strategy.

PS46-906-27 Involving local celebrities as ambassadors for increased attention to TB: experiences from India

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Background and challenges to implementation: In India, celebrities - actors, sportspersons, artistes - are often involved as ambassadors for social issues. Their involvement draws greater attention to the issues they endorse and has the potential to trigger behavior change. The TB programme in India received a significant boost recently when the country's best-known actor became a TB ambassador.

Intervention or response: In a diverse, multi-lingual country, the involvement of local celebrities is essential. REACH identified and involved celebrities in Bihar, Odisha and Jharkhand as State TB Ambassadors. The ambassadors included a former world number 1 archer and a youth icon; a popular television actor; an internationally renowned sand artiste; a popular stand-up comedian and a well-respected musician. All ambassadors were identified with the consent of the respective State TB Offices. Communication materials featuring the ambassadors were developed and handed over to the state for dissemination. All ambassadors were engaged pro-bono.

Results and lessons learnt: 16 short films and 15 audio messages featuring ambassadors were developed. These highlighted many issues including basic symptoms, treatment adherence and issues related to stigma. In two states, the government bought air time for Rs. 1.5 million to disseminate the campaign. Posters featuring ambassadors were shared with all districts across the state. In Odisha, on World TB Day, an ambassador created sand-art on TB that was seen by several thousands of visitors to the local beach. In Bihar, the ambassador interacted with elected representatives to brainstorm solutions to the state's TB problems.

Conclusions and key recommendations: The involvement of celebrities and icons has resulted in the creation of communications materials that local audiences could identify with - featuring men and women who spoke their language, thus meeting the need for content in regional languages. This process also resulted in the timely utilization of the states' allocated budget for advocacy and communications.

PS46-907-27 Edutainment positively impacts the transfer of TB messages to high school students in Rehoboth, Namibia

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Background: Namibia is among the top ten countries with the highest per capita burden of Tuberculosis (TB), with a total of 9154 cases reported in 2016. Hardap region is one of the most affected, with a case notification rate of 648/100 000 in 2016. Age group 15-19 years contributed over 9% of the TB cases in Hardap since 2015. Reaching all age groups with key messages on TB remains a challenge. Edutainment is defined as technologies used to entertain with the purpose to educate while seeking to make education more attractive to young people and students. This presentation aims to assess the impact of edutainment in teaching TB messages in a local high school.

Methods: The Lucky Specials, a full-length feature film that educates viewers about TB, was screened at M&K Gertze High school in Rehoboth to students between the ages of 14-19 years, in order to confront them with the current social and scientific realities of TB. A 9-part pre-test and post-test assessment, designed to measure TB-related knowledge, attitudes and practices of the students, was administered to assess the impact of the intervention.

Results: 133 students participated. The mean score on the questionnaire increased from 5.4 in the pre-test to 8.0 in the post-test, and the difference was statistically significant ($p < 0.01$), using a t-test for paired samples.

Conclusions: The results suggest that edutainment may add value in teaching key messages on TB in high schools. The animated TB messages portrayed in the Lucky Specials were appreciated by the selected audience and Lucky Specials should be screened in all schools in Namibia. This assessment was done on a small scale but this type of intervention has the potential for bigger impact if rolled out all over Namibia.

PS46-908-27 Establishing a structured media engagement programme to improve reporting on TB in India

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Background and challenges to implementation: The news media, and newspapers in particular, remain a trusted source of health information in India. Improving the frequency and quality of reporting on TB can therefore give readers access to valuable and accurate

information on TB symptoms, diagnosis and treatment. **Intervention or response:** In 2010, REACH began engaging with journalists in India through a structured programme. At the core of this intervention was a fellowship programme for local language journalists, intended to improve their understanding of TB and encourage high-quality reporting on local TB issues. In addition, one national media fellowship was awarded each year to senior journalists, to explore one TB-related issue at the macro level. All Fellows attended capacity-building workshops and received ongoing support and mentorship through the fellowship period.

Results and lessons learnt: Over 8 years, 77 print journalists from 16 states wrote over 300 articles on TB in 10 languages. These were published in over 95 publications. 28 journalists received 32 awards for excellence in TB journalism. Over 140 journalists received regular information and updates on TB. 54% of Fellows continued to report on TB beyond the Fellowship period and 26% demonstrated interest in improving their capacity to report on TB. This intervention established and strengthened links between journalists and TB experts including researchers, doctors, health workers, local TB authorities and affected communities.

Conclusions and key recommendations: The structure of engagement created through this intervention has brought TB onto the radar of journalists and spurred their long-term interest in reporting on TB. The Fellowship programme has demonstrated the long-term impact of investing in building the capacity of local language media and dispelled the premise that TB is not newsworthy. Overall, this media engagement programme has demonstrated a highly replicable model for increased reporting on TB and other health issues, particularly in other high-burden countries where there is limited media reporting on TB.

PS46-909-27 Knowledge about tuberculosis and its impact on MCH care services among mothers in south Asia: results of a nation-wide cross-sectional household survey

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Background: The purpose of the present study to understand whether and what extent women know tuberculosis and aware of program over the past decades in Bangladesh, Pakistan, Nepal and India. Tuberculosis among women might be under-reported in developing countries. It has been supported by the results from several studies comparing active and passive case-finding strategies.

There are very few studies have been focused on issues. So, study aim to explore inequities in knowledge, attitudes and practices regarding tuberculosis and its association with maternal and child health services.

Methods: We analysed pooled data from the Demographic and Health Survey conducted between periods 1990 to 2016. Bivariate and multinomial logistic regression analyses are performed to find the correlates of correct knowledge of TB transmission. Correct knowledge about tuberculosis transmission use as a dependent variable and the explanatory variables are: socio-economic and demographic data.

Results: Knowledge about TB correctly reported by approximately range 6 to 8% of women, and is significantly associated with MCH services (ANC, FP, Institutional delivery, immunization), education and media by using multinomial logistic regression. The likelihood of correct knowledge is (Odds-3.9) higher with ≥ 11 years of education than with no/primary. A significantly higher (Odds-1.5) is found who have media exposure. Correct knowledge about TB transmission is very low among married women in Bangladesh. Factors such as education, media, household environment, could play an important role in improving knowledge about transmission among women in these all countries.

Conclusions: Knowledge about TB transmission in the general population of in these countries is very poor and misconceptions about transmission. Among traditional mass media, only the radio is associated with knowledge. TB control program should include more information about transmission in its IEC messages and alternative mass media such as radio could be considered when delivering messages about TB.

PS46-910-27 Applying integrated communication strategies to increase tuberculosis prevention knowledge and case identification capacities in West Coast District, Western Cape Province, South Africa

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Background and challenges to implementation: World Health Organization (2017) estimates that South Africa has 154,000 missing tuberculosis cases, and urges for intensified case-finding. Educating communities, and availing information about TB services in their areas is key to improving case notification and patient outcomes. In Cederberg Sub-District, Western Cape Province, where TB incidence was 837/100,000 in 2016, the USAID Tuberculosis South Africa Project designed an integrated communication strategy to improve case finding and treatment initiation.

Intervention or response: Stakeholders received 'Basic TB Management and Interpersonal Communication for Communities' training prior to conducting community

dialogues and door-to-door screening in Citrusdal and Clanwilliam in February and March 2018

Cross-promotion of messages on community radio and social media was done both to disseminate TB information and promote community TB screening activities.

Results and lessons learnt: Sixty-one stakeholders were trained to increase knowledge and capacities to identify TB symptoms, refer individuals to health facilities, and speak about TB with others. 770 people received individualised TB information verbally and in pamphlets. Of these, 416 were screened for TB, with 66 presumptive cases identified. Thirty-one were tested at their local health facility. Two tested positive for TB and were initiated on appropriate treatment. One contact under five years-old was initiated on Isoniazid Preventive Therapy. Two interviews were broadcast on a local community radio station with listenership of 40,000. Information was shared with 2,226 Facebook and Twitter followers generating conversations; notably about inadequate knowledge surrounding TB diagnosis and treatment, and challenges adhering to treatment because of side effects.

Conclusions and key recommendations: These integrated communications strategies were useful in disseminating personalised information about TB, in screening people for TB, and engaging people in TB care. Despite the relatively low yield, these training and communication strategies are important to improving quality and perception of TB care. Communication aimed at reducing TB stigma in these communities will be prioritised in future efforts.

PS46-911-27 Do the social media sites of India's top political leaders vouch for commitment to end TB by 2025?

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Background: WHO's ENDTB strategy sets 90% reduction in TB epidemic by 2035 and SDG aims that to 80% by 2030. On the contrary, India's 2017-25 National Strategic Plan for TB and commitment in the Parliament target to EndTB by 2025 much ahead of 2030/35. During 2017, India rolled out - daily drug regimen, universal DST, enhanced molecular diagnostic techniques (CB-NAAT), Active Case Finding (ACF) and nutrition support incentives to TB patients. Leaders interface with public through social network on an issue and this paper aims to find out the rise or fall of political will for TB by top leaders.

Methods: Leaders were classified into two categories-National & State. At national level tweets of Prime Minister (PM), Health Minister (HM) and Ministry of Health & Family Welfare (MoHFW) reviewed during Jan-March 2017 and that of 5 Chief Ministers (CM)

- Haryana, Odisha, Maharastra, Kerala & Madhya Pradesh from 5 regions - North, East, West, South and Central India respectively at the state level. Tweets were categorized into TB & Non-TB health issues. Under TB, those were studied further on HIV-TB, meetings, ENDTB plan, drugs, diagnosis, notification, Partner and ACF.

Results: TB was found adequate space with 76 tweets on issues of HIV-TB(4), meetings(45), ENDTB plan(18), Drugs(2), Diagnosis(3), Notification(1), Partner(1) and ACF(2) of HM & MoHFW. Out of ~1800 tweets of PM, TB had 2 and a special mention in national broadcast on radio. PM has taken TB as one of three key health issues of India for periodic review. Out of 5 CMs all of them found showing their commitment to End TB by 2025 through their social interactions.

Conclusions: Trend of social media along with policy and programmatic actions by top leaders run in tandem to END TB by 2025. It still needs to penetrate into the ancillary domains of other ministries and all law makers of the country.

PS46-912-27 Social media application facilitates fast treatment initiation among drug-resistant TB patients: Cambodia experience

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Background and challenges to implementation: Cambodia has introduced Bedaquiline (Bdq) and the shorter treatment regimen (STR) for multidrug-resistant tuberculosis (MDR-TB) in late 2017, and 32 patients have been enrolled on the STR and six patients on Bdq-containing regimens coming from various parts of the country. Patient condition, consent, and test results need to be relayed from one responsible staff to another, and entails waiting time for patients. For contribute to high quality treatment and care of patients, the national TB program has implemented better communication tools among staff managing MDR-TB.

Intervention or response: The Cambodian National Center for Tuberculosis and Leprosy Control (CENAT) uses the Facebook (FB) Messenger application on the mobile device utilizing features of instant sending of messages from central level to provincial treatment facilities, from laboratories to managing MDR-TB staff, and vice versa.

Members of the messenger group called “MDR-TB Network” include CENAT and laboratory staff, implementing NGO (Cambodia Health Committee) medical coordinators, provincial TB supervisors, and facility

staff. They do person-to-person or group chats, make audio and video calls for case discussions allowing instant sharing of patient updates, test results, images and screenshots of chest films, electrocardiogram tracings, etc.

Results and lessons learnt: Using FB messenger is among the main reasons for the fast empiric treatment initiation from initial consultation with an average of 4.5 days noted in at least three provinces implementing Bdq and the STR. Health care providers value and consider the network as a tool to provide prompt technical assistance, particularly on complicated cases.

Conclusions and key recommendations: Digital health approaches through a social media application bridges the distance among DR-TB providers, and results in prompt service delivery, reducing patient waiting time and avoiding delay in treatment initiation, thereby potentially increasing chances of cure and preventing transmission. Further assessment is needed to study the impact of this approach in patient outcomes.

PS47 Found and reported: but what tuberculosis treatment outcome

PS47-913-27 *M. africanum* (MTBc Lineage 6) has worse treatment outcome than *M. tuberculosis sensu stricto* (Lineage 4)

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Background: To determine the rate of smear conversion for different *M. tuberculosis* lineages using classical and vital staining microscopy techniques in assessing treatment response of new pulmonary tuberculosis patients in Bamako, Mali.

Methods: Between February 2015 and March 2018, we conducted a prospective cohort study of smear positive pulmonary tuberculosis patients in Bamako. Confirmed *Mycobacterium tuberculosis* complex (MTBc) isolates underwent genotyping by spoligotyping to allow for lineage classification. Patients were followed at 1-month (M), 2M and 5M with Auramine (AR) and Fluorescein di-acetate (FDA) vital staining microscopy to measure smear conversion. Good treatment outcome was defined as AR smear conversion at 5M. Patients with Xpert defined RR were excluded from analysis.

Results: Nine hundred and fifty patients completed first line standard therapy (category one) and had an isolate available for typing. Fourteen (1.5%) of patients were excluded based on RR detected at 2 or 5 months. The prevalence of HIV coinfection was 9.4%, and 72.5% of all patients were male. The most widely represented lineage was the modern Euro-American (lineage 4, 55.5%), followed by lineage 6 (*M. africanum* type 2, 20.5%). Ancestral lineages combined (L1, L5 and L6, plus *M. bovis* (0.8%)) amounted to 26.7%, and were associated with HIV infection relative to L4 (OR (95% CI); 0.55(0.32-0.96)). The smear conversion rate was greater for lineage 4 compared to lineage 6 in both techniques at all time points, (OR (95%CI); AR 1.45(1.05-2.0) and FDA 1.42 (0.98-2.07)). Indeed, treatment outcome was better for lineage 4 patients compared to those infected with lineage 6 (OR (95% CI); 1.42 (1.04-1.94)).

Conclusions: All six major human lineages identified outside of Ethiopia are found in Bamako, with a substantial proportion of ancestral lineages. We found that patients diseased with lineage 4 convert earlier than those in genotype lineage 6.

Keywords: Smear conversion, MTB lineages, Bamako

PS47-914-27 Disparities in tuberculosis treatment outcomes between rural and urban populations in Zambia

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Background: The burden of tuberculosis (TB) is higher in urban than rural settings due to overcrowding, high HIV prevalence and occupational transmission. The effectiveness of TB control in rural sub-Saharan Africa especially in countries where HIV prevalence is high is unknown. We evaluated the difference in anti-TB treatment outcomes between urban and rural populations and risk factors for unfavorable treatment outcomes.

Methods: In a retrospective observational study of new TB patients who were treated for TB between 2006 - 2013, we evaluated associations between location of treatment and treatment outcome using mixed effects logistic regression.

Results: We analyzed data for 21,057 new TB cases, of whom 65% attended urban health facilities. Fifty-four percent were male and mean age was 33 years (SD; 17). 11,539 (47%) were co-infected with HIV and 88% of these initiated cART. Unfavorable anti-TB treatment outcomes occurred in 2,617 (12%) patients, of whom 41% were rural. Unfavorable outcomes were due to death (41%), lost to follow up (36%) and treatment

failure (23%). Location was not associated with death (adjusted OR: 1.1; 95% CI; 0.8 1.5). Patients in rural locations were more likely to fail treatment and be lost to follow up (adjusted OR 1.28; 95% CI 1.1 1.8). Females had a 33% reduced chance of failure and loss to follow up (adjusted OR 0.67; 95% 0.5 0.7). Patients who were initiated on anti-TB treatment 14 days or more after registration had a 60% higher chance of death compared to those initiated within 14 days of registration (adjusted OR 1.6; 95% CI 1.3 2.1).

Conclusions: TB disease patients in rural locations have higher unfavorable treatment outcomes than those in urban locations. Therefore, TB control programs must develop specific strategies to address the challenges of TB treatment access and quality of care in rural areas.

PS47-915-27 Treatment outcomes of tuberculosis patients seeking care in the private sector in India

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Background: Of the estimated 2.8 million incident TB cases in India, ~1.5 million are diagnosed and treated each year under the government's Revised National TB Control programme (RNTCP). Remaining patients either go undiagnosed or seek treatment in private sector. While RNTCP routinely records and reports treatment outcomes of all TB patients it registers, there is limited information on the treatment outcomes of patients treated in private sector. The Global Fund supported Project Axshya implemented interventions in 40 urban cities in India to engage private qualified practitioners for TB notification.

Methods: A prospective study during the period April 2016-December 2017 was implemented to document overall disease burden and treatment outcomes in private sector. Private practitioners were mapped, sensitized and engaged for TB notification by the project. Treatment outcomes were assessed for patients who completed at least 9 months of anti-TB treatment. Variables like age, sex, type of TB, treatment initiation date etc. were collected and analysed.

Results: Overall 51,429 cases were notified during the study period. The demographic profile of 49,782 patients was available. 60% were male, 90% were new TB cases, 78% had pulmonary TB, ~1% were drug-resistant and ~7% were pediatrics. Majority were diagnosed clinically. Treatment outcomes were available for 3934 patients. Outcomes were obtained from the practitioner or patient. 58% completed their treatment and 37% were lost to follow up, about 2% died and 1% failed treatment (Table 1).

Conclusions: Large proportion of TB patients were notified through systematic engagement with the private sector. Nearly 60% completed treatment but more than 30% were lost to follow up. Due to lack of follow-up mechanisms, it is difficult to trace patients, ensure treatment completion and document outcomes in the private sector. Private practitioners need to ensure that their patients complete the prescribed treatment and provide treatment adherence support to patients for better outcomes.

Variable		N	%
Age	<15years	167	4
	15-44years	2308	59
	>44years	1235	31
Gender	Not recorded	230	6
	Male	2500	64
	Female	1430	36
	Not recorded	4	0
Type of TB	Pulmonary	3049	78
	Extra-pulmonary	872	22
	New TB	3827	97
	Retreatment TB	94	2
	Not recorded	11	0
Microbiological confirmation for diagnosis	Yes	812	21
	No	2410	61
	Not available	691	18
Treatment Outcomes	Treatment completed	2261	58
	Loss to follow up	1463	37
	Switched providers	69	2
	Died	85	2
	Treatment failed	56	1
	Total	3934	

[Table 1. Demographic and clinical profile of TB patients and their treatment outcomes notified from urban cities under Project Axshya]

PS47-916-27 Predictors of relapse among people with smear-positive pulmonary tuberculosis disease in Iraq

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Background: Relapse constitutes a burden on people with tuberculosis (TB) and the health system due to the need for a longer course of treatment and the increased risk for developing drug resistance.

This study aimed at finding factors predicting relapse and the rate of relapse during the first 18 months following successful treatment of sputum positive pulmonary TB patients.

Methods: This longitudinal study followed for 18 months people who were enrolled in the national drug resistance survey 2013-2014 and were successfully treat-

ed for smear positive pulmonary TB. The outcome was developing relapse. Age and sex adjusted logistic regression used to estimated predictors of relapse.

Results: The study followed 862 persons (ex-patients). Twenty one patients developed relapse during this cohort follow up with a relapse rate of 2.4% (1.6%-3.8%). Majority (90.5%) of relapse events occurred in the first nine months after treatment and a peak (five events of relapse) observed at month eight after treatment. Last event of relapse was observed at month 15 after treatment completion. Significant predictors for TB relapse according to this study were previous history of imprisonment, OR= 3.84 (1.24-11.87) and previous treatment for TB, OR= 2.63 (1.09-6.92). Other studied factors (e.g. sex, age, marital status, occupation, BMI, family size, residence, education, distance to health care facility, job, smoking, etc) were not significantly predicting relapse of TB disease according to this study.

Conclusions: Imprisonment and retreatment are predictors for TB relapse.

PS47-917-27 TB treatment outcomes among recurrent TB patients in Zambia

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Background: Recurrent TB comprise between 13 - 20% of cases notified globally. Understanding the magnitude of recurrent TB and its treatment outcomes is critical because recurrent TB cases are at increased risk of Multi-Drug Resistant TB. We examined the prevalence of recurrent TB among TB cases and compared the risk of unfavorable treatment outcomes between rural and urban settings.

Methods: We conducted a multicenter retrospective review of TB program data routinely collected between 2006 - 2013 in a setting with a high prevalence of both HIV and TB. To assess for associations between explanatory and outcome variables we used binomial logistic regression. The primary outcome was death.

Results: Of the 25,533 TB cases 3,566(13.9%) were recurrent TB cases. The prevalence of recurrent TB cases was 15.3% in urban and 11.3% in rural areas among all TB cases. Fifty-seven percent were male and median age was 36.3 (S.D: 14.8). The causes of recurrent TB were relapse (77%), loss to follow up (1%), failure (1%) and other (21%). In urban areas 66.7% of recurrent TB cases were HIV positive and 46.6% HIV positive in the rural. For treatment outcomes 7.5% were cured, 80.9% completed treatment, 5.5% died, 2.9% lost to follow, 3.2%

failed treatment. In both the univariable and multivariable analysis rural area was associated with death (Adjusted OR:1.7; 95% CI: 1.0 - 2.7). Males had 40% reduction in the odds of death (adjusted OR 0.6; 95% CI: 0.4 - 1.0). Among cases with HIV those not initiated on cART were twice likely to die (adjusted OR: 2.2; 95% CI: 1.2 - 3.1).

Conclusions: Recurrent TB was high in both rural and urban with rural areas having worse treatment outcomes. A well-organized patient monitoring system adapted to each setting such as effectively administered DOTS can help early detection of recurrent cases and improve case management.

PS47-918-27 Predictive risk model of failure in pulmonary tuberculosis treatment in HIV co-infected patients in Portugal

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Background: In Portugal, like in other low incidence countries, Tuberculosis (TB) tend to concentrate in groups at higher risk of becoming ill, such as Human Immunodeficiency Virus (HIV) infected patients. TB control in this group, particularly of pulmonary cases (PTB), is crucial, as increased rates of treatment failure are more likely.

This study aims to develop a predictive risk model of treatment failure for PTB-HIV co-infected cases.

Methods: PTB cases older than 15 years, notified in the Portuguese TB surveillance database (SVIG-TB), from 2000 to 2012 in the Continent, were analyzed and stratified by TB-HIV co-infection.

PTB treatment failure included the WHO categories ("failure", "default", "death", "transferred out") and predictors studied were sociodemographic, behavioral, disease-related and treatment-related factors.

Statistical analysis was based on binary logistic regression models. A predicting multivariate risk model of failure was carefully developed and assessed and turned into a nomogram.

Data concerning the identification of patients were anonymized.

Results: TB-HIV co-infection prevalence was 17.6%. Treatment failure rate in PTB-HIV co-infected cases was 29.6%, thus five times greater than in non co-infected (6.5%, $p < 0.001$).

Statistically significant crude OR estimated for predictors were: IV drug users (OR=1,79; IC95%: 1,51-2,13), retreatment (OR=1,73; IC95%: 1,42-2,10), community residence (OR=1,45; IC95%: 1,13-1,87), homeless (OR=1,66; IC95%: 1,21-2,26)

The independent failure factors for TB-HIV co-infected patients found in multivariate analysis were: IV drugs users (OR=2.17; 95% CI: 1.45-3.26), homeless (OR=2.99; 95% CI: 1.10-8.11) and retreatment cases (OR=1.67; 95% CI: 1.10-2.54).

Conclusions: Treatment success rate in PTB-HIV co-infected cases is lower than the 85% WHO minimum threshold.

Treatment failure is much more severe in the sub-group of HIV co-infected patients. Such result shows the need for a stronger, selective commitment of the National Program to counteract it in this sub-group, taking advantage of the now identified predictors.

PS47-919-27 Facteurs associés à l'abandon du traitement antituberculeux à Douala, Cameroun

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Background: L'émergence des souches de bacille de Koch résistants au antituberculeux constitue en défi en matière de lutte antituberculeuse. L'abandon du traitement en constitue un déterminant.

L'objectif de ce travail était de déterminer les facteurs associés à l'abandon du traitement antituberculeux à Douala.

Methods: Nous avons mené une étude cohorte rétrospective du 01 Janvier 2014 au 31 Décembre 2016 à partir du registres et des fiches de suivi du traitement antituberculeux dans 23 centres de traitement antituberculeux. Les variables étudiées étaient l'âge, le sexe, la forme clinique de la tuberculose, l'examen des crachats à la fin du deuxième mois, le statut VIH et le traitement antirétroviral ainsi que la prophylaxie au cotimoxazole pour les patients VIH positifs.

La recherche des facteurs associés à l'abandon du traitement antituberculeux ab été faite grâce à un modèle de régression logistique.

Results: Parmi les 11596 patients inclus dans cette étude, 6578 (56,7%) étaient de sexe masculin. L'âge moyen des patients était de $35,5 \pm 15$ ans. La tuberculose pulmonaire à microscopie positive était la forme clinique la plus fréquente avec 6718 patients soit 57,9%. Les nouveaux cas de tuberculose représentaient 88,5% de la population d'étude tandis que la séroprévalence de l'infection à VIH était de 33,1%. Au cours du traitement, 2055 étaient perdus de vue soit une prévalence de 17,7%. La tuberculose pulmonaire à microscopie négative [odds ratio (OR) 1,73], la tuberculose extrapulmonaire (OR 2,22) et la non mise sous traitement antirétroviral (OR 1,38) étaient les facteurs indépendamment associés à l'abandon du traitement antituberculeux.

Conclusions: Le taux d'abandon du traitement antituberculeux reste élevé dans la ville de Douala. Un renforcement de l'éducation thérapeutique des patients tuberculeux sous traitement et la prise en charge adéquate de l'infection à VIH permettraient de réduire l'incidence de l'abandon du traitement.

PS47-920-27 Performance measurement dashboard for data-driven management of a TB control project in Indonesia

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Background and challenges to implementation: Challenge TB is a 5-year KNCV-led USAID funded global project supporting the National TB Program of Indonesia with implementation of the national strategic plan for TB. Performance monitoring throughout the project is important to keep the implementation on track and meet the expected outcomes.

In order to strengthen data-driven decision making in the project, a dashboard was developed to provide real time insight in the performance of each district, and progress towards the successful implementation of strategic interventions.

Intervention or response: The CTB project defined 36 indicators based on the program specific priority interventions, divided in two sets. First, the system indicators: engagement of all providers in TB services, TB-HIV collaboration, expansion of electronic reporting at primary care level, expansion of TB control in prisons, sputum smear quality assurance, GeneXpert access and utilization, sample transportation networks, district TB budget allocation, and PMDT scale-up. Second, the patient outcome indicators (aligned with NTP standards): TB-HIV, childhood TB, TB-DM, TB case notification, LTBI management, SL-LPA testing, MDR-TB diagnosis and treatment enrollment, treatment success rates, etc. The progress of indicator values towards quality thresholds are monitored quarterly using color coding: Red (< 50% target achieved), Orange (≥50% - < 75% target achieved), Yellow (≥75% - < 100% target achieved) and Green (≥100% target achieved).

Results and lessons learnt: Between Oct 2016 and Sep 2017 the overall performance increased from 66% to 79%. The dashboard is able to show the dynamics in performance on each of the indicators. A major barrier for using the dashboard is the slow reporting to the current surveillance system, hampering "real time" feedback on interventions and progress, which is mitigated through training and on the job support.

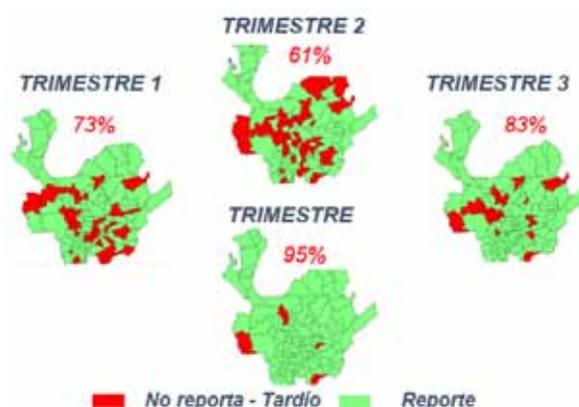
Conclusions and key recommendations: The dashboard is a useful instrument to keep track of performance and progress in the districts. The indicators provided useful information in each district for prioritization of interventions.

PS47-921-27 Innovation in information systems processes: generating impact in decision making in Antioquia, 2017

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Background and challenges to implementation: In the department of Antioquia for the year 2016 2,643 cases of tuberculosis were reported in all forms, with an incidence of 40 cases per 100,000 inhabitants reported by the Public Health Surveillance system, the percentage of success of the treatment is 75% for the 2015 and 70% for 2016, information reported through the tuberculosis control program information system, evidencing under-reporting and poor quality of the reported information. For 2017, the strengthening of the management of the system in the department of Antioquia was prioritized to improve decision making and impact on the results of the indicators with opportunity and data quality.

Intervention or response: To increase the registry, improve the opportunity and the quality of the data, the processes in information systems management were reviewed, identifying gaps that were intervened from the characterization of the 125 municipalities that are part of the report, making the revision and the follow-up of the records sent quarterly, feedback from found and adjusted findings, workshops were held in 9 regions of the department in management of information systems, monitoring and evaluation of the tuberculosis program, generating a positive impact.



