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ABSTRACT BOOK

WORLD CONFERENCE ON LUNG HEALTH 2022 OF THE INTERNATIONAL UNION AGAINST TUBERCULOSIS AND LUNG DISEASE (THE UNION)

**VIRTUAL EVENT
8 – 11 NOVEMBER 2022**

Since its foundation in 1939, the mission of the Research Institute of Tuberculosis, Japan Anti-Tuberculosis (RIT/JATA) has been to contribute to domestic and global tuberculosis control by conducting various studies, providing technical support as well as performing activities for international cooperation and collaboration.

Our Vision

- ▶ A world where no one suffers from tuberculosis

Our Mission

- ▶ Our mission is to eliminate TB suffering through development and implementation of comprehensive TB control strategies.



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AIMS AND SCOPE

The International Journal of Tuberculosis and Lung Disease is an official journal of The Union. The Journal's main aim is the continuing education of physicians and other health personnel, and the dissemination of the most up-to-date information in the field of TB and lung health. It publishes original articles and commissioned reviews not only on the clinical and biological and epidemiological aspects, but also on community aspects: fundamental research and assessment of field projects and action programmes for TB control and the promotion of lung health. The Journal welcomes articles submitted on all aspects of lung health, including cost-benefit analysis, legislation, epidemiology, intervention studies and health systems research.

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The Union World Conference on Lung Health 2022 Virtual Event, November 8 – 11

SYMPOSIA: TUESDAY 8 NOVEMBER 2022

SP-01 Clinical experience from BPaL operational research in Asia, Africa and EEC

South Africa's experience: Clinical experience of BPaL across Nix-TB, ZeNix and BPaL Clinical Access Program

P. Howell,¹ ¹Sizwe Tropical Disease Hospital, Johannesburg,, Johannesburg, South Africa.
e-mail: phowell@witshealth.co.za

South Africa is a leader in the drug-resistant tuberculosis research space, both in pioneering R&D of shorter regimens, providing access to new or repurposed medicines, and implementation of groundbreaking guidelines. Dr Howell has worked with the BPaL regimen since 2015 as well as other ongoing pretomanid work.

She will discuss the clinical experience of BPaL across Nix-TB and ZeNix clinical trials, and operational research through the BPaL Clinical Access Program.

Clinical experience from BPaL OR leading up to scale-up in Kyrgyzstan

A. Toktogenova,¹ ¹NTBLCP, Kyrgyzstan, Bishkek, Kyrgyzstan.
e-mail: atyrkul7@gmail.com

Kyrgyzstan started enrolling patients on BPaL OR since August 2021. Preliminary analysis of the first cohort of TB patients of the BPaL OR in the Kyrgyz Republic showed high rates of culture conversion and the importance of adequate safety monitoring and management. Dr Toktogenova has been coordinating this initiative as the NTP Manager in the country and will share the clinical experience of the OR.

Clinical experience from BPaL OR in the Philippines

I. Flores,¹ ¹National TBMAC, San Fernando, Pampanga, Philippines. e-mail: docging1003@gmail.com

Dr. Irene Flores is the principal investigator of the Philippines BPaL Operational Research (OR) program. She will present the program's experience with the BPaL regimen to date as it enrolls 100 patients at 12 sites in the Philippines by the end of 2022.

This effort, which has been formally endorsed by the national Department of Health, is carried out through the Tropical Disease Foundation, a Manila-based organization dedicated to TB treatment innovation.

Clinical experience of BPaL observed in the OR in Ghana and Ecuador

C. Merle,¹ ¹WHO Special Programme for Research and Training in Tropical Diseases (WHO-TDR), Geneva, Switzerland. e-mail: merlec@who.int

In November 2019, the Special Programme for Research and Training in Tropical Diseases (TDR) and the WHO Global TB Programme launched ShORRT (Short, all-Oral Regimens For Rifampicin-resistant Tuberculosis), an operational research package to assess the effectiveness, safety, feasibility, acceptability, cost and impact (including on health-related quality of life) of the use of all-oral shorter treatment regimens for adults and children with MDR/RR-TB. Dr Merle, scientist at TDR, coordinates this initiative. She will share the country experience with OR for BPaL regimen.

SP-02 Towards TB-sensitive social protection programmes: understanding barriers and formulating solutions

WHO's guidance on social protection for people affected by TB

D. Pedrazzoli,¹ ¹World Health Organization, Geneva, Switzerland. e-mail: pedrazzolid@who.int

This presentation will provide an overview of the upcoming WHO's guidance on social protection for people affected by TB, including its development process, main contents, and implementation framework. It will also showcase a selection of case studies, led by either national TB programmes (NTPs) or by UN agencies (e.g. ILO, WFP) in collaboration with NTPs or other government entities, that feature in the guidance.

These case studies will provide lessons learnt, successes and challenges in the implementation of socio-economic support to people affected by TB.

Assessing the TB-sensitivity of social protection programs: a generic study protocol

D. Carter,¹ ¹London School of Hygiene and Tropical Medicine, London, United Kingdom.
e-mail: Daniel.Carter1@lshtm.ac.uk

The evidence base supporting a positive impact of social protection programmes on TB outcomes continues to grow and consolidate. However, important questions remain about how well people with TB are able to access existing social protection programmes.

In this presentation, we describe a flexible mixed-methods protocol for assessing important supply-side and demand-side barriers that impact access to social protection through questionnaires, focus groups, and analysis of secondary literature and data.

We discuss how the results of this protocol can assist TB policymakers in strengthening existing intersectoral collaborations to improve access to social protection for people with TB.

Enhancing access to social protection for TB patients: challenges and opportunities in the Western Pacific Region

K. Rahevar,¹ ¹World Health Organization, Manila, Philippines. e-mail: rahevark@who.int

This presentation will provide an overview of the key findings resulting from the implementation of a mixed-methods approach for the assessment of the TB-sensitivity of existing social protection programs.

This exercise involved the Philippines, Laos and Mongolia and aimed to identify barriers to access to social protection from TB patients in these countries and possible solutions. Emerged evidence will be discussed separately and across countries so to identify lessons in common and highlight country specificities.

The presentation will conclude by illustrating a research and operational roadmap to maximise access to social protection from TB-affected communities in these countries.

SP-03 Advancing the TB-HIV response by addressing advanced HIV disease

Update on global TB/HIV burden and policy

A. Baddeley,¹ ¹World Health Organization, Geneva, Switzerland. e-mail: baddeleya@who.int

Scale-up of collaborative TB/HIV activities has saved an estimated 9 million lives since 2005 but TB is still the main cause of death among people with HIV, accounting for a third of all AIDS deaths.

This presentation will give an overview of the latest data on TB/HIV burden and coverage of collaborative TB/HIV activities, together with an update on the latest WHO guidance to address TB/HIV and advanced HIV disease.

Perspective from a survivor of advanced HIV disease and TB

S. Watiti,¹ ¹The National Forum of PLHIV Networks in Uganda (NAFOPANU), Kampala, Uganda.
e-mail: stephen.watiti@gmail.com

Stephen Watiti will share his perspective as a survivor from advanced HIV disease, MDR TB, severe bacterial infection, CCM and cancer.

Understanding high TB mortalities through death audits; a perspective from Siaya county, Kenya

M. Wambura,¹ ¹National Tuberculosis, Leprosy and Lung Disease Program Kenya, Kisumu, Kenya.
e-mail: mary2.wambura@gmail.com

Siaya county is one of the 47 counties in Kenya that is high burden for both TB and HIV with HIV prevalence of 16%. Mortality among TB/HIV is high at about 14%. Mortality Audits are carried out using predefined standard audit forms routinely. Patient audit records are routinely extracted from the Kenya national TB surveillance system, TIBU, and mortality audit forms. Systematic mortality audits with the help of structured mortality audit forms have the capacity to reveal areas that can contribute to improve systems and outcomes in TB control both for the HIV positive and negative TB patients.

Integration of the AHD package into TB/HIV care; case study from Malawi

P. Nyasulu,¹ ¹Department of HIV, STI and Viral Hepatitis in the Malawi Ministry of Health, Lilongwe, Malawi.
e-mail: pnyasulu@itech-malawi.org

In Malawi, 41% of people attending HIV services had advanced HIV disease in 2021. This presentation will give an overview of the progress, challenges, and opportunities for expanding access to services for advanced HIV disease, including through the TB services and how this relates to the WHO recommended AHD package of care.

Living with HIV but dying from TB: What do we need to do to get to zero deaths?

H. Ayles,¹ ¹London School of Hygiene and Tropical Medicine, Lusaka, Zambia.
e-mail: helen@zambart.org.zm

Despite the widespread availability of life-saving anti-retroviral therapy for HIV, people living with HIV are still dying of TB at an unacceptable rate. TB is a curable disease and so why do so many people living with HIV still die from TB? How can we reduce these deaths? This talk will explore the existing knowledge and research gaps that remain for us to achieve our target of zero deaths from TB.

SP-04 Stool-based diagnostics: a game-changer for hard-to-diagnose populations?

The landscape of stool-based diagnostics and results of stool-processing studies.

M. Ruhwald,¹ ¹FIND, the global alliance for diagnostics, Geneva, Switzerland. e-mail: morten.ruhwald@finddx.org

This presentation will start with an introduction on the need for and opportunities presented by stool-based diagnostics in certain populations. This will be followed by an overview of stool sample processing methods and the current policy.

The remainder of the presentation will be dedicated to results of FINDs work on stool-based diagnostics and stool sample processing.

The Global Laboratory Initiative practical manual for stool testing using Xpert Ultra and lessons learned for implementation of stool testing in children and PLHIV.

P. de Haas,¹ ¹KNCV Tuberculosis Foundation, The Hague, Netherlands. e-mail: Petra.deHaas@kncvtbc.org

The Global Laboratory Initiative (GLI) practical manual on stool provides information on the choice of stool processing methods and practical consideration for stool testing implementation. Next to this rich guidance, the results of experiments performed to gather more insights on optimal stool storage conditions, sampling strategy and robustness of the stool testing are available that will support countries while introducing stool testing. Furthermore, due to a paucity of data, stool testing is not yet recommended for (HIV-infected) adults with presumptive pulmonary TB, a pilot implementation conducted in Vietnam shows promising results.

TB-Speed results of using stool samples for diagnosis of tuberculosis in vulnerable children.

M. Bonnet,¹ ¹French National Research Institute for Sustainable Development, Montpellier, France.
e-mail: maryline.bonnet@ird.fr

In order to improve the diagnosis of tuberculosis among vulnerable children unable to produce sputum and to offer a simple alternative to sputum, the TB-Speed project included stool sample in its innovative diagnostic approach for children living with HIV with presumptive TB and for children admitted with severe acute malnutrition or severe pneumonia.

Uptake and feasibility of stool sample collection and yield of Xpert Ultra from stool in these different groups of children will be presented. Results of the performance of three centrifuge-free processing methods of stool sample prior Ultra testing will be also presented.

A novel stool DNA isolation technique for diagnosing TB disease by qPCR and M tuberculosis drug resistance by targeted sequencing.

A. Kay,¹ ¹Baylor Global TB Program, Houston, United States. e-mail: alexander.kay@bcm.edu

This presentation will present preliminary findings from a multinational study on the diagnostic accuracy of a novel stool quantitative PCR for detection of M tuberculosis. The stool DNA isolation methodology for this assay also enables targeted next-generation sequencing for the detection of mutations associated with M tuberculosis complex drug resistance to thirteen antibiotics. The presentation will demonstrate the potential for obtaining disease confirmation and comprehensive M tuberculosis drug resistance profiles from stool.

Future directions of non-sputum based TB diagnosis.

C. Lange,¹ ¹Research Center Borstel, Leibniz Lung Center, Borstel, Germany. e-mail: clange@fz-borstel.de

Conventional diagnosis of tuberculosis can be challenging due to slow diagnostic processes or, in the case of young children, patients with extrapulmonary tuberculosis and some people living with HIV, unavailability of sputum specimens for a microbiologically confirmed diagnosis.

Detection of M. tuberculosis antigen or DNA from urine or stool, identification of tuberculosis-specific volatile compounds from exhaled breath or pathogen-free diagnosis from host RNA or metabolomic signatures from peripheral blood are currently explored to improve the diagnosis of tuberculosis in the field.

This presentation will give an overview of the current state of these developments and their potential for the future.

SP-05 What will it take to eliminate TB stigma? Engaging communities in implementation research to develop person-centred TB stigma interventions

Considerations for the design and evaluation of TB stigma reduction interventions

A. Daftary,¹ ¹York University, York, Canada.
e-mail: adaftary@yorku.ca

Stigma is a complex social phenomena, connected to intersecting determining factors, enabled through diverse pathways, and emergent in numerous visible and hidden forms. Reducing TB stigma calls for context-specific strategies, and robust approaches to the evaluation of such strategies. Current approaches are however too varied and may preclude required long-term investments into stigma mitigation.

This talk will outline discuss standardized and validated methods to inform the design, implementation and scale-up of TB stigma mitigation efforts.

Developing TB survivors as peer research associates for stigma research

P. Tisile,¹ ¹TB Proof, Cape Town, South Africa.
e-mail: ptisile@gmail.com

TB survivors have critical insider knowledge and contextual experiences that give them an unmatched ability to provide support to people affected by TB and reshape TB care narratives to improve quality of care delivery and patient engagement. While peer research associates (PRAs) have been increasingly used in fields such as cancer and HIV research, little is known about their potential role in improving person-centred TB care delivery and supporting implementation research.

From the perspective of a TB PRA, Ms. Tisile will discuss insights from conducting community-based stigma assessments in the form of surveys and in-depth interviews in Khayelitsha, Cape Town.

The Roots and Impacts of TB Stigma and the protective effects of Empowering treatment

M. Baiguerel,¹ ¹Center for Health Promotion and Research, Ngaoundere, Cameroon.
e-mail: erikamyriam18@gmail.com

TB patients in Cameroon report high levels of TB stigma (26.0%) and moderate to severe depression (29.2%). High TB stigma scores were correlated with alcohol use disorder (β .317, F 7.815, p = .006) and incurring debt, disavings, and/or experiencing hunger due to TB in multivariate analysis (β .988, F 5.019, p = 0.027).

Perceived good quality of care, resilience, and provision of emotional, nutritional, economic, or psychological

supports (β -.334, p =.023) were associated with lower TB stigma in partial correlation analysis (β F4.548, p =.035).

Self-reported adherence was high, but was negatively associated with receiving stigmatizing care in the health system and positively associated with receiving compassionate care.

Stigma measurement and the evaluation of "From the Inside Out"- a self-stigma management toolkit among people with TB and MDR-TB in Vietnam

L. Redwood,¹ ¹University of Sydney, Sydney, Australia.
e-mail: lisajredwood@gmail.com

There is an increased need for accurate stigma measurement and reduction initiatives in high TB and MDR-TB burden countries. Ms. Redwood will share her finding from her PhD research in Vietnam. She will cover the burden of stigma, depression, and health-related quality of life in people with TB and MDR-TB in Vietnam. Following this, she will present the preliminary results of a self-stigma and shame reduction intervention among people with TB and MDR-TB in Vietnam.

Exploring the intersections between stigma, caste and racism as they relate to TB policy and practice

A. McDowell,¹ ¹York University, New Orleans, United States. e-mail: mcdowell.andrew@gmail.com

There is growing recognition of the need for TB elimination efforts to align with an antiracism agenda. Dr. McDowell will discuss insights from his research in India, to explore intersections between access to care, stigma, caste and race.

Based on a longitudinal study of rural Indian families as they access TB care, the talk reveals ways TB infection control (TB-IC) measures put in place by caregivers are often experienced as caste-based discrimination and stigma. The effects of experiences are linked to health outcomes. McDowell argues for the inclusion of anti-casteist and anti-racist perspectives during the design and implementation of TB-IC measures.

SP-06 Evaluation of a standardised TB treatment regimen in patients with multidrug-resistant tuberculosis: STREAM Stage 2 final results

Overview of STREAM Stage 2 trial design and implementation

N. Gopalan,¹ ¹National Institute for Research in Tuberculosis, ICMR-NIRT, Chennai, India.
e-mail: gopalannaren@yahoo.co.in

This session will provide an overview of the STREAM Stage 2 trial design including treatment regimens, follow-up schedule, and outcomes assessed. The session will also include a summary of the major protocol amendments over the 6+ year implementation period.

Efficacy Results from STREAM Stage 2

R. Goodall,¹ ¹MRC CTU at UCL, London, United Kingdom.
e-mail: r.goodall@ucl.ac.uk

This session will present primary efficacy analysis results for comparisons between the all oral 9 month regimen and the control regimen. It will also present results for comparison between the control regimen and the 6 month regimen containing bedaquiline and an injectable.

Safety Results from STREAM Stage 2 trial

B. Kirenga,¹ ¹Makerere University Lung Institute, Kampala, Uganda. e-mail: brucekirenga@yahoo.co.uk

This session will present an overview of safety results in terms of adverse events and serious adverse events, and comparisons between trial regimens.

Health Economics Analyses

L. Rosu,¹ ¹Liverpool School of Tropical Medicine, Liverpool, United Kingdom.
e-mail: laura.rosu@lstm.ac.uk

This session will present the health economic data that was collected alongside the trial for the two 9-month regimens and the 6-month regimen. This includes patient and health system costs as well as quality of life data up to week 76. Cost-effectiveness of each regimen compared to standard of care will also be presented.

STREAM Stage 2 Results Dissemination

M. Kipiani,¹ TB management and Control Service at the National TB Program; Tbilisi, Georgia, Tbilisi, Georgia.
e-mail: maiagegechkori@yahoo.com

This session will provide an overview of our stakeholder engagement strategy for dissemination of trial results and cover the breadth of work done in consultation with site teams and Community Advisory Boards to achieve dissemination to trial participants, National TB programmes, healthcare workers, and the wider community.

SP-07 Large-scale implementation of short-course TB preventive treatment regimens: experiences from the field

Scale up of short course preventive treatment for TB – Evidence to Policy, Policy to Practice

M. Gombe,¹ The Aurum Institute, Harare, Zimbabwe.
e-mail: mgombe@auruminstitute.org

The IMPAACT4TB project implements innovative strategies to deliver 3HP to high-risk groups in 12 project countries. Experience from this project will be used to support global scale-up and contribute to meeting the global EndTB targets.

This session will describe the lessons learnt during implementation of short regimens, including demand creation through engagement with civil society organisations, use of evidence to ensure decisions about use, feasibility and scale-up of these new regimens are based on latest available scientific practice, value for money analysis to prepare business cases for MOH, and working with manufacturers to ensure affordability and access to nationalise short-course regimens.

Scale up of short course preventive treatment for TB – Evidence to Policy, Policy to Practice

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on latest available scientific practice, value for money analysis to prepare business cases for MOH, and working with manufacturers to ensure affordability and access to nationalise short-course regimens.

Implementation of 3HP in Pakistan

H. Hussain,¹ IIRD, Singapore, Singapore.
e-mail: hamidah.hussain@ird.global

Pakistan ranks 5th among high TB burden countries. A private-sector health care provider, Indus Hospital and Health Network, initiated a ZERO TB initiative in Karachi to implement a comprehensive approach to ending TB.

This approach included the scale-up of TPT among high-risk groups. This also included the scale-up of 3HP and 1HP, including children.

The PEARL project - update from Kiribati

B. Marais,¹ University of Sydney, Sydney, Australia.
e-mail: ben.marais@sydney.edu.au

Population-wide interventions offer opportunities to eliminate tuberculosis (TB) and leprosy, but data on the implementation of combined approaches are limited in high-burden settings. A comprehensive TB and leprosy elimination approach, including screening and treatment of active disease and infection is being implemented in Kiribati.

We aim to demonstrate feasibility and to evaluate the effect of this approach on disease incidence rates, as well as TB transmission. Treatment of TB infection, one of the key interventions, include the use of 12 weekly doses of isoniazid and rifapentine (3HP). Pragmatic adherence support strategies tailored to the particular setting will be implemented.

Providing 3HP to people living with HIV in a differentiated care model

M. Mapingure,¹ ICAP at Columbia University, Harare, Zimbabwe. e-mail: mpm2189@cumc.columbia.edu

Zimbabwe's Ministry of Health and Child Care (MoHCC) has scaled up multiple differentiated service delivery models including facility-based individual models such as fast-track. These fast-track visits occur quarterly and involve ART pickup among other things, which reduces time spent at the facility. Integrating TPT into the fast-track model has the potential to enhance coverage and treatment completion. ICAP in collaboration with MoHCC and the Zimbabwe National Network for PL-HIV assessed the integration of 3HP into the fast track model.

SP-08 Enabling gender equity in TB: gender-sensitive solutions in TB policy and programme

A personal experience with TB and a call for gender-sensitive and identity-conscious approaches to address TB inequities and injustice

T. Kunor,¹ ¹WHO Civil Society Task Force on TB, London, United Kingdom. e-mail: tenzinkunor@gmail.com

Tuberculosis (TB) affected communities and individuals offer experience, people-centred initiatives, and community-led accountability, crucial to efforts to end TB. Tenzin Kunor shares his powerful and moving lived experience of multidrug-resistant TB.

Emphasising the importance of social identities and systems of privilege and oppression that impact individuals' experience with TB, he calls for gender-sensitive and identity-conscious approaches that are culturally- and community-relevant to address TB inequities and injustice.

What gender equity in TB means and could look like

A. Daftary,¹ ¹York University, York, Canada. e-mail: adaftary@yorku.ca

To unpack what gender equity in TB means and could look like the following questions are addressed: What is equity and what does an equitable outcome mean in TB? Where does gender fit into the umbrella structure of (social) equity, and specifically what aspects of gender matter (or should matter) in TB? What are the threats to gender equity when it comes to TB? How can some of these threats be addressed or mitigated to enable gender equity in TB?

Solutions to addressing gender inequities to accessing TB care and prevention: Findings from the Stop TB Partnership's Communities, Rights and Gender assessments

A. Herna Sari,¹ ¹Rekat Peduli Indonesia, Surabaya, Indonesia. e-mail: anihernasari@gmail.com

The Stop TB Partnership's Communities, Rights and Gender assessments are multi-stakeholder participatory processes to support countries in identifying TB key and vulnerable population data gaps, human rights and gender barriers to TB services, and subsequent solutions to address inequalities to accessing TB care and prevention.

Findings have identified, for example, that the types of barriers to services that men experienced are unique; stigma manifests differently for men and women; there

is also further evidence on the experience of men who are members of key and vulnerable populations. Here country examples are given of solutions being implemented to foster gender-transformative programming.

Development and evaluation of gender-sensitive TB interventions for community settings in Nigeria

C. Ugwu,¹ ¹Zankli Research Centre, Karu, Nigeria. e-mail: 119153@lstmed.ac.uk

The DESTINE research was developed through The LIGHT Consortium in response to men's high tuberculosis burden and disadvantages in detection and reporting in Nigeria. The research programme seeks to demonstrate the effect of a gender-sensitive intervention for actively finding people with tuberculosis in community settings.

This presentation will cover the evidence emerging from its qualitative research component on the factors affecting access to tuberculosis care and how they interact. It will also highlight key findings from the scoping review on gender-based interventions, as well as the co-creation of a bespoke gender-sensitive intervention with key tuberculosis stakeholders in the country.

Where women lead, change happens: Empowering women to end the tuberculosis epidemic

M. Murenga,¹ ¹TB Women, Nairobi, Kenya. e-mail: maureenmurenga@gmail.com

Empowering women will be critical for the success of reaching the goal of ending the tuberculosis epidemic. Women in affected communities and women's advocates need to be engaged in efforts to design and enhance access to TB services, especially in high HIV and TB burden settings. Human rights and equity challenges should be effectively addressed to ensure that socio-cultural barriers and stigma are effectively eliminated, providing women access to high-quality care, free of catastrophic costs and social repercussions. All working to end TB must commit to do much more to engage affected communities and enable equitable access to care.

SP-09 Designing future-ready TB diagnostic systems using diagnostic network optimisation (DNO): uptake and impact of DNO recommendations from country experiences

Value for Money of investments in laboratory systems strengthening- access, efficiency and equity perspectives

H. Albert,¹ ¹FIND, Cape Town, South Africa.
e-mail: Heidi.albert@finddx.org

DNO is a highly contextual and adaptable approach that can be applied in a range of contexts to generate evidence for strategic planning and to inform investment decisions, including domestic funding and donor funding requests. Achieving improved access to services in different settings may require tailored approaches based on the local epidemiology, health systems infrastructure and geography, and DNO enables decision makers to examine trade-offs of different options based on access, equity and efficiency, hence enabling the greatest impact of investments.

This presentation explores dimensions of value for money that can be explored using DNO and use for decision making.

Scaling up access to molecular testing and implementation of optimal sample referral system towards achieving universal DST in ten Indian states

A. Beri,¹ ¹Foundation of Innovative New Diagnostics (FIND), Delhi, India. e-mail: archana.beri@finddx.org

India's NTP aims to scale up rapid TB molecular and drug resistance testing to support achieving universal TB testing in line with National Strategic Goals of the country. To achieve this vision, improved last mile access to testing and utilization of available diagnostic capacity is essential.

This presentation will provide an overview of planning and implementing sample referral system using diagnostic network and route optimization (RO) analysis. This seeks to provide detailed planning of referrals, sample transport routing designs (including type of route), cost estimates and the number of vehicles/human resource required to meet routing needs. Implementation of the recommended sample referral network design and monitoring its impact on India's NTP will be described.

Embedding data driven decision-making for TB diagnostic systems in Pakistan's TB National Strategic Planning processes

S. Tahseen,¹ ¹National TB Reference Laboratory, National Tuberculosis Control Programme, Islamabad, Pakistan.
e-mail: sabira.tahseen@gmail.com

Pakistan has an estimated TB incidence in 2020 of 573,000, of which 48% patients were notified. Building on recent progress, the National TB Control Programme's National Strategic Planning process is underway and will inform upcoming donor funding requests. Pakistan has initiated a DNO analysis to design an optimal network to address the shift to upfront WRD testing for all presumptive TB patients, consider private sector demand, optimize placement of GeneXpert 10-colour devices, guide expansion of chest X-ray and explore opportunities for integration with other programmes. This presentation will describe the DNO scope definition, approaches to stakeholder engagement, and present preliminary findings.

Mapping tuberculosis testing capacity in national laboratory networks of Africa: how can DNO address gaps through the ASLM LabCoP?

M. Massinga Loembé,¹ ¹African Society for Laboratory Medicine (ASLM), Libreville, Gabon.
e-mail: mmassinga@aslm.org

The LabMap program of the African Society for Laboratory Medicine (ASLM) and Africa CDC has collected GIS data on laboratory testing capacity across 15 African countries. This landscaping exercise has evidenced gaps existing between international or national norms for access (ie: essential diagnostics list) and actual availability of diagnostic tools at each tier of the laboratory network. DNO can help bridge the identified gaps by recommending options for adding testing capacity or effectively leverage existing multi-disease testing instruments.

Furthermore, the ASLM Laboratory Systems Strengthening Community of Practice (LabCoP) allows countries and stakeholders to co-create knowledge and identify solutions to improve laboratory services and networks. Here we propose use of the LabCoP theory of action to develop use cases for DNO and improve availability and access to TB diagnostics.

SYMPOSIA: WEDNESDAY 9 NOVEMBER 2022

SP-10 Two-month Regimens Using Novel Combinations to Augment Treatment Effectiveness for Drug-sensitive Tuberculosis (TRUNCATE-TB Trial)

Overview of the TRUNCATE-TB trial design and conduct

E. Burhan,¹ ¹Persahabatan Hospital, Jakarta Timur, Indonesia. e-mail: erlina_Burhan@yahoo.com

This presentation will describe the rationale for the trial and for the key components of the innovative trial design; and describe the overall trial conduct including overcoming the challenges arising from the COVID-19 pandemic.

Efficacy and safety results from the treatment strategy

N. Paton,¹ ¹National University of Singapore, Singapore, Singapore. e-mail: nick_paton@nus.edu.sg

This presentation will describe the outcomes from the randomised comparison of the treatment strategy with standard treatment and explore how modifications might further enhance potential advantages of the 2-month treatment strategy approach.

Implementation of whole genome sequencing and impact on trial results

C. Suresh,¹ ¹National University of Singapore, Singapore, Singapore. e-mail: mdcceli@nus.edu.sg

This presentation will describe the implementation of comprehensive whole genome sequencing in the trial and its added value for determining trial primary outcomes, as well as exploring the emergence of drug resistance.

Pharmacokinetics and pharmacodynamics of the trial regimens

C. Cousins,¹ ¹National University of Singapore, Singapore, Singapore. e-mail: christopher.cousins@ucl.ac.uk

This presentation will explore the pharmacokinetics and pharmacodynamics of key drugs used in the TRUNCATE-TB trial in order to determine optimal dosing strategies for future ultra-short drug-susceptible TB regimens.

Feasibility and acceptability of the 2-month treatment strategy

N. Donato,¹ ¹Lung Center of the Philippines, Quezon City, Metro Manila, Philippines.
e-mail: nerissa.donato@gmail.com

This presentation will describe the feasibility and acceptability of implementing the TRUNCATE-TB treatment strategy from the perspective of a clinician in a busy TB clinic, as well as patient experiences gathered during the trial.

SP-11 Private sector engagement to end TB in Africa

Private sector engagement in TB control in Southern Africa

C. Chamdimba,¹ ¹African Union Development Agency (AUDA-NEPAD), Johannesburg, South Africa.
e-mail: chimwemwec@nepad.org

In support of countries in Southern Africa to strengthen their pandemic preparedness and cross-border disease control, AUDA/NEPAD has conducted a landscape analysis. The engagement of the private sector is outlined as a key priority area in support of coverage and quality of TB control and occupational lung services. The study has informed interventions in Malawi, Lesotho, Mozambique, and Zambia to strengthen coordination and support private sector engagement in TB control for increased access to quality ensured service.

Scaling up PPM as part of the national plan to Ending TB in Nigeria

C. Anyaike,¹ ¹National Tuberculosis, Leprosy and Buruli Ulcer Control Programme, Nigeria, Abuja, Nigeria.
e-mail: chuxxanyaike@yahoo.com

Nigeria has made rapid progress in engaging private providers in their TB services through PPM programs in the last several years. The National Program is providing the stewardship to various stakeholders involved in PPM, as outlined in a recent landscape analysis, emphasizing the potential impact in finding the missing people with TB, improving quality of services, and improving efficiencies.

Providing TB and HIV services to mining populations in northern Tanzania

R. Abeid,¹ ¹SHDEPHA+Kahama, Kahama Municipal, Shinyanga Region, Tanzania.
e-mail: rabiabeid@gmail.com

The mining sector, though a vital economic sector in Africa, is associated with high levels of Tuberculosis. The challenge of TB in the mining sector is compounded by high rates of HIV, unfavourable working and living conditions which increase the miners' risk of contracting the communicable disease.

The challenge of TB in the mines is further complicated by labour migration patterns and weak mine health regulatory systems, leaving mining companies to self-regulate on dust control. The unique relationships between TB and HIV; TB and poverty; and TB and mining requires multi-sectoral integrated approach to end TB by 2030

SP-12 Digital health technologies for providing person-centred tuberculosis care: country experiences and suggested strategies for scale-up

Digital Adherence Technologies in TB care: overview of the experience from five countries

K. van Kalmthout,¹ ¹KNCV Tuberculosis Foundation, The Hague, Netherlands.
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The Unitaaid-funded ASCENT (Adherence Support Coalition to End TB) project started in 2019. It aims to help people affected by TB in Tanzania, South Africa, Ukraine, Ethiopia and the Philippines to successfully complete treatment using digital technologies such as smart pill boxes, medication sleeves and video supported treatment. In this session, implementation experiences will be shared.

Synthesising evidence on the impact of digital adherence technologies on health outcomes and implementation issues of employing adherence technologies, among people being treated for tuberculosis disease

K. Fielding,¹ ¹London School of Hygiene and Tropical Medicine, London, United Kingdom.
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A systematic review found limited evidence of the effect of digital adherence technologies on improving health outcomes for persons on tuberculosis treatment. Updated global guidelines made a conditional recommendation with very low certainty of evidence for tracers and/or digital medication monitors offered to tuberculosis patients. In the last few years there have been a plethora of studies reporting on digital adherence technologies, and implementation studies have generated important data on implementation challenges.

Here, we will report on an updated systematic review on the use of digital adherence technologies on improving health outcomes and systematic review synthesising data on implementation challenges.

The use of digital adherence technologies to improve TB treatment outcomes: results from the TB MATE study in South Africa

S. Charalambous,¹ ¹The Aurum Institute, Johannesburg, South Africa. e-mail: scharalambous@auruminstitute.org

TB Mate is a cluster-randomised trial being conducted in 18 primary health clinics in South Africa. The study is enrolling drug-sensitive TB (DS-TB) patients. All participants are provided with monitors: intervention arm

participants had visual/audio reminders for medication intake; standard of care monitors had no reminders.

In the intervention arm, weekly adherence reports are generated, and participants receive intensified support depending on number of missed doses. TB Mate is comparing adherence to TB medication amongst persons with supported by medication monitor and differentiated care approach (intervention) versus standard care. We will share results on treatment outcomes, feasibility, and cost.

How digital adherence technologies helped mitigate the impact of Covid-19 on TB services in Philippines

J. Alacapa,¹ ¹KNCV Tuberculosis Foundation (Philippines), Innovations for Community Health, USAID CLAIMHealth/Panagora, Metro Manila, Philippines.
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The COVID-19 pandemic exposed challenges in the Philippines healthcare system, resulting in a Tuberculosis notification drop of 37% in 2019-2020. Lockdown policies restricted mobility, and the treatment's paternalistic approach via daily face-to-face dosing couldn't pivot.

Through the pioneering efforts of the Philippine KNCV-ASCENT project, with the Department of Health, digital adherence technologies supported the shift to community and home-based treatment and allowed for greater flexibility for healthcare workers and patients, resulting in more person-centred care.

Critical success factors were strong government buy-in and recognition as a COVID-19 recovery strategy, the use of research evidence, and stakeholder co-design.

Programmatic Introduction of Digital Adherence Technology in Ethiopia: A stepwise approach towards national scale up

T. Letta,¹ ¹The Ministry of Health of the Federal Democratic Republic of Ethiopia, Addis Ababa, Ethiopia.
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Ethiopia is one of the early adopters of digital adherence tools (DAT's) for TB care, following a stepwise approach. At baseline, stakeholder consultations were held during the selection of the DAT types, following which the framework and infrastructure for the interventions was set up. Then the feasibility and acceptability of the DAT was assessed in a run-in phase before moving to the main trial phase.

Key challenges included issues with procurement and supply chain of DAT's, adherence platform configuration and customization, research protocol approval process and network coverage problem in some areas.

SP-13 TB and forced migration: what do we know and what should we do?

What do we know? The epidemiology of TB among forced migrant populations.

D. Zenner,¹ ¹Queen Mary University, London, United Kingdom. e-mail: d.zenner@qmul.ac.uk

Persons experiencing forced migration are at high risk of TB, because of multiple interacting factors, including those which facilitate transmission, those which weaken immune response or those which prevent appropriate timely care often as a result of complex socio-economic and security environments in their country of origin, and sometimes during transit and arrival. TB outcomes will also be worse. Forced migrants should be priority populations for TB care, yet accurate epidemiological data is scarce.

This introductory talk aims to summarise, what is known and what else should be known about these populations.

Lessons from the frontline: TB in first reception centres on the Romanian border

I. Margineanu,¹ ¹Rijksuniversiteit Groningen, University Medical Centrum Groningen, Groningen, Netherlands.
e-mail: ismargineanu@gmail.com

The war in Ukraine took Romanian authorities and NGOs by surprise. The first refugee centres set-up were ad-hoc efforts by volunteers, without governmental supervision. Despite medical advice and assistance and reasonable resources, optimum hygienic conditions were impossible to achieve.

The first waves of refugees arrived during wintertime with a large proportion of children. The focus of medical attention, apart from mental health and managing chronic conditions, were infectious diseases, mostly respiratory, including pneumonias, COVID-19, and TB. The presentation will discuss the set up and operation of a large refugee centre in Romania and implementation of prevention strategies for infectious diseases.

Lessons from the frontline: Afghanistan evacuation efforts

D. Posey,¹ ¹Centres of Disease Control and Prevention, Atlanta, United States. e-mail: dxp8@cdc.gov

For many years, the United States were offering permanent immigration to individuals (and their dependents) who worked for the US government. During 2021, overseas screening activities were rapidly expanded in advance of a planned US military withdrawal from Afghanistan. However, after Kabul fell, the United States evacuated approximately 70,000 Afghans to the United

States and quickly established an onshore tuberculosis screening program across several US military bases while addressing other public health concerns, such as COVID-19 and measles.

The presentation will cover how tuberculosis screening was performed, rates of detection, and challenges and lessons learned in implementing this program.

Lessons from the frontline: Key challenges for TB control and elimination in the Middle East—TB in refugees, migrants and internally displaced populations

N. Wilson,¹ IOM, Amman, Jordan.
e-mail: nwilson@iom.int

The Middle East Response (MER) funded by the Global Fund through IOM covers supports TB prevention and control in Yemen, Syria, Iraq, Palestinian Territories, Lebanon and Jordan. Protracted conflicts have caused region-wide displacement of people with lasting damage to health systems. COVID-19 and travel restrictions have imposed additional constraints on mobile populations.

This presentation will describe TB control within the MER highlighting epidemiology of TB in mobile populations, the challenges they face and strategic directions for the future.

Whizzy gadgets – the combined COVID and TB testing among refugees in Moldova and the Middle East – reporting from a joint IOM/FIND project

C. Gilpin,¹ IOM, Geneva, Switzerland.
e-mail: cgilpin@iom.int

The ongoing COVID-19 pandemic coupled with conflicts across Europe and the Middle East led to disruption of essential tuberculosis services. Given similar presentations in both diseases have, IOM together with FIND provide antigen rapid diagnostic tests (Ag-RDTs) to accelerate testing access. IOM has supported testing for COVID-19 and TB in persons with respiratory illness in the Middle East.

Ag-RDTs self-tests have also been distributed to Ukrainian refugees in Moldova at border crossings and shelters along signposting health services. The use of Ag-RDTs allows rapid COVID-19 and TB detection, helping to better triage persons to appropriate care for TB and COVID-19.

SP-14 Contemplating tobacco endgame in low- and middle-income countries through sustenance of tobacco control policies

Tobacco Free Generation (TFG) End Game Strategy in Philippines- a case study

H. Nung Koong,¹ Tobacco Free Generation International Limited, Singapore, Singapore.
e-mail: koonghn@gmail.com

The Tobacco-Free Generation International (TFGi) Endgame Approach, first published in 2010 by Dr Koong HN, has been nurtured to its current global phenomena (2 cities implementing a local TFG law 2017 and 2011; New Zealand, Malaysia and Denmark announced ~ 2021/2022) via a social movement, one year later. The presentation will show three critical elements for adoption:

- i. The vital need for a preceding social media publicity before any legislative attempts: contrasting the Balanga City, Philippines experience versus the negative mass discourse from the lack of such social media.
- ii. The almost-free and harmonious positive publicity from a youth/young-adult led social movement.
- iii. The ease of learning the TFGiEndgame narrative through customised TFG workshops.

This is the necessary FIRST step for any LMICs to unravel the deeply, entrenched and intertwined global blindspots that muddle societal understanding. Thereafter, each advocate/learner has the mastery to guide the subsequent social, structural and political discourse.

Establishing Tobacco Endgame Hub: Experiences from Australia & India

A. Jones,¹ The International Union Against Tuberculosis and Lung Disease, Sydney, Australia.
e-mail: ajones@theunion.org

This presentation aims to cover the main processes involved in the establishment of endgame hubs in Australia and India. What are the key goals, steps, results and lessons learned from these two vast countries in their mission and efforts to achieve tobacco endgames.

Establishing Tobacco Endgame Hub: Experiences from Australia & India

S. Goel,¹ Department of Community Medicine & School of Public Health, Post Graduate Institute of Medical Education & Research (PGIMER), Chandigarh, India., Chandigarh, India. e-mail: sonugoel007@yahoo.co.in

This presentation would cover the processes involved in establishment of endgame hubs in Australia and India. One which is well established since long (Australia)

would describe the journey so far and its contributions while the Indian one, which is still in its nascent stage highlight the its need, requirements in the current context.

SP-15 Tackling barriers in access to rapid molecular TB testing in remote areas: the Truenat experience

Truenat roll-out under the Stop TB/USAID introducing New Tools Project: filling gaps in access to testing in hard-to-reach places

L. Mupfumi,¹ ¹Stop TB Partnership, Geneva, Switzerland.
e-mail: lucymu@unops.org

The introducing New Tools Project (iNTP), a collaboration between the Stop TB Partnership and USAID, is the largest multi-country roll-out of the Truenat technology (9 countries in Africa and Asia). The Project aims to support countries in reaching the UNHLM targets for the detection and treatment of TB and drug-resistant TB.

The presentation will focus on the Truenat package offered to countries under the iNTP, including the available pricing and service and maintenance offered, connectivity functionalities as well as the implementation guidance developed by Stop TB and USAID. Early evidence of the impact of the iNTP will also be shared.

Support package for the Truenat assay implementation at the peripheral level

E. Reisdorf,¹ ¹IDDS, Rockville, MD, United States.
e-mail: Erik.Reisdorf@icf.com

The Truenat assay is being implemented for the first time at the peripheral level in nine countries supported by Stop TB partnership and the USAID IDDS project. Providing ongoing support to sites with minimal expertise with rapid molecular diagnostic tools is critical to ensure successful implementation.

The IDDS support package includes two components:

1. External Quality Assessment (EQA); and,
2. TB rapid molecular diagnostic “superusers” to provide ongoing mentorship and supervision.

This presentation will discuss the piloting of the support package and lessons learned.

Early experience of Nigeria in implementing Truenat in peripheral health care settings and in active case-finding activities

N. Nwokoye,¹ ¹KNCV Tuberculosis Foundation Nigeria, Abuja, Nigeria. e-mail: nnwokoye@kncvnigeria.org

In November 2021, Nigeria started the implementation of Truenat instruments provided through the Stop TB/USAID New Tools Project, with support from KNCV Nigeria and the IHVN.

Over the first four months of implementation, 13,248 tests were performed, with utilization rates steadily increasing (63% in March 2022) and error rates steadily decreasing (3% in March 2022).

In addition to using the instruments in peripheral settings to fill gaps in patient access to rapid molecular testing, Nigeria couples the instruments with ultraportable X-ray equipment for active case finding in communities.

Improving patient-centered primary care in the Philippines: early experience implementing Truenat

R. Basilio,¹ ¹Research Institute of Tropical Medicine in the Philippines, Muntinlupa City, Philippines.
e-mail: monbasilio@gmail.com

The Philippines started using Truenat in April 2022, with 38 Truenat instruments provided through the Stop TB/USAID introducing New Tools Project and with implementation support from the USAID’s TB Innovations and Health Systems Strengthening Project.

The country is positioning Truenat in hard-to-reach areas together with ultraportable X-ray equipment, as part of its efforts to improve the efficiency in TB/primary care service delivery.

This presentation will focus on the early country experience in starting to use Truenat and show complementarity with existing testing resources in the system, including lessons learned in installations, training, and effective use.

SP-16 Child contact case management: promising strategies and models of care to close the policy–practice gap

Designing Decentralized Pediatric TB Prevention Services Using a Task-sharing Approach between the TB clinic and the Health Extension Worker in Ethiopia: a qualitative study

N. Salazar-Austin,¹ ¹Johns Hopkins University School of Medicine, Baltimore, United States.
e-mail: nsalaza1@jhmi.edu

Developing innovative health care delivery models to accompany WHO-endorsed short-course TB Preventive Treatment (TPT) regimens is essential to reduce TB-associated child morbidity and mortality. Integrated community case management (iCCM) improves child survival through community-based services. The CHIP-TB cluster randomized trial will assess whether integrated community-based pediatric TB prevention services is feasible, acceptable and effective in increasing TPT uptake among child contacts < 15 years in Ethiopia and South Africa.

Here we present pre-trial formative work exploring context-specific implementation strategies needed to support contact investigation, TPT initiation and follow-up by health extension workers in Ethiopia.

Decentralized model of care for child contact investigation and TPT management in Cameroon and Uganda: CONTACT study results

M. Bonnet,¹ ¹French National Research Institute for Sustainable Development, Montpellier, France.
e-mail: maryline.bonnet@ird.fr

One of the challenges for child contact investigation and tuberculosis preventive treatment (TPT) management is the necessity to bring children to the facility. We will present results of a cluster randomized controlled trial that evaluated the impact (TPT initiation and completion and TB case detection) of a community-based intervention for child contact investigations and TPT management in Cameroon and Uganda.

The intervention includes contact screening in the household, referral of symptomatic contacts to the facility for investigation and 3 months rifampicin-isoniazid TPT initiation and follow-up of asymptomatic contacts <5 years old or 5-14 years and HIV-positive at the household.

Family-centered approaches for child contact management: experiences from Brazil

A. Trajman,¹ ¹Federal University of Rio de Janeiro, Rio de Janeiro, Brazil. e-mail: atrajman@gmail.com

The Family Health Strategy, the recommended model of primary care in Brazil, was successful in reducing overall mortality and improving TB treatment outcomes. An evaluation of the bottlenecks in the contact investigation and TB Preventive Treatment (TPT) cascade of care followed by tailored interventions in Family Health clinics increased the numbers of contacts starting TPT.

The family-centered approach has also been shown to improve cost-effectiveness of TPT interventions in LMIC. An intervention package including TST training, implementation of CAD, educational material and digital tools for surveillance will be discussed as potential solutions for TPT scale-up in Brazil and other LMIC.

Supporting national roll-out of contact investigation interventions targeting families and children in Vietnam: reflections on planning, budgeting and monitoring requirements for successful implementation

A. Innes,¹ ¹FHI 360, Bangkok, Thailand.
e-mail: ainnnes@fhi360.org

The Vietnam National Tuberculosis Program has implemented community campaigns since 2020 to detect TB disease and infection. Household contacts (primarily families) of adult pulmonary TB patients diagnosed within two years were evaluated during home visits.

Parents were counseled to bring children to the campaigns. Since 2020, a total of eight provinces that contain approximately 25% of Vietnam's TB burden evaluated 18,402 household contacts of whom 3,546 were <15 years old.

We diagnosed 105 Xpert-confirmed TB patients (of whom 5 were patients <15 years old) and 4,024 with TB infection (245 were children <15 years old).

SP-17 Systemic neglect of tuberculosis in indigenous peoples, the hidden pandemic

Combating TB within Canada's First Nation communities through culturally competent practices

T. Campbell,¹ ¹Northern Inter-Tribal Health Authority, Prince Albert, Canada. e-mail: tinacampbell@nitha.com

Ms. Campbell will discuss how the Northern Inter-Tribal Health Authority (NITHA) is working to combat tuberculosis within the First Nations of northern Saskatchewan and how cultural competence is essential to that plight. She will additionally address driving forces of the TB burden and underlying barriers to TB management in the Indigenous populations of Canada.

Addressing inequities in tuberculosis care of indigenous Venezuelans

J. Villalba,¹ ¹Mayo Clinic, Rochester, United States. e-mail: villalbanunez.julian@mayo.edu

Tuberculosis remains an active problem in indigenous populations; however, there continues to be inadequate research on the topic worldwide. Dr. Villalba will discuss current tuberculosis trends in indigenous peoples and provide context from his own experiences working with indigenous communities in Venezuela.

Prevalence of pulmonary tuberculosis among the tribal populations in India

B. Thomas,¹ ¹Formerly ICMR-National Institute for Research in Tuberculosis (Retired), Chennai, India. e-mail: beenaelli09@gmail.com

Tribal peoples make up nearly 8.6% of India's population. These groups are disproportionately impacted by TB. Dr. Thomas will discuss the methods utilized to perform a comprehensive survey of the tribal groups in India to better understand the prevalence of TB. She will also discuss her work about knowledge of TB within tribal groups as well as what factors may influence care-seeking behaviors among indigenous peoples of India.

Participatory Action Research to develop a better understanding of tuberculosis with Aboriginal communities in northern New South Wales, Australia, for health system change

S. Devlin,¹ ¹North Coast Public Health Unit, Lismore, Australia. e-mail: sue.devlin@my.jcu.edu.au

Systemic racism is the root cause of societal and health service issues that sustain ongoing transmission of TB in Aboriginal communities. Ending TB transmission in Aboriginal communities requires shifting the power imbalance towards Aboriginal people. Aboriginal peoples' voices must be privileged in the governance, design & delivery of TB policy, programs, services, and research. To end inter-generational TB affecting Aboriginal families, health services must engage ongoing deep listening with Aboriginal people and act together. Health system change is required to amplify and sustain effective grassroots TB prevention initiatives in northern New South Wales.

This talk includes "Uncle Richard", an Aboriginal elder and Traditional Knowledge Custodian of the Gumbayngirr Nation.

SP-18 What the pandemic taught us: TB programming during COVID-19 and beyond

Navigating the impact of COVID-19 on TB programming – how a change in approach to information turned a pandemic into success

P. Lungu,¹ ¹National Tuberculosis and Leprosy Control Zambia, Lusaka, Zambia. e-mail: lungupatrick99@gmail.com

The Zambia NTP navigated the negative COVID-19 pandemic impact on their programme performance by instigating a national TB situation room with weekly online review meetings. This allowed the programme to react to issues timely and efficiently. Through this process, the programme managed to improve and exceed its pre-pandemic performance. This session will share the experience, lessons learned, and impact on the future strategy.

National TB Control Program Adaptive Plan: Experience and challenges

A. Fabella,¹ ¹Department of Health- Disease Prevention and Control Bureau, Marikina City, Philippines. e-mail: rmfabella@doh.gov.ph

The Department of Health, Philippines organized an overall agency-wide adaptive plan or the “new normal” to guide the government on how it will move forward and cope owing to the experience of the COVID-19 pandemic and its socio-economic effects. The NTP Adaptive Plan provided specific measures and adjustments to the implementation of TB care guidelines to ensure the sustainability of TB care and the Updated Philippine Strategic TB Elimination Plan, it also served as the basis for specifying the investment requirements as input to the annual budget. The session will provide feedback on the process of planning and challenges faced.

Principles and guidance for planning a resilient TB programme - WHO tools & guidelines to support the planning process

S. Labelle,¹ ¹World Health Organization, Geneva, Switzerland. e-mail: labelles@who.int

A national strategic plan (NSP) for TB is a key strategic document that guides national authorities and stakeholders in how to comprehensively address the TB epidemic through interventions within the health sector and in other sectors.

Following significant global developments in TB and public health, including new tools and approaches to TB programming and planning, WHO is releasing a new guidance for developing an NSP for TB.

The session will highlight the key updates from the previous guidance, and present the key principles, good practices, components, and recommended process for national TB strategic planning.

User-experience-design & co-creation approaches to develop tailor made tools and approaches to facilitate evidence-based, country-led planning & decision making

E. Efo,¹ ¹KNCV Tuberculosis Foundation, The Hague, Netherlands. e-mail: egwuma.efo@kncvtbc.org

The rapid global spread of the COVID-19 pandemic threatened TB programming from early/mid-2020 onwards, creating additional challenges for NTPs and their partners during the last planning cycle.

In response, KNCV engaged selected PCF early-adopter countries in a user-experience-design & co-creation exercise, developing tailor-made tools and approaches, facilitating evidence-based, country-led planning & decision making. This included shifting from predominately external expert-dependent in-person TA to national capacity development supported by virtual/remote assis-

tance and mentoring. The co-creation process allowed adapting the PCF approach by identifying strengths, limitations, and opportunities to co-create more robust, responsive, and user-friendly approaches and tools for future users.

Using the People-Centred Framework for TB programming to plan our way out of the pandemic – introducing the PCF Knowledge Hub & toolkit

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The People-Centred Framework Approach (PCF) for TB programming is a standardized approach to facilitate person-centred, optimized, and evidence-based TB programming. In 2019-2020, ten early adopter countries used the tool for developing their national TB strategic plans and funding requests to major external funding sources. Under the current scenario of national TB programmes being impacted by the ongoing global pandemic, the PCF can help NTPs in planning their way out of the pandemic. In this presentation, we will introduce the PCF knowledge hub and toolkit to support country planning efforts.

SP-19 Advancing the science of TB education and counselling to improve patient-centred TB care in low- and middle-income countries

Steps toward a patient-centered framework for TB treatment literacy interventions

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Patient-centered care includes involving patients as empowered partners in their own care. Treatment literacy is necessary to support shared decision-making and participation in treatment decisions. However, there is no consensus operational definition of TB treatment literacy, and the content of treatment literacy materials varies widely. This talk will discuss steps toward developing a framework for TB treatment literacy interventions, a review of existing materials, and research priorities.

Peer Navigation to Enhance TB Education and Counseling for Individuals Diagnosed with TB and HIV-TB in Uganda

J. Davis,¹ ¹Yale School of Public Health, New Haven, United States. e-mail: lucian.davis@yale.edu

This presentation will describe the results of a two-part study in which we developed a multi-component, peer navigation strategy for providing TB education and counseling to persons living with and without HIV in Uganda and then evaluated its feasibility and effects on TB knowledge using a pragmatic, pre-post implementation design.

Counselling and peer support to improve outcomes for people with DRTB/HIV in South Africa: Staff training, patient experiences, and lessons for future practice

B. Seepamore,¹ ¹University of KwaZulu-Natal, Durban, South Africa. e-mail: Seepamoreb@ukzn.ac.za

Patient-centred care may improve outcomes and care engagement for people living with DRTB-HIV. A randomized trial of adherence support for people living with DRTB/HIV examined a psychosocial support (staff training, patient education, intensive individual counselling, group support). Staff training employed an interactive approach to counselling and treatment literacy, including role-plays and peer feedback. Individual counselling used motivational interviewing to actively engage participants in positive changes and strategize about barriers. Adherence support groups were a venue for peer support, psychosocial education, guest speakers, and skill building. Ongoing mentoring and supervision highlighted the importance of training a psychosocial workforce for public health.

Patient education and counselling for people affected by TB: lessons learned from COVID-19 and HIV and the path forward for TB

A. Daftary,¹ ¹York University, York, Canada. e-mail: adaftary@yorku.ca

People-centred, equity-oriented approaches in TB demand that we reimagine TB-related education and counselling. This talk will draw on tenets and methods of patient education to help inform the next generation of TB programming. Examples will be drawn from HIV, where approaches are driven by patient empowerment, principles of social justice, and partner/family involvement, and COVID, where community health literacy and access to information, through technological and social innovation, have been prioritized. Opportunities for knowledge transference on community engagement and patient education that support high-quality, patient-centred TB care will be presented.

SYMPOSIA: THURSDAY 10 NOVEMBER 2022

SP-20 TB disease: where does the threshold lie and why does it matter?

Voices from the past - Modelling new natural history

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As a new paradigm recognising the spectrum of tuberculosis (TB) has emerged, it has become necessary to revisit axioms about disease progression following *Mycobacterium tuberculosis* (Mtb) infection. This presentation will bring together historical and contemporary literature with a modelling framework that acknowledges distinct states across the spectrum of Mtb infection and TB disease. We will provide estimates of progression to each disease state and quantification of diverse pathways to and within TB disease states. This better understanding of pathways within states of Mtb infection and TB disease offers an opportunity for more effective TB prevention and treatment efforts.

Peering into the future - The natural history of asymptomatic disease

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Current dogma presents latent TB infection as a quiescent state, where the bacteria is inactive and that 'reactivation' precedes progression to active TB. The latent phase is often described as the multiple years which intervene between the time of documented TB exposure and the period of symptom onset. This presentation will illuminate the natural history of disease progression in recent TB contacts who progress to microbiologically-positive TB over 5-years. We will demonstrate the degree and diversity of active pathology which exist in individuals defined as having 'latent TB' and posit that active TB disease exists for years before symptoms.

Squishy symptoms - How much of sputum-positive-TB-disease is subclinical and how much does it matter?

L. Stuck,¹ ¹Amsterdam Institute for Global Health and Development, University of Amsterdam, Utrecht, Netherlands.
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Sub-clinical pulmonary tuberculosis (scTB) is a potential barrier to control and elimination. However, definitions for scTB are numerous and disputed and have significant bearing on the importance of scTB.

This presentation will describe results from a re-analysis of prevalence surveys to explore the impact of shifting the symptom threshold on the proportion scTB, and will explore the implications, in particular for current screening rules and the definition of scTB.

To treat or not to treat - Results from a systematic review of the management of Culture negative TB

A. Gray,¹ ¹University College London, London, United Kingdom. e-mail: adamgray2@nhs.net

It is recognised that some people have pulmonary tuberculosis that is apparent radiographically, but despite rigorous testing do not have culturable Mtb in their sputum. These individuals are at high risk of disease progression. Treatment is often given by clinicians though discouraged in clinical guidelines and the optimal treatment is not known.

Here we present the findings of a systematic review and meta-analysis of clinical trials comparing treatment with no treatment in this group. We find significant reduction in progression to microbiologically confirmed disease in those treated with multidrug rifampicin based regimens more effective.

What patients want: Discrete Choice Experiments for treatment of symptomatic culture negative individuals

W. Kamchedzera,¹ ¹Malawi-Liverpool Wellcome Trust Clinical Research Programme, Blantyre, Malawi.
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Treating individuals likely to progress to active TB disease can reduce the current TB burden. Research on patients' preferences for the management of incipient TB is vital.

Here we present the results of a discrete choice experiment conducted with 128 participants in Malawi to elicit preferences for the management of culture negative TB.

This involved framing a scenario where microbiological tests for TB were negative but a novel test placed them at high risk of disease progression over 12 months. Par-

participants choose between treatments with different attributes or no treatment. We found that participants strongly preferred treatments that prevent Mtb transmission.

SP-21 Innovative approaches and tools to find and treat missing people with TB

Global Fund TB strategic Initiative : Finding Missing people with TB and supporting innovative approaches in countries

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The Global Fund to Fight AIDS, Tuberculosis and Malaria has supported countries in adopting innovative approaches to find and treat missing people with TB which includes DSTB, DRTB as well as TB prevention through catalytic funding. This includes the TB strategic Initiative 'Innovative approaches to find and treat missing people with TB'.

The session will highlight key elements of the strategic support as well as innovative approaches developed and implemented with partners for impactful TB programming and improving the TB care cascade including TB prevention and community led monitoring.

Country adaptation and use of WHO Prevent TB application: Philippines' End TB App Suite

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In 2021, the Philippine DOH, supported by WHO, launched the End TB App Suite. It aims to provide a complete digital solution in the fight against Tuberculosis, and aims to support the government in reaching its TB elimination targets while providing an innovative tool during the time of the pandemic.

Inspired by the WHO Prevent TB app, the app suite has similar elements with additional functionalities, divided into four apps, covering distinct areas: Care TB focuses on patient care; Race TB supports surveillance; Lead TB is used for programmatic management and supervision, and Guide TB focuses on e-learning.

Country adaptation and use of WHO Prevent TB application: experience from India and future plans

R. Kumar,¹ ¹Ministry of Health and Family Welfare, Government of India, NEW DELHI, India.
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Nikshay, a case-based digital surveillance tool under the National TB Elimination Programme (NTEP) for India, adopts life cycle approach tracking TB care cascade. Albeit the initial focus of Nikshay was on granular monitoring of diagnosis and treatment while brushing on aggregate information on TPT, the evolving intricacies of TPT management necessitated subsuming it as an integral component of the surveillance workflow.

In this vein NTEP with WHO-India support piloted Prevent TB App and incorporated a case-based approach to TPT monitoring. Iterative feedback on the App usage emboldened the de novo Nikshay TPT module with enhancements from the learnings.

OneImpact Community-led Monitoring – Innovation for action, advocacy and accountability in TB.

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OneImpact community-led monitoring (CLM) is supporting National TB programmes to reach TB prevention, diagnosis, and treatment targets, using a rights-based approach to TB. Conceptualized by Stop TB Partnership, Dure Technologies and communities, OneImpact empowers people with TB to claim their rights, access services, and report and eliminate TB stigma and discrimination.

Through an innovative mobile application and system, it facilitates the participation of people with TB in the response to activate a human rights-based, people-centred response. In doing so, it combats TB challenges at individual and community levels while generating essential information to combat them at the programmatic level.

OneImpact CLM Mozambique – Key Successes and Lessons Learnt

H. Hallstrom,¹ ¹Associação Mocambicana para a Ajuda de Desenvolvimento de Povo para Povo (ADPP), Mozambique, Maputo, Mozambique.
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In 2019- 2020 Associação Mocambicana para a Ajuda de Desenvolvimento de Povo para Povo (ADPP) successfully adapted and pilot tested OneImpact in Mozambique, with demonstrated results and contributions towards TB prevention and treatment goals.

Today with the support of Stop TB Partnership, Centre for Disease Control and Prevention (CDC), GIZ-Back up, and the Global Fund, ADPP continues to expand

and prioritize community-led monitoring as a key intervention to promote and protect the rights of people affected by TB in Mozambique and to support TB programmatic goals and performance targets.

SP-22 Updated WHO guidelines on the management of TB in children and adolescents

Development and validation of treatment-decision algorithms for children being evaluated for pulmonary tuberculosis: an individual participant data meta-analysis

K. Gunasekera,¹ ¹Yale School of Public Health, New Haven, United States.
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This talk describes the development of a data-driven algorithm to support treatment decision-making among children being evaluated for pulmonary tuberculosis in resource-limited, high tuberculosis-incidence settings.

We describe the assembly of individual participant data of children being evaluated for presumptive pulmonary tuberculosis from multiple, diverse settings and use of modeling methods to quantify the contribution of clinical and imaging findings to risk of pulmonary tuberculosis.

We discuss implementation considerations that informed algorithm development from this model, strengths and limitations of this data-driven algorithm-building approach, and guidance for future work to externally validate treatment-decision algorithms.

Assessing severity of disease to determine treatment duration for children and adolescents with drug-susceptible TB, experiences from the SHINE trial

C. Chabala,¹ ¹University of Zambia, Lusaka, Zambia.
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The new WHO guidelines include a strong recommendation on 4-month treatment of non-severe forms of TB, based on the findings of the SHINE trial; important implementation considerations for this recommendation are around assessing the severity of disease to determine treatment duration; this assessment can be based on CXR features, bacteriological results and clinical signs and symptoms.

We share the clinical experience of assessing TB severity in children in Zambia and important considerations for implementing the WHO recommendations.

Experiences with the short intensive treatment regimen for children with TB meningitis

R. Solomons,¹ ¹Stellenbosch University, Cape Town, South Africa. e-mail: regan@sun.ac.za

TB meningitis is one of the most serious and fatal forms of extrapulmonary TB. The 6-month treatment regimen for TBM, consisting of rifampicin, isoniazid, pyrazinamide and ethionamide, which is now recommended by WHO as an alternative to the standard 12-month regimen, has been used in South Africa for over 30 years.

The 6-month treatment regimen has been found to be efficient and safe in drug-susceptible TBM. Ethionamide as the fourth drug in our setting has a manageable side effect profile, however availability can be challenging.

Implementing decentralized and integrated TB services for children under 5 years: evidence and lessons learned generated by the INPUT study in Cameroon

B. Tchounga,¹ ¹Elizabeth Glaser Pediatric AIDS Foundation, Yaoundé, Cameroon.
e-mail: btchounga@pedaids.org

Using evidence from the INPUT clustered randomized study, we will review the challenges and lessons learned from implementation of the CaP-TB project in Cameroon, focusing on integration and decentralization of TB services for children <5 years.

We will discuss final study results, comparing the effect of CaP-TB interventions on pediatric TB case finding and treatment cascades versus standard-of-care.

The presentation will also review acceptability and feasibility of project interventions, documented through the qualitative assessment conducted as part of the study. Implications for successful implementation of integrated and decentralized models of care recommended by new WHO guidance will be discussed.

Civil society perspectives on implementation of the new recommendations on child and adolescent TB

A. Khan,¹ ¹Association for Social Development, Islamabad, Pakistan. e-mail: ccp@asd.com.pk

The evidence-based new TB guidelines recommend family-centred integrated TB care, using new technologies and drugs. In this talk I will provide considerations about implementing these in a developing country programmatic context, as a member of the civil society.

These include key consideration on implementation challenges and how civil society can help to:

i. Bring services closer to children and families – a balance between access and cost?

- ii. Scale-up implementation of new diagnostic technologies e.g., Xpert ultra on stool specimens, and;
- iii. Ensure uptake of new shorter drug susceptible TB formulations and all oral DR-TB regimen and improve outcomes among children.

SP-23 Tobacco industry in the pharmaceutical sector: coping with the double-headed serpent

The “changing face” of the tobacco industry

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The tobacco industry remains a key contributor of global deaths but is now donning the cloak of a pharmaceutical and healthcare industry.

Vaping: Tobacco Industry is destroying the future of children

A. Bush,¹ ¹Imperial College UK, London, United Kingdom.
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The novel vaping products of the tobacco industry are not harmless. The short and long term effects of e-cigarette use will be discussed. The concerns of Pediatric Community will be underlined.

Can the industry turn into a medical company?

E. Dagli,¹ ¹Health institute Association, Istanbul, Turkey.
e-mail: elifzdagli@gmail.com

The tobacco industry recently invested into respiratory technology and medical cannabis companies. This talk will discuss what the the industry plans for future and will try to answer the questions about the sincerity of the transformation.

SP-24 Practical considerations for implementing and scaling up a new DR-TB regimen: experience from early BPAL-adopting countries

A practical implementation guide for programmatic introduction of the BPAL regimen

S. Staples,¹ ¹THINK TB and HIV Investigative Network, Durban, South Africa. e-mail: s.staples@think.org.za

The BPAL implementation guide, developed by THINK and partners with support from the Stop TB Partnership's TB REACH, is a comprehensive guide to the operationalization of the BPAL regimen with an aim to assist countries in successful and safe BPAL implementation. This presentation will describe the rationale for the guide and its relevance in low- and middle-income countries, especially as WHO has recommended programmatic use of BPAL containing regimens. It will also give an overview of the Guide, including toxicity management, pharmacovigilance, regulatory implementation and lessons learnt from earlier trials and experienced clinicians.