[Map of the report of the Tuberculosis Control Program by municipalities of Antioquia, year 2017.]

Results and lessons learnt: In 2017, the management of the reports reported by the municipalities was measured quarterly, starting in the first quarter with 73%, second

quarter 61%, third quarter 83% and in the fourth quarter 95%, showing that the strategies used impacted positively in the tuberculosis program information.

Conclusions and key recommendations: It contributed to improve the register with quality and opportunity for decision-making at the departmental level, obtain cohorts of patients with greater precision in less time, identify institutions that have difficulties in complying with the indicators to be timely intervened. This activity can be socialized in a meeting with the national level in order for other departments to adopt the strategies implemented.

PS48 Understanding drug-resistant tuberculosis

PS48-922-27 Genotyping of drug-resistant tuberculosis strains for isoniazid resistance using first-line line probe assay in Karachi, Pakistan

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Background: The presence of *KatG* and *InhA* mutations determine isoniazid (INH) susceptibility in tuberculosis (TB) patients. Understanding the prevalence of these mutations may provide insight into whether high-dose INH or ethionamide (Eto) are viable options for drug-resistant (DR-) TB patients. Data describing these mutations have not previously been reported in Pakistan. We aim to describe the prevalence of *KatG* and *InhA* mutations, as well as their association with previous INH treatment in Karachi, Pakistan.

Methods: This is a descriptive study of consecutive TB patients with isolates resistant to isoniazid from two health centers (January-November 2017). First-line Line Probe Assay (LPA) was performed through GenoType MTBDRplus v2. We report frequency of patient characteristics and resistance patterns, and prevalence of the *KatG* and *InhA* mutations, including prevalence within those with Eto resistance and with prior INH use.

Results: Ninety-six individuals met eligibility criteria with a mean age of 29.4 (SD: 13.6), 44 (45.8%) were male, and 93 (96.9%) had pulmonary TB. Resistance testing identified 77 (80.2%) had MDR-TB, 10 (10.4%) had INH mono-resistance, and 5 (5.2%) had XDR-TB. LPA identified 72 (75.0%) with *KatG* mutation, 16

(16.7%) with *InhA* mutation, and 1 (1.0%) with both mutations. Of the 58 (74.4%) individuals who reported previous INH use, 48 (82.8%) had *KatG* mutation while 6 (10.3%) had *InhA* mutation. Of the 17 (17.1%) with Eto resistance, 11 (64.7%) had *KatG* mutation while 6 (35.3%) had *InhA* mutation.

Conclusions: Increased use of LPA in Pakistan may identify subgroups at high-risk of *KatG* and/or *InhA* mutation, for whom accelerated decisions regarding use of Eto or high-dose INH for DR-TB treatment may lead to more effective regimens.

PS48-923-27 Trend of multidrug and fluoroquinolone resistance in Mycobacterium tuberculosis isolates from 2010 to 2014 in South Korea

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Background: This study was conducted to evaluate the recent prevalence and trend of anti-tuberculosis (TB) drug resistance with a focus on multidrug-resistance (MDR) and fluoroquinolone resistance in South Korea. **Methods:** We retrospectively reviewed the drug susceptibility testing results of culture-confirmed *Mycobacterium tuberculosis* isolates collected from 2010 to 2014 at seven tertiary hospitals in South Korea.

Results: A total of 5,599 cases were included; 4,927 (88.0%) were new cases and 672 (12.0%) were previously treated cases. The MDR rate has significantly decreased from 6.0% in 2010 to 3.0% in 2014 among new cases, and from 28.6% in 2010 to 18.4% in 2014 among previously treated cases ($P < 0.001$ and $P = 0.027$, respectively). The resistance rate to any fluoroquinolone was 0.8% (43/5221) in non-MDR-TB patients, as compared to 26.2% (99/378) in MDR-TB patients ($P < 0.001$). There was no significant change in the trend of fluoroquinolone resistance among both non-MDR-TB and MDR-TB patients. Among the 43 non-MDR-TB patients with fluoroquinolone resistance, 38 (88.4%) had fluoroquinolone mono-resistant isolates.

Conclusions: The prevalence of MDR-TB has significantly decreased from 2010 to 2014. The prevalence of fluoroquinolone resistance among non-MDR-TB patients was low, but the existence of fluoroquinolone mono-resistant TB may be a warning on the widespread use of fluoroquinolone in the community.

PS48-925-27 MDR/XDR-TB strain mobility in South Africa

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Background: Klopper et al. (2018) recently described a group of MDR/XDR *M. tuberculosis* (*Mtb*) strains (AA1SA), only seen in South Africa. Closer investigation showed that the group could be separated into several strain families, or clusters. These endemic clusters are the ideal subject to study country-wide strain mobility because their distribution is not confounded by immigration from elsewhere.

Methods: We sequenced the complete genomes of 200 *Mtb* strains associated with AA1SA tuberculosis episodes from the Eastern Cape (ECP), Free State, Gauteng and Western Cape (WCP) provinces and studied their genetic history using phylogenetic methods.

Results: Our results show that MDR/XDR AA1SA strains are particularly abundant in the ECP and WCP. Rare basal strains, with fewer DR conferring mutations, can also be found elsewhere and have likely been around since 1960. The MDR/XDR strains cluster in two subclades (A1 and B), that show notably distinct distributions and histories. Sub-clade A1 is almost exclusively found in the WCP, where it rapidly established itself as a result of two or three additional DR conferring mutations. Sub-clade A migrated to the ECP on rare occasions, but without establishing itself there. Sub-clade B differs from A1 by 4 DR conferring mutations, but matches in phenotypic DR profiles. Sub-clade B appears more mobile and able to establish itself, originating in the ECP but on multiple occasions expanding into the WCP and establishing itself there as a result of local transmission. Sub-clade B also appears in other provinces but has so far failed to establish itself there for reasons unknown.

Conclusions: Our research reveals that MDR/XDR strain families show notably varied within-country geographic mobility, despite matching phenotypic DR profiles. Further research is required to identify the driving forces behind this mobility. We recommend improved genetic monitoring of strain mobility to better anticipate, control and prevent the geographical expansion of MDR/XDR tuberculosis.

PS48-926-27 Updated TB drug resistance in Japan, 2012-2013

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Background: Ryoken TB consortium has conducted 14 anti-tuberculosis drug resistance surveys (DRS) since 1952 for every 2-5 years. This is the 15th DRS conducted in 2012-2013 to provide the updated TB drug resistance situation in Japan.

Methods: Ryoken is a TB research consortium composed of 141 hospitals. The participation was voluntary, and 48 facilities contributed for data collection in this study. The quality assured anti-TB drug susceptibility testing (DST) data was collected from those hospital laboratories through 2012-2013. The treatment history information was collected from national registration system, and matched with laboratory data for analyses.

Results: A total of 8,681 DST data sets was collected. Due to the data security policy of each local government, only 2,560 patients (29.5%) were analysed for treatment history. The combined resistances of isoniazid (INH) and rifampicin (RIF) were 5.3% and 1.6%, respectively (n=8,681). A total of 107 multidrug-resistant (MDR; 1.2%) and 13 extensively drug resistant (XDR; 0.1%) *M. tuberculosis* was identified. Just as limited information, the INH and RIF resistant cases among new and previously-treated patients were 5.2%/21.1% and 1.6%/12.7% in analysed 2,560 patients. The initial INH resistance showed significant increase compared to the data in 2007 (Ryoken. IJTLD 2015). A total of 99 MDR-TB was analysed separately for second-line drugs, and confirmed 23 XDR-TB strains. So the XDR-TB among MDR-TB in this period was 23.2%. the resistance against levofloxacin and pyrazinamide was 3.0% and 2.1% (combined resistance, n=8,681).

Conclusions: The 15th Ryoken DRS was conducted in 2012-2013. The combined data indicated increasing trend of drug resistance in major for drugs (INH, RIF, streptomycin and ethambutol). It also showed the increasing trend of M/XDR-TB in Japan. Japan used to show decreasing trend of anti-TB drug resistances until 2007, though the resurgence of drug resistant TB is anticipated.

PS48-927-27 Prevalence of MDR-TB in Indonesia: results from the first national anti-tuberculosis drug resistance survey

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Background: The first national anti-tuberculosis (TB) drug resistance survey was conducted in Indonesia between February 2017 and March 2018 to determine the prevalence of resistance to all first- and second-line drugs used for the treatment of TB in the country.

Methods: Subjects with sputum smear-positive pulmonary TB were enrolled from 70 health facilities distributed in 40 districts throughout the country. Survey sites were selected using a probability proportion to size approach. In addition to smear microscopy all cases underwent Xpert MTB/RIF testing, and those found positive to TB received culture and drug susceptibility testing using MGIT960 technology. Whole genome sequencing is also being conducted on all cases with rifampicin resistance, all previously treated cases rifampicin-susceptible TB and 35% of new cases with rifampicin-susceptible TB.

Results: A total of 3200 sputum smear-positive TB patients were enrolled, and 2,603 included in the survey, including 2,123 new and 480 previously treated TB cases. The prevalence of cases with rifampicin resistance was 2.4% (95%CI 1.5 - 3.6%) among new cases and 14.6% (95%CI 9.6-21.7%) among previously treated cases. The prevalence of multidrug-resistant TB (MDR-TB) cases was 1.3% (95%CI 0.7-2.2%) in new cases and 11.4% (95%CI 6.8-18.4%) in previously treated cases. Among 74 cases diagnosed with MDR-TB, 13 cases had pre-extensively drug resistant TB (preXDR -TB) and four cases had XDR-TB.

Conclusions: The first national anti-TB drug resistance survey in Indonesia showed a prevalence of MDR-TB in line with the findings of similar surveys conducted in other countries of the region. Detection and treatment of MDR-TB should be prioritized to ensure low transmission of MDR-TB in the community and all TB cases complete standardized TB treatment. Results of whole genome sequencing are awaited and will provide information on levels of resistance to pyrazinamide, fluoroquinolones and aminoglycosides which will be critical for the design of future treatment regimens in Indonesia.

PS48-928-27 Genetic diversity of multidrug-resistant Mycobacterium tuberculosis Central Asian Strain isolates from Nepal and comparison with neighboring countries

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Background: Multi-drug resistant Tuberculosis (MDR-TB) is an emerging threat for successful TB control in Indian subcontinent region. Central Asian strain (CAS) family has been reported as one of the dominant families contributing to MDR-TB in South Asia including Nepal, India and Pakistan. The aim of this study was to better understand the genetic characteristics of MDR-TB CAS family isolates circulating in Nepal, as well as in neighboring countries.

Methods: A total of 145 MDR-TB CAS family isolates collected in Nepal from 2008 to 2013 were analyzed by spoligotyping and mycobacterial interspersed repetitive units-variable number of tandem repeats (MIRU-VNTR) analysis. We also compared these data with published data from India and Pakistan to investigate possible epidemiological link through construction of Minimum spanning tree (MST).

Results: Spoligotyping analysis exhibited CAS1_Delhi SIT26 (n=60) was the predominant lineage among MDR-TB CAS family in all three countries. However, by combining two genotyping methods, spoligotyping and MIRU-VNTR, 60 isolates were further discriminated into 49 different types and 5 clusters. These clusters composed of 14 isolates with clustering rate (23.3%), which suggesting a possible ongoing transmissions.

Conclusions: Based on MST data from neighboring countries, we elucidated an evolutionary relationship between the two countries, Nepal and India, which could be explained by their open borders. This study identified the evolutionary relationships among MDR-TB CAS1_Delhi (SIT26) subfamily isolates from Nepal and those from neighboring countries.

PS48-929-27 Predominance of Mycobacterium tuberculosis Beijing clade and its association with drug resistance in north-eastern parts of India

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Background: The socio-cultural and demographic characteristics of the North-Eastern region (NER) of India are different from rest of the country and the population predominantly belongs to Mongoloid race. This study was aimed to characterise the MTB isolates from the region and find out if the circulating lineages had any difference in their drug resistance pattern.

Methods: A total of 218 MTB culture isolates from MDR suspected cases (1 each from 1 patient) of the North East region (NE) were included in the study. All donor patients were HIV seronegative. All isolates were reconfirmed as MTB using standard methods. Genotyping of isolates was performed using a commercially available spoligotyping kit (M/s Ocimum Bio-Solutions). DNA for Spoligotyping was extracted using QIAGEN kit (Hilden, Germany). Drug Sensitivity testing of isolates was done using the SIRE kit, BACTEC MGIT960. We examined the rate of drug resistance between Beijing and non-Beijing strains.

Results: Out of 218 MTB cultures received from the local intermediary laboratory, 159 isolates could be genotyped as remaining were not suitable for subculture. Overall, Beijing clade was most predominant [98, 61.6%], followed by CAS [23, 14.5%], EAI (10, 6.2%; 10) and T (2, 1.3%). Of the 159 isolates 103(64.8%) isolates were MDR while 28(17.6%) were sensitive to all four drugs and remaining 28 (17.6%) isolates were mono or poly-resistant for various drugs. Out of 103 MDR isolates, 83 (80.6%) were Beijing, 15 (14.6%) CAS, 2 (1.9%) T, and 3 (2.9%) EAI lineage. Of the total 98 Beijing isolates, 88 (89.8%) were resistant to one or more drugs.

Conclusions: The Beijing genotype of MTB was found most predominant in the North-Eastern region of India. This genotype was also found highly (p value < 0.001) associated with drug resistance. Hence this part of India is highly vulnerable for MDR and XDR-TB.

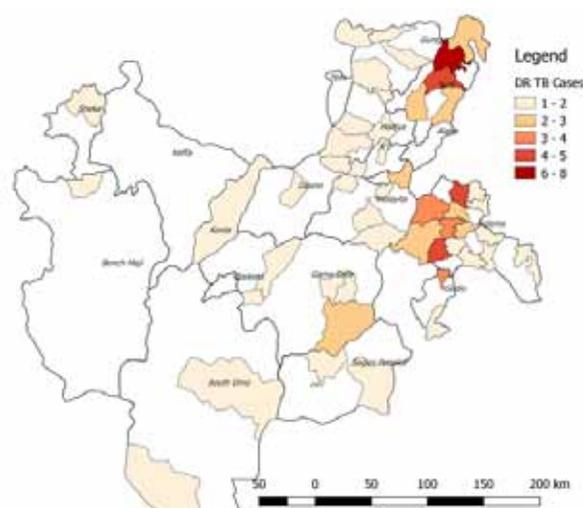
PS48-930-27 Demographic characteristics and geographic distribution of drug-resistant TB patients enrolled in six treatment initiation centres of SNNPR, Ethiopia

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Background: Exploring demographic and other related characteristics of drug resistant TB (DR-TB) patients could guide DR-TB case finding activities. This analysis aims to assess specific demographic and other related features of DR-TB patients enrolled in all 6 DR-TB treatment initiation centers (TICs) of the Southern Nations Nationalities and Peoples Region (SNNPR), Ethiopia.

Methods: A facility based cross-sectional study was conducted on DR-TB patients who were enrolled at the 6 TICs from July 2015 to June 2017. A data extraction tool was prepared to capture demographic characteristics and basic clinical history. The TIC focal persons were used to collect data after being oriented on how to extract data from the MDR-TB register.



[DR TB Case Distribution in South Nations, Nationalities and People Region (2015 -2017)]

Results: A total of 127 DR-TB cases were enrolled in the 6 TICs during the study period. About 57% (73) were male and the median age was 27 years [interquartile range(IQR) of 25: 1st IQR:14 and 3rd IQR:35]. Eleven percent (14) were under 15 years of age. About 98%

were pulmonary TB cases and 80% had previous treatment history. Ninety percent (114) received their follow up treatment in the nearby treatment follow-up centers. Eighty percent (103) were from northeast and east of the SNNPR, which showed “clustering” of DR-TB cases in certain localities.

Conclusions: In the region, the majority of notified DR-TB cases were male, young and with a history of previous TB treatment. And most of the DR-TB cases were found to be notified in a limited number of localities in the region. This implies rigorous, intensive and strengthened active DR-TB case finding should be implemented in these localities to identify many more DR-TB cases. Thus, spatial pattern analysis should be practiced in similar resource constrained areas as it helps a lot to intervene and efficient resource allocation.

PS48-931-27 Do patients incur out-of-pocket expenditures prior to multidrug-resistant tuberculosis treatment? A cost analysis study from South India

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Background: Though diagnosis of tuberculosis (TB) and the treatment thereof is offered free of cost through Revised National Tuberculosis Control Programme (RNTCP) in India, many patients incur significant out-of-pocket expenditures (OOPE) prior to enrolment. Multidrug-resistant TB (MDR TB) treatment is more complex, more difficult to manage and costlier than drug-sensitive TB. Therefore we estimated direct and indirect OOPE incurred by presumptive MDR patients prior to treatment initiation in Mangalore, Karnataka, India.

Methods: We interviewed 40 patients who registered for MDR treatment in Mangalore from August 2016 to April 2017. Direct and indirect costs associated with diagnosis and evaluation prior to MDR treatment registration were collected through face to face interviews. Expenditure incurred was expressed in USD and summarised using medians with interquartile ranges (IQR) and proportions.

Results: The direct and indirect median (IQR) costs incurred were \$105 (\$49-306) and \$51 (\$2-306) respectively; median (IQR) cost associated with coping mechanisms (loans, selling off assets, and donations) prior to MDR

TB treatment was \$640 (\$324-1360). Taken together, these costs exceeded 130% of the median annual income (\$608 [\$228- 912]).

Conclusions: OOPE is catastrophic even prior to treatment initiation of MDR TB patients way forward could be understanding the various aspects of financial crises and take measures specific to each one of them.

PS48-932-27 Increasing trend of drug-resistant TB among new TB patients and its implications in two large regions of Ethiopia

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Background and challenges to implementation: Because of limited access to diagnostic facilities, only TB patients with a history of anti-TB treatment are prioritized for anti-TB drug sensitivity testing, leaving new TB patients enrolled for drug-susceptible TB treatment with limited options. In this study, we analyzed the trend of drug-resistant TB in new patients among all drug-resistant TB patients enrolled in treatment.

Intervention or response: The National TB Program of Ethiopia, with support from the USAID-funded Challenge TB and Heal TB projects and other partners, expanded TB drug sensitivity testing sites from 3 to 51 sites in the Amhara and Oromia regions—representing 60% of the nearly 100 million people in Ethiopia—primarily by rolling out GeneXpert diagnostics. The projects assisted with developing guidelines and standard operating procedures and trained health workers. DR-TB treatment was expanded to accommodate the increasing number of patients. These interventions have increased the notification and treatment of drug-resistant TB. We used the quarterly segregated two-year (October 2014-December 2016) trend of drug-resistant TB enrollment among new patients from routinely reported data from the Amhara and Oromia regions.

Results and lessons learnt: Of 692 patients enrolled in second-line anti-TB drugs, 146 (21.1%) were new TB patients. The proportion of new TB patients among all enrolled DR-TB patients increased from 7.8% at baseline to 30.2% during the last reported quarter. The yield of interventions directed at increasing case detection has been shown in the growing share of DR-TB case detection among new TB patients-

Conclusions and key recommendations: The rate of drug-resistant TB among new patients has increased over the last two years. This suggests improvements in case detection capacity. It also highlights that new TB

patients make up a significant proportion of DR-TB patients, indicating the need to implement universal drug sensitivity testing.



[Trend of drug-resistant TB case enrollment and % of new TB patients]

PS48-933-27 Whole genome sequencing of multidrug-resistant tuberculosis isolates in Singapore, 2005-2017

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Background: It is known that mycobacterial interspersed repetitive unit-variable number tandem repeat (MIRU-VNTR) lacks discriminatory power, especially for Beijing strains, resulting in overestimation of TB community transmission. Whole genome sequencing (WGS) has recently been shown to provide better delineation of TB outbreaks.

Methods: The National TB Notification Registry captures the drug susceptibility pattern of all *Mycobacterium tuberculosis complex* (MTC) isolates in Singapore via electronic linkage to the two mycobacteriology laboratories in the country. From 2005, spoligotyping and MIRU-VNTR was performed on all multidrug-resistant (MDR) isolates at the Central TB Laboratory, Singapore General Hospital. WGS was retrospectively performed on MIRU-clustered isolates.

Results: There were 288 MDR-TB cases diagnosed in Singapore from 2005 to 2017. The majority (80%) were foreign-born. Spoligotyping and 24 loci MIRU-VNTR on 279 of the MDR isolates identified 23 clusters with at least two MDR cases in each cluster (cluster size ranging from 2 to 18). All but two clusters comprised isolates belonging to the Beijing family; 94/103 (91%) of the MIRU-clustered isolates versus 95/176 (53.9%) of the non-MIRU clustered isolates were of the Beijing strain. WGS on 81 (78%) of the 103 MIRU-clustered isolates

decreased the number of clusters from 23 to 7, and the number of patients in clusters from 103 to 37. The two largest WGS clusters (n=16, n=7) comprised mostly local-born patients whereas the larger MIRU clusters which were not WGS-clustered comprised mostly foreign-born patients.

Conclusions: We demonstrate the usefulness of WGS in delineating MDR-TB clusters in Singapore.

PS49 Tuberculosis among prison inmates

PS49-934-27 Nationwide chest X-ray screening for active TB in Thai prisons

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Background: Tuberculosis (TB) screening in prisons helps ensure that active TB is identified early to reduce poor treatment outcomes and the risk of TB transmission. There are options of TB screening, but chest x-ray (CXR) is recommended in high-risk groups including prisoners if resources permit. This study was to assess the proportion of TB patients among screened prisoners and evaluate the contribution of the screening to case-notification in prisons.

Methods: This study used data from a nationwide TB screening campaign in all prisons during March-December 2017. The algorithm for screening and diagnosing TB in prisons included both symptom-based screening and CXR, then by sputum microscopy or Xpert MTB/RIF test for confirmation. Treatment for TB or MDR-TB was provided to the patients by the hospitals where the prisons are registered under the Universal Health Care Scheme (UC). Disaggregated data by prisons, screening results, laboratory results and final diagnoses were entered via a web-based system. Descriptive analyses were used to assess the frequencies and proportions.

Results: Of 285,367 prisoners in 143 prisons, 99.3% were screened. Overall, 17,025 (6.0%) had positive screening due to symptomatic and/or abnormal CXR suggestive of TB. Among 283,272 prisoners screened, 2,473 tuberculosis cases (873/100,000) were detected; these included 2,183 bacteriologically confirmed cases (1,638 cases of Xpert-positive TB and 545 cases of smear-positive TB). Ninety one patients were identified as Rifampicin Resistance (RR-TB) detected by Xpert. The contribution of the screening to TB case notification in prisons in 2017 was 72.7% (2,191/3,014).

Conclusions: Mass radiography helped identify more active TB cases than the routine programme. If the mass radiography in prisons is endorsed by the Ministry of Public Health and covered by the UC, the burden of TB in this high-risk population will be decreased.

PS49-935-27 The contribution of mass screening to overall case finding in 10 prisons in Tigray Region, Northern Ethiopia

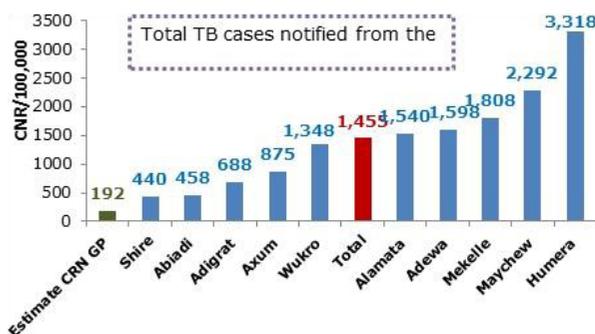
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Background and challenges to implementation: The burden of TB among prisoners is documented to be higher than that of the general population. However, the actual contribution of mass screening to case finding is not well studied.

Intervention or response: Using the national standard operating procedure, we provided an off-site training on TB and TB-HIV to health care providers working in 10 prisons. Additionally, on-site supportive supervision and orientation on standard mass TB screening tools was provided. This was followed by providing essential supplies, including falcon tubes, and the prisons were linked and networked with the Woreda health office, GeneXpert testing sites, and nearby postal hubs. Inmates and staff were considered presumptive TB cases if they had total score of 2 or more based on Presumptive TB screening criteria (cough of >2 weeks [=2], sputum production [=1], loss of weight in last three months [=1], loss appetite [=1], and chest pain [=1]). The sputum samples were tested with the Xpert MTB/RIF assay.

Results and lessons learnt: Of 12,716 (97%) prison inmates and staff screened for TB, 18% (2,315) were found to be presumptive TB cases. Of these, 1,933 (83.5%) were tested by GeneXpert, and 20 DS-TB cases were identified. An additional 23 TB cases were diagnosed clinically and notified during the mass screening. TB cases identified through the one-time mass screening comprised 23.2% (43) of the total number of TB cases reported (185) during this period from the prisons. The overall case notification rate in the 10 prisons was 1,455 per 100,000 (185/12,993).

Conclusions and key recommendations: A one-time mass screening alone contributed to nearly 25% of TB cases reported from 10 prisons in the Tigray Region. This practice should be replicated and strengthened in prisons in Tigray and other similar settings in Ethiopia.



[Figure: Case notification rate in 10 correctional centers of Tigray, 2016-2017]

PS49-936-27 Active TB case finding in prisons: experience of the Challenge TB project in Democratic Republic of Congo

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Background and challenges to implementation: Systematic screening TB cases among high risk population like prisoners can complement the passive case finding. DRC prisons conditions are crowded with inadequate infection control, absence of health workers in some prisons and nutrition issue. We will present the results and lessons learnt of Challenge TB (CTB) project interventions implemented by International Union against TB and lung Diseases (UNION).

Intervention or response: Active TB screening among prisoners have been conducted in 16 prisons of 8 CTB supported provinces since 2015. Advocacy of prison administration, sensitization, entry screening, caught surveillance and contact investigation have been strengthening in these prisons, using symptom screening and sputum smear, while those requiring conduct chest X-rays are referred.

Results and lessons learnt: During three years of the project of 10,362 sensitization prisoners, 10,081 were noted as presumptive TB cases and were tested among which 514 were diagnosed TB patients. 472 (92%) were initiated on DOT and 42 (8%) on second line treatment. DR TB patients were isolated within the prison, while patients released before treatment completion were referred to a facility next to them. For DR TB patients biological follow-up exams and nutrition support were provided by project. The followings lessons were learnt: timid participation of the nearest or prison health teams, requirement of prior authorization from the prison authorities, inadequate quality of health services or even

lack of access to diagnosis and treatment like X-rays, Xpert and other diagnostics (biochemistry, ECG, audiometry etc.), undernourishment of prisoners and inadequate follow-up of treatment after release from prison. **Conclusions and key recommendations:** Strengthening collaboration with prison administration and health staff training can improve TB detection in prisons and promote care, prevention and treatment. However follow-up of released non completed TB treatment prisoners is still high challenge.

PS49-937-27 Can regular mass TB screening in a central prison increase TB case notifications?

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Background and challenges to implementation: Infectious diseases like tuberculosis (TB) pose serious threats in Malawian prisons and the world at large; and present significant challenges for prison and public health authorities. The Malawi National TB Programme (NTP) has been collaborating with Prison Health Services for many years in order to improve TB control in Malawian prisons.

Intervention or response: Malawi NTP developed policy for TB control in prisons; and had put in place surveillance mechanism in all prisons, however, TB case notifications remain low. As part of improving TB case notifications in prison, NTP, with support from Challenge TB, decided to start conducting bi-annual mass TB screening at Maula Prison (a central prison). The screening process included symptom screening using the four TB cardinal symptoms (cough, fever, night sweats and weight loss). Chest x-ray screening was introduced in 2017. Bi-annual TB screening was conducted within the prison premises from first quarter 2015 to fourth quarter 2017. Those eligible for sputum examination were requested to submit spot and early morning sputum specimens. All sputum specimens were examined using Xpert MTB/RIF assay. All MTB+/RIF+ and indeterminate results were repeated in order to confirm results.

Results and lessons learnt: TB case notifications at Maula Prison have increased with this approach. There was a 29% noticeable annual increase in the number of prisoners diagnosed with TB from 2015 (66 prisoners) to 2016 (85 prisoners). There was also a 28% increase from 2016 to 2017 (when 109 prisoners were diagnosed with TB). Majority of these TB cases were diagnosed during mass TB screening and were mostly bacteriologically positive.

Conclusions and key recommendations: Mass TB screening at Maula Central Prison has resulted in increase in TB case notifications. This intervention could

arrest the spread of tuberculosis in Malawian prisons. The intervention has been expanded to other central prisons and some small and medium sized prisons in the country.

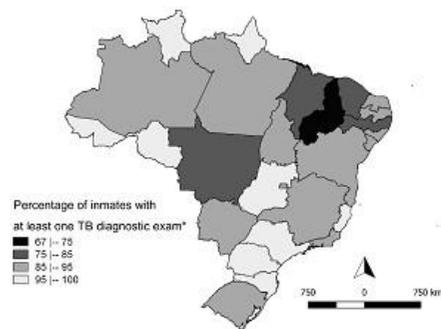
PS49-938-27 Tuberculosis in inmates: access to laboratory diagnosis in Brazil

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Background: In Brazil, in 2017, 10.5% of the new tuberculosis (TB) cases occurred in inmates, being therefore a priority population for the end of TB in the country. Access to quality TB diagnosis as well as drug-resistance detection becomes a priority to contain the disease transmission in overcrowded environments, such as Brazilian's prisons. In this sense, we analyzed the access to TB laboratory diagnosis by inmates in Brazil.

Methods: We conducted a cross-sectional study of new pulmonary TB cases in inmates, diagnosed in 2016, from the Brazilian National Information System for Notifiable Diseases. We calculated the frequency distribution of the diagnosis cascade preconized for this population by the Brazilian Ministry of Health, Sputum Smear or Molecular Rapid Test, Culture and Sensitivity Test (ST) for all suspect cases. Additionally, the access to TB diagnosis tests was presented on a map by Brazilian States.

Results: 6,423 new pulmonary TB cases were registered in prison population in 2016. 93.2% of them had access to at least one laboratory test for TB; however, culture exam was not performed in 53.7% of the positive cases. Among those that had a positive result for culture, 64% had access to the ST, of which 4.3% presented some type of resistance to TB treatment drugs. Regarding geographic distribution, access to laboratory tests was lower in the Northeast region of the country and higher in the South and Southeast regions (Figure 1).



[Figure 1. Percentage of inmates with at least one tuberculosis diagnostic exam according to Brazilian States 2015

*Culture exam, sputum microscopy or MTB GeneXpert]

Conclusions: Despite national recommendations, the proportion of cases that had access to Culture and ST was unsatisfactory. This may favor the disease transmission, including resistant strains. Although this population is sentenced to liberty deprivation, they should not be deprived of their human rights of accessing quality health care. It is urgent to guarantee universal access to laboratory diagnosis, including ST, to adequate therapeutic care for this population.

PS49-939-27 Underserved prison settings in Uganda contribute to missed TB cases: the case of Mukono District

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Background and challenges to implementation: The TB prevalence and incidence in Uganda are estimated at 253 and 234 per 100,000 respectively. Every year, 46% of expected TB cases are missed; men are four times more likely to have TB compared to women and are more likely to be missed. Prison settings especially in low resource settings are known to increase risk for TB.

The USAID Defeat TB project is a five-year technical assistance mechanism for TB control in focus districts with high TB burden and mobile populations including Mukono. The project supports activities to find the missed TB cases especially among key affected populations.

Intervention or response: Methodology: We assessed TB service delivery among prisons in Mukono District using the Ministry of Health standard checklist and identified gaps in TB screening and Infection control. We then conducted a cross sectional systematic TB screening activity using the intensified case finding guide at 3 prisons in the district that are host to 231 prisoners.

Results and lessons learnt: Of the 231 prison inmates (90% male) screened for TB, 94 men were presumed TB cases and evaluated using Gene Xpert of which 3 (1.3%) were found to be MTB positive. This translates into a prevalence of 1300/100,000 which is 5 times higher than in the general population. This also corresponds to a lesser number needed to screen among prisons compared to the general population. The 91 presumptive TB cases which were MTB negative on Gene Xpert were scheduled for further clinical and radiological evaluation.

Conclusions and key recommendations: There are missed opportunities for TB case detection and prevention in prison settings in Uganda. We recommend prioritization of the prison settings for intensified TB case finding and prevention efforts.

PS49-940-27 Promoting the rights of prisoners to tuberculosis care and prevention in Kenya

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Background and challenges to implementation: The TB pandemic in prisons is a serious human rights issue. Prisoners should enjoy the same standards of health care available in the community without discrimination on the grounds of their legal status. Prisons are often high-risk environments for TB transmission because of severe overcrowding, poor ventilation and limited access to health care. A retrospective study based on data from death registers in 13 Kenyan prisons found TB to account for up to 30% of the mortality. WHO recommends improving TB situation in prisons through increasing capacities of prison staff and collaborative activities to improve health access.

In 2016 Amref received funding from Global Fund to conduct TB prevention and care interventions in 15 high volume prisons.

Intervention or response: Amref supported training of 376 prison wardens and 75 Health Care Workers from prison facilities on comprehensive service package including TB screening upon entry to prisons, health education and management of TB patients. The wardens screened inmates at admission to prisons, peer educators (inmates) continuously offered TB health education, infection prevention messages and referred coughers to health facilities for diagnosis. Quarterly outreaches to screen and refer inmates with TB signs and symptoms were conducted and identified cases promptly initiated on treatment thus reducing transmission in prison settings.

Results and lessons learnt: Between January 2016 and December 2017 TB screening at admission was consistently done. In addition 74 outreaches to prisons for health education and TB screening were done in 15 prisons. Of the 16,174 prisoners screened, 4,202 (25%) were presumptive and 138 (3%) diagnosed with TB and initiated on treatment. Of the 75,706 and 85,188 TB patients notified by the National TB program in 2016 and 2017 respectively, 2% were from prisons.

Conclusions and key recommendations: Improving TB prevention and care in prisons leads to prompt diagnosis and initiation of treatment thus promoting prisoners right to health.

PS49-941-27 Best practices towards ending TB in correctional facilities: experience from India

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Background and challenges to implementation: According to WHO, the level of TB in prisons has been reported to be up to 100 times higher than that of the general population. TB in prisons may account 25% of a country's TB burden. Late diagnosis, inadequate treatment, overcrowding, poor ventilation and repeated prison transfers increases TB transmission. Delays in detection and treatment of TB must be minimised to reduce further transmission of infection. Several factors contribute to delayed TB diagnosis in the prison system. Initial screening specifically targeting TB is rarely applied. This paper attempts to assess the prison intervention conducted by Project Axshya through passive and active symptom screening approach.

Intervention or response: Project Axshya is being implemented in 285 districts across the country with the objective of enhancing access of vulnerable and marginalized populations to TB services. In the initial period, the intervention was conducted by sensitising inmates on the signs and symptoms of TB through awareness activities. In order to cut the transmission chain and to reach out to large number of inmates, later the approached was changed to active screening. All the inmates underwent a general health check-up including blood pressure, blood sugar testing and TB symptom screening.

Results and lessons learnt: It is found that significantly more number of inmates participated and could be sensitised and screened in the active symptom screening approach, as this non-stigmatised approach has given the opportunity to participate in wide numbers. Also more number of PTBPs identified through the active screening (7.8 % vs. 0.2%) with TB positivity rate of 5% vs. 4%.

Indicator ↓ / Approach →	Passive screening approach (Oct 15- Dec 16)	Active symptom screening approach (Jan 17- Dec 17)
No. of prison inmates screened and sensitised	39454	46449
Number of PTBPs identified	77 (0.2%)	3628 (7.8%)
Number of PTBPs tested for TB	73 (95%)	3133 (86%)
No. diagnosed as TB (all forms)	3 (4%)	147 (5%)
No. put on treatment under NTP (DOTS)	3 (100%)	136 (93%)

[Comparative analysis of Passive and active screening approach in correctional facilities]

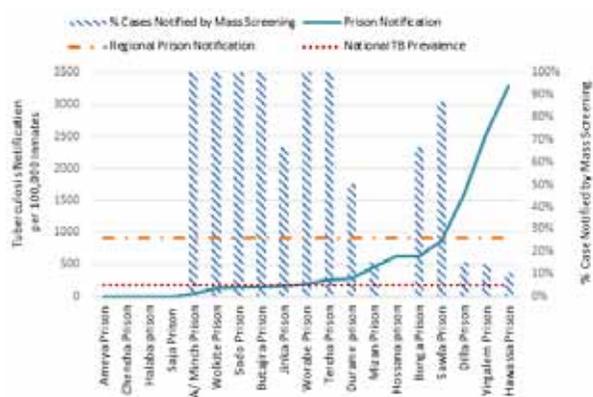
Conclusions and key recommendations: As per WHO recommendations, every prisoner should have unrestricted access to the correct diagnosis and treatment of communicable diseases, mainly TB. In correctional facilities, active TB symptom screening approach yields comparatively better results than passive approach. This calls for new approaches to control TB in the high-transmission settings.

PS49-942-27 Contribution of mass screening to case finding in USAID/CTB supported prisons in SNNPR, Ethiopia

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Background: Ethiopia is a high tuberculosis (TB) burden country. Prisons are priority settings for TB prevention and control because of the high TB burden in these settings. Thus, we assessed the contribution of mass screening to case finding in the prisons of the Southern Nations, Nationalities and Peoples Region (SNNPR), Ethiopia.

Methods: In SNNPR, USAID/Challenge TB (CTB) project provided support to improve case finding in prison settings. Interventions included training for health care workers serving prisoners; regular mentorship and supportive supervision; and technical and financial support to conduct mass screenings amongst the prisoners. Acid fast bacilli (AFB) smear microscopy, Genexpert (when available) and Chest X-ray (for smear and Xpert negative cases) were used at routine diagnostic tests. Prisoners that remained symptomatic were re-examined for TB within three months after antibiotic trial.



[Tuberculosis Disease Burden in Prisons in SNNPR Regional State, April - Aug 2017]

Results: During April to August 2017, 83% (19/23) prisons were supported for mass screening, which was conducted over a period of two weeks. Two thousand four (9%) symptomatic cases were identified out of 23,477 prisoners screened. Of these, 49 TB cases were identified and treated. Follow-up screening identified 10 additional cases. Routine health services in prisons identified 172 more TB cases within the same calendar year. The combined notification in all prisons was 910 per 100,000

inmates, which is 5x higher than the national prevalence (177). USAID/CTB supported mass screenings contributed directly in the identification of 26% (59/231) of new TB cases. It contributed 100% in 6 prisons and >50% in 4 more.

Conclusions: Prisons in SNNPR have variable TB burden ranging from no cases to as high as 3,300 per 100,000 inmates. Mass screening contributed a quarter of the overall TB cases notified from the prisons and it should be considered for implementation in selected prisons depending on the performance of the routine prison health services.

PS49-944-27 Effect of urban DOTS expansion in Kabul prisons on tuberculosis treatment outcome: a document review

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Background and challenges to implementation: Before 2015, no complete TB services or reporting system existed in Kabul prisons, resulting in low case finding (40 all form TB cases in 2014) and a treatment success rate (TSR) of 80%. The NTP, with support from the USAID-funded Challenge TB project expanded the urban DOTS approach, which involves public and private health care providers in TB control efforts, to two main prisons in Kabul to address this gap.

Intervention or response: After conducting a baseline assessment, and signing a memorandum of understanding with the in line ministries, the CTB project trained medical staff on TB case management, provided recording and reporting formats, and supervised, monitored and provided feedback to prison TB clinics. The NTP and CTB technical teams reviewed data from 2015-2017 using the standard NTP reporting tool and compared the information with existing surveillance data.

Results and lessons learnt: In 2015, 115 all form TB cases were registered in Kabul prisons, 102 were successfully treated (89%), four patients died (3%) and nine (7%) were not evaluated. In 2016, 209 all form TB cases were registered and 201 (96%) successfully treated, three patients (1%) died and four (2%) were not evaluated.

In 2015, of 5,449 TB cases registered in Kabul health facilities, 4,416 were successfully treated (TSR of 80%); 141 died (2.5%) and 510 (9%) were not evaluated. In 2016, of 6,108 all form TB cases diagnosed in public health facilities, 5,152 (84%) were successfully treated, 95 (1.5%) died and 450(7%) not evaluated (Table 1).

Conclusions and key recommendations: Urban DOTS services in Kabul prisons made significant improvements to the TSR. Prison TB clinics may have a higher TSR

because they might employ a better follow-up mechanism and enrolled TB patients are in a controlled area making it easier to access the patient and provide daily medication. We recommend engaging other prisons in TB services.

Year	% Treatment success rate in Kabul health facilities(HFs)	% Died	% of not evaluated cases in Kabul HFs	Treatment success rate in prisons health facilities (%)	% Died	% of not evaluated cases in prisons
2015	81%	2.5%	10%	89%	3%	8%
2016	85%	1.5%	7%	96%	1%	1%

[Comparison of treatment outcomes in prisons and other urban health facilities in Kabul]

PS49-945-27 Identifying efficient mass screening strategies for tuberculosis in Brazilian prisons using a mobile diagnostic unit

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Background: Prisoners have high burden of tuberculosis globally, and the WHO recommends periodic mass screening for early identification of tuberculosis cases among inmates. In Brazil, which has the third largest incarcerated population in the world, mass screening is not widely performed due to resource constraints. We aimed to identify efficient tuberculosis screening strategies in prisons through use of a mobile diagnostic unit in which multiple modalities were performed.

Methods: We constructed a mobile tuberculosis screening unit on a truck, which contains an x-ray machine with digitizer, lead shielding, and a GeneXpert machine. In two prisons in the state of Mato Grosso do Sul, we invited all inmates to participate in a screening study. Each participant was interviewed using a standardized questionnaire and screened for tuberculosis by chest x-ray (with automated interpretation) and two sputum samples for smear microscopy, culture, and Xpert MTB/RIF.

Results: Between November, 2017 and March, 2018, we recruited 3,007 inmates, and 164 (5.4%) declined to participate. Among 2,843 participants, high rates of drug

use (57%), alcohol use (48%), smoking (52%) and previous TB (12%) were reported. In total, 100 (3.5%) had microbiologically confirmed pulmonary tuberculosis. Among the 100 cases, 92 were detected by Xpert, and 8 were positive by culture but negative by Xpert. Three of the cases were HIV co-infected, no rifampin-resistant cases were identified, and all patients received treatment upon notification.

Conclusions: Using a mobile diagnostic unit, we identified 100 cases of pulmonary tuberculosis in two prisons over a period of just five months. Prevalence was 3,500 per 100,000, and most cases could be detected by a single sputum sample tested by Xpert. An additional 2,500 inmates will be screened by September, 2018, and the yield of various screening algorithms including symptom combinations, x-ray, and Xpert will be presented at the conference.

PS50 Towards quality management of tuberculosis laboratory networks: approaches and experiences

PS50-946-27 Quality control of sputum samples to increase the proportion of bacteriologically confirmed tuberculosis: a multicenter randomized controlled trial

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Background: The diagnosis of tuberculosis (TB) should be based on bacteriological detection of the bacillus, for which the quality of sputum samples is critical, but the percentage of bacteriologically confirmed cases of TB in China has decreased far below the recommended level. To increase the proportion of bacteriologically confirmed TB, we designed a pragmatic procedure for sputum quality control (QC).

Methods: A multicenter randomized controlled trial enrolled 980 adults age ≥ 15 years with suspected TB from three counties in China during the entire year 2017. Half of the participants (490) were randomly assigned to an intervention group that received instruction and sputum induction if necessary by a health-care worker, and 490 to the control group for expectoration without observation. The primary outcome was the proportion of pa-

tients detected positive by smear, culture or molecular assay (EasyNat or Xpert). Secondary outcomes were sputum quality and the proportion of cases detected by the individual diagnostic methods and cases started on treatment. This study is registered with Chinese Clinical Trial Registry (<http://www.chictr.org.cn/>), number ChiCTR-IOR-17012476.

Results: The bacteria-positivity rates were significantly better in the intervention group: overall (159/490 [32%] vs. 122/490 [25%], odds ratio OR 1.45 [95% CI 1.10-1.91], $p=0.009$); for smear (83/490 [17%] vs. 55/490 [11%], OR 1.60 [95% CI 1.11-2.32], $p=0.010$); for culture (135/490 [28%] vs. 104/490 [21%], OR 1.41 [95% CI 1.05-1.89], $p=0.021$); and with molecular assays (132/490 [27%] vs. 89/490 [18%], OR 1.66 [95% CI 1.23-2.26], $p=0.001$). A higher proportion of intervention versus controlled patients provided adequate spot-sputum sample of over 3 mL (387/490 [79%] vs. 210/490 [43%]; $p < 0.001$). The improvement in case detection was greater in younger patients (aOR 1.27 [95% CI 1.05-1.53] for every 10 years younger).

Conclusions: Instruction on producing a sputum and sputum induction when necessary significantly increased the proportion of bacteriological confirmation among pulmonary TB patients.

PS50-947-27 Introduction of a quality management system in a national reference laboratory

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Background and challenges to implementation: High-quality laboratory services are an essential component for tuberculosis care and control. A strong laboratory quality management (QM) system is critical to ensuring the quality of testing. A minimal QM system is composed of quality control (QC), external quality assessment (EQA), standard operating procedures (SOP) and competency assessment (CA). Here we describe the implementation of a QM system in a National Reference Laboratory (NRL) in Germany and the impact on microscopy and culture results.

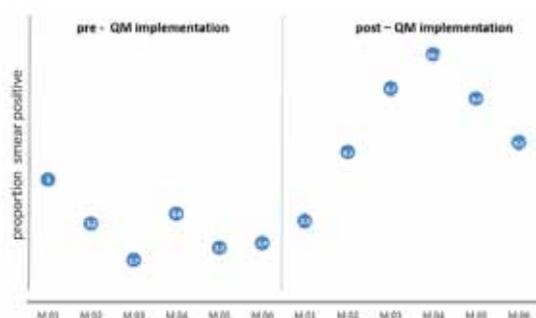
Intervention or response: Following a change in senior leadership in 2015 the new head of the NRL prioritised the implementation of a QM system within a change management framework. QM for analytical procedures included: development of SOPs, batch control, positive and negative controls, internal QC, training and CA of technicians and routine review of quality indicators.

Over a period of 6 months fully quality managed fluorescence microscopy was implemented. The proportions of smear positive respiratory samples before and after implementation of QM were compared. The second

analytic process selected for QM was decontamination and culture. Contamination rates before and after full implementation of QM were determined.

Results and lessons learnt: The proportion of smear positive respiratory samples significantly increased from 3.09 (95% CI 2.1-4.3%) pre QM-implementation to 6.9% (95% CI 5.1-9.1%) post QM-implementation ($p < 0.01$) (figure 1). Contamination rates in liquid culture decreased from 14.6-29.0% in the years 2013-2015 to less than 10% post QM-implementation.

Conclusions and key recommendations: Introduction of QM is resource and staff intensive, but leads to significant improvement in laboratory performance. In the context of a laboratory not used to QM appropriate change management is essentially to ensure a sustainable culture change.



[Figure 1. Proportion of smear positive respiratory samples by month before and after implementation of quality management]

PS50-948-27 Quality components affecting the quality of TB laboratory diagnostics services in public health centers in central Uganda

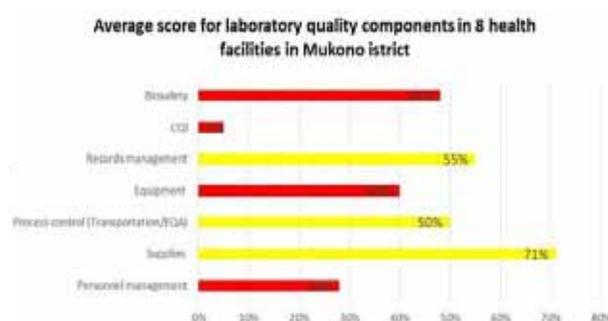
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Background and challenges to implementation: The national TB prevalence survey conducted in Uganda in 2014/15 found a higher TB burden (253/100,000) than was previously estimated, indicating the challenge ahead to achieve the global target of ending tuberculosis by 2030. The strategies to end TB include early diagnosis of TB and drug susceptibility testing, highlighting the critical role of laboratories. In the absence of detailed information on the quality of TB laboratory services in Uganda, a situation analysis of various quality components of TB laboratory services was conducted by USAID Defeat TB project.

Intervention or response: The focus district was Mukono district located in central Uganda, which has 17 public health facilities. Eight high volume health facili-

ties were purposively selected for assessment. Assessors used a customized checklist tool comprised of seven elements based on International Organization for standardization (ISO) 15189:2012. To complete the assessment, assessors reviewed records, observed laboratory operations, and followed a specimen through the laboratory. The quality component performance grading was; "red" is below 50%, requires significant improvement; "orange" is between %50- 80%, some improvement necessary; "green" is above 80%, in good standing.

Results and lessons learnt: At least 3/7 components scored fairly, between 50% -80%. The rest were below 50% and thus required significant improvement. The TB laboratory services supplies component scored highest with 70% and above in all health facilities. The lowest was continuous quality improvement (CQI) with 5%. However, laboratory teams were knowledgeable on good laboratory practice though not all were familiar with concepts of Laboratory Quality Management Systems.



[Figure 1. Average score for laboratory quality components in 8 health facilities in Mukono district]

Conclusions and key recommendations: This formative assessment highlights the priority areas for technical assistance to optimize laboratory performance. The USAID Defeat TB project is using CQI approaches to implement changes including; appointing TB laboratory focal person, integrated onsite mentorships, trainings, integrated TB sample transportation with Hub system, and preventive machine maintenance.

PS50-949-27 External quality assurance for ensuring quality and diagnostic services in TB

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Background and challenges to implementation: BRAC, a non-government organization, is implementing TB control program for 92 million people in Bangladesh. In collaboration with National TB control program (NTP), BRAC has expanded the laboratory network and ongoing quality assurance system to 42 districts.

The organization is following the National guidelines of EQA to monitor the performance of its laboratories in an unbiased manner and help the facilities create credible results to physicians, patients and health authorities.

Intervention or response: A total of 26 EQA laboratories have been established to check the quality of 767 peripheral laboratories in BRAC supported area. Additionally, to increase accessibility to TB diagnostics, outreach sputum collection centres are arranged below sub-district level. Training of laboratory workers on AFB microscopy has been conducted. An Internal Quality Control team is working to maintain the quality of these laboratory services and quality of DOTS. Regular feedback is subsequently provided in order to develop technical competency of laboratory personnel.

Results and lessons learnt: Up to September 2017, 2.36 million slides were examined for diagnosis and follow up at BRAC supported peripheral laboratories, 0.0019% of which were found to be discordant slides by the second controller. Previously, the percentages of discordant slides were 0.0044% and 0.0030%, in the year 2015 and 2016, respectively.

Conclusions and key recommendations: The use of EQA makes it possible to find the definite error made by laboratories and take immediate measures to resolve the issue thereby strengthening the on-going laboratory activity. EQA system helps to assure that the laboratory diagnosis is of standard quality.

PS50-950-27 Continuous quality improvement approach rapidly increases GeneXpert utilization, reporting and tuberculosis case notification: lessons from Kampala, Uganda

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Background and challenges to implementation: WHO endorsed Gene-Xpert testing for TB diagnosis because its more sensitive and can detect both drug resistant and sensitive TB in two hours. A Gene-Xpert machine of four modules has a daily sample test rate of 16 samples per day; At baseline, weekly data showed low Gene-Xpert utilization in Kampala city with only 55% (12/22) Gene-Xpert machines reporting test results to the national TB and leprosy program (NTLP) through GxAlert system. In comparison to expected weekly targets of 2800 samples tested, only 368 TB samples test results and 42 positive cases were reported to NTLP in week one

of January 2018. A rapid assessment identified gaps in documentation and stock monitoring; irregular machine maintenance and no designated staff to monitor these processes. We aimed at increasing Gene-Xpert utilization and reporting tested results using CQI approach.

Intervention or response: Using CQI approach, NTLP supported by USAID Defeat TB project engaged a multidisciplinary team of mentors who included laboratory supervisors, Information technology and logistics experts in 25 laboratories in Kampala city. Staff were mentored to document, order and update stock cards; and monitor a reporting log. A schedule to service Gene-Xpert machines and analyze samples was implemented daily. Laboratory staff supported sample collection at TB screening entry points at the facility. A designated staff and laboratory teams met weekly to review performance.

Results and lessons learnt: Within four weeks, samples tested doubled from 368 to 873, reported test results and TB cases notified increased from 55% and 42 TB cases to 95% and 183 cases respectively as shown in figure 1 below. Capacity of laboratory staff to maintain Gene-Xpert machine functionality was enhanced.

Conclusions and key recommendations: Using continuous quality improvement (CQI) approach rapidly increased Gene-Xpert utilization, GxAlert reporting and TB case notification in an urban setting. Introducing or scaling up mentorship in similar setting can enhance efforts toward finding missing TB cases.

PS50-951-27 Preparing TB C&DST laboratories under the RNTCP for NABL accreditation in India

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Background and challenges to implementation: As Revised National TB Control Program (RNTCP) scales up universal DST, it is imperative to ensure quality of TB diagnostics across TB Culture and Drug Susceptibility Testing (C&DST) laboratories in India. Under The Global Fund project (Oct15-Dec17), Central TB Division (CTD) with Foundation for Innovative New Diagnostics (FIND) as its sub-recipient planned to support 7 sites to improve quality and apply for National Accreditation Board for Laboratories (NABL) accreditation as per ISO 15189.

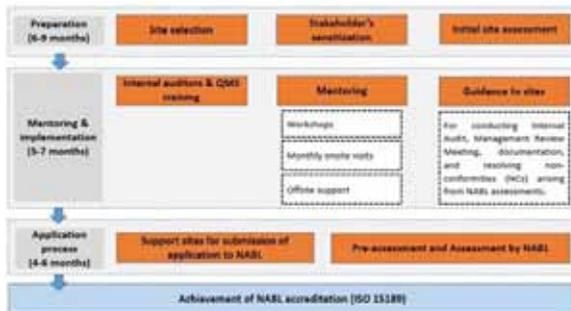
Intervention or response: A comprehensive and customized approach was developed to strengthen Quality Management System (QMS) at the identified 14 TB C&DST Laboratories and prepare towards NABL accreditation over 15-18 months as shown in figure. This included:

- i. Site selection based on criteria such as adequate manpower, infrastructure & equipment, participation in proficiency testing program, and staff commitment to improve quality
- ii. Stakeholders' sensitization meeting to explain needs, process and challenges for accreditation and share mentoring plan,
- iii. Initial site assessment using FIND's TB QMS Harmonized Checklist by trained ISO 15189 assessors,
- iv. Internal Auditors and QMS training for site staff,
- v. Mentoring over six months through two workshops, monthly onsite visits and offsite support for improving QMS implementation,
- vi. Guiding sites for conducting Internal Audit, Management Review Meeting, documentation, and resolving non-conformities (NCs) arising from NABL assessments.

Results and lessons learnt: Eleven of fourteen sites successfully applied for NABL accreditation. One site achieved accreditation. Two sites completed final assessment and eight sites completed pre-assessment.

Challenges overcome while preparing included documentation on legal identity of laboratory, identification of NCs, corrective actions, organogram, risk assessment, etc. QMS was strengthened by development and implementation of a Quality Manual, Safety Manual, Clinician Manual and Quality System Procedures.

Conclusions and key recommendations: Structured mentoring approach is required for supporting sites to improve QMS complying to international accreditation standards.



[Supporting sites towards NABL accreditation ISO 15189]

PS50-952-27 Rapid scale-up of liquid culture and DST facilities under the RNTCP to increase access to universal DST

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Background and challenges to implementation: World Health Organization recommends 1 TB Culture and Drug Susceptibility Testing (C&DST) laboratory per 10,000,000 population. Till 2015, India's Revised National Tuberculosis Control Program (RNTCP) had 64 C&DST laboratories. Foundation for Innovative New Diagnostics (FIND) supported establishing 46 laboratories and 15 more were planned under The Global Fund (TGF) supported project (Oct15-Dec17). Site assessments were completed by Nov16. FIND had the unprecedented challenge to upgrade labs within 10 months to align with the national TB elimination goals.

Intervention or response: FIND initiated the process for upgrading 14 labs in Mar18. Simultaneously, 33 different kinds of equipment and 41 different types of consumables were procured and delivered to these sites. Vendor was identified in Jun17 to upgrade these sites as a turn key project through an RFP mechanism. FIND conducted intensive discussions with vendor to finalize designs and develop a micro-plan for upgrading labs for Liquid Culture and DST (LC-DST) facilities. This was carried out in stages i.e.

- i. Civil, electrical and plumbing works;
- ii. Panelling, interiors & flooring;
- iii. AHU placement & ducting;
- iv. BSC installation & its ducting;
- v. Dry-run & validation and
- vi. Training & handover.

Besides using pre-designed quality checklists, FIND regularly monitored work-progress through site visits, meetings, phone calls and sharing site pictures at each stage (see figure).



[Upgrading Sites for Liquid Culture and DST Facilities]

Results and lessons learnt: Eleven of fourteen sites were successfully completed by Mar2018 and remaining 3 will be completed by May18, thereby significantly increasing national diagnostic capacity. Challenges like providing adequate power supply, access to site, road permits, slow civil works completion by institute lead to delays in work completion and timelines were extended. **Conclusions and key recommendations:** Large number of sites were upgraded to LC-DST facilities within a record time of <1 year. Strong planning and coordination between vendors, FIND and the sites was a key to smooth upgrading of facilities.

PS50-953-27 External quality assessment of chest X-ray interpretation for TB triage and diagnosis in Myanmar

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Background: WHO has reconsidered CXR as a high sensitivity triaging and diagnostic tool placed early in TB diagnosis algorithms. The main limitation of CXR lies in low specificity due to significant inter-rater variation. To strengthen TB diagnosis in Myanmar, the objective of this study was to measure inter-rater agreement of CXR interpretation between readers at different level of the health system.