Implementing a novel regimen in a large country with diverse settings and considerations: learnings from South Africa

N. Ndjeka,¹ ¹TB Control and Management, National Department of Health South Africa, Pretoria, South Africa.
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South Africa has been a leader in the research agenda for new TB therapies, serving as a hub of research expertise and enrolling patients in the clinical study of the BPAL regimen in TB Alliance's Nix-TB and ZeNix studies. Building on the success of those trials, the national BPAL Clinical Access Program (CAP) began enrolling patients in December 2020. Dr. Norbert Ndjeka will discuss preliminary experiences from the CAP and discuss how South Africa can continue to be a leader in adopting new technologies to fight DR-TB, including by scaling up access to six-month, all-oral regimens.

Introducing BPAL in the United States

C. Haley,¹ ¹Southeastern National Tuberculosis Center, University of Florida, Gainesville, United States.
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Since USFDA approval August 14, 2019 of the all-oral BPAL regimen, Bedaquiline, Pretomanid and Linezolid given 6 months (extendable to 9) for treatment of a specific type of highly treatment-resistant tuberculosis, this novel regimen has been widely implemented throughout the country.

This session will describe the challenges and successes of early implementation into clinical practice and the monitoring measures used to enhance patient safety and tolerance. Data from more than 100 patients treated with BPaL will be presented to highlight the positive clinical outcomes that have enabled this regimen to become the U.S. standard of care for drug-resistant TB.

SP-25 Airborne infection prevention and control: the key to preventing the next pandemic

Prioritizing & managing IPC risks in health facilities in the era of TB & COVID-19

A. Kansal,¹ ¹National Institute of Tuberculosis and Respiratory Diseases (NITRD), New Delhi, India.
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The emergence of COVID-19 has highlighted the need for airborne IPC practices in health facilities to be improved. Globally more than 115,000 healthcare workers have been infected and died from COVID-19, mostly infected in their workplaces.

This session will present the various risks emerging in all parts of health facilities around the world resulting from design in the era of climate change, global warming, increased air conditioning use.

Also, the process of identifying COVID-19 and TB risks, surveillance systems and the process of prioritizing these risks in the development of a facility IPC programme for healthcare facilities.

Commodities supply & management for a successful IPC programme

G. Mustapha,¹ ¹KNCV Tuberculosis Foundation, The Hague, Netherlands.
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IPC commodities are critical to an effective IPC programme and several commodities have been identified as needed for IPC ranging from policies, germicidal UV fixtures, respirators and masks.

The supply chain requirements for sourcing these commodities and their management to the point of use is critical to maintain adequate supplies. Major shortages of critical IPC commodities were observed during the COVID-19 pandemic and there have never been enough commodities for TB control as well.

This presentation looks at the process of identifying, quantifying, procuring and managing the distribution to the point of care.

Airborne IPC interventions based on rapid turnaround time for COVID-19 and TB diagnosis to reduce transmission

G. Volchenkov,¹ ¹Vladimir Regional TB Control Center, Vladimir, Russian Federation. e-mail: vlchnkv@yahoo.com

Rapid diagnostics are critical for reduction of airborne transmission risk of TB, COVID-19 and other respiratory infections. Adequate triage and testing algorithm makes early diagnosis, effective isolation and prompt treatment of COVID-19, TB and other infections possible. All airborne IPC interventions if targeted by rapid diagnosis can be much more efficient. Monitoring patients contagiousness allows reducing isolation and hospitalization time therefore further reducing transmission risk and treatment cost.

This session will look at the use of existing rapid diagnostic tests to guide IPC interventions and prevent airborne infection transmission.

SP-26 The effect of the COVID-19 pandemic on quality and pathways to TB care in India, Indonesia and Nigeria

Quality of care for individuals with chest symptoms in Patna before and during the COVID-19 pandemic in India

B. Daniels,¹ ¹Georgetown University, Washington, United States. e-mail: bd581@georgetown.edu

Challenges to care-seeking for individuals with TB in Patna, India became evident from data surveys and in-depth interviews with individuals with TB in Patna in 2022 after the Delta wave. How have these changed from pre-pandemic times?

Are individuals with TB symptoms having more complex pathways to care in Indonesia since the pandemic

L. Huria,¹ ¹McGill University, Montreal, Canada.
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This presentation compares pathways to care for individuals with TB in an urban setting in Indonesia, before and after the onset of the COVID-19 pandemic. The results show a large increase in care-seeking delays, and changes in numbers of encounters within the public or private sectors, using data from surveys conducted between 2017-2019, and 2021-2022

Private Sector Healthcare Seeking for Tuberculosis in the time of COVID-19: Experiences from two Nigerian Cities

C. Oga-Omenka,¹ ¹University of Waterloo, Waterloo, Ontario, Canada. e-mail: cogaomenka@uwaterloo.ca

The presented results will describe the health-seeking pathways to TB care for individuals during the COVID-19 pandemic. This will include quantification of the delays throughout the TB care cascade that individuals with TB and individuals with symptoms of TB faced.

Implications and recommendations for TB care

B. Lestari,¹ ¹Department of Public Health, Faculty of Medicine Universitas Padjadjaran, Bandung, Indonesia. e-mail: bony.wiem@gmail.com

What points in care-seeking are particularly challenging for individuals with chest symptoms, and how do these differ between the public and the private sector? Survey results will be presented, along with recommendations for TB program interventions that are responsive to these results.

SP-27 Mobilising communities against TB

Where does the community stand in the collective effort to combat TB in high burden settings?

T. Anh,¹ ¹Woolcock Institute of Medical Research, Hanoi, Vietnam. e-mail: thuanh.nguyen@sydney.edu.au

Dr. Thu Anh will discuss the work of her team and their community partners in mobilizing communities and Engaging community leaders to galvanize participation in TB screening and treatment to decrease TB in Vietnamese communities.

Community engagement for implementation research in Lima, Peru

D. Puma,¹ ¹Socios En Salud Sucursal Perú, Lima, Peru. e-mail: dpuma_ses@pih.org

Ms. Puma will describe the role of community engagement performed during the implementation of a community-based chest x-ray screening program for TB in Lima, Peru, including the involvement of the community in informing the implementation strategies that are tested, and the dissemination of research results through social media and community journal clubs.

Educating My Community

G. Makanda,¹ ¹TB Proof, Western Cape, South Africa. e-mail: makandagoodman@gmail.com

Mr. Makanda, a TB advocacy officer, will discuss challenges and successes in engaging his community of Kayelitsha, South Africa to address its TB burden.

SP-28 Full value assessment of novel TB vaccines: combating pandemics today and tomorrow

Health impacts of novel TB vaccines in low- and middle-income countries

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Tuberculosis remains a serious global health issue, particularly in low- and middle-income countries. The introduction of novel vaccines is a key strategy to reach elimination goals. We developed and calibrated a tuberculosis infection transmission model to evaluate the impacts of novel vaccines. A novel adolescent/adult vaccine introduced between 2028-2047 could prevent 3.6 (3.3–3.9) million deaths before 2050, including 1.6 million in the WHO South-East Asian region.

Accelerated introduction similar to the pace of COVID-19 vaccines could approximately double the lives saved. Investment is required to support vaccine development, manufacturing, prompt introduction and scale-up.

Economic and broader impacts of novel TB vaccines in low- and middle-income countries: a modelling study

A. Portnoy,¹ ¹Harvard T.H. Chan School of Public Health, Boston, United States. e-mail: aportnoy@mail.harvard.edu

Articulating the broader health and economic impacts of novel TB vaccines is key to make the case for continued investment and support a range of decisions for development and adoption by global and country stakeholders. We estimated potential epidemiological and socioeconomic outcomes of novel TB vaccine introduction, as well as changes in household financial vulnerability to catastrophic costs.

From a societal perspective (including productivity gains and averted patient costs), vaccination was projected to be cost-effective in 75 of 105 low- and middle-income countries (LMICs) and cost-saving in 57 of 105 LMICs, including 96% of countries with higher TB burden.

How will the Full Value Assessment of Novel TB Vaccines support Indian country level decision making?

K. Rade,¹ ¹WHO India, Delhi, India.
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These Full Value Assessment of Novel TB Vaccines results are crucial to inform country level decision making, to support the research and development of novel/repurposed TB vaccines, and to plan for their eventual roll out.

I will present my thoughts on the how these results will support decision making in India, and how I believe these results can be made even more useful to country decision makers.

Implications of the Full Value Assessment of Novel TB Vaccines for South African country level decision making

S. Charalambous,¹ ¹The Aurum Institute, Johannesburg, South Africa.
e-mail: scharalambous@auruminstitute.org

I briefly will describe the ,South African TB Think Tank‘ and how it supports the South African government’s TB decision making. I will go on to present my thoughts on how these Full Value of Assessment of Novel TB Vaccines results could support TB vaccine introduction and implementation decision making, and what gaps might remain.

Implications of the Full Value Assessment of Novel TB Vaccines for global level TB vaccine decision making

M. Tufet,¹ ¹GAVI, Geneva, Switzerland.
e-mail: mtufet@gavi.org

These results are really useful to guide global stakeholders in their R&D coordination, and potential licensure, manufacture, and scale-up funding of new TB vaccines. I will present GAVI’s view on how these results will support our decision making, and what additional evidence would be useful to support global vaccine decision-making.

SYMPOSIA: FRIDAY 11 NOVEMBER 2022

SP-29 Use of diagnostic algorithms to improve tuberculosis diagnosis in children

Development and validation of a TB treatment decision algorithm for children in low-and middle-income countries – an individual patient data meta-analysis

J. Seddon,¹ ¹Stellenbosch University, Cape Town, South Africa. e-mail: james.seddon@imperial.ac.uk

As part of the 2022 WHO child and adolescent TB guideline development process, individual patient data for nearly 5,000 children were brought together from multiple geographically diverse child TB diagnostic studies.

Modelling approaches were used to quantify the contribution of different clinical and radiological characteristics to discriminate children with TB from children with other diseases. These were then used to construct an algorithm to guide decisions around initiation of TB treatment for children.

The model was internally validated and has subsequently been incorporated into the implementation guide accompanying the WHO child and adolescent TB guideline.

Feasibility and performance of specific diagnostic algorithms for highly vulnerable groups: children living with HIV and children with severe acute malnutrition

C. Chabala,¹ ¹University of Zambia, Lusaka, Zambia. e-mail: cchabala@gmail.com

Diagnosis of tuberculosis is challenging particularly children with severe acute malnutrition (SAM) and children living with HIV/AIDS (CLWHA). Prompt diagnosis and treatment is cardinal in reducing tuberculosis-associated mortality in these vulnerable groups. We conducted two prospective multicenter studies in children with SAM and CLWHA to evaluate the utility of diagnostic algorithms that incorporate clinical parameters, chest radiography, abdominal ultrasound and use of Xpert Ultra on respiratory and stool samples.

We report on the external validation of the PAANTHER TB treatment decision algorithm in CLHIV with presumptive tuberculosis and the feasibility of developing a diagnostic algorithm for children with SAM.

Cost effectiveness of using different tuberculosis diagnostic algorithms in highly vulnerable groups: children living with HIV and children with severe acute malnutrition

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In sub-Saharan Africa, 27% of TB cases are associated with undernutrition, whereas children with severe acute malnutrition (SAM) are largely asymptomatic.

Compared to a standard of care, we assessed the cost-effectiveness of implementing new diagnostic prediction scores from the TB-Speed project for children with SAM, as well as the estimated effect of the recently recommended WHO algorithm.

Integrating TB diagnostic algorithms into IMCI (Integrated Management of Childhood Illness) approaches for children in primary healthcare

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Decentralization, integration, and family-centred care are essential to reducing morbidity and mortality of pediatric TB. The IMCI allows the integration of algorithms at the lowest level of care where TB diagnostic support is limited. In TB high burden countries, TB screening and diagnosis need to be better integrated and tailored to the needs of children under 5 years old, with Pneumonia, HIV or Severe Acute Malnutrition.

Operational research in different settings is critical to bring the most benefits without overburdening the primary levels of childhood healthcare.

Role of new biomarkers for future TB diagnostic algorithms in children

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Under-diagnosis remains the major obstacle in overcoming childhood TB. The performance of diagnostic algorithms might be improved by including biomarker-based testing approaches. Test candidates currently undergoing evaluation target mycobacterial antigens (i.e., lipoarabinomannan) and markers of the host immune response (i.e., protein or transcriptomic signatures, cellular immune assays). To successfully reach those children most vulnerable of dying from TB, novel assays are needed at all different levels of health care, carefully considering the technical and infrastructural requirements of each test.

Here, we aim to summarise the available evidence of novel assay performances presently undergoing evaluation and contextualise their potential application.

SP-30 Is digital X-ray and CAD/AI a game-changer in the fight against TB?

Resources for the implementation of AI-based digital X-ray for TB detection and results from a qualitative study of pilot project users

Z. Qin,¹ ¹Stop TB Partnership, Geneva, Switzerland. e-mail: zhizhenq@stoptb.org

This presentation features newly available global resources for large-scale rollout of CAD-based digital X-rays on CAD marketplace (ai4hlth.org), vendor selection, practical strategies for threshold score calibration, and training modules and materials.

The presentation will also show the perspectives of program coordinators and clinical staff from 6 country pilot projects using ultra-portable digital chest x-ray machines in combination AI.

Is mainstreaming chest X-ray screening using artificial intelligence-powered computer-aided tuberculosis detection cost-effective in public health facilities?

R. Francisco,¹ ¹Independent Consultant, Quezon City, Philippines. e-mail: francisco.ruth@gmail.com

Mainstreaming chest x-ray (CXR) screening with artificial intelligence-powered computer-aided detection (AI-powered CAD) is a promising solution for finding missing patients with tuberculosis (TB). We assessed the cost-effectiveness of mainstreaming CXR screening with AI-powered CAD or human reading for intensified TB case finding (ICF) vis-à-vis symptom-based screening.

Using data from a pilot in two public hospitals in the Philippines showed that AI-powered CAD use for ICF was cost-effective: the incremental cost-effectiveness was ₱43,376 per disability-adjusted life-year averted compared to ₱47,667 for human CXR readers. Both CXR screening alternatives remain cost-effective under different scenarios (i.e., higher discount rate, lower benefits, higher costs).

Scaling up the use of digital X-ray with CAD for active TB case-finding in Nigeria: implementation experience from mobile units to ultra-portable systems

A. Ihesie,¹ ¹USAID Nigeria, Abuja, Nigeria. e-mail: austinihesie@yahoo.com

Nigeria is the 2nd highest contributor to Global missing TB cases. The focus of current efforts is on innovative strategies to find missing TB cases through improved access to high-quality TB diagnostics for underserved populations. The country was among early implementers of

the Mobile digital X-ray units with CAD, commencing in 2017. In December 2021, under the New Tools Project, it scaled-up the use of Ultra-Portable Digital X-ray/CAD systems and within 4 months of implementation screened 28,842 persons for TB and diagnosed 775 (21%) TB cases. We describe our evolving implementation experience for scale-up and integration of this innovative tool.

Evaluating the use of ultraportable X-rays and CAD software for TB screening during the COVID-19 pandemic in Viet Nam

L. Nguyen,¹ ¹Friends for International TB Relief (FIT), Hanoi, Vietnam. e-mail: lan.nguyen@tbhelp.org

This presentation will share how ultraportable X-rays and CAD software were used to continue community-based TB screening during periods of COVID-19 social distancing restrictions in Ha Noi and Ho Chi Minh City which prevented routine mass mobilization of participants. We will present operational experiences for using these tools, an evaluation of TB yields and an assessment of the added value of CAD-assisted X-ray reading.

Using mobile CAD system for digital chest X-ray in four KwaZulu Natal districts, South Africa

L. Duckworth,¹ ¹THINK: TB and HIV Investigative Network, Durban, South Africa. e-mail: l.duckworth@think.org.za

This presentation will share the experience in establishing mobile digital x-ray services (with AI-powered CAD) in four USAID TB-LON funded districts in Kwazulu-Natal, South Africa. Results from the first three months will be presented, including the number of asymptomatic people with Presumptive TB X-Rays who were confirmed as having GeneXpert-positive TB. Demographic data on TB diagnosis by age, gender, and HIV status will also be presented, together with lessons learned from widespread screening, in asymptomatic individuals, versus targeted screening strategies.

SP-31 Joining forces for integrated, people-centred care for TB and comorbidities

An introduction to the WHO Framework for collaborative action on TB and comorbidities

A. Baddeley,¹ ¹World Health Organization, Geneva, Switzerland. e-mail: baddeleya@who.int

Integrated, people-centred TB care and prevention of TB/HIV and other key comorbidities lie at the heart of the World Health Organization's End TB strategy and are critical for achieving End TB Strategy targets. People-centred care requires close collaboration between health programmes to ensure alignment of planning, policy, tools, human resource capacity, and essential products and technologies.

This presentation will provide an overview of WHO's Framework for collaborative action on TB and comorbidities which aims to establish and strengthen collaboration across health programmes and across sectors for delivering people-centred services for TB and comorbidities.

The syndemicity of TB comorbidities: interviews with survivors from 11 high-burden countries

A. Daftary,¹ ¹York University, York, Canada. e-mail: adaftary@yorku.ca

A rapid qualitative assessment involving 24 former patients was undertaken in 2021 to help inform the WHO framework on people-centered care for TB comorbidities. Participants had experienced one or more comorbidities during TB treatment, including: diabetes, mental health issue, substance (drugs/alcohol) use, tobacco use, HIV, and/or hepatitis C virus. Comorbidities intersected with and reinforced the impacts of each other culminating in syndemic illness experiences.

Mental health comorbidity was pervasive, stigmatizing, and commonly precipitated by TB. Collaborative multidisciplinary teams, active triage, peer support, and material resources were crucially recommended, together with patient involvement in referral decisions, to enable a people-centred response.

Integrating tuberculosis screening and testing in COVID-19 health facilities in the City of Manila, Philippines

M. Santiago,¹ ¹Family Health International 360, Makati, Philippines. e-mail: MSantiago@fhi360.org

The COVID-19 pandemic has greatly affected the provision of tuberculosis (TB) services particularly screening and testing in the Philippines. Integrating TB screening

and testing in COVID-19 isolation and swabbing facilities ensures the continuous provision of these services at the point of care.

This presentation will show how strategic leveraging of COVID-19 programs' facilities and resources can help increase TB testing and notification.

Case study from India: Introducing and scaling up TB-HIV interventions in a concentrated HIV epidemic setting

S. Mattoo,¹ ¹Central TB Division India, Delhi, India. e-mail: mattoos@rntcp.org

India's experience on TB-HIV collaborative action since 2001 has demonstrated efforts to develop/update frameworks, training modules, surveillance and scale up co-located services at national level till 2012. By 2019, single-window TB-HIV services, HIV testing in all presumptive TB, rapid molecular test, daily regimen and 3 Is (ICF, IC, IPT), interventions in TI, LWS, prisons and closed settings were provided. Key enablers for TB-HIV activities in India include co-location of services, standardised joint recording, reporting, supervision, monitoring, and review. Integrated digital platforms are being explored. In 2021, 95% of TB patients received HIV test and 96% PLHIVs were screened for TB.

Case study from Madagascar: introducing and scaling up assessment, counselling and management of undernutrition in TB patients

N. Xaba,¹ ¹World Food Programme, Johannesburg, South Africa. e-mail: nonhlanhla.xaba@wfp.org

Madagascar has some of the highest rates of malnutrition globally. According to the WHO Global TB Report estimates 47% of TB episodes in 2020 were attributable to undernutrition. This presentation will show how close collaboration with key stakeholders, including the World Food Programme, the national TB programme and the institute for nutrition have worked together to scale up assessment and counselling and management of undernutrition among people attending TB services.

SP-32 TB-PRACTECAL: final trial results and the case for programmatic roll-out

TB-PRACTECAL Trial results

C. Berry,¹ ¹Médecins Sans Frontières, Newcastle, Australia. e-mail: Catherine.berry@london.msf.org

TB-PRACTECAL is a phase III trial comparing bedaquiline, linezolid and pretomanid with moxifloxacin (BPALM) to the control (standard of care). In October 2021, an interim analysis showed that BPALM was non-inferior to the control with the modified intention to treat population showing 11% unsuccessful outcomes versus 48.5% in the control for the primary composite outcome by 72 weeks of follow-up. Final efficacy & safety results for all 4 arms are presented.

Key planned subgroups and sensitivity analyses describing fluoroquinolone resistant and COVID-19-affected subgroups as well as the cohort following implementation of the 2019 WHO guidelines will be presented.

TB-PRACTECAL regimens: key safety aspects for clinicians

I. Motta,¹ ¹Médecins Sans Frontières, Turin, Italy. e-mail: ilaria.motta@london.msf.org

BPAL-based regimens carry a range of potential toxicities including myelotoxicity, neurotoxicity, liver dysfunction and QT-prolongation. In October 2021, secondary analyses were presented showing that BPALM had fewer grade ≥ 3 or serious adverse events by week 72 compared with the standard of care. We present analyses on the key adverse events which clinicians might expect if using BPAL-based regimens.

TB-PRACTECAL: the economic case for 24-week BPAL-based treatments for drug-resistant TB

S. Sweeney,¹ ¹London School of Hygiene and Tropical Medicine, London, United Kingdom. e-mail: sedona.sweeney@lshtm.ac.uk

We will present the results of an economic evaluation estimating the incremental cost-effectiveness of the three PRACTECAL regimens (BPALM, BPALC and BPAL) to treat people with rifampicin-resistant TB, as compared with WHO standard of care regimens.

Total TB-related costs and disability-adjusted life years (DALYs) were estimated over a 20-year time horizon using a Markov model along with their cost-effectiveness and impact on participant poverty levels. An incremental cost-effectiveness ratio was estimated assuming replacement of the current standard of care with each investigational regimen.

Capturing patient-reported experiences and quality of life outcomes in the TB-PRACTECAL clinical trial (PRACTECAL-PRO)

B. Stringer,¹ ¹Médecins Sans Frontières, London, United Kingdom. e-mail: beverley.stringer@london.msf.org

PRACTECAL-PRO aimed to understand participants' perspectives on treatment outcomes. 136 participants completed the Short Form 12 (SF-12) and St George's Respiratory Questionnaire (SGRQ) at baseline, 12, 24, and 48 weeks. Healthy volunteers (age/sex-matched) completed these measures once.

Interviews with 55 participants explored health perceptions and benefits/ hassles of therapy. At baseline, trial participants reported worse respiratory-related (SGRQ) and general health related (SF-12) quality of life than healthy volunteers.

SGRQ Total score at week 48 differed between investigational and standard of care arms. Health improvements were framed as including regular health advice and monitoring; increasing confidence of treatment working.

The case for programmatic roll out of BPALM

B. Nyang'wa,¹ ¹Médecins Sans Frontières, Amsterdam, Netherlands. e-mail: bern.nyangwa@london.msf.org

Following on from the evidence-base that TB-PRACTECAL has provided, MSF is moving forward to accelerate adoption of BPAL-based regimens for DR-TB. Early operational research use, programmatic support and concrete action on drug and diagnostics access are all critical for getting 6-month treatments to patients as soon as possible.

We will examine the opportunities and barriers to implementation and reflect on the outstanding questions which need to be answered.

SP-33 Evidence and research gaps identified during the development of policy guidelines for tuberculosis

Compilation of research gaps from recent WHO policy guidelines

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WHO guideline development groups document research gaps as they arise during the course of evidence review. In 2022, WHO compiled and published research gaps extracted from the latest updates of WHO guidelines on TB (2013–2021).

This session aims to share highlight of these research gaps to support decision-makers who fund and implement research to consider evidence needs of TB programmes and policy makers.

A look into the future of TB preventive therapy

M. Frick,¹ ¹Treatment Action Group, Brooklyn, United States. e-mail: mike.frick@treatmentactiongroup.org

Preventive treatment for TB infection has significantly evolved, with options of short-term therapy now available for as little as one month. The TB prevention landscape can be transformed with the availability of new tools such as sensitive tests for TB infection, biomarkers of risk of progression to active disease and better treatment options for contacts of people with drug-resistant TB. This session will explore this and additional research needs in discovery.

Demand for rapid non-sputum based technologies for screening and diagnosing TB

R. Hasan,¹ ¹Aga Khan University, Karachi, Pakistan. e-mail: rumina.hasan@aku.edu

Accurate non-sputum-based test for TB detection is a key priority, especially for children. Lack of validated biomarker(s) in non-sputum samples continues to be a challenge in operationalizing this vision.

This presentation will discuss the potential of such technologies and tests in closing the diagnostic gap from a country context (once available), and additional needs in resources and collaboration required to accelerate further research and development.

Implementation science to optimise TB care for children and adolescents

C. Chabala,¹ ¹University of Zambia, Lusaka, Zambia. e-mail: cchabala@gmail.com

Recent update to WHO policy guidance on the management of TB in children and adolescent identifies several evidence gaps to inform future policy update. This includes implementation research on potential child and adolescent TB-related service models to improve prevention, contact investigation, diagnosis and treatment. This presentation will highlight examples of innovative service delivery approaches, which are succeeding in expanding access to TB services for this population group.

SP-34 Providing TB care in conflict settings: an overview of global guidance and lessons from Afghanistan, Ethiopia and Ukraine

New WHO guidance on TB prevention and care among refugees and other populations in humanitarian settings

K. Viney,¹ ¹World Health Organization, Geneva, Switzerland. e-mail: vineyk@who.int

Current conflicts in several parts of the world, as well as health emergencies, underpin the need to ensure access to health services for all people affected by TB. During this presentation we will feature the new inter-agency field guide on TB prevention and care among refugees and other populations in humanitarian settings, published in March 2022 by WHO, in collaboration with UNHCR and the US CDC.

The field guide provides an overview of key actions needed to prepare for and deliver effective TB prevention and care (diagnosis, treatment and prevention) services for refugees and other populations during humanitarian emergencies.

Afghanistan's experience in strengthening TB care in a conflict environment

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In 2021, the National TB Program (NTP) reported 50,710 all-form TB cases in Afghanistan. However, case notification was lower than in 2019 (52,770), demonstrating a 4% decline likely due to COVID-19's impact combined with August's 2021 change in government.

In this presentation, we will share experiences of the USAID-funded Assistance for Families and Indigent Afghans to Thrive project collaborating with the NTP and partners implementing TB-control and prevention activities in this challenging environment, focusing on supporting TB case finding, community-based Directly Observed Treatment Short-course and laboratory diagnosis to detect and treat missed drug-resistant patients in seven provinces.

Ethiopia's resilient health system under the multiple shocks of conflict and COVID-19

D. Datiko,¹ ¹USAID Eliminate TB Project, Management Sciences for Health, Addis Ababa, Ethiopia.
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Ethiopia has experienced shocks to the health system, including conflict and COVID-19. The conflict has affected about 20% of the population, and 700 health facilities and laboratories mainly in the northern part of the country.

This symposium aims to share lessons learned from the USAID-funded Eliminate TB Project, National TB Program, and stakeholders from implementing and re-summing TB services in this environment. Together, these partners have implemented mitigation efforts that have led to recent increases in the number of districts that have re-engaged in TB services, improved case finding, and identified patients that have returned to TB treatment.

Challenges faced by the Ukrainian TB programme during the recent war

N. Deyanova,¹ ¹Organization for Appropriate Technologies in Health, Kyiv, Ukraine.
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War disrupts country health systems leading to limited access to services. When the war in Ukraine started in February 2022, it was feared that this would have immediate negative impact on TB services in Ukraine. Using the national electronic recording and reporting system, we continued to monitor the progress during the war. By the end of March 2022, the rate of patient enrolment did not change much, and adherence remained good, but the proportion of patients with no information increased significantly. We will also highlight how the collaboration between the national program and partners has contributed to mitigating the impact.

Lessons learnt, challenges and good practices in advancing TB identification and care in refugee settings during emergency situations and longer-term responses

S. Harlass,¹ ¹United Nations High Commissioner for Refugees, Geneva, Switzerland.
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In this presentation we will share experiences on global partnerships, funding, community-based responses, and improved access to diagnostics as well as treatment support has led to advances in TB care in refugees and what remains to be done to reach 2030 targets in refugee populations.

Country experiences from Pakistan, East Africa, Jordan and Southern Africa will be presented. Reference will be made to the application of the Guidance on TB prevention and care among refugees and other populations in humanitarian settings: an interagency field guide.

SP-35 From domestic resource mobilisation to global policy-making: how can TB get its 'fair share' of financing?

Increasing financial sustainability through domestic resource mobilisation in Ethiopia

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With declining external funding, increased programmatic needs, and catastrophic out of pocket (OOP) costs for TB, Ethiopia's experience represents a struggle many countries are facing. Mobilizing domestic resources has been a critical part of Ethiopia's TB strategy.

This presentation will discuss the justification, development, and implementation plans for Ethiopia's Domestic Resource Mobilization Strategy roadmap for TB, which sets out the country's goals to finance 20 percent of TB program costs from domestic sources and reduce out-of-pocket expenditure by 30 percent.

Public financing of TB partners: Government outsourcing of TB services in Bangladesh

M. Nurul Amin,¹ ¹Ministry of Health and Family Welfare, Bangladesh, Dhaka, Bangladesh.
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Bangladesh is at a critical juncture as it moves to upper middle-income status and transitions away from donor support. Approximately 80 percent of TB services at the

sub-district level in Bangladesh are provided by NGOs and CSOs, primarily funded through the Global Fund. This presentation will discuss Bangladesh's plans to establish a sustainable pathway for government-led and -financed outsourcing of TB services to these TB partners.

India's experience with blended finance, and potential applications for TB

N. Rao,¹ ¹USAID, Mumbai, India. e-mail: nrao@usaid.gov

India has been a pioneer of applying market-based solutions and innovative financing to public health problems. SAMRIDH is a healthcare blended finance facility that combines commercial capital with public and philanthropic funds to drive greater resources towards market-based health solutions to improve access to healthcare.

This presentation will discuss the blended financing approach and explore possible applications of these innovative financing solutions to TB in India.

Creating policy dialogue to support equitable, needs-based, evidence-driven allocation of funding for TB

J. González Anaya,¹ ¹Izzi Telecom, Mexico City, Mexico. e-mail: josea_gonzalez@outlookpro.mx

The Covid-19 pandemic has demonstrated the critical relationship between health and the economy, highlighting an urgent need to improve dialogue between health sector and macroeconomic leaders.

This presentation will discuss how improving TB outcomes at both national and global levels requires a constructive multi-sectoral dialogue that is not limited to publicly financed healthcare; and that decision-making, by both donors and governments, should address the asymmetry between the financing needs and the allocation of resources for TB.

SP-36 Laying the groundwork for the success of new TB vaccines

Update on the pipeline of late-stage TB vaccines

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Numerous phase 2b or 3 efficacy trials of prevention of disease, prevention of recurrence and therapeutic TB vaccines are planned or ongoing.

The presentation will give an update on the pipeline of late-stage TB vaccine trials, and recommendations from the Global Plan to support advancement of this pipeline.

The case for TB vaccines

R. White,¹ ¹London School of Hygiene and Tropical Medicine, London, United Kingdom. e-mail: Richard.white@lshtm.ac.uk

Tuberculosis remains a serious global health issue, particularly in low- and middle-income countries. The introduction of new/repurposed TB vaccines could be a useful strategy to reduce the global TB burden.

In this presentation, I will present the highlights of the latest research on the potential direct and broader health and economic impacts of new/repurposed TB vaccines. This evidence should be useful for TB vaccine research, adoption and implementation decision-making by global and country stakeholders.

Introducing the WHO roadmap for global introduction of new TB vaccines

B. Giersing,¹ ¹World Health Organization, Dept of Immunization, Vaccines & Biologicals, Geneva, Switzerland. e-mail: giersingb@who.int

Coordination of various stakeholders and early planning along the vaccine introduction pathway will be needed to accelerate uptake and impact for TB vaccine candidates approaching regulatory approval in the next 3-5 years.

The presentation will give an overview of the WHO Roadmap for Global Introduction of New TB Vaccines intended for adults and adolescents and the Evidence Considerations for Vaccine Policy initiatives aimed at articulating the activities and evidence needed to pave the way to global introduction of new TB vaccines, once licensed.

Vaccine trials in India and lessons learnt for the introduction of adult TB vaccines

D. Christopher,¹ ¹Christian Medical College, Vellore, India. e-mail: djchris@cmcvellore.ac.in

Results and the updates on TB vaccine trials in India will be discussed, with a view towards the broader challenges and opportunities for vaccine implementation in India.

SP-37 Vulnerability and resilience of TB and COVID-19 care services during military and humanitarian crises: experience of USAID and PATH support for Ukraine

Overview of TB and COVID-19 prevention and care in Ukraine on the eve of Russia's military invasion

K. Gamazina,¹ ¹PATH, Kyiv, Ukraine. e-mail: kgamazina@path.org

A 40% decrease in TB detection rates in 2020, followed by a two-year COVID-19 epidemic, reversed a decade of progress toward ending TB in Ukraine. The TB/COVID-19 Recovery Plan was developed under the National TB Program with the support of international donors/partners, and its implementation began in early 2022 to support the decentralization of TB service management and involvement of primary healthcare services into outpatient TB cure and care.

This, along with mobilization of local NGOs and communities to provide psychological and social support to people affected by TB, has become crucial for sustainability of TB control activities.

Principles and priorities of USAID assistance in TB and COVID-19 prevention and care in Ukraine before, during and after Russia's military invasion.

K. Denysova,¹ ¹USAID, Kyiv, Ukraine. e-mail: kdenysova@usaid.gov

Fostering Millennium Development Goals and UN Political Declaration on TB eradication, USAID stood hand-by-hand with Ukrainian counterparts in their efforts to maximize TB response and mitigate adverse impacts of COVID-19 on achievement of National TB Strategy objectives. This assistance has evolved over time in line with political dynamics in and around Ukraine, where hostilities have become key to rethinking the cooperation scope and scale.

The experience of successful implementation of USAID projects in challenging environments of social and political transition, large-scale military conflict, and postwar recovery in Ukraine may be exemplary for those who are looking for motivation and inspiration.

Response measures to support TB service delivery in territories affected by hostilities and civil crisis in Ukraine

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

TB services in Ukraine have been drastically affected by the large-scale military conflict following Russia's military invasion: essential infrastructure has been damaged or destroyed, health care workers have been forced to flee, and functioning facilities are overloaded due to an influx of internally displaced persons (IDPs).

Several response measures have been implemented, from emergency food provision in TB hospitals to procurement of mobile X-ray stations for TB screening in IDP camps. Lessons from this crisis underscore the need for early emergency preparedness efforts to mitigate risk and ensure resiliency of TB prevention and care efforts.

COVID-19 prevention and control in an environment of wartime mass migration and displacement

R. Rodyna,¹ ¹PATH, Kyiv, Ukraine. e-mail: rrodyna@path.org

The fragile COVID-19 prevention and treatment system that Ukraine had built through massive national efforts and support from the international community was immediately compromised due to Russia's invasion.

To prevent uncontrolled outbreaks of COVID-19 and other communicable diseases, particularly among IDPs, a number of urgent public health measures have been introduced, including capacity building, deployment of mobile teams to conduct risk assessments in IDP locations, outreach by immunization teams, improved vaccine supply, and information dissemination.

The effectiveness of efforts to reduce COVID-19 risks in combat environments will be at the center of this discussion.

Rebuilding and resiliency: post-conflict TB and COVID-19 service recovery

G. Dravniece,¹ ¹PATH, Kyiv, Ukraine. e-mail: gdravniece@path.org

Russia's devastating military intervention in Ukraine has multiple implications for TB and COVID-19 prevention and care. Although TB care provision only ceased in completely destroyed areas, the entire system of TB and COVID-19 detection, treatment, and prevention has

been affected, due to the mass migration of people affected by TB and medical personnel, severe damage to supply chains and logistics infrastructure, unavailability of auxiliary and maintenance services, and shortages of material and financial resources.

Selecting appropriate interventions to address immediate and long-term needs, in alignment with evolving country priorities and constraints, will be a major recovery planning challenge.

ABSTRACT PRESENTATIONS TUESDAY 8 NOVEMBER 2022

ORAL ABSTRACT SESSION (OA)

OA-01 Digital innovations to improve TB control

OA01-200-08 Delft Light Backpack (DLB) portable digital X-ray for pre-diagnostic TB screening: results from a scale-up intervention in Nigeria

B. Odume,¹ C. Ogbudebe,¹ C. Eze,¹ M. Tukur,¹ N. Nwokoye,¹ O. Chukwuogo,¹ D. Nongo,² A. Ihesie,² R. Eneogu,² C. Anyaike,³ T. Lagundoye Odusote,² O. Oyelaran,²
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Background and challenges to implementation: Nigeria is ranked sixth in TB burden in Africa with a 70% gap in TB case notification. To bridge the gap in TB case notification, the National TB Program adopted innovative active TB case finding (ACF) strategies. KNCV TB Foundation Nigeria piloted the use of portable digital x-ray (PDX) with artificial intelligence (AI) for TB ACF targeting most-at-risk populations (MARPs) and the lessons learnt from the pilot informed the scale up of this intervention. We present the results and lessons learnt in the scale up of this innovative intervention in Nigeria.

Intervention or response: The USAID new tools project funded the procurement and deployment of PDX to six states under the KNCV TB LON 1 and 2 project for TB ACF targeting MARPs and hard to reach population. Each PDX was assigned to a trained radiographer with an assistant.

Target populations were mapped out and prior to each community outreach, engagement, and awareness creation on TB was done. All clients were screened using a parallel screening algorithm that included the WHO four symptom screening and PDX CAD4TB with the threshold set at 50.

All identified presumptive TB were evaluated with GeneXpert, Truenat or TB LAMP and bacteriological negative results had their x-ray films and symptoms sent for radiologist review for clinical diagnosis.

Results/Impact: Starting from Dec 2021 to March 2022, 17,261 (M 12,350; F 4,911) clients were screened for TB, 2,764 (M 1,893; F 871) presumptive TB identified and 2,639 (M 1,819; F 820) evaluated. All the 437 (M 337; F 100) TB cases diagnosed were enrolled on treatment across the six intervention states. See Fig 1 for the TB screening efficiency of the DLBs.

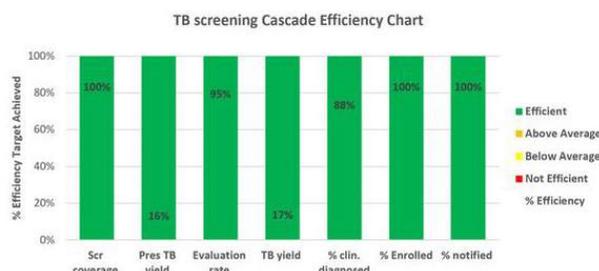


Figure 1. DLB TB screening Cascade Efficiency Chart

Conclusions: This intervention was found very efficient in identifying missing TB cases among the hard-to-reach and MARPs including men. It is recommended for scale up to more states in Nigeria.

OA01-201-08 Transporting sputum specimen through a digitally fluent 'RiderforHealth' software by community-based riders to enhance the accessibility of quality TB diagnosis in Pakistan

S. Raza,¹ A. Rashid,¹ A. Tahir,¹ F. Naureen,¹ K. Aamir,¹ ¹Mercy Corps, Public Health, Islamabad, Pakistan. e-mail: adtahir@mercy Corps.org

Background and challenges to implementation: Accessibility to Microscopic and Gene Xpert Facilities is remote particularly in the rural districts of the country, contributing to the number of undiagnosed TB Cases and limited TB Care and Prevention.

Intervention or response: Mercy Corps Pakistan, under its TB Program, is implementing a digitally fluent mechanism of Specimen Transportation in 50 Districts of the Country to enhance access to TB testing and RR determination.

The Project is supported by a contextually developed 'RiderforHealth' software, backed by an online data-driven dashboard, generating gender-disaggregated data of the samples transported in each district from Basic Health Units to Rural Health Centers and Private Hospitals for Microscopy and Gene Xpert Testing.

The transportation of samples takes course through Community-Based Riders who by using the mobile application transport the specimen within their assigned geographical areas to the designated 427 Public and Private Health Care Facilities, earning for themselves a monthly remuneration based on the KMs covered. Each sample is updated by a Medical Practitioner at the respective Health Care Facility by scanning a dashboard-

generated QR Code (scanned by the rider as well) as part of the transportation mechanism such that both the testing and the rides are updated onto the dashboard.

Results/Impact: 13,148 Samples have been successfully transported and tested since December 2021 through 179 Community-Based Riders, with 9,303 samples tested at Gene Xpert sites, out of which 96 samples have been RR Determined. 43% of the tested specimen are women and girls, while 56% of the tested specimen constitute men and boys. 169 Samples are transported daily on an average.

Conclusions: A digitalized mechanism of Specimen Transportation generating gender-disaggregated data of the tested specimen contributes to RR Determination and access to TB detection, prevention, and care.

OA01-202-08 Optimizing clinical TB diagnosis in portable digital X-Ray (PDX) driven community active case finding for TB using a virtual radiologist-linkage platform in Nigeria

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Background and challenges to implementation: In Nigeria, improving TB case finding has always been prioritized due to the significant gap of about 70% in TB case notification. The KNCV TB Foundation under the USAID funded TB LON project introduced the use of PDX with artificial intelligence (AI) in pre-diagnostic TB screening during community based active TB case finding. We reviewed the results from this intervention to showcase the impact of an optimized system for clinical TB diagnosis using the PDX in finding missing TB cases.

Intervention or response: Eight Delft Light Backpack (DLB) PDX were deployed across 6 states in Nigeria for community active TB case finding targeting most at risk population. In a bid to optimize TB yield, keep track of x-ray requests and institute a quality control system for clinical TB diagnosis, a real-time platform, the XMAP for x-ray reporting was also introduced. The XMAP utilizes digital films taken during screening to facilitate clinical diagnosis by referring them virtually from the field straight to the radiologists for interpretation and reporting.

Results/Impact: Data from January to March 2022 implementation period shows the TB cascade from the eight DLBs, *table above*. Pre-diagnostic TB screening for 23,990 clients using the DLB identified 2,710 presumptive TB. Out of 2,198 presumptive TB with negative bacteriological results sent for clinical diagnosis through the XMAP digital reporting platform, 302 (60%) were suggestive of TB by the radiologists.

S/N	State	All Clients Screened with DLB	All Presumptive TB identified	Pre-sumptive TB with cough and sputum	Presumptive with cough and sputum with negative bacteriological diagnosis	Chest X-ray referred to Radiologist for clinical diagnosis	Clinical diagnosed TB cases	Total diagnosed TB cases (Bacteriological & Clinically diagnosed)
1	Benue	2,710	354	353	335	333	79	96
2	Kano A	3,474	309	308	288	41	13	83
3	Kano B	4,090	434	434	422	230	86	98
4	Cross River A	1,245	142	141	84	20	14	21
5	Cross River B	2,608	283	270	261	222	34	43
6	Delta	4,314	566	564	372	92	20	38
7	Katsina	3,044	257	257	213	132	36	78
8	Nasarawa	2,505	365	315	223	45	20	48
Total		23,990	2,710	2,642	2,198	1,115	302	505

Conclusions: The XMAP facilitates CXR interpretation for clinical TB diagnosis by radiologists irrespective of the location where the TB screening services were provided. It also facilitates diagnosis among presumptive TB with negative Xpert results accounting for 60% (302) of all diagnosed TB cases that would have otherwise been missed. It is therefore recommended as an add on while using the DLB PDX in community TB ACF intervention to improve TB case yield, timely diagnosis and linkage to treatment.

OA01-203-08 Scaling up ultra-portable digital X-ray with computer-aided detection (CAD) In Nigeria, early experiences and results from the Introducing New Tools Project Nigeria

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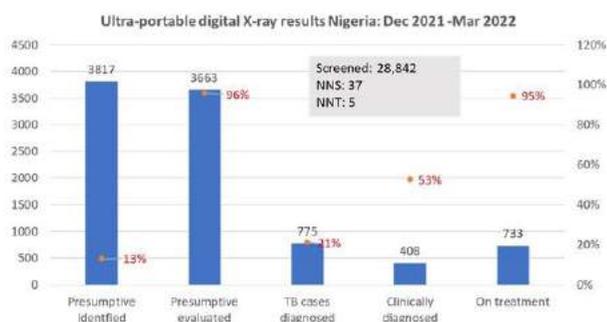
Background and challenges to implementation: Nigeria accounts for 4.4% of Global TB burden and is the 2nd highest contributor to Global missing TB cases. In October 2021, the country received 10 Ultra-Portable digital Xray (uPDX) systems with Computer-Aided Detection (CAD), under the USAID-funded/STOP TB Partnership introducing New Tools Project (iNTP). The project aimed to improve access to high quality, innovative screening, and diagnostic tools for TB. Implementation in-country was through USAID TB Partners-KNCV and IHVN. Nigeria was 1st among iNTP countries to roll-out the uPDX and we describe our early implementation experience and results.

Intervention or response: The implementation strategy for roll-out of uPDX with CAD in Nigeria involved engagement of National TB Program (NTP) and Stake-

holders for integration into National guidelines; Training of field and program staff; Set-up and Installation; field roll-out and follow-up. The 10 uPDX systems were deployed to 8 high TB burden states. Hotspot analytics and epidemiological data were used to target populations for screening including special population groups. A parallel screening algorithm using the W4SS and CXR guided screening and identification of presumptive with CAD threshold score set at 50.

Results/Impact: We identified enablers to the prompt roll-out to include adequate engagement of NTP, acceptability and close collaboration among stakeholders; KNCV's prior technical experience on use of digital CXRs and CAD; targeted HR engagement; technical support of STOP TB, IDDS and service support by DELFT.

Early results show that among 28,842 people screened within 4 months of implementation (Dec 2021 – March 2022), 3,817 (13%) were identified as presumptive, while 775 persons were diagnosed with TB (53% clinically). To diagnose 1 TB case, the Number-needed-to-screen was 37, while the Number-needed-to-test was 5.



Conclusions: The uPDX with CAD has significantly improved the ability of the TB program to take high-quality TB care to Hard-to-reach and vulnerable/underserved populations. This is critical to finding missing TB cases.

OA01-204-08 Sensitivity and specificity of computer-aided detection for presumptive TB identification by chest X-ray during active case finding activities in the Philippines

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Background and challenges to implementation: The Philippines ranks 4th with highest number of incident tuberculosis (TB) cases globally. Due to the coronavirus disease 2019 (COVID-19) pandemic, TB screening activities were greatly affected, resulting in 37% fewer TB notifications in 2020. There is need to strengthen active TB case finding (ACF) through more sensitive screening tools.

Intervention or response: Several ACF models have been implemented using mobile vans with digital chest x-ray (CXR) equipped with computer-aided detection (CAD) to screen different high-risk groups for TB. CAD software may improve CXR performance in investigating individuals with presumptive TB. Between May 2021 and January 2022, data of those with CXR and Xpert MTB/Rif tests were collected during ACF implementation. CXR screening was assessed using its sensitivity and specificity compared to Xpert MTB/Rif serving as the gold standard for TB diagnosis.

Receiver Operator Characteristic (ROC) analysis was used to determine the area under the curve and the threshold that simultaneously maximizes sensitivity and specificity (Youden's index).

Results/Impact: A total of 266 MTB positive and 362 non-TB cases were selected from pool of screened clients. At threshold of 0.5, the sensitivity was 95.9% and specificity was 30.4% with accuracy of 58%. The ROC curve for CAD for the detection of presumptive TB was 0.8263 (95% CI: 0.79, 0.86). The threshold that maximized the sensitivity (74.1%), specificity (76.5%) and accuracy (76%) of CAD simultaneously was 0.91 with Youden's index of 0.506. More smokers (32%) were found among those with TB but both groups had the same proportion of TB history (22-23%).

High risk groups	TB cases (n=266)	Non-TB cases (n=362)	Total (n=628)
Smokers	77 (32%)	64 (20%)	141 (25%)
Diabetic	17 (7%)	19 (6%)	36 (6%)
TB contacts	33 (13.9%)	24 (7.5%)	57 (10%)
With Previous TB history	53 (22%)	74 (23%)	127 (22%)

Table 1: Descriptive analysis of some risk factors.

Threshold	Sensitivity	Specificity	Accuracy
0.4	96.2%	28.5%	57.3%
0.5*	95.9%	30.4%	58.1%
0.6	92.1%	41.2%	62.7%
0.7	89.5%	50.8%	67.2%
0.8	83.5%	62.2%	71.2%
0.91**	74.1%	76.5%	75.5%

* TBIHSS AI score cut-off

**Youden's Index

Table 2: Sensitivity and Specificity of CAD at different thresholds.

Conclusions: CAD software can detect presumptive TB with modest accuracy among different high-risk groups in local setting. There is likely a larger role for CAD software as a triage test at the primary care level settings where access to radiologists is limited. However, further studies are needed to better assess heterogeneity in specific sub-groups.

OA01-205-08 Piloting interactive voice response system (IVRS) based communication with TB patients to improve bank account seeding for direct benefit transfers (DBT)

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Background and challenges to implementation: Government of India provides TB Patients with \$ 6.55 per month of treatment as nutrition support *via* Direct Benefit Transfers (DBT). Notified patients need to be informed about the DBT scheme and followed-up for collection of Bank Account Details. DBT uptake is limited due to unavailability of bank details of patients, largely attributable to paucity in human resource at sub-district level to engage with patients, competing priorities and increasing notifications, further aggravated by the restrictions in movement due to COVID-19.

Intervention or response: A digital communications campaign through Interactive Voice Response System (IVRS) was piloted in twenty-one districts of Bihar for three months. Intervention included weekly- scheduled automated phone calls, automated Short Message Services (SMS) and access to on-demand connect through a central toll-free number. Information regarding the DBT scheme and bank detail submission were shared with patients. Sampled patients were surveyed to understand message comprehension and retention. Seventeen districts of Bihar served as non-intervention controls.

Results/Impact: IVRS-based interventions enabled rapid, repeated (weekly) connect to large number of patients. 98187 beneficiaries were targeted under the pilot. 47% of them were successfully connected, with high listenership duration (61% listening to complete messages) and high levels of comprehension of messages. Account seeding improved by ~21% higher than base rate. The odds of seeding bank accounts increased by more than 55% (95% CI 33.5% - 94.5%) amongst patients more than 4 months into treatment.

Conclusions: IVRS-based communication aided rapid outreach to large number of patients and complemented programme staff's efforts in sensitizing patients about DBT schemes and submission of bank account details. IVRS calls acted as reminders/nudges for patient response while also providing a channel for patients to share service-related feedback. This may be used for patient education on treatment, drug refill, follow-up, entitlements and provide a medium for continued engagement with patients through course of treatment.

OA01-206-08 Improving TB detection through TB screening using ultra-portable chest X-ray with artificial intelligence in the municipality of Cainta, Rizal province, Philippines

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Background and challenges to implementation: The Philippines is among the top 30 high TB-burden countries, with an estimated annual incidence of 539 per 100,000 population. Tuberculosis notifications decreased by 37% between 2019 and 2020, due to disruptions brought on by the COVID-19 pandemic. Although a gradual recovery was observed by the end of 2020, TB notification remains below pre-pandemic levels.

Intervention or response: The USAID's TB Platforms for Sustainable Detection, Care and Treatment Project, in collaboration with the Center for Health Development CALABARZON, and Fujifilm Philippines implemented TB screening using an ultra-portable chest X-ray (UP-CXR) with Artificial Intelligence (Lunit AI) to improve access to TB screening, in Geographically Isolated and Disadvantaged Areas (GIDAs). The UP-CXR with AI provides an instant reading and is linked to a rapid diagnostic test (Xpert MTB/Rif), aimed at reducing the turnaround time from screening to diagnosis and treatment initiation and early loss to follow up.

Results/Impact: Over 3 weeks, 536 patients were screened for TB using symptoms and chest X-ray, 267 (50%) of whom were presumed to have TB. Two hundred three (76%) patients were tested using GeneXpert. Compared to other active TB finding activities which have a molecular testing rate of 25%, using the UP-CXR with AI increased the molecular testing rate to 76%. The use of AI also facilitated an average turnaround time from screening to testing of 1.3 days which is significantly lower than the average turn-around time of 69.7 days when using chest X-ray without AI.

Conclusions: The use of CXR with AI can increase efficiency in implementing the TB cascade, shortening turnaround times and reducing loss to follow-up. Studies on the feasibility and cost-effectiveness of UP-CXR in remote and disadvantaged settings will help inform decisions on adoption and scale-up.

OA01-207-08 Feasibility and quality of digital chest radiography for childhood TB diagnosis at district hospital level in high tuberculosis burden and low-income countries

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Background and challenges to implementation: Most children diagnosed with TB are not bacteriologically confirmed. Chest X-ray (CXR) plays an important role in diagnosis but access to good quality CXR remains a major challenge in low-income countries. Use of digitalized X-ray can solve some of the quality issues and facilitate the transfer of images for quality control

Intervention or response: As part of the TB Speed Decentralization study, we implemented digital CXR using DR plate on existing analogic radiography machine in two district hospitals (DH) per country in Cambodia, Cameroon, Cote d'Ivoire, Mozambique, Sierra Leone and Uganda. CXR were transferred to a central internet server as FTPS files and downloaded by clinicians (at DH or from primary health centres referring children for CXR) and national e-readers. We assessed the feasibility (uptake) of CXR taking, and interpretation and the proportion of CXR of good quality as defined in a standardized reading report and documented the reasons why CXR were not done

Results/Impact: Of 3506 children with presumptive TB, after excluding those referred for CXR but who did not attend the DH, 1869 (53.3%) came for CXR including 108 referred twice (after 1 week antibiotic course), resulting in a total of 1977 CXR to be performed. Of them, 1780 (90.0%) were performed, 1773 (99.6%) classified as good quality and 1771 (99.5%) were interpreted. Reasons for not performing CXR (N=197) included 73 re-

ported technical problem with X-ray machine (37.1%), 44 problems with interconnection of the DR plate (22.3%), 34 non-specified technical problems (17.3%), 30 electrical problems (15.2%), 12 absence of radiographer (6.1%), and 4 administrative issues (2.0%).

Conclusions: CXR using digital plates on analogic radiography machine was feasible as shown by the high uptake with a high proportion of good quality X-ray using digitalized system. Failure of the digitalized system were mainly due to either connectivity or electrical issues.

OA-02 Strengthening national-and global policies: lessons learnt

OA02-208-08 Analysis of Global Fund COVID-19 Response Mechanism 2021 (C19RM 2021) investments supporting TB activities in 20 countries

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Background: The Global Fund provided support to countries to fight COVID-19 through the C19RM. An analysis was undertaken of the C19RM's 2021 investments aimed at supporting people with TB and TB programs in 20 priority countries. The aim of the analysis was to review the investments that could directly and indirectly benefit the national TB responses supported by the Global Fund; analyse the type of investments; highlight potential COVID-19 investments that can contribute to strengthening TB programs.

Design/Methods: Global Fund C19RM 2021 funding requests and budgets for 20 high priority Global Fund countries were reviewed for investments to support TB. The investments were categorised into Direct (Activities specific to TB), Contributory (Activities that target COVID-19 or other diseases, but also comprehend activities for TB) and Indirect (Not specific to TB, but can help by way of spill-over). The countries were Bangladesh, Cambodia, Cameroon, Congo, Ethiopia, Ghana, Indonesia, Kenya, Myanmar, Nigeria, Pakistan, Peru, Philippines, South Africa, Tanzania, Uganda, Ukraine, Vietnam, Zambia, Zimbabwe.

Results: For the 20 countries analyzed, USD \$159M was the total final approved amount that could benefit TB programs, USD \$95M was a direct TB investment. 41% of the investment that could support TB programs were included under the Case Management, Infection Prevention & Control, Diagnostics & Laboratory interventions. The two biggest cost categories accounting

for 40% of investments were linked to health products equipment and health products non-pharmaceutical, ie X-ray equipment and Personal Protective Equipment.

Conclusions: In the 20 countries analyzed there is a potential additional \$67M investment within the Global Fund C19 RM 2021 outside mitigation for TB activities that could support TB programs. Global Fund supported countries need to be aware of the investments in the Covid 19 response that could further strengthen the TB program and support the TB response.

OA02-209-08 Towards universal health coverage in Viet Nam: lessons from the enrollment of people with tuberculosis in the National Social Health Insurance scheme

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Background: Vietnam has made significant progress towards universal health coverage (UHC) through a government-provided Social Health Insurance (SHI) scheme, and over 90% of the general population is currently enrolled. However, 63% of TB-affected households face catastrophic costs. In late 2022, reimbursements for TB care will be expanded by the national SHI.

Design/Methods: This was a collective case study, with naturalistic design and theoretical sampling of persons without SHI using a mixed method, interpretivist approach. Using data from a pilot that enrolled people with TB in SHI, we employed descriptive statistics and framework analysis of in-depth individual interviews to identify the challenges faced by people with TB. Additionally, we conducted a national legislation review related the integration of TB care into SHI.

Results: From the quantitative analysis of the pilot data, we found that 78.8% of participants who began TB treatment without SHI were able to enrol. The median days it took between treatment enrolment and the issuance of the SHI card was 33. 18.3% of eligible households were never enrolled in SHI, mainly due to missing documentation (89.5%).

From the qualitative framework analysis, three challenges were identified:

1. The cost of SHI enrolment was perceived as high;
2. SHI enrolment was viewed as tedious and complicated;
3. Some face difficulties meeting the administrative requirements to enrol in SHI.

From the legislation review, we identified nine legal documents guiding the integration of TB and SHI. However, no specific provisions have been made for the uninsured initiating TB treatment.

	Percentage of participants enrolled in SHI	78.8% (82 out of 104)
	Median days between TB treatment start and SHI issue	33
Quantitative results	Average household members included in SHI enrolment	2.4
	Average cost for SHI enrolment	1,551,492 VND/67.75 USD
	Proportion of participants never enrolled	18.2% (19 out of 104)
Qualitative results	Theme 1: People with TB perceive the cost of enrolment in SHI as high, especially for low-income families in Viet Nam.	
	Theme 2: People with TB perceive the SHI enrolment process as tedious and complicated.	
	Theme 3: Some people with TB face difficulties in meeting the administrative requirements to enrol in SHI.	
Legislation review	Law of Health Insurance, 2013: increases co-payment rate and transitions to household-based registration for health insurance, rather than individuals.	
	Circular 36/2021/TT-BYT, 2022: defines the beneficiaries, medical expenses related to TB diagnosis and treatment eligible for SHI reimbursement.	

Conclusions: While the Government of Vietnam has made huge strides in achieving UHC and ensuring accessibility to affordable TB medicines through SHI, questions remain on how changes in TB financing will affect uninsured populations. Specific provisions are required to address challenges that can leave people with TB unassisted and paying out-of-pocket for care.

OA02-210-08 Can effective and sustained advocacy to government increase domestic funding for TB control - experience from Nigeria

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Background and challenges to implementation: Nigeria is among 14 countries with highest TB and TB HIV burden and is included in 8 countries contributing 2/3rd of global total TB cases. Poor TB treatment coverage in the

country can be traced to funding gaps for implementing TB interventions and activities. The observed funding gap of 70% in Nigeria mirrors TB treatment coverage gap of 70%^[1]. This paper aims to demonstrate the role of effective and sustained advocacy to government for increased domestic funding for TB control.

Intervention or response: KNCV TB Foundation Nigeria through support of USAID from 2021 engaged coordinating consultants in 14 TBLON 1 and 2 project states to conduct sustainable capacity assessment. Road maps and action points from these assessments informed a strategic advocacy to the state governments to improve funding for TB control. Capacity of state TB program managers and state health insurance schemes were also built on annual strategic planning processes, budgeting as well as developing memos for fund release and request to approving authorities.

Results/Impact: In February 2022, Kano state government released 4.1 million naira, Benue state released 5 million naira for TB control services while Plateau state released 9 million naira for purchase of motorcycles to strengthen TB program logistics across the state.

The graph below (Figure 1) shows increased annual budgetary allocation across selected TBLON 1 and 2 states.

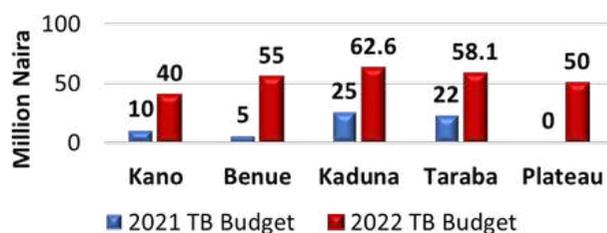


Figure 1. Increase in TB budget allocation.

Conclusions: Funding gaps in TB control in Nigeria can be improved through continuous advocacy to the state governments for increased funding allocation and release.

Sustained domestic resource mobilization activities has a key role in achieving the National strategic plan towards access to quality TB diagnosis, care and treatment in Nigeria.

Keywords: Domestic resource mobilization, Funding gaps, TB diagnosis and control.

OA02-211-08 Integration of TB and HIV control with national AMR plans: evidence from the 2021 Global Tripartite Survey

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Background: Compounded by the risk of anti-microbial resistance (AMR), TB and HIV are pervasive infectious epidemics that potentiate each other and have resulted in heavy health system burdens. Such complex consequences of AMR on infectious diseases catalyzed the development of National Action Plans (NAPs) to combat AMR globally.

Since 2016, the progress of the NAPs has been monitored annually with the Tripartite AMR Country Self-Assessment Surveys (TrACSS) launched by the WHO, FAO, and OIE. We analyzed the progress of the NAPs and their integration with TB and HIV control.

Design/Methods: Using publicly available 2021 TrACSS data, we analyzed the progress of the NAPs and their integration with TB and HIV control using cross-tabulations, Pearson's, and McNemar's Chi-square analyses in Stata-15 statistical software.

Results: By WHO regions, 41 AFRO countries (25.2%), 11 SEARO (6.8%), 50 EURO (30.7%), 23 AMRO (14%), 21 EMRO (12.9%), and 17 WPRO (10.4%) submitted responses.

Only 5(3%) had no NAP, 18(11%) were under development, 45(27.6%) had developed the NAP, 63(38.7%) were implementing, and 32(19.6%) were actively monitoring after implementation. NAPs linked to TB control were 62(65.3%) with 54(56.8%) linked to HIV.

This difference in the TB and HIV integration with NAPs was statistically significant (McNemar's Chi² = 5.33, McNemar's exact = 0.039).

Regional locations however did not modify this linkage of TB (Pearson Chi² = 7.64, Fisher's exact = 0.202) or HIV (Pearson Chi² = 6.04, Fisher's exact = 0.285) to the NAPs.

Conclusions: Ninety-seven percent of the countries had AMR plans either existing or under development. However, not all were linked to TB (65.3%) or HIV (56.8%) control. This non-exhaustive coverage highlights potential gaps in efforts to curb the dual TB/HIV epidemic and reveals the need for stronger integration across the TB/HIV domain on one hand, and AMR on the other.

OA02-212-08 A global survey of national TB programmes: policies, practices, and challenges of systematic screening for TB disease

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Background: The policies and practices around implementation of TB screening vary globally, and factors driving these are poorly understood. We aimed to understand these, and the challenges of screening for TB disease, to provide information for policy makers, funding agencies and academics to help maximise the effectiveness of screening.

Design/Methods: Following the publication of the updated WHO TB screening guidelines, we designed an online survey to explore policies and practices around TB screening. We invited National TB Programmes of all countries reporting >1000 TB cases per year to participate (123 countries). There were 23 questions designed to explore 3 key areas:

1. Policies and practices for screening for TB disease, including implementation, priority populations, funding, and reporting of screening data.
2. Screening tools and confirmatory testing used.
3. Use of screening technologies, including the use computer-aided diagnostics (CAD).

Results: 59 countries responded from all WHO regions, representing 81% of the global TB burden. 49 (83%) countries report an existing strategic plan to increase screening for TB disease and 38% reported that the COVID-19 pandemic has increased the priority of screening. High priority groups include child and adult household contacts (identified as high priority by 93% and 86% of countries respectively), people in penitentiary institutions (identified by 86%); and people living with HIV (identified by 83%). 66% of countries aim to expand use of chest x-ray (CXR).

However, 80% reported at least 1 barrier to doing so, 89% of these citing high equipment costs or funding. Only 4 countries (9%) report using CAD in most TB screening settings.

Conclusions: Most countries plan to increase screening for TB disease and to increase CXR based screening. However, a high proportion of countries report signifi-

cant barriers to implementing this, especially in high TB burden countries. Efforts to support screening should focus on overcoming these.

OA02-213-08 The “Tibay ng Dibdib” strategy: an intersectoral dialogue to engage and empower local leaders in achieving TB elimination in Tarlac, Philippines

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Background and challenges to implementation: The province of Tarlac has an annual TB incidence of 539 per 100,000 population. Home to 1,503,456 residents, there are about 8,104 individuals in the province at risk for developing TB every year. However, in 2021, only 4,913 (61%) were notified and enrolled in treatment. The local government unit continues to implement relevant laws for TB, Universal Health Care, and local government directives to ensure the continuity of TB services. Effective policies are needed at the local level to ensure sustainable financing and the availability of TB services.

Intervention or response: The USAID’s TB Platforms for Sustainable Detection, Care and Treatment Project implemented the “*Usapang Dibdiban*” (“Heart-to-heart talk”) with Tarlac’s local chief executives, legislative officials, and TB program managers. A series of TB dialogues were conducted with local officials to raise their awareness of the TB situation in their communities and strengthen their ownership and commitment to TB programming and implementation of TB detection and treatment services.

Results/Impact: The strategy led to the introduction of policies on prescription-based dispensing of TB medications, mandatory notification, and TB response during disasters. Local TB ordinances were developed, leading to the creation of a local TB council, which leads the implementation of locally appropriate TB interventions including patient support groups and TB social protection programs. Through supplemental budgeting, the strategy led to an increase of 18,875,816 (US\$ 361,956) in Tarlac’s annual TB budget for the year 2022, which will be used to find and treat 1,135 more TB patients.

Conclusions: Local government decision-makers play a pivotal role in achieving sustainable TB elimination using Universal Health Care reforms. Intersectoral TB dia-

logues engage and empower decision-makers to lead the fight against TB, by developing a clear understanding of TB challenges, fostering ownership of the local TB situation, and inspiring future leaders to take action on TB elimination in their communities.

OA02-214-08 Civil society advocacy interventions to ensure sustainable funding for comprehensive TB care package in Ukraine

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Background and challenges to implementation: In Ukraine, treatment success for the 2018 cohort of DR-TB patients was 50.5%, and loss to follow-up was 15.6%. Since 2019, PATH and local NGOs have implemented patient-centered psychosocial support in twelve oblasts for 930 DR-TB patients, and decreased loss to follow-up to 3.2%. It is essential to increase domestic funding allocations to sustain these successful services during the transition from donor to local funding.

Intervention or response: STBCEU worked with NGOs to identify domestic resources to sustain psychosocial support for TB patients. STBCEU conducted a needs assessment of 12 NGOs' advocacy experience, capacity and designed targeted trainings and tools to build NGOs' capacity on the resource mobilization for patient-centered TB services. Then NGOs developed advocacy action plans to attract local funding. STBCEU provided support and mentoring while NGOs implemented these action plans.



Figure. NGOs' advocacy actions timeline.

Results/Impact: During June–December 2021, NGOs raised US\$59,370 in local funding to support TB patients mainly to cover cost of computer tomography scanning, food and hygiene packages, medicine for side effects management, and for other targeted interventions. Lviv Oblast Council provided US\$3,500 to open a COVID-19 and TB hotline, through which four medical experts have fielded more than 400 calls since October 11, 2021. To date, six NGOs have achieved their advocacy goals.

Conclusions: Strengthening the role and capacity of civil society to raise funds for their vital role in supporting TB care was shown to be feasible and successful in reducing loss to TB follow-up care. Given the current crisis in Ukraine, we anticipate that the role of civil society

will be even more important in the coming years for re-establishing comprehensive, uninterrupted TB care. The 12 NGOs with which we worked have strong capacity to fundraise and guide interventions and will be able to resume raising funds and providing essential supportive care in the years to come.

OA02-215-08 Resilient community structures: a key gateway to improved TB treatment success rate, despite COVID-19 pandemic

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Background and challenges to implementation: Poor compliance to treatment is considered one of the most serious challenges of TB prevention and care. Adherence to TB treatment is crucial to avert disease transmission and achieve cure since patients who interrupt treatment are at increased risk for the development of drug resistance TB and death.

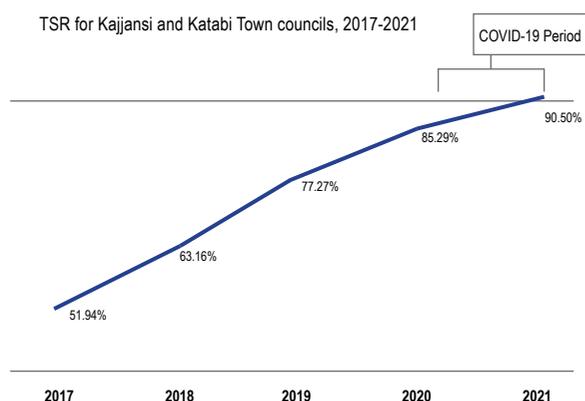
During the COVID 19 pandemic, both patients and HCWs could not travel to HFs to access services as result of the lockdown.

Intervention or response: During 2018 through support from the USAID Defeat TB activity three Community linkage facilitators (CLFs) were engaged to support the six diagnostic and treatment units (DTUs) in Kajjansi and Katabi Town Councils in Wakiso District.

During the COVID 19 crisis, the USAID Defeat TB further supported CLFs to deliver medicines patients who could not travel to the health facilities and conducted physical follow up for patients who could not return to the health facility. CLFs from the same locality as the patient were tasked to look for these patients and return them to care. Through awareness creation the CLFs were able to solicit the support of the local cultural and political leaders.

Results/Impact: Through these efforts the treatment success rate (TSR) of the DTUs in Kajjansi and Katabi Town Councils improved by 38.56 percentage points from 51.94% to 90.5%. Despite COVID-19 in 2020, the continuous engagement of the CFLs, contributed to improving the TSR further from 85.29% to 90.50% in 2021 (Fig 1) thus mitigating the threats of COVID-19 unwinding the realized gain.

Conclusions: The CLFs are critical part of the health system in Uganda and are vital health facility team members who significantly contribute to early detection and treatment of TB. Their intervention improves the TSR which is essential in reducing TB-related morbidity and mortality thus combating the rising threat of multi-drug resistant TB and achieve the goal of ending TB.



OA02-215-08 Figure. TSR for Kajjansi and Katabi Town councils, 2017 - 2021

OA-03 Management of DR-TB

OA03-216-08 Active screening and management of adverse events during multidrug-resistant tuberculosis treatment – Dharavi, India

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Background and challenges to implementation: Every month, >350 persons with MDR-TB are on treatment in Mumbai’s Dharavi slum; however, only one in three successfully complete MDR-TB treatment. The management of adverse events (AEs) among persons with MDR-TB is a significant challenge to the programme, often leading to unsuccessful treatment outcomes. Healthcare workers have limited knowledge about the type, frequency, and severity of AEs occurring among those on MDR-TB treatment. We developed a mechanism to actively screen and manage AE in this slum with high burden of MDR-TB.

Intervention or response: Municipal Corporation of Greater Mumbai, SHARE INDIA, and the U.S. Centers for Disease Control and Prevention implemented a comprehensive person-centric intervention for persons affected by MDR-TB in Dharavi. Key components were active screening for AE through monthly home visits by trained field coordinators using a standardised tool, and follow ups telephone to track them throughout the referral cycle for redressal of AE.

Results/Impact: From December 2020–February 2022, 758 persons were registered for MDR-TB treatment, and all (100%) were enrolled in the intervention. A total of 413 (54%) persons reported 1848 AE episodes. Commonly reported AEs were gastro-intestinal symptoms (19%), arthralgia (15%), and peripheral neuropathy (9%) (Table 1).

Among those with AEs, 377 (91%) were referred for further management, and 332 (88%) fully resolved AEs. The majority of the AEs were managed at primary health institutions (33%) or MDR-TB outpatient clinics (19%). A change in regimen was required in 69 (18%) persons with MDR-TB. During the intervention period, only 10 (1.3%) persons with MDR-TB were lost to follow-up.

Adverse event	Mild	Moderate	Severe	Grand Total
Gastro-intestinal symptoms	171 (9%)	163 (9%)	11 (1%)	345 (19%)
Arthralgia	139 (8%)	132 (7%)	7 (-0%)	278 (15%)
Peripheral neuropathy	78 (4%)	84 (5%)	0 (0%)	162 (9%)
Giddiness	21 (1%)	64 (3%)	5 (-0%)	90 (5%)
Loss of hearing	12 (1%)	48 (3%)	0 (0%)	60 (3%)
Visual Disturbances	19 (1%)	39 (2%)	0 (0%)	58 (3%)
Dermatitis	28 (2%)	28 (2%)	0 (0%)	56 (3%)
Headache	20 (1%)	33 (2%)	1 (0%)	54 (3%)

Table 1: Common adverse event reported by persons with MDR-TB and its severity in Dharavi slum, Mumbai (Dec 20-Feb 22) [AE episodes (n)=1848]

Conclusions: Our person-centric approach successfully managed persons affected by MDR-TB through active, regular (yet simple) screening and monitoring for AEs. Prompt identification of AEs helped in AE management for most of the persons with MDR-TB within the public sector, and very few were lost to follow-up.

Keywords: MDR-TB, slum, Mumbai.

OA03-217-08 Barriers to achieving treatment success in drug-resistant tuberculosis patients in India: a systematic review

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Background: More than 40% of people with drug-resistant (i.e., multidrug- or rifampin-resistant) tuberculosis (TB) in India experience unfavorable treatment outcomes. We conducted a systematic review to identify factors associated with experiencing unfavorable treatment outcomes in drug-resistant TB patients in India.

Design/Methods: We searched PubMed, Embase, and Web of Science to find studies published between January 2000 and May 2021 using search terms for TB, India, and loss to follow-up, including treatment success and treatment failure. Two independent reviewers identified relevant studies and extracted findings regarding factors associated with drug-resistant TB patients experiencing unfavorable treatment outcomes. After assessing quality of the studies, we reported variables with statistically significant adjusted effect estimates in relation to unfavorable treatment outcomes in multivariable regression analyses in cohort studies.

Results: Of 4,516 studies screened by systematic search, 16 met the inclusion criteria, of which eight reported findings from multivariable regression analyses. Patient-related factors significantly and independently associated with higher risk of unfavorable treatment outcomes among drug-resistant TB patients included: male sex (vs. female sex), older age, history of previous TB, longer time to treatment initiation, presence of cavitation, ambulatory treatment initiation, resistance to ≥ 5 drugs, culture conversion time > 4 months, medication non-adherence, low body mass index, and alcohol use. Health-system related factors significantly and independently associated with higher risk of unfavorable treatment outcomes included having a different DOT provider in the intensive and continuation treatment phases (vs. having same DOT provider) [Figure 1].

Conclusions: Multiple challenges contribute to unfavorable treatment outcomes among drug-resistant TB patients in India. Early identification of highly drug-

resistant strains, provision of nutritional support, treatment of alcohol use disorder, behavioral interventions to reduce medication nonadherence, and consistent care by the same providers may be strategies to improve treatment outcomes in this patient population.

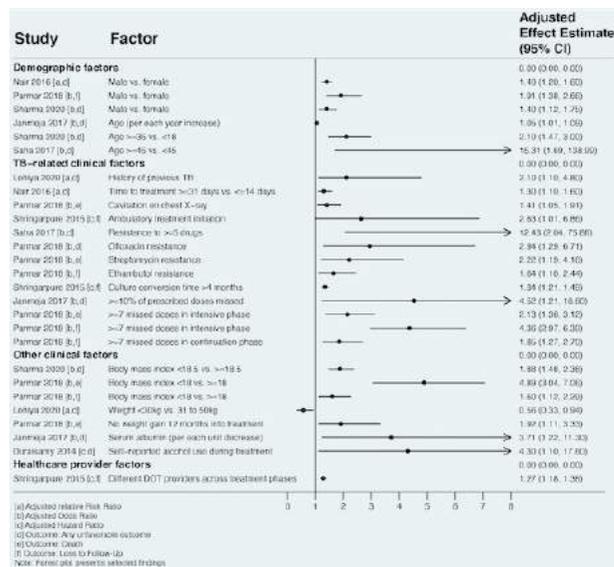


Figure 1. Factors associated with unfavorable treatment outcomes among drug-resistant TB patients in India.

OA03-218-08 High prevalence of bedaquiline resistance in difficult to treat drug resistant tuberculosis patients in Médecins Sans Frontières Clinic, Mumbai

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Background and challenges to implementation: National TB Elimination Program (NTEP) introduced Bedaquiline (BDQ) since 2016, but there is limited data on the issue of emerging BDQ resistance. Lack of BDQ drug susceptibility test (DST) and implementation of testing guidelines. Short duration of BDQ in treatment regimen contributing to resistance.

Intervention or response: The Médecins sans Frontières (MSF) clinic in Mumbai provides integrative care to drug resistant tuberculosis (DRTB) patients with advanced resistance profiles. Patient who failed treatment

in past and in need of new and repurposed drugs are referred to the clinic and evaluated by multidisciplinary team. All patient who are BDQ exposed (86) or contact (2) of patients failed on BDQ based regimen are subjected to BDQ DST in accredited lab. The resistant cohort was treated with delamanid, carbapenem +/- BDQ and other optimized background regimen (OBR) based on DST and exposure history.

Results/Impact: Out of 88 culture positive samples subjected to BDQ DST from Dec 2020 till Feb 2022, 22.7% (20/88) were resistant. In 20 resistant cases, 55% (11/20) are male with median age of 27.5 years (18 – 58). Majority of patients, 80% (16/20) with pulmonary TB and rest disseminated. The cohort comprised 95% (19/20) extensively drug-resistant (XDR) patients with mean exposure to BDQ 6 months and other group A drug is 17 months. More than 70% patients had bilateral disease and 45% with grade III breathlessness many needing inhalers and O2 support. Concomitant resistance to Cfz, Lzd and FQ was found among 25% (5/20), 35% (7/20) and 95% (19/20) patients, respectively. In the resistance cohort, 2 refused treatment, 39% (7/18) died, 11% (2/18) failed and 50% (9/18) are still on treatment. Our cohort shows high unfavourable outcome in early treatment experience.

Drug exposure and resistance pattern			Clinical Profile		
Drug	Median exposure (in months)	Resistance pattern (%)	Indicator	No. of patient (n=20)	%
Bedaquiline	6	100% (20/20)	Bi-lateral lung involvement	14	70%
Linezolid	15	35% (7/20)	Lung cavities	15	75%
Fluoroquinolones	20	95% (19/20)	Breathless ness- Grade III	9	45%
Clofazimine	15	25% (5/20)	Inhalers	16	80%
Second line injectables	9	45% (9/20)	O2 Support	5	25%
Ethionamide	24	NA	Severe Malnutrition (BMI < 16)	13	65%
PAS	6	NA	Comorbidities	4	20%
Cycloserine	22	NA	At least 1 grade III ADR in past	11	55%

Conclusions: High prevalence of BDQ resistance in previously treated patients, scale up use of BDQ DST routinely in order to ensure early access to effective regimens.

OA03-219-08 Antimicrobial and synergistic effects of MMV Pathogen Box compounds on resistant strains of Mycobacterium tuberculosis

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Background: In order to accelerate the discovery of novel drug compounds, the MMV group has developed the Pathogen Box, a collection of 400 drugs that have demonstrated biological activity against specific pathogenic organisms. However, activity against resistant forms of several key pathogens, including *M. tuberculosis*, has not been sufficiently explored. *M. tuberculosis* is an established WHO critical priority pathogen that is increasingly becoming untreatable due to the emergence and spread of multi-/extensively drug-resistant strains. New agents and therapeutic options to complement available drug regimens for treatment are urgently needed.

This study explored the antibiotic potential, including synergistic effects of MMV Pathogen Box compounds against multi-/extensively drug-resistant *M. tuberculosis*.

Design/Methods: GeneXpert MTB/RIF and MTB-DR_{plus} assays were used to confirm the identity and resistance profile of *M. tuberculosis*. Micro broth dilution assay was used to determine pathogen-specific MIC and MBC of the five selected Pathogen Box compounds against MDR MTB. A checkerboard assay was used to determine synergy between the five compounds and with isoniazid (INH) and rifampicin (RIF). Time-kill kinetics was performed to determine if the compounds are bactericidal or bacteriostatic.

Results: GeneXpert MTB/RIF and MTBDR_{plus} assays confirmed that *M. tuberculosis* isolates were at least resistant to RIF and INH, harboring *rpoBMUT1(D516V)* and *KatGMUT1(S315T1)* mutations. MMV676603, MMV687146, MMV687696, MMV687180, and MMV153413 showed potent activity against MDR MTB at a MIC and MBC of 0.078125 and 0.15625, 0.0391 and 0.078125, 0.078125 and 0.078125, 0.078125 and 0.078125 and, 0.625 and 0.625µM, respectively.

The five Pathogen Box compounds were bactericidal and were either synergistic or additive with fractional inhibitory concentration index ranging between 0.23 to 0.90.

Conclusions: This study demonstrated that these five Pathogen Box compounds have potent activity against multi-drug-resistant *M. tuberculosis* and have the potential to be developed as primary or adjunctive therapy to improve treatment outcomes in patients with active tuberculosis.

OA03-220-08 Health-related quality of life and psychological distress among TB patients after treatment for drug-sensitive TB in four African countries

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Background and challenges to implementation: Few studies explore the psycho-social impact of TB following successful TB treatment completion. We explore health-related quality of life (HRQoL) and psychological distress of patients at treatment completion and at 6 months post-treatment completion.

Intervention or response: A multi-country observational TB cohort study among adult patients receiving treatment for pulmonary TB through national TB programs in four African countries.

The Medical Outcomes Short Form-36 (SF-36; score from 0-100) questionnaire and Kessler Psychological Distress Scale (K10; score from 0-40) were administered to patients at treatment completion and 6 months post-treatment completion.

Regression was used to identify factors associated with poor HRQoL or reported any form of psychological distress (K10>20) at treatment completion.

Results/Impact: 1378 adults (66% male; median age 34 years IQR:18-43; 42% HIV positive) were included. Patients reported higher HRQoL scores (less disability) at both treatment completion (physical component summary score; PCS mean 53.1 and mental component summary score; MCS mean 55.7) and at 6 months post-treatment completion (PCS mean 56.7 and MCS mean 56.1) compared to treatment start (PCS mean 37.9. and MCS mean 42.1).

Similarly, there was a significant decline in the proportion that reported any form of psychological distress at treatment completion (3.4%) and at 6 months post-treatment completion (2.6%) compared to treatment start (41.4%).

HRQoL and psychological distress trajectories in response to TB treatment were heterogeneous across countries. Females and those 30 years and older were more likely to report a lower PCS or MCS at treatment completion. At treatment completion, being female and from South Africa were associated with any form of psychological distress.

Conclusions: Our results suggest ongoing psychological support for females, older adults, and those living in settings with a high prevalence of mental illness to improve how people perceive their quality of life and mental well-being as an essential goal of TB treatment.

OA03-221-08 Adverse events during linezolid treatment in multidrug-resistant tuberculosis in Sweden 2015-2018

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Background: Linezolid is an effective drug against multidrug-resistant tuberculosis (MDR-TB) but treatment is associated with frequent and severe adverse events (AE). This study aimed to investigate factors associated with linezolid AE in persons diagnosed with MDR-TB in Sweden.

Design/Methods: We performed a retrospective cohort study of all persons diagnosed with MDR-TB in Sweden 2015-2018 and treated with linezolid. Data was collected from medical records. The first occurrence of an AE was defined according to Common Terminology Criteria for Adverse Events, 2017. A Cox regression model was used.

Results: In total, 62 persons received a linezolid-containing MDR-TB regimen. Mean age was 27 years, 40.3 % (n=25) were women and a successful end of treatment outcome was seen in 90.3 % (n=56). Median linezolid treatment was 8.7 months (IQR 4.5-13.6). Linezolid starting dose was 600 mg (range 200-600) for 96.8 % (n=60) of persons. Linezolid was withdrawn due to AE in 69.4 % (n=43), of which 37.2 % (16/43) restarted linezolid. AEs due to peripheral neuropathy, myelosuppres-

sion and opticus neuritis were seen in 50.0 % (n=31), 46.8 % (n=29) and 6.5 % (n=4) of persons, respectively. The overall incidence was 65.8 and 80.6 per 1000 person-months for peripheral neuropathy and myelosuppression, with the highest rates observed in the first six months (Table 1). Treatment with an average dose of ≥10 mg/kg was associated with a higher risk of peripheral neuropathy (HR 3.29, 95% CI 1.08-10.1, p=0.037) compared to <7 mg/kg. Having a comorbidity was associated with a higher risk of myelosuppression (HR 2.33, 95% CI 1.11-4.86, p=0.025).

	Incidence per 1000 person-months (95 % confidence interval)			
	Overall	0-3 months	>3-6 months	>6 months
Peripheral neuropathy	65.8 (46.3-93.6)	49.6 (24.8-99.1)	130 (78.2-215)	41.2 (20.6-82.5)
Myelosuppression	80.6 (56.0-116)	171 (113-260)	47.4 (17.8-126)	20.4 (6.59-63.3)
Opticus neuritis	6.66 (2.50-17.8)	5.95 (0.84-42.2)	7.15 (1.01-50.8)	6.84 (1.71-27.4)

Table 1. Incidence of adverse events per 1000 person-months in persons treated with linezolid-containing regimens for multidrug-resistant tuberculosis in Sweden 2015-2018.

Conclusions: About half of persons treated with linezolid-containing MDR-TB regimens experienced peripheral neuropathy or myelosuppression resulting in frequent cessation of linezolid. Careful monitoring is needed, especially in the first six months, for persons treated with linezolid-containing MDR-TB regimens. Future research should focus on preventative measures.

OA03-222-08 Treatment outcomes of WHO-conforming longer all-oral multidrug-resistant tuberculosis regimens

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Background: In 2019, WHO revised its hierarchy of drugs for the design of longer individualized regimens for multidrug- or rifampin-resistant tuberculosis (MDR/RR-TB). The effectiveness of regimens designed according to this guidance has not been evaluated.

Design/Methods: Our objective was to report on the frequency of treatment success according to fluoroquinolone susceptibility and the number of Group A, B, and C drugs included in the baseline regimen. We conducted a secondary analysis of participants in the endTB Observational Study, who initiated regimens containing bedaquiline and/or delamanid for MDR/RR-TB between April 2015 and September 2018. Treatment outcomes were assigned based on WHO 2013 definitions. We excluded individuals with unknown fluoroquinolone resistance, who received an aminoglycoside, polypeptide, or carbapenem during treatment, and who received fewer than four likely effective drugs.

Results: We included 572 patients for analysis. Fluoroquinolone susceptibility was documented in 353 (61.7%) and fluoroquinolone resistance in 219 (38.2%). In all, 462 (80.8%) experienced a successful end-of-treatment outcome. The frequency of treatment success was high across all groups, ranging from 72.1% to 90.0% (Table). Heterogenous regimen compositions and drug durations within categories precluded meaningful comparisons of effectiveness.

# of likely effective Group A drugs	# of likely effective Group B & C drugs*	Fluoroquinolone resistance	N	End-of-treatment outcome (n, %)				
				Favorable	Unfavorable		LTFU or no data n (%)	Not evaluated n (%)
					n (%) [95% CI]	Failure n (%)		
Exactly 3	1 Group B + 0 Group C	FQ-S	65	55 (84.6) [73.8, 91.6]	1 (1.5)	4 (6.2)	5 (7.7)	0 (0.0)
	>=1 Group B + >=0 Group C**		71	59 (83.1) [72.6, 90.2]	0 (0.0)	8 (11.3)	4 (5.6)	0 (0.0)
	0 Group B + >=1 Group C		10	9 (90.0) [57.4, 100.0]	1 (10.0)	0 (0.0)	0 (0.0)	0 (0.0)
Exactly 2	>=2 Group B and/or Group C	FQ-S	139	102 (73.4) [65.5, 80.1]	4 (2.9)	16 (11.5)	17 (12.2)	0 (0.0)
Exactly 2***	>=2 Group B and/or Group C	FQ-R	184	162 (88.0) [82.5, 92.0]	4 (2.2)	10 (5.4)	7 (3.8)	1 (0.5)
Exactly 1	>=3 Group B and/or Group C	FQ-S	68	49 (72.1) [60.4, 81.4]	1 (1.5)	14 (20.6)	2 (2.9)	2 (2.9)
Exactly 1	>=3 Group B and/or Group C	FQ-R	35	26 (74.3) [57.8, 86.0]	1 (2.9)	3 (8.6)	5 (14.3)	0 (0.0)

* All groups are mutually exclusive
 ** Patients in this group are mutually exclusive of the four-drug regimen "Exactly 3 and 1 Group B + 0 Group C" and therefore all had at least 5 likely effective drugs. All other groups had a mix of 4-drug and more than 4 drug regimens.
 *** 100% in this category had bedaquiline and linezolid as the two Group A drugs.

Table. End-of-treatment outcomes among patients receiving an all-oral regimen conforming to 2019 WHO guidance for MDR/RR-TB, stratified by number of Group A, B & C drugs in the baseline regimen and fluoroquinolone resistance (N=572).

Conclusions: This analysis of all-oral longer individualized regimens designed in accordance with 2019 WHO guidance reveals high frequencies of treatment success. Future research designed to address the heterogenous, evolving nature of longer, individualized MDR/RR-TB regimens should examine which combinations of drugs maximize safety/tolerability and effectiveness.

OA03-223-08 Relative bioavailability of delamanid tablets dispersed in water in healthy adult volunteers

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Background: Delamanid is a novel antituberculosis drug used for treatment of drug-resistant tuberculosis. It is available as a 50mg tablet and recently also as a 25mg dispersible tablet formulation. To improve delamanid access for children, we evaluated the effects, including relative bioavailability, of dispersing the 50mg tablet to inform its practical use for children in settings where the 25mg dispersible formulation is not yet available.

Design/Methods: The relative bioavailability of delamanid 50mg tablets administered in dispersed form versus swallowed whole, was investigated in a phase I single-dose, open-label, randomized, four-period, cross-over study in South Africa.

Healthy adult participants were randomly assigned 1:1:1 to separately receive two of three dose strengths of delamanid after a meal, as whole tablets followed by dispersed tablets, or *vice versa*. The dose strengths were 25mg ($\frac{1}{2} \times 50\text{mg}$), 50mg and 100mg ($2 \times 50\text{mg}$). Sampling was scheduled for two days after each dose, and at 168 hours after the fourth dose. The pharmacokinetics of delamanid and its metabolite DM-6705 were analyzed using nonlinear mixed-effect modelling approach. The precision of the estimated effect of formulation on bioavailability was determined with log-likelihood profiling.

Results: 26 participants contributed 763 and 714 observations of delamanid and DM-6705, respectively. Two-compartment models jointly described both analytes with delayed absorption and first-order elimination. The mean absorption time of dispersed tablets was typically 73% (90% confidence interval: 68-79%) of whole tablets. The two administration methods were not significantly different regarding either bioavailability or its variability. The bioavailability of dispersed tablets was estimated to be 107% of whole tablets, with 90% confidence interval of 99.7-114%, fulfilling the formal bioequivalence criterion.

Conclusions: Dispersed 50mg delamanid tablets have the same bioavailability as tablets swallowed whole and can therefore be used in children and other patients who cannot swallow whole tablets, improving access to treatment.

OA-04 Integrated care - how it helps in improving access

OA04-224-08 Integrating tuberculosis screening and testing in COVID-19 health facilities in the city of Manila, Philippines

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Background and challenges to implementation: Several tuberculosis (TB) systematic screening activities have been implemented in the City of Manila, Philippines. However, due to the coronavirus disease 2019 (COVID-19) pandemic, case finding activities were either suspended/postponed or conducted at limited capacity. This resulted in >60% reduction in TB case notification in 2020.

Intervention or response: On August 25, 2021, integrated TB screening and testing was introduced in 3 COVID-19 facilities in the City of Manila. In isolation facilities, persons with confirmed COVID-19 were offered sputum collection for Xpert MTB/Rif assay regardless of TB signs and symptoms. In the swabbing facilities, persons undergoing COVID-19 testing were initially screened for respiratory symptoms (cough, fever, dyspnea) regardless of duration. Those with no respiratory symptoms were offered chest x-ray (CXR) through a mobile van equipped with artificial intelligence. If respiratory symptoms present or CXR suggestive of TB, sputum collection for TB testing was done.

Indicators	Isolation Facility	Swabbing Facility	Combined
Participation rate of clients for TB screening	37% (1,388/3,743)	68% (3,729/5,460)	56% (5,117/9,203)
Presumptive TB rate	NA	13.8% (513/3,729)	NA
Sputum collection rate	99.7% (1,384/1,388)	99% (508/513)	99.5% (1,893/1,901)
Sputum testing rate	99.7% (1,380/1,384)	98% (497/508)	99.2% (1,877/1,892)
Yield rate	2.7% (38/1,384)	1.0% (37/3,729)	1.5% (75/5,113)
Number needed to screen to detect one BC-TB case	36 (1,384/38)	101 (3,729/37)	68 (5,113/75)
Number needed to test to detect one BC-TB case	36 (1,380/38)	13 (497/37)	25 (1,877/75)

Results/Impact: 5,113 people were screened for TB between August 25, 2021 - January 31, 2022 at COVID-19 facilities. The participation rate was low at 56% due to client's perception of low TB risk and fear of exposure to

SARS-COV-2, and the prioritization of COVID-19 clinical management and perceived difficulty in specimen collection by staff. Sputum collection and testing rates were high at 99.5% and 99.2%, respectively. Facilitating factors were the deployment of 2 medical technologists to perform Xpert MTB/Rif testing, commitment from Manila Health Department and TB laboratories, availability of adequate laboratory supplies, and presence of sputum transportation. Bacteriologically confirmed TB (BC-TB) was diagnosed in 75 persons. The number needed to screen to find one BC-TB was 68. Yield rate was 1.5%.

Conclusions: Integrating TB services in COVID-19 health facilities is doable through strategic collaborative design and human resource augmentation, thereby, expanding provision of TB screening and testing and ultimately increasing TB notification through COVID-focused services.

OA04-225-08 Trends in private sector notifications in India: experience from Joint Effort for Elimination of Tuberculosis project

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Background and challenges to implementation: Private sector engagement is critical in achieving India TB elimination goals. This necessitates large scale sustainable interventions focused on the private sector.

Intervention or response: FIND India implemented the “Joint Effort for Elimination of Tuberculosis (JEET)” project in collaboration with National TB Elimination Programme (NTEP), India, supported by the Global Fund since 2018. Out of the 101 districts where the project was rolled out, FIND had implemented the resource intensive Patient Provider Support Agency (PPSA) model in 21 districts across 5 states (Andhra Pradesh, Telangana State, Karnataka, Punjab, and West Bengal) facilitating case notifications, bacteriological confirmation by Xpert MTB/RIF, and treatment adherence. The project activities were fully implemented by 2019 beginning and completed by March 2022.

Results/Impact: Records from Government of India’s web-based TB notification portal (Nikshay) were analysed from 2017 (baseline) to 2021 for the 21 PPSA project districts across 5 states. Overall, the number of TB patients notified from the private sector increased by 166% from 13,288 in 2017 to 35,306 in 2021. The notification rate more than doubled from 31 to 80 per 100,000 in 2021. The percentage of microbiologically confirmed TB case notifications from these PPSA geographies increased from 30% (4,007/13,288) in 2017 to 40% (13,992/35,306) in 2021. Throughout the project periods, over 80% notified patients had successful TB treatment outcomes.

Conclusions: Despite the adverse impact of COVID-19 on TB notifications in 2020 and 2021, the project JEET has made significant impact in engaging the private sector in line with the NTEP’s national strategic plan for TB elimination. Scaling up and sustaining these interventions will be critical to consolidate the gains made by the project.

OA04-226-08 Stakeholder engagement improved uptake and turnaround time of GeneXpert test results in Ethiopia

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Background and challenges to implementation: Effective specimen referral is critical for early sputum pick up, shipment, test performance, and result feedback. In Ethiopia, the system is designed in an integrated manner and run by the postal courier service under the coordination of the Ethiopian Public Health Institute. It is essential to track the effectiveness of the referral system at each level of health service and identify challenges to take appropriate actions.

Intervention or response: The USAID Eliminate TB Project collaborated with and trained 58 regional laboratory professionals, clinicians, directors, postal couriers, and program coordinators to improve specimen referral for GeneXpert and turnaround time (TAT). Acceptable TAT is when a specimen is referred, and the result delivered within 24 hours. After the training, the USAID Eliminate TB Project assessed two GeneXpert sites, seven public TB diagnostic facilities, postal office, 13 public-private mix (PPM), Adama Public Referral Laboratory, and the town health office.

Results/Impact: Total sputum tested by GeneXpert centers increased from 90 in June 2021 to 227 in September 2021. The proportion of specimen referred with acceptable TAT improved from 48% to 65% (figure 1).

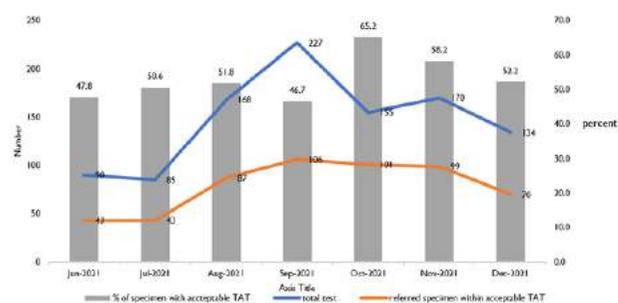


Figure 1. The trend of GeneXpert test and TAT, June 2021-December 2021.

Conclusions: The engagement of relevant stakeholders in specimen transportation improved specimen tested using GeneXpert and TAT. Hence, a continuous coordination and review of specimen referral performance indicators and implementation of an improvement plan are highly recommended.

OA04-227-08 How to improve access to TB care for the nomads? Review of barriers and enablers for Sahel nomadic populations

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Background and challenges to implementation: Tuberculosis (TB) control in nomadic populations represents a major public health problem in sub-Saharan Africa.

Intervention or response: Barriers and enablers of TB care for nomads were identified through a literature review and survey conducted among the National TB Programs (NTPs) of six Sahelian countries:

Burkina Faso, Chad, Niger, Mali, Mauritania, and Senegal. A conceptual framework was developed. Data retrieved from twenty-eight peer-reviewed papers or collected through the survey were regrouped in 5 categories: health system related factors, socioeconomic factors, cultural, political and environmental factors.

Results/Impact: The large distance between nomadic camps and health care facilities and the absence of TB-specific programmatic interventions for nomads were the main barriers identified. The establishment of a multi-ministerial national committee in charge of nomadic populations, the mapping of nomadic transhumance roads, the identification of gaps in health service provision and community engagement for defining fit for purpose solutions are key elements to improve TB control in nomadic population.

Conclusions: Some countries in the region successfully implemented interventions to overcome the barriers to TB care. These interventions should be more widely

shared to inform other countries for the development of appropriate strategies for which community engagement is essential.

OA04-228-08 The predictors of TB yield: improving efficiency of TB control by comparing various TB case finding interventions in Nigeria

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Background and challenges to implementation: In 2020, Nigeria ranked 6th among the 30 high burden countries for tuberculosis (TB) and 1st in Africa for TB incidence. In a country of over 200 million, there is a need to prioritize high-yielding interventions to ensure efficient utilization of limited resources to screen, identify missing TB cases and link them to treatment.

Intervention or response: Data analyzed was from the 2022 Q1 implementing period of the TB LON 1&2 Project implemented by KNCV Nigeria with support from USAID, cutting across 14 states. Seven directly attributable TB case finding interventions were identified (Intensified case finding, ICF, in public and private facilities; Targeted Community Outreaches, TCO; Portable Digital X-ray, PDX-driven community case finding; ICF targeting Nomads; Contact Investigation, CI; & the WOW Truck-driven community case finding), compared and the proportion of their numbers needed to screen (%NNS) and test (%NNT) to identify TB patients assessed using MS Excel.

Results/Impact: A total of 2,173,657 persons were screened for TB, with the Portable Digital X-ray (PDX) & Contact Investigation (CI) yielding the highest at 2.3% NNS each (The average across all interventions was 0.6%). Further analysis of the 162,832 persons presumed to have TB and tested for TB revealed the PDX led most interventions with a 20.6% NNT (the Average was 8.0%). Based on %NNT_TB, other interventions with high TB yield included CI and ICF_Public.

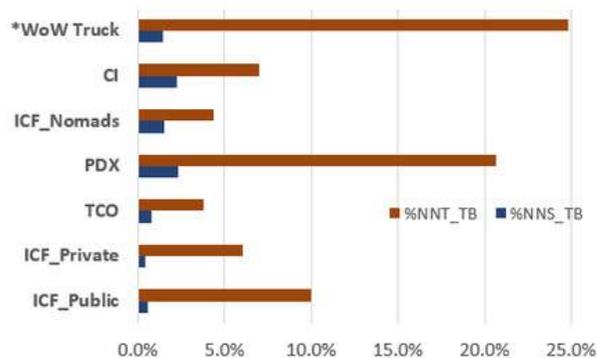


Figure. TB yield by various interventions in Q2 2022. *WOW Truck is also furnished with a PDX which may account for its high %NNT_TB.

Conclusions: Tuberculosis control requires multiple interventions to achieve. However, certain interventions have higher efficiency in terms of surveillance and early detection in particular locations.

The portable digital chest x-ray device coupled with AI and a real-time referring/reporting digital platform has shown the best yields in a resource-limited setting and should be considered for scale-up & optimization while sustaining efforts in other interventions for a multi-pronged response.

OA04-229-08 Scale-up of 99DOTS for TB treatment supervision: Intervention reach and treatment outcomes

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Background: Evaluations of 99DOTS, a digital adherence technology for supporting and supervising TB treatment adherence, have shown variable uptake and effectiveness. We evaluated whether a multi-component implementation strategy (*i.e.*, enhanced 99DOTS) including:

1. Provision of low-cost phones to patients who lack access,
2. Task-shifting of adherence monitoring and patient follow-up to community health workers, and;
3. Automated task lists to facilitate follow-up could improve the uptake and effectiveness of 99DOTS-based TB treatment supervision in Uganda.

Design/Methods: We introduced enhanced 99DOTS at 18 health facilities already using 99DOTS for TB treatment supervision (99DOTS experienced facilities) and 12 health facilities using routine community-based DOT (99DOTS naïve facilities).

We compared reach (proportion enrolled on 99DOTS) and effectiveness (proportions completing treatment, completing intensive phase and lost to follow-up) outcomes before and after the introduction of enhanced 99DOTS using data on all adults initiating treatment for drug-susceptible pulmonary TB. Confidence intervals (CIs) were adjusted for clustering at the facility level by bootstrapping with 1,000 repetitions.

Results: At the 18 99DOTS experienced facilities, the proportion of patients enrolled on 99DOTS in the first month of treatment increased from 48.7% (n=1156/2373) in the routine 99DOTS period (August 2019-April 2020) to 85.1% (n=2175/2556) in the enhanced 99DOTS period (July 2020-June 2021), a difference of 36.4% (95% CI 33.9-38.8, p<0.001). At the 12 99DOTS naïve facilities, 85.9% (n=1713/1994) of patients were enrolled on 99DOTS in the enhanced 99DOTS period. At both 99DOTS experienced and naïve facilities, the proportions completing treatment, completing the intensive phase, and lost to follow-up were similar before and after the introduction of enhanced 99DOTS (Table).

	99DOTS experienced health facilities (n=18)			99DOTS naïve health facilities (n=12)		
	Pre-intervention (n=2373)	Post-intervention (n=2556)	P-value	Pre-intervention (n=1447)	Post-intervention (n=1994)	P-value
Enrolled onto 99DOTS	1156 (48.7%, 95% CI 42.5-55.0)	2175 (85.1%, 95% CI 81.4-88.2)	<0.001	-	1713 (85.9%, 95% CI 81.3-89.5)	-
Treated successfully	1852 (78.0%, 95% CI 74.2-81.5)	1997 (78.1%, 95% CI 73.8-81.9)	1.0	1287 (87.1%, 95% CI 79.9-92.0)	1776 (89.1%, 95% CI 84.0-92.7)	0.86
Completed intensive phase	2006 (84.5%, 95% CI 81.5-87.1)	2179 (85.3%, 95% CI 81.6-88.3)	0.94	1355 (91.7%, 95% CI 86.6-95.0)	1857 (93.1%, 95% CI 89.7-95.5)	0.85
Lost to follow-up	176 (7.4%, 95% CI 4.9-11.1)	159 (6.2%, 95% CI 4.3-8.8)	0.85	108 (7.3%, 95% CI 4.0-12.9)	105 (5.3%, 95% CI 3.1-8.8)	0.74

Conclusions: Our enhanced 99DOTS implementation strategy resulted in high uptake (>85%) of 99DOTS but did not improve treatment outcomes. 99DOTS is a viable alternative to DOT for most patients, but other interventions are needed to meet END TB targets.

OA04-230-08 Digital adherence monitoring of tuberculosis treatment in Ukraine: analysis of adherence levels and patient-provider communication before and during the war in Ukraine

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Background: Existing evidence on how war influences treatment adherence suggests it is harmful, though data are limited. When Russia invaded Ukraine in February 2022, it had a major impact on implementing the Adherence Support Coalition to End Tuberculosis (ASCENT) cluster-randomized trial evaluating the effectiveness of digital adherence technologies on tuberculosis treatment outcomes.

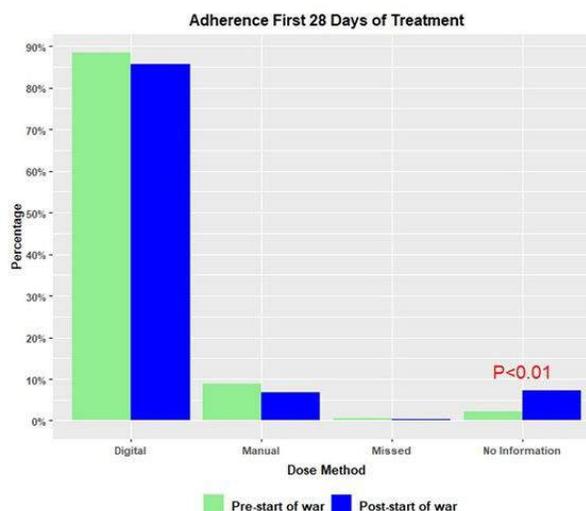
We aimed to determine if adherence levels changed during the first month of treatment pre-start and post-start of the war.

Design/Methods: We analyzed adherence data from the first 28 days of treatment for participants on drug-sensitive TB regimen, who used smart pillboxes in the ASCENT project in Ukraine, for the period 07/2021-01/2022 (pre-start war period) and 24/2-24/3/2022 (post-start war period).

Adherence data were recorded by a digital platform. Digital adherence was based on the platform receiving a signal that the box was opened. Manual adherence was recorded when the box was not opened, but healthcare workers marked drugs were taken according to the person's self-report, or a missed dose if drugs were self-reported as not taken.

When neither was recorded, the platform recorded "no information". We compared the proportion of digital and manual adherence and no information levels for pre-start and post-start war periods.

Results: This analysis included 591 participants (499 pre-start) from Donetsk, Mykolaivska, Odeska, Lvivska, and Zakarpatska regions. Median age (44.0 years pre-start vs 43.6 post-start), percentage male (66% pre-start vs 67% post-start) and digital adherence (88% pre-start vs 86% post-start) were similar by group. The proportion with no information, however, was higher in the post-start group (2.3% vs 7.3%; $p < 0.01$).



Conclusions: Overall (digital plus manual) adherence was similar pre-war and during the first month after the war started and high at least 90%. The increase in proportion with no information suggests disruptions in patient-provider communication due to the war, which will likely worsen if the war is protracted.

OA-05 Improvements in access to care

OA05-231-08 A combined holistic approach to increase tuberculosis cases in Cambodia: a result of program monitoring data of 96 points of care in 2022 in Cambodia

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Background and challenges to implementation: Cambodia transitioned out of the list of high 30 tuberculosis (TB) burden countries and was recognized for its success in reducing the disease. However, progress toward ending TB was impeded by persons missed by the health systems ¼ 53% of TB cases were undiagnosed and untreated in 2021. A holistic approach to increasing TB case detection, notification, care, and prevention is critical to ending TB in Cambodia.

Intervention or response: Community Mobilization Initiatives to End Tuberculosis (COMMIT) is a five-year USAID-funded project that implements a multi-sectoral

approach using locally generated solutions and community engagements to improve TB case finding, TB prevention, linkage to diagnosis, and treatment support in Cambodia. The combined interventions included one-off roving, snowball, community TB screening, hospital linkage, bi-directional screening of TB and diabetes, contact investigations, screening and provision of TB preventive treatment. COMMIT operates in 96 points of care, including ten referral hospitals and 86 health centers in Cambodia. We aim to highlight the program's 15 months achievement from January 2021 to March 2022.

Results/Impact: Despite the challenges posed by the COVID-19 pandemic, COMMIT maintained most of the operations. In total, we screened 91,926 people, of which, 26,895 were tested for TB. We detected 2,384 people with all forms of TB, and 99% enrolled treatment. 526 persons diagnosed with pulmonary TB were identified, and their close contacts (n=2,841) were evaluated. 2,406 (84.7%) were eligible for TB preventive treatment (TPT). 80.4% of those who were eligible for TPT initiated treatment. The treatment regimens prescribed were 3HP: 12 weeks once-weekly isoniazid-rifapentine (n=266), 3RH: 12 weeks once-daily isoniazid-rifampicin (n=757), and 6H: 24 weeks isoniazid (n=912).

Conclusions: COMMIT's multisectoral and multiprong approach to TB could increase case detection and improve TB prevention efforts in Cambodia. The experience, data, and lessons learned are pivotal in informing relevant programs and policies on the path toward ending TB in the country.

OA05-232-08 Narrowing the gap on missing TB cases through clinical diagnosis using XMAP in Northern Cross River state (NCRS)

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Background and challenges to implementation: Tuberculosis (TB) is one of the deadliest infectious diseases in the world. Early detection and treatment along with prevention is key to ending TB. Poor quality sputum could be responsible for non-detection of some TB cases which may account for a huge part of the missing TB cases in NCRS. The XMAP, a digital x-ray reporting platform was introduced to optimize clinical Tb diagnosis to narrow the gap in missing TB cases.

Intervention or response: The XMAP is a web-based application piloted by KNCV TB Foundation Nigeria, to provide complete yet prompt clinical evaluation of the chest radiographs of presumptive TB by engaged Radiologists. Bacteriologically negative presumptive TB clients had their chest X-rays and clinical symptoms uploaded on the XMAP for clinical diagnosis.

Based on the Radiologist review, the results are then classified as:

1. Suggestive,
2. Not suggestive,
3. Unconfirmed.

The southern WoW truck and the pilot DLB carried out TB active case finding (ACF) in NCRS in Q1, 2022, across 3 LGAs, at the start of XMAP in January 2022.

Results/Impact: Across the 3 LGAs, a total 915 presumptive TB was identified and 821 was tested with Genexpert (GXP) with 790 negatives, 726 of the GXP negative were sent for x-ray review on the XMAP and 119 was diagnosed and placed on treatment, these 119 TB cases would have been missed, and they would have infected many more people with TB. Clinical diagnosis through the XMAP platform contributed 74% and 79 % of all the TB cases diagnosed by WoW and DLB respectively.

	WOW	DLB	TOTAL
No. Presumptive TB	632	283	915
No. presumptive TB tested with Genexpert	551	270	821
No. presumptive Genexpert-negative	529	261	790
No. presumptive sent to XMAP	504	222	726
Total no. TB cases diagnosed	115	43	158
TB case yield from XMAP	85	34	119
% clinical diagnosis through XMAP	74	79	75

Table. January to March data for Southern WoW Truck and DLB in NCRS.

Conclusions: Early results from XMAP has shown that clinical diagnosis for TB is crucial, in narrowing the diagnostic gap and finding the missing TB cases in Northern Cross River state and Nigeria at large.

OA05-233-08 Bridge TB care: preliminary evaluation of a cross-border tuberculosis patient referral programme from Japan

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Background and challenges to implementation: Japan is a middle, reaching low-tuberculosis (TB)-burden country, with 12,739 patients newly notified in 2020 (rate of 10.1 per 100,000). However, the number and the proportion of foreign-born TB patients have constantly been increasing. One of the critical issues is the high proportion of transfer-out, which comprises approximately 15% of treatment outcomes and about half of them move out of Japan. There has not yet been a systematic programme to refer TB patients moving out of Japan.

Intervention or response: The Research Institute of Tuberculosis introduced a cross-border TB patient referral programme, “Bridge TB Care” (BTBC), in 2019 to refer TB patients moving out of Japan to TB care in the destination country, to follow them up to the end of their treatment course, and to report the treatment outcomes back to the public health centre in Japan.

Results/Impact: As of April 2022, BTBC had received requests for international referrals of 88 patients. After excluding those who had cancelled their travel or finished their treatment before departure, we enrolled 77 patients, including seven multi-drug resistant TB patients from ten countries. The median age was 26 years old, 66.2% were males, and 72.7% were diagnosed with pulmonary TB. 28.6%, 22.1%, and 15.6% left for Vietnam, the Philippines, and China, respectively. 83.1% (64/77) were confirmed to have accessed a medical facility. Of the 13 whose access to a medical facility could not be confirmed, 53.8% (7/13) subsequently became lost-to-follow-up. The treatment status of the 77 patients enrolled is summarized in Table 1. The treatment success rate was 79.0% (49/62 of the due date was before April 15, 2022).

Treatment status	N	%
Those of treatment completion due date was before April 15, 2022	62	100
Treatment success confirmed (*1)	49	79.0 95% CI [67.4 – 87.3%]
Lost to follow-up confirmed (*2)	12	19.4 95% CI [11.4 – 30.9%]
Treatment result not yet confirmed	1	1.6
Still on treatment (*3)	15	-

TB: Tuberculosis

CI: Confidence Intervals

*1: One multi-drug resistant tuberculosis (MDR-TB) patient included.

*2: Two MDR-TB patients included.

*3: Four MDR-TB patients included.

Table 1. Treatment status of 77 patients who were referred via Bridge TB Care programme, from September 2019 to April 2022.

Conclusions: Few cross-border referral programmes for TB patients currently operate globally. BTBC’s experience can potentially contribute to building valuable evidence for such programmes to ensure the continuity of TB patient care across the border.

OA05-234-08 The MOVE IT Model: increasing access to TB diagnostics for private sector patients in Tarlac City, Philippines

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Background and challenges to implementation: In 2020, of the TB patients notified in the private sector in the Philippines (under the mandatory notification scheme), only 5% were bacteriologically confirmed (BC), while 95% were clinically diagnosed (CD). One reason for this is the private sector’s low access to rapid TB diagnostic testing laboratory (RTDL). There are significant risks associated with a high number of CD patients enrolled in treatment, including the increased likelihood of incorrect treatment and drug resistance.

Intervention or response: The USAID’s Platforms for Sustainable Detection, Care and Treatment Project, in collaboration with the Department of Health, implemented the **MOVE-IT Model**, a strategy linking private healthcare providers (hospitals and clinics) without access to GeneXpert testing to a public RTDL facility, through an intermediary facility known as the „MOVE-IT Hub“. The MOVE IT hub is a private health facility that serves as the focal facility to collect sputum, store, transport, and provide network services for TB patients from referring private providers, for a convenience fee. GeneXpert test results are returned to the referring providers for further management.

Results/Impact: Preliminary results from the first 3 months of implementation (November 2021 to February 2022) show that through the strategy, 27 sputum and gastric specimens were collected from referring private providers and tested. Within the health facility network, the number of patients tested increased from 7% (4 out of 56) to 48% (27 out of 56). The number of bacteriologically confirmed patients increased by 21 percentage points, from 1(5%) to 7 (26%).

Conclusions: The MOVE-IT model demonstrates the potential of public-private partnerships in bringing TB services within TB patients’ reach, especially those in the private sector. It demonstrates a sustainable model for leveraging public and private resources to achieve common TB goals. With continued collaboration and supply of resources, it is expected that bacteriological confirmation from the private sector will continue to increase.

OA05-235-08 Convergence and divergence TB treatment support services between TB health facilities and people with TB in two East African countries

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Background: TB treatment adherence remains a significant challenge in high-burden countries, making the availability of treatment support services vital for improving TB outcomes, reducing TB transmission, and preventing the development of drug-resistant TB. Facilities offer various treatment support services, but these must align with what people with TB need and desire to support adherence and treatment completion. This study examines the availability of treatment support services reported by health facilities compared to desirability and self-reported receipt of those services.

Design/Methods: Quality of TB services assessments (QTSA), conducted in Ethiopia and Uganda between 2020–2021, include data from 401 public and private facilities across different levels offering TB services and 1,040 people enrolled in TB care. Data related to the availability of TB treatment support services reported by health facilities were compared to support services desired and received by people with TB to map gaps and unmet needs.

Results: Significant gaps were seen between the TB treatment support services facilities reported providing and the TB support services people with TB indicated receiving in both countries. TB treatment support services desired by people with TB in Uganda more often aligned with the services facilities reported providing compared to Ethiopia. Divergence between services desired and services received were observed in all services examined in Ethiopia and all but one of the services examined in Uganda.

Conclusions: The study revealed significant gaps between the services desired and received by people with TB. This highlights the need to prioritize TB services that are most responsive to the needs and desires of people with TB. Such action can help national TB programs refocus on how TB services are organized and delivered, particularly in resource-limited settings, in order to ensure treatment adherence, improve treatment outcomes, and minimize the catastrophic costs of TB.

OA05-236-08 Deployment of multiple diagnostic technologies for TB diagnosis: a gap-bridging strategy to case finding

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Background and challenges to implementation: Nigeria is one of the high-burden Tuberculosis countries globally. The National Tuberculosis Control Programme (NTP) adopted and implemented the WHO-recommended policies on new diagnostic technologies for diagnosis of TB disease. These include GeneXpert Dx System in 2011, Urine Lateral Flow Lipoarabinomannan (LF-LAM) assay for TB diagnosis among PLHIV with advanced disease, TB loop-mediated isothermal amplification (TB-LAMP), and TrueNat MTB plus/MTB-RIF Dx Systems, to improve TB diagnostic access in the country.

Intervention or response: USAID-funded KNCV TB Foundation LON 1&2 Project implemented in 14 states in Nigeria and in collaboration with the NTP, supported the validation and deployment of new TB diagnostic technologies in Nigeria. There are 13 GeneXpert sites in 3 states namely: Akwa Ibom, Cross River and Rivers, located in urban and semi-urban areas; 2 TB-LAMP machines located in rural areas and 6 TrueNat machines situated in primary healthcare centres in rural areas. The data covers June 2021 to March 2022.

Results/Impact: 111,477 tests were conducted using the GeneXpert system, with 9,949 positives identified (9% positivity yield). Six thousand, six hundred and

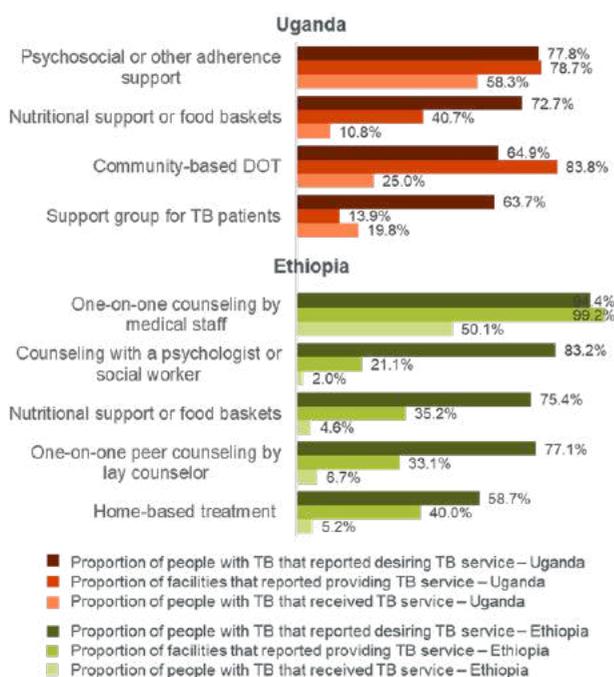


Figure. Comparison of TB treatment services offered by health facilities and TB treatment services received by people with TB in Uganda and Ethiopia.

thirty-seven tests were performed using the TB-LAMP with 419 positive cases identified (positivity yield of 6%). Four (4) rifampicin-resistance cases confirmed in a GeneXpert site. The 6 TrueNat sites tested 1965, 128 positive cases (positivity yield of 7%) and 2 rifampicin-resistance cases. The introduction and deployment of TB-LAMP and TrueNat identified improved access to diagnosis leading to the detection of 547 cases within the underserved locations.

Serial Number	Diagnostic tool	Number of samples tested	Number of TB cases identified	Positivity yield (%)
1	GeneXpert	111477	9949	9
2	TB-LAMP	6637	419	6
3	TrueNat	1965	128	7

Conclusions: TB-LAMP and TrueNat systems have filled the void in areas where the primary diagnostic tool, (GeneXpert) is absent. Targeted deployment of multiple technologies for TB detection can help bridge the TB diagnostic gap. Innovative diagnostic solutions that are nimble for the infrastructurally-challenged rural settings are needed for scale up for TB case finding.

OA05-237-08 Improving private sector access to high quality TB diagnostic services in Gresik, East Java Province, Indonesia

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Background and challenges to implementation: Gresik Regency in East Java Province, Indonesia, has 161 private health providers in total (general practitioners, clinics, and hospitals). In Q4-2019, a minority of private providers (5%) had access to GeneXpert (GX) testing despite nine GX machines with 39 functional modules in the district.

Intervention or response: In 2020, USAID TB Private Sector Activity supported the District Health Office (DHO) to optimize GX as the primary TB diagnostic tool. This began with developing a regional GX network and specimen transportation system, particularly to support facilities with insufficient resources. This included facilitating collaboration between private health providers and *Puskesmas* (public primary health centers) for specimen collection and transportation to GX laboratories. The DHO provided equal access for all health providers, including private sector, to Global Fund reimbursed specimen packaging and transportation. The DHO allocated local budget for provision of sputum pots and consumable items to all health providers. To strengthen policy implementation, the DHO distributed

a circular letter and provided training on the specimen packaging, filling the request form for sputum examination, and transportation tracking system to all health providers. Quarterly, the DHO reviews the progress of GX utilization involving professional organizations in Gresik to improve policy implementation.

Results/Impact: The proportion of TB presumptive, identified by private health providers, who were tested by GX significantly increased from 35% (35/99) in Q4-2019 to 86% (478/558) in Q1-2022. This was achieved through engagement with almost all (94%) private health providers in the district Public-Private-Mix network by Q1-2022, a significant improvement from only 5% (12/161) in Q4-2019.

Conclusions: The DHO plays an important role in defining strategy, coordinating with other key stakeholders, and ensuring equal access to resources, resulting in increased use of GX as the primary TB diagnostic tool by private health providers. Regular monitoring and evaluation of access to GX testing are crucial to improve policy implementation.

OA-06 How could we improve contact investigation?

OA06-239-08 Evaluation of three computer aided diagnostic packages in household contacts for the detection of microbiologically confirmed prevalent TB, incident TB and asymptomatic disease by FDG-PET/CT

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Background: The WHO now recommends the use of Computer Aided Diagnostics (CAD) to facilitate the reading of chest X-rays (CXR) performed for systematic screening of TB disease. CXR potentially aids the detection of asymptomatic disease. We evaluated three CAD software against microbiological and radiographic ([¹⁸F]-fluoro-2-deoxy-D-glucose positron emission/computed tomography (FDG-PET/CT)) reference standards for prevalent and incident TB.

Design/Methods: We recruited adult household contacts of drug-resistant TB in South Africa. 483 participants were extensively investigated for TB at baseline, with CXR and 3 sputa (induced if needed) for culture. 247 participants additionally underwent baseline FDG-PET/CT imaging to detect asymptomatic disease. Participants were followed up for at least 3 years without preventive therapy, three additional sputum samples were sent for culture between years 2-3. We evaluated 3 CAD software CAD4TBv7, qXRv3 and Lunitv4.9.0 to detect prevalent (baseline) and incident (follow-up)

TB and FDG-PET/CT evidence of asymptomatic TB disease, by calculating the area under receiver operator curve (AUC ROC).

Results: Amongst the 483 participants included, there were 23 prevalent and 38 incident TB cases. The AUC ROC to detect microbiologically confirmed prevalent TB was: CAD4TB 0.87 (95% confidence interval 0.77-0.96); qXR 0.88 (0.79-0.97); Lunit 0.91 (0.83-0.99).

Using a fixed specificity of 80% to detect prevalent TB, corresponding sensitivity was 100%, 90% and 85% for Lunit, qXR, and CAD4TB respectively. 14.1-15.6% of those above the 80% specificity CAD threshold score were considered “false positive” but subsequently progressed to incident TB.

Against a gold standard of FDG-PET/CT the AUC ROC for radiographic evidence of asymptomatic TB was CAD4TB 0.75 (0.67-0.83), qXR: 0.81 (0.74-0.88); Lunit 0.82 (0.74-0.89).

Conclusions: The CAD software performed well in identifying culture positive prevalent TB but missed roughly 15% of progressive TB when compared to FDG-PET/CT imaging for asymptomatic disease. A substantial proportion of those above threshold went on to develop incident disease.

OA06-240-08 Application of artificial intelligence enabled chest X-ray screening to support TB case detection in the Yangon region

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Background and challenges to implementation: Yangon bears the highest TB burden in Myanmar, housing 24% of the country’s DR-TB cases. 74% of people in Yangon receive their first care from private general practitioners (GPs).

However, there are significant gaps within TB care provided by the private sector, including lack of systematic screening for TB and contact tracing.

Intervention or response: PATH and Myanmar Medical Association implemented an intervention supported by the Stop TB Partnership’s TB REACH initiative to accelerate TB case detection in Yangon. An artificial intelligence based chest X-ray (CXR) software, qXR was deployed for TB screening at seven private health centres from August 2020 to October 2021. CXRs were acquired by the software directly from the digital X-Ray machine or uploaded using the qTrack application and instant AI results were used as clinical decision support by GPs. The radiologist opinion was received subsequently within two days.

2389 consecutive TB symptomatic patients or contacts were included in this analysis. The participants were divided into two groups i.e. household contacts of TB

patients (Group 1) and patients visiting private clinics identified as TB presumptive by clinician (Group 2). Agreement between radiologist report and qXR and its strength was computed using Cohen's kappa.

Results/Impact: The mean age of the patients was 37.6 and females constituted 56% of this sample. 569 of 2389 CXRs had signs of TB as per radiologist report.

The overall agreement between qXR and radiologist for Group 1 was 91.3% and Group 2 was 82.9%. The Cohen's kappa for Group 1 and Group 2 was 0.55 and 0.66 respectively.

Overall, 80 patients were confirmed with TB using GeneXpert. qXR flagged 78 (97.5%) and the radiologist flagged 70 (77.7%) of these cases.

Conclusions: Using CXR AI as part of a systematic screening process is a valuable tool for GPs in accelerating diagnosis of TB.

OA06-241-08 Impacts of stool-based testing on childhood TB case notification in Kano state northwestern Nigeria

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Background and challenges to implementation: Nigeria is ranked the highest TB burden country in Africa and 6th globally. Childhood TB notification has remained low due to difficulties in diagnosing TB in children.

Apart from the traditional diagnostic methods such as gastric lavage for lavage for GeneXpert and chest X-ray for clinical diagnosis, new diagnostic option using the stool for GeneXpert was piloted and scaled up in Nigeria by KNCV TB Foundation to improve childhood TB diagnosis in Nigeria.

This paper aims to share results and lessons learnt from the implementation of the stool based GeneXpert testing in one of the 14 states supported by KNCV Nigeria under the TB LON project.

Intervention or response: In October 2021, KNCV Tuberculosis Foundation Nigeria selected high volume TB facilities in Kano state for implementation of the stool-based test. Laboratory staff were trained on stool sample collection, analysis using GeneXpert machines and documentation of results using adapted state TB recording and reporting tools for children 0-14years

Results/Impact: There was a steady progress in TB yield among stool sample tested from November 2021 as shown in (fig 1) and this contributed also to an overall increase in childhood TB case notification in the State.

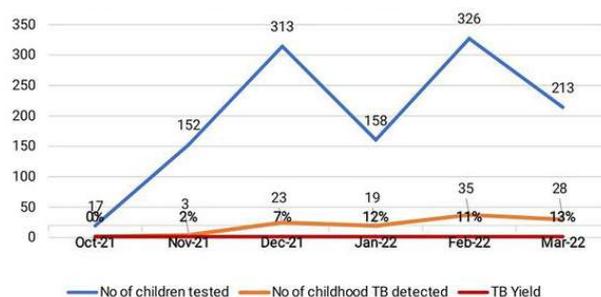


Figure. Trend of childhood TB yield using stool analysis in Kano state.

Conclusions: The TB yield from the stool-based test consistently increased from 2% to 13%. This method is recommended for scale up across other sites to help bridge the gap in childhood TB case notification in the state.

OA06-242-08 A systematic review of the number needed to screen for active tuberculosis among children

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Background: Improving detection of pediatric tuberculosis (TB) is critical to reducing morbidity and mortality among children. We conducted a systematic review to estimate the number of children needed to screen (NNS) to detect a single case of active TB across different screening modalities, geographic locations, risk groups, and settings (community, healthcare system, institutions).

Design/Methods: We searched four databases (PubMed, EMBASE, Scopus, and the Cochrane Library) for articles published from November 2010-February 2020. We included studies of TB active case finding (ACF) in children using symptom-based screening, chest x-ray, Xpert, or underweight status. Active TB diagnosis was defined according to individual study criteria (including clinical diagnoses), as sputa-based diagnostics are not widely used in children.

We indirectly estimated the weighted mean NNS for a given modality, geographic location, risk group, and setting using the inverse of the weighted prevalence. We assessed risk of bias using a modified AXIS tool.

Results: We screened 27,221 titles and abstracts, of which we included 30 studies of ACF in children < 15 years old. Most of the studies were conducted in countries with medium or high TB incidence (27/30) and did not require microbiologic confirmation of active TB (23/30). Symptom-based screening was the most common screening modality (weighted mean NNS 257 [range: 5-undefined], 19 studies). The weighted mean NNS was lower among children with HIV for all screening modalities (8 studies, see Figure).

The weighted mean NNS was lower in both inpatient (216 [18-241]) and outpatient (67 [5-undefined]) health-care settings compared to community (1,117 [28-5,146]) school settings (464 [118-665]). Risk of bias was low.

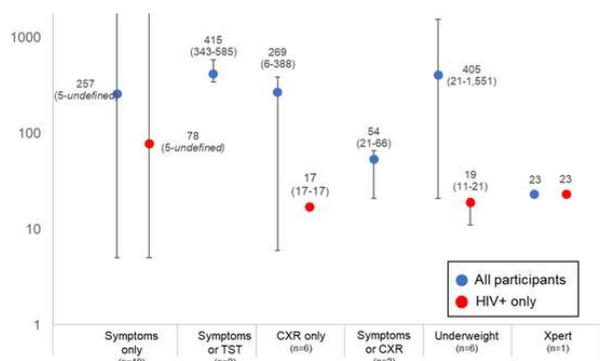


Figure. Number needed to screen to detect a single case of TB among children.

Conclusions: While substantial heterogeneity in the screening modalities and populations limited our ability to make inferences, we identified a potential opportunity to increase TB screening in healthcare settings. Case finding interventions should incorporate both the evidence presented in this review and the local context.

OA06-243-08 Tuberculosis yield among Contacts of non-Pulmonary Bacteriologically Confirmed Index TB patients in the urban setting of Central Uganda

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Background: The World Health Organization (WHO) recommends systematic and active investigation of TB contacts. However, lower priority is given to contact investigation among other non-pulmonary bacteriologically confirmed (PBC) patients, it thus contributes to the scarce information on the yield of TB among contacts of index TB patients without microbiological confirmation (non-PBC patients). This study therefore aims at establishing the yield of TB among contacts of PBC and non-PBC index TB patients in the urban setting of central Uganda.