Methods: Seven facilities located in Yangon and Mandalay regions were included in the study. In each facility, CXR performed for all presumptive TB patients were randomly selected during last quarter 2017. CXR read by TB staff at facility level were blindly rechecked by in-country controllers 1 and 2 and international controller considered as gold standard. Degree of agreement between readers was measured by kappa coefficient (k) using following classification: $k \leq 0.20$ poor, 0.21-0.40 fair, 0.41-0.60 moderate, 0.61-0.80 good, and 0.81-1.00 very good.

Results: Out of 851 TB presumptive patients included in the study, 836 CXR were read at facility level. The median age of patients was 41 years and 49% was female. At facility level, 46% of patient's CXR were normal, 32% suggestive TB, 9% healed TB, 8% suggestive of disease other than TB, 5% inconclusive, and 0% not readable. Kappa was 0.48 (95% confidence interval: 0.43-0.52), 0.53 (0.49-0.57), and 0.57 (0.53-0.61), between gold standard versus respectively, TB staff, controller 1, and controller 2. Kappa was 0.51 (0.46-0.55), 0.47 (0.43-0.52), and 0.50 (0.46-0.54), between TB staff versus respectively, controller 1 and controller 2, and between controller 1 versus controller 2. All levels of inter-reader agreement were moderate.

Conclusions: Moderate kappa with 6 results classification is acceptable. EQA on CXR should be maintained to improve level of agreement. Maintaining 6 results classification is essential to consider CXR as a diagnosis tool. Not readable classification is not properly used reaching the highest disagreement rate.

PS50-954-27 Quality improvement support improves TB diagnosis through intensified TB case finding at care entry points in Kampala

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Background and challenges to implementation: Despite high TB burden, Uganda is still grappling with declining TB case notifications. The burden of TB is found to be higher in urban areas (504 per 100,000 persons) than rural in areas (370 per 100,000 persons). Kampala has the highest TB burden and misses about 50% of the TB cases due to TB case finding inefficiencies.

Intervention or response: The National Tuberculosis and Leprosy Programme (NTLP) with the support of the USAID funded TRACK TB project used quality improvement (QI) approaches to address case finding inefficiencies.

We conducted an integrated performance assessment of health facilities on standards of TB, TB-HIV and MDR TB care, mentored facility providers and applied continuous QI methods to address gaps in TB case finding. Health providers from 45 facilities in Kampala were trained in QI using the national QI curriculum focusing on case finding. To improve TB screening the following strategies were adopted:

- (i) Assigning focal persons at triage to supervise documentation in out-patient department (OPD) register;
- (ii) Introduced intensified case Finding (ICF) tools at all care entry points,
- (iii) Orienting all health workers at care entry points on TB screening.

Results and lessons learnt: The total OPD attendance increased from 344,279 in Jan-Mar 2016 to 415,628 in Jul-Sept 2017. TB screening among OPD attendance increased from 134,551(39.1%) to 340,007(81.8%) patients. The presumptive TB cases identified increased initially from 6,180 in Jan-Mar 2016 to 8,028 in Jul-Sept 2017. There was an improvement in newly confirmed TB cases identified from 715 to 946 in the same period giving a yield of 340 cases/100,000 which is about two thirds of the Kampala prevalence of 504/100,000.

Variables	Jan-Mar 2016	Apr-Jun 2016	Jul-Sep 2016	Oct-Dec 2016	Jan-Mar 2017	Apr-Jun 2017	Jul-Sep 2017
OPD attendance	344,279	369,036	347,983	254,506	389,310	459,164	415,628
TB screened cases	134,551	250,853	207,126	164,012	273,882	292,720	340,007
Presumptive TB cases	6180	9836	6957	5926	6,375	8,499	8,028
Confirmed TB cases	715	815	911	796	724	757	946

[Table 1: TB screening cascade at health facilities]

Conclusions and key recommendations: The QI initiatives improved the capacity of facility health workers in TB case finding and notification. The facility QI teams need to be strengthened to ensure they are functional to sustain and improve case finding and case notification.

LATE BREAKER PRESENTATIONS FRIDAY 26 OCTOBER 2018

ORAL ABSTRACT SESSIONS

OA13 The HIV-TB and diabetes late-breaker session

OA13-3347-26 Association of diabetes mellitus with treatment outcome of drug resistant tuberculosis patients in Pakistan from 2010-14

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Background: Drug-Resistant Tuberculosis is a major challenge to national TB control programmes. In 2015; there were 580,000 estimated incident DR-TB patients in the world, whereas, the treatment success rate of patients enrolled in 2013 were reported 52%. Pakistan is among the high burden countries for drug-susceptible and drug-resistant tuberculosis. In 2015; there were estimated 14,000 new DR-TB Patients. Treatment success rate of DR-TB in Pakistan was 69% in 2013 which is better than global treatment success rate. Diabetes mellitus is one of the leading non-communicable diseases which are on the rise. Global Diabetes report 2016 estimates that 1.5 million deaths are directly caused by diabetes in 2012. The aim of the study was to assess the effect of diabetes mellitus on unfavourable treatment outcome of drug-resistant tuberculosis patients enrolled for treatment (2010-14)

Methods: A cross-sectional study based on retrospective record review of all patients with DR-TB enrolled at 24 Programmatic Management of Drug-Resistant Tuberculosis sites of Pakistan during June 2010 to December 2014. Treatment outcomes were also extracted from the DR-TB registers and were based on WHO designated definitions

Results: A total of 5,811 patients started second-line anti-TB treatment from June 2010 to December 2014. All diabetic patients had type two diabetes. Overall 4,009 (68.9%) of patients had favourable treatment outcomes. No significant association found between diabetic status and poor treatment outcome (risk ratio [RR] 0.90, 95%CI 0.74-1.05). However, it was observed that the death rate was higher in patients with diabetes compared to patients without diabetes (20.8% vs. 16.6%) but the difference was not statistically significant.

Conclusions: Diabetes mellitus is not associated with unfavourable outcomes of DR-TB. There is a need for record of glycaemic control in DR-TB Patients in order to access the severity of diabetes and its impact on DR-TB management and outcomes.

Treatment Outcomes	Total	Favorable outcomes	Cured	Completed	Unfavorable outcomes	Failure	Lost to Follow-up	Death	Not evaluated
Total	5811	4009 (68.9%)	3861 (66.4%)	148 (2.5%)	1802 (31.1%)	230 (4.0%)	427 (7.3%)	984 (16.9%)	161 (2.8%)
Without Diabetes	5302 (91.2%)	3671 (69.3%)	3530 (66.6%)	141 (2.7%)	1631 (30.7%)	210 (4.0%)	394 (7.4%)	878 (16.6%)	149 (2.8%)
With Diabetes	509 (8.8%)	338 (66.4%)	331 (65.0%)	7 (1.4%)	171 (33.6%)	20 (3.9%)	33 (6.5%)	106 (20.8%)	12 (2.4%)
Risk Ratio					0.9 (0.74-1.05)				

[WHO defined treatment outcomes of drug-resistant tuberculosis patients with diabetes mellitus in Pakistan; 2010-14]

OA13-3449-26 Novel point-of-care LAM assay for the detection of tuberculosis in people living with HIV with superior sensitivity

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Background: Most tuberculosis-related deaths in HIV patients could be prevented with earlier diagnosis and treatment. The only commercially available tuberculosis point-of-care (POC) test (Alere LAM assay) has insufficient sensitivity. A next-generation urinary POC assay (Fuji LAM assay), developed for superior diagnostic accuracy, was assessed.

Methods: Independent, blinded assessment of the Fuji assay was performed according to manufacturer's guidelines on urine samples from three independent inpatient cohort studies conducted at two South African district hospitals. Diagnostic accuracy, against both microbiological (MRS) and composite reference standards (CRS), and in comparison with the Alere assay, was analysed.

Results: A total of 968 newly admitted patients living with HIV were included, with a microbiologically-confirmed tuberculosis prevalence of 62% and a mean CD4 count of 149 cells/ μ l. Against the MRS, the pooled sensitivity of the Fuji assay (75.8% (95%CI 72.3-79.1)) was

31% higher compared to the Alere assay (44.7% (95% CI 40.7-48.7)). Specificities were 96.0% (95% CI 93.0-97.8) and 98.2% (95% CI 95.8-99.2) against a CRS, respectively. In the subgroup of patients with $CD4 \leq 100$ cells/ μ l, the Fuji assay had a sensitivity of 87.1% (95% CI 83.4-90.1) versus 58% (95% CI 53.0-62.9) with the Alere assay. The yield of sputum-based diagnostics was substantially limited by the proportion of patients able to produce sputum (on day 1 of admission only 153 of 420 (36.4%) patients whereas 418 (99.5%) provided urine). This resulted in only 26.6% of patients being diagnosed with TB on day 1 using sputum Xpert MTB/RIF (G4) in the one cohort with systematic screening regardless of symptoms. In contrast, Alere diagnosed 43.3% and Fuji yielded 64.5% of diagnoses.

Conclusions: The Fuji LAM assay offers markedly superior diagnostic sensitivity, while maintaining specificity, in comparison to the Alere LAM assay. Given the superior diagnostic yield on day one of admission, this assay could transform tuberculosis diagnosis for people living with HIV who require hospitalisation.

	Microbiological Reference Standard (MRS) ¹ N=968		Composite Reference Standard (CRS) ² N=968	
	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Fuji LAM	75.8% [72.3-79.3]	91.0% [87.7-93.5]	69.0% [65.5-72.4]	96.0% [93.0-97.8]
Alere LAM	44.7% [40.7-48.7]	95.1% [92.4-96.9]	40.7% [37.1-44.4]	98.2% [95.8-99.2]
Difference (Fuji LAM - Alere LAM)	31.2% [22.6-39.3] significant	-4.1% [-17.9-9.8] not significant	28.4% [20.7-35.7] significant	-2.2% [-18.4-14.1] not significant

[Diagnostic accuracy of the novel Fuji LAM assay compared to the Alere LAM assay]

OA13-3277-26 Feasibility and acceptability of integrating paediatric TB and HIV case finding with integrated community case management of malaria, pneumonia and diarrhoea in Uganda

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Background: Childhood TB and HIV remain significant causes of under-five morbidity and mortality in Uganda, yet only 50% and 58% of children with TB and HIV respectively are diagnosed. To assess the feasibility and acceptability of incorporating TB and HIV components to the integrated Community Case Management of malaria, pneumonia and diarrhoea (iCCM) platform, UNICEF and WHO supported Ministry of Health to pilot the adapted WHO/UNICEF TB-HIV-iCCM guidelines in 3 districts.

Methods: WHO trained national trainers on the generic WHO/UNICEF TB-HIV-iCCM guidelines who incorporated TB and HIV components into the national iCCM packages. Packages were piloted in Wakiso, Sheema and Kayunga districts involving 18 trained health workers and 220 trained village health team members (VHTs) who were also mentored and supervised. VHTs assessed children in an integrated manner, identified and referred children at risk of TB and HIV to 13 linked facilities. Data on assessed cases, key informant interviews and focus group discussions was collected and analysed.

Results: From January to September 2017, 8,645 under 5-year-old children were assessed by VHTs using an integrated approach. Out of these children, 48 (0.6%) had TB exposure, 19 (0.2%) had HIV, 69 (0.8%) had known HIV exposure with unknown status and 96% were of 'unknown HIV exposure'. Stakeholders positively embraced the integrated approach and recognised its potential impact on TB and HIV case finding. However, stigma, non-disclosure of HIV status, non-uptake of referrals and weak community-facility linkages, minimal patient tracking and limited supplies negatively impacted children's access to TB and HIV services.

Conclusions: It is feasible to integrate paediatric TB and HIV risk assessment with iCCM without any negative impact on VHT's assessment for 'standard' illnesses. Revision of national iCCM guidelines to include TB and HIV is important to guide scale up of the integrated approach. Stigma, counselling, referrals, and health systems constraints need to be addressed.

OA13-3282-26 Effect of extensive tuberculosis screening before and after ART initiation in HIV-infected adults with $CD4 < 100$ /mm³: data from the ANRS 12290 STATIS trial

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Background: From 09/2014 to 04/2018, the STATIS randomized clinical trial evaluated systematic empirical tuberculosis (TB) treatment *vs.* extensive TB screening guided therapy in HIV-infected adults initiating antiretroviral therapy (ART) with $CD4 < 100$ /mm³ in Cambodia, Ivory Coast, Vietnam and Uganda. Here, we assessed the effect of the extensive TB screening before and after ART initiation on TB case detection.

Methods: In the extensive TB screening arm, ART-naive adults ready to start ART with no evidence of TB underwent systematic urine lipoarabinomannan (LAM), chest X-ray (CXR) and sputum Xpert MTB/RIF in addition to symptom assessment. After ART initiation, symptom screening followed, when positive, by CXR, Xpert MTB/RIF and urine LAM was repeated at 4 and 8 weeks. Sensitivity and negative predictive value of different screening tests was calculated using sputum Xpert MTB/RIF as reference standard.

Results: Overall, 525 patients (mean age 36 years, 57.8% male, 70.5% with CD4 < 50 cells/mm³) were analyzed. Before ART initiation, TB was detected in 39/370 (10.5%) and 12/155 (7.7%) patients with CD4 < 50 cells/mm³ and ≥ 50 cells/mm³, respectively (p=0.32). Xpert MTB/RIF was positive in 33/51 (64.7%) patients. Among asymptomatic patients, there was no positive Xpert MTB/RIF when CD4 count was ≥ 50 cells/mm³ and 9/119 (7.6%) when CD4 count was < 50 cells/mm³ (p=0.03). CXR and urine LAM had the highest negative predictive value in this last group (Table). By 8 weeks after ART initiation, 36/474 (7.6%) additional TB cases were detected: 27/331 (8.2%) among patients with CD4 < 50 cells/mm³ and 9/143 (6.3%) among patients with CD4 ≥ 50 cells/mm³ (p=0.48).

Conclusions: Extensive TB screening before and after ART initiation can detect a significant number of TB among severely immunosuppressed HIV-infected adults. At ART initiation, TB screening using CXR or urine LAM might be preferable than symptom screening alone in patients with CD4 < 50 cells/mm³.

	Overall		CD4 < 50 cells/mm ³		CD4 ≥ 50 cells/mm ³	
	SE, % (n/N)	NPV, % (n/N)	SE, % (n/N)	NPV, % (n/N)	SE, % (n/N)	NPV, % (n/N)
> 1 symptom	71.0 (22/31)	94.8 (165/174)	60.9 (14/23)	92.4 (110/119)	100 (8/8)	100 (55/55)
CXR	51.6 (16/31)	96.1 (371/386)	52.2 (12/23)	96.0 (263/274)	50.0 (4/8)	96.4 (108/112)
Urine LAM	32.2 (10/31)	95.1 (405/426)	43.5 (10/23)	95.6 (284/297)	0 (0/8)	93.8 (121/129)

[Sensitivity (SE) and negative predictive value (NPV) of symptom screening, chest X-ray (CXR) and urine lipoarabinomannan (LAM)]

OA13-3312-26 Mortality risk doubled in tuberculosis patients with diabetes not receiving metformin

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Background: Diabetes mellitus (DM) increases the risk of developing tuberculosis disease (TB), however its impact on unfavorable TB treatment outcomes is primarily based on retrospective studies. We assessed the impact of DM and use of metformin on TB treatment outcomes including all-cause mortality.

Methods: We conducted a prospective cohort study of patients with pulmonary TB with and without DM in India. Sputum specimen positive for acid-fast bacilli or GeneXpert-positive or culture positive TB cases with DM (HbA1c ≥ 6.5% or fasting glucose ≥ 126 mg/dl or random blood glucose > 200 mg/dl or self-reported DM history/treatment) or without DM were enrolled and evaluated for 18 months. Univariable and multivariable Poisson regression was performed to assess the effect of DM and use of metformin on a composite unfavorable TB treatment outcome of failure, recurrence and all-cause mortality.

Results: Of 756 enrolled, 202 (27%) had TB with DM and 554 (73%) had TB without DM. Of the 202 with DM, 105 (52%) reported metformin receipt. DM was not independently associated with increased risk of unfavorable treatment outcomes (adjusted relative risk [aRR] 1.17; 95% CI: 0.78 - 1.77, p=0.45) (Table).

Outcomes	Yes N (%)	No N (%)	Rate per 100PY	Unadjusted RR (95% CI)	Adjusted RR (95% CI)
Overall					
*Unfavorable outcomes					
No DM (n=554)	113 (20%)	441 (80%)	21.6	Ref	Ref
DM (n=202)	42 (21%)	160 (79%)	26.2	1.21 (0.83 - 1.74)	1.17 (0.78 - 1.77)
**All-cause mortality					
No DM (n=494)	41 (8%)	453 (92%)	8.4	Ref	Ref
DM (n=209)	22 (11%)	187 (89%)	14.2	1.73 (1.03 - 2.91)	1.28 (0.70 - 2.31)
Use of metformin among TB-diabetics***					
*Unfavorable outcomes					
On metformin (n=105)	16 (15%)	89 (85%)	18.7	0.87 (0.51 - 1.47)	0.87 (0.48 - 1.57)
Not on metformin (n=97)	26 (27%)	71 (73%)	34.6	1.60 (1.05 - 2.45)	1.41 (0.89 - 2.24)
**All-cause mortality					
On metformin (n=113)	8 (7%)	107 (93%)	9.3	1.10 (0.51 - 2.35)	0.99 (0.42 - 2.34)
Not on metformin (n=94)	14 (15%)	80 (85%)	20.5	2.58 (1.40 - 4.76)	2.03 (1.05 - 3.94)

*Unfavorable outcome includes treatment failure, recurrence and all-cause mortality.
**Recall ratio
***comparator=No DM
†adjusted for sex, age, household income, smoking, alcohol and body mass index and daily vs. intermittent

[Tuberculosis treatment outcomes by diabetes mellitus (DM), and use of metformin]

However, subgroup analysis restricted to DM patients found that metformin use was associated with lower risk of unfavorable TB treatment outcomes (aRR, 0.55; 95% CI: 0.28-1.07, p=0.08) after adjusting for potential confounders. Assessing individual treatment outcomes among patients with DM, metformin use was not as

sociated with lower risk of failure or recurrence but not receiving metformin was significantly associated with a 2-fold increased risk for all-cause mortality (adjusted hazard ratio, 2.03; 95% CI: 1.05-3.94, $p=0.04$) adjusting for age, sex, household income, body mass index, smoking and alcohol dependence (Table).

Conclusions: Not receiving metformin doubled the mortality risk among TB patients with DM, indicating anti-mycobacterial and host-directed therapy potential of this widely prescribed anti-DM drug.

OA13-3267-26 Co-existent burden of malnutrition and diabetes in Filipino people with Tuberculosis

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Background: Estimated TB incidence in the Philippines in 2016 was 555/100,000 population.

The END TB strategy recommends “All persons with TB need to be assessed for nutritional status and receive nutritional counselling and care according to need” and “all persons with TB should be screened for diabetes”. However, very little Filipino data exists to support policy implementation planning.

Methods: A cross-sectional study with active tracing sought to enroll all persons registered in public TB-DOTS clinics in Metro Manila ($n=3$, including 1 with an HIV clinic) and rural Negros Occidental ($n=2$). Research nurses assessed HbA1C, C-reactive protein (CRP) (Alere Affnion) and hemoglobin (Hemocue 301+) from finger-prick samples and conducted anthropometry. Diabetes was defined as HbA1C $\geq 6.5\%$ or current diabetes treatment. HIV screening required additional consent.

Results: 637 persons (70% male), aged 18-81 years (mean 45 years) with TB were enrolled. The prevalence of malnutrition (body mass index [BMI] < 18.5 kg/m²) was 36.6% (232/634), diabetes 9.2% (54/589) and moderate or severe anemia (hemoglobin < 11 g/dl), 13.6% (86/632) (Table 1). Malnutrition and anemia were more prevalent in rural clinics (Table 1) in women ($p < 0.001$), and; although they decreased in continuation compared to intensive treatment phase ($p=0.01$ & $p=0.002$), moderate & severe malnutrition and anemia remained high at 13.0% (16/123) and 8.1% (10/123) in months 5-6 of treatment. Neither were associated with HIV status. Diabetes was associated with higher BMI ($p < 0.001$) but was also detected in patients with malnutrition (5 mild, 2 moderate and 1 severe thinness). Of 24 persons on dia-

betes treatment, 56.5% (13/23) were poorly controlled (HbA1C $\geq 8\%$).

Conclusions: Malnutrition and diabetes are common in Filipino persons with TB and can co-exist in the same individual. Malnutrition and anaemia remain prevalent in the final months of treatment. Further investigation to determine malnutrition and diabetes associations with adverse treatment outcomes is ongoing in a prospective cohort.

	Urban (Manila)		Rural (Negros)		All (combined)		p-value
	N	n (%)	N	n (%)	N	n (%)	
Malnutrition	336		298		634		0.048
Non-wasted (BMI ≥ 18.5 kg/m ²)	228 (67.9)		174 (58.4)		402 (63.4)		
Mild (BMI < 18.5 -17.0 kg/m ²)	52 (15.5)		50 (16.8)		102 (16.1)		
Moderate (BMI < 17 -16.0 kg/m ²)	22 (6.5)		33 (11.1)		55 (8.7)		
Severe (BMI < 16 kg/m ²)	34 (10.1)		41 (13.8)		75 (11.8)		
Diabetes	325		264		589		0.316
No	299 (92.0)		236 (89.4)		535 (90.8)		
Yes	26 (8.0)		28 (10.6)		54 (9.2)		
Anaemia	336		296		632		0.038
Not anaemic (hbg $\geq 12/13$ g/dl F/M)	242 (72.0)		185 (62.5)		427 (67.6)		
Mild (hbg $< 12/13$ -11 g/dl)	55 (16.4)		64 (21.6)		119 (18.8)		
Mod or severe (hbg < 11 g/dl)	39 (11.6)		47 (15.9)		86 (13.6)		
HIV	338		299		637		<0.001
No	229 (67.8)		39 (13.0)		268 (42.1)		
Yes	74 (21.9)		2 (0.7)		76 (11.9)		
Unknown	35 (10.4)		258 (86.3)		293 (46.0)		

[Table 1: Prevalence of co-morbid malnutrition, diabetes, anemia and HIV by urban/rural clinic site]

OA11 The Union student late-breaker session on lung health

OA11-3314-26 Predictors for treatment outcome among drug-susceptible tuberculosis patients in The Netherlands

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Background: Since drug-susceptible tuberculosis (DSTB) is the most common diagnosis among TB cases in The Netherlands, targeting drug treatment among this group is essential to control drug-resistance and occurrence of new cases efficiently. The objective of this contemporary study was to analyze predictors for poor outcome of TB treatment among DSTB patients in The Netherlands.

Methods: We performed a retrospective inception cohort study using the Netherlands Tuberculosis Registry (NTR). We included adult patients with DSTB who started their treatment between 2005 and 2015. A set of potential predictors was examined using multivariate logistic regression analyses with two separate outcomes, i.e. unsuccessful treatment and TB mortality.

Results: Among 5,674 cases identified, the majority of patients were foreign-born (72%). The cumulative incidence for unsuccessful treatment and mortality were 2.6% and 2.0%, respectively. Significant predictors for unsuccessful treatment were age 18-24 years (Odds ratio (OR) 2.04, 95% confidence interval (CI) 1.34-3.10), homelessness (OR 2.56, 95% CI 1.16-5.63), prisoner (OR 5.39, 95% CI 2.90-10.05), and having diabetes (OR 2.02, 95% CI 1.03-3.97). Furthermore, predictors for mortality were age 74-84 years (OR 5.58, 95% CI 3.10-10.03), age above 85 years (OR 9.35, 95% CI 4.31-20.30), having a combination of pulmonary and extra-pulmonary TB (OR 4.97, 95% CI 1.42-17.41), having a central nervous system (OR 120, 95% CI 34.43-418.54) or military TB (OR 10.73, 95% CI 2.50-46.02), drug addiction (OR 3.56; 95% CI 1.34-9.47), and renal insufficiency/on dialysis (OR 3.23, 95% CI 1.17-8.96).

Conclusions: Our study showed that the outcome of DSTB treatment was as successful in foreign-born patients as in native-born patients. To avoid transmission and the development of drug resistance, special attention should be given to certain high-risk patients.

OA11-3348-26 A disputed *rpoB* mutation associated with rifampicin mono-resistant TB in Khayelitsha, South Africa

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Background: Rifampicin mono-resistant tuberculosis (RMR-TB) comprises 18% and 38% of all rifampicin-resistant TB (RR-TB) globally and in South Africa (SA). National surveys from SA show increasing RMR-TB among TB patients from 2001-02 (0.4%) to 2012-14 (2.9%); factors associated with this rise in RMR-TB are unknown. To assess possible differences in the emergence of rifampicin-resistance, we compared mutations conferring rifampicin-resistance between isolates from routinely diagnosed RMR-TB and multidrug-resistant TB (MDR-TB) patients in Khayelitsha, SA.

Methods: Stored pre-treatment isolates from RR-TB patients (diagnosed 2013-15) were re-cultured and whole genome sequencing (WGS) was performed. TB profiler was used to identify resistance-conferring mutations in *rpoB* and strain lineages. *rpoB* mutations were classified as high/moderate and minimal confidence in conferring rifampicin-resistance.

Results: WGS was conducted on 201 available stored pre-treatment isolates from 647 routinely diagnosed patients across 2013-15 (33 RMR-TB [16%], 168 MDR-TB [84%]). Among RMR-TB isolates, 9/33 (27%) had no *rpoB* mutation, while the predominant mutation in the remainder was L511P (9/24; 38%), reported as minimal confidence in conferring rifampicin-resistance. These isolates were not clonal based on WGS. The remaining 15/24 (62%) isolates had *rpoB* mutations with high/moderate confidence in conferring rifampicin-resistance. Among the 168 MDR-TB isolates, 21 (13%) had no *rpoB* mutation and 106/147 (72%) showed the high confidence S531L mutation. In contrast to RMR-TB, the L511P mutation was present in only 0.7% (1/147) MDR-TB isolates ($p < 0.01$, compared to RMR-TB). Lineage

4 predominated among RMR-TB isolates (14/24; 58%), while MDR-TB isolates were predominantly lineage 2 (104/147; 71%).

Conclusions: The predominance of the *rpoB* L511P mutation among RMR-TB isolates suggests a different evolutionary mechanism of rifampicin-resistance. Given the association of *rpoB* L511P with low-level rifampicin-resistance among RMR-TB isolates, it is possible that different treatment approaches could be effective for these patients. Moreover, there have been no clinical trials to optimise treatment of these patients.

OA11-3399-26 Manufactured-cigarette use and rolled-cigarette use in South East Asian countries: which product makes smoker more dependent?

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Background: Nicotine dependence of various tobacco products helps in its continued use and results in dose-dependent carcinogenic risk. This study estimates and compares dependence potential of manufactured- and rolled-cigarette in SEA countries.

Methods: Global Adult Tobacco Survey data of India, Indonesia, Bangladesh and Thailand (first-wave) was analyzed for dependence and its outcome indicators. Considering reliability and inter-country comparison, time-to-first-smoke (TTFS) and cigarette-per-day (CPD) were taken as indicator of nicotine dependence. Dependence outcome indicators like inability-to-quit and poor quit-intention were analyzed. The scoring for TTFS (range: 0-3) was done as per heaviness of smoking index scoring. The dependence scoring (range: 0-6) was estimated by taking into account TTFS, inability to quit and quit-intention. Analysis was done for exclusive users only.

Results: Exclusive use of manufactured- cigarette in SEA ranged between 0.8% in Indonesia to 9.3% in Thailand. Similarly exclusive use of rolled-cigarette was ranged from 0% in Bangladesh to 7.1% in Thailand. Mean CPD for rolled-cigarette was higher than that of manufactured-cigarette. Significantly higher proportion of rolled-cigarette users (range: 40.9-76.1%) smoked within 30 minutes of waking up than manufactured-cigarette (range: 32.8-57.8%) users. The proportion of rolled-cigarette using it within five minutes of waking up was 1.1 to 2.78 times higher than that of manufactured cigarette. Country wise mean TTFS score was higher for rolled- than manufactured cigarette. Mean dependence score was significantly higher across countries for rolled-cigarette (range: 4.4-5.45) than manufactured cigarette (3.2-4.16). The association between standard TTFS and dependence score was significant, positive and strong ($r > + 0.7$) for each country.

Conclusions: The higher dependence potential of locally made, less regulated and more dangerous rolled-cigarette than that of manufactured cigarette is a significant public health concern and needs to be addressed by contextual interventions. Dependence score can be used to measure the dependence potential of tobacco products.

OA11-3339-26 Mapping tuberculosis treatment outcomes in Ethiopia

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Background: This study aimed to determine whether the prevalence of poor TB treatment outcome varied geographically across Ethiopia at district and zone level and whether such variability was associated with socioeconomic, behavioural, health access, and climatic conditions.