Design/Methods: We abstracted data from the Uganda national TB contact investigation registers present at the health facilities for the period January 2018 to August 2020. The screening yield for both PBC and non-PBC, timing of TB diagnosis among contacts were determined. Logistic regression was used to examine association between TB classification category of the contacts and index TB patients.

Results: From January 2018 to August 2020, 234 persons were diagnosed with TB from a total of 14,275 contacts traced for both PBC and non-PBC TB index patients at 48 facilities. Of these, 42.7% were contacts of non-PBC index patients. TB screening yield was higher among contacts of non PBC (2.0%) compared to (1.4%) among contacts of PBC index patients. For both groups, over 80% of their contacts were diagnosed with TB within 3 months.

On multivariate logistic regression being young <15 years (adjusted odds ratio [aOR] 5.38, 95% CI [2.6 -11.3] p=<0.05) and being positive for HIV (aOR 2.11, 95% CI [1.1-4.1] p=0.03) were associated with type of TB diagnosed from contacts.

Conclusions: TB yield among contacts of non-PBC index case is nearly the same for contacts of PBC index cases. To improve TB case-finding, emphasis should be placed on contact investigation for household and close contacts of all other index cases with pulmonary tuberculosis regardless of whether PBC or non-PBC during intensive phase of treatment.

OA06-244-08 Mobile proprietary patent medicine vendors tuberculosis screening: impact on case finding in high burden LGAs in Osun State

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Background and challenges to implementation: Proprietary Patent Medicine Vendors (PPMV) being the health-care provider of the first instance in the community is strategic in improving TB case finding in the community. They serve as the first point of patient consult in most

communities by offering over-the-counter (OTC) drugs for common symptoms including patients presenting with symptoms suggestive of TB.

Tuberculosis Local Organization Network 3 (TB LON 3) project implemented by IHVN with funding from PEPFAR through USAID identified this window of opportunity to increase case finding in Osun state by supporting these set of informal providers to screen their clients for TB clinically and refer identified presumptive clients to designated facilities for further evaluation.

Intervention or response: To improve TB case finding among PPMVs, the TB LON 3 project reached out and engaged the Mobile PPMVs in 3 high burden Local Government Areas in Osun State, namely Iwo, Irewole, and Isokan. The trained PPMVs move from house to house to sell OTC drugs and integrated TB screening services with their customers. Using the WHO 4 clinical screening questions for their clients, presumptives are identified and referred to designated facilities for further evaluation and treatment for confirmed TB cases.

Results/Impact: By engaging the services of the Mobile PMVs in Q1 of 2021, the TB case finding increased from 8 in Q4 2020 prior to the intervention to 139 in Q1 2022 which represents a 1637% increase in case finding between Q4 2020 and Q1 2022.

Quarter	Number Diagnosed
Q4 2020	8
Q1 2021	70
Q2 2021	107
Q3 2021	95
Q4 2021	151
Q1 2022	139

Conclusions: TB case findings can be increased by building the capacity of the Mobile PPMVs to reach out to communities and populations that are hitherto not routinely availed of TB screening services. The mobile PPMV on-the-go intervention is part of the strategy that has resulted in the 64% increase in TB case finding recorded in the Osun State TB Program between Q1 2021 and Q1 2022.

OA06-245-08 Case yield from household contact screening of tuberculosis index patients in Karachi, Pakistan

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Background: Nearly 40% of people affected by TB in Pakistan are not diagnosed each year. National and international guidelines recommend screening household contacts of index TB patients. However, not all index patients or contacts are eligible. As a result, many contacts, a large number of whom may have TB disease, remain unscreened.

Design/Methods: We conducted a prospective cohort study under programmatic conditions in Karachi, Pakistan from January 2018 - December 2019, to screen all household contacts of all TB index patients. We disaggregated these according to guidelines into eligible (those with bacteriologically confirmed pulmonary TB or children <5 years) or ineligible (those with clinically diagnosed or extrapulmonary TB ≥5 years) index patients, and eligible (children <5 years or symptomatic individuals) or ineligible (asymptomatic individuals ≥5 years) contacts. We calculated TB case yields for different types of index patients and contacts, comparing the odds of diagnosing a contact with TB after adjusting for age and sex.

Results: Of 39,168 household contacts from 6,362 index patients, 21,035 completed clinical assessment for TB disease with a medical officer, and 416 were diagnosed with all forms of TB. The case yield from eligible contacts of TB index patients ineligible for screening under current guidelines (2,950 index patients, yield of 6.26%) was similar to the yield (3,411 index patients, yield of 6.03%) from eligible index patients (Odds Ratio 0.99 [0.82 – 1.20]). Screening ineligible contacts of all index patients (15,165 contacts, yield of 0.36%) had a significantly lower, but non-zero, yield than screening eligible contacts (5,870 contacts, yield of 6.15%).

Conclusions: Broadening Pakistan's TB contact screening guidelines to include clinically diagnosed and extrapulmonary index patients ≥5 years could double the number of cases detected at a similar level of effort. However, efforts to end TB need to consider the role and cost-effectiveness of screening asymptomatic household contacts ≥5 years.

OA06-455-08 Mapping the relationship between tuberculosis burden and case notifications in Uganda

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Background: Identifying spatial variation in tuberculosis (TB) burden can help national tuberculosis programs effectively allocate resources to reach all people with TB. However, data limitations pose challenges for TB subnational burden estimation. National TB prevalence surveys are conducted infrequently and are not powered for subnational burden calculations, whereas case notifications are collected continuously but may have varying completeness across space and time.

Methods: We developed a small-area modeling approach to integrate geo-positioned prevalence survey data, case notifications, and geospatial covariates to jointly estimate spatial variation in TB incidence and space-time variation in case notification completeness across 145 districts in Uganda during 2015-2019.

We simultaneously fit two surfaces in a spatially structured Bayesian hierarchical model. TB incidence was estimated using cluster-level estimates from the national 2014 - 2015 TB prevalence survey transformed to incidence and case notifications adjusted for geospatial covariates of health system access, while case notification completeness was estimated based on the ratio between incidence estimates and case notifications over space and time.

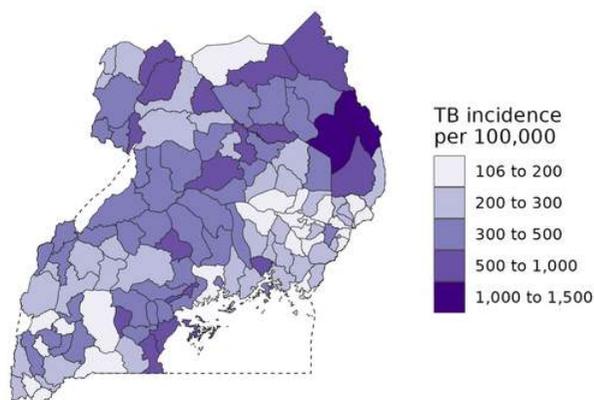


Figure: Estimated pulmonary TB incidence by district in Uganda, 2019

Results: We estimate that pulmonary TB incidence among adults varied >10-fold across the districts of Uganda in 2019, ranging from 106/100,000 in Butaleja, Eastern Region to 1,500/100,000 in Moroto, North-Eastern Region.

Additionally, case detection has increased nationwide from 2015 to 2019. District-level estimates of TB incidence had an average 95% uncertainty interval range of 128/100,000, which was five times more precise than a model using TB prevalence survey data alone.

Conclusion: A combined modeling framework that integrates TB case notifications, TB prevalence survey data, and geospatial covariates yields more precise estimates of TB burden than alternative models using a single data source.

This joint estimation approach provides useful insights for TB program operation and can be adapted to the data contexts in many countries with high TB burden.

OA-07 Cost and cost-effectiveness of TB interventions

OA07-246-08 Cost-effectiveness of decentralizing pediatric tuberculosis diagnosis services in seven low-income and high TB burden countries: a model-based analysis of the TB-Speed decentralization study

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Background: WHO has recently recommended decentralization of health services to improve children's access to TB diagnosis and treatment but evidence on cost-effectiveness is scarce. We sought to assess the cost-effectiveness of decentralizing childhood TB diagnostic approaches at district hospital (DH) or primary health center (PHC) level.

Design/Methods: The TB-Speed Decentralization study (NCT04038632) randomized two health districts of Cambodia, Cameroon, Côte d'Ivoire, Mozambique,

Sierra Leone, and Uganda to implement systematic screening, naso-pharyngeal aspiration and stool sampling, and Xpert Ultra testing, either at PHC-level (PHC-focused strategy), or at DH-level referring children with presumptive TB from PHCs (DH-focused), with digital chest X-ray at DH for both. We modelled the intervention in Zambia (TB-Speed country). We assessed the cost-effectiveness of these strategies against a standard of care representing national TB programs (SOC) from a health system perspective. Study data, literature, and expert opinion were used to parametrize a decision tree model of patient care and outcomes. Costs (2021 USD) for each step of the interventions (care pathways) were estimated by ingredients-based costing. We modelled costs and disability-adjusted life years (DALYs) for each strategy, and incremental cost-effectiveness ratios (ICERs) with respect to the SOC.

Results: Compared to the SOC, the DH-focused strategy was more cost-effective than the PHC-focused strategy across all countries. We estimated moving from SOC to the DH-focused strategy cost between \$572 (95% uncertainty range [UR]: \$509–\$648) and \$617 (UR: \$549–\$695) per additional TB diagnosis depending on the country. ICERs for DH-focused strategy versus SOC ranged between \$142 and \$159 per DALY averted. The probability of cost-effectiveness by threshold is shown in Figure 1. Higher prevalence of TB in children attending health facilities was associated with increased cost-effectiveness.

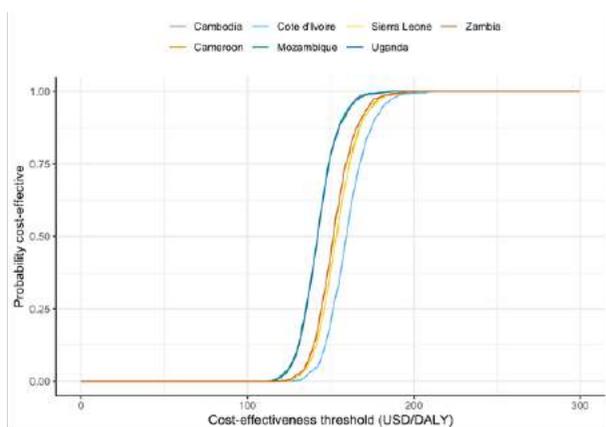


Figure 1. Cost-effectiveness acceptability curves by country for cost per disability-adjusted life year (DALY) averted analysis for the DH-focused strategy compared to the standard of care strategy.

Conclusions: DH-focused decentralization of TB case detection is likely to be cost-effective compared to SOC in all countries studied at thresholds under \$200 per DALY.

OA07-247-08 An integrated macroeconomic-health model for estimating the economic impact of tuberculosis

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Background: The economic evaluation of the benefits of tuberculosis (TB) policies typically take a micro-economic perspective, focussing on the health sector costs and health gains of policies. Extending economic analyses beyond the partial equilibrium (health sector) perspective into the general equilibrium (macro-economic) domain may provide further evidence to support investment in TB services. Computable General Equilibrium (CGE) models are one approach to this challenge. CGE models are multi-sector macro-economic (or whole-economy) models and are recommended by the WHO as a tool for health policy analysis.

Design/Methods: We developed an integrated macro-economic framework for analyzing the relationship between tuberculosis and the macro-economy. The framework combines a dynamic epidemiological model of TB, a demographic model and a CGE model, stratified into socio-economic household quintiles. We demonstrate the framework by applying it to estimate the effects of TB on gross domestic product (GDP) in India.

Results: Our preliminary results suggest that the estimated value of TB in India between 2021 and 2040 is 182 billion USD (0.27% of GDP). Approximately 90% of the estimated economic losses are the result of reductions in labour supply due to TB morbidity (11%) and mortality (81%). While the largest absolute costs are borne by households in the highest socio-economic quintile the relative effect is greatest in poorer households with those in the lowest quintile experiencing losses equivalent to 0.53% of household income compared with 0.24% in the highest quintile.

Conclusions: TB has significant effects on the Indian economy beyond health sector spending. The use of a CGE modelling framework can provide additional evidence to support investment in TB services and to validate simpler approaches to estimate the macro-economic impacts of TB.

OA07-248-08 Cost-effectiveness of post-arrival screening for incipient TB among migrants to the United States

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Background: Most TB cases in the US occur among foreign-born individuals, and current guidelines recommend screening and treatment for latent TB infection (LTBI) among migrants from high TB burden countries. However, the current LTBI screening tool (Interferon Gamma Release Assay, IGRA) has a low positive predictive value for future TB.

We estimated the potential cost-effectiveness of host blood RNA signature tests to identify incipient TB among recent migrants to the US.

Design/Methods: We developed a discrete event simulation model projecting lifetime TB-related outcomes for migrants from Mexico, China, India, the Philippines, and Vietnam entering the US in 2019 (55% of all immigrants).

We compared three post-arrival screening strategies:

- I. No LTBI or incipient TB screening;
- II. Screen all with IGRA, provide treatment for LTBI;
- III. Screen all with IGRA followed by an RNA signature test for IGRA positives, provide treatment for incipient TB (Figure 1).

We assumed the RNA test cost \$300USD with 90% sensitivity for TB cases developing within two years and 75% specificity (WHO Target Product Profile). We performed cost-effectiveness analyses from a societal perspective, with costs and quality-adjusted life-years (QALYs) discounted at 3% annually.

Results: Without intervention (Strategy-I), we estimated 2766 TB cases over the lifetime of the study cohort. Strategy-II (IGRA) and Strategy-III (IGRA+RNA) averted 56.8% and 15.0% of total TB cases, respectively.

At a willingness-to-pay threshold of 100,000 USD/QALY gained, Strategy-II was cost-effective for migrants from India, China, the Philippines, and Vietnam. Neither Strategy-II nor Strategy-III was cost-effective for Mexico. Strategy-III was dominated for all.

Sensitivity analyses showed that Strategy-III could be cost-effective if RNA signatures could identify TB cases developing >5 years later.

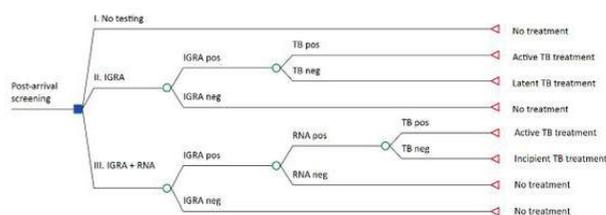


Figure 1. Post-arrival screening strategies.

Strategy-I: No screening for LTBI or incipient TB upon arrival. Strategy-II: All individuals in the study cohort are screened for LTBI with IGRA. IGRA-positive individuals with active TB ruled out are treated for LTBI. Strategy-III: All individuals in the study cohort are screened with IGRA first. Those who tested positive with IGRA are screened with a host blood RNA signature test to rule out individuals at low risk of future TB. RNA-positive individuals with active TB rules out are treated for incipient TB.

IGRA, Interferon Gamma Release Assay; RNA, host blood RNA signature test; pos, positive test result; neg, negative test result.

Conclusions: Using RNA signatures to identify and target treatment for incipient TB is not cost-effective for our study cohort, compared to treating all IGRA-positives, unless TB cases developing further in the future can be identified.

OA07-249-08 Cost-utility analysis of artificial intelligence powered intensified case screening finding strategies in two urban centers in Mega Manila, the Philippines

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Background: Computer-aided detection using artificial intelligence (AI) has gained more attention in tuberculosis intensified case finding activities (ICF) to improve early detection in high-risk settings. Through USAID support, the Philippines piloted a qure.AI-powered outsourced mobile van x-ray ICF set-up in outpatient departments of two large urban hospitals in Mega Manila. While there is a push, there is limited cost-effectiveness evidence.

Design/Methods: We utilized a model-based decision analytic tree cost-utility analysis with a societal perspective, focusing on the costs incurred by the TB control sector and patient productivity losses and projecting over a 10-year time horizon at a 7% discount rate. We compared the actual ICF set-up (“Scenario 3” or “ICF QXR” in Figure 1) to three alternative scenarios: “Scenario 1” or Passive Case Finding (PCF) using only

symptom screening before Xpert MTB/RIF Xpert assay (“PCF SX”); “Scenario 2” or PCF using human-read X-ray screening before referring for Xpert testing (“PCF CXR” or the standard-of-care); and “Scenario 4” or ICF using human-read X-ray (“ICF CXR”).

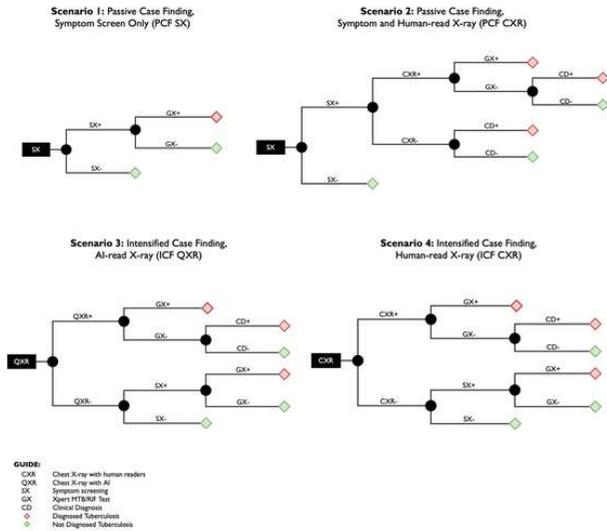


Figure 1. Decision tree algorithms for the four screening scenarios evaluated.

Results: One-year expenses for patients ranged from PHP 12.4 million (~USD 248,000) for Scenario 1 to PHP 27.9 million (~USD 558,000) for Scenario 4. Compared to the GDP-threshold computed as PHP 163,702.00 (USD 3,247.04) per DALY avoided based on 2020 GDP, all scenarios were affordable, with only Scenario 3 (ICF QXR) revealed to be dominant or outperforming the SOC Scenario 2. Scenario 1 was the least expensive but also avoided the fewest DALYs. Even after discounting and accounting for companions in Scenario 3 and Scenario 4, the order of cost-effectiveness remained maintained. Findings remained robust even after sensitivity analysis was conducted.

Conclusions: Adopting AI technology for ICFs in a hospital environment has a very high cost-utility. Further real-world comparative evaluation or pragmatic trial is recommended to establish stronger cost-effectiveness evidence to support such an approach over traditional case-finding activities.

OA07-250-08 Patient incurred costs for individuals using digital adherence technologies to support tuberculosis treatment adherence: findings from the ASCENT multi-country study

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Background: Digital adherence technologies (DATs) may reduce the number of visits to a health facility compared to the traditional Directly Observed Treatment Strategy through remote daily monitoring. Patient costs contribute to poor adherence if it becomes a barrier to medication collection and may exacerbate impoverishment.

As part of the ASCENT project, we examined factors associated with patient incurred costs of individuals using DATs for tuberculosis treatment support in Ethiopia, South Africa, the Philippines, and Tanzania.

Design/Methods: We estimated the cost per treatment episode from a patient perspective using cross-sectional patient cost surveys with 323 participants of the ASCENT trial.

Self-reported income was used to rank individuals into terciles of monthly income for each country. We calculated total costs as the sum of direct - and time costs and converted them to USD.

Time was valued using self-reported individual income. Using a gamma generalized linear model with log link, we examined the factors associated with total episode costs. Explanatory variables included DAT used, country, and individual income.

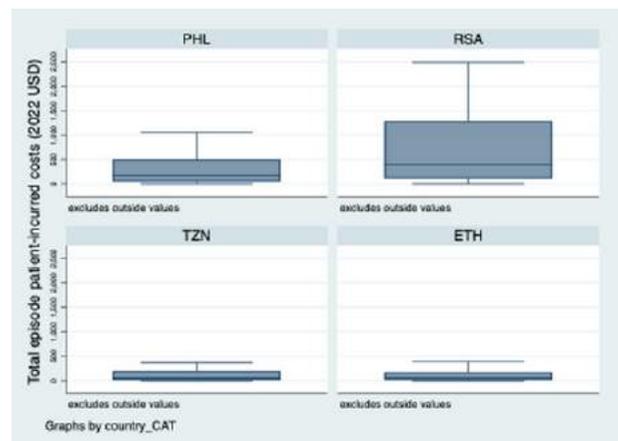


Figure 1. Total episode patient-incurred costs in 2022 USD. PHL: Philippines, RSA: South Africa, TZN: Tanzania, ETH: Ethiopia. USD: United States Dollars.

Results: The mean cost per treatment episode per person was US\$473 (SD: 1507); US\$19 (SD: 43) in the poorest tercile, and US\$1296 (SD: 2416) for the wealthiest. Indirect costs and the time taken to travel to health facilities was the main driver of these costs. Higher patient episode costs were associated with receiving care in South Africa compared to the Philippines OR=2.41 [95% CI:1.45; 4.01, p-value<0.001]; and being wealthy OR=34.56 [95% CI:23.42; 50.99, p-value<0.001].

Conclusions: Costs incurred by individuals on tuberculosis treatment using DATs remain high. The time cost of travelling to health facilities is a driver of episode costs. Further work is required to assess whether DATs can reduce patient incurred costs and poverty induced by ill health.

OA07-251-08 Costs incurred by individuals undergoing TB care in low-, middle-, and high-income settings: a systematic review

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Background: One of the WHO End TB Strategy targets is to eliminate the burden of out-of-pocket (OOP) costs for households impacted by TB. Understanding of this economic burden is limited due to sparse economic data on the OOP expenditures incurred by individuals undergoing TB diagnosis and treatment. In order to improve the current knowledge and help inform decisions on cost-effective TB care, research needs to be conducted to understand the OOP costs incurred by individuals while undergoing TB treatment and identify the main drivers of costs.

Design/Methods: We conducted a comprehensive systematic review to examine the costs incurred by patients undergoing TB care in low-, middle-, and high-income country settings. Main drivers of costs were identified by examining key cost components and assessing how variations impacted overall patient costs. Studies were included if they used WHO or WHO adapted patient costing questionnaires such as USAID, StopTB, or TB|CTA, to report direct (medical and non-medical) and indirect (time lost and loss of income) patient-related costs associated with TB care. Studies were independently assessed by three reviewers with key costing data extracted and compared across differing parameters to identify key drivers of cost including differing urban settings, patient types and economic settings.

Results: 790 studies were screened with 45 meeting inclusion criteria. A large proportion of studies were conducted within the last 5 years (44% from 2017-2021), 33% included patients with drug-resistant TB (DR-TB) within their study population and 62% analyzed study

populations with HIV-positive patients. Total costs for TB care ranged from \$0.67-\$19,153.80, diagnostics ranged from \$3.21-\$2682.10 and treatment ranged from \$4.40-\$4894.39.

Conclusions: The largest drivers of cost were medication, hospitalization, and loss of income. 71% of studies, reported individuals suffering from social consequences or resorting to coping mechanisms in varying degrees to manage the burden of TB-related costs.

OA07-252-08 Do catastrophic costs due to tuberculosis predict unfavourable tuberculosis treatment outcome? A systematic review and meta-analysis

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Background: Patients with tuberculosis and their households often experience medical and non-medical out-of-pocket expenditures and lost income. When the total of these costs due to tuberculosis exceed 20% of pre-illness annual household income then they are considered to be catastrophic in case they make completion of tuberculosis treatment unaffordable and consequently unachievable. Eliminating catastrophic costs due to tuberculosis is one of three targets for ending tuberculosis prioritised by the World Health Organisation. We aimed to assess the evidence that catastrophic costs due to tuberculosis predict unfavourable tuberculosis treatment outcomes.

Design/Methods: We did a literature search of PubMed, Scopus and Web of Science electronic databases using Prisma-P guidelines with search terms „(tuberculosis OR TB OR Koch disease) AND (catastrophic costs OR catastrophic household costs)“. We then selected and characterised relevant studies and performed a meta-analyses of their findings.

Results: The literature search identified 441 publications including 193 unique studies. Screening their title and abstracts found 120 potentially relevant studies, full-text review of which identified three studies that clearly informed our research aim. Wingfield et al 2014 studied 765 unselected patients whereas Fuady et al (2020) and Guidoni et al (2021) both studied 282 and 310 unselected patients only with drug-susceptible tuberculosis. Meta-

analysis of these studies demonstrated that catastrophic costs due to tuberculosis predicted 2.3-times greater odds of unfavourable treatment outcome (95% confidence intervals=1.7-3.1, $P<0.001$, figure upper panel). A sensitivity analysis including a potentially eligible fourth study Plesca et al (2021) of 287 selected patients only with drug-resistant tuberculosis who had already completed at least two months of therapy also showed that catastrophic costs due to tuberculosis significantly predicted unfavourable treatment outcome (figure lower panel).

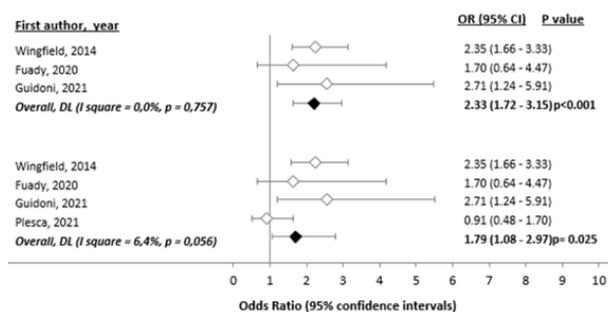


Figure 1. Catastrophic costs predictive of unfavorable TB outcomes (20% threshold).

Conclusions: Patients and their households that experience catastrophic costs due to tuberculosis are at increased risk of suffering unfavourable tuberculosis treatment outcomes.

OA-08 Causes and effects of DR-TB

OA08-253-08 Determinants of catastrophic cost incurrence in households impacted by MDR-TB in Ho Chi Minh City, Viet Nam

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Background: People receiving multidrug-resistant tuberculosis (MDR-TB) treatment and their households have an increased likelihood of experiencing catastrophic costs (CC), yet their risk factors are poorly understood.

Design/Methods: Data were collected from 94 people with MDR-TB taking a nine-month regimen using a longitudinal adaption of the WHO TB Patient Cost Survey between October 2020 to April 2022 in ten districts of HCMC. Participants were surveyed within two weeks of treatment initiation, after the first month of continuation phase and after the end of treatment. Costs were converted from the local currency to US\$ (VND1 = US\$ 0.000043, 2020-2022, OANDA). The CC threshold was defined as total costs exceeding 20% of annual pre-TB household income. Logistic regression analysis was used to identify independent variables associated with CCs.

Characteristics	Experienced CC (N=81) n (%)	Univariable Logistic Regression		Multivariable Logistic Regression	
		cOR [95% CI]	p-value	aOR [95% CI]	p-value
Years of age, median (IQR)	42 (33-56)	0.99 [0.95-1.03]	0.64	0.98 [0.93-1.03]	0.36
Male	62 (77)	2.04 [0.60-6.98]	0.26	1.19 [0.25-5.66]	0.83
Wealth Quintile 1-3 (Less Wealthy)*	55 (68)	7.05 [1.79-27.80]	0.01	5.58 [1.25-24.83]	0.02
Lost job due to MDR-TB treatment	69 (74)	3.33 [1.01-11.05]	0.05	2.82 [0.56-14.22]	0.21
Breadwinner	40 (49)	5.37 [1.12-25.75]	0.04	3.58 [0.65-19.65]	0.14
Any form of social protection	78 (96)	11.56 [2.22-60.07]	0.00	4.42 [0.60-32.82]	0.15

* Quintiles based on Multidimensional Poverty Index using Principal Component Analysis including 12 asset variables; Abbreviations: CC – catastrophic cost, HH – household, MDR-TB – Multidrug-resistant tuberculosis

Table.

Results: Within the study population, 86% (95% CI: [77.49-91.86]) of participants experienced CC, with a high proportion found among males (77%) and poorer households (68%). Most participants received some form of social protection (93%), especially among people experiencing CC (96%). Households where the affected person lost their job (aOR=2.82, 95% CI: [0.56-14.22]) and were the family's breadwinner (aOR=3.58, 95% CI: [0.65-19.65]) seem to have higher odds of experiencing CC, while poorer households also remained significantly associated with CC in the fully adjusted model (aOR=5.58, 95% CI: [1.25-24.83]).

Conclusions: These results indicate that people with MDR-TB in HCMC, Viet Nam that belonged to poorer households had higher odds of experiencing CC despite almost universal access to some form of social protection. Additional strategies to mitigate CC among people with MDR-TB, especially the most vulnerable, are urgently required.

OA08-254-08 Care for patients with MDR-TB and AUD during COVID pandemic

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Background: The provision of MDR/RR-TB treatment remains a global challenge, made only more complex through the COVID-19 pandemic. We compare MDR/RR-TB treatment adherence via home-based directly observed treatment (DOT), out-patient facility DOT, video (VOT) and in-patient DOT in patients with harmful alcohol use or alcohol use disorder (AUD) during the COVID pandemic. All patients also received patient-centred, psycho-social support and harm reduction throughout treatment.

Design/Methods: Cohort study with patients starting treatment between January 2019 and November 2021 included, with censure in February 2022. Mixed effects logistic regression used to analyse risk of non-adherence by treatment/month. Non-adherence was taking <90% of prescribed treatment in a month.

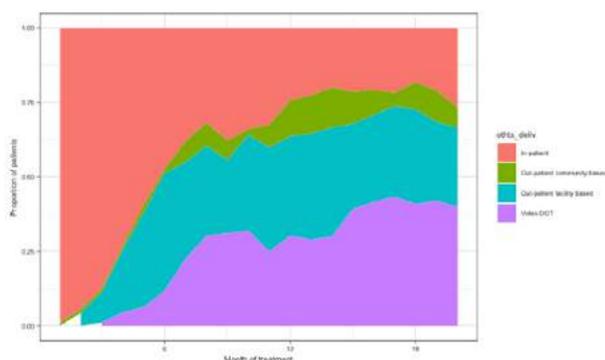


Figure 1. Break down of type of DOTs over the course of treatment.

Results: There were 89 patients included in the analysis. Mean overall adherence was 90.3% and mean adherence for in-patient, VOT, home-based and out-patient facility settings were 98.1%, 92.4%, 97.4% and 79.1%. Enrolment in VOT increased over time, but average adherence at VOT decreased over time, likely linked to changes in enrolment criteria where more people became eligible for VOT during Covid-19. The odds ratio of poor adherence was 3.8 (95% CI:1.7-8.7) at an out-patient fa-

cility, 0.3 (95% CI:0.05-1.5) when home-based and 0.07 (95% CI:0.03-0.2) for in-patient, with VOT as the reference. Patients who attended VOT, home-based, facility DOT had differences in age, self-reported motivation to complete treatment, and psychiatric or physical disease. In mixed-effects logistic regression, after adjustment for patient characteristics and time-on-treatment, the odds of non-adherence at in-patient, home-based and VOT were not statistically different but facility-based DOT remained the worst (AOR:18.1 (95% CI:2.6-127.7)).

Background and challenges to implementation: The provision of MDR/RR-TB treatment remains a global challenge, made only more complex through the COVID-19 pandemic. We compare MDR/RR-TB treatment adherence via home-based directly observed treatment (DOT), out-patient facility DOT, video (VOT) and in-patient DOT in patients with harmful alcohol use or alcohol use disorder (AUD) during the COVID pandemic. All patients also received patient-centred, psycho-social support and harm reduction throughout treatment.

Intervention or response: Cohort study with patients starting treatment between January 2019 and November 2021 included, with censure in February 2022. Mixed effects logistic regression used to analyse risk of non-adherence by treatment/month. Non-adherence was taking <90% of prescribed treatment in a month.

Results/Impact: There were 89 patients included in the analysis. Mean overall adherence was 90.3% and mean adherence for in-patient, VOT, home-based and out-patient facility settings were 98.1%, 92.4%, 97.4% and 79.1%. Enrolment in VOT increased over time, but average adherence at VOT decreased over time, likely linked to changes in enrolment criteria where more people became eligible for VOT during Covid-19. The odds ratio of poor adherence was 3.8 (95% CI:1.7-8.7) at an out-patient facility, 0.3 (95% CI:0.05-1.5) when home-based and 0.07 (95% CI:0.03-0.2) for in-patient, with VOT as the reference. Patients who attended VOT, home-based, facility DOT had differences in age, self-reported motivation to complete treatment, and psychiatric or physical disease. In mixed-effects logistic regression, after adjustment for patient characteristics and time-on-treatment, the odds of non-adherence at in-patient, home-based and VOT were not statistically different but facility-based DOT remained the worst (AOR:18.1 (95% CI:2.6-127.7)).

Conclusions: This person-centred, psycho-social support and harm reduction intervention maintained good levels of adherence through the COVID-19 pandemic. Adherence at an out-patient facility was worse than VOT or home-based DOT, even after adjusting for patient characteristics. Video DOT was increasingly popular, but may not be the right option for all patients.

OA08-255-08 Burden of rifampicin-resistant tuberculosis on total tuberculosis treatment regimen costs in WHO European region countries: a TBnet study

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Background: Tuberculosis care carries high costs for health care systems. Drug cost of treating rifampicin-resistant tuberculosis (RR-TB) are much higher than for drug-susceptible tuberculosis. We estimated the proportion of annual total drug cost spent for RR-TB among all notified tuberculosis cases in European countries.

Design/Methods: Participants in 41 countries in the WHO European region provided data on cost and availability of tuberculosis drugs. Regimen costs were calculated for the standard drug-susceptible regimen (rifampicin, isoniazid, ethambutol, pyrazinamide) and for a long conventional RR-TB regimen including bedaquiline, moxifloxacin (if not available, replaced by levofloxacin), linezolid, cycloserine/terizidone, and clofazimine for 18 months.

Annual national drug regimen costs were estimated based on notification data reported by WHO/ECDC for the year 2019. We assumed that all notified RR-TB cases received the long course treatment. Extensively drug-resistant tuberculosis cases were excluded.

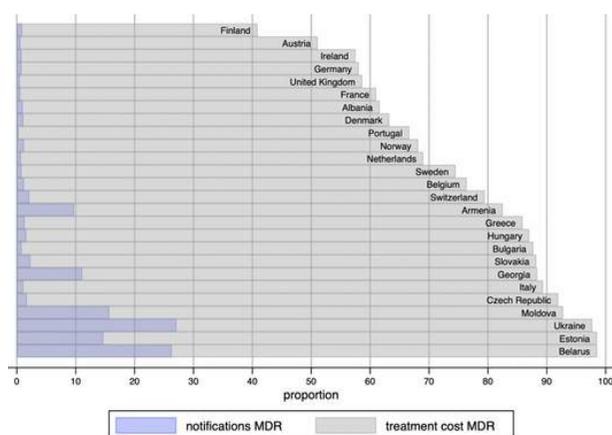


Figure 1. Proportion of pulmonary RR-TB cases among all notified cases (blue bar) and proportion of regimen cost for treatment with a long-course Bedaquiline based regimen for RR-TB among total drug cost for treatment of all notified cases in European countries (grey bar) in 2019.

Results: Overall, 41 countries provided data on drug cost. A regimen for treatment of drug-susceptible tuberculosis was available in all countries. The long conven-

tional RR-TB regimen with a treatment duration of 18 months was available in only 31 countries, and cost data was available for 26 of them. In all countries except for Finland, countrywide RR-TB regimen costs were higher than costs for drug-susceptible tuberculosis, regardless of the proportion of pulmonary RR-TB among all notified tuberculosis cases (ranging between 0.2% [Spain; Serbia] and 27.1% [Belarus, Ukraine]) (Figure 1).

Conclusions: Although representing only a small proportion of all tuberculosis cases in most European countries, RR-TB treatment regimens account for a large majority of total tuberculosis drug costs. In particular in countries with a high burden of RR-TB and overall lower resources for healthcare, the cost burden for treatment of RR-TB is extremely high. These results call for more affordable RR-TB drug costs to improve access to treatment in Europe.

OA08-256-08 The effect of malnutrition on sputum culture conversion and treatment outcomes among people with multidrug-resistant tuberculosis: a systematic review and meta-analysis

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Background: Malnutrition is associated with weakened cell-mediated immunity, decreased drug absorption, and heightened disease severity. Particularly, undernutrition is a risk factor for tuberculosis (TB) with a population attributable fraction of 1.9 million cases globally in 2020. However, evidence on the effect of malnutrition on TB treatment outcomes remains inconsistent and poorly understood.

We thus aimed to evaluate the effect of malnutrition on sputum culture conversion and treatment outcomes among people with MDR-TB.

Design/Methods: We searched published articles from Medline, Embase, Scopus and Web of Science databases without restricting the year of publication. Meta-analysis with a random-effect model was used to estimate Odds Ratio (ORs) and Hazard Ratios (HRs), with 95% confidence interval (CI). In the presence of heterogeneity, subgroup analysis, meta-regression and sensitivity analysis were performed. Moreover, both Egger's and Begg's tests were carried out to check out the potential publication bias of the included studies.

Results: We included 60 studies comprising a total of 32201 people with MDR-TB. The pooled prevalence of undernutrition among people with MDR-TB was 49.2% (95% CI: 42.6, 55.7). Undernutrition was significantly associated with lower sputum culture conversion (HR: 0.73, 95% CI: 0.63, 0.85), and higher mortality

(OR: 2.85, 95%CI: 2.12, 3.85) as well as higher unfavourable treatment outcomes (OR: 1.77, 95%CI: 1.51, 2.07). However, overweight was not significantly associated with mortality (OR: 0.81, 95%CI: 0.63, 1.05) nor unfavourable outcomes (OR: 1.24, 95%CI: 0.71, 2.16).

Conclusions: Undernutrition was significantly associated with unfavourable treatment outcomes, including mortality as well as delayed sputum culture conversion among people with MDR-TB.

OA08-257-08 Emergence of resistance to bedaquiline in Karakalpakstan, Uzbekistan

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Background: WHO recommends the use of bedaquiline (Bdq) in longer as well as shorter multidrug-resistant tuberculosis (MDR-TB) treatment regimens. However, resistance to this new drug is now emerging. A recent systematic review found relevant frequency of acquired bedaquiline resistance in patients on bdq containing regimens (Mallick J. et. al.). There are no standardized regimens and limited treatment options for patients with resistance to bedaquiline.

We aim to describe the characteristics and share our experience from management of patients with MDR-TB with resistance to Bdq.

Design/Methods: We performed a retrospective study of routinely collected data for patients treated for MDR-TB in Karakalpakstan between January 2015 and March 2022. We included 64 patients with confirmed bedaquiline resistance on phenotypic drug susceptibility testing (DST) at any point before, during or after TB treatment. We describe the baseline characteristics, treatment, and follow-up of these patients while on TB treatment.

Results: Twelve (18.8%) patients showed primary Bdq-resistance, seventeen (26.6%) patients acquired resistance during treatment and thirty-five (54.7%) patients had no baseline DST or exposure history to bedaquiline. There were forty-three male patients representing 67.2% of the total cohort. The treatment regimens for these patients included clofazimine (93%), linezolid (84%), delamanid (79%), cycloserine (63%), and bedaquiline (53%). The interim clinical outcome for the 43 patients whose treatment history were available are; twenty-one (48.8%) on treatment, seven (16.3%) treatment completed or cured, six (14%) treatment failure, five (11.6%) died, and four (9.3%) lost to follow-up.

Conclusions: Our programmatic data gives an overview of the emergence of resistance to Bdq in a TB programme using bedaquiline for management of MDR-TB. Primary resistance to bedaquiline was present in almost a fifth of patients, highlighting the need for baseline DST to Bdq. Follow-up DST should be performed for patients on Bdq containing regimens who fail to culture convert.

OA08-258-08 Coverage, timeliness and effectiveness of conditional cash transfers for people with drug resistant tuberculosis in Zimbabwe: a mixed methods study

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Background: The END TB strategy recommends social protection to mitigate the socio-economic impact of tuberculosis (TB) on households. Zimbabwe started implementing a conditional cash transfer (CCT) programme for people on drug resistant TB (DR-TB) treatment in 2013. The programme has not yet been evaluated.

We aimed to:

- i. Determine proportion of people receiving CCTs and effectiveness of CCTs in improving treatment outcomes,
- ii. To explore the experiences of people with DR-TB with registering for the programme and;
- iii. To understand the impact of CCTs from the perspective of people with DR-TB.

Design/Methods: Data from 2014-2021 were extracted from TB registers and from CCT payment records held by the National TB Programme. Sixteen in-depth interviews were conducted with people who were completing treatment or had completed treatment within the last two months.

Poisson regression, adjusted for province, year of treatment, age and sex was used to investigate associations between receiving CCTs and successful treatment outcomes among people who were in DR-TB care for ≥ 3 months after treatment initiation. Qualitative data were analyzed using thematic analysis.

Results: A total of 481 people were included in the quantitative study. Of these, 53% (254/481) received CCTs at some point during treatment. People who exited DR-TB care within three months were 73% less likely to receive CCTs (prevalence ratio (PR) =0.27 [95% CI: 0.18-0.41]). Among those who were alive and in care three months after treatment initiation, CCT recipients were 32% more likely to have successful outcomes versus those who did not (adjusted PR=1.32, [95% CI:1.00-1.75]). Qualitative results revealed lack of knowledge about availability of CCTs among people with DR-TB and missed opportunities by healthcare providers to provide information about availability of CCTs. Delays and inconsistencies in disbursements of CCTs were frequent themes.

Conclusions: CCTs were associated with successful treatment outcomes. Improvements in coverage, timeliness and predictability of disbursements are recommended.

OA08-259-08 The effectiveness and safety of an all-oral ultra-short regimen in China: preliminary results of a randomized controlled trial (TB-TRUST study)

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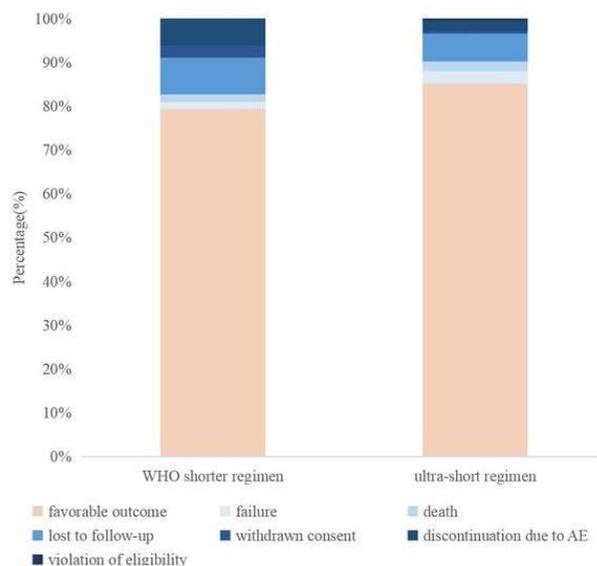
Background: Research on variants of the shorter rifampicin-resistant tuberculosis (RR-TB) treatment regimen was urgently needed. We here launched a non-inferiority randomized controlled trial, Refining MDR-TB Treatment Regimens for Ultra Short Therapy (TB-TRUST), aiming to evaluate the effectiveness and feasibility of an all-oral ultra-short regimen in China.

Design/Methods: The multicenter trial recruited RR-TB patients who susceptible to fluoroquinolones and aminoglycosides. Participants were randomly divided into the ultra-short arm and the control arm with a ratio of 1:1. The control arm used the WHO injectable-containing shorter regimen. In the ultra-short arm, pyrazinamide-susceptible patients received levofloxacin, linezolid, cycloserine, and pyrazinamide for 24 weeks, and pyrazinamide-resistant patients replaced pyrazinamide with clofazimine for 36 weeks.

The primary outcome was a favorable status at 84 weeks after randomization. The sample size was calculated as 354. Data used in this preliminary study were updated at April 1st, 2022.

Results: Of 354 patients who underwent randomization, 262 completed treatment. The favorable status reported was comparable between two groups (85.1% [142/170] in the ultra-short arm and 79.3% [149/175] in the control arm, P=0.15). Unfavorable outcome was reported in 14.9% of participants in the ultra-short arm (2.3% death, 2.9% failed, 6.3% lost-to follow-up, 0.6% with-

drawn consent, 2.3% discontinuation due to adverse event [AE], 0.6% violation of eligibility criteria) and in 20.7% in the control arm (1.7% death, 1.7% failed, 8.4% lost-to follow-up, 2.8% withdrawn consent, 6.1% discontinuation due to AE). AEs were reported by 70% of participants; the most common AEs were hyperuricemia (70.1%), QTc prolongation (35.1%), and anemia (26.6%) in the ultra-short arm, and hyperuricemia (52.6%), elevated liver enzyme (49.4%), QTc prolongation (44.9%) in the control arm.



Conclusions: The preliminary results showed that the refined ultra-short regimen was noninferior to the WHO injectable-containing shorter regimen in terms of the effectiveness and safety in patients with fluoroquinolones susceptible RR-TB. (ClinicalTrials.gov number, NCT03867136)

OA08-260-08 Can T-wave morphology abnormalities identify patients at risk of clinically-relevant QT prolongation during drug-resistant tuberculosis treatment?

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Background: STREAM Stage 1 was a randomised controlled trial for patients with rifampicin resistant TB, comparing a Short versus Long treatment regimen. Clinically-relevant QT/QTcF prolongation (≥ 500 ms or increase in ≥ 60 ms from baseline) was more common amongst Short regimen participants, who received high

dose moxifloxacin and clofazimine. T-wave morphology abnormalities may be a useful early biomarker for QT prolongation that increases the risk of malignant ventricular arrhythmia.

Design/Methods: ECGs were selected from baseline, early and late time-points on treatment in 200 participants (Short 142; Long 58) with available ECGs.

The sample included all 82 participants with available ECGs who developed clinically-relevant QT prolongation and 118/191 who did not, representative of the study population based on country, gender and age.

ECGs were blinded to regimen, time-point and QT interval. T-wave morphology was categorised as normal or abnormal (notched, asymmetric, flat wave, flat peak or broad) (Figure 1). Differences between groups were assessed using Chi Square tests (paired/unpaired, as appropriate).



Figure 1. Examples of abnormal T wave morphology seen in ECGs from participants in STREAM Stage 1 (notched, asymmetric, flat wave (a), flat peak (b) or broad).

Results: At baseline, 23% (45/200) of participants displayed ≥ 1 abnormal category, increasing to 45% (90/200, $p < 0.001$) at the late time point. An increased frequency between baseline and late time-points was observed for notched 2% (3/200) vs 11% (22/200), $p < 0.001$; flat peak 0% vs 7% (14/200), $p < 0.001$ and broad 2% (4/200) vs 13% (26/200), $p < 0.001$, categories.

T-wave abnormalities were more common in Short regimen participants ECGs 38% (88/234, $p = 0.008$) compared to Long regimen 21% (16/76), and ECGs in participants who developed clinically-relevant QT prolongation, 44% (56/128, $p = < 0.001$). T-wave abnormalities occurred prior to a $QT/QTcF \geq 500$ ms in 53% of participants (Long 2/5; Short 14/25).

Conclusions: T-wave morphology abnormalities occurred in Stream Stage 1. Differences existed between regimen, time-point and whether or not clinically-relevant QT prolongation occurred. The abnormalities observed may allow early detection of patients at risk of QT prolongation.

OA-09 Transmission of MTBC strains in human and animal populations

OA09-262-08 Mycobacterium bovis cattle from Morocco show close phylogenetic relationships to isolates from France, Spain, Portugal, and Algeria

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Background: Livestock production is a fundamental pillar of the Moroccan economy; however, the problems facing this industry are complex, with a major factor being infectious diseases. Bovine tuberculosis (bTB) caused mainly by *Mycobacterium bovis* (*M. bovis*) has generated considerable direct and indirect economic losses, in addition to the unknown human health burden caused by zoonotic TB.

Previous studies have shown likely *M. bovis* transmission links between Morocco and Southern Europe, however, due to the limitations inherent with the methods used, more definitive conclusions could not be determined.

Design/Methods: In this study, we employed whole genome sequencing on *M. bovis* isolates from Morocco, and a representative selection of *M. bovis* isolates from different countries publicly available in NCBI. Single nucleotide polymorphism analysis was performed using the vsnp bioinformatics pipeline developed by the National Veterinary Services Laboratories.

Results: We analyzed 784 *M. bovis* isolates, 99 of them from humans. Most Moroccan isolates fell within EU2 (37) and EU3 (13) clonal complexes, while interestingly only one was classified as EU1, and others fell outside the currently defined clonal complexes. Moroccan *M. bovis* showed a close phylogenetic relationship with isolates from Portugal, Spain, France, and Algeria, which are geographically aligned with Morocco, and have historical and economic ties. The human *M. bovis* isolates clustered with cattle isolates from Morocco, however, the genetic relationship was not very close.

The present study provided an initial understanding of *M. bovis* genetic diversity and relatedness in Morocco and neighboring countries.

Conclusions: Ultimately, large sample sizes, different hosts and countries are necessary to fully delineate *M. bovis* transmission within the animal-human interface.

OA09-263-08 Isolation of *Mycobacterium orygis* from free ranging spotted deer and blackbuck in Chennai, India

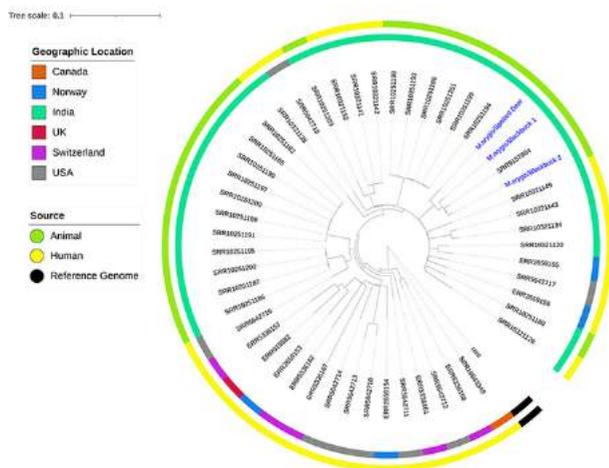
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Background: Wildlife tuberculosis is an underreported and unexplored area of research in a high TB burden country like India. Here we report the isolation of *Mycobacterium orygis*, a member of *Mycobacterium tuberculosis* complex (MTBC) from free ranging wild ungulates, namely two black bucks (*Antelope cervicapra*) and one spotted deer (*Axis axis*) from the Guindy National Park, a densely populated place in Chennai, India.

Design/Methods: Postmortem analysis upon natural death revealed pale-yellow lesions in lungs and lymph nodes. Tissue samples were harvested, homogenized, decontaminated and inoculated in solid and liquid media.

DNA extracted from cultured isolates were subject to PCR (MPT64 gene), spoligotyping and whole genome sequencing (WGS) (Illumina).

Results were assessed with Galaxy/vSNP. Phylogenies were constructed with RAxML. RD Analyser and RD-Scan were used to localize the regions of difference within the sequences.



Results: The cultured isolates were sensitive for first line

anti-TB drugs and were confirmed as *M. orygis* by PCR, spoligotyping (ST587) as well as WGS. The isolates appeared well clustered with other globally reported *M. orygis* isolates in the phylogenetic tree.

The deletion of RD7 to RD10, RDOryx_1, RDOryx_4, RD12Oryx, RD301 and RD315 substantiated these isolates as *M. orygis*. The SNP difference within the isolates ranged from 40-110 SNPs ruling out the possibility of any transmission as the SNP-based cut-off for this ranges from 3 -14 SNPs

Conclusions: We were not able to identify the source of *M. orygis* infection in the animals, but it would be prudent to take into account the free ranging transmission because of the increased human-animal interaction in the area. Since it is well known that the pathogen is capable of causing infection in both human and animal hosts, systematic surveillance and screening of spotted deer, black buck as well as humans in the vicinity is essential for successful implementation of the One Health approach.

OA09-264-08 African buffalo (*Syncerus caffer*) samples in novel transport medium used with Xpert MTB/RIF Ultra provides rapid and safe detection of *Mycobacterium bovis* in maintenance hosts

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Background: Bovine tuberculosis caused by an important zoonotic pathogen, *Mycobacterium bovis* (*M. bovis*), is responsible for substantial economic losses and potential human health risk when livestock and wildlife are infected. In South Africa, African buffaloes (*Syncerus caffer*) are key maintenance hosts of *M. bovis*. Confirmation of infection requires culture from infected specimens.

Unfortunately, mycobacterial culture has sub-optimal sensitivity and is time-consuming. Post-mortem examination of infected animals, sample collection, transport and storage of tissue specimens are considered a potential human health risk.

Therefore, we evaluated the combined use of inactivating PrimeStore Molecular Transport Medium (PSMTM) and GeneXpert MTB/RIF Ultra (Ultra) for the detection of *M. bovis* infection from buffaloes with known infections.

Design/Methods: Swabs of gross pathological lesions (n = 16) from known *M. bovis* infected buffaloes (n = 13) were stored in PSMTM at ambient temperature until Ultra testing.

Additionally, all swabbed tissue samples were cultured in parallel. As a negative control cohort, oral swabs (n = 119) from *M. bovis*-unexposed buffaloes (n = 119) with varying nontuberculous mycobacteria (NTM) infections from geographically distinct wildlife farms (n = 3) were collected, stored in PSMTM, transported at ambient temperature, and tested using Ultra.

Agreement between tests was calculated as Cohen's kappa coefficient using GraphPad Prism Software. McNemar's test was used to compare Ultra results from tissue swabs and tissue cultures using GraphPad software. P-value < 0.05 was considered statistically significant.

Results: *M. tuberculosis* complex DNA was detected by Ultra in 13/16 tissue swabs and 9/16 matched tissue homogenates from culture-confirmed *M. bovis* positive buffaloes. MTBC DNA was detected in 14/116 oral swabs from *M. bovis*-unexposed, NTM infected animals, showing the potentially high specificity of Ultra with PSMTM swabs.

Conclusions: PSMTM sample processing, in combination with the Ultra, has the potential to provide a safe, rapid screening test for zoonotic *M. bovis* in wildlife.

OA09-265-08 Genetic profiling of *Mycobacterium tuberculosis* complex (MTBC) strains from slaughtered cattle in Chennai, India

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Background: Bovine TB has been a chronic illness that has been affecting cattle and causing mortality and economic losses in India as well as across the globe for the past century.

This study identified the presence of *Mycobacterium tuberculosis* complex (MTBC) organisms in slaughtered cattle in Chennai India.

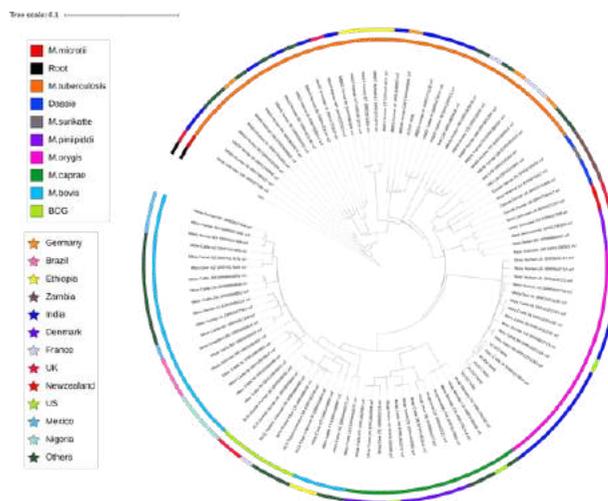
Design/Methods: A total of 153 lymph node (LN) samples (85 bronchial LN and 68 mediastinal LN) collected from 113 animals were used in this study. Culture, molecular (PCR and spoligotyping) and whole genome sequencing methods (WGS) (Illumina) were used for species identification from these sites.

WGS results were assessed with Galaxy/vSNP. Phylogenies were constructed with RAxML. RD Analyser and RDScan were used to localize the regions of difference (RD) within the sequences.

Results: Six out of 113 (5.3%) animals were positive for MTBC by culture, of which *M. tuberculosis* was isolated from one animal, and *M. orygis* from the other five. Strikingly, no *M. bovis* was found. Drug susceptibility testing revealed that one of the *M. orygis* isolates was phenotypically resistant to isoniazid and ethambutol,

antimycobacterial agents typically used in human TB care.

WGS and phylogenetic analyses show that the isolates recovered have relatively restricted genetic diversity, with evidence of sharing of identical or closely related isolates amongst cattle, consistent with cattle-to-cattle transmission. RD analyses confirmed an intact RD1 region in all six samples presence of intact RD239 and RD236a region in the *M. tuberculosis* isolate while the *M. orygis* isolates showed the deletion of RD7 to RD10 and the presence of RD4.



Conclusions: Our studies suggest that bTB in India is likely to be different than elsewhere and highlight an urgent unmet need to better understand the epidemiology of bTB and develop rational strategies to accelerate the control of bTB in India and other regions where the disease remains endemic.

OA09-266-08 Candidate host-directed therapeutics for tuberculosis differentially restrict *M. tuberculosis* complex lineages growth in-vitro

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Background: The rise of multi-drug resistant tuberculosis (TB) and poor treatment outcomes of some drug-susceptible TB mandate novel treatment approaches such as host-directed therapeutics (HDTs).

However, reliable tools are lacking to evaluate HDT efficacy and determine the impact of host and Mycobacterium tuberculosis complex (MTBC) genetic diversity, which affects treatment response. Our study sought to address this gap to better inform the development of HDTs for TB.

Design/Methods: Clinical isolates representing major MTBC lineages circulating in Africa were transfected with reporter-gene-tagged plasmids and used to assess the direct inhibition of three promising tyrosine kinase inhibitors (TKIs) in-vitro using the standard colony-forming unit (CFU) and SpectraMax i3x to measure bacilli growth.

We developed an in-house application for semi-automated data extraction, management, and visualisation of the massive data generated by CFU, absorbance, fluorescence, and luminescence readouts.

We also developed statistical models to analyse HDTs drug sensitivity and predict growth outcomes effectively and efficiently.

Results: The growth pattern of *Mtb*-lineage2, *Mtb*-lineage4, *Maf*-lineage5, *Maf*-lineage6 and *M. Bovis* were analysed and showed significant differences detectable with all the readouts.

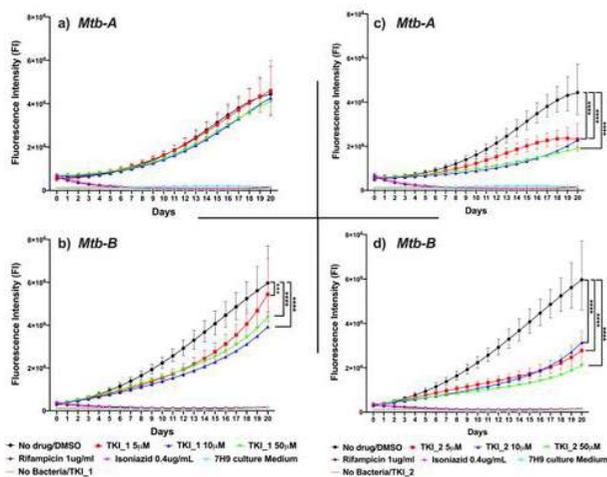


Figure 1. Tyrosine kinase inhibitors (TKI) direct restriction of *M. tuberculosis* complex lineages growth in-vitro. Daily fluorescence measurement of the growth of *Mtb*-A (a & c) and *Mtb*-B (b & d) in presence of different concentrations (Red=5mM; Blue=10mM, Green=50mM) of TKI_1 and TKI_2 respectively. Controls conditions include Black=bacteria + drug diluent DMSO; Pink=bacteria + Isoniazid 0.4mg/mL, Purple=bacteria + Rifampicin 1mg/mL; Cyan=culture media only 7H9 and Brown=only 7H9 + TKI. P-value represent difference between the growth of the bacteria without drug and in the presence of different drug concentration over 20 days.

*= $p < 0.05 - 0.01$, **= $p < 0.01 - 0.001$, ***= $p < 0.001 - 0.0001$, ****= $p < 0.0001$.

However, only the fluorescence, luminescence, and absorbance readouts were suitable for evaluating drugs' effect on the bacteria. HDTs, including those in clinical trials for TB (TKI_1), directly restricted the growth of some MTBC lineages but not other clades, whereas others HDTs (such as TKI_2) significantly inhibited all the tested MTBC lineages (Fig1).

Conclusions: We show for the first-time tyrosine kinase inhibitors HDTs' direct inhibition of clinical MTBC lineages in-vitro. The direct inhibition varies with the type of HDT drugs and MTBC lineages. Our assay is suitable for preselecting HDT drugs for testing in clinical trials to ensure that they are efficacious against all MTBC lineages.

OA09-267-08 Integrating surveillance and genomic data to reveal tuberculosis transmission clusters in Southern Taiwan

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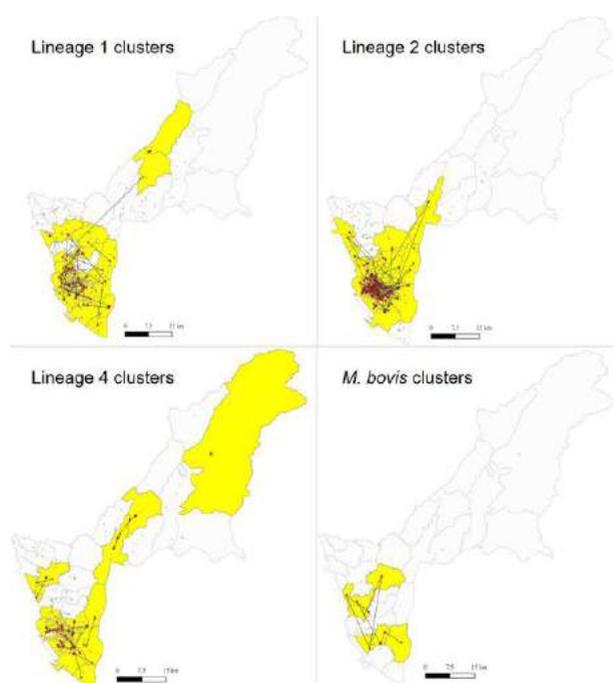
Background: Tuberculosis (TB) incidence in Kaohsiung, a metropolitan area in Southern Taiwan, was 49.3 per 100,000 in 2019. The reduction rate of TB incidence in Kaohsiung was lower than the national average, suggesting potential unidentified sources of infections in the communities. In Taiwan, conventional TB surveillance relies on case reporting and contact tracing, subject to time delay and recall bias.

This prospective study aims to integrate whole genomic sequencing (WGS) data of *Mycobacterium tuberculosis* (MTB) and case surveillance data to infer transmission clusters.

Design/Methods: MTB isolates were obtained from notified TB cases in Kaohsiung from 2018 to 2021. Snippy (v.4.6.0) pipeline was used to align reads and identify core single-nucleotide polymorphisms (SNPs). We applied a probabilistic transmission approach, Transcluster, to incorporate sampling dates, SNP distances, and spatial weights for cluster analysis. Spatial weight was determined by pairwise comparisons of residential, occupational, and other known locations. A higher probability of transmission was given if the cases had overlapped locations or at a closer distance.

Results: Among 1,777 TB isolates analyzed, lineage 1, lineage 2, lineage 4, and *M. bovis* accounted for 43%, 35%, 21%, and 1% of infections, respectively. Lineage 2 tended to have big clusters (> 20 cases) which were located in the city center, while other lineages had medium-sized (5-12 cases) or small clusters (< 4 cases) distributed in both urban and suburban areas. Pairwise comparisons showed that 50 pairs had overlapped footprints at households, hospitals, universities, prisons, or coastal industrial parks; however, only half of these were genetically similar, and these are mainly from the same households or have been to the same hospitals.

Conclusions: By incorporating genomic and surveillance data, several unknown and recent transmission clusters were identified. Control actions should be strengthened in the areas showing clustered cases.



OA-10 Clinical trials and operational research for new treatment for TB (adults and Children)

OA10-268-08 Pregnancy outcomes for patients treated with new and repurposed drugs for drug-resistant tuberculosis

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Background: Drug-resistant tuberculosis (DR-TB) carries significant morbidity and mortality risk. Care of DR-TB in pregnancy is challenging; the impact of in-utero exposure to anti-tubercular drugs is largely unknown, with little information to inform decisions about DR-TB treatment during pregnancy.

Design/Methods: Pregnancy outcomes were collected in a pharmacovigilance programme supporting a clinical trial (TB-PRACTECAL; N=552) and an observational cohort (endTB; N=2,906). We present birth outcomes reported by participants.

Results: Between 01-Apr-2015 and 31-Mar-2022, 58 pregnancies in 53 women were notified from 10 countries. Patients became pregnant a median of 261 (range, 0-727) days from treatment start. No maternal deaths occurred. Treatment was changed/interrupted during pregnancy in 17.0% (9/53) of mothers. Treatment outcome was successful in 97.3% (36/37) of mothers in endTB and 100% (7/7) of mothers who completed TB-PRACTECAL. Known pregnancy outcomes (N=52) included: 30 live births (one twin pregnancy), 20 elective abortions, and 3 miscarriages.

Of the 30 neonates, 16 were born to mothers treated during pregnancy with bedaquiline, 11 clofazimine, 7 second-line injectables, 5 delamanid, 2 bedaquiline-pretomanid-linezolid-clofazimine (exposure: 21 and 64 days), and 1 bedaquiline-pretomanid-linezolid-moxifloxacin (exposure: 3 days).

For 4 neonates, mothers became pregnant within 6 months of bedaquiline last dose. Median birthweight (N=24) was 3,015 (range,1,270-4,200) grams. Two babies were born prematurely (30-31 weeks). Low-birthweight was reported in eight babies (33.3%; 8/24). One low-birthweight baby died from complications unrelated to tuberculosis. One baby was treated for DR-TB. No malformations were reported.

Characteristics	endTB Observational cohort	TB- PRACTECAL	Total
Number of pregnant women	16	16	53
Median (min-max) days on DR-TB treatment at pregnancy start	219 (0-678)	329 (104-727)	261 (0-727) [#]
DR-TB treatment outcome assigned	37	7	44
Favourable	36 (97.3%)	7 (100%)	43 (97.7%)
Unfavourable	1 (2.7%)	0	1 (2.3%)
Known pregnancy outcomes	38	14	52
Number of live births	20*	10	30*
Number of low-birthweight neonates	8	0	8
Number of elective abortions	17	3	20
Number of spontaneous abortions	2	1	3

[#]Including 1 participant in endTB and 12 participants in TB-PRACTECAL who became pregnant during follow-up after treatment completion.

*Twins delivered.

Table. Pregnancy and DR-TB treatment outcomes of mothers enrolled in the endTB observational cohort and the TB-PRACTECAL clinical trial.

Conclusions: These results support evidence that effective DR-TB treatments may improve maternal outcomes and prevent perinatal transmission. However, further research is required on how these perinatal outcomes compare to other cohorts not affected by TB or exposed to different TB treatments, and factors contributing to low-birthweight in babies born to mothers with DR-TB. A global registry is urgently needed to assist parents and clinicians with decision-making.

OA10-269-08 Monitoring for hepatotoxicity among HIV-positive patients on ART and isoniazid and rifapentine for treatment of tuberculosis infection

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Background: Hepatotoxicity is a potentially serious adverse drug event among people taking rifapentine and isoniazid. Few studies have evaluated hepatotoxicity in those taking ART and newer TB preventive treatment regimens.

Screening for liver function at initiation and during follow-up will greatly increase costs and reduce feasibility of treatment regimens.

Current guidelines generally do not include screening or monitoring for liver adverse events, but using clinical trial data, one can determine whether this is required. As part of the WHIP₃TB trial, weekly rifapentine-isoniazid for three months (3HP) was given once or annually.

We investigate liver function test results at screening and follow-up among HIV-positive people taking 3HP in South Africa, Mozambique, and Ethiopia.

Design/Methods: HIV-positive adults on ART were enrolled in the trial. Liver function tests were done at screening, and months 1 and 2 post-treatment initiation. Using Division of AIDS grading for liver function tests (AST, ALT, or Bilirubin) and for hepatic disease, we defined grade 3-4 events as hepatotoxicity.

Results: A total of 4994 (70% female; median age:41 years(IQR 34-48years)) participants were screened and 3610 were initiated on 3HP. At screening, 10(0.2%) participants had abnormal liver enzymes and were excluded from the study.

At follow-up, abnormal liver function was 8(0.2%) at month1 and 18(0.6%) at month2. A further four (0.1%) participants had a hepatitis event and, in total, 26(0.8%) had some form of liver abnormality at follow-up.

	Screening N=4430	Month 1 N=3334	Month 2 N=3219
Grade			
0	3825(86.9)	2775(83.2)	2680(83.3)
1	522(11.9)	492(14.8)	468(14.5)
2	47(1.1)	59(1.8)	53(1.7)
3	7(0.2)	6(0.2)	11(0.3)
4	2(0.1)	2(0.1)	7(0.2)

Conclusions: Liver abnormality at screening and follow-up among persons starting 3HP was low in these three settings. It is not necessary to screen for liver function abnormality prior to TPT initiation or during follow-up in routine implementation.

OA10-270-08 Predictors of treatment outcomes in children with rifampicin-resistant tuberculosis: a global individual patient data meta-analysis

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Background: Current rifampicin-resistant tuberculosis (RR-TB) treatment in children remains complex and long due to limited paediatric data with newer drugs and shorter regimens.

Design/Methods: A systematic review and individual patient data (IPD) meta-analysis included published and unpublished data from children and adolescents (0-19 years) treated for RR-TB between 1994-2020; IPD on demographic, clinical, and treatment characteristics and outcomes were pooled. Children with missing TB treatment regimen, duration, or outcome were excluded. Clinical and demographic characteristics were described and, along with the use of drugs by WHO group, were evaluated as predictors of favourable vs. unfavourable outcome (treatment failure or death) using mixed-effects logistic regression models. Missing data were imputed using multiple imputation.

Results: We included 20395 children from 57 cohorts, 63% from India, 30% from South Africa. The mean (SD) age was 14.7 (4.8) years, 89.6% were bacteriologically confirmed, and mean (SD) treatment duration was 15.3 months (8.3) months. Overall, 16825 (82.5%) had treatment success, 722 (3.5%) treatment failure, and

2848 (14%) died. Of 17764 children with documented HIV status, 13.8% were HIV-positive. HIV positivity, prior TB treatment, older age, AFB positivity, male gender and pulmonary disease were associated with lower odds of favourable outcome ($p < 0.001$).

Increased odds of favourable outcome were associated with inclusion of two (aOR 1.4; 95%CI [1.09,1.8]; $p < 0.001$) or three (aOR 2.1; 95%CI [1.6,2.8], $p < 0.001$) group A drugs (bedaquiline, linezolid, levofloxacin/moxifloxacin).

Conclusions: In this largest ever paediatric RR-TB IPD, treatment success was high despite high bacteriological confirmation rates and high HIV prevalence. Young children and those with clinically diagnosed RR-TB were underrepresented. The use of multiple group A drugs resulted in better outcomes, which supports new WHO guidelines for all-oral regimens in all children. Improved paediatric RR-TB treatment surveillance is need to generate more outcomes data on new drugs and regimens, especially in young children.

OA10-271-08 Treatment outcome of the pre-XDR-TB patients in Ukraine with BPaL under OR conditions

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Background: Clinical implementation of the BPaL regimen is developed only for Operational Research (OR), not for routine practice.

Design/Methods: BPaL implementation started in Ukraine in November 2020 at the National TB Institute, under TB Reach “Pilot Study to Evaluate the Effectiveness and Safety of the BPaL Treatment Regimen in Ukraine” project implemented by OATH together with KNCV as an OR.

A patient selection, monitoring system and treatment was conducted according to approved OR Protocol. The International Advisory Council was established, comprising National TB Institute, OATH, KNCV, PATH, and Ukraine’s NTP to ensure efficient selection of patients with pre-XDR-TB or failure/intolerance of previous MDR-TB treatment.

Results: During November 2020 to December 2021, 145 patients were screened, 137 were eligible for enrolment on the BPaL and 121 of them continued treatment without exclusion criteria. 97 of them ended BPaL before 03.2022 and were registered treatment outcome for them.

There were received follow treatment outcome: “cure” and “treatment completion” – in 90 (92,8 %), Died – in 1 (1,0 %), LTFU – in 2 (2,1 %), SAE and permanent

interruption of the BPaL regimen due to AE(s) - in 4 (4,2 %) patients, respectively. AEs (including SAE) were registered in 79 (81,4 %), SAEs - in 37 (38,1 %) of patients. Permanent dose reduction of Lzd due to AE(s) were registered in 42 (43,2 %), temporary interruption of Lzd due to AE(s) - in 4 (4,1 %), permanent interruption of Lzd due to AE(s) - in 8 (8,2 %), temporary interruption of the BPaL regimen due to AE(s) - in 14 (14,4 %), permanent interruption of the BPaL regimen due to AE(s) - in 4 (4,1 %) of patients respectively.

Conclusions: Ukraine is the first country in the world started BPaL under OR conditions with excellent results: favorable outcome were received in 92,8 % of patients.

OA10-272-08 Validation of machine readings of QT interval during monitoring in the STREAM Stage 1 trial

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Background: STREAM Stage 1 was a randomised-controlled trial in rifampicin-resistant TB, comparing a Short versus Long regimen. Participants received regular ECG monitoring using machine-generated readings to identify QT prolongation, which was more frequent in Short regimen participants.

This sub-study compares machine with gold-standard manual readings to investigate whether they are reliable, accurate and/or affected by treatment.

Design/Methods: All participants with available ECGs at baseline, an early (weeks 1,2,3 or 4) and a late (weeks 12,24 or 36) time-point on treatment were identified. A representative sample (by country, age and gender) of 118/191 participants was selected, enriched by all who developed QT/QTcF ≥ 500 ms or ≥ 60 ms increase from baseline (n=82). There were 142 Short and 58 Long regimen participants.

ECGs were blinded to regimen and time-point; QT intervals were calculated by Tangent method and compared to automated readings. A difference of ± 20 ms is commonly considered acceptable in cardiological practice. Machine/manual differences were assessed using Bland-Altman plots by regimen and time-point.

Results: Mean (SD) differences between machine and manual QT measurements varied with time-point, but not regimen: +19ms (8.4) and +19.4ms (9.2) at baseline, 23.47ms (11.82) and 25.59 (10.61) at the early time-point and +24.3ms (13.3) and +23.6ms (13.7) at the late time-point on the Short and Long regimens, respectively.

Variance of the discrepancies increased on treatment but was unrelated to length of QT interval. Of the 10 measurements outside the limits of agreement (LOA) in Figure 1, all but two ECGs had evidence of T wave morphology abnormality.

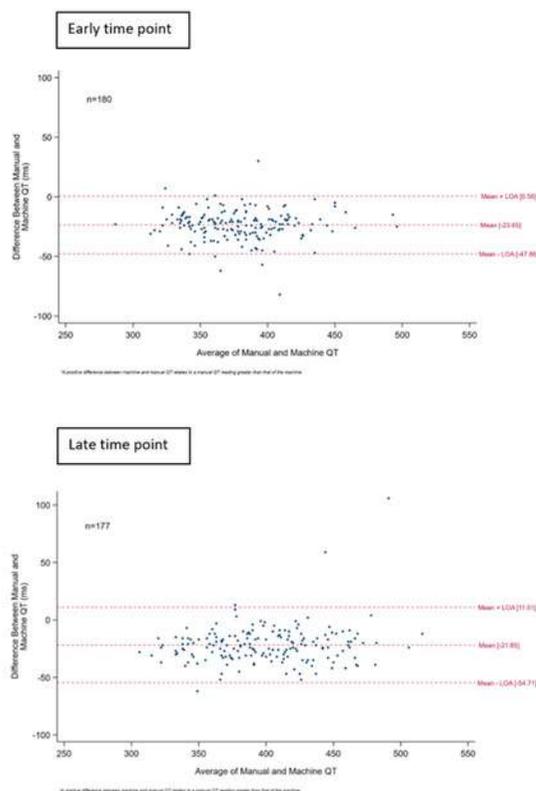


Figure 1. Bland-Altman plots comparing the difference between manual and machine QT interval readings for both regimens at the early and late time point.

Conclusions: Compared with manual readings, machine readings overestimated the QT interval by 22.5ms on average but were otherwise reasonably reliable. Less reliable readings (a large discrepancy outside LOA) occurred infrequently and may be affected by abnormal T wave morphology. These ECGs might benefit from a manual QT measurement and cardiologist input.

OA10-273-08 High rate of adverse drug reactions with a novel triple-dose tuberculosis retreatment regimen: interim findings of TRIDORE

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Background: High-dose rifampicin (R) and isoniazid (H) are known to be safe but were not yet combined in a single regimen. TRIDORE (TRIPle-DOse RE-treatment: Clinicaltrials.Gov.=NCT04260477) is an ongoing pragmatic open-label multi-stage randomized clinical trial in nine Niger National Tuberculosis Program clinics supported by Damien Foundation.

The primary objective of this study is to determine whether a 6-month first-line regimen with triple-dose of both rifampicin (R) and isoniazid (H) is non-inferior (10% margin) in terms of safety compared to a normal-dose regimen in previously treated patients with rifampicin-susceptible recurrent tuberculosis (TB) to overcome resistance. Here we report interim findings.

Design/Methods: Consenting participants were randomly assigned to either the intervention arm (6R³H³ZE; R³ at 30 mg/kg, H³ at 15 mg/kg, and normal-dose pyrazinamide (Z) and ethambutol (E), supplemented with pyridoxin) or the control arm (6RHZE, all drugs throughout).

In addition to routine monitoring, liver function tests (ALT) were performed at fixed intervals. The primary safety endpoint was the occurrence of any TB drug-related grade 3-5 adverse event (AE).

Results: Between March 2021 and February 2022, 127 patients were enrolled, of whom 62 and 65 were treated with 6R³H³ZE and 6RHZE, respectively. Of 127, 111 (87.4%) were male and median age (IQR) was 37 (30-48) years.

Co-infection with HIV, hepatitis B, and/or hepatitis C was present in respectively 3 (2.4), 13 (10.2%), and 3 (2.4%) patients. The median BMI at enrolment was 18.1 (16.3-19.7) kg/m².

Grade 3-5 drug-related AE were significantly more frequent when triple dose was used (5/62 vs 0/65, p=0.03, difference weighted for site 8%; (95% CI:1.0,14.3)).

Table 1 on the following page shows secondary endpoints.

	Intervention (N = 62) n (%; 95% CI)	Control (N = 65) n (%; 95% CI)	p-value ^a	% difference between intervention and control ^b % (95%CI)
Primary endpoint				
Grade 3-5 drug-related AEs ^c	5 (8.1; 3.5,17.5)	0 (0.0; 0.0,5.6)	0.03	8 (1.0,14.3)
Secondary endpoints				
Any adverse event (regardless of grading / relationship with TB drugs)	18 (29.0; 19.2,41.3)	11 (16.9; 9.7,27.8)	0.1	11 (-2.6,25.1)
Grade 3-5 AEs (regardless of relationship with TB drugs)	11 (17.7; 10.2,29.0)	2 (3.1; 0.9,10.5)	0.008	14 (3.7,24.0)
Any serious adverse events	11 (17.7; 10.2,29.0)	2 (3.1; 0.9,10.5)	0.008	14 (3.7,24.0)
Treatment change (any reason)	7 (11.3; 5.6,21.5)	0 (0.0; 0.0,5.6)	0.006	11 (3.1, 18.7)
Death	4 (6.5; 2.5,15.4)	1 (1.5; 0.3,8.2)	0.2	5 (-2.2,11.6)
Hepatotoxicity ^d	4 (6.5; 2.5,15.4)	0 (0.0; 0.0,5.6)	0.05	6 (0.1,12.3)
ALT Grade 1 or 2 without jaundice	7 (11.3; 5.6,21.5)	4 (6.2; 2.4,14.8)	0.4	5 (-4,14.5)

^a Assessed as probably or definitively related & Fisher's exact test

^b Grade 3 or higher increase of ALT, or grade 2 increase with jaundice

^c Weighted for treatment site. To be non-inferior, the upper bound of the CI around the difference should be below the 10% non-inferiority margin, as pre-defined in the study protocol. For endpoints with the upper bound of the CI larger than 10%, non-inferiority was not shown.

AE: adverse event; CI: confidence interval; TB: tuberculosis

Table 1. Interim safety results of a triple-dose versus normal-dose first-line regimen.

Conclusions: Our interim data shows a significant association between the occurrence of grade 3-5 drug-related AEs and the use of triple-dose rifampicin and isoniazid. We plan to adapt the experimental high-dose regimen, informed by both safety and effectiveness analyses.

OA10-274-08 Use of a pediatric formulation of delamanid for the treatment of children with rifampicin-resistant tuberculosis: early outpatient experience from Khayelitsha, South Africa

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Background and challenges to implementation: Children are a vulnerable population when it comes to tuberculosis (TB), including rifampicin-resistant forms of the disease (RR-TB). While children with RR-TB are reported to have excellent treatment outcomes, treatment is characterized by highly centralized care and limited pediatric formulations of second-line drugs.

Intervention or response: We report here a cohort of 8 children who received treatment with the new pediatric formulation of delamanid as part of a community-based program in the peri-urban township of Khayelitsha in Cape Town, South Africa. Children between the ages of three and six years were preferentially treated with delamanid using weight-based dosing. The pediatric formulation of delamanid (a 25 mg, dispersible, mango-flavored tablet) was obtained through a named-patient-basis administered by Otsuka Pharma.

Results/Impact: Between February 1, 2021 and February 28, 2022, eight children aged six years or under in Khayelitsha were deemed eligible for treatment with the pediatric formulation of delamanid.

Four of the eight children have completed treatment and are clinically cured. Three of the children are responding to treatment clinically and are likely to be cured, and one child was only recently initiated on treatment. The pediatric formulation was well-liked by all eight children and their caregivers who felt it was easy to prepare and administer and had a pleasant taste. Two of the eight children (25%) had their delamanid stopped prior to 24 weeks because they developed Grade 3 hallucinations and nightmares, a newly described adverse event associated with delamanid use, although it bears mentioning that nightmares can be common in young children and there were no other behavioral or mood changes reported in these children.

Conclusions: Children with RR-TB need to be able to receive this delamanid formulation under programmatic ambulatory conditions. These formulations are an important part of the decentralized pediatric TB services that have recently been recommended by the World Health Organization.

E-POSTER SESSION (EP)

EP-01 TB and modelling: COVID-19, new vaccine and treatment outcome

EP-01-600 Sub-national impact of COVID-19 on TB notifications and recovery from nine countries

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Background and challenges to implementation: The COVID-19 pandemic led to massive decreases in TB detection globally. Different patterns including recovery have been described from national level data. TB REACH interventions are designed to improve case detection and carefully document sub-national data. We used TB REACH data from projects implemented in 2020 and 2021 to characterize sub-national variations in both the initial reduction and recovery from the COVID-19 pandemic.

Intervention or response: TB REACH partners report quarterly TB notification data for districts in which interventions are implemented and for a control population, including a 3-year baseline. We selected 15 projects from 9 countries with a total of 28 areas (15 intervention and 13 control) based on the following criteria: clear reduction in TB notifications seen as a result of the COVID-19 pandemic in 2020 and availability of at least two quarters for 2021. Using linear trends, three predictions for all forms (AF) notifications were calculated; one based on pre- (Q2-2020) and two on post- COVID19 trends (Q2-2020 and Q2-2021). These predictions were used to calculate the drop in notification in Q2-2020 and the level of recovery in Q2-2021 (Figure). Interrupted time series analysis will still be done.

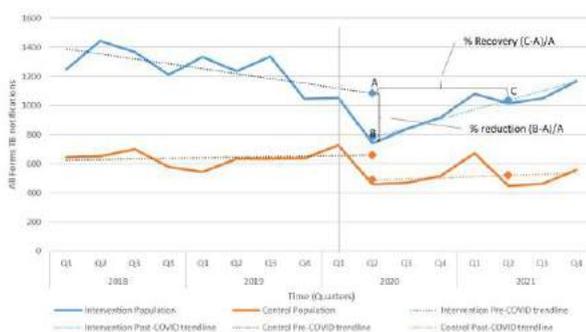


Figure. All forms tuberculosis notification data of 1 project showing the various trend lines and calculations.

Results/Impact: All projects showed a drop in notification in Q2-2020 followed by a diverse set of patterns. The severity of the initial drop varied: results show a median reduction between the two predictions of Q2-2020 notifications of 43% (inter quartile range [IQR] 32%-50%) ranging between 20 to 70%. By Q2-2021 21 of 28 populations had at least a 10% lower notification compared to pre-COVID-19, with a median of -23% (IQR: -9% - -31%).

Conclusions: A year after the first reductions were seen, only a fraction of the populations has reached notifications similar to pre-COVID-19. It is important to understand which factors influence recovery and whether case finding activities can accelerate the process.

EP-01-601 Differences in individual and spatial characteristics of diagnosed drug-resistant TB cases before and after COVID-19 national lockdowns in KwaZulu-Natal, South Africa

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Background: The COVID-19 pandemic has impacted the incidence and detection of TB disease worldwide; however, the effect of COVID-19 is unlikely to have been homogenous across populations. We sought to understand the impact of COVID-19 lockdowns on individual and spatial characteristics of persons diagnosed with drug-resistant TB in KwaZulu-Natal, South Africa between 2018–2021.

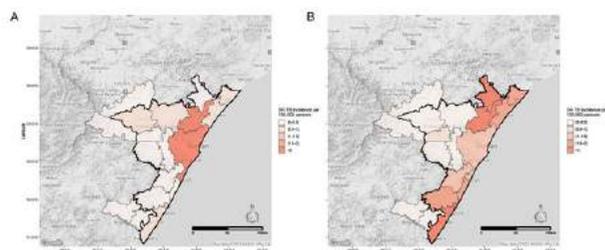
Design/Methods: This was a cross-sectional analysis of temporal changes in drug-resistant TB diagnoses. Information on drug-resistant TB cases was collected from the CONTEXT prospective cohort study and local municipality characteristics were collected from Statistics South Africa. We compared time periods before and after the national lockdown announcement on March 26th, 2020. Individuals were geocoded by diag-

nostic facility to local municipalities and stratified on sample collection date. We used Bayesian conditional autoregressive models and relative-risk surface maps to examine spatial correlates and patterns of drug-resistant TB incidence.

Results: Between October 2018–May 2021, there were 95 and 74 drug-resistant TB cases diagnosed prior to and after the lockdown, respectively. Compared to cases diagnosed before the lockdown, cases diagnosed after were less likely to have a fuel source for heating, piped water, or a flush toilet (p -values ≤ 0.02).

Before the lockdown, TB incidence at the community level was negatively associated with having electrical lighting, and positively associated with owning a stove or internet access.

After the lockdown, incidence at the community level was negatively associated with having a flush toilet and electrical lighting, and positively associated with owning a stove. Predominantly rural northeastern and southwestern municipalities had significantly greater relative-risks for drug-resistant TB diagnosis after the lockdown (Figure).



Conclusions: We observed that TB cases diagnosed after the lockdown had worse living conditions, fewer resources, and more adults in their household. This work provides valuable insight into the regional and local impacts of COVID-19 mitigation strategies on TB control.

EP-01-602 Impact of COVID-19 pandemic on tuberculosis care cascade in KwaZulu-Natal, South Africa: An interrupted time series analysis, 2019-2021

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Background: COVID-19 pandemic related disruptions on routine tuberculosis (TB) services need to be quantified with real-world data. South Africa (SA) introduced a national lockdown in March 2020. We describe the impact of these COVID-19 restrictions on routine head count, systematic TB screening, testing of presumptive cases and treatment initiations in health care facilities of the 11 health districts in KwaZulu-Natal (KZN), South Africa.

Design/Methods: Anonymized quarterly TB programmatic data collected between 1st January 2019 and 31st December 2021 were utilized. In this interrupted time series analysis, we used descriptive statistics and Poisson regression models to estimate the impact of the SA pandemic restrictions on trends.

Results: Following lockdown, the headcount and screening decreased by 1,446,430 and 1,258,693 respectively. In Poisson regression models (Table 1), lockdown was associated with a 22% (Incidence rate ratio [IRR] 0.78, 95%CI: 0.73 to 0.84) and 23% (IRR 0.77, 95%CI: 0.70 to 0.83) decrease in headcount and screening respectively.

	Crude IRR (95% CI)	p-value	Adjusted IRR* (95% CI)	p-value
Head count				
** Lockdown	0.81 (0.78 to 0.84)	<0.001	0.78 (0.73 to 0.84)	<0.001
*** Quarter	0.97 (0.96 to 0.99)	<0.001	1.00 (0.99 to 1.02)	0.255
TB screening				
** Lockdown	0.84 (0.79 to 0.88)	<0.001	0.77 (0.70 to 0.83)	<0.001
*** Quarter	0.98 (0.97 to 0.99)	0.008	1.01 (1.00 to 1.03)	0.020
Presumptive TB testing				
** Lockdown	0.98 (0.80 to 1.20)	0.880	0.61 (0.48 to 0.78)	<0.001
*** Quarter	1.01 (0.99 to 1.04)	0.170	1.08 (1.04 to 1.12)	<0.001
TB Treatment Initiation				
** Lockdown	0.79 (0.69 to 0.89)	<0.001	0.63 (0.51 to 0.77)	<0.001
*** Quarter	0.98 (0.95 to 1.00)	0.109	1.04 (1.01 to 1.07)	0.013

IRR: Incidence rate ratio, listed as result of Poisson regression analysis.

*IRR adjusted for autocorrelation and time (quarter)

**Lockdown was treated as a binary variable (0=pre-lockdown and 1=lockdown)

***Quarter was treated a continuous variable

Table 1. Effects of COVID-19 lockdown on TB-treatment cascade, Kwazulu-Natal, South Africa; 2019-2021.

Furthermore, the number of tests performed and treatment initiations declined by 64,912 and 3,468 respectively following lockdown. There was an associated 39% decrease (IRR 0.61; 95% CI: 0.48 to 0.78) for testing and 37% decrease (IRR 0.63, 95% CI: 0.51 to 0.77) for treatment initiations.

Subsequent to easing of lockdown, trends showed negligible but statistically significant increases in successive quarters of TB screening by 1.5% (IRR 1.015; 95% CI: 1.00 to 1.02), tests performed by 8% (IRR 1.081; 95% CI: 1.05 to 1.12) and treatment initiations by 4% (IRR 1.04; 95% CI: 1.01 to 1.07) respectively.

Conclusions: Lockdown has severely impacted routine TB services with an overall decrease observed across the care cascade. There is a need for monitoring of the National TB Recovery Plan allowing for adjustment strategies to ensure the success of the plan against the backdrop of the COVID-19 pandemic.

EP-01-603 Multi-country calibration of a tuberculosis model for the evaluation of the potential impact of new vaccines in low- and middle- income countries

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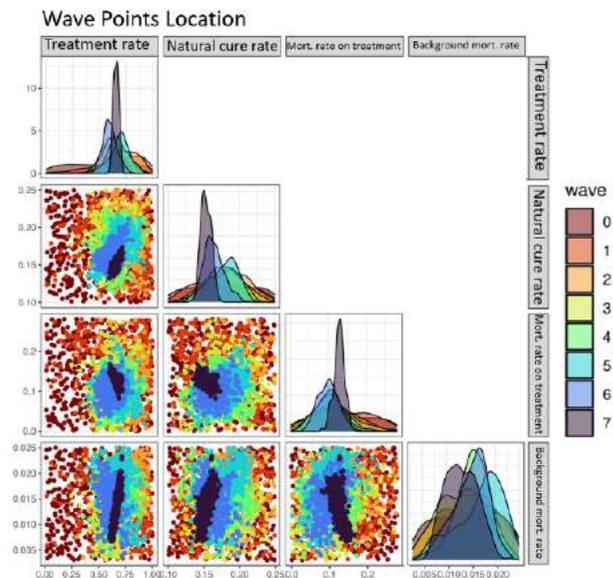
Background: Tuberculosis is one of the leading causes of death from a single infectious agent and new, effective tuberculosis vaccines are critical for meeting the END-TB targets. Modelling allows us to evaluate the potential impact of new vaccines, but the credibility of the obtained results strongly relies on our ability to calibrate the model to empirical data.

To provide robust estimates, we aimed to calibrate a tuberculosis model to 115 low- and middle- income countries, using the new R-package *hmer*.

Design/Methods: A compartmental deterministic dynamic model of *Mycobacterium tuberculosis* transmission and progression was developed. The model was fit to 9–13 target measures, by varying 19–22 input parameters.

Calibration was performed using the package *hmer*, which implements history matching with emulation, a framework that works iteratively, progressively removing parts of the input space that cannot match the data. The attached image shows the distribution of pairs of parameters for points remaining at the end of each iteration (wave).

The process identifies a set of points representing all possible conditions under which the model can match the data.



Results: Of the 115 analysed countries, 105 were successfully calibrated and one had inconsistent data. The *hmer* visualizations and derivative emulation tools provided strong evidence that the remaining 9 uncalibrated models were misspecified and could not be calibrated to the target ranges.

Conclusions: By allowing us to easily and efficiently perform history matching with emulation, *hmer* made it possible to calibrate a multi-input, multi-output tuberculosis model to more than 100 countries, producing a robust evaluation of the potential impact of new tuberculosis vaccines in low- and middle- income countries. This demonstrates that *hmer* can play a key role in addressing the current lack of methodologies to robustly calibrate complex models to empirical data and therefore constitutes a useful addition to the epidemiologist's calibration tool-kit.

EP-01-604 Quantifying the health impact and cost-effectiveness of new tuberculosis vaccines in South Africa

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Background: New tuberculosis (TB) vaccines are urgently needed to meet the End TB goals. However, more research on how these vaccines could be effective in high HIV burden settings is needed. South Africa (SA) has one of the highest TB/HIV rates globally. With promising new TB vaccines in development, we estimated their potential impact and cost effectiveness in SA.

Design/Methods: We developed and calibrated a dynamic age-structured transmission model of TB/HIV coinfection to SA data. TB vaccines were introduced from 2030 to 2050 and assumed to prevent disease with variable duration of protection. Incidence, mortality rate reductions and cases averted were estimated by comparing vaccination to no-vaccination scenarios. In addition to duration of protection, we varied targeted age groups and vaccine efficacy with respect to individuals' HIV and ART status.

A cost model was developed to estimate net cumulative costs. Due to HIV/TB coinfection in South Africa, we estimated additional costs due to HIV treatment as a result of increased life-expectancy due to reduced TB mortality. Costs and disease adjusted life years (DALYs) were discounted by 3% per year and incremental cost-effectiveness ratios (ICER) compared to a willingness to pay threshold of \$2,480/DALY averted.

Results: Increasing vaccine efficacy and longer duration of protection resulted in high reduction in incidence and mortality in 2050. More cases are averted when vaccines are effective in all individuals compared to HIV-negative and HIV-positive on ART individuals only. For all vaccine duration and efficacies, vaccination was cost-effective from a societal perspective.

Conclusions: New TB vaccines could have the most impact in high HIV burden settings, if they are efficacious in all individuals. These findings could be used by vaccine developers, and help inform key decision making for future TB vaccination strategies in SA.

EP-01-605 Getting TB case-finding back on track after the COVID-19 pandemic

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Background and challenges to implementation: The COVID 19 pandemic caused disruptions in the delivery of TB care services that resulted in 17.1% decline in TB case notification for the period April - June 2022 immediately after its outbreak. In order to revamp TB case notification across the country, the Uganda National TB and Leprosy Program (NTLP) designed and implemented a coordinated country-wide community TB screening intervention called the Community Awareness, Testing, Prevention and Treatment to end TB in Uganda – CAST TB campaign. We aimed to document results from this intervention.

Intervention or response: The NTLP mobilized implementing partners across the country to orient community healthcare workers in TB education and screening, provide personal protective equipment and information education and communication materials. Over a period of five days, community healthcare workers from villages across Uganda carried out community TB education, door to door screening using the WHO symptom screen and collection of sputum from persons with presumptive TB. Sputum was carried by hub riders to GeneXpert sites for testing or sputum microscopy. Results were relayed back to community healthcare workers through phone calls. Patients diagnosed with TB were referred to the nearest health facility to be initiated on TB treatment. Data was captured electronically.

Results/Impact: From March 16th to 20th 2022, 25124 villages were reached, 731,408 households visited and 1,376,522 persons screened for TB; of those, 189,042 had presumptive TB and sputum samples were collected from 135,939 presumptive TB patients. At the end of the five days' campaign, 4,149 patients were diagnosed with TB. This has increased the country's case notification by 26% between Jan – March 2022.

Conclusions: A country-wide coordinated community-based campaign led to a large scale increase in TB case notifications over a short period of time. Periodic efforts to increase TB case detection can help countries recover from the COVID 19 pandemic.

EP-01-606 Impact of COVID-19 on treatment outcomes of drug-resistant tuberculosis in Ethiopia

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Background and challenges to implementation: Ethiopia is one of few countries with a treatment success rate of 70%; higher than the global average of 59%. We evaluated the impact of COVID-19 on drug-resistant tuberculosis (DR-TB) treatment outcomes since the first case was reported in Ethiopia in March 2020.

Intervention or response: Using the routine district health information system, all DR-TB patients with documented treatment outcomes since October 2018 were included in the analysis. We compared the treatment outcomes six quarters before (October 2018-March 2020) and six quarters after (April 2020-September 2021) the emergence of COVID-19.

Results/Impact: DR-TB treatment outcomes were available for 95.3% (1,907/2,002) of patients (1,088 before and 819 during COVID-19 emergence). Unfavorable outcomes were reported for 19.1% (208/1,088) before and 19.4% (159/819) after the emergence of the COVID-19 pandemic (OR 1.02; 95% CI [0.81, 1.28]). However, DR-TB related mortality was 4.8 times higher among patients during the COVID-19 the pandemic, 73.6% (117/159) versus 36.5% (76/208) before COVID-19 (OR 4.8; 95% CI [3.08, 7.55]). During the COVID-19 pandemic, DR-TB patients who were on a long treatment regimen had a 1.6 times risk of having unfavorable outcome versus those on a short treatment regimen (24.3% [83/341] versus 16.6% [80/482], OR 1.62; 95% CI [1.14, 2.28]), while no difference was observed before COVID-19 (22.2% [212/957] versus 19.5% [33/169], OR 1.17, 95% CI [0.78, 1.76]). During the pandemic, there was a 2.8 times risk of mortality among DR-TB patients who were treated by a long treatment regimen compared to those treated with a short regimen, (59.0% [49/83] versus 33.8% [27/80], OR 2.83, 95% CI [1.49, 5.34]).

Conclusions: While the overall favorable treatment outcomes were similar before and after the emergence of the COVID-19 pandemic, the five-fold higher increase in mortality during the COVID-19 pandemic, especially among those receiving a long treatment regime, is worrisome and requires further evaluation.

EP-01-607 Ensuring quality healthcare in pandemic

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Background: In the recent times of pandemic it has been very difficult for patients with tuberculosis to visit the healthcare facility for routine follow up. As a result of this the number of lost to follow up patients and those with treatment drop outs had significantly increased. Keeping this in mind we started tele opd for patients on anti tuberculosis treatment.

Aims and objectives:

1. To study the viability of tele opd for tuberculosis patients
 2. To study the overall patients satisfaction with tele opd
- Design/Methods:** Sample size:100 patients on anti tuberculosis treatment

Inclusion criteria:

1. Patients aged 18 years and above
2. Patients on anti tuberculosis treatment for at least 1 month
3. Patients on regular follow ups in our TB opd
4. Patients with basic technical knowledge of using smartphones

Exclusion criteria:

1. Patients unable to consent
2. Patients with comorbidities
3. Patients with drug resistant tuberculosis
4. Patients with no mobile internet facilities

Methodology: We arranged tele consultation with our patients on a regular basis twice a month. Tele consultation consisted of video calls of approximately 15 minutes with pulmonologist. Patients satisfaction was studied with likert scale after each consultation.

Results:

1. Study population was male predominant with 55% males and 45% females
2. Most common age group in our study population was 48+/-8 (p<0.01)
3. 98% of our tele consultation appointments went as per schedule
4. Patients responded well with only 2% patients required hospital visit
5. Drop out rate was 1%
6. Overall satisfaction was 100%
7. 99% patients complete 6 months of anti tuberculosis therapy without any significant adverse event

Conclusions: Tele Pulmonology is a step ahead in future. If implemented systematically would lead to favourable and desire outcomes. It would also reduce significantly the overall cost of treatment and provide great comfort to end users.

EP-01-608 Contribution of community DOT: evaluation of follow-up results at 2 months of treatment

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Background and challenges to implementation: In the context of the COVID 19 pandemic, the National Tuberculosis Program in Togo has implemented community DOT in order to ensure proper monitoring of the treatment of tuberculosis patients. The objective of this study is to determine the contribution of community DOT in the management of TB patients by evaluating the conversion rate at two months of treatment.

Intervention or response: Prospective here-elsewhere type study whose data was collected from April to July 2021 on 8 sites (4 intervention sites and 4 control sites). A reasoned choice made it possible to select the study sites. A chi-square test of homogeneity made it possible to make a comparative analysis of the bacilloscopy conversion rate at two months of treatment in the two groups.

Results/Impact: A total of 182 patients were included (91 for each group: intervention and control). The analysis of the results shows a male predominance of patients both in the intervention group and in the control group with a respective proportion of (57.14%) and (71.43%) with the age group of 25. at 34 the most represented in the 2 groups. Of all the patients, about 15.38% were HIV positive. This proportion is 18.68% in the intervention group against 12.09% in the control group. Overall we note that 92.05% of patients in the intervention group had a negative bacilloscopy at M2 against 67.90% in the control group. The chi-square test for homogeneity at the 5% threshold shows that the difference is significant with a p-value equal to 0.00.

Conclusions: This analysis shows that community DOT has a positive impact on the conversion of patients' bacilloscopy results after 2 months of treatment.

EP-01-609 Using the continuous quality improvement collaborative approach to address the low tuberculosis treatment success rate: lessons from Uganda

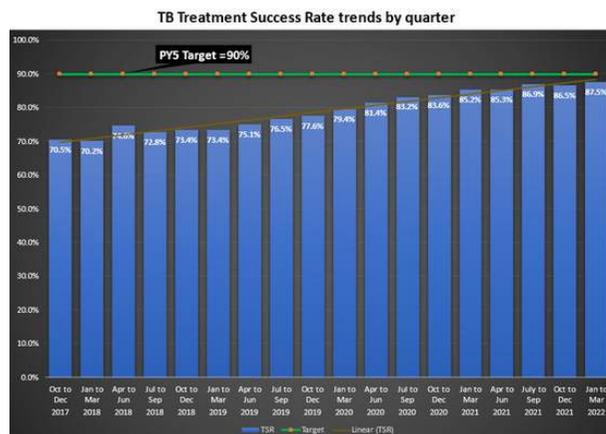
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Background and challenges to implementation: WHO's End Tuberculosis Strategy aims to achieve 90% Treatment success rate (TSR) for all notified patients. The global TSR for drug susceptible TB remains below tar-

get at 85%. In Uganda, the national TB treatment success rate (TSR) remained suboptimal at 72% with high patient loss to follow up (13%), Deaths (8%), not evaluated (6%) and failed treatment (1%). The MOH NTLP with support from the USAID Defeat TB project, set up a national level TSR improvement initiative to address the performance gap. We describe the successful application of continuous quality improvement approach to improve TSR.

Intervention or response: A multi-disciplinary TSR Improvement Technical Working Team was established to review the performance data, conduct a root cause analysis, and synthesize a package for improving TSR. A demonstration national TSR improvement collaborative was established. Site QI teams were coached to apply the model for improvement and the package through plan-do- study- act cycles of learning while using data to monitor progress. Process indicators were used to monitor progress and the MOH reporting system was used to track the impact of the initiative on the TSR.

Results/Impact: TSR improved from 73.8% to 87.5% for the Apr- Jun 2018 and the Jan- Mar 2021 cohorts respectively (Figure 1). Similarly, the cure rates improved from 58.7% to 72.7% for the respective cohorts (Figure 1). LTFU reduced from 13% to 5%, Deaths from 8% to 6.3%, Not evaluated from 6% to 0.62 % and treatment failed from 1% to 0.58%.



Conclusions: The QI collaborative approach and focus on systems for retention of TB patients in care achieved rapid and sustained TSR improvement despite the disruptive effects of the COVID-19 pandemic. We recommend the replication of the approach in similar settings to achieve and sustain the global target for TB TSR.

EP-02 TB and infection control

EP-02-610 Implementation of TB infection control (TBIC) in MDR-TB treatment initiating centers (TIC) in Amhara and Oromia regions, Ethiopia

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Background and challenges to implementation: Tuberculosis infection control is a combination of measures aimed at minimising the risk of tuberculosis transmission among populations. The effectiveness of Tuberculosis transmission control at health care facilities may depend on the proper and full package implementation of control measures.

Intervention or response: A cross-sectional descriptive study was conducted in selected fifteen hospitals in Amhara and Oromia regions from January-July 2019. The assessment was conducted by direct observation, documents review and interviews with the facility heads.

Results/Impact: In Amhara and Oromia TICs were evaluated for the implementation of TBIC. WHO adapted TBICs guidelines was available in 8/15 (53%) of the hospitals and 7/15 (47%) hospitals had a written TBIC policy. 2/15 (13%) hospitals have full-time focal person, and 3/15 (20%) periodically evaluated the practice. Regular TBIC risk assessments were conducted in 6/15 (40%) hospitals, and only 4/15 (27%) of them screened HCWS for LTBI. Standard operating procedure for infrastructure renovation and maintenance available only in 1/15 (7%) of the hospitals. The facility design, patient flow and triage system comply with national TBIC policy in 3/15 (20%) hospitals.

Among 157 high risk workplaces, 132 (84%) had natural mode of ventilation and 24 (15%) had mixed mode of ventilation. 94/157 (60%) of the workplaces were cross ventilated. 31% workplaces had ACH measure of <12, whilst 47 (30%) and 61 (39%) workplaces had 12-20 and >20 respectively. Fit test apparatus was available in 10/15 (67%) of the hospitals and only 6/15 (40%) of them have at least one staff trained to perform Fit testing for users of particulate respirators.

Conclusions: The study showed that TBIC implementation was low in the selected TICs. Consequently, the HCWs were not getting appropriate care. Therefore, more attention has to be given for proper implementation to minimize risk of acquiring Tuberculosis

EP-02-611 Integrated COVID-19 and TB services to help recover TB care and prevention services in the COVID-19 pandemic: results from a multi-country survey

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Background: In many countries, tuberculosis (TB) services have been disrupted by the measures undertaken to control COVID-19, which resulted in declines in TB notifications. Approaches that integrate both TB and COVID-19 services have potential to recover disrupted services. Therefore, we assessed trends in COVID-19 and TB notifications and interventions and activities taken to retain TB care and prevention services in Kyrgyzstan, Nigeria, Tanzania, and Viet Nam.

Design/Methods: We designed a data entry tool in Excel to collect quarterly surveillance country-data (Quarter (Q) 1 2018- Q1 2021) on TB notifications from National Tuberculosis Programs or Global Tuberculosis Program TB on COVID-19 notifications from the online database "Our World in Data" on the "Coronavirus Pandemic (COVID-19)".

Additionally, we designed a survey tool in MS Forms to collect country-specific survey data on COVID-19 measures, such as lockdowns, reported affected TB care and prevention services, and reported employed strategies to recover and retain those services from country-representatives. We used Excel to visualize trends in TB and COVID notification data, and used SPSS to perform descriptive statistics.

Results: We observed declining TB notification trends for Kyrgyzstan and Viet Nam, whereas the trend was fluctuating for Tanzania and increasing for Nigeria. All countries reported reduced TB screening and testing activities and employed the following strategies to recover and retain their services: digital solutions for adherence support, capacity building, and M&E; adjustment in medication supply/delivery & quantity, including home delivery, pick up points, and month supply; integrated TB/COVID-19 screening & diagnostic platform; and the use of community health care workers.

Conclusions: Integrated service delivery approaches that employed digital health solutions contributed to maintaining TB services during COVID-19 pandemic.

EP-02-612 Improving tuberculosis infection prevention and control practices in healthcare facilities, China, 2017-2019

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Background: China's tuberculosis (TB) burden is second highest in the world. TB Building and Strengthening Infection Control Strategies (TB BASICS), an intervention combining training, mentorship, and routine evaluations, was implemented in nine healthcare facilities in China during 2017–2019. The TB BASICS framework capacitates facility-level infection prevention and control (IPC) teams to analyze and address TB transmission risks and promote effective risk management through a continuous quality improvement approach.

Design/Methods: TB BASICS risk assessments were conducted in 57 inpatient, outpatient, and laboratory departments in nine healthcare facilities across six provinces. We focus on 15 outpatient departments across the nine facilities that completed baseline assessments. Assessments included 18 administrative, 10 environmental, and six personal protective equipment (PPE) indicators and were conducted quarterly for 18 months. For facilities with multiple outpatient departments, facility-wide averages were calculated and used in analyses.

Results: At baseline, one facility scored $\geq 70\%$, but 8/9 (89%) reached this target by 15 months. While overall scores increased continuously from a baseline average of 49% to 81% at final evaluation (Figure), facility-level scores fluctuated during follow-up. Initial score improvements were generally greater, with an average overall percent change of 46% during the initial nine months, compared to 13% during the final nine months.

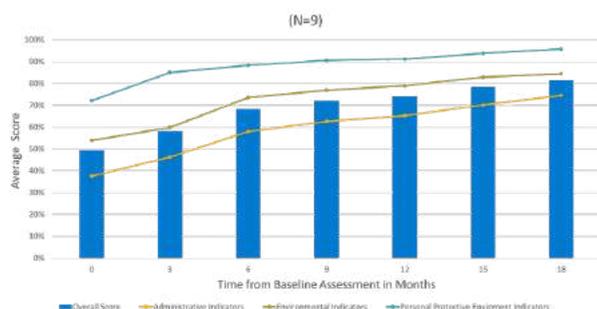


Figure. Average IPC scores overall and by indicator type.

Greatest changes were seen in the first six months. Throughout follow-up, average administrative scores were lowest, while PPE scores were highest. The five

lowest-scoring administrative indicators related to separating presumptive or confirmed TB patients; low scores were often attributed to space constraints.

Conclusions: IPC scores among outpatient departments increased following TB BASICS implementation. Improvement slowed after six months, which may suggest additional support or infrastructure adjustments are needed for more challenging indicators, particularly separating TB patients. The TB BASICS model has potential for application to broader IPC efforts to reduce transmission of respiratory infections in healthcare facilities.

EP-02-613 Implementation of a novel tool to assess healthcare worker TB screening and management practices in Nigeria

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Background and challenges to implementation: Healthcare workers (HCWs) are at increased risk for tuberculosis (TB) due to routine workplace exposure, particularly in resource-limited settings with high TB burden. Infection prevention and control (IPC) measures, including routine HCW screening practices and policies to manage TB cases among HCWs, are essential to prevent nosocomial transmission. We developed and implemented a novel tool to assess current health facility policies to screen and manage TB among HCWs.

Intervention or response: Following a review of Nigerian and global guidelines, key domains for establishing TB occupational health programs were identified, including screening practices, managing suspected cases of HCW TB and latent TB, and return-to-work policies. A novel HCW TB screening and management tool was developed to assess facility-level implementation of these key domains. Following validation, trained IPC staff administered the tool to TB officers in 29 PEPFAR-supported health facilities in northern Nigeria between July and November 2021.

Results/Impact: Of the 29 facilities surveyed, only seven (24%) conducted TB symptom screening for HCWs as a routine practice. Eighteen facilities (62%) had no

mechanism to monitor exposed HCWs under quarantine, and 55% reported having no registry for HCWs presumed to have TB. Nonetheless, 69% of facilities reported good practice of TB testing, treatment, and work restriction for HCWs with presumptive TB.

Most facilities reported having a return-to-work policy for HCWs with confirmed TB (90%) with some variation: resuming after sputum-smear conversion at 2–3 months (38%), after treatment (24%), or once cured (28%).

Conclusions: We found limited implementation of IPC policies and practices to identify and manage HCWs exposed to TB in Nigeria. Gaps identified must be addressed to mitigate occupational TB infection risks in health facilities. Results from facility assessments using our tool will inform the development and strengthening of TB occupational health policies and programs throughout Nigeria.

EP-02-614 Treatment efficacy of a novel short-course regimen with isoniazid plus rifapentine for latent tuberculosis infection: preliminary results from a murine model

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Background: Tuberculosis preventive treatment (TPT) for high-risk individuals is a crucial component of End TB Strategy. Despite many existing TPT regimens, people are still searching for a shorter regimen with higher efficacy and better tolerance. We assessed the efficacy of a novel one-month thrice-weekly isoniazid plus rifapentine (1H₃P₃) regimen in a murine model of latent tuberculosis infection (LTBI).

Design/Methods: BALB/c mice were immunized with a recombinant strain of bacillus Calmette-Guérin (rBCG30) following challenge with a low-dose of *Mycobacterium tuberculosis* (*M. tuberculosis*) H37Rv. Isoniazid (66.7 mg/kg) and rifapentine (7.5 mg/kg) were administered thrice-weekly by gavage for 4 weeks. Treatment efficacy was assessed based on the colony forming unit (CFU) counts of *M. tuberculosis* in the lungs and spleens, and compared between groups at different time points.

Results: At the initiation of treatment, the bacterial burden in the lungs and spleens of LTBI mice was 4.07 ± 0.10 and 3.18 ± 0.53 log₁₀ CFU/g, respectively. It decreased rapidly to 0.62 ± 1.40 log₁₀ CFU/g and 0.32 ± 0.71 log₁₀ CFU/g after 2 weeks of treatment. At the end of treatment, all the 1H₃P₃-treated LTBI mice turned culture-negative, except for one mouse with 1.59 log₁₀ CFU/g in the lungs. Meanwhile, the untreated LTBI mice all remained culture-positive. The lung and spleen CFU counts were listed in Table 1.

Regimen	Mean lung CFU (log ₁₀ /g) ± SD (no. of mice)			Mean spleen CFU (log ₁₀ /g) ± SD (no. of mice)		
	Day 0	Week 2	Week 4	Day 0	Week 2	Week 4
Untreated	4.07 ± 0.10 (3)	3.27 ± 0.46 (4)	1.38 ± 1.89 (5)	3.18 ± 0.53 (3)	2.25 ± 1.53 (4)	3.02 ± 0.72 (5)
1H ₃ P ₃		0.62 ± 1.40 (5)	0.32 ± 0.71 (5)		0.70 ± 0.96 (5)	0 (5)

Table 1. *M. tuberculosis* CFU counts of LTBI mice during treatment.

Day 0 corresponds to the initiation of treatment; no. of mice indicates the number of LTBI mice allocated to each treatment arm; 1H₃P₃ indicates the 4-week thrice-weekly isoniazid (66.7 mg/kg) plus rifapentine (7.5 mg/kg) treatment regimen.

Conclusions: This novel 1H₃P₃ regimen exhibited potent bactericidal activity in the experimental paucibacillary LTBI murine model. Our data provide preclinical evidence supporting further evaluation of this short-course regimen in clinical trials.

EP-02-615 Addressing TB and diabetes co-infection in Bangladesh by utilizing diabetic network

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Background and challenges to implementation: Globally, 10–15% of persons with all forms of tuberculosis (TB) are associated with Diabetes Mellitus (DM). Research has established that DM is associated with up to 3–4-fold increased risk of TB. The association between DM and TB is strong and negatively influence each other in terms of morbidity and mortality if not managed properly. To address the issue, USAID's Alliance for Combating TB in Bangladesh (ACTB) partnered with the Diabetic Association of Bangladesh (BADAS) to utilize its multi-component approach to increase access to TB services for diabetics by improving prevention, early diagnosis and quality of care for persons with diabetes and TB.

Intervention or response: The diabetic network includes 108 centers in Bangladesh engaged in providing overall healthcare services including rehabilitation for diabetics. The key approach for this TB-DM initiative included active screening of persons with TB by dedicated staff, counselling and orientation of facility providers and persons with TB, and strong networking with TB diagnostic and DOTS centers.

Results/Impact: From October 2020 to March 2022, a total of 4,552 persons with TB were diagnosed (72% male and 38% female) from 46,749 presumptives by screening 939,120 diabetics visiting 108 diabetic centers

nationwide. Among those diagnosed, 3,183 were bacteriologically confirmed, 524 were clinically diagnosed and 845 had Extra Pulmonary TB cases, and 15 had Drug-Resistant TB. Interestingly, among all the persons diagnosed, 73% were diabetics, and rest were pre-diabetics.

However, while comparing with no intervention, only 195 persons with TB were diagnosed in a year through this network; whereas, within the first year of intervention (October 2020 to September 2021), this annual number increased to 2,128 persons with TB which is almost 11 times higher.

Conclusions: With the success of this TB-DM integrated screening and follow-up model, similar scale-ups are recommended in other government and private facilities in Bangladesh where diabetics are served.

EP-02-616 Feasibility of linking clients presenting with TB symptoms in South Africa's private sector to timely testing and treatment in public sector: Connect TB Study

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Background and challenges to implementation: South Africa's private sector receives up to 38% of primary care visits. Previous research among private General Practitioners (GPs) in eThekweni, a district with high TB and TB-HIV rates, showed less than optimal TB testing referral and HIV enquiry. We implemented a pilot study to link symptomatic clients of GPs to public sector TB testing and treatment. Challenges included GP participation, assessing HIV status, reducing client visits, and case notification.

Intervention or response: The KwaZulu-Natal Department of Health and National Health Laboratory Service provided GPs with specimen jars for spot sputum collection and TB testing by GeneXpert MTB/RIF Ultra. We developed an e-form on an established medical referral app (Vula) to organise specimen transportation to public laboratory, secure real-time communication of

test results, and provide nationally recommended management guidance to GPs. Client details recorded by GP included phone numbers to enable adherence support, preferred treatment location, and HIV status or test result. Clients were sent text messages for treatment referral or symptom follow-up. People with TB were phoned monthly by adherence facilitators to troubleshoot barriers and document treatment milestones for provider feedback and verification against District notification data.

Results/Impact: In total, 158 (50.5%) private GPs consented to participate, with 128 (81.0%) completing Vula training. Sixty-one GPs submitted ≥ 1 specimen over 11 months ($n=571$). HIV status was recorded for 89% of clients. Of 107 clients diagnosed with TB, 102 initiated TB treatment (99 publicly, 3 privately), two died before culture diagnosis, and three were lost to follow-up. Documentation from adherence support calls facilitated progress and outcome data reporting to GPs and Department of Health.

Conclusions: Connecting people with TB between private and public sectors was feasible through Vula and public sector collaboration, although GP uptake was limited. Future scale-up could include incorporation into forthcoming national health insurance system and/or modest provider incentives for testing and referral.

EP-02-617 Facility-based active case finding for early detection and treatment of TB in Bangladesh

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Background and challenges to implementation: Early diagnosis and treatment of TB prevents new TB infections and deaths. Active Case Finding (ACF) for TB is a WHO-recommended intervention for TB detection at early stage. USAID's Alliance for Combating TB in Bangladesh (ACTB) activity under the National Tuberculosis Control Programme (NTP) initiated facility-based ACF to increase TB diagnosis and reduce transmission.

Intervention or response: USAID's ACTB has been conducting ACF activities at 40 health facilities in 22 districts of Bangladesh since August 2021, under the guidance of NTP. Using NTP-endorsed TB screening tools, trained screeners conducted symptom-based screening for TB presumptives among the individuals visiting the outpatient departments and inpatient wards of the facilities. In coordination with the respective facilities and DOT centers, the screeners facilitated evaluation of the TB presumptives by the physicians; assisted TB presumptives in the diagnostic channels for chest X-ray, GeneXpert®, microscopy, and other investigations; and ensured TB treatment enrolment and follow-ups.

Results/Impact: During August'21-March'22, from 40 health facilities, the ACF activity diagnosed 6,757 persons with TB by screening 2,125,154 individuals. Persons with Extrapulmonary TB (predominance of gland TB) were 35%. Table-1 shows the breakdowns, including adult and child ACF data.

Indicators	Adult	Child	Total Numbers
Patients screened for TB	1,406,283	718,871	2,125,154
TB presumptive identified	42,467(3%)	18,128(3%)	60,595(3%)
TB presumptive tested	37,638(89%)	15,812(87%)	53,450(88%)
Persons with all forms of TB diagnosed	5,530(15%)	1,227(8%)	6,757(13%)
Pulmonary-Bacteriologically confirmed	2,889(52%)	299(24%)	3,188(47%)
Pulmonary-Clinically diagnosed	766(14%)	400(33%)	1,166(17%)
Extrapulmonary	1,865(34%)	528(43%)	2,393(35%)
Persons with TB who started treatment	5,498(99%)	1,157(84%)	6,654(98%)

Table-1: ACF at 40 facilities (Aug-2021 to Mar-2022)

Conclusions: The ACF was implemented to increase TB diagnosis and reduce transmission, allowing early detection and treatment of persons with TB. The Government of Bangladesh and other TB burden countries can replicate this ACF model at all health facilities to increase TB case detection and effective treatment.

EP-02-618 Effect of pharmacogenetics on pharmacokinetics of first line anti tubercular drugs in pediatric tuberculosis

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Background: Despite many effective Anti-TB Drugs (ATDs) and several revisions in the dosing regimens, tuberculosis (TB) remains a disease with high morbidity and mortality. The pharmacokinetics (PK) data in children raises concerns about the suboptimal plasma concentrations attained that lead to treatment failure and emergence of resistance. Gene polymorphism studies indicate that metabolism of first-line ATDs is influenced by genetic variations and plays a major role in drug dosing.

Design/Methods: A literature search was undertaken through PubMed, EMBASE and MEDLINE till 21st April 2022 with the keywords “Anti-tubercular drugs (ATDs)”, “Pharmacokinetics”, “Pharmacogenet-

ics”, “Tuberculosis”, “polymorphism” with the limitation to “title”. The relevant review articles, randomized controlled trials, and other types of clinical research articles related to PK and Pharmacogenetics (PG) in pediatric population were included for the review.

Results: This review discusses the available PK and PG data of first line ATDs in children in relation to efficacy and treatment failures. Various studies propose that with the current dosing regimens, the concentration of all first-line ATDs are lower than the target therapeutic concentrations desired.

While response to treatment depends on multiple factors, sub-therapeutic serum concentrations of drugs could potentially lead to unsatisfactory treatment outcomes. N-acetyl transferase2 (NAT2) slow acetylator status, Cytochrome P450 2E1 (CYP2E1) single nucleotide polymorphisms and Glutathione S-Transferase M1 and T1 (GSTM1 and GSTT1) null genotype have a moderate effect on genetic susceptibility to liver injury. These polymorphisms affect the treatment of TB in children and are key regulators of hepatotoxicity in children.

Conclusions: Plasma drug concentrations achieved in the serum are amongst the most important determinants of clinical response to a drug accounting for both toxicity and efficacy. With the failure to ensure adequate control of the childhood TB burden, studies on drug concentrations associated with the revised drug dosing and genomics are a need of the hour.

EP-02-619 Anti-tubercular drug-induced liver injury in children: implications and recommendations for management

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Background: In developing nations with high tuberculosis (TB) burden, anti-tubercular therapy (ATT) is the commonest cause of anti-tubercular drug-induced liver injury (ATDILI). The spectrum of ATDILI ranges from asymptomatic transaminases elevation to fulminant hepatic failure. In this review, we assess the factors associated with ATDILI in pediatric TB patients and its impact on the treatment of childhood TB.

Design/Methods: A literature search was undertaken through PubMed, EMBASE and MEDLINE till 21st April 2022 with the keywords “Anti-tubercular drugs (ATDs)”, or “hepatotoxicity”, or “hepatitis in pediatric TB patients”, or “drug-induced hepatitis in children”, or “drug-induced liver injury in children” with limitation to “title”. The relevant review articles, randomised controlled trials, and related clinical research articles were studied for writing this review.

Results: In this review, various risk factors associated with ATDILI in children have been proposed: malnutrition, pre-treatment hypoalbuminemia, co-existence of chronic liver disease (CLD), HIV and hepatitis B or C virus co-infections have been found to be the most important ones.

Extensive disease at onset (like disseminated TB or neuro-tuberculosis), use of pyrazinamide beyond 30mg/kg/day and empirical treatment with ATT have been found to predispose to a complicated course. Various genetic factors, such as Cytochrome P450 2E1 (CYP2E1), N-acetyl transferase2 (NAT2) polymorphism and homozygous null mutation of Glutathione S-Transferase M1 and T1 (GSTM1 and GSTT1) genes have been identified as predisposing factors.

Though various guidelines for adults and children are available for management of this condition, none are evidence-based due to lack of randomised control trials.

Conclusions: ATDILI secondary to ATT has been showing an increasing trend. Prompt clinical recognition and discontinuation of all hepatotoxic drugs is the most essential step. Various risk factors and predictors of severity are proposed in this review. These factors should be taken into consideration as a guide to monitor the patients during treatment.

EP-03 Broader approach for implementation of TB active case finding and preventive strategies

EP-03-620 Paradigm shift in classification of eligible index TB clients for contact investigation: a review of selected tertiary health facilities in Plateau and Nasarawa States Nigeria

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Background and challenges to implementation: In September 2018, the United Nations convened the first-ever High-Level Meeting (UNHLM) to accelerate the global response for ending the TB epidemic by 2035.

To achieve this elimination target, a broader approach towards implementation of TB active case finding and preventive strategies are needed. This includes TB contact investigation and treatment of latent TB infection (LTBI).

Intervention or response: In depth review of contact investigation reports from two tertiary institutions in Nigeria: University of Jos Teaching Hospital, Plateau state and Dalhatu Araf Specialist Hospital Lafia, Nasarawa State was conducted. Looking at all index TB cases that were contact traced and were followed through the TB diagnosis cascade.

This article is to showcase the need to extend contact investigation eligibility beyond bacteriologically diagnosed index TB cases to include individual who were diagnosed of pulmonary TB with chest X-ray. As contacts traced among these group of patients have in turn yielded new bacteriologically confirmed TB cases.

Results/Impact: During the period of review January 2021-February, 2022.

Total of 1783 all form Pulmonary index TB cases (508 (28%) Pulmonary clinical TB cases) were contact traced with total of 3432 contacts identified and screened (902 (26%) contact of pulmonary clinically diagnosed index TB Patients) with 1114 Presumed of having TB (337 (30%) among screened contacts of Pulmonary clinically diagnosed index TB Patients) yielding total of 291 TB cases (93 (32%) TB case detection among pulmonary clinically diagnosed presumed of having TB). 100% (291) diagnosed patients were successfully commenced on treatment.

Indicators	Pulmonary Clinically diagnosed	Pulmonary Bacteriologically diagnosed	Total all forms	Proportion Pulmonary Clinical cases cascade
Index TB Cases	508	1275	1783	28%
Contacts Identified	102	2530	3232	26%
Contacts Screened	102	2530	3232	26%
Presumptive Identified	337	777	1114	30%
Presumptive Evaluated	337	777	1114	30%
Diagnosed TB cases	93	198	291	32%
Commenced on Treatment	93	198	291	32%

Conclusions: Extension of Contact Investigation Index Patient Eligibility to all form of Pulmonary TB patients (bacteriologically and clinically) has contributed to increasing the yield of TB case detection and breaking chain of TB transmission within communities.

EP-03-621 Knowledge, attitude, and practice assessment to engage community pharmacies in tuberculosis patients detection: a multi-centre cross-sectional study in Indonesia

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Background: Suboptimal tuberculosis patient case detection (TBDP) and subsequent delays in treatment are worsened by the COVID-19 pandemic. The community pharmacy is reported as the place for first aid medication among patients with TB. We, therefore, analysed knowledge, attitude, and practice (KAP) on TBDP of community pharmacy personnel, aiming to find innovative strategies to engage community pharmacies in TBDP.

Design/Methods: A multi-centre cross-sectional study was performed in four areas representing Indonesia's eastern, central and western parts. Pharmacists and pharmacy technicians who worked in pharmacies were assessed. Descriptive and multivariable regression analyses were used to define factors associated with the KAP on TBDP.

Results: A total of 1,129 participants from 979 pharmacies, comprising pharmacists (56.6%) and pharmacy technicians (43.4%), were included. Most participants knew about TB.

However, knowledge related to TB symptoms, populations at risk, and medication for TB were still suboptimal. Most participants showed a positive attitude towards TBDP. They believed in their professional role (75.1%), capacity in TB screening (65.4%), and responsibility for TBDP (67.4%).

Nevertheless, a lack of TBDP practice was identified in most participants. Several factors significantly associated with performing the TBDP practice, such as TB training experience ($p < 0.001$), provision of a drug consultation service ($p < 0.001$), male gender ($p < 0.05$), a positive attitude towards TBDP ($p < 0.001$), short working hours ($p < 0.001$), and central city location of the pharmacy ($p < 0.05$).

Conclusions: Most participants showed good knowledge and attitude, which did not translate into actual TBDP practice. We identified that TB educational programs are essential in improving the KAP. A comprehensive local assessment is needed to develop effective strategies and guidance to engage the community pharmacy in TBDP activities.

EP-03-622 Using the door-to-door approach to improve community TB case finding in Kampala, Wakiso and Mukono districts

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Background and challenges to implementation: Globally, Uganda is one of the 30 high burden TB/HIV countries. In 2021, Uganda reported 69,162 new cases representing 84% TB case notification. In order to close this gap, the USAID Local Partner Health Services-TB Activity focused on improving community contribution to TB case notification through strengthening community systems for active TB case finding in the districts of Kampala, Mukono and Wakiso.

Intervention or response: Outreach teams composed of clinicians, laboratory personnel from 25 TB diagnostic and treatment units and community health workers were constituted. In consultation with local leadership, data-driven targeted integrated TB outreach activities were scheduled.

During the outreaches, teams moved from home to home providing TB messages, screening for TB symptoms, collecting sputum samples for GeneXpert testing. Test results were returned to patients by the community

health workers who supported linkage of diagnosed TB patients to treatment. Contact tracing was also conducted to identify additional TB cases.

Results/Impact: Between January to March 2022, 6,498 individuals were screened for TB, 1551 presumptive TB cases were identified and linked to diagnostic services, and 401 TB cases identified from the door-door TB screening initiative. This was an increase from 178 cases reported in July-September 2021 and 169 cases reported in October-December 2021. The community contribution to TB case notification also increased from 13% (July-September 2021) to 22.7% (January-March 2022).

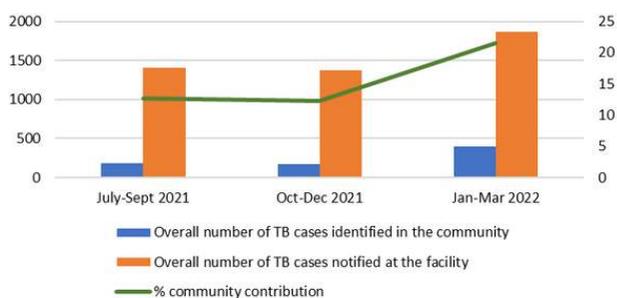


Figure. Quarterly progress on community case identification using a door-to-door approach.

Conclusions: Door-to-door approach is an effective way to increase TB case notification and should be scaled up for greater impact.

EP-03-623 Integration of HIV testing in a community intervention for tuberculosis screening among 5-14-year-old household contacts of tuberculosis patients in Cameroon and Uganda

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Background: Child contacts <5 years and people living with HIV are at a higher risk of developing severe forms of active TB disease once infected. Access to TB preventive treatment (TPT) is therefore critical. The multicenter, cluster-randomized trial (CONTACT) evaluated the impact of a community intervention for contact investigation and TPT management in Cameroon and

Uganda, targeting child contacts <5 years and contacts 5-14 years living with HIV. We present the results of integrating HIV testing in the household to identify contacts 5-14 years potentially eligible for TPT.

Design/Methods: Trained community health workers (CHWs) visited the households of TB index patients identified in seven urban/semi-urban and six rural districts or sub-districts and provided TB screening to child contacts. HIV voluntary counseling and testing were offered to all contacts (5-14 years old) whose HIV status was unknown by a CHW in Uganda and a community nurse in Cameroon after obtaining parental consent and the child's assent. We describe the cascade of care for HIV testing and the factors associated with the acceptance of HIV testing using a generalized linear mixed model.