Methods: A geospatial analysis was conducted using national TB data reported from June, 2015 to June, 2017. The prevalence of poor TB treatment outcome was calculated by dividing the sum of treatment failure, death and lost to follow-up by the total number of TB patients enrolled to the treatment. Binomial logistic regression models were computed and a spatial analysis was performed using a Bayesian framework. Estimates of parameters were generated using Markov chain Monte Carlo (MCMC) simulation. Geographic clustering was assessed using the Getis-Ord G_i^* statistic, and global and local Moran's I statistics.

Results: A total of 223,244 patients commenced on TB treatment were reported in Ethiopia, from 722 districts during the study periods. Of these, 63,556 (28.5%) were cured, 139,633 (62.4%) completed treatment, 6,716 (3.0%) died, 1,459 (0.65%) had treatment failure, and 12,200 (5.5%) were lost to follow up. The overall prevalence of poor TB treatment outcome was 9.0% (ranges, 1-58%). Hot-spots and clustering of poor TB treatment outcomes were detected in districts near the international borders in Afar, Gambelia, and Somali regions. Low wealth index (OR: 1.003; 95%CI: 1.00, 1.011), poor knowledge about TB (OR: 1.014; 95%CI: 1.002, 1.03), and annual mean temperature (OR: 1.148; 95% CI: 1.08, 1.21) were positively associated with poor TB treatment outcome.

Conclusions: This study showed significant spatial variation in poor TB treatment outcome in Ethiopia that was related to underlying socioeconomic status, knowledge about TB, and climatic conditions. Clinical and public

health interventions should be targeted in hot spot areas to reduce poor TB treatment outcomes and to achieve the national End-TB targets at low cost.

OA11-3307-26 Recurrent tuberculosis in the Netherlands

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Background: This study estimated the rates of reactivation and reinfection of tuberculosis (TB) patients diagnosed and treated in the Netherlands, after completed and interrupted treatment between 1993 until 2016. Additionally, risk factors for reactivation and reinfection were analyzed.

Methods: Retrospective cohort study of all culture-positive TB patients who completed or interrupted their treatment, registered in the Dutch Tuberculosis Register (NTR). All bacterial strains were typed with Restriction Fragment Length Polymorphism (RFLP) IS6110 and/or the Variable Number Tandem Repeat (VNTR) method. Reactivation was defined as an identical and reinfection as a non-identical *Mycobacterium tuberculosis* strain between two episodes. Cox regression analysis was used and person times in years (py) were calculated from the end date of treatment in the first episode until re-notification or 31 December 2016.

Results: A total of 16,283 patients were included. The overall rate of reactivation was 45 per 100,000 py for patients who completed their treatment and 219 per 100,000 py for patients who interrupted their treatment. The rate of reinfection for all included patients was 12 per 100,000 py. Among patients who completed treatment, male gender, poly/mono rifampicin resistance and a previous TB episode were independent risk factors for reactivation. Among patients who interrupted the treatment, directly observed treatment (DOT) and diabetes were significantly associated with reactivation. Extra-pulmonary TB was associated with a significant lower risk of both reactivation and reinfection. Even for patients who completed their treatment, the incidence rate of reactivation was >200 in the first two years and >50/100,000 py 2-5 years after treatment.

Conclusions: Patients with pulmonary TB are at risk for reactivation for at least five years after completing treatment. Good monitoring of these patients is indicated and guidelines should be in place to enhance early detection of recurrent TB.

OA11-3213-26 Prospective evaluation of candidate host immunological biosignatures as tools for the diagnosis of TB disease

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Background: The lack of simple, field-friendly point-of-care diagnostic tests remains one of the major challenges in the control of tuberculosis (TB), especially in resource-constrained settings. Host immunological biomarkers have previously been shown as potentially useful diagnostic tools for the disease.

Objectives: To validate recently identified host biosignatures and evaluate new candidate biomarkers as tools for the diagnosis of TB in six African countries.

Methods: Serum samples were collected from individuals who presented with symptoms requiring investigation for pulmonary TB at seven primary health care clinics situated in six African countries, prior to assessment for TB disease. Using a harmonized diagnostic algorithm comprising of laboratory, clinical and radiological findings, participants were later classified as having TB or other respiratory diseases. Biomarkers comprising a previously identified seven-marker serum protein biosignature (CRP, SAA, IFN- γ , IP-10, CFH, Apo-A1 and Transthyretin; replaced by Ferritin due to technical reasons), and other potentially new biomarkers selected from the literature were evaluated in all study participants using the Luminex multiplex platform.

Results: A total of 1004 participants, 278 of whom were diagnosed with active TB were included. The previously identified seven-marker biosignature validated on the new cohort with an area under the ROC curve (AUC) of 0.88 (95% CI 0.85-0.91) corresponding to a sensitivity of 84.3% and specificity of 77.7% respectively, regardless of HIV status or study site. A modified biosignature (CRP, SAP, NCAM, I-309 and GDF-15) diagnosed TB disease in a train sample set (n=677) with an AUC of 0.91 (95% CI 0.88-0.93).

Conclusions: We validated the previously identified seven-marker serum protein biosignature and furthermore, showed that refinement of the biosignature by substitution of some proteins with other biomarkers resulted in improved diagnosis of active TB, regardless of HIV status or African country sample origin. Our results pave the way for the development of a point-of-care screening test for active TB.

OA11-3295-26 Host biomarkers detected in Quantiferon Plus supernatants show promise as diagnostic candidates for active TB disease

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Background: The diagnosis of tuberculosis (TB) disease remains a challenge, especially in areas with limited resources. This is mainly due to limitations with the current TB diagnostic tests including poor sensitivity, costs, long turn-around times and the unavailability of rapid point-of-care tests. New TB diagnostic tests are therefore urgently needed. The QuantiFERON-TB Gold (QFT) Plus test is a recently introduced test for MTB infection. It is not known whether measurement of the levels of host markers other than Interferon-gamma in QFT Plus supernatants has potential in the diagnosis of TB disease.

Methods: We recruited participants presenting at a primary health care clinic in Cape Town, South Africa with symptoms requiring investigation for TB disease. Participants were later classified as TB or other respiratory diseases (ORD) based on the results of clinical and laboratory tests. We evaluated the concentrations of 37 host biomarkers in QFT Plus supernatants of study participants using a multiplex platform.

Results: Out of 120 individuals included in our study, 35 (29.2%) were diagnosed with active TB. Multiple host markers detected in the nil (unstimulated) and antigen-stimulated tubes showed potential as diagnostic markers for TB. However, the main findings of our study included the identification of a five-marker biosignature in the unstimulated supernatants (Apo-ACIII, CXCL1, MIG, MCP-2, NCAM) which diagnosed TB disease with sensitivity and specificity of 87% and 78% respectively; and a four-marker TB1 and TB2 antigen-specific biosignature which diagnosed TB disease with sensitivity and specificity of 73% and 85% respectively, after leave-one-out cross validation. These biosignatures were not affected by HIV infection.

Conclusions: Host biomarkers detected in QFT Plus supernatants may be useful in the diagnosis of active TB disease, regardless of HIV infection. Further validation studies are needed before such markers may be considered as candidate biomarkers for a blood-based diagnostic test for active TB.

OA11-3369-26 Genotype based clusters and spatio-temporal pattern of multi-drug resistant tuberculosis (MDR-TB) from an outbreak area in Thailand

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Background: An outbreak of multidrug-resistant *Mycobacterium tuberculosis* (MDR-TB) in Tha Maka district of Kanchanaburi province accepted since 2008 (Jiraphongsa *et al.*, 2011). This district is divided into 17 sub-districts with the total number of citizen was 92,164. In 2016, a total of 190 TB patients were registered and the annual rate of MDR-TB in new TB cases reached 20.73 %, which was 10-times higher than the national figure of 2.2%. The previous studies have confirmed clonal outbreaks of MDR-TB strains, however their epidemiological linkages remains elusive. This study aim to describe genotype based clusters and spatio-temporal pattern of these MDR-TB cases.

Methods: Currently, we evaluated drug resistance, strain diversity, and genetic clustering in patients diagnosed with MDR-TB during 2013 and 2017. Phenotypic drug susceptibility testing obtained from National Tuberculosis Reference Laboratory. The spoligotype pattern and WGS data were performed and analyzed using next-generation sequencing machine at Medical Life Science institute, Department of Medical Science.

Results: A total of 40 MDR-TB patients were evaluated, of which 2 were extensively drug-resistant TB (XDR-TB). Spoligotyping identified 5 different strains, the Beijing genotype being most prevalent including 36 patients (90%). Whole genome sequencing analysis showed 4 lineages and 5 sub-lineages of MDR-TB patient. The majority of these strains belong to lineage 2.2.1.

This 2.2.1 sub-lineage could be further stratified into 4 genetic clusters based on clustering analysis. The largest genetic cluster included 26 MDR-TB patients. The spatio-temporal pattern provided evidence of community transmissions in all sub-districts since 2013 and at 2017, the cases are distributed in 10 out of 17 sub-districts.

Conclusions: WGS detected several sub-clusters and micro epidemics of MDR-TB. It is crucially important for outbreak characterization. All clusters have different spatio-temporal pattern, suggesting that they have differential transmission capability. Their transmission is a serious public health threat so that their household transmission rates should be studied.

OA17 The Union/CDC (Centers for Disease Control and Prevention) late-breaker session on TB

OA17-3194-26 Non-invasive detection of tuberculosis by oral swab PCR analysis

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Background: Diagnostic tests for tuberculosis (TB) usually require collection of sputum, a viscous material derived from human airways. Sputum can be difficult and hazardous to collect from some patients, and challenging to process in the laboratory. Oral swab analysis (OSA) presents an alternative sample type that is non-invasive and easier to collect than sputum.

Methods: Oral swabs were collected from South African adults including Xpert MTB/RIF confirmed TB patients (N=138), symptomatic patients without TB (N=34), and QuantiFERON(QFT)-negative controls (N=37). In Phase 1 (blinded to diagnosis), symptomatic patients were recruited when presenting at the clinic for TB investigations; in Phase 2 (unblinded), only Xpert MTB/RIF confirmed TB patients were recruited. Oral swabs were collected using two swab brands in 3 sessions within 7 days after recruitment. Three sites in the oral cavity were compared. Swabs were analysed using a blinded, manual, non-nested qPCR targeting IS6110.

Results: In Phase 1, 61 TB cases were identified. Sensitivity was 80.3% (49/61) for sputum Xpert MTB/RIF and 82% (50/61) for OSA (2 swabs). In sputum Xpert MTB/RIF positive confirmed TB cases (n=49), OSA (2 swabs) sensitivity was 91.8% (45/49). OSA specificity in non-TB patients and QFT-negative participants was 91.5% (65/71). In Phase 2, 89 Xpert MTB/RIF confirmed TB cases were recruited. OSA (2 swabs) sensitivity was 93.3% (83/89) relative to sputum Xpert MTB/RIF. Tongue swabbing yielded significantly better results than cheek or gum swabbing. Day 2 oral swabs yield better results than Day 1 swabs. The inexpensive PurFlock swab brand yield better results than the Omniswab brand.

Conclusions: Sensitivity of OSA was consistent in the 2 phases and was comparable to sputum Xpert MTB/RIF results in all TB cases. OSA shows promise as an alternative specimen for TB diagnosis and could facilitate TB case-finding in situations that are limited by the physical or logistical challenges of sputum collection.

OA17-3294-26 Resistance to moxifloxacin and pyrazinamide in patients with recurrent tuberculosis in KwaZulu-Natal South Africa

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Background: The WHO Global Development Pipeline includes the combination of pyrazinamide and moxifloxacin in several rifampicin-sparing regimens and short-course multidrug-resistant tuberculosis regimens. Limited information on resistance to these drugs at the population and individual level is available globally or in South Africa. Recent surveillance data using genotypic or phenotypic methods, report high levels of resistance to pyrazinamide (50%-70%) for MDR-TB isolates in South Africa and lower resistance to moxifloxacin (0.9%-14%). We determine resistance to these drugs in patients with recurrent tuberculosis.

Methods: Phenotypic and genotypic resistance testing methods was conducted at baseline on Mtb isolates from patients with recurrent tuberculosis in the Improving Retreatment Success trial. Minimum-inhibitory concentrations (MIC's) were done in triplicate using agar-proportion method and resazurin-microtiter assay for moxifloxacin and pyrazinamide respectively. Whole genome sequencing (WGS) was used to determine mutations in the *pncA*, *rpsA*, *gyrA* and *gyrB* genes. Drug concentrations for moxifloxacin and pyrazinamide were measured in plasma using HPLC/MS-MS.

Results: MIC data for moxifloxacin and pyrazinamide was available for 58 and 48 isolates respectively. MIC for moxifloxacin was 0.125mg/L in 36/58 (62%) and 0.25mg/L in 22/58 (38%) and ≥ 100 mg/L for pyrazinamide in 33/48 (69%), of which 26/48 (54%) were ≥ 3600 mg/L. WGS data showed four mutations in the *pncA* gene (S65S/T) and 19 *rpsA* (R212R). Neutral variants in the *gyrA* gene (E21Q, S95T, G247S, and G668D) were found in 87% of isolates. Median (interquartile range) AUC and Cmax for moxifloxacin and pyrazinamide were 13.12h·mg/L (11.68-14.73) and 1.63mg/L (1.48-1.80) and 350h·mg/L (279-450) and 28.0mg/L (22.0-34.1) respectively.

Conclusions: We found no resistance to moxifloxacin and high resistance to pyrazinamide using phenotypic methods. Drug levels were low overall but above MIC in all patients for moxifloxacin, but not pyrazinamide, in more than 70% of patients. Pyrazinamide resistance may be driven by mutations outside of the *pncA* gene in our patients.

OA17-3113-26 Prevalence of latent tuberculosis among household contacts of patients with multidrug-resistant tuberculosis in Vietnam

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Background: Contacts of multidrug-resistant (MDR-TB) have a high risk of exposure to tuberculosis (TB), and are a high risk population for developing the disease. This study aimed to measure the prevalence of latent TB infection among household contacts of patients with MDR-TB.

Methods: We undertook a cross-sectional survey among household members of patients with MDR-TB in Viet Nam who agreed to be screened for participation in the VQUIN MDR trial. Household contacts were recruited from 132 clinics within the Programmatic Management of Drug Resistant TB (PMDT) program across 10 Provinces of the country. Eligible contacts of all ages had a clinical examination, chest radiograph and submitted one spontaneous sputum sample for Xpert MTB/RIF test to exclude active TB. LTBI status was established based upon a tuberculin skin test result of at least 10mm.

Results: The overall prevalence of TST positivity was 1,488/2,004 (74.2%). The prevalence of TST positivity was higher in male contacts, and higher in adults. Among children, TST positivity increased with age. Table 1 summarises the prevalence of latent TB infection in this population. The prevalence of bacteriologically confirmed TB was 30/2,004 (1.5%).

Conclusions: The prevalence of LTBI was high among household contacts of patients with MDR-TB. Further research is required to evaluate the effect of medications to prevent progression to active disease among this high-risk population.

Category	TST positive/Test read, n (%), using cut-off point of 10 mm	TB incidence (confirmed by Xpert/culture)	Category	TST positive/Test read, n (%), using cut-off point of 10 mm	TB incidence (confirmed by Xpert/culture)
Age <15 years	231/398 (58.0)	1/398	Age 15 years and above	1257/1606 (78.3)	29/1606
BCG scar present	213/398 (92.2)		BCG scar present	543/683 (79.5)	
Male	134/234 (58.0)		Male	483/594 (81.3)	
Female	97/164 (42.0)		Female	774/1012 (76.5)	

[Prevalence of TST positivity among contacts in 10 Provinces of Vietnam]

OA17-3440-26 Pharmacokinetics, safety and optimal dosing of linezolid in children with multidrug-resistant tuberculosis

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Background: Linezolid is increasingly important for multidrug-resistant tuberculosis (MDR-TB) treatment in adults and children. However there is no linezolid pharmacokinetic or prospective long-term safety data in children treated for MDR-TB, and its optimal paediatric dose for MDR-TB treatment has not yet been characterized.

Methods: South African children routinely treated for MDR-TB in two observational studies had pharmacokinetic sampling after either a single dose or multiple doses of linezolid (10 mg/kg/dose twice daily if < 10y or once daily if ≥10y). Linezolid pharmacokinetic parameters were described using non-linear mixed effects modelling. Children receiving long-term linezolid for their routine treatment had clinical and laboratory monitoring. Adverse events were assessed for severity and attribution to linezolid. Model simulations were used to estimate paediatric weight-banded doses resulting in exposures approximating a 600 mg once daily dose in adults.

Results: Forty-eight children were included (mean age 5.9 years, range 0.6-15.3); 2 were HIV-infected, 31 received single dose linezolid and 17 received multiple doses. The final model was one compartment characterized by clearance and volume parameters which included allometric scaling to account for weight; no other evaluated covariates contributed to the model. Simulated optimal weight-banded once daily doses ranged from 14.5 mg/kg (children 5 to < 7 kg) to 8.2 mg/kg (children 43 to < 56 kg). Linezolid-related adverse event occurred in 10/17 treated long-term, including 5 with a Grade 3/4 event, which were all anaemia. Adverse events resulted in linezolid dose reductions (n=4), temporary interruptions (n=5) or permanent discontinuations (n=4).

Conclusions: Linezolid exposures were satisfactory in this cohort of children with MDR-TB, compared to current target exposures. Linezolid-related adverse effects were frequent and occasionally severe; careful safety monitoring is required. Compared to doses currently being used in many settings for MDR-TB treatment in children, lower doses may approximate target exposures and should be evaluated in children.

OA17-3415-26 The Conundrum of Xpert MTB/RIF Ultra 'trace' in a high burden setting: to treat or not to treat?

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Background: The recently released Xpert Ultra is an optimised assay replacing the Xpert G4. Amongst the changes are the use of two additional targets (IS6110 and IS1081) which resulted in improved sensitivity (88%) for the detection of TB particularly in HIV positive and smear negative cases together with a reduction in specificity (96%). The latter is driven primarily among Xpert Ultra trace positives with previous TB treatment history resulting in "false positives" when assessing against culture and has created uncertainty.

Methods: South Africa's National TB prevalence survey is currently ongoing with 50 of 110 clusters already completed. Two sputum samples are collected from each eligible participant, one for Xpert Ultra and one for Bactec MGIT 960 culture. We performed a sub-analysis of all Xpert Ultra trace positives in the survey to determine the clinical relevance by factoring in the culture results, previous history of TB treatment and chest X-ray (CXR) results.

Results: A total of 43 Xpert Ultra trace results were detected since the beginning of the survey with 41 having a matched culture sample. Of the 41, 15 (36.6%) were culture positive with an average time to positivity of 17 days (range 13 - 29 days), 23 (56.1%) were culture negative and 3 (7.3%) samples were contaminated. The proportion of patients with abnormal CXR were similar in culture positive (100%) and negatives (96%) cases. Among the culture negative patients, 17/23 (73.9%) had reported a history of previous TB treatment, and of those with a CXR (22/23), all were abnormal. Among culture positive patients, 11/15 (73.3%) had no previous history of TB and of these, all had an abnormal CXR.

Conclusions: A trace result accompanied with a history of previous TB treatment is most likely to be false positive TB, while new cases are more likely to be true positive indicating active TB disease.

OA17-3403-26 Significant progress in TB vaccine development: insights from a phase 2b placebo-controlled trial of M72/AS01E

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Background: A safe, efficacious tuberculosis (TB) vaccine is essential for achieving the Sustainable Development Goal of ending the TB epidemic by 2030. The safety and efficacy of the candidate TB vaccine, M72/AS01_E, was assessed. There have been significant key insights from the design, conduct and analysis of this trial.

Methods: This randomized, double-blind, placebo-controlled, phase 2b trial (NCT01755598) was conducted in Kenya, South Africa and Zambia. Human immunodeficiency virus-negative adults aged 18-50 years with latent *Mycobacterium tuberculosis* infection (LTBI) were randomised (1:1) to receive intramuscular injections of either M72/AS01_E or placebo at 30 days interval and followed for ≥2 years for pulmonary TB confirmed by sputum PCR or culture. For 80% power assuming a true vaccine efficacy (VE) of 70% and 2-sided 10% significance level, using a log rank test, 21 cases were required for a fixed sample design.

Results: 3573 participants received M72/AS01_E or placebo. In this proof-of-concept trial, VE for prevention of TB disease was 54% (90% CI: 13.9-75.4; p=0.04). M72/AS01_E had acceptable safety and reactogenicity profile. Trial insights: strong community engagement was critical to timely completion of enrolment and high retention rates; population mobility proved to be a challenge in follow-up; endpoint enrichment was achieved by enrolling only individuals with LTBI; baseline TB screening did not add much value; the assumption of annual TB disease incidence of 0.55% confirmed by the observed incidence of 0.6% in placebo group demonstrated the need for robust epidemiological data; both liquid culture and PCR should be used for TB confirmation, as PCR had only 80% sensitivity compared to culture cases in this specific context of active TB case finding.

Conclusions: M72/AS01_E had an acceptable safety profile and was efficacious. The design, conduct and analysis of this trial could guide future TB vaccine studies.

Funding: GlaxoSmithKline Biologicals SA (sponsor); Aeras (funded by BMGF, DFID UK, DGIS, AusAID)

OA17-3308-26 TB & leprosy free Majuro: early findings of a mass TB and leprosy screening and treatment program in the Marshall Islands

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Background: The Republic of the Marshall Islands (RMI) currently has the world's 11th highest TB incidence (422/100,000. WHO 2016 data). In 2017 mass TB screening in Ebeye island diagnosed active TB rate of 846/100,000 and greatly expanded local TB program capacity. In June 2018, the government of RMI began an ambitious program to screen and treat all persons in Majuro, its largest population centre, for active and latent tuberculosis.

Methods: All consenting individuals participated in screening according to an age-based protocol using tuberculin skin test (aged ≥ 5), symptoms, contact history and chest x-ray; if any of these were abnormal, sputum was collected for GeneXpert. Children < 10 received a TB-focused physical examination prior to consideration of chest x-ray. A screen for leprosy was incorporated for all individuals, as well as diabetes testing for adults with latent or active TB. Cases were reviewed by an expert panel to confirm diagnosis and initiate standard TB treatment. After ruling out active TB, individuals with latent TB were immediately commenced on treatment with short-course rifamycin-based therapy. Those under 5 were considered for latent treatment if they had documented household exposure to a TB case.

Results: As of August 1, 2018, one-half of the target population completed initial TB screening. Preliminary screening results are recorded in Table 1.

	First screening (at home)	Completed screening	Active TB diagnosis	Latent TB diagnosis	Recommended for latent TB treatment	Started latent TB treatment	New diagnosis of leprosy	Diabetes	New diagnosis of diabetes
Paediatric (0-14)	3,983	3,096	35	261	261	233	7	-	-
Adult (15+)	8,095	6,237	74	2163	1,909	1,856	19	594	190
Total	12,078	9,333	109	2424	2,170	2,089	26	594	190
Comment	51% of population reached second visit for on-going	77% completed second TST reading/eval	Initial active TB rate 1,168 per 100,000 screened	26% screened were diagnosed with latent TB	10% not medically eligible for treatment	96% of eligible patients started latent TB treatment	Initial Hansen's rate 27.9 per 10,000 screened	30% screened have previous history of diabetes or A1c >6.5	10% screened were newly diagnosed

[Table 1: Initial screening results for TB+Leprosy Free Majuro (Week 7 of 14, August 1, 2018)]

The initial rate of active TB is 1,168/100,000 screened. Overall TST-positivity was 26%. Among individuals offered treatment for TB infection, 96% have commenced treatment.

Conclusions: With strong national commitment and international technical support, it is possible to bring organized mass TB-prevention activities to large active case finding campaigns in high-burden countries. Initial data indicated a very high rate of acceptance of latent TB treatment. The added effect of mass TB prevention to an active case finding project could be quite significant but will likely take several years to assess.

OA17-3416-26 Addressing policy needs for controlling TB and multidrug-resistant TB (MDR-TB): a biosocial inquiry among patients in Pune city in Western Maharashtra, India

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Background: Globally, India carries the highest burden of tuberculosis (TB) and multidrug-resistant tuberculosis (MDR-TB) cases. We sought to understand the care-seeking experience and quantify delays in care for patients with TB using a mixed methods approach.

Methods: Using a structured interview tool and an in-depth interview guide, we interviewed 168 TB patients (117 non-MDR and 51 MDR) during Jan-July 2018. Differences between the two groups were calculated using Fisher's exact test and Mann-Whitney U test (Table 1).

Results: Overall, 64% patients were young (15-35 years) with a higher proportion in MDR group than Non-MDR. Seventy percent of patients resided in crowded localities such as slums and chawls with a higher proportion in the MDR group. Patients were predominantly housewives, students and unemployed. More MDR than non-MDR cases reported a history of TB; 66% had prior anti-TB treatment under the Revised National TB Control Program (RNTCP), 24% under the private sector and 10% in both sectors. Delays in initiating appropriate anti-TB therapy were considerable for both groups, but significantly higher for MDR-TB. Delays in MDR care were due to initial treatment in private sector, low suspicion for MDR, delay in using GeneXpert and inappropriate first-line treatment by some RNTCP providers. Furthermore, 30% patients among MDR and 19% among non-MDR group mentioned interruption for < 2 weeks in an ongoing treatment. Reasons include the lack of knowledge about TB, treatment side effects, poor counseling by health staff and that patients' own misconceptions.

Conclusions: A high proportion of young patients in the MDR group suggests that MDR-TB is being fueled by an ongoing DR transmission in crowded localities. Our analysis indicate target groups for suspecting TB and MDR and warns against the blanket use of first-line treatment. It also highlights the need for timely use of GeneXpert, and for improving counseling skills among TB care providers.

Parameter	MDR-TB (n=51)	Non MDR-TB (n=117)	p- value
Duration between onset of symptoms and start of appropriate anti-TB treatment	Range: 15 days to 1 year Median: 150 days (IQR: 60-395)	Range: 15 days to 3 years Median: 60 days (IQR: 30-90)	<0.01** (Mann-Whitney U test)
Young age group (15-35 years)	75%	58%	0.03* (Fisher's exact test)
Spend 24 hours in crowded locality	80%	65%	0.05 (Fisher's exact test)
Prior history of TB	72.5%	21.1%	<0.001** (Fisher's exact test)

[Table 1: Comparison between MDR-TB and Non-MDR-TB group]

Results: 6 were found to be positive among the 50 symptomatic farm workers and 21 cattle were found to be positive by comparative intradermal test (CIT). 6 animals were subjected to postmortem examinations deceased due to severity of the disease. Spoligotyping revealed the presence of East African Indian (EAI), MANU, U and orphan strain among the cattle whereas all 6 cattle handlers were identified to be EAI.

Two strains from cattle were identified as *M. orygis* by WGS and a single nucleotide polymorphisms (SNP) difference of 4, 7 and 16 was found between the strains indicating transmission at the animal-human interface.

Conclusions: To best of our knowledge this is the first study to screen cattle handlers and cattle simultaneously for tuberculosis in India. This study has brought to light the possibility of transmission of *M. tuberculosis* between human and cattle. This is the first report of isolation of *M. orygis* from Indian cattle. The study emphasizes the urgent need for the one health approach warrant a detailed epidemiological investigations where complex interaction of the environment, hosts and TB pathogens involved.

OA17-3302-26 Isolation and molecular typing of *Mycobacterium tuberculosis* isolated from farm workers and cattle from south India

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Background: Bovine tuberculosis (bTB) is one of the important areas of concern because of its serious impact it causes on economic losses and public health. Reverse zoonosis due to *M. tuberculosis* in bovine is increasingly being reported from high burden TB countries including India. We hypothesised transmission of *Mycobacterium tuberculosis* complex (MTBC) between farm workers and cattle is prevalent in Chennai region, south India.

Methods: A total of 271 farm workers and 167 cattle were screened for tuberculosis in 2 organized and 1 unorganized farms in Chennai. The samples were further analyzed by acid fast staining, culture, polymerase chain reaction (PCR), spoligotyping, drug sensitivity test (DST) and whole genome sequencing (WGS). Postmortem examinations were conducted for severely diseased cattle.

TBSCIENCE2018 ORAL ABSTRACTS

Parallel session on reducing transmission: what is the scientific basis behind for the reduction of transmission and the initiation of appropriate treatment?

3095 The effect of Beijing lineage on TB transmissibility and disease progression

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Background: Previous studies on the relative transmissibility and propensity to cause disease of the *Mycobacterium tuberculosis* (MTB) Beijing lineage have been inconclusive. Most of these followed household contacts (HHCs) of index patients infected with known MTB strains and included adults who may have been infected in the past or in the community. Here, we studied the impact of exposure to index patients infected with Beijing strains in child HHCs whom we deemed less likely than adults to have been exposed outside the household.

Methods: Over a 36-month recruitment period in Lima, Peru, we identified 4,500 index patients with suspected pulmonary TB, of whom the infecting MTB strain was ascertained in 2,530. We prospectively followed 4,468 HHCs aged 15 and younger of 2,136 index patients for TB infection with a tuberculin skin test (TST) at baseline, 6, and 12 months among those who had previously tested negative and for TB disease at baseline, 2, 6, and 12 months. We used a modified Poisson generalized estimating equation to estimate the risk ratio (RR) for baseline infection and Cox frailty proportional hazards models to estimate hazard ratios (HRs) for incident infection and disease.

Results: Among 4,468 child HHCs, 1,140 (25.5%) were infected at baseline, 530 (11.9%) converted their TST, and 206 (4.6%) developed disease during follow-up. Compared to child HHCs exposed to index patients with non-Beijing strains, those exposed to Beijing strains were more likely to become infected (adjusted HR, 1.70, 95% CI, 1.22-2.36) and develop disease (adjusted HR, 1.85, 95% CI, 1.03-3.32) during follow-up. We found no statistically significant difference in the risk for baseline infection (adjusted RR, 1.18, 95% CI, 0.97-1.43) among child HHCs exposed to Beijing strains compared to non-Beijing strains.

Conclusions: Children exposed to MTB Beijing strains were at higher risk for incident infection and disease compared to those exposed to other strains.

Parallel session highlighting the latest developments in the area of tuberculosis vaccines

3139 An incomplete vaccine? RD5-mediated secretion defect in BCG vaccine strains results in reduction of antigenic repertoire but little impact on protection

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Background: Although the BCG vaccine is widely used, it does not efficiently protect against pulmonary tuberculosis and an improved tuberculosis vaccine is therefore urgently needed. *Mycobacterium tuberculosis* uses different ESX/Type VII secretion (T7S) systems to transport proteins important for virulence and host immune responses. We recently reported that secretion of T7S substrates belonging to the mycobacteria-specific PE-PPE proteins of the PGRS and MPTR subfamilies required both a functional ESX-5 system and a functional PPE38-protein for secretion. *ppe38*-deletion increased virulence of *M. tuberculosis* strains (Ates et al 2018). Here we investigated the effect of the *ppe38*-encompassing RD5-deletion in BCG on immune responses elicited by this vaccine.

Methods: We use various in vitro and in vivo (mouse) methods that are detailed in Ates et al 2018 PLoS Pathogens 2018.

Results: The RD5-deletion in BCG was indeed associated with a secretion defect of all detected PE_PGRS and PPE-MPTR proteins (a total predicted 89 substrates), which could be partially complemented. Epitope mapping of the PPE-MPTR protein PPE10 provided evidence of its potential immunogenicity and allowed monitoring of T-cell responses from BCG/*M. tuberculosis* immunized mice, confirming the dependence of PPE10-specific immune-induction on PPE38-mediated

secretion. Restoration of PE_PGRS/PPE-MPTR secretion in recombinant BCG neither altered global antigenic presentation or activation of innate immune cells, nor protective efficacy in two different mouse vaccination-infection models.

Conclusions: The BCG vaccine strain is unable to secrete to major groups of PE-PPE proteins, some of which are immunodominant antigens possibly important for protection against tuberculosis. Many of these PE-PPE proteins also have been ascribed immunomodulatory characteristics, but we found no direct evidence of skewed immune responses elicited by BCG or Mtb strains with or without this secretion defect.

These unexpected finding stimulates a reassessment of the immunomodulatory properties of PE_PGRS/PPE-MPTR proteins, some of which are contained in vaccine formulations currently in clinical evaluation.

Parallel session Tuberculosis Surveillance and Research Unit meeting: innovations in the production and use of surveillance data

3244 Mixture analysis of tuberculin data to estimate incidence of *Mycobacterium tuberculosis* infection

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Background: Serial tuberculin skin tests (TST) have been used to estimate incident *Mycobacterium tuberculosis* (*M.tuberculosis*) infection in young children. However, ‘boosting’ of pre-sensitisation to mycobacterial antigens from BCG and/or repeat testing, complicate interpretation. We present a novel use of mixture analysis to determine the optimal cut-off to estimate incidence of *M.tuberculosis* infection in a population.

Methods: Children aged under 6 years of age resident within a demographic surveillance site in Malawi were recruited. TST was performed at baseline and repeated after 1-2 years.

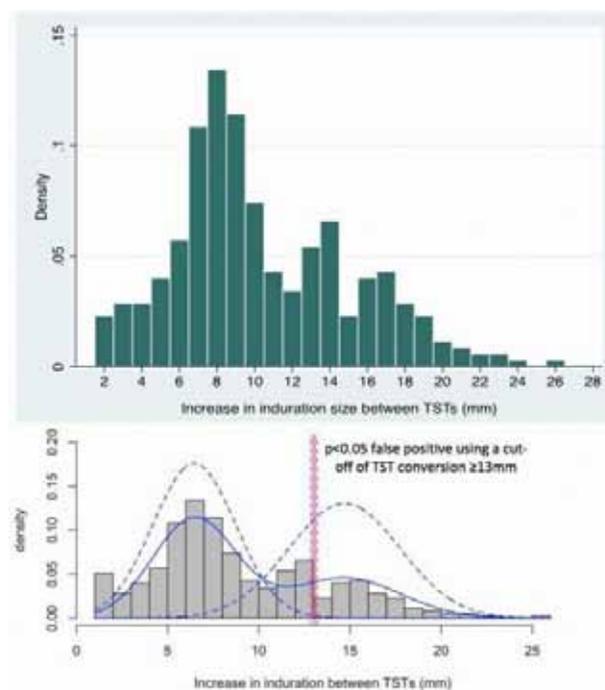
Mixture analysis of the tuberculin data was based on implementation of the Expectation Maximisation algorithm by fitting a finite mixture model to the observed profiles of the increment in induration size in mm. The fitted finite mixture model was used to identify a cut-off value that discriminated the two modes of the dataset,

corresponding to ‘boosting’ and true *M.tuberculosis* infection respectively. All analyses were undertaken in R and Stata 15.0.

Results: The median time between TSTs was 1.7 years (IQR: 1.1 to 2.6 years). The frequency distribution of all increments (range 2 to 26mm) between serial TSTs is shown in the Figure (a). Mixture analysis generated a two-component distribution; the mean (and standard deviation) were 6.5 (2.3), and 14.7 (3.1) for the 1st and 2nd peak respectively. The derived cut-off point using the finite mixture model was 12.8 (95% CI 12.6 - 13.0). See Figure (b)

A TST conversion of 13mm was chosen to define incident *M.tuberculosis* infection to minimise false positives. Among the 3066 children who underwent serial TST, 91 children TST-converted (3.0%), giving an incidence of 1.6 per 100 person-years (95% CI: 1.3 - 2.0 per 100py).

Conclusions: Estimates of incident *M.tuberculosis* infection risk in young children may provide a critical indicator of ongoing community transmission of *M.tuberculosis*.



[Figure. (a) Histogram of increase in induration size between 1st and 2nd TST [n=350] (b) 2-component mixture model based on implementation of Expectation Maximization (EM) algorithm to derive the cut-off value for TST conversion (KEY: grey bars = histogram bars; blue solid line = kernel density estimation of the distribution; blue dashed line = finite-mixture model; red solid line = cut-off value; red dashed lines = 95% CI around cut-off value)]

Parallel session on reducing transmission: what is the scientific basis behind for the reduction of transmission and the initiation of appropriate treatment?

3274 Automated algorithm for early identification of rifampicin-resistant tuberculosis transmission hotspots in Rwanda

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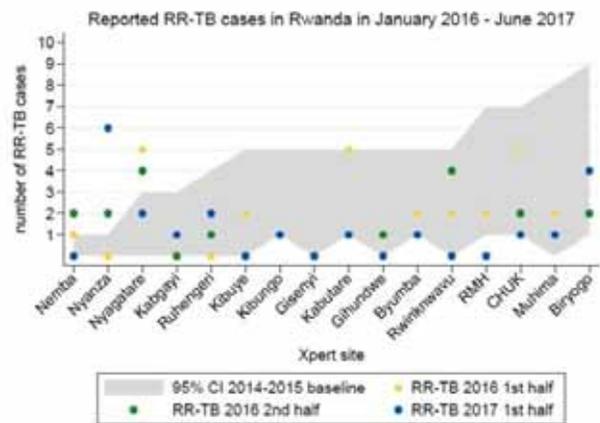
Background: Rwanda is moving towards using Xpert MTB/RIF (hereinafter called Xpert) as the initial diagnostic test for all presumptive TB patients. The utility of Xpert results for improving rifampicin-resistant TB (RR-TB) surveillance has not yet been explored. Leveraging on the existing connectivity platform in Rwanda, we explored whether routine retrospective Xpert data can be used for early identification of potential RR-TB transmission hotspots. Ultimately, we aim to develop an automated algorithm within the connectivity platform for RR-TB surveillance by the Rwandan national TB control program (NTP).

Methods: We gathered 118,760 Xpert results generated in 2012 -2017 from 46 Xpert sites in Rwanda. Employing Poisson regression on half-year data from 2014-2015, we modelled the expected number of RR-TB cases by Xpert site. We then compared these expected numbers with the actual half-year frequencies of RR-TB by Xpert site from January 2016 - June 2017.

Results: We observed missed probe E in 81% of all RR-TB cases detected. For most Xpert sites, the actual reported number of RR-TB cases were within the 95% confidence interval of expected numbers in previous years. Three sites with higher than expected number of RR-TB cases were identified, indicating unusual spatial clustering of cases that define potential transmission hotspots (Figure 1).

Conclusions: The utility of probe information on the distribution of RR-conferring mutations in this dataset is limited due to low heterogeneity in the individual probe results. Our study shows that retrospective routine Xpert data can be utilized to identify Xpert sites with unexpected RR-TB cases (Figure 1). An RR-TB case

above the expected range is a flag for the NTP to suspect an outbreak and investigate further on the case, whereas a case below baseline may indicate operational diagnostic issues. This algorithm may be run for half-year periods within the connectivity platform for early identification of potential RR-TB transmission hotspots.



[Figure 1. Reported half-year-RR-TB cases in Rwanda in January 2016 - June 2017 plotted against 2014 - 2015 baseline prevalence within 95% CI for the 16 Xpert sites analyzed.]

3297 Can we find the missing men in clinics? Clinic attendance by sex and HIV status in rural KwaZulu-Natal, South Africa

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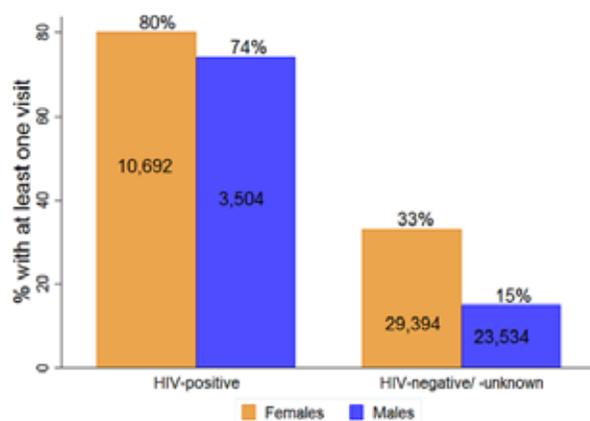
Background: African national TB prevalence surveys suggest that HIV-negative men are over-represented among people with undiagnosed TB, and thus are a key population for case-finding; it is unclear where case-finding efforts should be targeted. The aim of the study was to determine the frequency of primary healthcare clinic (PHC) attendance among HIV-negative men.

Methods: This study was conducted among adult (≥ 15 years) residents of a demographic surveillance area (DSA) in rural KwaZulu-Natal, South Africa. Since January 2017, all people attending the 11 PHCs in the DSA were asked their reason for attendance. This information was retrospectively linked with demographic surveillance data and HIV status from DSA sero-surveys. HIV status was defined as positive if the individual tested positive in the sero-survey or clinic attendance for HIV care was recorded; negative if tested negative between Jan 2014—Dec 2017 and had no HIV-related

visits; unknown otherwise. The frequency of clinic attendance during April 2017-March 2018 was calculated by sex and HIV status.

Results: Among 67,124 resident adults in the DSA, 27,038 (40%) were male; 14,196 (21%) were HIV-positive, 18,892 (28%) were HIV-negative and 34,036 (51%) were HIV-unknown. 24,382 (36%) resident adults visited a PHC at least once during the study period. Among HIV-positive individuals, 80% (N=8554) of women and 74% (N= 2593) of men ever visited a PHC for any reason (Figure 1). Among HIV-negative or HIV-unknown individuals, 33% (N=29,394) of women and 15% (N=23,534) of men ever visited a PHC. Overall, HIV care accounted for 43% (37,556/88,109) of all visits made by adults.

Conclusions: In this rural DSA population, HIV-negative and -unknown men rarely attend PHCs. Improving TB screening in clinics may not reach a key population with respect to undiagnosed TB. Additional strategies are likely to be needed to diagnose and treat TB earlier, particularly in men.



[Proportion of adults making ≥ 1 clinic visit (for any reason) during the study year]

Parallel session Tuberculosis Surveillance and Research Unit meeting: innovations in the production and use of surveillance data

3332 An evaluation of a systematic screening intervention among elderly populations in rural Cambodia

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Background: Cambodia, a high TB burden country, has seen a significant decrease in tuberculosis (TB) incidence from 575 (2000) to 380 per 100,000 (2015). However, the rate is only decreasing by 2.8% since 2010. Cambodia's elderly population (≥ 55 years) accounts for 50% of the TB burden and is often unable to access care. The Cambodian Anti-Tuberculosis Association (CATA) intervention aimed to increase the TB notification rate amongst elderly TB patients.

Methods: In 2017, CATA built on and expanded their successful approaches first piloted in a TB REACH Wave 3 intervention (2014) in 8 districts in rural Cambodia. Mobile teams equipped with a chest x-ray (CXR) and Xpert MTB/RIF Ultra (Xpert) visited health facilities to screen all elderly individuals. Those with an abnormal CXR or those with a normal CXR but with positive TB symptoms were subsequently tested with Xpert. Patients with positive Xpert results (Bac+) were linked to the National TB Program for treatment. TB case notification data from the intervention period (June 2017 - April 2018) was compared to a historical baseline and to a control population to assess impact.

Results: In 2017, 127 health facilities were visited, 53,098 elderly were screened by CXR, 9,705 (18.3%) were tested with Xpert, and 777 (8%) were found to be Bac+. New Bac+ TB notifications increased by 76% (all ages) and 151% (≥ 55 years) compared to a historical baseline. Adjusting for a 3-year trend and compared to a control group (standard care), there was a 45% increase (all ages) and a 65% (≥ 55 years) increase in TB case notifications during the intervention period.

Conclusions: CATA's intervention in 2017 was successful in finding additional TB cases in both elderly and all ages populations. This illustrates the importance of implementing sustainable active case finding interventions in Cambodia.

3368 High incidence of active tuberculosis in Eritrean and Somalian asylum seekers after arrival in the Netherlands: time for a screening programme for latent infection

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Background: The Netherlands is a low-incidence country for tuberculosis (TB). In 2017, 75% of 787 cases were foreign born. Asylum seekers from Eritrea and Somalia accounted for 23% of all cases. Upon arrival, migrants from high-incidence countries are screened for active TB. To inform policy makers on the value of additional screening on latent TB infection (LTBI), we analysed incidence rates of TB in Eritreans and Somalians in the first five years after arrival.

Methods: In this retrospective cohort study, we included Eritreans and Somalians (first applicants, family reunifications and invited refugees) who arrived in the Netherlands between 1-1-2013 and 31-12-2017 and calculated TB prevalence at arrival and incidence rates over the first five years after arrival, using data from the Immigration and Naturalisation Service and the National TB Register. A cox regression model was used to analyse the effect of age, sex and country of origin on TB incidence.

Results: The study population consisted of 21,182 Eritreans and 4,875 Somalians with median follow-up periods of 28 and 49 months. TB prevalence at entry screening was 274 (95% CI 211-354) and 328 (201-535) per 100,000 Eritreans and Somalians respectively. Incidence rates were 941 (809-1,090) and 1,107 (846-1,449) per 100,000 person-years in the first year after arrival, 591 (446-781) and 621 (423-912) in the third year, and 309 (44-2,195) and 81 (11-575) in the fifth year (Table).

	IR 1st year (95% CI)	IR 2nd year (95% CI)	IR 3rd year (95% CI)	IR 4th year (95% CI)	IR 5th year (95% CI)
Eritreans	941 (811-1,090)	755 (626-910)	591 (446-781)	150 (62-360)	309 (44-2,195)
Somalians	1,107 (846-1,449)	918 (678-1,242)	621 (423-912)	260 (135-500)	81 (11-575)

[Incidence rates (IR) per 100,000 person-years in Eritreans and Somalians in the 1st, 2nd, 3rd, 4th and 5th year after arrival in the Netherlands]

The hazard ratio (HR) was higher among Eritrean adults (≥ 18 years) and males (HR 3.5; 95% CI 2.5-4.9 and 1.6; 1.3-2.1), and among Somalian adults (3.6; 2.6-5.2).

Conclusions: The high TB incidence rates in Eritreans and Somalians in the first years after arrival support the introduction of LTBI screening for asylum seekers from similar high-incidence countries. A substantial number of TB cases and possible transmissions within the Netherlands could be avoided with screening and treating them for LTBI.

Parallel session on reducing transmission: what is the scientific basis behind for the reduction of transmission and the initiation of appropriate treatment?

3478 Deriving Mycobacterium tuberculosis transmission between risk-groups in low-incidence setting using MIRU-VNTR fingerprints and WGS combined

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Background: To better inform TB control policy in low-incidence countries, it is important to assess the extent of transmission between different risk groups, as for example immigrants from high- versus low-incidence countries and natives. Earlier estimates for transmission from non-natives to natives are mostly low, but quite divergent across EU countries, and transmission estimates between different nationalities are few. Many are based on low-resolution molecular fingerprinting techniques; the advent of whole genome sequencing (WGS) in the context of TB surveillance allows us to review these estimates.

Methods: To that end, we developed a framework to derive transmission between and within selected risk groups. We here focus on nationalities with relatively high TB burden in the Netherlands over the years 2016-2017. Both 24 loci-MIRU VNTR fingerprinting and whole genome sequencing (WGS) were carried out on all culture-positive isolates in the Netherlands in 2016 and 2017. We first derived a maximum likelihood phylogeny using a Bayesian approach (BEAST2), with a new addition using both VNTR and WGS data (BEASTvnr). We then applied a cluster-picking algorithm (Cluster Picker) to identify clusters of cases, assuming transmitted cases differ less than 12 SNPs from each other. Based on these clusters, transmission within and between nationalities could be traced. As a control, we use the same phylogeny (*i.e.* tree topology), but with randomly reassigned tips.

Results: Combining VNTR and WGS data offers a high-resolution phylogeny, that allows, through cluster analysis, to derive transmission rates between chosen risk groups. While most transmission occurs within nationalities, the extent of cross-nationality transmission differs between groups.

Conclusions: Sequencing data complements fingerprint data for the derivation of transmission among TB risk groups in low-incidence settings.

Parallel session highlighting the latest developments in the area of tuberculosis vaccines

3500 Imprinted DNA methylation perturbations persist after successful anti-tuberculosis therapy

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Background: Epigenetic modifications determine immune cell phenotype. Vaccines and infections induce long lasting epigenetic alterations to host immunity. While usually controlled by host immunity, deficits in cell-mediated immunity increase the risk of *Mtb* infection progressing to disease. Elucidation of epigenetic regulation of anti-mycobacterial immunity will help clarify mechanisms of immune exhaustion and identify novel host-directed immunotherapy.

Methods: Genome-wide DNA methylation (DNA MethylEPIC) and methylation-sensitive restriction enzyme (MSRE) PCR, gene expression (Nanostring and targeted rt-PCR gene expression) and flow cytometry-based *Mtb*-specific multi-dimensional immune profiling was completed among isolated CD4+ T cells and bulk peripheral blood mononuclear cells (PBMCs) provided by a cohort of HIV infected and uninfected individuals with TB and their asymptomatic household contacts.

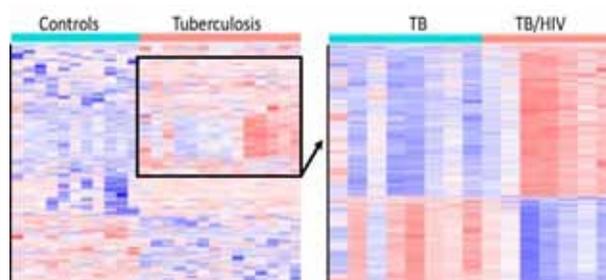
Results: DNA methylation studies demonstrated that TB patients had DNA hyper-methylation in the IL-7, IL-12, IFN- γ , and TCR -signaling pathways. These hyper-methylated differences were validated by MSRE-PCR. Pioneer and Transcription factors critical for cell-mediated immunity were also differentially methylated. A

distinct DNA methylation landscape discriminated TB diseased from TB-HIV co-infected individuals (Figure). To functionally validate alterations in DNA methylation, cells were stimulated with IFN- γ and demonstrated a decrease in IFN- γ -inducible gene expression among TB patients with hyper-methylation of the IFN- γ signaling pathway. Six months after the completion of successful Anti-tuberculosis therapy (ATT), participants with TB had persistent hyper-methylation of the IL-12, IFN- γ , and TCR-signaling pathways.

Conclusions: Chronic infections (LCMV in mice, and HIV and helminth infections in humans) induce persistent imprinted epigenetic alterations that alter host cell-mediated immunity. Similarly, our findings demonstrate that individuals who develop TB

i) exhibit DNA hyper-methylation of genes critical to intracellular cell-mediated immunity, and

ii) retain these perturbations for at least 6 months after the completion of successful ATT. Studies should evaluate if these persistent epigenetic perturbations inhibit vaccine immunogenicity or underlie recurrent TB.



[DNA Methylation Landscape discriminates asymptomatic *Mtb* infected from TB or HIV/TB.]

TBSCIENCE2018 POSTERS: TUESDAY, 23 OCTOBER 2018

3026 Multi-biomarker test for point-of-care screening for active tuberculosis: a five country multi-center test evaluation

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Background: Inexpensive rapid screening tests applicable at the point-of-care (POC) are vital to combat tuberculosis. Particularly, minimally invasive, non-sputum-based biomarker tests for all TB forms can help control transmission. Availability of such tests would significantly accelerate and streamline diagnostic approaches, improve cost-efficiency and decrease unnecessary costly GeneXpert referrals.

Methods: Multi-biomarker test (MBT) strips measuring levels of selections of up to six serum proteins simultaneously on one lateral flow (LF) strip were produced. The strips contain individual capture lines for selected analytes composing a biosignature that distinguishes TB patients from other respiratory diseases (ORD) in the same geographical setting. Quantitative signals are recorded with a low-cost, handheld reader compatible with the applied luminescent up-converting particle (UCP) label. Biomarker selection for application on MBT strips and algorithms used to distinguish potential TB and ORD are flexible.

Results: Results obtained with MBT strips correlate well with singleplex LF strips for each marker. Using LF tests for 5 selected biomarkers sensitivity and specificity achieved were 94% and 96% respectively based on a South-African cohort. Patients were designated TB positive when scoring a value above the cutoff threshold for at least 3 out of 5 biomarkers. Serum samples of potential TB patients collected at five medical research institutes (Ethiopia, Namibia, South-Africa, The Gambia, Uganda) were tested locally with MBT strips and results analyzed to obtain an overall pan-Africa applicable signature.

Conclusions: Evaluated POC applicable UCP-LF devices detecting serum biomarker signatures can help to distinguish active TB from ORD and as such can pri-

oritize highest risk patients for further care. Ongoing prospective studies evaluate the MBT strip with finger-stick avoiding requirement of a laboratory or trained phlebotomists.

3133 Interruption of anti-tuberculosis drugs among adolescent and young adults ages 10-30 years at Kapkatet county hospital, Kenya

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Background: Adolescents and young people represent a growing share of Tuberculosis (TB) worldwide. Adolescents account for over 40% of the total population in Kenya. UNAIDS report of 2017 flagged Kenya's population of school going teenagers of ages between 15-19 years as the most likely to stop treatment. The main objective is to highlight the interruption of anti-TBs among adolescent and young people at Kapkatet county hospital.

Methods: A retrospective study was done on adolescent and young adults ages 10-30 years old diagnosed with TB and started on treatment at Kapkatet county hospital within a period of three years between the periods of January 2015-December 2017. Ministry of health TB registers were used as source documents. Data was extracted and analysis done using SPSS version 21. Relationship associated factors and drug interruption was established. P- Value less than 0.05 was considered significance.

Results: A total of 300 adolescents and young adults were assessed during the review period. 63% (n=190) were male and 37% (n=110) female. Out of 300 adolescent who were on anti-TBs, 94% (n=282) were school going. At the end of the review period, only 60% (n=180) successfully completed treatment; 60% were female and 40% were male. On Anti-TB drug interruption, 40% (n=120) missed drugs and clinic appointments; 70% (n=84) were male. There was a positive correlation between male and female on drug interruption (P= 0.002).

Conclusions: Treatment failure was generally high and more focus should be put on males adolescent and young adults. Adolescents and young adults are likely to interrupt treatment both at intensive phase and at continuation phase of treatment related to stigma, bill burden, and duration of treatment, social support and school linkage. There should be structured friendly adolescence and young adult package of care and treatment to improve on anti-TB adherence.

3175 Referral pattern of TB patients to DOTS centre by practicing pediatricians of Punjab state, India - and its relationship to knowledge of DOTS programme

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Background: In India, a large segment of population turns to private health care providers for TB care. The operational research was done in five districts of Punjab i.e. Ludhiana, Jalandhar, Amritsar, Patiala and Bathinda to assess referral of TB cases to DOTS Centre by practicing pediatricians and the factors responsible and its relationship with knowledge of DOTS program.

Methods:

Study design: Observational case-control study.

Period of study: One year.

Material and methods: List of all registered pediatricians in the five cities was obtained and atleast 30% pediatricians (total enrolled = 139) were selected randomly by lottery method. Referral group involved Pediatricians who had referred at least one TB patient during last two quarters to DOTS centre for treatment. Non Referral group included pediatricians who did not refer any patient during this study. Data was collected on a pre-tested, structured questionnaire containing information about pediatricians and their knowledge of DOTS centre, DOTS therapy, TB case notification, TB case suspicion, diagnosis and treatment under RNTCP. The data so generated was analyzed.

Results: Of the enrolled paediatricians, 40% did not referral TB cases to DOTS centre. Fear of losing patient (71% vs. 30%) (p value=0.002) and apprehension about quality of drugs (66% vs. 34%) (p value < 0.001) was more in non-referral group. Accessibility to DOTS centre was more in referral group (67% vs 34%, p=0.02). There was significant difference regarding adequate knowledge of TB treatment (35% vs 17%) (p value=0.05). It was noted only 39% doctors were sensitization from the RNTCP program.

Conclusions: There was significant proportion of pediatricians who did not refer TB cases to DOTS centre in the state. The factors responsible can be improved by sensitizing paediatricians through workshops and CMEs conducted by RNTCP.

3240 Differences in metabolic risk factors for tuberculosis in close contacts with diabetes from two ethnicities impacting *M. tuberculosis* growth in peripheral blood mononuclear cells

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Background: Type 2 diabetes (T2D) is a highly prevalent risk factor for TB, but the effect size of this association varies across populations, which may be due to other metabolic and epidemiological factors besides hyperglycemia. The impact of these factors on containment of mycobacteria by immune cells is largely unexplored.

Methods: We performed a prospective cross-sectional study in adult close contacts of newly diagnosed pulmonary TB patients in South Africa (n=247) and the Texas-Mexico border (n=106) and assessed metabolic and sociodemographic characteristics. Peripheral blood mononuclear cells (PBMCs) were isolated from whole blood of contacts with T2D (n=36 in South Africa, n=32 in Texas-Mexico) and with normo- or intermediate glycaemia (n=52 in South Africa, n=68 in Texas-Mexico) and infected *ex vivo* with live *M. tuberculosis* H₃₇R_v to determine mycobacterial growth.

Results: The overall prevalence of T2D was 30.2% in Texas-Mexico and 17.4% in South Africa. Newly diagnosed T2D prevalence amongst TB contacts was high with 47% in South Africa and 34% in Texas-Mexico. Strikingly, the diabetic phenotype differed between Hispanics and South African Coloureds particularly in concentrations of triglycerides and cholesterol. *In vitro* growth of *M. tuberculosis* was significantly higher in PBMCs from T2D patients compared to normo-glycemic participants across both ethnicities, but did not differ between T2D patients using metformin vs. other or no T2D drugs. Mycobacterial growth was lower in PBMCs from contacts with serum cholesterol >200mg/dL in South Africa, whereas mycobacterial growth was higher in PBMCs from smokers.

Conclusions: Our findings suggest that expanding T2D screening from TB patients to their close contacts is effective to identify new T2D patients at risk for TB infection and disease. Our findings also demonstrate that contacts with T2D differ across ethnicities in characteristics that could further affect TB risk, including concentrations of serum lipids and smoking.