Results: Overall, 850 contacts (5-14 years old) declared by 372 index cases were screened for TB in both countries. Of them, 681 (80.1%) did not know their HIV status, 624 (91.6%) accepted testing, and 614 (90.2%) were tested. Of those tested, three (0.5%) tested positive. They were all linked to HIV care and initiated TPT. Data per country are presented in the table. None of the index cases (HIV status) and contact (gender, age, TB screening result, relation with the index case, district location) factors were independently associated with HIV testing acceptance.

	Global, n (%)	Cameroon, n (%)	Uganda, n (%)
Index cases	372	237	135
HIV-positive	81 (21.8)	48 (20.3)	33 (24.4)
Contacts 5-14 years	850	589	261
Contacts knowing their HIV status	169 (19.9)	82 (13.9)	87 (33.3)
Known HIV-positive	2 (1.2)	1 (1.2)	1 (1.1)
Contacts not knowing their HIV status	681 (80.1)	507 (86.1)	174 (66.7)
Accept test	624 (91.6)	455 (89.7)	169 (97.1)
Tested	614 (90.2)	449 (88.6)	165 (94.8)
Positives	3 (0.5)	2 (0.5)	1 (0.6)

Table 1. Cascade of care for HIV testing.

Conclusions: The high acceptance of HIV testing at the household level in both countries supports its integration in community-based TB contact investigation activities.

EP-03-624 Best practices of actively finding childhood TB cases in sub-national public tertiary facility: program experience in Oyo State, Nigeria

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Background and challenges to implementation: Nigeria accounts for 4.6% of the Global TB burden. The National Tuberculosis Program, over the years prioritized strategies to actively increase TB case-finding. This led to an increase in the treatment coverage from 27% in 2019 to 30% in 2020. Despite the gains recorded in case notification, childhood TB case finding is still poor.

In 2020, there was a drop in the proportion of childhood TB cases notified from 8% in the previous year to 6%. The childhood TB proportion in Oyo State was 5% lower than the national achievement in 2020.

Intervention or response: To increase childhood TB cases, we constituted a Pediatric TB Cascade management team (pCMT) to oversee case finding at various service delivery points (SDPs) where children congregate to access health services at a sub-national tertiary facility in Oyo state. The pCMT is made up of clinicians, nurses, medical records, and DOT officers in the facility. Health care workers from the SDPs were trained on childhood TB with attention on TB screening and referral of presumptive TB.

Results/Impact: The number of children screened for TB increased from 643 in quarter 4, 2021 to 1461 in Q1 2022 which represents a 227% increase. Ages 0 to 4 years accounted for 65% of those screened. The presumptive TB identified increased from 42 in the previous quarter to 97 in quarter 1 2022, with a 6.6% presumptive TB yield. All presumptive TB were evaluated using GeneXpert, with stool sample testing accounting for about 70%. The childhood TB proportion from the facility increased from 4% in the previous quarter to 14%. The age group 0 - 4 years accounted for 55% of the TB cases.

Conclusions: Involvement of facility stakeholders to oversee facility TB report from various pediatrics' service delivery points will increase access to TB services and help identify more childhood TB cases.

EP-03-625 Community active case finding: a mop up strategy for missing TB cases from the health system. A case study of Cross River State TB program

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Background and challenges to implementation: Nigeria still ranks high in the global TB index cases and has over 300,000 missing TB cases annually. The situation becomes more worrisome in view of the paucity of funds due to increasing demands from natural disasters, complex emergencies, emerging and re-emerging infections that limit social connectedness and further isolate the health system.

Intervention or response: Community tuberculosis active case finding (cTB ACF) by KNCV in 10 of the 18 local government areas (LGAs) of Cross River state started with the formation of the Local Government Community Screening Committee (LGCSC) comprising the Local government primary healthcare director, social mobilization officer, TBLS and ward focal persons. The LGCSC recruited all the community volunteers (CVs) from each ward in the LGAs. Each CV is supervised by a DOT officer closer to the ward while the DOT officer reports to the LGTBLS. The basic qualifications for CV were senior secondary certificate, basic health knowledge and must have lived in the ward for 10 years. The CVs were given mentorship and training on the overview of TB, infection control, TB screening and referral before their deployment to their wards for cTB ACF.

Results/Impact: TB cases diagnosed in cTB ACF maintained a steep trajectory with 2.1% (38) case contribution in quarter 1, 4.4% (71) in quarter 2, 10.5% (169) in quarter 3 and 10.7% (139) case contribution in quarter 4 with a total of 417 TB cases averaging 6.5% of the total TB cases diagnosed in the state in 2021.

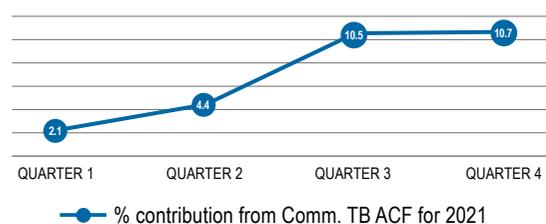


Figure. % contribution from Comm. TB ACF for 2021.

Conclusions: The steep trajectory displayed in TB case contribution from cTB ACF is a clear indication of the potentials inherent in cTB ACF to turn around the miss-

ing TB cases in Nigeria if it is deployed at the national level by all the stakeholders as a proven intervention to finding the missing TB cases from the health system.

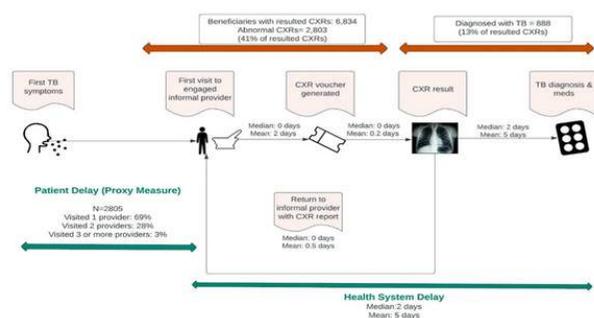
EP-03-626 Optimal strategies for reduction in TB diagnostic delay: model for engagement of less-than-fully-qualified providers (LTFQs)

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Background and challenges to implementation: First consultation with informal, Less-than-fully-qualified providers (LTFQs) is one of strongest risk factors for delayed TB diagnosis. Simulation models have estimated that moving test ordering earlier in the diagnostic pathway has a greater impact on diagnostic delay than improving diagnostic accuracy of the treating provider.

Intervention or response: The intervention engaged a network of LTFQs (AYUSH, RMPS, etc) and Chest X-ray (CXR) facilities across four districts of Gujarat and Jharkhand states. LTFQs were able to order free CXRs for symptomatic cases through a mobile platform; receive and interpret CXR results; and refer patients to formal qualified providers (FQs) for further diagnosis. Health system delays were monitored through the platform. Interviews were conducted with a patient sample to assess patient-level delays in initial care-seeking.

Results/Impact: 6,834 symptomatic cases with resulted CXRs were registered by 618 LTFQs from June 2021 to March 2022. 41% of resulted CXRs were abnormal; 13% of resulted CXRs were ultimately diagnosed with TB. A comparison group of 3,284 symptomatic cases registered by FQs yielded the same conversion rate of 13%, indicating that LTFQs were highly effective in screening and referring symptomatic cases with clinical acumen.



The median and mean health system diagnostic delay was 2 days and 5 days respectively. “Number of different providers visited” was used as a proxy measure for patient-level diagnostic delay. The engaged LTFQ was the first point-of-care for the majority of beneficiaries

(69%); 28% visited 2 providers; and 3% visited 3 or more providers. Switching from one LTFQ to another was limited with over 95% of cases returning to the same LTFQ with the CXR report, and rapid referrals made from LTFQs to a FQ within a median of 2 days from receiving a CXR result.

Conclusions: Operational models of engaging LTFQs for test-ordering can be optimized to reduce diagnostic delays and disease transmission.

EP-03-627 The role of mass chest radiography screening in TB active case-finding: a re-evaluation of the Kolín study

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Background: The Kolín study evaluated the impact of mass chest-radiography (CXR) screening for pulmonary TB active case-finding between 1960 and 1972 in the district of Kolín, Czechoslovakia. It is often cited as evidence against mass CXR screening, but given technological advances, it is important to re-evaluate the data to determine if the perceived lack of added epidemiological value of mass CXR screening still holds.

Design/Methods: We re-examined the data of the Kolín study to address two questions:

1. Whether TB incidence declined throughout the study period, and;
2. If there was a decline, to what extent this was due to mass CXR screening.

Results: We found that total and new cases declined annually by 13.6% (95% CI:9.4-17.9%) and 10.8% (95% CI:3.9-18.0%), respectively. Of note, TB prevalence increased noticeably in 1961 due to the first mass CXR screening, and subsequent peaks correspond to repeat instances of the mass screening.

Between study periods, there was a steeper decline in prevalence between 1960-1964 (annual decline of 17.2%, 95% CI:9.3-51.3%) compared to 1965-1972 (10.6%, 95% CI:1.1-20.9%); suggesting that the impact was largest in the first years after initiation of mass CXR screening.

Furthermore, mass CXR screening contributed to detecting 61% (148/241) of new TB cases, of which 16% (23/148) were smear-positive between 1960-1964. After this, detection declined to 38% (102/270); however, a larger proportion were smear-positive (29%, 30/102). CXR performance at detecting smear-positive cases was similar to the symptom-based passive case-finding approach.

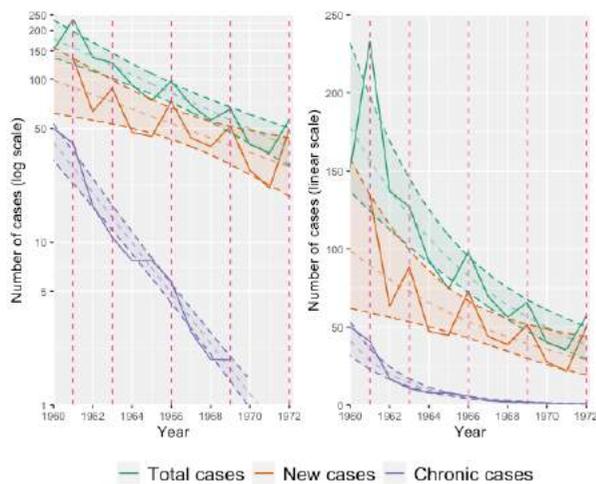


Figure. Number of bacillary pulmonary TB cases detected in Kolín, Czechoslovakia, from 1960 to 1972. Dotted vertical lines indicate when mass CXR screening took place.

Conclusions: The arguments surrounding the “impracticality” of CXR were fixed on its perceived lack of detection of smear-positive cases.

However, mass CXR screening performed very well at primarily identifying early cases (most less infectious) and likely contributed strongly to the decline in TB in Kolín.

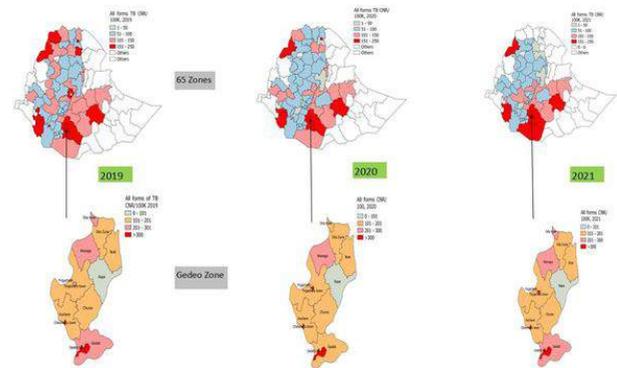
EP-03-628 Mapping the burden of TB in Ethiopia: a practical approach to develop targeted interventions

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Background and challenges to implementation: Ethiopia is one of thirty high-TB burden countries in the world with a TB incidence rate of 132/100,000 population. The distribution of TB is not uniform across the country. Mapping the TB burden setting can assist with tailoring interventions and prioritization of resources.

Intervention or response: The USAID Eliminate TB Project operates in 65 zones of Ethiopia. Data on all forms of TB cases notified in 2021 were extracted from National District Information Health System (DHIS2) for these zones. The TB case notification rate (CNR) per 100,000 population of each zone was calculated. Using the CNR per 100,000 population data, we mapped the USAID Eliminate TB project zones using Quantum GIS software. Among the high-burden zones, Gedeo Zone was mapped by district.

Results/Impact: Out of the 65 zones mapped, 9 (14%) zones had a CNR of 151 or more, while 11 (17%) were above the national TB estimate. The 9 zones contributed 26% of TB cases notified. Out of the 12 districts in Gedeo Zone, 9 (75%) were above the national TB estimate, while 3 (25%) were above a CNR of 300. In general, the concentration of TB cases is high in southern part of the country.



Trend mapping of TB burden for Zones and districts, 2019-2021, Ethiopia

Conclusions: There is variation in the CNRs across the regions and zones of Ethiopia. Mapping helps to display hot spot areas and facilitates the tailoring of interventions to ensure effective and efficient TB programming.

EP-03-629 Gender and tuberculosis in Nigeria: active household contact investigation - a veritable strategy for reaching men

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Background and challenges to implementation: Nigeria has the highest TB burden in Africa. Epidemiological data shows that more males are affected by Tuberculosis than females. Data from facility-based TB interventions report fewer men are screened and identified as presumptive TB however more men are diagnosed with TB.

Strategies for finding the TB cases do not specifically target men. To reach more men, USAID-funded KNCV Nigeria TB LON project modified their approach to household contact investigation (CI).

Intervention or response: In the modified approach, CI across TB LON project was made more flexible and patient-centred. Household CI was planned with the index patient to agree a suitable date and time for visits including evenings and weekends. Contact investigators were identified from the pool of community volunteers, TB

screening and DOTS officers who understood cultural settings. CI was extended to close contacts in neighbouring households. Symptom screening was done, and presumptive contacts evaluated and diagnosed TB cases linked to treatment. Reporting was weekly and quality improvement meetings monthly.

Results/Impact: In the implementation period April to September 2021, a total of 106,892 contacts were screened 53% were males and 47% females, 32,599 presumptive TB were identified 53% Males 47% females, 2101 TB cases were diagnosed 54% males and 46% females, 2053 patients were enrolled on appropriate treatment- Males 54%: females 46%.

Disaggregating data by age and sex, the category 35-44 years had 62% male and 38% female contacts screened, 62% male and 38% female presumptive TB identified, 61% Male and 39% female TB cases diagnosed. For age category 45-54 years, 59% Male and 41% female contacts were screened, 57% male and 43% female presumptive TB were identified, while 56% Male and 44% female TB cases were diagnosed. See Figure 1.

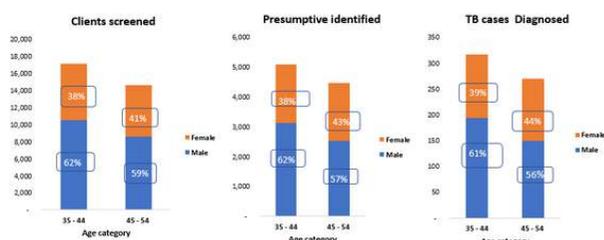


Figure 1. Age and sex disaggregation of clients screened, presumptive and TB cases detected.

Conclusions: Contact investigation when patient centered is a veritable tool for reaching men including those in the productive age group.

EP-03-630 Household tuberculosis contact tracing in Tajikistan: active case finding in a high DR-TB burden setting

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Background: Tajikistan has a high-burden of MDR-TB with an estimated 2400 cases in 2019 (26/100,000 population). With an average household size in Tajikistan of 6, each index case interacts with multiple household members, resulting in additional people infected each year. Contact tracing serves to identify those at highest risk of latent infection and active disease.

Although contact tracing of high-risk groups is widely included in global and national policies, this activity is rarely prioritized outside of low-burden, resource-rich settings.

Design/Methods: We conducted a prospective cohort study using routinely collected programme data from Dushanbe, Tajikistan. Over 36 months of contact follow-up, we collected baseline demographic data, TB symptoms, diagnostic test results, TB-disease related data, and the number with confirmed TB disease.

We calculated person-years of follow-up and the time from first assessment to confirmed TB amongst all contacts, stratified by age.

Results: We notified 6654 household contacts of 830 DR-TB index cases (8.1 contacts/case) from 2018-2021. Of these, 4016 contacts (60.4%) came for an initial evaluation. Over 36 months, we identified 50 new active DR-TB cases from 40 different index cases, over 2908 person years of follow-up.

Forty-nine (49) new cases were identified in the first year of follow-up. The average time from first assessment to disease progression was 71 days. Nine new cases were <5y and 29 were 5-14y.

Forty-nine of fifty (98%) had TB symptoms, 34/42 (82%) had chest X-rays consistent with TB, 10/33 (30%) sputum smears were AFB-positive, 29/30 TSTs (97%) were positive, and there were 30 positive TB cultures (16 MDR and 14 XDR). All were started on treatment. The number needed to screen to identify one confirmed case of DR-TB was 101.

Conclusions: DR-TB household contact tracing was feasible and productive in Tajikistan, a low-income country with an inefficient healthcare delivery system. This model should be replicated in similar settings.

EP-04 TB active case finding: impact, performance and acceptability

EP-04-631 Evaluating the programmatic performance of using chest X-ray for TB screening: the Nigeria experience

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Background and challenges to implementation: Computer-aided detection for TB (CAD) is increasingly being used globally in screening and testing algorithms to increase TB yield. The USAID-funded LON project led by KNCV implemented innovative approaches to the use of CAD in Nigeria. The strategies aimed to increase TB case-finding.

Intervention or response: We deployed three mobile digital Chest X-ray (CXR) units fitted with CAD for community TB case-finding activities. Two different approaches were used for TB screening. In the first algorithm, clients were initially screened using the WHO 4 symptoms and had their CXR done. All clients with a positive CAD score of ≥ 60 or a positive WHO 4 symptom screen had their sputum tested using GeneXpert for diagnostic evaluation. In a further subcategory, clients with a high CAD score of ≥ 80 that tested negative with GeneXpert were further reviewed by a consultant radiologist for clinical diagnosis. Hence all three WHO methods (symptom screen, CXR-CAD and wMRD) were used in this diagnostic algorithm. In the second approach, CXR was used as the initial screening for TB. Clients with CAD score of ≥ 60 had their sputum tested with GeneXpert. We analysed and compared the TB yield.

Results/Impact: From April 2020 to June 2021, 79,688 persons were screened for TB and 7,907 presumptive TB were identified resulting in a screening yield of 10% using both approaches. TB screening yield was 14.3% using CXR screening and 9% using WHO 4 symptom screen. TB diagnostic yield using sequential symptom screen with CXR-CAD followed by GeneXpert was 18.3% compared to 8.6% when using only CXR-CAD followed by GeneXpert.

Conclusions: TB screening using CXR-CAD showed a higher screening yield compared to the WHO 4 symptoms. When CXR-CAD is used in combination with WHO 4 symptom screen and GeneXpert as a single diagnostic algorithm the TB yield was far superior to CXR and GeneXpert alone.

EP-04-632 Performance based financing of community owned resource persons improves community TB case finding in a Nomadic population, a case in Karamoja region, Uganda

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Background: Performance Based Payments (PBP) are financing payments based upon the achievement specific measurable events that are accomplished and valued in advance by parties to the contract. There is evidence from a variety of settings that PBF can improve the performance of healthcare systems. We set out to evaluate the impact of PBF on TB case detection and treatment completion in remote Karamoja sub region, a region with very low TB case detection and treatment completion rates.

Design/Methods: Medici con l'Africa (CUAMM) in partnership with Program for Accelerated Control of TB (PACT) Karamoja, a project funded by the United States Agency for International Development (USAID) engaged Community Owned Resource Persons (CORPs) on a monthly performance-based contract (PBP). CORPs screened persons in the community for TB and referred symptomatic persons to their nearest health facility for further TB evaluation and diagnosis. They also tracked treatment interrupters and reinstated them on TB treatment. A retainer fee (USD 30) was given to each CORPs with additional payment (USD 25) for targets met for referral of patients with presumptive TB, tracking patients diagnosed with TB and linking them to TB treatment and tracking and returning to care of patients who interrupt TB treatment.

Results: From April 2020 to March 2022, CORPs referred 31,683 patients to health facilities (Figure 1).

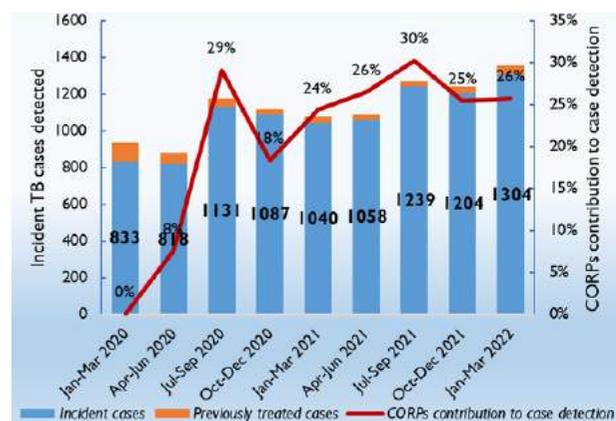


Figure 1: Trend of CORPs contribution to quarterly case detection in Karamoja region, Uganda.

Of these 2,139 were diagnosed with TB (22% of regional case detection). During the same period, loss to follow up reduced from 31% to 7% and treatment completion increased from 53% to 86%.

Conclusions: Performance based Payment of CORPs steadily improved community TB case finding and reduced loss to follow up in Karamoja region. We recommend performance-based payment for community TB control interventions in rural settings like Karamoja region.

EP-04-633 Contact tracing clinically diagnosed TB cases vs contact tracing bacteriologically diagnosed TB cases. An analysis of presumptive and diagnosed TB case yield

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Background and challenges to implementation: Contact Investigation is targeted at bacteriologically diagnosed pulmonary TB cases as they are believed to be infectious, while clinically diagnosed TB cases are not contact traced. With increase in clinically diagnosed cases, there is a need to investigate their contacts as they are a considerable number. KNCV TB Foundation Nigeria in collaboration with Imo State TB Control Program (STBLCP) investigated contacts of clinically diagnosed pulmonary TB cases and compared presumptive yield and TB case yield to ongoing contact investigation for only bacteriologically confirmed index cases in the program. The findings could advise whether the intervention would contribute significantly to TB case finding

Intervention or response: Trained contact tracers working in 14 LGAs in Imo state were instructed to investigate the household contacts of all pulmonary TB cases irrespective of method of diagnosis, while indicating such for the index patient. This was done for 9 months (June 2021 to March 2022).

Data was collected and analyzed to look at presumptive TB yield and confirmed TB case yield for both bacteriologically and clinically diagnosed

Results/Impact: From 122 Clinically diagnosed index patients, 648 contacts were identified and screened, 175 presumptive TB cases were identified and evaluated (presumptive yield of 27%), and 25 TB cases were diagnosed (TB Case yield of 14%). From 237 bacteriologically diagnosed index cases, 1326 contacts were identified and screened, 290 presumptive TB cases were identified and evaluated (presumptive yield of 22%) and 37 TB cases were diagnosed (TB Case yield of 13%).

June 2021 to March 2022						
No of Clinically Diagnosed Index Cases	No of Contacts Identified (Contact to Index Case Ratio)	No of Contacts Screened (Screening Coverage)	No of Presumptive TB Cases (Presumptive Yield)	No of Presumptive TB Cases Evaluated (Evaluation Rate)	No of Positive TB Cases Diagnosed (Case Yield)	Index Case to Diagnosed Case Ratio
122	648 (5)	648 (100%)	175 (27%)	175 (100%)	25 (14%)	5
No of Bacteriologically Diagnosed Index Cases	No of Contacts Identified (Contact to Index Case Ratio)	No of Contacts Screened (Screening Coverage)	No of Presumptive TB Cases (Presumptive Yield)	No of Presumptive TB Cases Evaluated (Evaluation Rate)	No of Positive TB Cases Diagnosed (Case Yield)	Index Case to Diagnosed Case Ratio
237	1326 (5.6)	1326 (100%)	290 (22%)	290 (100%)	37 (13%)	6

Conclusions: Contact tracing clinically diagnosed pulmonary TB cases has a slightly higher presumptive TB and case yield when compared to doing the same for bacteriologically diagnosed pulmonary TB cases. It also has a slightly better index case to diagnosed case ratio. Thus, contact investigation should be targeted at all diagnosed pulmonary TB cases.

EP-04-634 The effect of TB screening on TB treatment outcomes: results from the Zambian HPTN 071 intervention sites

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Background: HPTN 071 was a cluster randomised trial, conducted in 21 Zambian and South African communities. In intervention communities, house-to-house TB symptom screening and HIV testing with linkage-to-care was conducted over three consecutive rounds spanning 2014-2017. We investigated the effect of TB screening on TB treatment outcomes (treatment success and deaths) in the eight Zambian intervention communities. **Design/Methods:** People with TB picked-up through screening between 1/12/2015-31/12/2017 were identified using presumptive TB registers and linked to TB treatment registers (spanning 1/12/2015-31/12/2018) in intervention community clinics using probabilistic matching. The contribution of screening to new adult (≥ 15 years) bacteriologically-confirmed (smear/Xpert positive) notifications between 1/1/2016-31/12/2017 is summarised. Logistic regression (adjusting for age, gender, HIV-status and community) was used to investigate the association between case finding (screen vs passive case finding [PCF]) and treatment outcomes.

Results: Between 1/12/2015-31/12/2017, TB screening identified 422 people with undiagnosed TB, with 75% (316/422) linked to TB treatment registers. Screening contributed 15% (205/1374) of notifications meeting our case definition. Among 1374 starting treatment, median age was 33years (interquartile range 27-40), 69% (949/1374) were male, and 54% (731/1354) were HIV-coinfected. Case finding was not associated with treatment success (83% [171/205] screened vs 82% [962/1169] PCF; adjusted odds ratio [aOR] 1.26 [95% confidence interval {95% CI} 0.83-1.91], $p=0.28$).

The odds of treatment success was lower among people living with HIV (PLHIV) (81% [591/731] PLHIV vs 85% [530/623] HIV-negative; aOR 0.58 [95% CI 0.43-0.80], $p<0.001$). Case finding was not associated with deaths (3% [6/205] screened vs 4% [49/1169] PCF; aOR 0.74 [95% CI 0.31-1.77], $p=0.48$).

The odds of death was higher among PLHIV (6% [42/731] PLHIV vs 2% [12/623] HIV-negative; aOR 3.02 [95% CI 1.56-5.87], $p<0.001$).

Conclusions: In this observational analysis, there was no association between TB screening and TB treatment outcomes. Treatment outcomes were poor among PLHIV, highlighting their continued need for prevention and care interventions.

EP-04-635 Risk factors for treatment delays among TB patients detected through active case finding in Viet Nam

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Background: TB patients detected by active TB case finding (ACF) initiatives should be promptly linked to treatment in order to fully realise the potential transmission reductions from early detection.

Design/Methods: Between June 2020 and March 2022, we conducted 395 days of community-based chest X-ray (CXR) screening across six provinces of Viet Nam, resulting in the detection and treatment of 506 Xpert-positive TB patients. We calculated descriptive statistics for two cohorts of TB patients: those linked to treatment <30 days and ≥30 days after their detection. We then evaluated 12 variables for their association with treatment delays and fitted a multilevel logistic regression model using district and province as the random factors.

Results: 94 (18.6%) TB patients were initiated on treatment ≥30 days after their Xpert test date. In the univariate risk factor analysis, six variables showed significant differences between the patient cohorts: presence of

comorbidity (HIV, immune disease, and/or diabetes), prior history of TB, Trace Call, RIF-resistant or RIF-indeterminate Xpert results, detection after screening at an event >5 kilometres from the nearest District TB Unit, and screening between June 2020 and April 2021 (initial COVID-19 phase).

The multilevel logistic regression showed that having comorbidity (aOR = 2.30 [1.23-4.32]) and Trace Call, RIF-resistant or RIF-indeterminate Xpert results (aOR = 2.21 [1.28-3.82]) were independent factors for TB treatment delays.

	Total	No treatment delay*	Treatment delay*	OR (95% CI)	P-value†	Adjusted OR (95% CI)**	P-value***
All TB patients detected and linked to treatment	506	412 (81.4%)	94 (18.6%)	N/A	N/A	N/A	N/A
Comorbidity (HIV, immune disease, and/or diabetes)	72 (14.2%)	50 (69.4%)	22 (30.6%)	2.21 (1.20-3.99)	0.005	2.30 (1.23-4.32)	0.009
Prior history of TB	129 (25.5%)	96 (74.4%)	33 (25.6%)	1.78 (1.06-2.95)	0.018	1.67 (0.97-2.89)	0.065
Trace Call: RIF-resistant, or RIF indeterminate Xpert results	127 (25.1%)	91 (71.7%)	36 (28.3%)	2.19 (1.33-3.61)	0.001	2.21 (1.28-3.82)	0.005
Distance between screening location and nearest DTU <5 km	162 (32.0%)	123 (76.9%)	39 (24.1%)	1.67 (1.02-2.71)	0.029	1.59 (0.88-2.94)	0.143
Screening between June 2020 and April 2021 (initial COVID-19 phase)	345 (68.2%)	270 (78.3%)	75 (21.7%)	2.08 (1.18-3.78)	0.007	1.80 (0.88-3.68)	0.110

* No treatment delay: linked to treatment <30 days after TB detection

** Treatment delay: linked to treatment ≥30 days after TB detection

*** Multilevel logistic regression model with city/province and district as random factors

Conclusions: Nearly one-fifth of TB treatment after ACF occurred with a ≥30 day delay. National guidelines currently require a second Xpert test for all initial Xpert results which are not RIF-sensitive before patients are eligible for treatment. More rapid testing mechanisms should be developed to reduce these delays caused by confirmatory testing.

EP-04-636 Acceptability and feasibility of household child-contact investigation and preventive therapy management in Cameroon and Uganda: a qualitative assessment

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Background: The CONTACT study (Cameroon, Uganda) is a cluster-randomized trial evaluating a community intervention for TB contact investigation and TB preventive treatment (TPT) management. It includes index case counseling at the facility, community health workers (CHWs) home-based child contact screening and TPT monitoring, as well as referral of suspect or side effects cases.

Design/Methods: This final qualitative assessment focused on the acceptability and feasibility of the intervention. We conducted in-depth interviews with 24 health-

care providers and community leaders and 12 focus group discussions with 79 index cases (separated by gender). Transcripts were analyzed using ATLAS.ti 9.

Results: The TB standard of care limitations included distance, transport costs, and waiting time associated with the workload of limited human resources. Conversely, the community-based intervention was found acceptable and feasible by all participants. Determinants of acceptability included the index case's counseling that establishes a good provider-patient relationship and strengthens patients' self-efficacy and the legitimacy of CHWs.

Despite the anticipated fear of stigma, almost all participants reported family support following disclosure. Beneficiaries cited positive outcomes of the intervention including relief from transport, screening of all family members, and TPT efficacy. Initial counseling towards self-disclosure within or outside the family resulted in more children initiated on TPT, including child contacts of neighbors. Providers witnessed an increased number of child contacts on TPT and highlighted the coherence of the intervention in their context. The main drivers of feasibility were CHWs' financial motivation and training (confidentiality, counseling), household visit planning, and community leaders' support. Sustainability issues revolved around securing CHWs' incentives through advocacy at the district and national levels.

Conclusions: The community-based intervention is acceptable and feasible. The combination of home-based child contact screening and TPT management has the potential of preventing the onset of TB disease in millions of children from high-burden, limited-resource areas.

EP-04-637 Assessment of paediatric clinical records at a drug-resistant tuberculosis hospital in the Eastern Cape

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Background and challenges to implementation: Approximately 9.1% of TB cases reported in South Africa in 2020 were children under the age of 15 years, amounting to approximately 30 000. While active case finding has shown to increase the number of children accessing treatment, the quality of care provided to this vulnerable population is of interest. The program aimed to evaluate the completeness of clinical charts as a proxy for quality of care at a drug-resistant tuberculosis hospital in the Eastern Cape.

Intervention or response: The clinical records of paediatric patients identified through an active case finding intervention and treated at the hospital between January 2020 and December 2021 were assessed for completeness.

Results/Impact: A total of 52 records were assessed. Overall, records achieved a score of 66% for completeness. However, just 46% of patients were initiated on treatment within the recommended five days of diagnosis with some being initiated up to one month later.

Evidence of structured adverse event monitoring was lacking in 25% (n = 13) of charts. Most (96%) children were evaluated by a social worker including a home assessment, but occupational therapy assessments were only performed for 11% of children.

Positively, contact tracing and testing were often completed (72%; n = 39) and recorded. Clinical tests such as electrocardiograms (85%; n = 45), height and weight measurements (92%; n = 48), blood tests (94%; n = 49), bacteriology (100%; n = 52) and chest x-rays (87%; n = 46) were well-documented with the exception of visual acuity tests (19%; n = 10). Patients were dosed according to their weight (98%; n = 51) and patients and caregivers were educated about drug-resistant tuberculosis (98%; n = 51).

Conclusions: While there were many positive findings regarding clinical monitoring and social worker assessment of children, there were challenges identified in terms of timely treatment initiation and active adverse event monitoring.

EP-04-638 Contact tracing evaluation around bacteriologically confirmed pulmonary tuberculosis index cases in Cameroon after 12 months of implementation

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Background and challenges to implementation: Since October 2020, Cameroon has been one of the 8 countries in Sub-Saharan Africa benefiting from the support of the Union for the implementation of the CETA Project (Contribute to the Elimination of Tuberculosis in Francophone Africa).

One of the components of this project consists in improving the screening and prevention of tuberculosis (TB) among household contacts (children under 5 and people living with HIV-PLHIV) with contagious index tuberculosis cases. It is thus moving towards the current vision of the Cameroon National Tuberculosis Program (NTP) and the World Health Organization (WHO) via the "End TB" strategy.

Intervention or response: We are evaluating here the contact tracing around contagious index TB cases carried out in 20 pilot Diagnostic and Treatment Centers

(DTC) of the country from October 2020 to September 2021. These DTCs were selected according to a certain number of criteria: having notified at least 50 bacteriologically confirmed pulmonary TB cases the previous year; not being occupied by another partner carrying out the same activity; be securely accessible.

Results/Impact: After 12 months of activities, 5245 patients with bacteriologically confirmed TB were notified in these DTCs. 526 of them benefited of home visits for contact tracing.

As results we had:

- i. 770 children under 5 years seen at home (including 767 put on Isoniazid-INH, 345(45%) with INH treatment completed, 12(1,5%) diagnosed with tuberculosis);
- ii. 50 PLHIV seen at home (including 57 put on Isoniazid-INH, 15 (26%) with INH treatment completed, 6(12%) diagnosed with tuberculosis).

Conclusions: This contact tracing improved INH chemotherapy nationwide (26% of improvement in children under 5 years old in 2021 compared to 2020).

Besides, 2,2% of household contacts (children under 5 and HIV-PLHIV) were diagnosed with tuberculosis and treated.

However, closer monitoring of cases on INH is necessary because less than 50% completed the treatment (45% in children and 26% in PLHIV).

EP-04-639 Yield from alternative models of contact investigation: the KNCV Nigeria experience

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Background: To find the missing TB cases, Nigeria adopts systematic contact investigation (CI) as an effective method for the timely diagnosis of TB patients and provision of TB preventive treatment. To optimize yield from Contact investigation, different models have been deployed. KNCV Nigeria USAID-funded TB LON project compared the yield from alternative models of contact investigation

Design/Methods: For a successive 6-month period the yield from two models of Contact Investigation (CI) - active household CI implemented October 2020- March 2021 and cluster (the onion model) CI implemented April to September 2021 was compared.

In active household CI, trained contact investigators visited the households of bacteriologically confirmed index TB cases to investigate their household contacts while in cluster CI, in addition to visiting households of index patients and investigating their contacts, close contacts living within a 2km radius of the index patient location were screened in a house-to-house case search.

Results: Active Household CI- Index patients visited were 9,107- index patient coverage of 83%, 41,802 household contacts were screened out of which 12,659 presumptive TB were identified (presumptive TB yield of 30%) 12,166 were evaluated and 1,516 TB patients diagnosed (TB yield of 12%) with a number needed to test (NNT) of 8 and a Number needed to screen (NNS) of 28.

For Cluster contact investigation 11,043 index patients were visited - index patient coverage of 96%, 106,892 household and close contacts screened, 32,599 presumptive TB identified (30% presumptive TB yield) 30,757 presumptive TB were evaluated, 2,101 TB patients were diagnosed -TB yield of 7%, NNT was 15 and NNS was 50.

Model of CI	Index Patients visited (Index patient coverage)	Contacts screened	Presumptive identified (Presumptive TB Yield)	Presumptive evaluated	TB patients diagnosed (TB Yield)	NNT	NNS
Active Household CI	9,107 (83%)	41,802	12,659 (30%)	12,166	1516(12%)	8	28
Cluster (Onion) Model	11,043(96%)	106,892	32,599 (30%)	30,757	2101(7%)	15	50

Table 1. Yield from alternative models of contact investigation.

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tive TB identified (30% presumptive TB yield) 30,757 presumptive TB were evaluated, 2,101 TB patients were diagnosed -TB yield of 7%, NNT was 15 and NNS was 50.

Conclusions: Even though both models of CI had the same presumptive TB yield, active household CI had a higher TB yield. Cluster CI on the other hand gave a better index patient coverage with a higher absolute number of TB cases.

EP-04-640 Strategies of increasing case finding in a high TB burden country

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Background and challenges to implementation: Nigeria still maintains her position of being 6th among the high Tuberculosis burden countries. For several years all efforts to increase case finding, the treatment coverage rate for TB remained at <25%. In 2019, the National programme was named principal recipient of the GFATM grant, which provided the leverage for intervention mapping between the programme and other implementing partners in the country. Granular deep dive data analysis was done intermittently to gather evidence for decision making towards identifying, sustaining or upscaling intervention.

Intervention or response: Interventions were mapped in different states and regions to avoid double funding a particular area by either the programme or partners especially amidst resource constrain. This mapping was guided by programme data in which a group of interventions like Active Case Search (ACS) among Nomads were introduced in the Northern states of Adamawa, Taraba and Gombe, ACS among IDPs were introduced in Borno, Adamawa and Yobe, OPD screening introduced in all secondary and tertiary facilities in the country, DOTs expanded to improve access to both private and public health facilities (including those in hard-to-reach areas).

PPM engagement improved with the introduction of MOU signing with the facilities. Special community activities using CBOs for ACS and House-to-House case search implemented in 12 high TB burden states.

Results/Impact: Treatment coverage rate increased from a baseline of 24% in 2018 (106,533) to 27% in 2019 (120,266), 30% in 2020 (138,591) and 45% in 2021 (207,785). Analysing contribution to case finding shows that community contributed 33% (68,334) to the national case finding in 2021, PPM 28% (58,219), OPD

screening 6%, (13,029), IDP 1% (2668), Nomads 1% (2158), and the rest from other activities implemented in the facilities.

Conclusions: Good leadership/governance and consistent data use play key roles in moving from a point of low case notification to a point of improved treatment coverage rate.

EP-05 Clinical trials and operational research for new treatment of TB

EP-05-641 Development of a deep learning model for predicting tuberculosis treatment outcomes on time series CT scans

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Background: Qualitatively tracking lesion changes based on time series CT scans to evaluate treatment outcomes is an important but far more challenging task. We developed a novel three-dimensional (3D) deep learning model to predict tuberculosis (TB) treatment outcomes of success, no treatment response (NTR) and drug-resistant tuberculosis (DR-TB) cases by longitudinal CT scans.

Design/Methods: 421 patients (301 treatment success, 50 DR-TB and 70 no treatment response) with bacteriologically-confirmed TB comprising 1263 CT scans were retrospectively collected from Hospital A with IRB approval, and separated into training, validation and testing subsets (7:2:1). DR-TB was considered as positive and treatment success and NTR were considered as negative.

For each patient, CT scans taken prior to treatment and follow-up scans at the second month and the end of treatment were involved. Pretreatment CT scans were used to train a baseline model and follow-up scans were added to train the prediction model including procedures of feature extraction and feature maps subtraction. Slices of CT scans were combined into 3D images and then into 3D-Resnet50, and feature maps of three timepoints were subtracted from each other. After global average pooling of fusion features, classification of DR-TB were obtained by the fully connected layer.

Results: The baseline model achieved an AUC of 0.16 to predict DR-TB, showing that it was unable to make treatment outcome prediction. An enhanced AUC of 0.97 was obtained by the prediction model and accuracy, sensitivity, specificity, false positive rate and false negative rate were 0.886, 0.750, 0.903, 0.097 and 0.250, respectively, revealing that the developed model by using time series scans performs well for treatment outcome prediction of DR-TB.

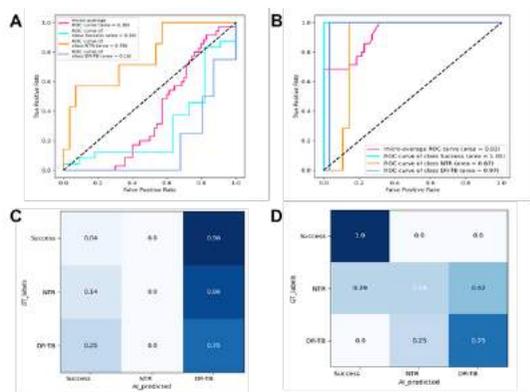


Figure 1. The evaluation performance of the baseline model and the prediction model on testing dataset. The red curve denoted micro-average AUC of one versus other two classes. (A) The ROC curves of the baseline model. (B) The ROC curves of the prediction model. (C) Normalized confusion matrix of the baseline model. (D) Normalized confusion matrix of the prediction model ROC, receiver operating characteristic curve; AUC, area under the curve. DR-TB, drug-resistant tuberculosis; NTR, no treatment response.

Figure 1.

Conclusions: This study demonstrated that the proposed prediction model with additional timepoint CT scans outperforms the compared baseline model, demonstrating the potential to identify TB patients who would fail the treatment and even transfer to DR-TB.

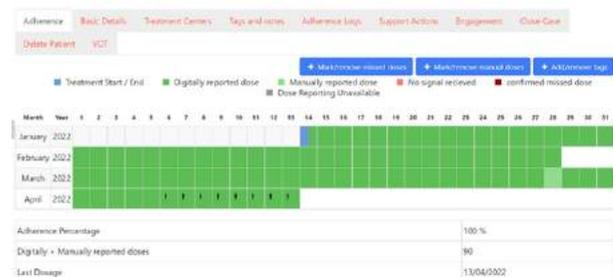
EP-05-642 Closing the TB adherence gap in Nigeria with digital adherence technologies

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Background and challenges to implementation: Nigeria accounts for two-thirds of all TB cases worldwide alongside 8 other countries with the greatest burden of TB, MDR-TB, and TB/HIV. The Directly Observed Treatment Short-course (DOTS) patient management strategy has some limitations of the additional cost of transportation incurred by patients' daily visits to the health facility and the availability of health care workers to support DOTS due to the dearth of human resources. Patient Adherence to TB treatment is essential for achieving better treatment outcomes and preventing the development of TB medication resistance

Intervention or response: Digital Adherence Technologies (DATs) have been demonstrated in various settings to be effective in improving TB patient adherence to treatment. KNCV Nigeria and partners are working closely with the National Tuberculosis Program (NTP) to implement two DATs models; Video Observed Therapy and 99DOTSLite within 8 states of Nigeria which were selected within the USAID-funded TB LON 1 and 2 project coverage area and reflect a mix of TB burden and gaps in treatment success rate.

Results/Impact: Two Success Stories have been documented from TB patients receiving TB treatment in DATs implementing facilities within 6 months of DATs implementation. A middle-aged relapsed TB patient was enrolled on 99DOTSLite in Sir Muhammad Sunusi Specialist Hospital, Kano, the patient confessed that the reminder messages received daily helped him stay consistent in taking his TB medication in his second round of treatment as opposed to the forgetfulness he experienced during his first treatment. Also, a patient enrolled on VOT in Federal Medical Center, Owerri submitted that sending videos daily provided an accountability mechanism for his medication intake to support his treatment adherence.



Conclusions: KNCV Nigeria will continue to support DATs implementation across implementing facilities to ensure TB patient treatment adherence for improved outcomes.

EP-05-643 Strengthening TB drug logistics management using quanTb for drug quantification and as an early warning system in Uzbekistan

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Background and challenges to implementation: In 2021, Uzbekistan began transitioning from donor to government funding of new tuberculosis (TB) drugs. To adapt to this change in procurement, the National TB Program (NTP) streamlined the procurement and logistics systems, ensuring the tools for quantification of TB drugs would work effectively for both the assessment of drug needs and planning from two sources.

Intervention or response: QuanTB is an electronic quantification and early warning system (EWS) designed to improve TB drug procurement. Between January 2021–January 2022, as TB drug procurement transitioned from donors to the state, the USAID Eliminating Tuberculosis in Central Asia (Activity) supported NTP in strengthening regional-level capacity for drug management, and improving stakeholder collaboration to ensure the continuous use of QuanTB during the transition.

Twenty-eight NTP specialists responsible for drug management in the country's 14 regions received training on QuanTB use and troubleshooting and data quality and analysis for tracking and decision-making. Since the training, the NTP has instituted quarterly analysis of TB drugs stocks using QuanTB, serving as an EWS so action to be taken to prevent impending stockouts or drug expiration.

Results/Impact: Increasing QuanTB system capacity improved TB drug need projections and data collection practices. Countrywide, regional warehouses reporting at least one TB medicine stock-out decreased by 43% (from 6 out of 14 in January 2021 to 0 by December 2021). The number of district TB facilities per region experiencing any TB drug stock-out decreased by 32% over the same period. Enhanced drug management prevented US \$18,378 in TB drugs from expiring and going to waste.

Conclusions: The NTP has successfully applied the QuanTB tool to forecasting and procurement planning for first- and second-line TB drugs procured under the state budget. QuanTB has become an effective tool for regular monitoring of TB drug supply risks at the regional and national levels.

EP-05-644 Telephonic adherence support for TB treatment: experience from a high TB burden urban setting in South Africa

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Background: Treatment adherence is critical for patient outcomes and End TB targets. While various Mhealth solutions have been suggested, recent data show no improvement in treatment outcomes unless linked to personal follow-up. With COVID-19 demanding remote care options, phone-based adherence support is a potential solution.

We aimed to determine the feasibility of a phone-based adherence model and report on adherence-related outcomes.

Design/Methods: We implemented a telephonic TB treatment adherence model, where TB clients of private-sector physicians were supported by trained laypeople (Adherence Facilitators [AFs]). AFs spoke isiZulu and English (local languages), received comprehensive training in TB symptoms, treatment and side effects, co-morbidities, motivational counselling, and harm reduction, and maintained a compendium of available support programmes.

Initial, one-week, and monthly calls were initiated with clients. Clients used a free “please-call” service for interim assistance. Call duration and discussion were recorded systematically, and reported collection dates were verified against clinic records. We report client demographics and uptake frequency, completion to date, and commonly alleviated barriers.

Results: Between May 2021–March 2022, 105 clients were diagnosed with pulmonary TB. Initial calls were successful to 103 (98%) clients, with 102 (97%) initiating treatment (98 in the public sector) and 96 (90%) accepting ongoing adherence support. Two foreign nationals with language barriers were not successfully linked to care. By April 2022, 638 support calls had been made (mean duration=9 minutes), and 35 clients (33%) had

completed treatment. Clients commonly discussed side effects (n=183 calls) and TB symptoms (n=127), while common barriers included clinic closures (n=31), work/childcare (n=12), and transportation (n=10).

Demographics	Overall n (%)	Accepted support n (%)	Self-adherent n (%)	Not initiated n (%)	Completed/ on track n (%)	LTFU/ treatment delay n (%)	Died on treatment n (%)
Sex							
F	42 (40)	38 (40)	3 (50)	1 (33)	38 (41)	3 (33)	1 (25)
M	63 (60)	58 (60)	3 (50)	2 (67)	54 (59)	6 (67)	3 (75)
Age group							
15-34	39 (37)	38 (40)	0 (0)	1 (33)	36 (39)	3 (33)	0 (0)
35-49	41 (39)	35 (36)	4 (67)	2 (67)	35 (38)	4 (44)	2 (50)
50-64	22 (21)	20 (21)	2 (33)	0 (0)	19 (21)	1 (11)	2 (50)
65+	3 (3)	3 (3)	0 (0)	0 (0)	2 (2)	1 (11)	0 (0)
HIV status							
pos	47 (45)	45 (47)	2 (33)	0 (0)	41 (45)	4 (44)	2 (50)
neg	49 (47)	44 (46)	4 (67)	1 (33)	44 (48)	3 (33)	2 (50)
unk	9 (8)	7 (7)	0 (0)	2 (67)	7 (7)	2 (22)	0 (0)

Acronyms: LTFU=lost to follow-up, pos=positive, neg=negative, unk=unknown

Conclusions: Telephonic adherence support offered a feasible, patient-centred model to support people with TB to treatment completion, with high levels of uptake and completion. Foreign nationals may be particularly vulnerable to initial loss-to-follow-up in this setting; language barriers may play a role.

EP-05-645 Consecutive missed doses and temporal patterns of non-adherence among tuberculosis patients: findings from the ASCENT multi-country study

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Background: Ensuring six months of treatment completed remains a critical strategy for improving treatment outcomes; however, little is known about patterns of non-adherence. As part of the ASCENT project evaluating the effectiveness of digital adherence technologies for tuberculosis treatment support, we examined individuals' treatment adherence patterns in Ethiopia, South Africa, Tanzania, Ukraine, and the Philippines.

Design/Methods: We summarised adherence patterns in a cohort of persons on drug-sensitive tuberculosis treatment who had the opportunity of six-month follow-up and who were enrolled in the smart pillbox arm of five pragmatic cluster-randomized trials. Daily digital adherence was defined as a pillbox opening on a day, recorded on the adherence platform. We used linear regression to model weekly digital adherence percentages

over time using fractional polynomials. The maximum number of consecutive doses not digitally confirmed is also summarised.

Results: Adherence data from 2,113 participants (37% female, median age 39 years) are summarised. A total of 1,805 (85%) missed at least one dose, and of these, 34%, 17%, and 8% had their maximum period of consecutive doses missed of one, two, and three days, respectively; 21% (423/1805) had at least eight days of consecutive doses missed. Weekly adherence percentages over time revealed an initial reduction in digital adherence (<10%) in the first month, excluding Ethiopia, before reaching a "middle plateau." Steeper declines in adherence were seen in Ethiopia, South Africa, and the Philippines in the final two months.

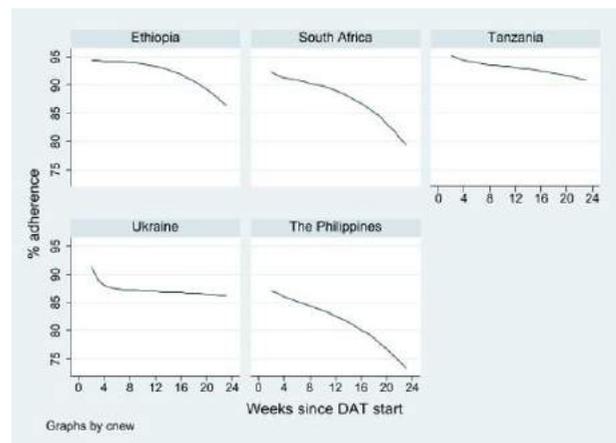


Figure 1. Weekly digital adherence percentage of TB patients modeled over 24 weeks in four countries: Ethiopia, South Africa, Tanzania, Ukraine, and the Philippines.

Conclusions: Digital adherence technologies offer a unique advantage in aggregating adherence data to help improve treatment delivery. Consecutive daily treatment interruptions were common among participants from these five countries, and to avert losses to follow-up, particular attention may be given during the first four weeks of treatment.

EP-05-646 Motivating persons with drug resistant TB to complete treatment: local TB response (LTBR) experience in Zambezia, Mozambique

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Background and challenges to implementation: Drug Resistant (DR) TB treatment outcomes in Zambezia is characterized by low rate of treatment success and high rates of death, lost to follow-up and not evaluated. Knowledge and awareness among persons affected by TB and their own families is limited, leading to incorrect intake of medication and lack of regular monthly clinical follow up.

The quality of services at Health Facilities often is limited due to insufficient training on management of persons with DR TB. This situation is aggravated by poor social conditions of many affected persons and lack of social support from authorities and civil society.

Intervention or response: USAID LTBR project provincial clinicians provided Technical Assistance, mentorship and on the job training to clinicians from health facilities (HF) on DR TB correct management and follow-up. The project implemented DOTS Plus strategy with Psychosocial Support (PSS) to all persons affected by DR TB in the province, providing a package of services, including TB&DR TB education, importance of treatment adherence and regular follow-up, contact screening, through well trained project community activists. Pill boxes were provided to ensure correct medication dosage and frequency. Monthly monetary subsidy of 540 MT (9\$) and cellphones to allow electronic payments were also provided to support transport costs to reach HFs.

Results/Impact: Zambezia province notified a total of 164 persons with DR TB in 2019, 226 in 2020 and 237 in 2021. Treatment success went from 59% in 2019 to 70% in 2020 and 71% in 2021, while death rate decreased from 24% in 2019 to 14% in 2020 and to 16% in 2021.

Conclusions: DOTS Plus/PSS is motivating factor to improve adherence and increase DR TB treatment outcomes. Provision of quality services to persons affected by TB and DR TB at the HFs, will improve treatment success rates and decrease death and lost to follow up rates.

EP-05-647 The assessment instrument of knowledge, attitude, and practice for community pharmacy personnel in tuberculosis case detection, drug monitoring, and community education

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Background: Community pharmacy is the potential facility to support TB elimination, especially in high prevalent TB countries. A validated instrument is needed for basic assessment to engage community pharmacies in TB.

We, therefore, developed a validated instrument to assess the knowledge, attitude, and practice (KAP) of pharmacy personnel in enhancing their role in TB case finding, drug monitoring, and community education.

Design/Methods: The study was started from the development phase, consisting of framework development, item generation, item screening, and pilot testing. We then validated the developed items with several analyses, i.e., participant characteristics, item discrimination, item difficulty, individual item content validity index (I-CVI), confirmatory factor analysis (CFA), adjusted goodness-of-fit index (AGFI), comparative fit index (CFI), non-normed fit index (NNFI), root mean squared error of approximation (RMSEA), and standardised root mean squared residual (SMRS).

Moreover, Cronbach's alpha and test-retest reliability were performed using Pearson's product-moment and intraclass correlation coefficient (ICC).

Results: A total of 63 items were defined from the item development phase. It consisted of sociodemographics (18), knowledge (18), attitudes (18), and practice (9) items. In the validation phase using 400 participants, we analysed that the score of I-CVI was 1, while the coefficient correlations of the test-retest reliability were 0.84 (knowledge), 0.55 (attitude), and 0.91 (practice).

We identified that the ICC were 0.91 (knowledge), 0.71 (attitude), and 0.95 (practice). The CFA model (χ^2/df) was 2.28, with the AGFI, CFI, NNFI, RMSEA, SMRS scores were 0.95, 0.99, 0.98, 0.06, 0.03, respectively. Cronbach's Alpha scores for the KAP were 0.75; 0.91; 0.95, respectively.

Conclusions: We successfully developed 63 validated items for assessing community pharmacy personnel's KAP in TB case detection, drug monitoring, and community education. The instrument can be considered for basic assessment to engage community pharmacies in supporting TB elimination.

EP-05-648 Comprehensive, integrated psychosocial support for people with DR-TB results in improved treatment outcomes in pilot regions of Tajikistan

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Background and challenges to implementation: The effectiveness of tuberculosis (TB) treatment in Tajikistan is not high. Among the cohort of cases diagnosed in 2020 with drug resistant (DR) TB, National TB Program (NTP) data shows that only 71% were cured. Tajikistan's poor treatment outcomes result largely from poor adherence to treatment/treatment interruption.

Intervention or response: The USAID Eliminating TB in Central Asia (Activity) introduced a set of psychosocial interventions for people with TB (PWTB) in its 18 pilot districts, which delivered in close collaboration with TB institutions, primary health care (PHC), health authorities and community leaders.

Trained outreach workers and community volunteers provide food packages and psychological and legal counseling to PWTB receiving outpatient treatment and escorted PWTB to health care facilities.

Exact services provided vary by region, as per the specific needs in the area. These interventions on the community level support PWTB in adhering to treatment, including timeliness and accuracy of drug intake.

Results/Impact: As a result of the integrated patient support provided to PWTB during outpatient treatment, including interaction between all relevant agencies and provision social support, DR-TB treatment outcomes in the Activity pilots improved.

In the period prior to Activity implementation, the treatment interruption was observed among 10% of DR-TB patients enrolled in treatment in 2018; and among 9% in the cohort enrolled in 2019.

After the launch of Activity interventions, treatment interruption among the 2019 cohort of DR-TB patients in the Activity pilots decreased to 3% and, among the 2020 cohort, to 1%. Treatment success rate reached 89% in the 2019 and 84% in the 2020 cohort.

Conclusions: Pilot implementation in Tajikistan demonstrates that integrated support for PWTB administered in concert with local agencies can reduce treatment interruption and improve treatment outcomes. This approach can be adapted and applied beyond the scope of these pilots.

EP-05-649 Sustained costs of 99DOTS following implementation in Uganda

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Background: 99DOTS is a Digital Adherence Technology (DAT) that has potential to improve treatment adherence for drug-susceptible tuberculosis (TB) in high burden settings. The Uganda National Tuberculosis and Leprosy Program (NTLP) recently approved 99DOTS for TB, but the routine costs of 99DOTS remain uncertain.

Design/Methods: DOT to DAT was a stepped-wedge randomized trial assessing the impact of 99DOTS on TB treatment outcomes in Uganda. As part of post-trial analysis, we conducted a time and motion (TAM) survey at 10 health facilities to assess the human resource needs required to sustain 99DOTS. TAM data was collected two ways: (a) using a self-reported "daily activities" form completed by trained community health workers (CHWs) and (b) direct observation of CHW household visits. TAM data were combined with NTLP salary estimates and resource data from the trial to estimate the post-implementation cost of 99DOTS-related activities. Costs were assessed from the health system perspective and reported as 2021 US dollars.

Median Cost per patient Activity	Observation Days (patients observed)	Median Time per Patient	Median time per day	Median Cost per patient
Enrollment	62 (96)	22 (10.7, 34)	0 (0, 24)	\$0.28 (0.11, 0.37)
Support Calls	111 (401)	4 (2.6, 7.5)	8 (0, 16)	\$0.05 (0.03, 0.09)
SMS	22 (34)	7.5 (5, 10)	0 (0, 0)	\$0.07 (0.05, 0.14)
Dashboard	110 (433)	2.1 (1.5, 6.3)	5 (0, 15)	\$0.03 (0.02, 0.09)
Other*	91 (N/A)	--	6 (0, 25)	--
Total 99DOTS	158 (1086)	9.4 (3.9, 26.1)	67 (36, 125)	\$0.14 (0.04, 0.32)

Results: 158 daily forms were collected from 34 CHWs. CHWs spent a median 14.1% (IQR: 7.5%, 26.0%), of their day performing 99DOTS-related activities. Household visits, travel, and enrollment required the most time. CHWs interacted with a median 6 (IQR: 2, 12) 99DOTS patients per day, spending 9.4 minutes (IQR: 3.9, 26.1) per patient. Directly observed TAM data were collected for 53 household visits, of which 50 were suc-

successful. Household visits lasted a median 150 minutes (IQR: 103, 187), with 48.1% of time spent traveling, 41.1% interacting with patients, and 10.8% spent in preparation or wrap-up. A median 4 people (IQR: 3, 5) were assessed per household visit. The daily cost of 99DOTS activities was \$0.70 per CHW (IQR: \$0.36, \$1.76), with a median cost of \$0.14 (IQR: \$0.04, \$0.32) per patient.

Conclusions: Decisions to scale-up DATs for TB treatment support should consider the sustained costs of routine implementation.

EP-05-650 Scope of 99DOTS Lite technology in optimizing coverage of adherence among TB & TPT beneficiaries under NTEP India

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Background and challenges to implementation: Ensuring optimal medication adherence through Digital Adherence Technologies (DAT) enables optimal treatment outcomes. The challenges associated with existing DATs has led to exploration of alternative approaches to digitally observe medication adherence.

In addition, roll out of TB Preventive Therapy (TPT) services is expected to increase eligible beneficiaries three-four fold, which in turn would require simple and cheap alternatives to existing technologies.

Intervention or response: 99 DOTS-lite' is a DAT, where-in a sticker with a Toll-Free number (TFN) is affixed on Anti-TB drugs. After consuming daily medication, patients make a free call to phone number on sticker. This yields a high confidence that the dose has been consumed and immediately the call gets recorded on the Nikshay Calendar-view as a dose consumed. This tool subsequently prioritizes patients for immediate follow-up by healthcare staff based on their reported adherence. This tool is extremely low cost (12 INR/0.16 USD per patient for logistics with additional platform costs) and allows different customizations.

Results/Impact: In a pilot eastern India, total of 1683 TB Patients were enrolled with an Digital adherence rate of 49% and overall Adherence rate of 73%. In one pilot in North India, 1866 Patients were enrolled across 5 districts with an Digital adherence of 38% and overall Adherence rate of 46%. Surveys conducted have shown that Staff have reported positive feedback in using 99DOTS

Lite, since the supply chain is extremely simplified and stickers are compatible with all existing form factors. Patients also cited that the availability of numbers on the blister serves as a ready reckoner to place a call and report adherence.

Conclusions: 99DOTS Lite is acceptable to patients and health workers. They cost significantly small proportion of cost of other DAT options, ensuring sustainability and deployment at scale. This technology when supported with alerts for missed reporting is expected to improve overall patient engagement.

EP-06 TB and MDR-TB treatment outcomes

EP-06-651 Treatment outcomes in young children with rifampicin-resistant TB regimens including bedaquiline and delamanid: a global individual patient data meta-analysis

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Background: Current rifampicin-resistant tuberculosis (RR-TB) treatment in children remains complex and long. There is limited access to the novel drugs bedaquiline and delamanid in young children due to few data on outcomes, dosing and safety.

We determined treatment outcomes in young children receiving RR-TB treatment regimens including bedaquiline or delamanid.

Design/Methods: A systematic review and individual patient data meta-analysis included children and adolescents (0-19 years) treated for RR-TB through March 2020 in published and unpublished data.

Among the subset of children <6 years of age treated with bedaquiline or <3 years of age treated with delamanid, a matched analysis was undertaken evaluating key outcomes using propensity-matching (age, sex) and exact matching (HIV status, previous TB treatment, bacteriologically-confirmed, AFB-positive).

Results: Overall, data from n=24,231 children from 44 studies were included. Children <6 years who received bedaquiline (n=40) vs. no bedaquiline (n=1992), were more likely to be HIV positive, have confirmed/smear-positive RR-TB, while favourable treatment outcomes were similar (75% vs 84.1%, respectively) in the two groups. Matched multivariate model regression showed no difference in treatment success with bedaquiline (aOR: 0.94; 95% CI 0.09-10.3). However, children treated with bedaquiline had significantly shorter treatment duration (13.3 vs. 16.4 months, adjusted effect 3.47 months; 95% CI; -6.0, -0.91) and were less likely to receive an injectable (aOR 0.12; 95% CI 0.05, 0.32). Only seven children <3 years of age received delamanid; all had favourable outcomes. Small numbers, and methodological limitations reduced the certainty of the evidence.

Conclusions: Few young children globally received bedaquiline or delamanid. Overall outcomes in young children with RR-TB were good. Bedaquiline use was significantly associated with shorter treatment duration and less injectable drug use. These data informed WHO 2022 guidelines recommending bedaquiline and delamanid in children of all ages. Further high-quality data is needed in children treated with these new drugs.

EP-06-652 Clinical audit to improve quality of DR-TB treatment in Indonesia

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Background and challenges to implementation: Treatment of drug resistant-TB (DR-TB) is challenging for patients and clinician, especially due to the frequent updates in the area of diagnosis and treatment. In 2017, Indonesian NTP supported by the Challenge TB Project/USAID developed clinical audit as a mechanism to identify clinical management issues, to conduct prompt actions for improving quality of care, as well as to learn best practices for DR-TB peer clinicians.

Intervention or response: In 2021, clinical audits were done in 46 hospitals in 11 provinces, reviewing 537 DR-TB patients on treatment. The audit involved national DR-TB experts/clinicians and NTP (as the auditor), as well as the health offices, referral laboratories, and NTP partners. The clinical audit were conducted in hybrid method, where the auditor attending through virtual meeting platform.

Results/Impact: Most of the DR-TB hospitals has recording and reporting issues, where 76% patients reviewed had incomplete/invalid treatment-related data on either the manual or online TB register system.

Other main findings were delay in treatment initiation (39% of patients reviewed were put on treatment >7 days after diagnosed), 25% patients reviewed did not do monthly sputum culture test for treatment monitoring, 21% patients were put on inappropriate DR-TB treatment regimen, inadequate adverse event management were identify in 21% patients, and 18% patients had no phenotypic DST at baseline.

Conclusions: Clinical audit is useful as a measure to identify clinical and programmatic issues related to DR-TB treatment. Currently the activity is only covering small proportion of DR-TB hospitals in Indonesia but have shown to be an effective way for capacity building and peer learning.

EP-06-653 Effect of mobile phone access to the uptake of digital adherence technologies in Nigeria

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Background and challenges to implementation: The Digital Adherence Technologies (DATs) project in Nigeria is implemented using two models, Video Observed Therapy (VOT) and 99DOTlite a modified version of 99DOTS to use Medication Labels. Patients enrolled on either of these models require feature/smartphones to use the DATs and with TB disease associated with the poor, a significant number of patients presenting at the health facilities have no mobile phones.

Intervention or response: To address this challenge, KNCV Nigeria adopted "access" to feature/smartphones as the eligibility criteria for consenting TB patients to enrol on any of the DATs.

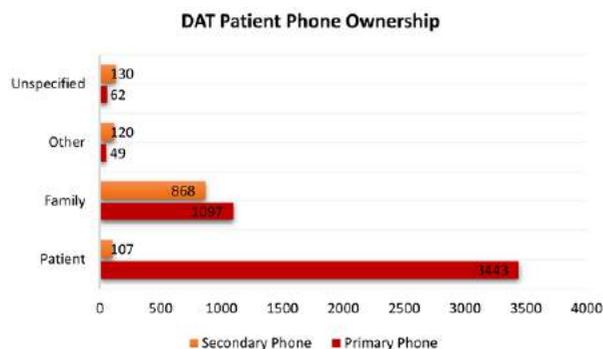
With access, the patient need not own a mobile phone but can leverage the mobile phone of any family member, treatment supporter or other relations within the household.