3285 Comparison of latent tuberculosis infection management between North Korean Refugees and South Koreans

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Background: The incidence of tuberculosis (TB) in North Korea is 561/100,000, seven times higher than that of South Korea. More than 1,000 North Korean Refugees (NKR) are escaping to South Korea every year, and these refugees can be the clues for unidentified TB policy of North Korea. We aimed to investigate the role of confirmatory Quantiferon-Gold In Tube (QTF) for LTBI diagnosis and the current status of LTBI treatment for NKR compared to South Koreans (SK).

Methods: Among the tuberculin skin test (TST) reactors (≥ 10 mm), the positive rate of QTF, TST size, and behaviors of LTBI treatment were compared retrospectively between the TB contacts of SK (n=126) and NKR (n=172).

Results: Among the total TST reactors (n=298), male-to-female ratio was 91(72.2%): 35(27.8%) in SK and 34(19.8%): 138(80.2%) in NKR group, respectively ($P < 0.001$). The mean age was higher in SK than NKR group (42.8 ± 9.9 vs. 35.4 ± 10.0 , $P < 0.001$). BCG scar rate was not different (66.7% vs. 73.5%, $P > 0.05$), and the mean size of TST was not different between two groups adjusted by sex, age, and BCG scar (16.57 ± 4.2 mm vs. 17.39 ± 3.9 mm). But, QTF positive rate was significantly higher in NKR than SK group [103/103 (100%) vs. 97/126 (77.0%), $P < 0.001$] among the TST reactors. Among the subjects who received LTBI treatment (n=272), difference of completion rate was not significant (SK 68% vs. NKR 65.9%), even though 4 month of Rifampin (SK:NKR, 82:90) or 9 month of Isoniazid (SK:NKR, 0:98) were prescribed.

Conclusions: The role of confirmatory QTF for TST reactors as LTBI screening for NKR seems to be extremely low. However, completion rate of LTBI treatment must be improved both in NKR and SK.

3292 A role of genetic variants and expression of interleukin-12 receptor subunit beta2 in protection against tuberculosis

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Background: Interferon-gamma (IFN- γ)-mediated immunity has a central role in protection against *Mycobacterium tuberculosis* (*Mtb*), and genetic variants in

the IFN- γ pathway have often shown associations with tuberculosis (TB). Interleukin-12 receptor subunit beta2 gene (*IL12RB2*) is expressed in Th1 cells together with another subunit, and forms a high-affinity heterodimeric receptor. In a previous study, promoter polymorphisms of *IL12RB2* were associated with leprosy, and had different transcriptional activities in Jurkat T cells (Ohyama H, *et al.* J Clin Pathol 58:740-743, 2005), but their role in TB remains unknown. The aim of this study is to explore immunogenetical significance of *IL12RB2* promoter variants on latent TB infection (LTBI) or active TB.

Methods: Three genetic variants in the 5' upstream region of *IL12RB2* (rs17109841, rs3762315, and rs3834764) were genotyped in 499 new smear-positive TB patients without HIV infection, 505 healthy individuals and 345 disease-free health care workers (HCWs) in Hanoi, Viet Nam. In HCWs, the state of LTBI was assessed, using results of the commercially available IFN- γ release assay (IGRA) for TB, and whole blood was further collected into tubes with RNA-stabilizing solution. Total RNA was extracted, and subjected to quantitative RT/PCR for *IL12RB2*.

Results: The frequency of an insertion allele of rs3834764 was significantly lower in the IGRA-positive HCWs than that in IGRA-negative HCWs ($P=0.041$, odds ratio [OR] 0.69, 95% confidence interval [CI] 0.48-0.99), although genotype and allele frequencies of these polymorphisms did not show associations between active TB and healthy groups, and the *IL12RB2* mRNA levels in the whole blood cells were not significantly different among the genotypes.

Conclusions: The insertion allele of *IL12RB2* rs3834764 may confer protection against transmission of TB or establishment of LTBI, presumably affecting the gene expression in T cells at sites of infection.

3303 Scoring TB severity from computerized-detection of lung lesions in CT scans for use in improving TB diagnostics and treatment

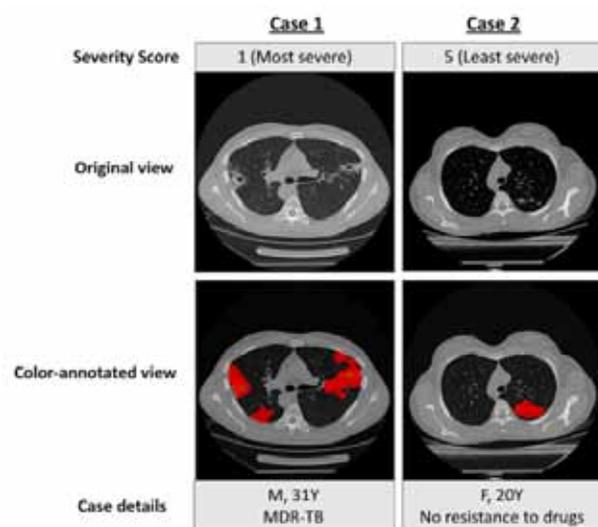
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Background: Medical imaging has great potential to influence TB transmission reduction through improving diagnostics and treatment. In particular, computed tomography (CT) information can be used to assess treatment efficacy. Here, we present results from using artificial intelligence-based detection of lung lesions in chest CT (CCT) for predictive TB severity scoring.

Methods: Using custom software, an expert radiologist annotated several types of lung lesions on CCTs from 502 TB patients (CCTs were obtained from the TB Portals -<https://data.tbportals.niaid.nih.gov>). A convolutional neural network was then trained on 198 annotated CCTs for automated lung lesion detection. Finally, a lesion-based TB severity assessment software was developed, and its results were compared to those produced by conventional statistical techniques using clinical, lab, and radiologist scoring data.

Results: TB severity scores generated by the CCT analysis software were found to be in agreement with experts' ones and outperformed conventional approaches based on TB patient clinical and lab data (test set contained CCT from 109 patients; the best RMSE=0.7840, over worst theoretically possible RMSE \approx 2.95, <https://www.imageclef.org/2018/tuberculosis>). Automatic lesion labeling has been incorporated into the TB Portals platform interface (<https://bit.ly/2uPz7Fj>), enabling users to toggle between original and color-annotated 3D and 2D views and helping non-experts visualize pathology (Figure 1). The quantitative severity score calculated from CCTs also provides additional information in the form of an extensive CCT descriptor that can be used to identify the key CCT slices with TB-associated lesions.

Conclusions: Computerized lesions annotation based on artificial intelligence techniques offers superior performance for calculation of TB CCT descriptors, which can be used for generating TB severity scores. Such information is valuable to treating physicians, but also to researchers evaluating treatment efficacy in clinical trials. Automation can also increase usage of image-based evaluation and decrease its associated labor.



[Figure 1. Computerized detection and annotation of lesions on CT images with different severity scores. Cavities (green color) surrounded with foci and infiltrates (red color) are present on Case 1. Only a small region with foci (red color) is on Case 2.]

3324 Improvements in the sensitivity of the Respiratory Aerosol Sampling Chamber (RASC): characterising exhaled bioaerosols from pulmonary TB patients

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Background: The RASC is a research tool designed to create a micro-environment for investigation of bio-aerosol from a single individual. Earlier work has shown a 43% detection rate of *Mycobacterium tuberculosis* by bio-aerosol culture in those with pulmonary TB. We describe improvements in the RASC to aid characterisation of the infectious TB particle and develop a real-time TB infectivity measure.

Methods: Optimization of the RASC:

Efficiency of Bio-aerosol capture

Releases of 2 μ m fluorescent beads and model spores in large (20 μ m particles) and small (<5 μ m particles) were performed to investigate system losses.

Sampling Protocol

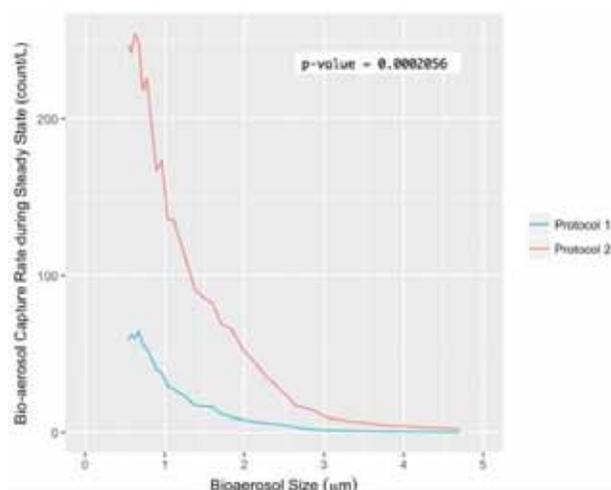
A change to continuous chamber air sampling via a single high flow (250L/min) cyclone collector (Bertin Coriolis) leading to lower CO₂ set-point and regulating constant chamber humidity and temperature. Protocol 1 involved initial contamination and short steady state sampling (median of 3800 PPM CO₂). Revised protocol 2 changed to continuous sampling with a lower steady state (median 1600 PPM CO₂). This revision led to decreased unsampled air volume at the end of the protocol.

Microbiological Detection

Liquid collected bio-aerosol samples are more amenable to non-culture based analytical methods increasing sensitivity over culture. Mass spectrometry of the supernatant for detection of specific mycobacterial lipids and metabolites and fluorescence microscopy of the re-suspended pellet for quantitative *Mtb* detection are being investigated.

Results: Large (>10 μ m) particles are rarely sampled by the RASC. Small particles (<5 μ m) are sampled at a rate of approximately 30% of the total released into the chamber.

Conclusions: Sampling of airborne bacilli is fraught with technical challenges. Efficiency of capture is often low, resulting in under-estimation of production from TB diseased individuals. Sampling systems need to maximise both capture rate and sensitivity of detection. Accurate quantification of *Mtb* production demands recognition and correction for these limitations.



[Comparison of mean bio-aerosol capture rates across size distributions for healthy controls]

3333 Analysis of high molecular weight complexes (Antigen 60) of *M.tuberculosis* and *M.bovis* BCG: towards discovery of biomarkers with higher specificity

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Background: Antigen 60, a high molecular weight (HMW) antigen complex extracted from *M.bovis* BCG (A60-BCG), has considerable antigenicity but is not specifically recognized by tuberculosis (TB) patient antibodies. HMW complexes from *M.tuberculosis* (A60-MTB) may possess unique proteins, and higher specificity.

Methods: HMW complexes (1,000-10,000kDa) extracted from lysate of sonicated gamma-irradiated MTB (strains H37Rv, CDC1551, HN878) using size exclusion chromatography and A60-BCG were trypsin-digested in-solution, analyzed by LC-MS/MS, and searched against Uniprot databases for MTB H37Rv and *M.bovis* BCG. Significant protein matches were analyzed using STRING for predictive protein-interaction analysis. A60-MTB and A60-BCG were probed with mouse monoclonal antibodies and patient IgG-antibodies (60 culture-confirmed TB and 40 provisionally diagnosed but confirmed non-TB) on western blot and ELISA, respectively. Antigenic reactivity in patient sera was analyzed using area-under-receiver-operator-curve analysis (AUC) and correlation.

Results: 129 proteins were common to A60-MTB (/CDC1551/H37Rv/HN878); 104 also common to A60-BCG, and 25 unique to A60-MTB. Majority of these

proteins are associated with the plasma membrane, with significant protein-protein interaction predicted among plasma membrane-associated proteins including dnaK (previously reported in bacterial extracellular vesicles). Anti-A60-CDC1551 and anti-A60-BCG IgG reactivity were significantly correlated in TB patients ($R^2 = 0.803$, p value ≤ 0.001), but less correlated in non-TB patients ($R^2 = 0.510$, p value ≤ 0.001). Anti-A60-CDC1551 IgG (AUC: 0.822, 95% CI: 0.75-0.904) better discriminates TB from non-TB patients compared to anti-A60-BCG IgG (AUC: 0.79, 95% CI: 0.702 - 0.878). LpqH was detected in A60-BCG and A60-HN878, but not in A60-CDC1551 or A60-H37Rv. Pooled TB sera showed unique reactivity to 50-60kDa bands in A60-CDC1551 and non-TB sera were uniquely reactive to 37-50kDa bands in A60-BCG.

Conclusions: A60-MTB is proteomically and antigenically distinct from A60-BCG, with higher specificity. Further investigation of proteins unique to A60-MTB may improve understanding of host-pathogen interactions and inform biomarker research towards improved diagnostics and reduced disease transmission.

3349 The prevalence of pulmonary tuberculosis and associated factors among prisoners in western Ethiopia

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Background: Tuberculosis (TB) is one of the major health problems in Ethiopia. Congregate settings like prisons are the most important conducive environment for the transmission of TB, but they are often given less attention. Therefore, this study was done to assess point prevalence of pulmonary tuberculosis (PTB) and associated factors among prisoners in Western Ethiopia.

Methods: A cross-sectional study was conducted from February to April 2018 among prisons in western Ethiopia. We used a symptom-based checklist as screening tool to identify prisoners with two or more week's symptom of cough and/or other constitutional symptoms as per the national guideline. About 4-5 ml of purulent spot and morning sputum sample was collected for AFB microscopy and GeneXpert, respectively. AFB microscopy was first done for all presumptive TB patients and sputum sample negative by AFB microscopy was transported to the nearby hospital for GeneXpert for confirmation. SPSS software package version 20.0 was used for analysis.

Results: Of 3395 prisoners screened, 32.1% were aged between 18 and 24 years, and 84 (2.5%) were presumptive TB cases. The point prevalence of PTB among prisoners was found 236 per 100,000 populations or 9.5% (8/84). One newly diagnosed PTB case was found to be Rifampicin resistant. About 56% and 15.5% of the pre-

sumptive TB suspects were smokers, and had BMI less than 18.5kg/m², respectively. Predictors identified for PTB were cough for more than four weeks'

Conclusions: The point prevalence of PTB among prisoners in western Ethiopia was found to be high. In order to reduce the burden of TB in prisons regular screening of the prisoners and routine screening of newly introduced prisoners should be in place. Strengthening the local health system and implementing targeted screening among contacts of index TB patients are more feasible strategies.

3358 Diabetes and intermediate hyperglycaemia similarly impact tuberculosis blood transcriptomes, causing enhanced inflammatory and reduced interferon responses

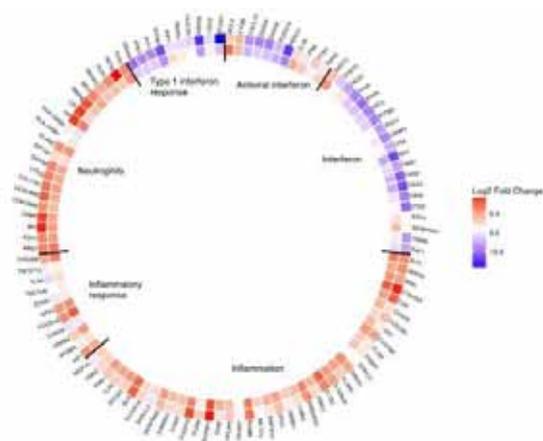
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Background: People living with diabetes have an increased risk of developing active tuberculosis, thereby contributing excessively to transmission. Blood transcriptomes are altered in active tuberculosis patients relative to healthy individuals. The effects of diabetes and intermediate hyperglycaemia on this transcriptomic signature were investigated, to enhance understanding of immunological susceptibility in diabetes-tuberculosis comorbidity, in order to develop intervention strategies targeting this group.

Methods: Whole blood samples were collected from active tuberculosis patients with diabetes (HbA1c $\geq 6.5\%$) or intermediate hyperglycaemia (HbA1c 5.7-6.5%), patients only with tuberculosis and healthy controls in four countries: South Africa, Romania, Indonesia and Peru. Differential blood gene expression was determined by RNA-seq (n=249).

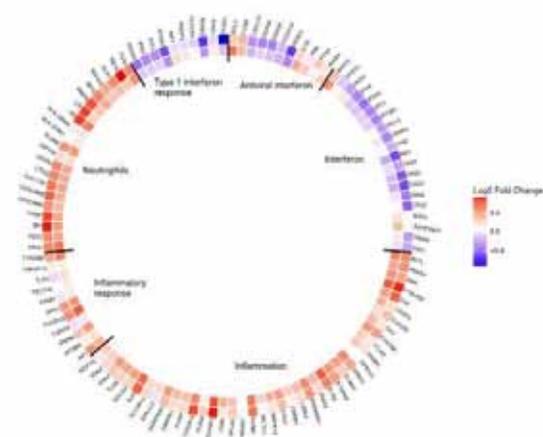
Results: Diabetes increased the magnitude of gene expression change in the host transcriptome in tuberculosis, notably showing an increase in innate, and decrease in adaptive immune responses. Strikingly, patients with intermediate hyperglycaemia and tuberculosis exhibited blood transcriptomes much more similar to diabetes-tuberculosis patients than to uncomplicated tuberculosis patients. Both diabetes-tuberculosis and intermediate hyperglycaemia-tuberculosis patients had a decreased type I interferon response relative to tuberculosis-only patients.

Conclusions: Aberrant transcriptomes reveal a mechanism of susceptibility to tuberculosis in people living with diabetes which consists of enhanced inflammation and reduced interferon responses. These immunological dysfunctions and pathology are present before diabetes is diagnosed and treated, showing that susceptibility exists even at intermediate levels of hyperglycaemia. These data warrant careful investigation of clinical disease outcome in intermediate hyperglycaemia patients with tuberculosis.



Summary of modular analysis. Fold changes of the genes within the top significantly differentially expressed modules are shown (adjusted p-value < 0.05). On the inside: IH-TB compared to TB-only. Outside: DM-TB compared to TB-only. Red=Up-, Blue=Down - regulated genes.

[Figure 1]



Summary of modular analysis. Fold changes of the genes within the top significantly differentially expressed modules are shown (adjusted p-value < 0.05). On the inside: IH-TB compared to TB-only. Outside: DM-TB compared to TB-only. Red=Up-, Blue=Down - regulated genes.

[Figure 2]

3360 Mycobacterium tuberculosis Complex Lineages and demographical risk factors as determinants of disease phenotypes from a moderate Tuberculosis burden country

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Background: Despite low infectious potential of extrapulmonary Tuberculosis (EPTB), it poses significant clinical challenges in case diagnosis and treatment monitoring. Understanding main demographical risk factors and current association of several pathogen-host factors plays a crucial role in speeding up diagnosis process and improving overall clinical experience. The objectives of this study were:

- (I) to examine the association of different lineages of mycobacteria with different level of disease severity of EPTB and compare it with pulmonary cases,
- (II) to investigate the main demographical risk factors for EPTB among adults and adolescents for the first time in Saudi Arabia.

Methods: A cross-sectional multicenter cohort study was carried out on extrapulmonary (n=1003) and pulmonary isolates (n=1089). All isolates were subjected to spoligotyping and 24-loci based MIRU-VNTR typing. The association between any two variables was performed using odd ratio and p values. Independent demographical risk factors among adults and adolescents were determined (n=902) using linear-univariate analysis and subsequently multivariate-regression model analysis.

Results: 'Ancestral' lineages and *M. bovis* were directly associated with lymph node tuberculosis and gastrointestinal tuberculosis respectively. In addition, 'modern' lineages, EAI showed significant association to central nervous system tuberculosis while Uganda-I to gastrointestinal tuberculosis. Gender was one of the main risk factors to lymph node and genitourinary TB. Moreover, nationality was identified as an independent risk factor to East-African-Indian lineage. Although our analysis showed no significant impact of aging as an independent risk for EPTB, this could be due to the pre-existence of high consanguinity rate in the population.

Conclusions: Our findings substantially contribute to emerging evidences that pathogen lineages influence disease phenotypes and epidemiological consequences. In addition, characterizing the main demographical risk factors for EPTB may also be crucial in optimizing diagnosis process and improving overall case management.

3362 Discrimination of early tuberculosis disease from latent tuberculosis infection and uninfected individuals with a transcriptional blood signature during active community-based screening

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Background: Reducing tuberculosis (TB) transmission is currently restricted by the failure to detect an estimated 3.3 million TB cases annually. The current tools we have to screen for TB disease are limited. In the majority of TB endemic settings, sputum smear microscopy is used to diagnose TB, but this test is insensitive for detecting pulmonary TB in its early stages. The objective of this study was to establish a concise gene signature that could discriminate between individuals with early TB disease, latent TB infection (LTBI) and those without infection.

Methods: This is a case control study nested within a cluster-randomised trial of population screening for active TB using Xpert MTB/RIF in a rural province of Vietnam. Active pulmonary TB in subjects with positive sputum Xpert was confirmed by sputum microscopy, culture and CXR. Whole blood samples from 303 participants, including 97 with active TB, 92 with LTBI diagnosed by IGRA testing and 114 uninfected individuals, were subject to transcriptomic analysis of target genes selected from a systematic review of previous transcriptional studies in TB. The optimal subset of differentially expressed genes for distinguishing cases and controls was selected using logistic regression with stepwise elimination with entry and retention probabilities set at 0.05.

Results: Analysis of 82 genes identified a pattern of differentially expressed genes in TB disease. A seven gene signature was identified that distinguished between TB disease and no TB disease with an AUC of 0.86 (95% CI: 0.80-0.91), and between TB disease from LTBI with an AUC of 0.88 (95% CI: 0.82-0.93).

Conclusions: This gene signature accurately distinguishes subjects with early TB disease from those without TB disease or infection, in the context of community-wide TB screening. This signature could be used as a non-sputum-based screening tool or triage test to detect prevalent cases of TB in the community.

3366 The protective effect or not of BCG vaccine in children and adults in an endemic region

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Background: Tuberculosis is a neglected disease which estimates one-third of world's population infected. In Brazil, BCG's vaccination is mandatory at birth. Vaccines are considered safe, preventive and cost-effective. However, World strategies for decrease tuberculosis haven't effectively succeeded, because of difficulties in precise diagnosis and delay on beginning treatment, despite vaccination. Recife (Pernambuco State, Brazil) is an endemic for tuberculosis (78.3 cases/100.000 hab). The study evaluated the protective action of BCG.

Methods: Two different groups of children (≤ 15 years), from hospitals of Recife, were analyzed: Group A (data collected 2003-2006) and Group B (2011-2016) and other group of adult (2011-2016). Gold-standard was clinical criteria and specific treatment response, according to WHO guidelines for TB. All statistical conclusion was made on 5% of significance and data were analyzed on SPSS by X^2 test and Binary logistic regression.

Results: In both children groups, there were no statistical difference ($p=0,26$) between have BCG scar and develop TB (latent or active), even in kids with contact with *bacilliferous* adult. To have BCG's scar and have or not TB in adults had statically difference, $p=0,02$. The variable "having contact with *bacilliferous* TB" was also measured on groups associated with TB diagnosis.

Conclusions: Analyzing results of BCG x have TB, it can be concluded that in high rate TB's region, to be vaccinated does not imply children protection against the disease but only protection in adults. When data were associated with "having contact with *bacilliferous* TB", *P* value increased. This may demonstrate that a confounding factor (time of exposition longer than 15 years) may be interfering with the conclusion. In adults, BCG showed protective effect to develop TB, however, time of exposed are higher than in children. Further studies with more patients and in other endemic regions should be performed, as so for a more effective vaccine against all forms of TB should be done.

3371 Comparing the efficacy of drug regimens for pulmonary tuberculosis: meta-analysis of phase III trials

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Background: Current first-line therapy for tuberculosis has evolved over seven decades and remained essentially unchanged for forty years. To identify outstanding knowledge gaps and improve the development pathway for new treatment regimens, a clearer understanding of the evidence base for the role of individual drugs and drug combinations is required.

Methods: A systematic review including phase III trials involving drugs proposed for treatment of people with newly-diagnosed pulmonary tuberculosis, with or without isoniazid resistance, was performed. Outcomes of interest were end-of-treatment (EOT), post-treatment (PT) or both combined. Risk of bias was assessed in five critical domains. Meta-analysis was performed using a random-effects model with the DerSimonian and Laird approach.

Results: 174 trials were included comprising 39,123 participants in 325 trial arms with 209 distinct treatment regimens. Few high-quality studies were identified, with widespread lack of blinding or allocation concealment. Isoniazid and rifampicin were critical in reducing the duration of treatment although only four included regimens excluded isoniazid. Any two-drug combination containing isoniazid at a duration of five months or more achieved EOT outcomes better than 90%. At 6 months duration the combined EOT and PT outcome for rifampicin-containing regimens was 5% (4.2%-5.4%) while for non-rifampicin containing regimens it was 13% (9.9%-17.4%). When given without isoniazid or rifampicin, pyrazinamide-containing regimens resulted in poor EOT outcomes (45% culture conversion at 6 months) and evidence supporting recommendations for current dosing and duration of pyrazinamide was limited.

Conclusions: The balance between duration of regimens and the potency of key drugs in short-course chemotherapy and the concept of regimen de-intensification was supported by this meta-analysis. However, the evidence base for current tuberculosis treatment regimens is strongly shaped by the historical pattern of development and is not as robust as is often assumed. Important questions remain unresolved and clinical trial activity in tuberculosis should be urgently renewed.

3372 The first genotyping and whole genome sequencing of *Mycobacterium tuberculosis* from Indonesian TB Prevalence Survey

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Background: Modern molecular methods can help TB surveillance for more deepen understanding of pathogen circulation in Indonesia. This study aims to genotyping *Mycobacterium tuberculosis* by MIRU-VNTR and spoligotyping standards and the making of a phylogenetic tree following with whole genome sequencing from Indonesian TB Prevalence Survey (Indonesian-TBPS)

Methods: The genotyping of 300 *Mycobacterium tuberculosis* isolates from Indonesian-TBPS was performed using 24-locus Mycobacterial Interspersed Repetitive Unit - Variable Number of Tandem Repeats (MIRU-VNTR) combined with spoligotyping. A phylogenetic analysis was performed and followed by whole genome sequencing using Next Generation Sequencing (NGS) for several specimens represent the clusters.

Results: Based on the strain analysis using MIRU-VNTR combined with spoligotyping, of the 172 strains identified, as many as 42 isolates (24%) were the Beijing strains, 34 isolates (19,7%) were EAI 5 genotype, 24 isolates were U genotype (13,9%), 18 isolates (10,5%) were T1 genotype and the rest were group into other genotypes. Following phylogenetic analysis formed 3 large groups containing at least 20 clusters. Further whole genome sequencing analysis representing clusters, it is known that the Beijing strain is 4 specimens, 3 EAI Manila specimens, 2 Harleem specimens, 2 LAM specimens and 1 Euro American S-Type specimen. While 7 other strains into the Euro American super lineage clade that has not been specific. Beijing strain followed by EAI Manila have more variant mutation with more SNP position than the other strains (16-29 SNP compare to 2-15). The SNP can be very related to TB drug resistance.

Conclusions: These are the first genotyping data from Indonesian-TBPS. It shows that Beijing strains are the most circulated *Mycobacterium tuberculosis* genotype in Indonesia followed by EAI 5, U and T1. The following drug resistance study should be performed in line with phylodynamic analysis of the pathogen.

3374 Variant identification approach profoundly affects transmission links inferred in TB genomic epidemiology studies

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Background: *M. tuberculosis* (*Mtb*) genomes are a potentially rich source of information that can be used to investigate transmission linkages. However, no consensus exists on how to identify *Mtb* genomic variants, making it difficult to interpret variation within a study and draw comparisons across studies. This is particularly problematic for *Mtb* since transmission inference often relies on the identification of a small number of genomic variants.

Methods: We systematically investigated how commonly used variant calling approaches influence transmission inference. We reanalyzed published short-read sequence data from a clonal outbreak of 86 Haarlem lineage *Mtb* isolates with commonly used mapping algorithms, variant callers, and filters. We inferred transmission links using single nucleotide polymorphism (SNP)-based distance thresholds. We additionally compared performance of commonly used pipelines and a deep convolutional neural network ("DeepVariant") in detecting true pairwise differences between simulated *Mtb* genomes.

Results: Applying different variant calling approaches leads to major pairwise SNP difference estimates for the same sequence data. With two frequently used pipelines, mean pairwise SNP differences were 2.8 (bwa/GATK) compared to 8.0 (smalt/samtools). Applying a common threshold for possible transmission of 6 (or 12) SNPs, this translates into 1312 (or 1386) transmission links (out of 6889 pairwise comparisons) predicted by bwa/GATK that are not predicted by smalt/samtools. With simulated outbreaks, DeepVariant achieved higher sensitivity (99.4%) for pairwise differences and fewer false positive calls (1.0 per genome), compared with the best published pipeline (sensitivity: 93.3% and 3.4 false positives).

Conclusions: Differences in commonly used variant calling approaches can lead to substantial differences in TB transmission inference, altering study conclusions. A deep learning approach outperforms standard approaches in identifying pairwise SNP differences. A shared variant calling approach will allow the TB research community to integrate data across studies and take full advantage of *Mtb* genomic variation for understanding transmission.

3379 Active case finding of pulmonary TB in a European refugee camp setting: lessons learnt from a mass screening of contacts in Oinofyta Hotspot in Greece

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Background: Within the context of the ongoing refugee crisis, a large number of people from high prevalence TB countries resides in refugee camps in Greece. Oinofyta camp was a temporary residence for a population of about 600 immigrants from Afghanistan, Pakistan and Iran. The camp was located within the premises of an abandoned factory building, characterized by limited space, poor ventilation and lighting. After diagnosing TB in 2 former camp residents, in-camp transmission has been suspected. In cooperation with Hellenic Center for Disease Control and Prevention (KEELPNO) we undertook an active case finding mass screening.

Methods: KEELPNO proposed a tuberculin skin test (TST) based two-step screening intervention. Initially the population of the camp underwent screening with TST. 5 mm was chosen as the cutoff for a positive skin reaction. Those with positive TST were subjected to chest x-ray. Although not part of the screening algorithm, those with positive TST were also questioned about typical TB symptoms. Those with positive x-ray were considered possible pulmonary TB patients and were sent to a tertiary hospital for TB workup, isolation and treatment.

Results: A total of 336 people were skin tested for TB. From those, 110 people had positive result (>5mm) including 17 children. 75 of them consequently underwent chest radiography. From those, only one patient had positive X-ray findings and referred to a tertiary hospital. 17,3 % of those with positive TST described at least one symptom of TB, the positive case included.

Conclusions: In our active case finding intervention we were able to identify one pulmonary TB case. With 32,7 % of the examined population exhibiting a positive skin reaction, massive administration of TST as first step of the mass screening procedure failed to narrow down substantially the number of contacts in need of further screening with X-ray.

3384 Clinical prediction tools to inform tuberculosis contact investigation

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Background: Efficient contact investigation strategies are needed for the early diagnosis of secondary TB cases and treatment of latent infections. In lower- and middle-income countries, contact investigation and preventive therapy are often not practiced. We develop clinical prediction tools that identify contacts of TB patients at elevated risk of progressing to active disease within a short period.

Methods: Between September 2009 and August 2012, we conducted a prospective cohort study in Lima, Peru in which we enrolled and followed 14,044 household contacts (HHCs) of 3,446 adult pulmonary TB patients. We used information collected in this study to predict concurrent and one-year incident disease among HHCs, including patient and HHC characteristics reportable by the index patients, detailed HHC characteristics, and HHC infection status. We used five-fold geographical cross-validation to select the best fitting regularized logistic regression models.

Results: Using information provided through interaction with the index patients alone, we predict concurrent and incident TB among HHCs with mean areas under the receiver-operating-characteristic curves ranging between 0.77 and 0.85 in external validation datasets. Of 10,947 HHCs who did not initiate preventive therapy (43% male, age: 33.0±18.2), 5.2% were diagnosed with concurrent (n=212) or one-year incident disease (n=362), meaning that one case is diagnosed for every 19.1 undifferentiated HHCs investigated. Using the prediction model, we estimate that 8% HHCs have a risk of over 10% and that this group makes up 43% of all concurrent or secondary TB cases. If efforts were focused on this high-risk group, the number of contacts needed to investigate to early diagnose one TB case is 4.0.

Conclusions: We present tools that identify high risk TB contacts based on patient reportable information at the time of their TB diagnosis alone. These tools could be the basis for initiating contact investigation and preventive therapy in resource limited settings.

3386 Interferon Gamma Releasing Assay implementation on BCG vaccine effectiveness pilot study in Indonesia

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Background: BCG vaccination has been used not to prevent TB infection but merely to provide substantial protection against the more severe types of disseminated TB. BCG vaccine effectiveness rate in Indonesia is still unknown. Interferon Gamma Release Assay (IGRA) have been shown to predominantly measure the presence of *M. tuberculosis*-specific effector memory T-cells, which are considered indicative of previous in vivo exposure to the bacilli. This study aimed to evaluate IGRA implementation as an additional assay to conventional TB diagnostic assay regarding BCG vaccine effectiveness

Methods: A total of 135 newborns and 346 adults aged ≥ 15 years old from 132 household were involved in the study. IGRA were measured twice in newborns at pre and 2 months following BCG vaccination. A comprehensive evaluation of previous TB history, present TB symptoms, chest X-ray examination and IGRA were taken for adult participant. Sputum smear microscopy and culture were examined for adults with present TB symptom and/or any abnormality in the chest X-ray.

Results: Only 97 out of 135 (71.85%) newborns that have complete IGRA results. In both pre and 2 months following BCG vaccination, IGRA results were negative for all 97 newborns. Based on present TB symptom and chest X-ray results, 282(81.50%) and 64(18.50%) adult participant were considered healthy and TB suspects respectively. 99 out of 282 (35.10%) healthy adults showed a positive IGRA result. 8 (12.5%) adult participants were diagnosed with active TB based on positive TB culture with only 1(one) positive TB case showed a negative IGRA

Conclusions: IGRA can be used as a part of TB diagnostic methods, but should not replace the standard TB diagnostic methods for diagnosing active TB. Knowing that progression to active TB is at its highest during the first years following infection, it is necessary to do a series of IGRA measurement to evaluate the BCG vaccine effectiveness.

3395 Prevalence and risk factors of latent tuberculosis infection in South Korea: the Korean National Health and Nutrition Examination Survey, 2016

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Background: South Korea has the highest tuberculosis (TB) burden among the Organisation for Economic Co-operation and Development (OECD) countries. Prevalence of latent tuberculosis infection (LTBI) in the nationwide population is an important indicator for assessing national TB control programme. The objectives of the study were to determine the prevalence and risk factors of LTBI in the South Korean population.

Methods: Interviews and tuberculin skin test (TST) were conducted among people aged 10 and more in 2016 as part of the Korean National Health and Nutrition Examination Survey (KNHANES), a nationally representative sample of the South Korean population. LTBI was defined as a TST measurement of ≥ 10 mm. Associations of age, sex, residence, education, father's education, body mass index (BMI), diabetes mellitus, current smoking, heavy drinking, Bacillus Calmette-Guérin (BCG) vaccination, previous TB history, close contact were assessed using multivariable logistic regression.

Results: A total of 2,051 participants underwent TST. Age- and sex-weighted prevalence of LTBI was 33.2% (95%CI: 30.9-35.6). Higher risk factors included age 25-34 (AOR=3.74, 95%CI: 1.75-8.01), age 35-44 (AOR=7.85, 95%CI: 3.68-16.73), age 45-54 (AOR=9.75, 95%CI: 4.58-20.76), age 55 and more (AOR=7.81, 95%CI: 3.62-16.86), male sex (AOR=1.69, 95%CI: 1.30-2.20), current smoking (AOR=1.66, 95%CI: 1.15-2.39), and previous TB history (AOR=4.21, 95%CI: 2.30-7.72).

Conclusions: The current level of LTBI in South Korea is still high in reaching the national TB control target. In addition to basic TB control measures, LTBI screening and treatment among high risk groups should be intensified in order to accelerate TB elimination in the country.

3404 Effect of OCT transporters genetic polymorphisms on the ethambutol pharmacokinetics, prediction from PBPK-model with IVIVE

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Background: Ethambutol is the first line Antituberculosis drugs for its prominent efficacy and susceptibility to the pathogen. Renal elimination is the major route via glomerular filtration and tubular secretion. For being a cationic compound, OCT membrane transporters facilitate the disposition of ethambutol, and attribute its PK/PD. Previously we showed that, genetic polymorphism in OCT1 and OCT2 transporters reduced its function. There is also reports in the clinics for significant interindividual variation in pharmacokinetics without mechanistic understanding. To address this issue, we aimed to evaluate effect of OCT2 variants on ethambutol transport and further PBPK model development to see effect on pharmacokinetics.

Methods: The transport experiments were conducted using human embryonic kidney cells transiently transfected with human OCT1 variants (P341L) and stably transfected with OCT2 transporter wild type and variants (T199I, T201M and A270S). Later, a full PBPK model for ethambutol was developed following permeability limited mechanistic kidney model (MechKim) in the SIMCYP simulator (Ver 17) using *in vitro* data to predict OCT2 genetic variants effect on ethambutol pharmacokinetics.

Results: The Clint of ethambutol in cells expressing genetic variants of OCT1-P341L (16% in KOR) reduced by 2-fold compared to OCT1-WT. Similarly, Clint of ethambutol in genetic variants of OCT2-T199I (1% in KOR), -T201M (2% in KOR) and -A270S (14% in KOR) were reduced 2.8-fold, 2.3-fold, and 1.6-fold compared with wild-type, respectively. The predicted pharmacokinetics showed the ethambutol AUC ratio as 1.41, 1.44 and 1.16 and CL were 28.8, 26.0 and 12.4 % lower respectively for T199I, T201M and A270S genetic variants subjects compared to wild type. OCT2-T199I and T201M genetic variants greatly reduced ethambutol clearance compared to wild type.

Conclusions: The genetic polymorphism in OCT1 and OCT2 transporters seems to influence on the reduction of ethambutol uptake which may help to personalized dosing in TB.

3420 Development and evaluation of rapid, low cost and affordable TB diagnostics

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Background: The early treatment of TB is currently hindered by the lack of rapid, accurate diagnostic tools, especially those that can be applied as a point-of-care device in the resource-constrained settings in developing countries. Alternatives do exist, but they either come at a high cost or lack the required sensitivity. Therefore, rapid, economical, and improved TB diagnostic tests are urgently needed. Our proposed tests (detection of antibodies in plasma; LAM antigen in urine and MPT64 in sputum) are rapid (20-25 minutes compared to 8 to 12 weeks for routine culture), low cost/ affordable (compared to \$10 for Xpert), do not require equipment, they are point of care easy to use tests in doctor's clinic & rural settings.

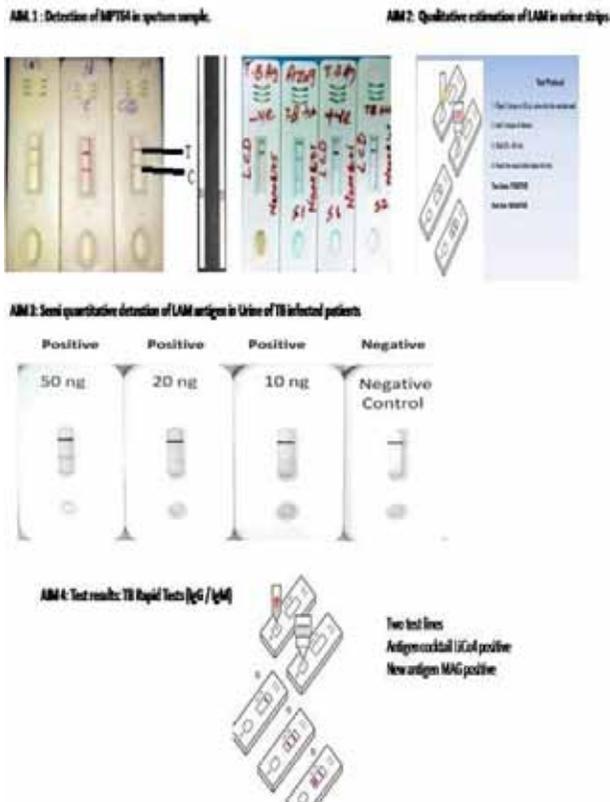
Methods: NEXT GENERATION TEST- TB-ST (IgG / IgM) & TB IgA): Membrane based lateral flow test to detects human IgG/IgM/IgA antibodies in patients with active Tuberculosis in serum, plasma or whole blood. The test consists: Special antibody binding protein (conjugated to colloidal gold particles) + two test lines.

TB Urine Strip Test: Rapid detection of the lipoarabinomannan (LAM) antigen of the outer cell wall in urine. A special monoclonal antibody is affixed to gold particles (conjugate). A membrane with immobilized LAM specific capture antibodies.

Detection of MPT64 in sputum: MPT64 (very stable protein & 8% of the total volume of the proteins secreted outside the cell) is secreted by *M. tuberculosis* in liquid/solid culture media or other biological fluids like sputum as soon as the pathogen starts dividing.

Results: For older tests :Sensitivity 56% & specificity >96% was found during pilot studies. The tests are under evaluation in JALMA (Reference Lab) in 444 presumptive TB patients.

Conclusions: TB-ST (IgG /IgM) & TB IgA: The total sensitivity can be increased in combination of IgA and IgG/M. Around 37% lives were saved through TB diagnosis and treatment b/n 2000-2013.



[Detection of Antigen and Antibodies for Rapid TB Diagnosis]

3424 Quantifying tuberculosis transmission between native and foreign-born populations in the Netherlands between 2009 and 2017 using variable number tandem repeat (VNTR) typing

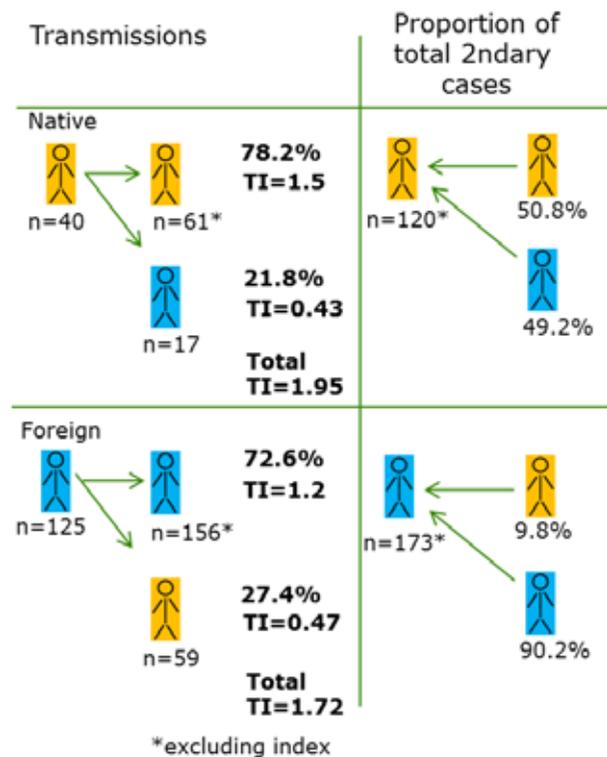
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Background: In the Netherlands, like in most low-incidence countries, TB incidence and epidemiology is strongly influenced by migration from high-endemic areas, and is further characterised by a low rate of transmission in the general population with occasional outbreaks. The aim of this study was to investigate transmission between native and foreign-born populations. **Methods:** 24-loci VNTR typing has been the genotyping method in the Netherlands since 2009 with backward typing of isolates 2004-2008. Clusters were defined if strains had 100% identical VNTR types. We limited our study to pulmonary TB patients with a new VNTR *Mycobacterium tuberculosis* strain occurring in 2009-2015 (index cases) and their clustered cases -occurring within two years of the indexes. The transmission in-

dex (TI) was defined as the number of cases within two years of the index case in the cluster, used as a proxy of transmission.

Results: 8,392 TB patients were notified in 2009-2017; 6,153 (73%) were foreign-born; 5,757 (69%) had VNTR typing results; Of these, 5,658 (98%) had a *M. tuberculosis* isolate and 2,801 (49%) had a unique fingerprint. 458 patients met our inclusion criteria (165 new clusters). Transmission between groups was comparable and bidirectional: 21.8% of cases resulted from native-foreign and 27.4% from foreign-native transmission. TI was similar for native and foreign-born index cases (1.95 and 1.72), as well as for native-foreign or foreign-native (0.43 and 0.47) (Figure). Due to the larger number of foreign-born patients, nearly half of the native secondary cases were presumably infected by a foreign-born TB patient.

Conclusions: Transmission from foreign-born patients to the native population is relevant in a low-incidence country, due to the high proportion of foreign-born patients. On an individual case basis, native and foreign-born patients generated similar number of secondary cases and transmission occurred as frequently from a native patient to a foreign-born patients, as vice versa.



[Transmission amongst native and foreign-born patients.]

3426 Estimating age-mixing patterns in contacts relevant for the transmission of *Mycobacterium tuberculosis* and other airborne infections

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Background: Age-mixing patterns can have substantial effects on infectious disease transmission dynamics and intervention effects. Data on close contacts (people spoken to and/or touched) is often used to estimate age-mixing. This is not appropriate for airborne infections such as tuberculosis, where transmission can occur between anybody 'sharing air' indoors. Directly collecting data on age-mixing patterns in casual contacts (shared indoor space, but not 'close') is difficult however. We demonstrate a method for indirectly estimating age-mixing patterns in casual indoor contacts.

Methods: We estimated age-mixing patterns in close, casual, and overall contacts using data from a social contact survey in South Africa. The age distribution of casual contacts in different location types was estimated from the reported time spent in the location type by respondents in each age group.

Results: Patterns of age-mixing calculated from contact time were similar between close and overall contacts, however patterns of age-mixing calculated from contact time were more age-assortative in overall contacts. There was also more variation by age group in total numbers of casual and overall contacts than in total numbers of close contacts. Estimates were robust to sensitivity analyses.

Conclusions: Patterns of age-mixing can be estimated for casual and overall contacts using data that can be easily collected as part of social contact surveys, and may differ from patterns in close contacts.

3464 Use of demand-driven approaches to improve the determination of TB burden amongst people living with HIV [PLHIV] across 28 health facilities in Nigeria

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Background: Nigeria is one of seven countries that contribute to 64% of the global burden of TB, ranking 6th ahead of S-Africa¹. Sub-Saharan Africa bears 70% of the global HIV burden²; Nigeria ranks 2nd in the region and 3rd globally with a prevalence of 3.4%³. Given that the burden of Tuberculosis among PLHIVs is 16-27% higher than in the general population⁴, innovative means to increase TB case finding among this group is essential.

Methods: CRS supports over 17,900 PLHIV's with comprehensive HIV care and treatment services distributed among 28 secondary health facilities across 5 states. Inconsistency in routine TB screening and documentation by health providers necessitated innovative approaches to determine TB status among PLHIV. An individualized approach was adopted involving an audit of patient charts to determine which clients had documented TB screening. Using awareness creation, health education, counselling and advocacy to PLHIV support groups, client's awareness and demand for TB screening during routine clinic visits was increased. Clients were also tracked through home visits, and/or phone calls and clinical TB screening was administered using the four cardinal questions.

Results: This approach led to a 23% increase in PLHIV screened for TB, with an associated 49% increase in the number of PLHIV who were initiated on Isoniazid Preventive Therapy. During the two-month period, 574 presumptive TB cases and 87 active cases were also identified.

Conclusions: Health worker-focused approaches to improving service delivery coverage have seen limited success and often do not reflect the huge cost incurred on interventions. Demand driven interventions to improve TB screening show significant promise as a complement to service-driven approaches in determining the burden of TB amongst PLHIVs.

3473 Evaluation of the National Electronic Drug-Resistant Tuberculosis surveillance system in South Africa, 2009-2013

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Background: Periodic evaluation of a surveillance system is important to ensure the effective and efficient operation of the program to fulfil its objectives. The electronic DR-TB register, EDRWeb was rolled-out in 2009 in South Africa, however, this is the first evaluation of the system since its inception. This report will outline the findings following the evaluation that was undertaken using data for patients initiated on DR-TB treatment between 2009 and 2013.

Methods: The 2001 Updated Guidelines for Evaluating Public Health Surveillance Systems, developed by the United States Centers for Disease Control and Prevention was adapted to evaluate the EDRWeb. Data was analysed from the 42 Drug Resistant tuberculosis units that had an active EDRWeb to assess the attributes of the system. Stakeholder perceptions on the utility and functionality of the system were investigated through the use of questionnaires.

Results: The EDRWeb was acceptable and simple, (59% and 91% respondents respectively) to capture the initial patient record, however 75% respondents needed more training on its functionality and capabilities. The system had limited usefulness, largely used as a data capturing platform than for data collation and reporting. This was largely attributed to the inadequate coordination of the introduction of the electronic reporting system, resulting in personnel being more accustomed to the paper-based tools.

Conclusions: The evaluation found that the system's usefulness could be improved by extending its capabilities beyond being a data capturing system only and a constant liaison and feedback between the system users. Following the EDRWeb upgrade, training was recommended and conducted for all active DR-TB units and this resulted in an improved system. The availability of improved data to stakeholders from the EDRWeb wherever they can be in the world bears testimony to the improved system leading to the decision to retire the reporting from paper based tools.

3480 Pharmacokinetics of ethionamide in children in an Indian setting

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Background: Adequate concentrations of 2nd line anti-tubercular therapy (ATT) are essential for the effective management of multi-drug resistant tuberculosis (MDR-TB). Doses of these drugs in pediatric age group are extrapolated from adult studies. However, children absorb, metabolize and eliminate drugs differently than adults which may lead to ineffective dosing when only adult data are used. The pharmacokinetics of these drugs in children is not well studied. We planned to study the pharmacokinetics of ethionamide in children with MDR-TB.

Methods: A pharmacokinetic study with limited sampling strategy of 5-point sampling was carried out in All India Institute of Medical Sciences, Delhi. Children with MDR TB on 2nd line ATT for at least 30 days were sampled at 0 (pre-dose), 1, 2, 3 and 4 hours post-drug. The separated plasma samples were analyzed by LC-MS/MS in MRM mode. C_{max} , T_{max} and AUC_{0-4} hours were calculated.

Results: Twelve children [girls:7 (58.3%), mean (SD) age: 133.1 (31.9) months] with rifampicin resistance on GeneXpert assay were enrolled. They tolerated ethionamide well, only four (33.3%) had increased thyroid stimulating hormone for which they were put on thyroxine hormone. The mean (SD) dose of ethionamide received was 16.9 (3.8) mg/kg/day in two divided doses

with a minimum of 12 hours interval between the last dose and first point of sampling. The median (IQR) C_{max} achieved was 10.69 (7.78, 20.86) $\mu\text{g/mL}$; mean (SD) T_{max} being 2 (1) hour. The median (IQR) AUC_{0-4} calculated was 28.01 (19.9, 41.79) $\mu\text{g/mL}\cdot\text{hr}$. None of the children had a C_{max} lower than the acceptable cut-off of 2.5 $\mu\text{g/mL}$. C_{max} or AUC_{0-4} were not affected by gender or age of the children; both were significantly correlated with the dose/kg body weight.

Conclusions: Children enrolled in this Indian study had acceptable plasma concentrations of ethionamide. They tolerated ethionamide well given in two divided doses.

3494 Challenges in childhood tuberculosis of Belarus

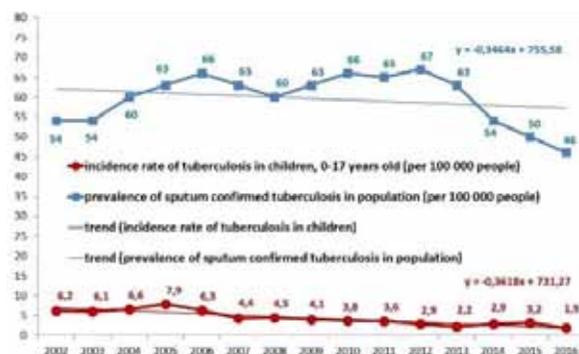
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Background: Study of incidence rate of tuberculosis in children is important for predicting the epidemic situation in the future and for the planning of tuberculosis prevention measures. The incidence rate of tuberculosis of children is closely linked to the spread of tuberculosis among adults.

The objective of this study was to examine tuberculosis incidence rates and patterns among children, prevalence of sputum confirmed tuberculosis among population in Belarus, analyzing data from 2002 to 2016.

Methods: The diagnosis was based on clinical, bacteriological, X-ray examination. We used data on child and adults population by the National Statistics Committee of the Republic of Belarus. We calculated incidence rates and prevalence of tuberculosis per 100,000 people.

Results: We have identified a decrease in the incidence rate of tuberculosis in children in 3.3 times: from 6.2 to 1.9 cases per 100,000 people for the period 2002-2016. The prevalence of sputum confirmed tuberculosis in population decreased only in 1.2 times: from 54 to 46 cases per 100,000 people. This is shown in Figure.



[Figure. Incidence rate of tuberculosis of children and prevalence of sputum confirmed tuberculosis]

The average incidence rate of tuberculosis in children was 4.44 cases per 100,000 people. The average prevalence of sputum confirmed tuberculosis in population was 59.6 cases per 100,000 people. Correlation between the incidence rate of tuberculosis in children and prevalence of sputum confirmed tuberculosis among population was absent between 2002 and 2016 (Correlation coefficient - 0.2). We assume that the true incidence of tuberculosis in children is higher than the reported incidence of tuberculosis in children in Belarus. Because the prevalence of sputum confirmed tuberculosis in population remains high. Therefore, it is necessary to improve screening for tuberculosis among children of Belarus.

Conclusions: Our study shows that a significant reduction in the incidence of tuberculosis among children is not true if the prevalence of sputum confirmed tuberculosis in population remains high.

3505 Turn around to diagnosis and treatment initiation and associated health facility related factors among patients attending private clinics in Lagos, Nigeria

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Background: Facility-related factors influencing turn-around time (TAT) to retrieval of genexpert result and TB treatment initiation have not been extensively studied in Nigeria.

Methods: Identified 27 peripheral private clinics were linked in 2015 with hub genexpert facilities. Retrospective analysis of sputum transport data over a 2 year period (January 2016-December 2017) was conducted. Data was extracted from sputum logbook and entered into SPSS for analysis

Results: The median TAT of Genexpert MTB/RIF assay (T4-T1) from date sent to date returned to the OPD of sending facility was 2 days (0-31, IQR=2.25). Median turnaround to treatment (T5-T1) after initial sputum collection was 3 days (0-44, IQR=4.25) for patients with positive Genexpert MTB/RIF assay while the median time from diagnosis to treatment (T5-T4) was 1.5 days (0-37, IQR=1.5).

Having sputum processed in a facility with resident genexpert, not-for-profit private facility and a facility with ad-hoc genexpert staff were all significantly associated with receiving result of genexpert diagnosis in the sending facility within 48 hours. On multivariate analysis, having HR support in the genexpert processing facility (OR-2.5, 1.8-3.3, $p < 0.001$); sending sputum from private not for profit private facility (OR 2.2, 1.6-3.0, $p < 0.001$) and having resident genexpert in the sending facility

(OR=17.6, 8.9-34.6, $p < 0.001$) were all significantly associated with early result Turnaround Time (T4-T1) within 48 hours of sputum collection. Presence of ad-hoc staff in genexpert hub facility and receiving MTB detected result within 48 hours of sample collection was associated with early treatment initiation (T5-T4) within 72 hours of diagnosis. On multivariate analysis, only receiving diagnosis result within 48 hours (OR-2.7, 1.2-6.0, $p = 0.013$) was significantly associated with early treatment initiation within 72 hours.

Conclusions: Resident genexpert machine and use of ad-hoc human resources at genexpert processing hub facility has reduced delay in TB diagnosis and improve genexpert result TAT but this did not have impact on treatment initiation.

3507 An estimate of the burden, potential missed care and diagnostic practices for tuberculosis amongst children admitted to government hospitals in Kenya

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Background: The true burden of TB in children remains unknown due to diagnostic challenges. TB is a leading cause of death, a "hidden epidemic" with approximately 65% of paediatric TB cases missed each year. We present preliminary results from a large longitudinal observational data set of hospitalised children in Kenya that estimate the burden of TB in children, using clinician documented TB diagnosis and or/decision to start anti-TB (referred to "Working TB Diagnosis") and the TB diagnostic practices highlighting potential missed care compared to recommended national guidelines. This will help guide development of interventions that could improve case detection of child TB in Kenya and other high burden countries.

Methods: This study was undertaken using routine in-patient paediatric data from the Clinical Information Network (CIN) a partnership between the Kenya Medical Research Institute, the Ministry of Health-Kenya, The Kenya Paediatric Association and 14 government hospitals spread across the country, for all admissions between 1st Dec 2015 to 30th Nov 2016. Descriptive exploratory analysis was done using Stata vs. 15 MP.

Results: There were 25,507 admissions in the calendar period, and 561 (2.2%) had a clinician assigned working TB diagnosis. Median age of these cases was 24 months (IQR 10, 60). Cough and fever were the commonest symptoms they presented with, and a history of TB contact was only elicited in 13.7% (77/561). 53 (9.5%) of the working TB cases died. Only 12.1% (68/561) were diagnosed using the guideline criteria (Table 1)

Conclusions: Most of the TB diagnoses were arrived at using less criteria than the guideline recommendations, and these present as potential missed care that could be contributing to the under-detected TB cases in children. More needs to be done to increase health care worker index of suspicion and use of TB diagnostic tests.

Scenarios Working TB Dx N= 561	Two or more of history ^a	Less than two of history	Two or more suggestive symptoms/ tests ^b	Less than two of suggestive symptoms/ tests	At least one bacteriological test done ^c	No bacteriological tests done
1. n= 68 (12.1%)	+		+		+	
2. n=123 (21.9%)	+		+			+
3. n=48 (8.6%)	+			+	+	
4. n= 183 (32.6%)	+			+		+
5. n= 15 (2.7%)		+	+		+	
6. n= 10 (1.8%)		+	+			+
7. n= 8 (1.4%)		+		+	+	
8. n= 80 (14.3%)		+		+		+

a Two or more of cough, fever, growth faltering or lethargy

b Two or more of history of TB contact, abnormal respiratory signs, chest X-ray or mantoux test order

c Either Genexpert, or smear microscopy of mycobacterium tuberculosis culture was done

[Diagnostic practices used by clinicians to diagnose TB in children]

Author Index

Bold indicates presenting author

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