Patients have the option of submitting a maximum of 3 alternative phone numbers for 99DOTlite and can log into the VOT app with any smartphone available using the login details provided at enrolment.

Results/Impact: DATs are made available to patients who own mobile phones and patients who do not own but have access to mobile thereby expanding the reach of DATs and removing the limitations to the enrolment of TB patients. Utilizing access to mobile phones as the eligibility criteria for DATs and not ownership contributed to the increased uptake of DATs across implementing health facilities.

Based on phone ownership data on primary phone numbers documented, 3,443 phone numbers were owned by the patients, 1097 were owned by family members and 49

by other members of the family. Also, 988 phone numbers were documented as secondary phone numbers to be leveraged for DATs in the event of the unavailability of the primary phone number.



Conclusions: Where TB patients do not own mobile phones, access to mobile phones should be employed as a strategy to increase the uptake of DATs.

EP-06-654 Barriers to achieving treatment success in previously treated tuberculosis patients in India: a systematic review

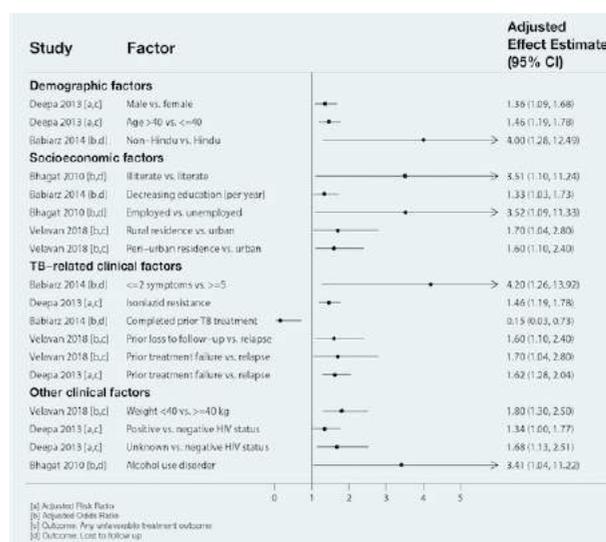
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Background: A higher proportion of previously treated tuberculosis (TB) patients in India experience unfavorable treatment outcomes (death, loss to follow-up, failure, or unevaluated) when compared to new TB patients. We conducted a systematic review to identify factors associated with unfavorable treatment outcomes in previously treated TB patients in India.

Design/Methods: We searched PubMed, Embase, and Web of Science to find studies published between January 2000 and May 2021 using search terms for TB, India, and unfavorable outcomes. Two independent reviewers identified relevant studies and extracted findings regarding factors associated with unfavorable treatment outcomes in previously treated TB patients. After quality assessment, we reported variables associated with statis-

tically significant adjusted effect estimates in relation to unfavorable treatment outcomes in multivariable regression analyses from cohort studies.

Results: Of 4,516 studies screened, 17 met the inclusion criteria, of which four reported findings from multivariable regression analyses. Factors significantly and independently associated with higher risk of unfavorable treatment outcomes among previously treated TB patients included: male sex (vs. female sex), age >40 years (vs. ≤40 years), non-Hindu religion (vs. Hindu), no education and illiteracy (vs. literate), employed (vs. unemployed), ≤2 symptoms at treatment initiation (vs. ≥5 symptoms), isoniazid mono-resistance present (vs. absent), noncompletion of prior treatment (vs. completion), prior treatment failure and loss-to-follow-up (vs. relapse), pre-treatment weight <40kg (vs. ≥40kg), positive or unknown HIV status (vs. HIV negative), and alcohol use disorder (vs. no alcohol use).



Conclusions: Multiple challenges contribute to unfavorable treatment outcomes in previously treated TB patients. Early diagnosis of isoniazid mono-resistance, treatment of alcohol use disorder, and nutritional supplementation to address undernutrition may be strategies to improve outcomes in this population.

In addition, some of these factors (e.g., loss to follow-up during prior treatment, low literacy) may inform approaches to triaging patients and providing intensive support to those at higher risk of poor outcomes.

EP-06-655 Uptake of 99DOTlite against video observed therapy: lessons from the DAT pilot in Nigeria

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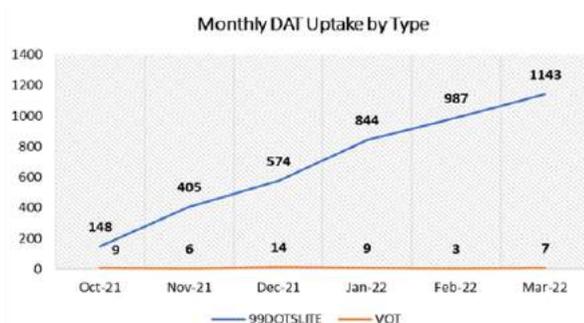
Background: 99DOTSlite and Video Observed Therapy (VOT) are the two models of Digital Adherence Technologies (DATs) implemented in Nigeria. Patients enrolled on 99DOTSlite are provided with medication labels with a unique hidden 3-digit code on each blister pack of TB medication. For VOT patients, the SureAdhere App is installed on their smartphones to enable them to send videos of daily medication intake via the app.

Design/Methods: We conducted a review of patients enrolled on DATs across the 8 states implementing DATs in Nigeria. The data is analyzed using DAT type to gauge uptake of the two models within a 6-month period between October 2021 to March 2022.

Results: The data showed a consistent trend in increased DAT uptake; however, this increase was not consistent with DAT types.

A breakdown of percentage contribution of DAT type by monthly enrolment numbers are as follows; October 2021 (99DOTSlite: 94% VOT:6%), November 2021 (99DOTSlite: 99% VOT:1%), December 2021 (99DOTSlite: 98% VOT:2%), January 2022 (99DOTSlite: 99% VOT:1%), February 2022 (99DOTSlite: 99.9% VOT:0.1%) and; March 2022 (99DOTSlite: 99% VOT:1%).

Patients who were previously enrolled on VOT were also switched to 99DOTSlite due to reasons such as technology fatigue and stigma-related issues.



Conclusions: Findings show that there is a higher uptake of 99DOTSlite among TB patients in DATs implementing health facilities, this is largely due to the ease of entry into this DAT type as well as stigma-related issues associated with persons receiving TB treatment which deter patients from sending videos using VOT.

EP-06-656 Barriers to achieving treatment success in new bacteriologically-confirmed pulmonary tuberculosis patients in India: a systematic review

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Background: New bacteriologically-confirmed pulmonary tuberculosis (NBCPTB) patients constitute the largest subpopulation of tuberculosis (TB) patients in India. One-seventh of these patients experience unfavorable treatment outcomes. We conducted a systematic review to identify factors associated with unfavorable outcomes in this subpopulation.

Design/Methods: We searched PubMed, Embase, and Web of Science to find studies published between January 2000 and May 2021 using search terms for TB, India, and unfavorable outcomes. After quality assessment, two independent reviewers extracted findings from studies that reported factors associated with NBCPTB patients experiencing unfavorable treatment outcomes. We report variables with statistically significant adjusted effect estimates in relation to unfavorable treatment outcomes in multivariable regression analyses.

Results: Of 4,516 studies screened, 25 met inclusion criteria, of which eight reported findings from multivariable regression analyses. Patient-related factors significantly and independently associated with higher risk of unfavorable outcomes included: age >45 years (vs. <=45 years), separated/divorced (vs. married, widowed, or single relationship status), not literate (vs. literate), illness duration >2 months (vs. <=2months), cavitory disease, lack of sputum conversion, subtherapeutic rifampin level, adverse drug reactions, treatment interruption, absence of diabetes, alcohol use disorder, and inadequate TB knowledge. Health system-factors significantly and independently associated with higher risk of unfavorable outcomes included: increasing number of providers visited before diagnosis, cost of travel as a barrier to clinic visits, having to pay for treatment, dissatisfactions with TB services, and inadequate patient-provider interaction or provider support [Figure 1].

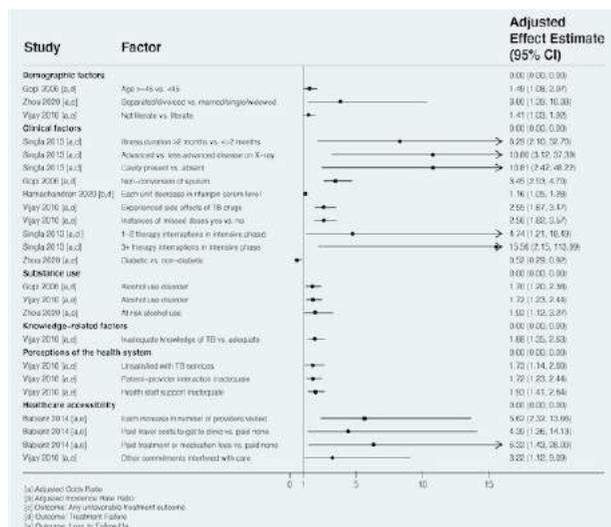


Figure 1. Factors associated with unfavorable treatment outcomes among new bacteriologically-confirmed pulmonary TB patients in India.

Conclusions: Multiple challenges contribute to unfavorable treatment outcomes in Indian NBCPTB patients. Ensuring therapeutic medication dosing, reducing medication nonadherence, treating alcohol use disorder, providing monetary support to facilitate clinic visits, and training providers to improve their interactions with patients may be strategies to improve outcomes in this patient subpopulation.

EP-06-657 Role of decentralized ambulatory drug-resistant tuberculosis care in treatment outcomes in Afghanistan

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Background and challenges to implementation: Drug-resistant tuberculosis (DR-TB) remains a global public health crisis, with only one in three people with DR-TB able to access lifesaving care and a low treatment success rate. This is a significant challenge for the Afghan health system. The National TB Program (NTP) began centralized programmatic management of drug-resistant tuberculosis (PMDT) in 2011 in Kabul, with few DR-TB cases enrolled for treatment. In 2019, the NTP decentralized PMDT service to other 3 provinces: Herat, Balkh, and Nangarhar. This study aims to evaluate the role of a decentralized approach and ambulatory care in DR-TB treatment outcomes.

Intervention or response: In 2019, the NTP equipped laboratories with GeneXpert and culture facility, and a sample transport system was established to perform drug susceptibility tests (DST) in the national reference

laboratory. In early 2020, ambulatory treatment was initiated for people with TB with their families. PMDT staff provided orientation counseling to families. The NTP shifted the injectable regimen to an 18-20 month oral Bedaquiline regimen, and NTP partners provided transportation costs for people with TB to attend their monthly follow-up

Results/Impact: In 2019, 353 DR-TB cases were enrolled in an 18-20 month treatment regimen in four PMDT sites. These people were followed during the pandemic period of 2020-2021. 246 people (70%) successfully completed the treatment, while 54 (15%) were lost to follow-up. 15 (4%) were not evaluated, 7 (2%) failed during the treatment and 31 (9%) died. The treatment success rate for the 2019 cohort was 70% in the aforementioned provinces, an improvement from 68% in 2018 and 63% in 2017 (Table 1).

Year	Cure rate	Com rate	Failure rate	LFU rate	Died rate	Not evaluated	Treatment success rate
2016	60%	1%	3%	22%	13%	1%	61%
2017	60%	3%	1%	23%	12%	1%	63%
2018	55%	13%	3%	17%	10%	1%	68%
2019	36%	35%	2%	14%	9%	4%	71%

Table. The trend of DR-TB treatment outcomes in Afghanistan

Conclusions: Treatment outcomes were significantly improved by decentralization of PMDT services, initiation of ambulatory treatment with the support of family members, shifting the injectable regimen to all-oral standard regimens, and providing transportation cost payment to people with TB.

EP-06-658 Digital nudges to support adherence and optimize health human resource: 99DOTS Lite experience from Uttar Pradesh, India

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Background and challenges to implementation: Because non-adherence to TB treatment leads to decreased quality of life and poor treatment outcomes, monitoring daily adherence is crucial; however, this remains a challenge in India. A phone-call based digital adherence technology, 99DOTS, has been adopted by the National TB Elimination Program (NTEP), but has limits related to its usability and lack of patient research.

Intervention or response: 99DOTS Lite is a simplified, improved version wherein a single toll-free number is provided to TB patients to report daily medication intake by phone. 1,618 patients scheduled to initiate TB treatment were linked with 99DOTS Lite in five dis-

districts of Uttar Pradesh between December 2021 and March 2022. Enrolled patients were from both public and private sector, had pulmonary tuberculosis (90% new case), were ages 15–80 years, with a male to female ratio of 1.7:1. They were provided a medicine box labelled with a toll-free number and counselled on how to report daily dosages. Adherence was monitored digitally on NIKSHAY dashboard (India's case-based TB management system). This dashboard aided health workers to monitor adherence and escalate cases (by phone or home visit) for missed doses.

Results/Impact: Interim findings show that on average, 42.4% of treatment days were reported digitally among enrolled patients. Interim digital adherence score (% of doses reported digitally by patients over treatment course during pilot) varied and was particularly low in districts with sub-optimal case escalation systems. Reasons for missed doses included: phone-related issues, forgetting to digitally report, transfer to other districts, medicine boxes supply logistics, and issues related to patient counselling.

Conclusions: The 99DOTS Lite pilot will run until September 2022. Interim findings help NTEP improve treatment adherence monitoring and supervision. Early findings suggest 99DOTS Lite has been easier for patients to use, and the case escalation system is crucial to follow up the missed doses and improve treatment adherence.

EP-06-659 Factors that influence uptake of digital adherence technologies in Nigeria

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Background: Digital Adherence Technologies (DATs) are recommended tools used to support TB patients to take their medication at a place and time that is convenient for them. By using any of the available DAT tools, patients are reminded to take their medications daily and this process can be observed digitally to provide patient-centred care based on adherence logs. This study examines the variables that support patient enrolment on DATs in Nigeria

Design/Methods: We analyzed facility-level data that tracks the enrolment of patients on DATs across supported facilities, reported weekly using an online data collection form. The data collection form was designed to capture data based on the DATs enrolment cascade from patients who started TB treatment or returning TB patients in their intensive phase to patients who declined enrolment on DATs

Results: Of the 1,117 reports received, 515 patients were found to have declined enrolment on any of the DATs. 32% of patients who declined did not own nor have ac-

cess to a feature/smartphone to enable enrolment, 20% of patients reported more than one reason for declining DAT including no access to phones, inability to use mobile phones and time constraints, 18% were not enrolled due to provider-related issues such as unavailability of smartphones to facilitate enrolment, 13% were not interested in DATs as patients were enrolled on a voluntary basis, 8% of patients owned phones but were unable to use them for DATs, 5% of patients complained of time constraints that may affect their commitment to using any of the DAT tools and another 3% reported other programmatic/technical related issues

Conclusions: Factors that influence DAT uptake in Nigeria include, patient access to mobile phones, quality of patient counselling and HCWs should be equipped with smartphones, or any technology required to digitally monitor patient adherence

EP-06-660 Developing digital adherence tool to improve TB treatment success rate in Papua, Indonesia: tool refinement process

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Background: Papua, the easternmost province in Indonesia, has continuously reported low tuberculosis (TB) treatment success rate, even prior to the COVID-19 pandemic. An alternative strategy to improve treatment adherence is through digital adherence monitoring and individualized remote support.

One of the tools, The Tuberculosis Treatment Support tools (TB-TST) has been used in Argentina. However, effectively implementing in new settings requires adaptation to fit with the unique community context.

Design/Methods: This is a mixed-method study using human-centered design to refine the TBT-TST patient app and an interactive provider dashboard for individuals with TB in Papua. First, the app was translated to Bahasa.

Second, interviewed to understand needs and preferences and usability testing with five Jayapura Hospital TB clinic patients and five members of SaCode community. In the third cycle, we collected feedback on high-fidelity wireframes informed by the second cycle data from five TB patients. For the provider dashboard, we conducted two refinement cycles. Focus group interviews with seven TB clinic nurses, followed by usability testing with three nurses.

Results: The iteration cycles for the patient app informed several major refinements on the report and progress page: a larger notification picture indicating the report was submitted, a clear calendar with color-coded explanations, and a new feature with a familiar picture for alarm and appointment functions.

In addition, we incorporated daily behavior change motivation quotes that will be highlighted on the home page. For the provider dashboard, significant refinements included a modified list of side effects based on Indonesia's guidelines and a mobile-friendly option to the computer-based interface to allow on-call nurses to monitor patients anytime using a mobile phone, especially to support those who report side effects.

Conclusions: The iterative process resulted in significant refinement and tailoring for the Papua setting and positive responses to incorporate the tool to support TB care in Papua.

EP-06-661 Treatment safety and outcomes of children treated for MDR/RR-TB in Papua New Guinea: a 6-year retrospective cohort

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Background: Papua New Guinea (PNG) has a high burden of pediatric tuberculosis and multidrug-resistant/rifampicin-resistant tuberculosis (MDR/RR-TB). Port Moresby General Hospital (PMGH) is the nation's central pediatric hospital, treating and diagnosing pediatric TB cases serving a large catchment area. We describe the treatment outcomes and safety of children treated for MDR/RR-TB at the PMGH.

Design/Methods: Retrospective routine data from 2016 to 2021 were collected in the pediatric TB clinic. Demographics, treatment regimens, safety and outcomes are described.

Results: During the 6-year study period, there were 153 children diagnosed with DR-TB, 71.2% by Xpert MTB/RIF. The median age was 6.4 years (interquartile range [2.6-10.6]) and 49.7% were girls. Children included 8.5% living with HIV, 32.7% with an MDR/RR-TB contact, and 39.9% with previous TB treatment. Children were treated with regimens using bedaquiline/delamanid (50.7%) following availability in 2019. From 2016-2019, long injectable regimens (27.8%), long non-

injectable regimens (9.7%), short injectable regimens (10.4%), and short non-injectable regimens (1.4%) were used. Of the 113 children with outcomes, 70.8% have completed treatment, 17.7% died, 8.0% were lost-to-follow-up, 2.6% transferred out and 0.9% had treatment failure (Figure). While on treatment, 12 (7.8%) children developed hearing loss, 4 (2.6%) arthralgia, 2 (1.3%) optic neuropathy and 1 (0.6%) rash. Children receiving bedaquiline/delamanid-based regimens had routine electrocardiograms, none of whom interrupted treatment due to QTcF prolongation.

Conclusions: This is the first report on treatment outcomes in children affected by MDR/RR-TB at Port Moresby General Hospital. Despite high rates of Xpert-confirmed child MDR/RR-TB, limited resources don't allow for confirmation of cure aligned with WHO definitions, and treatment failure rates might be underestimated. Nevertheless, high completion rates highlight that children achieve favorable MDR/RR-TB outcomes when diagnosed and offered treatment, even in limited-resources, TB high-burden settings.

EP-07 Access to quality care; use of new technologies

EP-07-662 Exploring potential of existing artificial intelligence to improve TB case finding: a case study of Nigeria Correctional Center Lafia, Nasarawa State, north central Nigeria

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Background and challenges to implementation: Nigeria ranks 6th among 30 countries high TB burden in the world. TB is a deadly air-borne disease which affects the lungs primarily as well as other body organs. Prison or correctional centers are well known sources of spread of TB as a congregate setting with poor ventilation, overcrowding and limited TB preventive services. The correctional center in Lafia, Nigeria is one of such settings with such challenges.

Intervention or response: TB screening among inmates of the Correctional Center, Lafia was carried out using a digital mobile x-ray machine equipped with the latest CAD4TB software (Version 7.0) for TB screening. Presumptive TB were identified by the CAD4TB software, with scores of 50 and above and provided sputum sam-

ples for molecular testing using GeneXpert MTB RIF. Inmates who tested positive were immediately enrolled on treatment. High Score X-rays from bacteriologically negative inmates were immediately sent to a Radiologist for secondary evaluation.

Results/Impact: 503 inmates (92% male, 7% female) from the Lafia Correctional Center were screened using the digital mobile x-ray with 33 X-ray films identified as presumptive TB cases (7%) requiring further evaluation using GeneXpert. Of this number, 12 were bacteriologically diagnosed with TB and another 12 with suggestive features of TB on X-ray following radiologist review of the films. The TB yield was 4.7% with the number needed to test at 1.4 and number needed to screen at 21



Conclusions: Exploring the use of digital X-rays with CAD4TB artificial intelligence software to improve TB screening of most at risk populations for TB can be efficient in finding missing TB cases especially in countries with high TB burden. It is therefore recommended that this intervention should be scaled up across other correctional centers and similar congregate settings in Nigeria.

EP-07-663 Enabling rapid TB triage in prisons using artificial intelligence software for reading digital chest X-rays

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Background and challenges to implementation: In low-resource settings such as prisons, a mobile chest X-ray (CXR) unit is used by health teams to systematically screen hundreds of persons each day. The challenge, however, is access to radiologist reading, which can take several days after which the patients need to be traced for followup. AI allows the result to be immediately available to the screening team, using which the patient is identified, placed into isolation, and enrolled for evaluation and treatment in the same instance.

Intervention or response: Health Through Walls conducts mass TB screenings and active case finding in overcrowded prisons of Haiti using mobile digital X-ray units, which were equipped with AI CAD software qXR for automated CXR interpretation. Persons identified

with chest radiographs suggestive of TB by qXR were immediately isolated from others to reduce spread and taken forward for confirmatory testing and treatment initiation. The disease management software qTrack, maintains electronic medical records and tracks patient journeys until treatment completion.

As of May 2022, nearly 3000 individuals have been screened for TB across 5 prisons in Haiti.

Results/Impact: A sample of 166 participants who were subjected to CXR screening and having a valid confirmatory result was available for analysis. All participants were male with mean age being 33.38.

Out of 166 participants, CXRs of 104 participants (62.6%) were found to be suggestive of TB by qXR. Out of these, 81 cases (77.9%) were microbiologically confirmed with TB using GeneXpert.

The overall agreement between qXR and the microbiological confirmatory test was 62.6%. The turnaround time (TAT) for radiologist review of CXR was as much as one week while the qXR results are instantly available.

Conclusions: The analysis highlights the potential of qXR in control environments such as prison facilities due to the its rapid turnaround and acceptable agreement rate. The results are limited due to the sample size.

EP-07-664 Digitally enhanced contact investigation to increase TB case finding in 43 districts in Indonesia

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Background and challenges to implementation: Contact investigation (CI) is part of the routine TB case finding strategy in Indonesia, carried out by healthcare workers (HCWs) and community cadres. However, monitoring of CI-related activities is challenging as recording and reporting often delayed. COVID-19 pandemic has further deteriorated CI implementation, urging the National Tuberculosis Program (NTP) and all partners to intensify TB case finding. SOBAT TB is a mobile- and web-based applications developed by Yayasan KNCV Indonesia to improve access to reliable TB information and case finding. TB self-screening, as its highlighted feature, assists identification of presumptive TB and household contacts for LTBI screening.

Intervention or response: YKI through USAID's TB Recovery initiative supported the NTP to implement SOBAT TB in 43 high TB-burden districts. Training on SOBAT TB utilization has been provided to a total 1,356 healthcare workers and 1,509 cadres since Novem-

ber 2021. SOBAT TB facilitates real-time recording and reporting of CI carried out at community level. The CI results are automatically notified to the HCWs and TB program managers, allowing prompt monitoring and follow up. This accelerates TB case finding and screening for individuals eligible for LTBI. SOBAT TB that has been integrated with the NTP's information system (SITB), reduces risks of inaccurate index case data, and ensure timely reporting of CI to the NTP.

Results/Impact: From November 2021 to April 2022, a total of 49,964 contacts have been investigated from 3,177 index cases in 43 districts. A total of 1,853 presumptive TB and 1,954 contacts with other risk factors (DM or HIV) requiring TB testing. Of that 598 have been tested and 40 were diagnosed with TB. Additionally, 7,019 household contacts are eligible for LTBI screening. Of that, 171 individuals have received TB preventive treatment.

Conclusions: SOBAT TB enhances the implementation of contact investigation at community level, especially in improving the quality of recording and reporting.

EP-07-665 The use of artificial intelligence software aided chest Xray screening for community active case finding in Kano, Nigeria

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Background: World Health Organisation (WHO) has recommended that chest Xray (CXR) screening can be used for tuberculosis (TB) case finding. CXR plays a pivotal role in supporting early diagnosis of TB, since a large number of individuals with TB are asymptomatic. Development of mobile digital x-ray systems with artificial intelligence (AI), with the accumulation of a large number of medical images provides new opportunities for machine learning and establishment of computer-aided detection (CAD) systems.

Design/Methods: A cross sectional study of Community active case finding activities across the same local government areas (LGA) using 2 arms of screening entry points, CXR with AI and modified WHO TB symptom screening questionnaire between October 2020 to September 2021 was done. Participants with a cough of any duration, fever, weight loss, and night sweats screened positive as TB presumptive (symptoms screening arm), while participants with a CAD4TB score of >60 screened positive as TB presumptive (CXR screening arm). All samples tested using Xpert MTB rif Ultra. Data was analysed using SPSS v20.

Results: Sixteen LGAs had separate participants screened using both methods. 943 presumptive TB found on CXR, and 116 (12%) diagnosed with TB. For modified symptom screening 4,272 presumptive TB identified and 115 (3%) diagnosed with TB. The difference in both presumptive TB and case yield from both arms was statistically significant $X^2(1, n=42,035) = 566.04, p = 0.00$; $X^2(1, n=5,215) = 168.49, p = 0.00$. An NNT of 8 using CXR screen and 39 using symptom screen was recorded.

Conclusions: AI aided CXR screen performs better than symptom screening in correlating with bacteriologic positive TB results. A lowered NNT bears the advantage of cost saving with more efficient use of sputum cups and Xpert cartridges. Bringing to scale AI aided CXR screening would be a cost efficient way to early TB detection in similar settings.

EP-07-666 Interim result of AI-powered portable CXR in boosting TB case finding in Katsina State, Nigeria

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Background and challenges to implementation: Digital solutions have been tremendously instrumental to TB control in Nigeria with coverage ranging from quality diagnosis to treatment monitoring. Of interest is the artificial intelligence (AI) powered portable digital XRay, otherwise referred to as DLB (Delft Light Backpack). The deployment of this tool is primarily aimed at community pre-diagnostic screening for TB in Katsina State, Nigeria to boost TB case finding.

With further innovation in the context of USAID-Funded TB LON 1&2, the films from this intervention can be visually reviewed by trained radiologist to address the gaps recorded in clinical diagnosis of TB at state and national levels.

Intervention or response: DLB was first deployed to prisons in Q1 2022, being congregate setting, and later to the community. The full report for Q1 2022 from DLB intervention in the state was reviewed. In addition, a 3-year review of case notification from prison was conducted.

Results/Impact: Overall, DLB assisted in notifying 57 cases across prisons in Q1 2022, in contrast to 24 and 26 cases notified in 2020 and 2021 respectively. By extension, LON project notified 897 in its first quarter of implementation in 2020, 1,433 in Q1 2021 and 1393 in Q1 2022. This translates to 2.6% case contribution from prison in 2020 and 2% in 2021.

With the deployment of DLB, the contribution doubled to 5%. Interim result from community screening shows 53 cases from 1732 screened populace translating to 3.0% yield. All these mean increased TB case finding in the state.

Conclusions: DLB has the potential to facilitate increased TB case notification which is invariably a predictor of effective TB control in line with the END TB strategy. National TB programs are encouraged to scale up the technology.

EP-07-667 WOW truck as a mobilization tool for community tuberculosis active case finding in Northern Cross River: comparing WOW truck and DLB

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Background and challenges to implementation: The wellness on wheel truck “WoW” is a special intervention, operationalized on a mobile truck housing a digital x-ray machine, and the Delft-light Backpack “DLB” is a portable digital x-ray machine that could be transported on motorcycle, both are usually deployed for TB community active case finding.

This study reveals the impact of the truck as a tool for mobilization and service patronage in face of low utilization of TB services In Northern Cross River State.

Intervention or response: The WoW and pilot DLB interventions are under the USAID-funded KNCV TB LON Regions 1 & 2 project in Nigeria, they are deployed for Tuberculosis active case finding (TB ACF) in the same local government area (LGA) after a one umbrella advocacy and community mobilization visits.

They both provide TB services ranging from clients screening, identification, and testing of presumptive and diagnosed cases are linked to treatment and notification to national tuberculosis program (NTP). In Northern Cross River State, TB ACF was carried out from January-March 2022 in 3 LGAs. Data was reviewed to compare client’s patronage among the 2 equipment.

	WOW	DLB	TOTAL	% WOW CONTRIBUTION
Screened	7840	2608	10488	75
Presumptive identified	632	283	915	69
Presumptive evaluated	630	281	913	69
Diagnosed TB cases	115	43	158	73
Treatment and notified to NTP	113	43	156	72

Table. January to March 2022

Results/Impact: A total of 10,488 clients were screened, 915 presumptive TB were identified and 911 of them evaluated out of which 158 TB cases were diagnosed, 156 were placed on treatment and notified to NTP. The

WOW truck contributed to 75%, 69% and 73% of screened, Presumptive and TB cases diagnosed. Communities received similar information prior to outreaches, but client’s patronage were higher for WOW truck.

Conclusions: Results from this study shows that client’s preference for WOW truck services are more compared to DLB, this advantage could be leveraged for more service delivery to communities

EP-07-669 “I am not working, even all my dreams are gone”: qualitative study to explore views regarding socioeconomic consequences associated with TB in rural Tanzania

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Background: Tanzania is among the 30 WHO identified high TB burden countries. The recent national TB patient cost survey showed that 44.9% of Tanzanians with TB faced catastrophic costs. We conducted qualitative interviews to understand the socioeconomic consequences of TB and impact on care seeking behaviour.

Design/Methods: This was a cross-sectional study nested in a multi-country, observational cohort study conducted in four African countries among adults (≥18 years) with pulmonary TB (TB Sequel).

During October-March 2021, we conducted interviews with TB patients or survivors and family to explore their experiences of the socioeconomic impact of TB. Participants were purposively selected and consented. Thematic analysis was used to identify and analyse main themes.

Results: Most respondents (30/57; 53%) reported facing financial and social consequences before, during and even after treatment. These included lack of money for transport/food while seeking care and self-perceived social stigma and discrimination. Direct medical (e.g., over the counter medication) and non-medical (e.g., transport/food) factors were viewed as obstacles to early treatment initiation.

Respondents expressed concern about their inability to participate in income production activities whilst sick or while seeking care. Consequently, this inability impacted food insecurity and financial hardship further. Some respondents reported using their savings to provide necessities, reducing the financial strength of the household even further. This financial burden then hampers the ability to seek or remain in TB care.

Often the most vulnerable sought care at traditional health practitioners which resulted in increased pre-diagnosis costs and delays in diagnosis leading to severe disease presentation, and increases in morbidity and mortality.

Conclusions: TB is known to be a disease of the poor. The End TB Strategy may not be fully realized if underlying social determinants of TB are not addressed. Appropriate social protection interventions should also be identified to mitigate the socioeconomic impact of TB.

EP-07-670 Food insecurity and asset sales: overcoming TB-related household expenditures in Ethiopia

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Background and challenges to implementation: As a chronic illness, TB can cause physical, social, and economic complications. TB related consequences can be seen at onset of the illness, as well as during and following treatment. Impacts can be worse in poorer segments of the population and in low-income countries like Ethiopia. This study aimed to determine the consequences of TB and coping mechanisms in Ethiopia.

Intervention or response: Using the standardized World Health Organization TB patient cost survey tool, a facility-based cross-sectional study was carried out in four regions of Ethiopia that are supported by the USAID Eliminate TB Project. TB patients were randomly selected, and the consequences of TB and coping mechanisms were described.

Results/Impact: Of the 403 TB patients that participated, 165 (40.8%) faced food insecurity, 157 (38.8%) lost their job, and 126 (31.2%) faced social exclusion or stigma. In addition, 63 (15.7%) TB patients reported that at least one member of their household temporarily withdrew from school because of TB. About 27.6% of TB patients used bank savings and cash to pay for the diagnosis and treatment of TB while 32.3% of patients borrowed money for these services. About 61.7% of patients sold assets, such as livestock and jewelry, to pay for the costs incurred due to TB illness and pay for household expenses.

Conclusions: Two-fifths of the TB patients and their households faced food insecurity and two-thirds sold their assets to overcome TB-related household expenditures. Collaboration between the National TB and Leprosy Program with the health insurance system is essential to establish social and community-based health insurance to avert the TB-related social consequences in Ethiopia.

EP-07-671 Impact of a digital adherence support intervention on TB treatment outcomes in a nomadic population: a case study of five facilities in Karamoja subregion, Uganda

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Background and challenges to implementation: There is evidence that mobile health technologies (mHealth) improve treatment outcomes among patients on Tuberculosis treatment. We assessed the impact of an mHealth tool (*CallforLife*[®]) on treatment outcomes among patients diagnosed with TB in a nomadic population in the Karamoja sub region-North Eastern Uganda.

Intervention or response: In 2020, the Infectious Diseases Institute (IDI) supported by the United States Agency for International Development (USAID) implemented the *CallforLife*[®]-(CFL) tool at five selected health facilities in the Karamoja subregion.

The CFL tool uses Interactive voice response technology (IVR) to send out pill reminders and clinic visit reminders to TB patients and records patients' adherence to TB medicines and subsequent treatment outcomes.

For this analysis, we compared treatment outcomes among patients who received the CFL intervention to overall treatment outcomes at the five health facilities.

We abstracted data for this analysis from the national district health information database (DHIS II). The proportion of patients successfully completing treatment was compared using Pearson's chisquare test.

Results/Impact: From October 2020 to March 2021, 210/458 patients at the five health facilities were enrolled on the CFL tool. Of these 62% were male and 50% had bacteriologically confirmed TB. There was no difference in age and sex between patients who were enrolled on the CFL tool and those who were not.

The proportion of patients successfully completing treatment was higher among patients enrolled on CFL compared to the overall number treated for TB at that health facility 91% vs 84% p<0.01.

Further, the proportion of patients lost to follow-up was lower among patients enrolled on CFL (4% vs. 8%; p = 0.03).

Conclusions: The implementation of CFL, a digital adherence tool was associated with improved treatment completion among patients diagnosed with TB in the Karamoja subregion.

EP-08 Access to quality care; improvements in case finding and early diagnostics

EP-08-672 Role of specimen referral systems on early detection of rifampicin resistant tuberculosis in Afghanistan

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Background and challenges to implementation: A significant challenge in Afghanistan is high rates of drug-resistant tuberculosis (DR-TB) in 2021, the case detection rate for DR-TB was 18%. Specimen referral systems play a critical role in ensuring access to laboratory services by allowing people with TB to receive care and treatment at one location, while their specimens are transferred to various levels of a tiered laboratory system for testing.

In 2017, the National TB Program (NTP) introduced and implemented sputum referral systems in 24 Afghan provinces to detect TB/Multi Drug Resistant-TB (MDR-TB). The study aimed to explore the role of sputum sample transportation on DR-TB case notification in Afghanistan.

Intervention or response: The NTP, with assistance from United States Agency for International Development (USAID)-funded and Global Fund (GF) TB projects, developed sample transportation guidelines and assessment tools, job aids to guide health care workers (HCWs), and register book. Among these 775 sites, 515 smear microscopy sites were involved in the sample referral and transportation mechanism to the GeneXpert sites for all suspected MDR-TB cases according to the country algorithm. Trained HCWs transported the samples to GeneXpert sites according to sample transportation guidelines and established incentive modalities supported by GF.

Results/Impact: From 2017-December 2021, a total of 34,735 sputum samples were transported from 852 health facilities to 77 GeneXpert sites. Of these, 32,206 (93%) were new bacteriologically confirmed TB (BC-TB) cases, and 480 (1.5 %) of them were diagnosed as Rifampicin Resistance (RR). Additionally, 2629 (7%) samples tested were previously treated TB cases, and 212 (8%) of them were detected as RR-TB.

Conclusions: Through the smooth implementation of specimen referral systems, NTP detected more TB/RR-TB cases and began treatments. We recommend expanding the system to all 775 smear microscopy sites to detect TB/RR cases to reach national TB/MDR-TB targets.

Variables	2017	2018	2019	2020	2021	Total
Number of samples transported for Xpert testing	500	6550	8467	9112	10106	34735
Number of new Bacteriological conform TB cases	150	6350	7863	8180	9663	32206 (93%)
Number of previously treated TB cases tested	350	300	604	932	443	2629 (7%)
Number of RR detected among New Bacteriological conform TB cases	25	115	118	95	127	480 (1.5%)
Number of RR detected among Previously treated TB cases	45	23	52	49	43	212 (8%)
Total Number of RR detected from all samples referred	70	138	170	144	170	692 (2%)

EP-08-673 Pre-treatment loss to follow up in adults with pulmonary tuberculosis: a qualitative evidence synthesis of patient and healthcare worker perspectives

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Background: Since 2018, over 14 million people have been treated for tuberculosis (TB) globally. However, pre-treatment loss to follow-up (PTLFU) has been shown to contribute substantially to patient losses in the TB care cascade with subsequent high community transmission and mortality rates. This qualitative evidence synthesis (QES) aimed to identify, appraise, and synthesize evidence on the perspectives of patients and healthcare workers on PTLFU.

Design/Methods: We registered the title with PROSPERO. We searched nine relevant databases up to 24 May 2021 for qualitative studies. Two review authors independently reviewed reports for eligibility and extracted data. We assessed methodological quality with the Evidence for Policy and Practice Information Center tool and synthesized data using the Supporting the Use of Research Evidence framework.

We assessed confidence in our findings using Confidence in the Evidence from Reviews of Qualitative Research (GRADE-CERQual).

Results: We reviewed a total of 1239 records and included five studies, all from low- and middle-income countries. Key themes reported by patients and healthcare workers were knowledge, attitude, and skills on TB and its management; healthcare workers' motivation to follow up with patients experiencing PTLFU; accessibility

and availability of facilities for TB care; resource and financial constraints; and communication challenges in the TB care cascade.

Poor communication between healthcare workers and patients caused by human resource and financial constraints was a key contributor to PTLFU. This, in turn, affected their interactions with patients. Using GRADE-CERQual, we had moderate confidence in most of our findings.

Conclusions: Our QES suggests that multiple factors related to patients, healthcare workers, and the healthcare system contribute to PTLFU. For optimal care, it will be necessary to improve healthcare worker-patient communication and address constraints faced by healthcare workers. TB services should be made available and accessible to patients by eliminating barriers such as poor referral systems and long waiting times.

EP-08-674 Implementation of the revised and updated TB contact investigation strategy in the Kyrgyz Republic

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Background and challenges to implementation: The TB contact investigation (CI) system in Kyrgyzstan was sub-standard and required improvements. Specialists of the Sanitary and Epidemiological Service (SES) conducted CI in only 50% of index cases, used microscopy results to identify index cases and made no household visits to identify contacts. Evaluation of TB contacts were performed once with no 24-month follow-up monitoring. On average, there were 2.6 contacts per index case and with 1.6% active TB cases identified among them. In addition to this evidence of ineffective TB CI, there were no uniquely designed data collection and reporting forms available to provide data on TB CI.

Intervention or response: The USAID Cure Tuberculosis Project helped to revise and update the TB CI processes by:

1. Including Xpert results are in criteria for index case;
2. Updated CI protocols to that in-person visit and permanent residence with each index case is now required.
3. Recruited and trained independent epidemiologists for extended CI protocol;
4. Revised the protocol for the examination of TB contacts at PHC;
5. Developed data collection and reporting forms for TB CI; and,

6. Trained PHC specialists on extended CI protocol.

Results/Impact: The implementation of the updated TB CI strategy was launched in two pilot regions in 2021. 90% of the identified index cases were covered by CI. On average, 4.4 contacts were identified for each index case, with 4.6% with active TB and 69.6% were children under 14.

Conclusions: The updated TB CI strategy in the Kyrgyz Republic has helped to increase the number of contacts and increase active TB cases detected among contacts, including children under 14 years of age.

EP-08-675 Improving bacteriological diagnosis of TB in resource-challenged high-burden primary healthcare centres using the Truenat: an early experience in south-south Nigeria

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Background and challenges to implementation: Nigeria has an estimated 400,000 incident TB cases according to Global Tuberculosis Report 2021. Diagnosis of tuberculosis (TB) remains difficult in resource-limited settings. WHO-recommended nucleic acid amplification tests (NAATs) offer rapid results, with diagnostic systems with infrastructural requirements suitable to resource limited settings for rapid diagnosis of MTB and detection of rifampicin resistance. We present our experience in adapting TrueNat in the real local settings in Nigeria.

Intervention or response: Nigeria has an estimated 400,000 incident TB cases according to Global Tuberculosis Report 2021. Diagnosis of tuberculosis (TB) remains difficult in resource-limited settings. Primary Healthcare (PHC) facilities in rural resource-limited settings were identified using the standardized National TB Programme-approved assessment checklist. Selected laboratory staff were trained as focal persons (FPs) and sites linked to the National Integrated Samples Referral Network (NiSRN) for sputum sample movement. The number of tests performed using TrueNat Duo was tracked from installations in December 2021. Laboratory FPs were interviewed to assess operational feasibility and challenges in the field.

Results/Impact: 1,965 presumptive cases were tested using TrueNat Duo, 128 TB cases detected, and 2 cases identified as rifampicin-resistant between December 2021 and March 2022. FPs identified poor power supply in rural settings as a major challenge. Despite being portable and battery-operated, the TrueNat system requires recharging. About 4-5hours of constant power supply is needed to power the batteries to full charge. The unavailability of external quality assurance (EQA)

mechanism for TrueNat testing was also an issue.

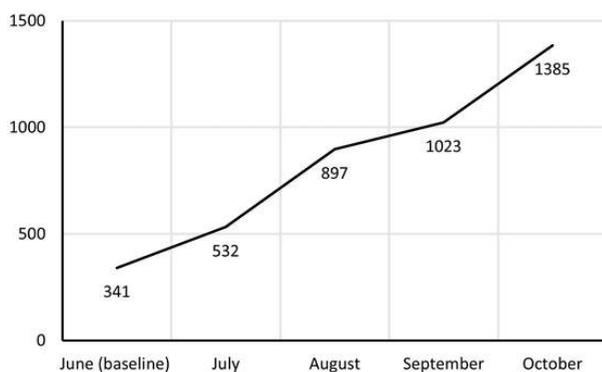
Conclusions: Deployment of TrueNat contributed to TB case detection in resource-challenged settings. Portable, mobile solar packs may improve its use in PHC and field settings for community outreaches. An EQA system is needed to validate the quality of results and competency of laboratorians involved in testing.

EP-08-676 Improving TB case finding in hospital outpatient departments: lessons from active TB screening in Nigeria urban slum areas

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Background and challenges to implementation: Nigeria has one of the highest tuberculosis (TB) burden in the world. Urban slum residents, numbering as high as 50 million in Nigeria, have been identified as a key affected population in recent strategic planning. However, questions remain about TB epidemiology in urban slums including how quickly intensified case finding interventions in hospital outpatient clinics could increase TB detection in this setting given ongoing transmission, a high HIV burden, and other social and economic factors.

Intervention or response: KNCV, through the USAID-funded TB LON project implemented active TB screening in hospital out-patient clinics in urban slums across 4 states in Nigeria to detect and predict TB disease. The targeted strategy involved capacity building, multi-symptom TB screening to identify early TB disease, specimen transport mechanism to laboratories, provision of laboratory tools and human resource support for TB diagnostics, capacity building for healthcare workers, and electronic data system for real-time performance monitoring. We reviewed the implementation data for the intervention period from July to October 2021 and compared monthly TB yield with baseline.



Results/Impact: In the month before this intervention started, the 28 hospitals notified 341 TB cases. During the intervention period, monthly TB notification increased from 562 in July to 1,385 in October, representing an average increase of 181% in TB case notification compared to the baseline (341). TB yield among tested was highest in clients attending the general out-patient department (19.5%), paediatric out-patient department (18.5%) and ART clinic (14.8%) but least among antenatal (5.1%) and accident and emergency (4.4%) clinics.

Conclusions: Depending on whether higher TB burden in urban slums in Nigeria is attributable to higher transmission or reactivation rates, active TB screening of hospital outpatient department attendees in urban slums significantly improved TB case finding. Innovation using real-time electronic data capture and analysis played a critical role in optimal performance monitoring.

EP-08-677 LTBR efforts to find missing persons with TB through monthly cough days in Sofala, Mozambique

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Background and challenges to implementation: Sofala is a province in central Mozambique divided by a corridor that connects the sea and the neighboring countries in the sub region of the continent. Districts located along the corridor are privileged with easy access to all facilities due to short distances and good roads differently of districts in north and south regions of the province, facing great challenges due to very long distances and poor access roads. Active Case Finding (ACF) activities are implemented at community and Health Facility (HF) levels, but there is a need to improve bringing innovative approaches to find more people with TB, targeting remote communities and high risk groups.

Intervention or response: Local TB Response is implementing ACF activities in 10 out of 13 districts in the province through Community activists and clinicians. In close coordination with Health Provincial Directorate (DPS), the project is conducting Monthly Cough Days (MCD) - a model of mobile clinic, integrating project and HF staff (clinician and lab technician), reaching selected communities previously mobilized to provide TB services (education, screening, sample collection to lab facilities and contact screening for contacts of persons with TB living in those communities). MCD are also conducted at district level prisons, targeting prisoners and guards with TB services.

Results/Impact: From Jan 2020 to March 2022, MCD were conducted in all 10 districts providing TB services to communities and prisons. A total of 6,360 persons

were reached with TB messages and TB screening, 25% (1,581/6,360) were identified with TB signs and symptoms and were investigated for TB. AS result of investigation, 22% (341/1,581) were diagnosed with TB with 33% (112/341) TB BC.

Conclusions: ACF through Monthly Cough Days mobile clinics targeting selected remote communities and high risk groups, is one of the strategies to find missing people with more yield (1 person with TB for each 5 screened).

EP-08-678 TB case-detection and notification in 3 correctional facilities in the Hhohho region of Eswatini

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Background and challenges to implementation: Eswatini's TB incidence is 319/100 000 (WHO, 2021), however, from March 2018 to April 2021, the 3 EGPAF-supported correctional clinics notified 0 TB cases, raising questions about the extent and quality of TB screening.

Intervention or response: Between May 2021 and September 2021, EGPAF, collaborating with NTCP, conducted refresher training for all 3 correctional clinics. Mass TB screening campaigns were thereafter conducted across all 3 facilities.

One facility approved screening of officers as part of the campaign. Health talks on sputum production were conducted for those with presumptive TB. Sputum samples were then collected and tested using Xpert MTB/RIF Ultra.

Those that could not produce sputum were referred to hospitals/health centres for clinical diagnosis. All contacts of confirmed TB cases were also evaluated for TB. Data was obtained from facility registers as part of routine data collection.

Results/Impact: 72 clients had TB signs/symptoms. 21/72 (29%) produced sputum, that was sent to the lab for testing. 3/21 (14%) active TB cases were detected and notified, 1 from each of the correctional clinics. 51/72 (71%) presumptive TB cases were referred to hospitals/health centres for clinical evaluation and TB was ruled out. Due to identification of active TB, quarterly TB screening campaigns and daily high-quality screening at the correctional clinics were adopted. Consequently 3 more cases were identified, by March 2022.

Conclusions: In a high TB incidence setting, correctional facilities should not continuously notify 0 cases. Daily high-quality TB screening at the correctional clinics and quarterly mass TB screening campaigns, with contact

tracing, are feasible, and promote early case-detection and treatment, which improve infection-prevention for inmates and officers. Other correctional facilities should emulate these practices.

EP-08-679 Am I TB-free?: changing the future course of TB using digital self-assessment tool for screening

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Background and challenges to implementation: Health self-assessment serves as a game-changing tool to initiate a patient's pathway to care. As digitalization transforms social and behavior change communication amidst the COVID-19 crisis, digital technologies for health must also evolve. A study found that a self-rated health questionnaire (SRH) can be a reliable indicator to assess the general health of a country's population.

Intervention or response: This study assessed the risk of TB using online self-administered TB screening tool among adult users. The tool's functionality, validity, and reliability, including initial findings from 9-month implementation were determined. The tool is composed of 10 questions asking users of their signs, symptoms, and risk factors for TB. It has an embedded algorithm that can provide a clinical recommendation to its user. The user is provided a list of facilities that they can visit for further testing.

	Female (n=4,036)	Male (n=2,068)	Total (n=6,104)
Age group			
20 and less	275 (6.8%)	171 (8.3%)	446 (7.3%)
21 to 40	2,878 (71.3%)	1,448 (70.0%)	4,326 (70.9%)
41 to 60	778 (19.3%)	374 (18.1%)	1,152 (18.9%)
above 60	105 (2.6%)	75 (3.6%)	180 (2.9%)
Previous Chest X-ray			
Yes	3,180 (78.8%)	1,510 (73.0%)	4,690 (76.8%)
No	856 (21.2%)	558 (27.0%)	1,414 (23.2%)
With at least 1 TB symptom			
Yes	2,313 (57.3%)	965 (46.7%)	3,278 (53.7%)
No	1,723 (42.7%)	1,103 (53.3%)	2,826 (46.3%)
With at least 1 TB risk factor			
Yes	1,045 (25.9%)	323 (15.6%)	1,368 (22.4%)
No	889 (22.0%)	443 (21.4%)	1,332 (21.8%)
N/A	2,102 (52.1%)	1,302 (63.0%)	3,404 (55.8%)
Recommendation			
Annual Chest Xray	1,045 (25.9%)	323 (15.6%)	1,368 (22.4%)
GeneXpert	2,102 (52.1%)	1,302 (63.0%)	3,404 (55.8%)
Immediate Chest x-ray	889 (22.0%)	443 (21.4%)	1,332 (21.8%)

Table 1. Characteristics of users of online self-assessment tool.

Results/Impact: Sixty-eight online users were included in tool pretesting, 95% of them found it was relevant and 91% would recommend it to others. Tele-health consultation with TB doctors served as the gold standard for validity. Sensitivity was 75% and specificity 100%.Kappa (a) statistic was 0.85 ($p < 0.0001$) for reli-

ability. The tool was found to have 97%-100% concurrence with doctors' findings and 99% concurrence with their recommendations ($p < 0.0001$).

During the 9-month implementation, 6,104 users accessed the tool of which 66% were female. Fifty-four percent had at least 1 TB symptom, 76.8% had chest X-ray (CXR) in the past year, and 22% reported at least 1 TB risk factor. Within the tool's recommendation for either "Immediate CXR", "Annual CXR", or "GeneXpert test", 56% of the total users were advised to undergo rapid TB diagnostic testing.

Conclusions: Based on sensitivity and specificity tests, the online self-assessment tool is a reliable tool for online users who aim to know about the status of their lung health.

EP-08-680 Establishing specimen transportation model to ensure access to TB diagnosis in Chernihivska oblast, Ukraine

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Background and challenges to implementation: In Ukraine, inefficient or nonexistent specimen transportation systems delay access to TB diagnostics. Service re-prioritization due to the COVID-19 pandemic worsened this situation for TB patients, particularly those in remote areas. Thus, the diagnosis of bacteriologically confirmed pulmonary TB dropped in Chernihivska oblasts by 62% between April–June 2020 compared to the prior quarter.

Intervention or response: To ensure access to TB and HIV diagnosis, treatment, and monitoring, the USAID-funded Support TB Control Efforts in Ukraine Project (STBCEU) established a transportation model in project-supported regions in Ukraine.

The system transports specimens for TB and HIV diagnosis and treatment monitoring, COVID-19 tests, and TB and ART drugs when required. Established to improve TB diagnostics, the system has been developed to work across disease areas.

Rayons deliver samples to facilities, where the transportation system collects them for delivery to GeneXpert facilities and oblast TB dispensary. STBCEU developed an SOP for all steps, including sample collection, storage, transportation, and results notification. The system is regularly monitored and adjusted as needed.

The transportation model launched in Chernihivska oblast in December 2020, with six routes covering the region.

Results/Impact: In 2021, the transportation system in Chernihivska oblast conducted 216 trips and covered 75,915 km. It delivered 1,308 samples for TB diagnosis: 10% ($n=126$) TB samples were found MBT positive and 25% ($n=32$) had Rif+ results.

Overall, the transportation system was responsible for the diagnosis of 34% of all bacteriologically confirmed pulmonary TB cases and 53% of all Rif+ cases in Chernihivska. By the end of 2021, Chernihivska oblast achieved 71% of its pre-COVID detection rate.

	Total TB case notifications in the oblast		TB case notifications attributed to transportation system (n [% of total])	
	Bac. confirmed cases	Rif+ cases(#)	Bac. confirmed cases	Rif+ cases
Jan–Mar, 2021	98	21	29 (30%)	11 (52 %)
Apr–Jun, 2021	86	14	35 (41%)	7 (50 %)
Jul–Sep, 2021	95	17	35 (37%)	8 (47 %)
Oct–Dec, 2021	92	8	27 (29 %)	6 (75 %)
TOTAL	371	60	126 (34 %)	32 (53 %)

Table. Transportation system contribution to bacteriologically confirmed and Rif+ cases in Chernihivska oblast, January–December 2021.

Conclusions: STBCEU's successful integrated specimen transportation system pilot has aided continuity of TB diagnosis in the region. Through advocacy and guidance to national partners, the system was replicated and expanded to all 12 project regions, four of which fund the system from their budget.

EP-08-681 Strategic planning to expand access to GeneXpert diagnosis network using laboratory spatial analysis in Vietnam

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Background and challenges to implementation: Rapid and accurate TB diagnosis is essential for effective TB care and epidemic response. The USAID-funded Infectious Disease Detection and Surveillance (IDDS) project analyzed the demand and access to GeneXpert (GX) testing in Vietnam to inform procurement and placement of instruments.

Intervention or response: Microscopy and GeneXpert testing data and geospatial data were used to determine the current testing capacity and analyze coverage, accessibility, and allocation of the diagnostic network with small- and large-scale expansion to meet anticipated demand. The expected demand was estimated using the number of patients using smear microscopy in 2019 per facility.

The population coverage of GX testing service in Vietnam was analyzed by determining the population percentage residing within a 5–50km radius of:

- a. An existing GX facility,
- b. Existing/additionally planned GX facilities, and;
- c. Any TB facility in Vietnam.

To assess GX network accessibility, the proportion of non-GX facilities located beyond feasible driving distance were analyzed, based on:

- a. Existing GX facilities and;
- b. Existing/additionally planned GX facilities.

Rifampicin resistance and screening activities/algorithms using CXR were not included.

Results/Impact: Using a generic method based on epidemiologic context and program targets, an estimated 1.38–1.42 million cartridges would be required to identify 75% of estimated incident and retreatment cases at coverage of 75%. Estimates based on program data are lower, and range from 0.99–1.13 million cartridges per year. Vietnam will require 1,200 GX modules and at least one million GX cartridges per year to replace microscopy as the initial diagnostic test for TB and rifampicin-resistant TB.

Reported performance		Algorithm: Xpert/AAT & basic HV cartridges	Algorithm: Xpert/AAT & extended HV cartridges	Algorithm: Xpert/AAT & basic HV cartridges			Algorithm: Xpert/AAT & extended HV cartridges		
Target case finding (as % of estimated)	Target AIT coverage as % of estimated PLWV enrolled plus 7.5% repeat	Cartridges required per year	Cartridges required per year	Module capacity required per year					
				Medium utilization	High utilization	Low utilization	Medium utilization	High utilization	Low utilization
75	75	2,285,796	1,924,156	1838	1492	3574	1892	1471	2648
	plus 7.5% repeat	1,843,306	1,423,511	1926	1557	3767	2036	1582	2847

Projected performance		Algorithm: Xpert/AAT & basic HV cartridges	Algorithm: Xpert/AAT & extended HV cartridges	Algorithm: Xpert/AAT & basic HV cartridges			Algorithm: Xpert/AAT & extended HV cartridges		
Target case finding (as % of estimated)	Target AIT coverage as % of estimated PLWV enrolled plus 7.5% repeat	Cartridges required per year	Cartridges required per year	Module capacity required per year					
				Medium utilization	High utilization	Low utilization	Medium utilization	High utilization	Low utilization
80	80	1,935,455	1,386,015	2198	1709	3077	2270	1766	3118
	plus 7.5% repeat	1,553,610	1,106,213	2363	1856	3308	2440	1896	3416

Table 1: Projected No. of cartridges and modules needed per year if Xpert is used as initial diagnostic test for all presumptive TB patients. (upper) at 75% performance target, (lower) at 80% performance target. Low utilization: 500 tests per module and year, medium utilization: 700 tests per module and year, high utilization: 900 tests per module and year.

Table 1.

Conclusions: This spatial analysis provided a framework for Vietnam NTP's efficient and targeted GX expansion. Geospatial analysis of coverage and accessibility showed that strong linkage of all non-GX and GX facilities is needed to reach high population coverage, which could be achieved through a nationwide specimen referral system.

EP-09 TB Access to quality care; the importance of integrated care and the involvement of the private sector

EP-09-682 Engaging indigenous community-based organizations can improve access to TB care services; lessons from the Karamoja subregion, North Eastern Uganda

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Background and challenges to implementation: Community based active case-finding interventions increase the scope of TB care services by reaching key vulnerable populations with limited access to healthcare services. Engaging indigenous organizations to provide care to communities increases acceptability and ownership of healthcare services.

We aimed to document the contribution of an indigenous community-based organization to TB care in Nakapelimoru Subcounty, Kotido district, Karamoja subregion, North-eastern Uganda.

Intervention or response: The Warrior Squad Foundation (WSF) is a community-based organization serving the indigenous population of Nakapelimoru subcounty. Nakapelimoru is one of the sub-counties with the lowest TB case detection rates in the region. The Program for Accelerated Control of TB (PACT) in Karamoja funded by the United States Agency for International Development (USAID) trained and supported the WSF team to carry out; community dialogues on TB, door-to-door TB screening, contact tracing, linkage of diagnosed TB patients to treatment and support for linkage to treatment and retention in care to patients diagnosed with TB.

Results/Impact: From July 2021-March 2022, the WSF engaged 9,000 community members in TB dialogues. About 8,500 community members were screened for TB and referred 296 of those presumptive with TB for sputum examination. A total of 39 TB patients were identified and started on treatment up from seven (7) during the previous nine Months (Figure 1).

Conclusions: Engaging a local community-based organization resulted in an exponential increase in the number of patients diagnosed with TB in Nakapelimoru subcounty. This intervention should be scaled up to reach vulnerable populations.

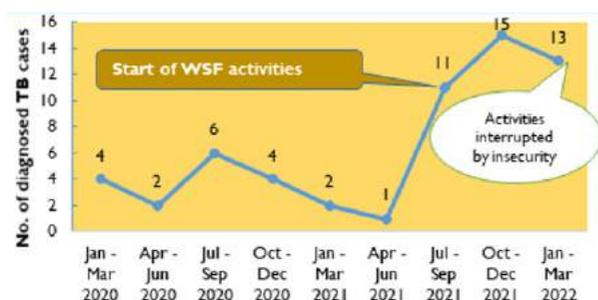


Figure 1. Trend of newly diagnosed TB cases in Nakapelimoru Sub county.

EP-09-683 Public-private mix for tuberculosis faces challenges and opportunities in Ethiopia

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Background and challenges to implementation: Engaging all care providers is a key component to end the tuberculosis (TB) epidemic. In Ethiopia, the engagement of private providers increased from 20 in 2006 to over 1,000 in 2021, but their contribution to TB case detection remained low at 15-17%. Hence, this study describes the challenges and opportunities for improvement.

Intervention or response: A structured tool was used to collect information from 199 public-private mix (PPM) facilities in four regions (42 towns) by the USAID Eliminate TB Project in October 2021. Reports and manuals were reviewed to supplement the findings.

Results/Impact: About 37% (42/113) PPM sites had no anti-TB drugs, 47% (94/199) had not participated in EQA in the last 6 months, and 59% (117/199) were not linked for sample transport. Forty-seven percent (85/199) of sites have no trained provider, and 22% of PPM-DOTS sites have no unit TB registration book indicating that PPM sites are not considered during distribution of recording materials.

Inadequate investment in the PPM program is one of the challenges to expanding to new sites. The current national PPM TB model does not consider incentivizing the private sector. The Ministry of Health signs an agreement with PPM sites to provide drugs and commodities free of charge.

The current community-based health insurance (CBHI) in Ethiopia is also not practically considering beneficiaries from the private sector.

Conclusions: PPM sites are not adequately supported by the district health system, resulting in low contribution from these sites. Hence, PPM sites could fully be embraced and integrated into the Primary Health Care Unit support system to maximize their contribution in TB case notification. It is advisable to pilot incentivized performance-based PPM models for a sustainable PPM TB program either through CBHI or other means.

EP-09-684 Does gender-based violence (GBV) exist within TB settings? Lessons learned from Kano State

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Background and challenges to implementation: KNCV TB LON 1& 2 project continued to collaborate with the Integrated Child Health and Social Services Award 3 (ICHSSA3) a USIAD Implementing partner, to conduct community gender-based activities in Kano state. Planning meetings were held at the state level with all the Community Base Officers (CBOs) from both USAID partners in attendance in a bid to synergize activities that would yield high screening outcomes for both Tuberculosis (TB) and Gender-Based Violence (GBV) activities.

Intervention or response: A 2-pronged approach was initiated for both GBV and TB screening integration during enrollment visits. With the assistance of the KNCV Wellness on Wheels (WoW) Truck, large numbers of people are screened for both TB and GBV. Harmonization of both TB and GBV data is done monthly to validate and follow-up manage patients appropriately.

Results/Impact: From April 2020 -March 2022 of collaborative activities, the intervention yielded 914 clients who have been reached as part of the targeted population. This is a result from a six-days combined field screening activity.

This activity was able to reach 7603 clients who were screened for TB of which 203 were screened for GBV. From those reached, 203 (2%) were screened for GBV. Of the persons screened, 3186 were presumed to have TB. Total TB cases evaluated 2898 of which 211 were diagnosed to have TB. GBV yield among total cases diagnosed was 1.4% (3 cases).

Of the 3 patients exposed to GBV, one (1) was positive for HIV and one (1) was a malnourished child. All exposed patients were referred for GBV care and management by ICHSSA 3.

Conclusions: The results of collaborative effort suggests the possibility of missed GBV cases within TB settings. It is optimistic that more GBV cases will be uncovered if these collaborative field activities are continually implemented at a larger coverage within Nigerian communities.

EP-09-685 Integrative health care approach for vulnerable indigenous communities of southern Mexico: a right to care and education in tuberculosis response

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Background and challenges to implementation: According to the World Health Organization (WHO), there were between 23,000 and 39,000 new cases of TB in Mexico in 2020, 6.2% were reported in indigenous communities. Comprehensive assessment in the progress of vaccination and intentional tuberculosis (TB) screening, early diagnosis and treatment, and the development of educational person-centered training tools for vulnerable indigenous communities is limited. This poster presents data gathered by the NGO Medical IMPACT during seven health brigades conducted in 2021 and 2022, in difficult-to-reach regions of southern Mexico, where access to essential TB prevention and care is seriously affected and local health services are unavailable.



Intervention or response: Deployment of health brigades, each consisting of 15 -18 healthcare providers (HCPs) to selected communities living under multiple vulnerabilities, with a big indigenous population, across the states of Guerrero, Oaxaca, Puebla, and Yucatan. For a two-week period, health care diagnosis and treatment stations were placed. Workstations prioritized TB related symptoms and signs. When necessary, nursing would screen and vaccinate for BCG. Other vaccines were available through a cold network process.

Results/Impact: Health brigades had a wide reach; almost 4,000 health interventions were conducted; vaccination regimens were completed and reinforced with 1,314 applied vaccines; 2 people were referred to the public sector and CENAPRECE to be evaluated for TB; and 50 educational sessions were held.

Conclusions: Despite the heterogeneity of the visited communities, the irregular supply of vaccines and infrastructure challenges were recognized as factors affecting communities' health. Although we encountered technical obstacles, the focus on risk groups made it possible to reach individuals who required vaccination and refer those who needed to be evaluated for TB to the public sector and CENAPRECE. By combining efforts with culturally integrated didactic material, communities were able to obtain a better understanding of vaccination and TB, as well as dispel myths, and inaccurate beliefs and preconceptions.

EP-09-686 Assessing the key barriers for improving the chest radiography testing of people with TB like symptoms (PTS) identified by the informal providers - RIPEND project experiences

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Background: TB-ALERT INIDA with funding support from the Stop TB Partnership's TB Reach Wave 6 grant implemented a project to enhance the quality of TB care for patients seeking medical care from informal providers. An intervention called 'Sampark Dhatha' was implemented in which a local public transporter is engaged to ferry patients with TB symptoms to health facilities with Chest X-Ray facilities. To ascertain the challenges faced by informal providers in getting Chest X-Ray done for their PTS and to describe the uptake of the 'Sampark Dhatha' intervention by PTS a mixed method parallel design study was taken up.

Design/Methods: The qualitative part involved interviews with informal health care providers to ascertain the challenges they face in getting their patients undergo chest X-Ray. The quantitative part involved description of the routine project data on the number of Sampark

Dhathas engaged, number of trips made by the sampark dhathas, number of persons with TB symptoms transported, number of patients who underwent chest X-Ray and the number of patients who were diagnosed on TB.

Results: Nonavailability of Chest X-Ray facilities in the nearby health facilities, concerns for cost incurred by patients in visiting & getting it done at a private health facility and the lack of capacity of the informal providers to read Chest X-Ray reports were some challenges. During the period April 2020 to September 2021, 5 Sampark Dhathas were engaged under the RIPEND project. They made 227 visits transporting 1635 patients to health facilities to undergo Chest X-Ray. Of the patients transported, 357 (22%) were diagnosed with TB.

Background and challenges to implementation: TB-ALERT INDIA, a non-governmental organisation, with funding support from the Stop TB Partnership's TB Reach Wave 6 grant is implementing a project to enhance the quality of TB care for patients seeking medical care from informal providers. Under this project, an intervention called 'Sampark Dhatha' is being implemented in which a local public transporter is engaged to ferry patients with TB symptoms to health facilities with Chest X-Ray facilities.

Conclusions: There is an urgent need to engage with the informal providers to ensure that their patients undergo Chest X-Ray as part of TB diagnostic process. Sampark dhatha is a feasible intervention to support patients with TB symptoms to undergo chest X-ray at health facilities.

EP-09-687 Acceptability of Kalinga Health Hub as a tuberculosis interface agency among private care providers in Marikina City, Philippines

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Background: The actual burden of tuberculosis in the Philippines is not known as only half can be traced in the national databases. Reduction of bacteriological confirmation can also be observed over the past years. This suggests a gap in diagnosis, notification, and treatment, especially in the private sector whereby a majority of patients seek initial care.

This study aimed to assess the acceptability of the Kalinga Health Hub, an intermediary social enterprise clinic, which was established as an attempt to bridge the notification gap among the private sector.

Design/Methods: The study utilized a qualitative descriptive approach to retrospectively elicit insights of private physicians who have partnered with the Hub. A total of 12 physicians were interviewed, all of whom are existing partners with varying degrees of participation with the Hub model. A sociodemographic survey was done to supplement the interviews.

Results: The interviews suggest multifaceted factors influence physicians' perception and extent of involvement in their partnership with the Hub. Intrinsic factors include their clinical practice characteristics and knowledge on the Hub and the national protocols for TB care. Extrinsic factors, such as patients' sociodemographic attributes, colleagues' and patients' feedback, locality's health system dynamics, and COVID-19 pandemic, also play pivotal roles in their sustained partnership.

Lastly, the Hub's engagement schemes and service quality are found to be key attractive features for the physicians to initiate (and continue with) their partnership.

Conclusions: The physicians' perception on the Hub model was generally positive as they found the idea of an intermediary Hub – that is service capable, patient-centered that conforms to public providers' accessibility – to be appealing.

Partnering with the Hub seemed to be beneficial as it resulted in increased awareness of and compliance with the TB guidelines. Using their feedback on the model, the model's approach can be revisited and refined before scaling-up the intervention.

EP-09-688 A public-private mix program to improve detection of tuberculosis in mountainous aboriginal regions in Taiwan

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Background and challenges to implementation: The incidence of tuberculosis (TB) in Taiwan's mountainous aboriginal regions (MARs) was 3 times higher than the national incidence. The main strategy for active TB detection in MARs is using Chest X-ray (CXR) screening arranged by public health bureaus.

However, more than 50% MARs-registered people couldn't get this service due to not living in their registered households. The screening rate in 2018 was only 20%.

Intervention or response: To reach the target population, since 2018, a new strategy by engaging cooperative hospitals and clinics where people registered in MARs are used to seeking medical treatment was endorsed. In 2021, a new public-private mix (PPM) program, which reimbursed those facilities by achieving 5 indicators

(number of CXR, timeliness of data uploading, automatic interface rate of CXR result, case tracking, API using) was implemented to find TB cases actively.

Results/Impact: The number of cooperative facilities increased from 14 in 2018 to 67 in 2021, providing a total of 36,054 CXR screenings (Figure).

The CXR screening rate in MARs for people aged 35 years and up remained 37% in 2020 and 2021. The cooperative facilities accounted for 39% of all CXR services in 2021, an increase of 14% of 2020.

In 2021, 68.7% cooperative facilities joined the PPM program. Sixty percent of the screening results of 8,540 CXR was submitted to the TB Case Management system timely through automatic interface in 2020 while 26% increase of CXR conducted and 38% increase of results automatically submitted in 2021.

Nineteen TB cases was detected by cooperative facilities in 2021 compared to 6 in 2020 and 68% of TB patients were found asymptotically in 2021.

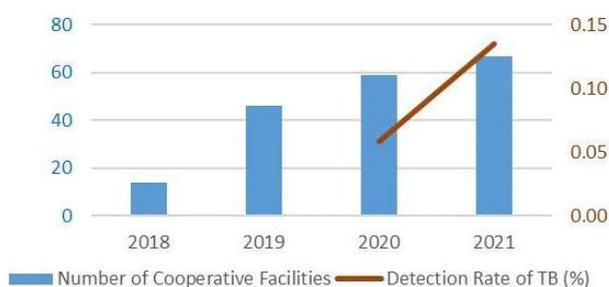


Figure. Yearly increasing trend of numbers of cooperative facilities and the detection rate of tuberculosis.

Conclusions: The PPM program increased the willingness of cooperative facilities to provide CXR to people registered in MARs. The preliminary results sheds light on how PPM can play an important role in active case finding for MARs.

EP-09-689 Increasing tuberculosis notifications among smear negative chest symptomatic through private sector engagement for CXR screening under Project Axshya

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Background and challenges to implementation: Sputum smear microscopy was the primary method for diagnosis of pulmonary tuberculosis before the scaling up of CBNAAT testing under the National TB program. The sensitivity of Microscopy is compromised in many situations and Chest x-ray (CXR) examination is often neglected due to various constraints. The availability of chest radiography in public is limited, and accessibility

to these services are often constrained by distance. In contrast, services in the private sector increase out-of-pocket expenditure.

Intervention or response: The Union in 2018-21 implemented Project Axshya and conducted Active Case Finding (ACF) in 108 Districts. Axshya Surveillance Units was a unique method for ACF. Volunteers reached out to the pulmonary Index cases House Holds for contact screening in the scattered hamlets of a village in hard-to-reach areas with a population size of 3000 to 5000. Under this study, we traced back the erstwhile sputum negative chest symptomatic and visited their households, and offered them CXR services in 8 Districts. Increased the number of Project Supported CXR centers through collaboration with the private sector. Sensitized community volunteers on tracing back the smear-negative Presumptive TB patients for CXR within their geography and used Xpert for confirmation.

Results/Impact: Despite COVID 19 constraints, the total number of identified Chest symptomatic increased in those units. Due to the engagement of more private CXR centers, the total number of CXR screenings increased from 1617 to 3315 in the next year. It increased the overall notification in those Units from 400 cases to 602 cases, a 50% increment in total notification due to more people undergone CXR Screening.

Period (P6-P13) of Intervention Studied	2019-20				2020-21			
	P6	P7	P8	P9	P10	P11	P12	P13
Total CXR Examined in Axshya Surveillance Units (ASU)	201	328	500	588	3315	732	1303	1218
Total Notified in ASU from CXR (Public & Private)	89	91	103	117	13	180	230	179
Total ASU Notification	256	353	330	344	53	402	512	434
Contribution of CXR in ASU Notification	34.8%	25.8%	31.2%	34.0%	24.5%	44.8%	44.9%	41.2%

Conclusions: It is advised to efficiently diagnose tuberculosis, the NTEP and future projects should strive to conduct a CXR examination of smear-negative chest symptomatic. Optimal use of more sensitive screening tests and private sector engagement for CXR screening can improve diagnostic yield in a programmatic setting.

EP-09-691 Use of WHO collaborative procedure for accelerated registration to facilitate access to quality-assured tuberculosis medicines in Uzbekistan

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Background and challenges to implementation: As Uzbekistan transitions from procurement of TB medicines supported by the Global Fund to Fight AIDS, Tuberculosis and Malaria (GFATM), the government decided to continue acquiring these products through the Global Drug Facility (GDF). The GDF now supplies all TB medicines, procured with domestic and GFATM funding. However, these medicines are not registered in Uzbekistan. Lack of registration impedes importation, ultimately delaying supply of these life-saving drugs. The WHO Collaborative Procedure for Accelerated Registration is an effective mechanism for helping countries optimize available resources, using reliance principles for timely and efficient registration of WHO prequalified products. Uzbekistan is a participating member of the WHO procedure, but it has never used this mechanism for medicine registration.

Intervention or response: The USAID Promoting the Quality of Medicines Plus (PQM+) program, implemented by USP, assessed the registration function of the National Medicines Regulatory Authority; trained staff on WHO requirements; and facilitated the development of this procedure and WHO guidelines for manufacturers. National TB Program, GDF, and PQM+ facilitated interactions between TB medicines manufacturers and the Medicines Regulatory Authority in Uzbekistan, ultimately helping manufacturers submit their dossiers for accelerated registration.

Results/Impact: Advocacy at various levels, coordination, and collaboration between national and international partners—combined with technical assistance from PQM+—resulted in the following:

- The first two WHO prequalified anti-TB medicines were registered in 35 days.
- Four additional dossiers were submitted for registration through the WHO procedure.
- The government reduced the registration fee for products prequalified through the WHO procedure by 40%.

Conclusions: With combined efforts of the National TB Program, government, and international partners, the WHO procedure was operationalized in Uzbekistan.

Opportunities for expedited registration and reduced fees encourage manufacturers of WHO prequalified medicines to register their products. In return, this ensures uninterrupted access to quality-assured WHO prequalified TB medicines in Uzbekistan.

EP-10 The cost of TB treatment

EP-10-692 Two-third of TB patients and their families experienced catastrophic costs in Ethiopia

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Background and challenges to implementation: Tuberculosis (TB) patients incur high costs when seeking diagnosis, care, and treatment. To understand the magnitude of this financial burden, the USAID Eliminate TB Project collaborated with regional health bureaus to carry out TB patient cost survey ever conducted in Ethiopia from November 2020 to March 2021.

Intervention or response: A facility-based cross-sectional survey was conducted in four regions, using World Health Organization TB patient cost survey tool to estimate the percentage of TB-affected households facing catastrophic costs, defined as total TB-related costs exceeding 20% of annual household income.

Results/Impact: A total of 433 TB patients participated in this study. The mean and median ages were 33.6 and 30 years, respectively. The mean and median income was \$544 and \$222, respectively. Of the surveyed households, 66.1% faced catastrophic costs. Farmers were 74% (AOR: 0.26, 95% CI [0.11, 0.62]) and 66% (AOR: 0.34, 95% CI [0.18, 0.61]) more likely to experience catastrophic costs compared with government and self-employed TB patients, respectively. Taking medication at home with a treatment supporter reduced incurred catastrophic costs by 48% (AOR: 0.52, 95% CI [0.33-0.84]).

Compared with TB patients enrolled in the community-based health insurance (CBHI) scheme, TB patients supported by their family without CBHI experienced twice the level of catastrophic costs (AOR:1.91, 95% CI [1.08, 3.36]). TB patients with medical reimbursement experienced 85% lower catastrophic costs compared to those with CBHI (AOR: 0.15, 95% CI [0.085, 0.27]).

Conclusions: In Ethiopia, two-thirds of TB patients and their households faced a substantial financial burden due to TB, despite the availability of free TB services. Expansion of existing CBHI, facility-based health insurance, and reimbursement schemes are essential to meet the needs of TB patients and for the early detection of missed TB cases. Engaging a family DOT treatment supporter is recommended to reduce costs due to TB treatment.

EP-10-693 Provider costs of using medication monitors and a differentiated care approach to improve TB treatment adherence in South Africa

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Background: Digital Adherence Technologies (DATs), with a Differentiated Care Approach (DCA), may improve adherence to tuberculosis (TB) treatment. Costing would be essential to guide policy decisions on large-scale implementation of DAT. We undertook a costing study within the TB Monitoring and Adherence Endpoints study, evaluating the costs of using Wisepill evriMED 1000 device (medication monitor) triggering a DCA, involving short message service, phone calls and home visits in South Africa.

Design/Methods: Between June 2019 - August 2020, we conducted a costing study from a provider perspective in three districts. We purposively selected one intervention and one control primary health care clinic/district aiming for a mix of rural/urban, busy/quiet and large/small clinics. Provider costs were collected using a bottom-up activity-based costing approach. Clinic-level time and motion studies were conducted; providers were observed and interviewed on time spent on clinic visits, generating reports, follow-up phone calls and home visits to TB patients.

Unit costs were analyzed and reported as cost/TB patient in the control and intervention (monitor and differentiated care) arms. All costs were converted using 1 USD = 16.46 SA Rand.

Results: Provider costs related to escalation for non-adherence including phone calls and home visits ranged between \$2.91 - \$8.34/TB patient at intervention (I) clinics with no cost at control (C) clinics. Shared costs such as data management support ranged between \$11.06 - \$17.64 at intervention clinics. The largest cost drivers at intervention clinics were the monitors (47.87% - 49.86%), data management support (22% - 35%) and escalation activities (6% - 16%). The total cost per patient ranged between \$48.81 - \$50.94 (intervention) and \$27.63 - \$29.26 (control).

Cost category	I	C	I	C	I	C
	GP 019	GP 009	KZN 517	KZN 518	WC 521	WC 525
Medication monitor	\$24.38 (49.86%)	\$24.38 (83.60%)	\$24.38 (47.87%)	\$24.38 (88.26%)	\$24.38 (48.17%)	\$24.38 (83.34%)
Phone and accessories	\$0.31 (1%)	\$0.00 (0%)	\$0.52 (1%)	\$0.00 (0%)	\$0.29 (1%)	\$0.00 (0%)
Wisepill Platform hosting & reminders	\$3.70 (8%)	\$2.07 (7%)	\$3.75 (7%)	\$2.07 (7%)	\$4.20 (8%)	\$2.07 (7%)
Adherence monitoring	\$ 2.63 (5%)	\$ 2.46 (8%)	\$ 1.35 (3%)	\$0.97 (4%)	\$2.14 (4%)	\$2.60 (9%)
Data management	\$12.47 (26%)	\$0.00 (0%)	\$17.64 (35%)	\$0.00 (0%)	\$11.06 (22%)	\$0.00 (0%)
Escalation for non-adherence (DCA)	\$5.07 (10%)	\$0.00 (0%)	\$2.91 (6%)	\$0.00 (0%)	\$8.34 (16%)	\$0.00 (0%)
Training	\$0.25 (0%)	\$0.26 (1%)	\$0.37 (0%)	\$0.21 (0%)	\$0.21 (0%)	\$0.21 (0%)
Total cost per patient	\$48.81	\$29.17	\$50.94	\$27.63	\$50.62	\$29.26

Table 1: Cost per patient (\$USD) of using a medication monitor (Wisepill evriMED 1000 device) with a Differentiated Care Approach

Conclusions: Innovative ways to lower the provider cost of DAT and DCA should be considered before scaling-up. Negotiating a lower cost for monitors with manufacturers and increasing efficiencies in data management and escalation activities should be prioritized.

EP-10-694 Illness, coping, and catastrophic costs for tuberculosis care in Pune, India

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V. Mave,^{2,4} J. Golub,^{1,4} H. Sohn,⁵ TB Aftermath
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Background: Many people with tuberculosis (TB) in India experience a large financial burden following completion of treatment. The magnitude and characteristics

of this financial burden in programmatic settings remain uncertain.

Design/Methods: This analysis used a TB patient cost questionnaire, modified from the WHO costing questionnaire, administered to people enrolled in a trial of TB outcomes after treatment completion (“TB Aftermath”) between February 2021 and April 2022 from six government TB Units in Pune, India. The questionnaire included questions on demographics, socio-economics status (SES) and costs incurred from TB treatment initiation through treatment completion. SES was defined by the Kuppaswamy wealth index, and TB illness costs included treatment, hospitalization, and lost wages, plus financial coping costs. All costs were reported as mean per-patient costs with 95% confidence intervals. Catastrophic costs were defined as total illness costs exceeding 20% of annual household income. All costs were assessed in 2021 US Dollars.

Results: Of 224 participants, 30% were categorized as “lower” or “upper-lower” SES. The mean cost of TB illness was \$266 (95% Confidence Interval (CI): 192, 340), with treatment composing 65% of all illness costs. Twenty-seven (8%) individuals experienced catastrophic costs, of whom eleven were “lower” or “upper-lower” SES. People with multidrug-resistant and extra-pulmonary TB had higher mean illness costs, \$772 (95% CI: 48, 1495) and \$331 (95% CI: 250, 412) respectively, compared to \$243 (95% CI: 174, 312) for drug-susceptible TB. Therefore, a higher proportion of these individuals experienced catastrophic costs (30% and 18%, respectively). 61 individuals (27%) borrowed money or sold assets to finance TB care (mean: \$97.67, 95% CI: 62.57, 132.59). Overall, 37% of all illness costs were covered by borrowing or sale of assets.

EP-10-695 An analysis of costs and pathways to care after a negative TB evaluation August 2021-April 2022

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Background and challenges to implementation: Studies show that Persons who were living with TB upon testing negative after completion of medication need further support. That support comes with costs and in this study we find out that the costs are characterized as: social, spiritual, psychological, mental, physical, financial, and cultural aspects which must be fulfilled to ensure completeness and full recovery. We followed 197 Persons in 6 TB Survivor Support Clubs in Kenya to characterize the costs and pathways to care after a negative TB evaluation.

Intervention or response: A person recuperating needs reconnection, reassurance and counselling which restores dignity and at the same time prepares them for self-esteem building. These individuals return to the clinic or hospital for regular checkup, rebuild and reconnect with members of the social networks and pursue means to support themselves.

We conducted a cross-sectional study of 197 patients with a negative TB evaluation at six (6) TB Survivor Support Clubs in Machakos, Kajiado, Nairobi Counties. Patients were traced 9 months post-evaluation using contact information from TB registers.

We collected information on healthcare visits and implemented locally validated cost characterizing questionnaires to assess the social, psychological, mental, physical, cultural, and financial impact of their symptoms post-evaluation.

Results/Impact: 197 (100%) surveyed participants returned to healthcare facilities post-evaluation, with a median of 3 visits each. All incurred catastrophic costs (i.e., spent >30% annual household income); 100/197 reported indirect costs related to lost work. All 197 responded that costs are incurred before and after they test negative are financial, social, cultural, mental, psychological, and physical.

Conclusions: Costs after a negative TB evaluation need to be captured by existing definitions of non-TB catastrophic health reports as these affect bio-social-cultural-medical facets of life. This can inform better policy, planning and programming if we are to eradicate TB by 2030 and shows the relevancy of TB Survivor Support Clubs.

Type of Cost	Cost Category	Drug-Susceptible Tuberculosis (N= 214)		Multidrug-Resistant Tuberculosis (N= 40)		Extra-Pulmonary Tuberculosis (N= 189)	
		Number of patients reporting (%)	Mean cost per patient (95% CI)	Number of patients reporting (%)	Mean cost per patient (95% CI)	Number of patients reporting (%)	Mean cost per patient (95% CI)
Cost of Illness (2021 USD)	Treatment	214 (100%)	151.25 (124.56, 177.52)	0 (0%)	646.29 (60.83, 1,232.02)	108 (100%)	233.69 (172.59, 295.29)
	Hospitalization	45 (21%)	91.96 (27.81, 155.90)	5 (50%)	125.56 (-51.92, 302.64)	36 (33%)	67.18 (58.97, 137.33)
	Total Cost of Illness	214 (100%)	243.11 (174.39, 312.64)	0 (0%)	771.58 (48.25, 1,494.88)	108 (100%)	331.07 (249.76, 412.27)
Number of Patients Experiencing Catastrophic Costs (%)		24 (11%)		3 (30%)		19 (18%)	
Coping Costs (2021 USD)	Amount Borrowed for TB Expenses	59 (28%)	45.04 (51.49, 120.44)	2 (20%)	155.09 (-51.05, 261.23)	38 (33%)	112.31 (68.24, 159.33)
	Value of Assets Sold for TB Expenses	11 (5%)	0.95 (1.09, 16.21)	0 (0%)	0 (0, 0)	5 (4%)	4.34 (-1.77, 10.46)

Table 1. Costs of TB care and coping costs by type of disease.

Conclusions: Despite free TB care in India, many people experience large costs. New strategies/strengthening existing ones are needed to reduce the financial burden of TB care.

EP-10-696 Impact and cost-effectiveness of TB preventive therapy for household contacts and people with HIV

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Background: Although tuberculosis (TB) preventive therapy (TPT) is highly effective, cost and feasibility limit its use. Household contacts of people with TB are a high-risk population who might benefit from broader TPT scale-up. Unfortunately, there is little evidence on the cost-effectiveness of TPT for household contacts – especially older children and adults.

Design/Methods: We developed a state-transition model to simulate weekly isoniazid-rifampentine for 12 weeks (3HP) for people with HIV (PWH) and household contacts in 29 high-burden countries that have procured 3HP, comparing costs, outcomes, and cost-effectiveness to a comparator scenario of no contact investigation or TPT over ten years.

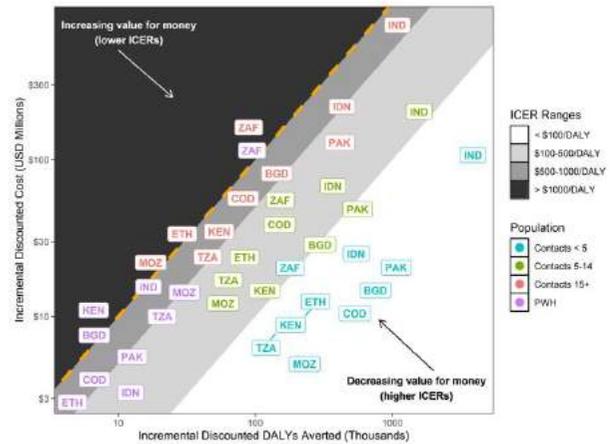
Our model integrates data from IMPAACT4TB, an initiative to scale up TPT for PWH and household contacts in 12 high-burden countries, and from published sources to simulate screening and diagnostic algorithms; TPT initiation, toxicity, and completion; and subsequent risks and timing of reactivation, treatment, and mortality.

Our primary outcome was the incremental cost-effectiveness ratio, expressed as incremental discounted costs (in 2020 USD) per incremental discounted disability-adjusted life year (DALY) averted.

Results: Over ten years across 29 countries, scaling up TPT (including contact investigation) was projected to prevent 264,000 [95% CI 106,000-489,000] cases and 352,000 [163,000-639,000] deaths among contacts <5 (\$22-228/DALY averted); 264,000 [94,000-527,000] cases and 153,000 [46,000-357,000] deaths among contacts 5-14 (\$106-492/DALY averted); and 822,000 [293,000-1,628,000] cases and 115,000 [63,000-185,000] deaths among contacts ≥ 15 (\$307-2523/DALY averted) (Figure).

Among PWH, TPT could prevent 187,000 [135,000-246,000] cases and 23,000 [13,000-37,000] deaths (cost-saving to \$2816 per DALY averted). Cost-effectiveness was generally most favorable for child contacts and similar for adult contacts and PWH.

Conclusions: TPT is likely cost-effective not only for PWH and child contacts, but also for older contacts. Given the large burden of TB among contacts over five, providing TPT to these individuals should be given increased prioritization and funding.



Each marker represents a country-specific estimate of discounted incremental DALYs averted (x-axis) and discounted incremental costs (y-axis) from implementing TPT among 4 different target populations (colors) compared to a scenario of no TPT, in the 10 countries modeled with the highest estimated number of incident TB cases (Bangladesh [BGD], Congo DRC [COD], Ethiopia [ETH], India [IND], Indonesia [IDN], Kenya [KEN], Mozambique [MOZ], Pakistan [PAK], South Africa [ZAF], Tanzania [TZA]). TPT costs < \$1000/DALY averted for those country-population combinations that fall to the bottom-right of the dashed orange line. Filled areas of the graph indicate incremental cost-effectiveness ratios (ICERs) for example, the graph indicates that the incremental cost-effectiveness ratio for TPT among contacts < 5 and contacts 5-14 for South Africa (ZAF) is between \$100 and \$500 per DALY averted, while for contacts over the age of 15 and PWH the incremental cost-effectiveness ratio is slightly greater than \$1000 per DALY averted.

EP-10-697 Shortening treatment for latent TB infection in Canada with 3HP: a cost-effectiveness analysis

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Background: A short-course regimen of 3 months of weekly rifampentine and isoniazid (3HP) has been recommended by WHO as alternative to treat latent TB infection. We assessed the cost-effectiveness of implementing novel shortened treatment using 3HP administered by DOT compared with existing standard of care, 9 months of daily isoniazid (9H) administered through self-administered treatment (SAT) in Ottawa, Canada.

Design/Methods: A Markov model was developed to simulate individuals with LTBI treated with self-administered 9H and directly observed 3HP in Ottawa Canada. The primary outcome was measured in quality-adjusted life years (QALYs) with model parameters including probability of treatment initiation, completion, adverse event and costing data derived from a local implementation study of 3HP in Ottawa. Published literature was also reviewed to derive additional epidemiological data. One way and probabilistic sensitivity analyses were performed.

Results: Over a 30-year period, treatment with DOT 3HP resulted in an incremental cost of \$1,724 CAD per QALY gained, as such 3HP with DOT would be considered highly cost-effective compared with 9H SAT in the Canadian setting. From the health system perspective, treatment using 3HP in Ottawa resulted in an incremental cost of \$186 compared to 9H per person

treated, and an incremental effectiveness of 0.11 additional QALYs with 3HP compared with 9H. Rates of 3HP initiation and completion as well as risk of fatal adverse events were key drivers of cost effectiveness. In scenario analysis where both 3HP and 9H were considered to administered as SAT, 3HP was cost saving compared with 9H.

Conclusions: The finding of this study suggests that using 3HP results in increase QALYs compared to 9H in Ottawa, Canada. 3HP may be a cost-effective alternative to 9H, particularly depending on willingness to pay threshold, and if the effectiveness of 3HP can be maintained without DOT.

EP-10-698 Putting our best cost forward: a comparative analysis of cross-sectional and longitudinal approaches for TB patient costing studies

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Background: Economic barriers can limit patient access to healthcare, resulting in worse tuberculosis (TB) outcomes. National costing surveys have been carried out in several countries to estimate costs incurred by TB-affected families. However, inaccuracies in cost estimates can make it difficult to compare the economic burden of TB across different countries.

We aimed to compare the cost estimates calculated through the cross-sectional and longitudinal survey designs in Nepal.

Design/Methods: We analysed data from a longitudinal costing survey conducted between April 2018 and October 2019 in Nepal.

Cost estimates were calculated by using three approaches:

1. Longitudinal: Costs estimated from interviews applied at three points in time during TB treatment;
2. Cross-sectional1 (CS1): Costs extrapolated by using data collected during the intensive phase;
3. Cross-sectional 2 (CS2): Costs extrapolated by using data collected during the continuation phase.

The prevalence of catastrophic health expenditure (CHE) was estimated for each approach.

Results: We found that CS1 may have overestimated the total TB treatment cost, whilst CS2 underestimated it (CS1: US\$150.04; IQR 63.05-276.29; CS2: US\$91.63;

IQR 37.53-296.60; longitudinal: US\$119.42; IQR 51.98-275.99, $p=0.000$). All approaches reported that the indirect costs contributed at least two thirds to the total costs of the intensive phase. The prevalence of CHE was similar for CS1 and longitudinal (64% vs 61%), but CS2 estimated lower prevalence compared to longitudinal (53% vs 61%, $p < 0.05$).

Conclusions: The longitudinal approach is the most suitable design as it generates more accurate cost estimates and captures variations of TB's economic burden during the treatment. However, in resource constraint settings, longitudinal costing surveys may be burdensome.

Further studies comparing cross-sectional and longitudinal designs can generate evidence on the proportional differences in cost estimates. We can then calculate a correction factor to adjust costs collected through a cross-sectional design.

EP-10-699 A comparison of outcome and cost efficiency of community tuberculosis active case finding (cTBACF) by local and other volunteers in Cross River State

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Background and challenges to implementation: Community tuberculosis active case finding (cTB ACF) is one the intervention strategies used by KNCV TB Foundation in active TB case finding because of the believe on the intervention's inherent power to find the missing TB cases in Nigerian communities which has plateaued for some year now. The increasing demand for fund by natural disasters and complex emergency for over a decade made it very important to implement TB interventions with minimal input but high output/outcome. Cost efficiency vis-a-vis outcome therefore becomes a paradigm for efficient cTB ACF.

Intervention or response: Community TB ACF is implemented in 13 local government areas of Cross River state using two outreach methods by: volunteers who reside within the outreach locality (local volunteers) and volunteers residing outside the outreach locality (other volunteers). Data for the outreach outcomes were obtained secondarily from submitted weekly reports from the commencement of the outreach methods and the cost of the intervention was obtained from the payment vouchers and attendance submitted at the end of every outreach while the percentage difference in intervention outcomes and cost were calculated manually.

Results/Impact: Presumptive TB evaluated and TB cases diagnosed by the local volunteers were 60% and 325% higher respectively while the numbers screened for TB

by other volunteers was 15% higher. TB yield was 5.2% and 1.9% for local and other volunteers respectively and 211% higher in favour of the local volunteers. The cost of implementation is 34% higher for other volunteers.

Particulars	Numbers screened	Presumptive TB Tested	TB cases diagnosed	TB Yield (%)	Cost/TB Case (₺)
Local volunteers	2961	658	34	5.2	3,353
Other volunteers	3409	412	8	1.9	4,500
Percentage difference	15%	60%	325%	211%	34%

Conclusions: Community TB ACF has a better outcome and cost efficiency when screening is handled by volunteers who are part of the environment and if this model is adopted nationally by all the stakeholders has the ability of bringing greater intervention outcome with less resources.

EP-10-700 Household costs incurred when seeking and receiving paediatric tuberculosis services: a survey in Cameroon and Kenya

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Background: Elimination of catastrophic costs due to TB is one of the three targets of the End TB Strategy. No data has yet been reported on the costs experienced by households of children receiving TB services. We quantified the economic impact on households with children seeking and receiving TB services during the Catalyzing Pediatric TB Innovations (CaP-TB) project in Cameroon and Kenya.

Design/Methods: As a sub-study of the INPUT stepped-wedge study evaluating the effect of CaP-TB integration of TB services in paediatric entry points, we designed a cross-sectional facility-based survey with retrospective data collection using a standardized questionnaire

adapted from the WHO TB patient cost generic survey instrument and translated to French. Parents of children receiving TB services during the CaP-TB project were interviewed between November 2020 to June 2021. Direct medical, direct non-medical, and indirect costs for TB services were analyzed following WHO recommendations. All costs are presented in 2021 US dollars.

Results: A total of 56 parents' representing their households (Cameroon, 26 and Kenya, 30) were interviewed. The pooled median estimated household costs were \$201 (IQR; \$113 - 349); \$240 (\$129 - 657) in Cameroon and \$178 (\$111- 262) in Kenya. The main cost drivers (Figure 1) were direct non-medical costs (transportation and food), and indirect costs (parent/guardian time lost). Approximately 45% of households reported experiencing dissaving (taking a loan, selling an asset) to deal with costs related to TB. Using a threshold of 20% of household income, 77% of households experienced catastrophic costs (58% in Cameroon and 93% in Kenya). **Conclusions:** Accessing and receiving TB services for children results in high levels of cost to households, despite free CaP-TB project services. Strategies to reduce costs for TB services for children need to address indirect costs or explore decentralization.

**ABSTRACT PRESENTATIONS
WEDNESDAY
9 NOVEMBER 2022**

ORAL ABSTRACT SESSION (OA)

OA-11 Expanding active case finding in vulnerable populations

OA11-275-09 The yield from the integration of traditional birth attendants in tuberculosis case finding in Niger state, north-central Nigeria

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Background and challenges to implementation: Niger state is estimated to have 12,786 Tuberculosis (TB) cases with barely 28% detected in 2020. One of the key challenges with TB case finding in the state is accessibility to TB services, especially at the community level. The state through the TB public-private mix intervention sought to increase access to TB services in the community by integrating Traditional Birth Attendants (TBA) into the program.

Intervention or response: Between 2020 and 2021, a total of 68 TBAs were actively engaged, trained on TB management, and mapped to TB treatment facilities. Linkage Coordinators (LC) were engaged to facilitate complete referrals.

The TBAs symptomatically screened clients accessing their services and those presumed to have TB had their samples collected and transported to diagnostic facilities by the LCs. They sometimes conducted outreaches within the community. The Local Government TB Supervisors (LGTBLS) supervised the process to ensure adherence to the National TB Program (NTP) guidelines.

When results were released, clients confirmed to have TB were contacted and linked to the nearest treatment facility to commence treatment. Data was collated from the NTP recording tools and analyzed using Excel.

Results/Impact: Out of the referrals made by the TBAs, a total of 415 TB cases were diagnosed and 400 (96%) were started on treatment. In 2020, TBAs contributed 2% to the total TB cases notified by the private sector in the state but increased to 18% in 2021.

The linkage mechanism facilitated by the LCs with support from the LGTBLs contributed to the high enrolment rate recorded.

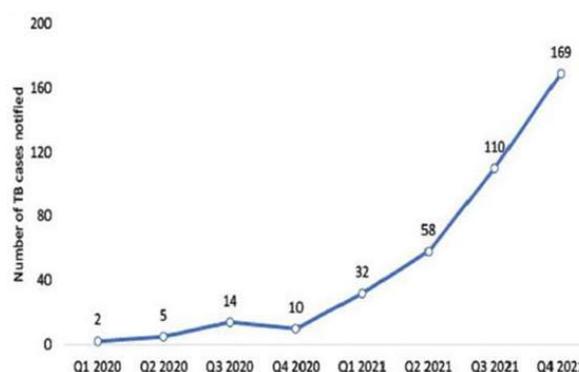


Figure 1: Trend of TB notification from referrals made by TBAs from Q1 2020 to Q4 2021.

Conclusions: This study demonstrates the great potential in the integration of maternal health and TB services. The presence of this cadre of health providers within the community should be harnessed toward ending TB, especially in low-resource settings.

OA11-276-09 Expanding contact investigation through spot to tent approach; Plateau State experience

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Background and challenges to implementation: Contact investigation is a useful intervention for finding individuals with TB early, to reduce spread to household members and other contacts of TB patients. Neighbors of TB patients may be at risk of acquiring TB or may have been the source of infection to the index case. Expanding contact investigation beyond the patient's household is an innovative approach to finding more TB cases. We explored the contribution of a spot-to-tent approach to contact investigation in TB case finding in Plateau state.

Intervention or response: We trained 17 community volunteers to implement contact investigation. They were assigned to TB treatment facilities in all the 17 LGAs

in the State. They conducted home visit to the patients, to screen household contacts. Apart from the household contact, they also screened the patients' neighbors living within a 2 KM radius typically described as spot-to-tent approach. They collected sputum from identified presumptive TB and sent for diagnostic evaluation. Diagnosed cases are linked to treatment. KNCV team conducted weekly reviews with the team to ensure quality of the intervention. Spot-to-tent approach was implemented from July 2020 – August 2021.

Results/Impact: Between July- Oct 2020, there was a surge in the number of clients screened for TB, presumptive identified and TB cases diagnosed. There was an overall increase of 44% in screening, 41% in presumptive TB identified and 78% in TB cases diagnosed. Between November 2020 and April 2021 spot-to-tent approach was suspended, screening, presumptive and case finding from contact investigation also dropped by 40%, 7% and 53% respectively compared to previous months when spot-to-tent was used. When the spot-to-tent was re-introduced in May-August 2021, the case finding improved by 30%, 36% and 53% respectively.

Conclusions: Implementation of spot-to-tent approach in contact investigation is a useful intervention for early TB case detection and finding missing TB cases.

OA11-277-09 GeneXpert Ultra in pregnancy: implications and complications

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Background: Subclinical TB is common in pregnancy, limiting assessment of drug sensitive and drug resistant TB (DR-TB). GeneXpert Ultra (GXPU) has better sensitivity than culture. We used GXPU to estimate active TB prevalence, including subclinical and DR-TB, in pregnant women in India.

Design/Methods: The Pregnancy Associated Immune Responses to Tuberculosis and HIV in India and South Africa (PARTHISA) study enrolls women during pregnancy through 21 days postpartum. We exclude women on TB treatment for >2 weeks or in the last two years.

Symptomatic women and asymptomatic women with latent TB infection are screened with two sputum samples for GXPU, AFB smear, liquid and solid cultures. Thrice yearly external quality assurance and weekly quality controls are done. Characteristics of women with high vs paucibacillary (low, very low, trace) GXPU results were compared using chi-square and Mann Whitney's test.

Results: Of 98 women screened, 19 had *M.tuberculosis* (MTB) detected by GXPU (15 pregnant, 4 postpartum). None reported a TB contact and 6 (32%) were living with HIV. Of the 19, 4(21%) had high versus 15(78%) with paucibacillary MTB ($p=0.0004$). Of the 15 paucibacillary cases, 9(47%) were asymptomatic. (Table 1) Three of four from high GXPU and 2 of 15 from paucibacillary group had abnormal chest Xray. Based on culture, GXPU had 100% sensitivity and 76% specificity. Six (32%) of the 19 cases had DR-TB: 3 with rifampicin-resistance by GXPU (very low MTB) but not culture; 3 with resistance to Isoniazid/Pyrazinamide/Streptomycin by culture (2 high and 1 low MTB by GXPU). Of the 6 DR-TB cases, 3 diagnosed by GXPU were asymptomatic, two of whom had HIV.

	Total	High / Medium positive- GXPU	%	Paucibacillary disease (low / very low / Trace)- GXPU	%	p value
Active/subclinical TB	19	4	21	15	79	0.0004
Antenatal (AN) enrolment	15	2	13.3	13	86.7	0.0001
Median Gestational Age weeks(IQR) [n=15]	16.2 (12.2-21)	25 (20-30.1)	-	16.2 (12.1-20.2)	-	0.1
Asymptomatic	9	0	-	9	100	NA
Chest Xray-Abnormal	5	3	60	2	40	0.5
Median CD4 cells/ mm ³ (for HIV only, n=6) (IQR)	614 (336-964)	-	-	614 (336-964)	-	NA
MGIT or LJ MTB positive	7	4	57	3	43	
Drug Sensitive	4	2	50	2	50	0.6
Drug Resistant (Non-Rif)*	3	2	66.7	1	33.7	
DR-Rifampicin-GXPU	3	0	-	3	100	NA

*no rifampicin resistance was detected by culture drug sensitivity testing
Abbreviations: TB: Tuberculosis; MGIT: Mycobacteria Growth Indicator Tube; LJ: Lowenstein Jensen cultures; GXPU: Gene Xpert Ultra; Rif: Rifampicin; IQR: Inter Quartile Range.

Conclusions: Considerable number of subclinical and DR-TB cases were diagnosed by GXPU during pregnancy. The low culture confirmation questions initiation of TB treatment for pregnant women based on GXPU, alone, especially given lack of safety data on DR-TB treatment in pregnancy.

OA11-278-09 Expanding intensified TB case finding for high-risk groups in Vietnam's general hospitals using the Double X strategy

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Background and challenges to implementation: The Vietnam National Tuberculosis (TB) Program (NTP) aims to increase detection and treatment of TB disease. Routine, passive TB case finding previously focused on people who visited TB facilities, missing opportunities in non-TB facilities to evaluate people with symptoms and risk factors for TB. Applying the Double X (2X) strategy in general hospitals aimed to increase intensified TB case finding (TB ICF).

Intervention or response: From January-December 2021, the Vietnam NTP implemented 2X ICF in 36 general hospitals of seven provinces with USAID support. This protocol expanded TB screening to outpatients in diabetes clinics, outpatients with respiratory symptoms, and inpatients with lung disease. The triage algorithm to obtain chest X-ray (CXR) films varied by risk group: outpatients with respiratory symptoms of any duration; diabetics with TB symptoms, hemoglobin A1C (HbA1C) >9%, or blood glucose >10 mmol/liter; and inpatients with lung disease with or without symptoms. The 2X ICF protocol leveraged chest X-ray (CXR) films, which are already ordered for those with respiratory symptoms or lung disease, further requiring CXR analysis for abnormalities from pulmonary TB. If CXR films were abnormal for TB, patients were referred for Xpert testing.

Results/Impact: We obtained 140,022 CXR films, of which 8,136 (5.8%) were abnormal for TB, leading to 7,562 (92.9%) people tested with Xpert and 1,652 (21.7%) Xpert-confirmed pulmonary TB patients. This yielded 1,179 Xpert-confirmed TB patients/100,000 CXR. Outpatients with respiratory symptoms comprised the largest proportion of patients evaluated with 2X ICF (n=77,192, 55.1%) and had the highest yield of TB detection (n=998, 1,293/100,000 CXR).

Conclusions: The 2X ICF strategy was high yield for detecting active TB disease while using non-TB health facilities, where patients often present, to streamline evaluation. This decreases patient burden and leverages existing resources. This protocol showed the feasibility of integrating TB ICF into routine activities of Vietnam's general health care system.

Risk group	Symptom screening	No. evaluated with CXR	No.(%) abnormal CXR	No.(%) tested with Xpert	No.(%) Xpert confirmed TB	TB case Yield/ 100,000 CXR
Outpatients with respiratory symptoms	Any respiratory symptoms	77,192	3,819 (4.9%)	3,658 (95.8%)	998 (27.3%)	1,293
Inpatients with lung diseases	Not required	33,161	2,633 (7.9%)	2,382 (90.5%)	426 (17.9%)	1,285
Diabetic patients	TB symptoms or HbA1C>9% or blood glucose level>10 mmol/liter	29,669	1,684 (5.7%)	1,522 (90.4%)	228 (15.0%)	768
Total		140,022	8,136 (5.8%)	7,562 (92.9%)	1,652 (21.7%)	1,179

2X Intensified case finding at 36 health facilities in Vietnam in 2021.

OA11-279-09 Higher number of community than household contacts among people with drug-resistant tuberculosis, South Africa

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Background: Although transmission of drug-resistant (DR) TB in community settings is likely a substantial driver of the ongoing global epidemic, further research is needed to inform interventions to interrupt transmission. We describe characteristics of household and community contacts of people with DR TB in KwaZulu-Natal, South Africa.

Design/Methods: This is an ongoing, cross-sectional study of persons with pre-XDR/XDR TB in KwaZulu-Natal province, South Africa. We conducted in-depth interviews to elicit commonly visited locations and characteristics of named close contacts at each location in the past 2 years. Close contacts were defined as individuals "touched, talked to, or spent time near." Descriptive analysis of contacts was stratified by location of contact: household vs community (defined as non-hospital or non-institutionalized settings, e.g., work, school, religious institutions, markets).

Results: From February 2019 to April 2022, 307 people with pre-XDR/XDR were identified to date. Complete interview data are available for 197: Median (IQR) age: 36 (30-43), 43% female, 69% HIV+. A total of 2,026 named close contacts were reported: 949 (47%) at household locations and 1,077 (53%) at community locations. The number of close contacts in community locations (median (IQR)=6(3-9)) was higher than in household locations (median (IQR)=5(2-8); Figure). This difference was largest among persons aged 45-54 who reported a median of 6 contacts in community vs. 3.5 contacts in household locations. Overall, contact age was weakly positively correlated with participant age among community contacts, suggesting age-assortative mixing (Figure).

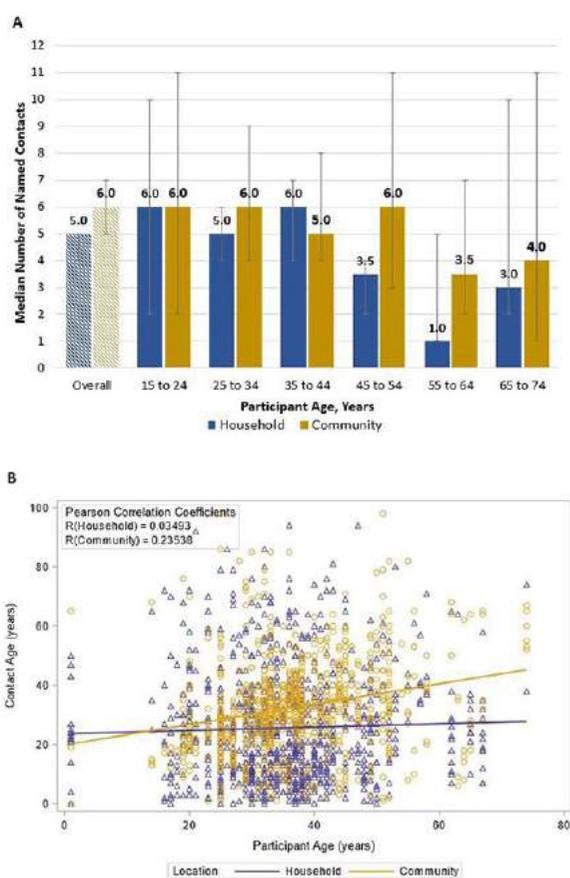


Figure. Median number of named contacts per pre-XDR/XDR TB participant (A) and contact age (B) by participant age among household and community contacts, KwaZulu-Natal, South Africa.

Conclusions: Close contacts in non-household settings represent a substantial proportion of persons at risk for infection and disease, particularly among working-age individuals. Given the potential for an even higher number of non-named contacts in community locations, TB prevention and care efforts must consider interventions in community settings to reduce transmission.

OA11-280-09 Facilitating and inhibiting factors for the introduction of digital adherence tools for TB care: analysis of pilot data from a multi-country, cluster randomized trial

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Background: Digital adherence technologies (DATs) facilitate adherence to tuberculosis treatment, but little is known about factors affecting their introduction and use in high TB burden settings.

We report data from the pilot phase of our study which is implementing the smart pillbox and SMS self-report using labels.

Design/Methods: This is a cross-sectional analysis of pilot data from cluster-randomized trials conducted in South Africa, Ethiopia, Ukraine, and Philippines between October 2020-October 2021. We conducted thematic analysis of qualitative data from interviews with healthcare workers (HCWs) and other implementing staff.

Furthermore, we used data from quarterly funder reports, facility visits, and research managers summaries. Quantitative data on adherence levels were extracted from the adherence platform to describe digitally-reported doses by the DAT and manual doses captured by the HCW, based on person's self-report.

Results: Adherence data were available for 2247 patients (36% female, median age 37 years). Digitally-recorded adherence percentage ranged by country; 69%-88% using the pillbox compared with 61%-87% for the labels. Manually-recorded adherence was higher in the labels group. Inhibiting factors for use of the labels at the individual-level were old age, illiteracy, phone-sharing and SMS fatigue; Contextual inhibitors included lack of electricity and poor network; Technological inhibitors include need for airtime balance and non-functional SMS code. HCW's reported that privacy, family support, reminder SMS's, technological savviness, and reduced facility visits facilitated the use of labels. HCWs reported that participants found the pillbox easy to use and have reduced facility visits. Inhibiting factors for the pillbox include difficulty to travel with, stigma, alarm dysfunction, poor network, and difficulties with continuity due to staff turnover.

Country	Ethiopia	The Philippines	South Africa	Ukraine
Median Age, years	30	42	40	41
% Female	42%	31%	40%	33%
% Digital Adherence	88%	69%	82%	85%
% Manual Adherence	9%	27%	6%	10%
% Combined Adherence	97%	96%	89%	94%
% Smart Pill Box Users	77%	39%	68%	100%
% Label users	23%	61%	32%	N/A

Table 1 Demographic summary and digitally and manually recorded doses per country.

Conclusions: Digital adherence was higher in patients using pillboxes, but several enablers and barriers should be considered before countries decide on the type of DAT.

OA11-281-09 Engaging local non-government organizations (NGOs) to scale up active case finding

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Background and challenges to implementation: Ukraine has one of the highest DR-TB burdens in the WHO *EU Region*, and annually an estimated 50% of DR-TB cases are not notified. The COVID-19 pandemic compounded DR-TB detection and treatment challenges: the number of DR-TB patients diagnosed dropped nearly 40% between the first and second quarters of 2020.

Intervention or response: PATH trained civil society representatives from 12 oblasts to build active case finding (ACF) skills and strengthen collaboration with health system. Beyond training, STBCEU developed ACF tools and job aids for social workers, a contact investigation algorithm, and informational flyers for contacts of TB patients. Since April 2020, NGO social workers have conducted systematic ACF among household and close contacts that have been provided to them by the DR-TB patients.

After comparing patient-listed contacts against those previously gathered by medical workers, they conducted home visits to motivate and refer newly listed contacts for TB examinations, supporting transportation when necessary. Also, they followed up with previously identified contacts to ensure timely re-examination.

Results/Impact: Between April 2020 and December 2021, medical providers identified 1,221 contacts of 930 index DR-TB patients, and social workers detected an additional 796 contacts.

Of these, 787 (98.9%) completed evaluation 19 (2.4%) were diagnosed with TB, and seven (0.9%) were diagnosed with LTBI and started TB preventive therapy. The

remaining 761 contacts received leaflets alerting them to repeat examination should TB symptoms arise. Of 289 previously identified contacts who were followed up by social workers, eight (2.8%) were diagnosed with TB and 21 (7.3%) with LTBI.

Summary of NGO social worker engagement in active case finding	Apr-Sep 2020	Oct-Dec 2020	Jan-Mar 2021	Apr-Jun 2021	Jul-Sep 2021	Oct-Dec 2021	Total
Contacts identified	81	153	172	182	94	114	796
Contacts who completed evaluation	73	152	172	179	96	115	787
Contacts diagnosed with active TB	1	5	4	2	3	4	19
Contacts diagnosed with LTBI	3				3	1	7
Contacts started on TPT	3				3	1	7
Re-examined contacts		51	76	62	43	57	289
Contacts diagnosed with active TB		2		1		5	8
Contacts diagnosed with LTBI		1	4			16	21
Contacts started on TPT			4				4

Conclusions: The ACF model that engage civil society proved highly effective in identifying missed TB cases and timely treatment start.

Close collaboration among NGOs' social workers and health services is critical. This model is recommended to be used for other regions within and outside of Ukraine.

OA11-282-09 Markedly increased childhood case notification through the engagement of orphanages in a hard-to-reach, high tuberculosis burden local government area in Anambra state, south-east Nigeria

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Background and challenges to implementation: World Health Organization estimates that 15% of incident Tuberculosis (TB) cases in a specified locality are children aged 0-15 years. Ogbaru Local Government Area (LGA) has a high TB burden and is located in a riverine and hard to reach area in Anambra State.

In the first and second quarters of 2019, only 5 (12%) and 2 (7%) of notified TB cases in Ogbaru LGA were children. The orphanages in the LGA were overcrowded with malnourished children not routinely screened for TB, making them high TB risk areas.

Intervention or response: In the third quarter of 2019, five selected high-volume orphanage homes within Ogbaru LGA were engaged in TB active case search. Outreaches were conducted to each orphanage and caregivers were trained to conduct TB clinical screening for children within the orphanage on arrival and monthly for 9 months using the national algorithm for pediatric TB clinical screening. Sputum samples were collected from the children and caregivers showing signs and symptoms. Children who were unable to expectorate were referred to pediatricians for further review and investigations. This intervention took place from Q3 2019 to Q1 2020. The national TB program recording tools were used for data collection and statistical analysis carried out using Excel.

Results/Impact: A total of 371 children were clinically screened for TB across the five homes, out of which 325 presumptive were identified and evaluated for active TB. A total of 61 confirmed TB cases were identified amongst the orphaned children and started treatment. The proportion of Childhood TB cases notified by the LGA increased from 8% pre-intervention average to 53% average during the 9 months intervention period.

Conclusions: Orphanages, when overcrowded and located in high TB burden areas are potential high TB risk areas for children. Systematically engaging them for TB clinical screening will improve TB case notification among children.

OA-12 Modelling the impact of TB control strategies

OA12-283-09 New tuberculosis vaccines in India: quantifying the potential health and economic impacts of adolescent/adult vaccination with M72/AS01E-like and BCG-revaccination-like vaccines

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Background: India suffers the largest global burden of tuberculosis. Eliminating this burden will likely require novel vaccines or vaccination strategies, such as M72/AS01E, or BCG-revaccination of adolescents, which have both recently completed Phase IIb trials. To maximise the benefit of novel approaches, it is important to investigate how variation in delivery strategies and vaccine profile will affect vaccine impact.

We evaluated the health and economic impacts of vaccination strategies in India while incorporating differences in vaccine characteristics and decisions regarding delivery.

Design/Methods: We developed and calibrated an age-stratified compartmental dynamic model of tuberculosis in India. Assuming current trends continue, we projected baseline epidemiology to 2050 (“no-new-vaccine”), and subsequently simulated scenarios over 2024–2050 with characteristics of the M72/AS01E and BCG vaccines consistent with trial data. We varied vaccine profile characteristics and delivery strategies to evaluate differences in impact.

We estimated the cumulative cases, treatments, and deaths averted by 2050 compared to the “no-new-vaccine” baseline, as well as the cost-effectiveness of each vaccine scenario.

Results: We found a 55% efficacy M72/AS01_E-like prevention of disease vaccine, efficacious with current infection, introduced in 2030 routinely to 9-year-olds and as an adolescent/adult campaign could avert approximately 10 million cases, 6 million treatments, and over 1 million deaths between 2030 and 2050. A 45% efficacy prevention of infection BCG-revaccination-like vaccine, efficacious in those with no current infection, introduced in 2027 as routine vaccination of 9-year-olds could avert over 5.5 million cases, 3.2 million treatments, and 600 thousand deaths. All scenarios were cost-effective.

Conclusions: M72/AS01_E-like and BCG-revaccination-like vaccines may substantially reduce the tuberculosis burden in India over the next decades and would be a cost-effective intervention. Investment in vaccine development and delivery should be prioritised, and focus placed on maximising vaccine efficacy during development, with prompt introduction and rapid scale-up when a vaccine becomes available.

OA12-284-09 The global impact and cost-effectiveness of multidrug- and rifampicin-resistant tuberculosis household contact management in children for 2019: a modelling study

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Background: Estimates suggest at least 30,000 children develop multidrug- or rifampicin-resistant tuberculosis (MDR/RR-TB) each year. Despite household contact management (HHCM) being widely recommended, it is rarely undertaken.

Design/Methods: We used mathematical modelling to evaluate the potential country-level and global impact and cost-effectiveness of MDR/RR-TB HHCM for children <15 years living with a newly diagnosed case of MDR/RR-TB.

We compared a baseline of no HHCM to several HHCM strategies and tuberculosis preventive therapy (TPT) regimens, calculating the impact on MDR/RR-TB cases, deaths, and health system costs.

All HHCM strategies involved the screening of children for prevalent TB disease but with TPT either not given or targeted dependent on age, HIV status and tuberculin

skin test (TST) result. We evaluated the use of fluoroquinolones (levofloxacin and moxifloxacin), delamanid and bedaquiline as TPT.

Results: Compared to a baseline without HHCM, HHCM for all adults diagnosed with MDR/RR-TB in 2019, would have entailed screening 227,000 (95% uncertainty interval [UI]: 205,000-252,000) children <15 years globally, and averted 2,350 (95% UI: 1,940- 2,790) tuberculosis deaths, costing an additional \$63 (95% UI: 74-95) million. If all household MDR/RR-TB child contacts received TPT using levofloxacin, 2,440 (95% UI: 1,900-3,060) incident tuberculosis cases and an additional 870 (95% UI: 650-1,130) deaths would have been prevented. Incremental cost-effectiveness ratios were lower than half of per capita gross domestic product for most interventions in most countries. Targeting only children <5 years and those living with HIV reduced incident cases and deaths averted, but improved cost-effectiveness. TPT using delamanid increased impact compared to levofloxacin.

Conclusions: HHCM for MDR/RR-TB is cost-effective in most settings, and could avert a substantial proportion of MDR/RR-TB cases and deaths in children globally

OA12-285-09 Impact of reversion of M. tuberculosis immunoreactivity tests on the estimated annual risk of infection

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Background: A key metric in tuberculosis epidemiology is the annual risk of infection (ARI), which is usually derived from Mycobacterium tuberculosis (Mtb) prevalence surveys using immunoreactivity tests, e.g. the tuberculin skin test (TST) in children.

However, deriving the ARI implicitly assumes persistent immunoreactivity in infected individuals. While this assumption is known to be incorrect, the impact of reversion is often not accounted for.

Design/Methods: We used a compartmental model of Mtb infection to quantify the impact of reversion on ARI estimation using age-specific empiric estimates of reversion for TST and interferon-gamma release assay (IGRA). The naïve ARI (not accounting for reversion) was compared against each true ARI (up to 50% reversion).

Results: Annual reversion probabilities up to 2.5% increase the true ARI by less than 25%. Similarly, no substantial increases are seen for any reversion probability for age less than one year. Using empirical data on TST reversion (22.2%/year for 0-19yo), the true ARI is 2-5 times higher than the naïve in the 8-12 age range; this is maintained until age 60, when there is at least a 5-fold increase in true ARI relative to naïve ARI. Applying empirical reversion probabilities for IGRA (9.9%/year) showed a 1.5-2-fold underestimation among 12-18 year-olds. Declines in ARI over time did not affect results. The exploratory analysis evaluating the estimated ARIs from published TST surveys illustrates how the true ARI would be at least two times higher when accounting for reversion.

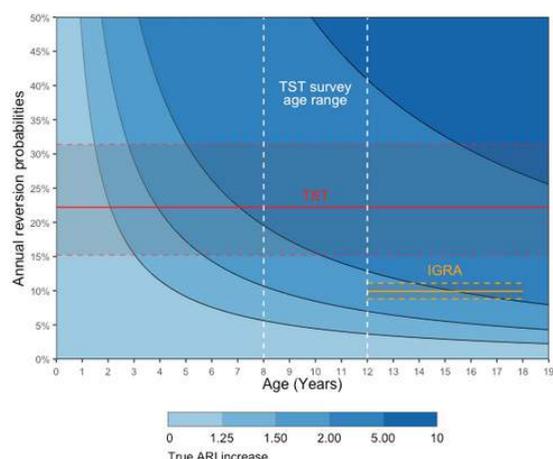


Figure. True ARI increase: true (varying reversion levels) to naïve ARI (no reversion) ratio.

Conclusions: Ignoring reversion leads to a stark underestimation of the true ARI in populations, changing our understanding of *Mtb* transmission intensity. While there are other contributing factors for TB immunoreactivity exist, future surveys should quantify and adjust for reversion probabilities to provide a more accurate reflection of the burden and dynamics of *Mtb* infection.

OA12-286-09 Impact and yield of tuberculosis infections (TBI) screening and treatment in immigrant groups in a low-prevalence country: a transmission modelling approach

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Background: Recent WHO guidelines recommend TB preventive treatment in populations at high risk of developing TB, such as persons living with HIV and TB contacts. It also recommends low burden countries to consider systematic testing and treatment for TB infection in immigrants from high-burden countries.

Replacing TB disease screening by TBI screening could prevent development of TB disease among migrants post arrival, thereby potentially aiding low TB incidence countries in working towards pre-elimination levels as defined in the WHO END TB Strategy.

Here, we investigated the potential long-term impact on TB incidence, of screening for TBI in three target groups: immigrants from high-incidence countries, asylum seekers, and the established Eritrean community.

Design/Methods: To that end, we formulated a mathematical model for TB transmission within the Netherlands. This was calibrated to the Dutch situation, and incorporated epidemiological data of three implementation studies carried out in the target groups considered. We used TB incidence categories: 50-100/100,000 ; 100-200/100,000 ; and >200/100,000 population. The time window for assessment was 20 years; we assumed no transmission between nationalities, and excluded transmission from 1st to 2nd generation immigrants.

Results: Using the calibrated transmission model, we estimated that per 10,000 persons screened, and relative to X-ray entry screening, LTBI screening would avert 10, 20, and 11 TB patients, respectively, among immigrants from countries with a TB incidence of 50-100, 100-200, and >200 /100,000 persons. For asylum seekers this number would be 102 TB patients, and for settled Eritrean migrants 44 TB patients.

Conclusions: Targeted TBI screening has greatest impact among asylum seekers and settled Eritrean migrants, followed by immigrant groups from respectively intermediate, then high- and low-incidence countries.

OA12-287-09 Improving estimates of social contact patterns for the airborne transmission of *Mycobacterium tuberculosis* and other respiratory pathogens

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Background: Data on social contact patterns are widely used to parameterise age-mixing matrices in mathematical models of infectious diseases. Despite this, little at-

tention is given to how social contact data are collected and analysed, or how the types of contact most relevant for transmission may vary between different infections. In particular, most studies focus on close contacts only – people spoken to face-to-face. This may be appropriate for infections spread primarily by droplet transmission, but it neglects the larger numbers of ‘shared air’ casual contacts who may be at risk from airborne transmission of pathogens such as *Mycobacterium tuberculosis* (*Mtb*), measles, and SARS-CoV-2.

Design/Methods: We conducted social contact surveys in communities in two provinces of South Africa in 2019 (Western Cape and KwaZulu-Natal). In addition to close contact data, we collected data on places visited and people present, allowing casual contact patterns to be estimated. Using these data, we estimated age mixing patterns relevant for i) droplet, ii) non-saturating airborne transmission, and iii) *Mtb* an airborne infection where saturation of household contacts occurs.

Results: Estimated contact patterns by age did not vary greatly between the three transmission routes/infections, in either setting. In both communities, relative to other adult age groups, overall contact intensities were lower in 50+ year olds when considering contact relevant for airborne transmission (ii and iii) than when considering contact relevant for droplet transmission (i)

Conclusions: Our findings provide some reassurance that the widespread use of close contact data to parameterise age-mixing in transmission models of airborne infections may not be resulting in major inaccuracies. The contribution of older age groups to transmission may be over-estimated, however.

There is a need for future social contact surveys to collect data on casual contacts, to investigate whether our findings can be generalised to a wider range of settings, and to improve model predictions.

OA12-288-09 Factors for medication adherence among adult TB patients using digital adherence technologies: sub-analysis from cluster randomized trials

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Background: The Adherence Support Coalition to End TB (ASCENT) project is conducting pragmatic cluster-randomised trials in five countries, with the aim of improving treatment outcomes by supporting treatment adherence using DATs.

The aim of this sub-analysis is to identify factors associated with adherence among patients in the intervention arm in four of the five countries.

Design/Methods: A subset of patients in the ASCENT project across South Africa, Tanzania, Ukraine, and the Philippines enrolled onto a DAT (smart pillbox or SMS self-report using labels) with an opportunity of >6 months follow-up define the population. Daily adherence was measured based on digital confirmation with the DAT (smart pillbox opening or short message services sent).

Patient-level adherence was defined as the count of confirmed doses by the DAT/days doses should have been taken. Factors associated with adherence were analysed using negative binomial regression with a random effect at the facility-level and the results are presented as crude rate ratios.

Results: 784 patients are included in the analysis. Median adherence percent combining across DATs was 66.8% (IQR: 38.7% - 88.3%) for the Philippines, 90.1% (IQR: 76.7% - 97.2%) for South Africa, 92.9% (IQR: 82.4% - 97.8%) for Tanzania, and 89.0% (IQR: 79.4% - 96.2%) for Ukraine.

Adherence was highest among patients over 58 years in Ukraine (90.50%) and among male patients in Tanzania (88.12%). Patients aged 38-47 years had higher levels of adherence versus 18-27 years in Tanzania (1.26, [1.06 - 1.50]) and South Africa (1.22, [1.06 - 1.40]) (Table 1).

	The Philippines		South Africa		Tanzania		Ukraine		
	Average adherence	Rate ratio [95% CI]	Average adherence	Rate ratio [95% CI]	Average adherence	Rate ratio [95% CI]	Average adherence	Rate ratio [95% CI]	
18-27	56.45%	1	79.85%	1	76.20%	1	87.71%	1	
28-37	62.97%	1.01 [0.70 - 1.47]	79.21%	1.04 [0.91 - 1.20]	89.14%	1.24 [1.04 - 1.49]	85.64%	0.97 [0.87 - 1.09]	
Age group (yrs)	38-47	60.01%	1.00 [0.71 - 1.40]	87.25%	1.22 [1.06 - 1.40]	89.35%	1.26 [1.06 - 1.50]	84.89%	0.94 [0.85 - 1.05]
	48-57	63.09%	1.30 [0.95 - 1.77]	86.01%	1.15 [1.00 - 1.33]	86.69%	1.15 [0.94 - 1.40]	84.23%	0.96 [0.85 - 1.07]
	58+	66.57%	1.20 [0.84 - 1.71]	84.02%	1.17 [1.00 - 1.38]	89.41%	1.22 [1.02 - 1.47]	90.50%	1.00 [0.89 - 1.13]
Sex	Male	63.10%	1	81.24%	1	88.12%	1	85.63%	1
	Female	58.53%	0.88 [0.70 - 1.11]	87.37%	1.06 [0.98 - 1.14]	87.09%	1.02 [0.93 - 1.12]	87.12%	1.07 [1.01 - 1.14]

Table 1: Negative binomial regression between medication adherence and select predictors.

Conclusions: In this analysis adherence varied by country and was highest in 38-47 years for Tanzania and South Africa. An increase in sample size and inclusion of other demographic and clinical characteristics will improve the insights on adherence in this population of patients.

OA12-289-09 Accuracy and costs of screening and diagnostic algorithms for the early detection of tuberculosis

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Background: WHO's 2021 TB (<https://extranet.who.int/tbknowledge/node/1274>) screening guidelines recommend the use of new and established screening tests for early detection of TB disease. Implementers often face a challenge to combine these tests into an algorithm that optimizes accuracy and/or efficiency.

Design/Methods: We present estimates of accuracy, yield, and costs of a range of different screening and diagnostic algorithm options described in the WHO TB screening operational handbook. We calculated the performance of the algorithms, including yields of true- and false-positive diagnoses, predictive values, and direct costs for delivering these services (overall and per person screened), in hypothetical populations with TB prevalence ranging from 0.5% to 2%. All algorithms include diagnostic evaluation with a rapid molecular test.

Results: Algorithms including symptom screening in combination with CXR in parallel or in a sequential negative manner have the highest yield, followed by the algorithm that uses CXR alone and then followed by the algorithm that uses mWRD as a screening test. The number of false-positives and false negatives is smallest in the parallel and serial negative screening algorithms.

The performance of the algorithms also varies with the prevalence of TB in the population being screened. For all algorithms, the risk of a false-positive diagnosis increases as the prevalence declines. At a TB prevalence of 0.5% in the screened population, all the algorithms have a positive predictive value of less than 75% (i.e. 25% have a false positive diagnosis). The cost per person screened and cost per true case detected are comparable for all CXR algorithms, while they are significantly higher for screening with mWRD.

Conclusions: Selection of appropriate screening algorithms requires careful consideration based on the objectives of the screening programme and prior to costing the preferred/selected screening strategy as part of the National Strategic Plan for Tuberculosis.

OA-13 Transmission dynamics of TB and MDR-TB

OA13-290-09 Multidrug and pre-extremely drug resistant tuberculosis in Mozambique

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Background: Worldwide, an estimated 9.9 million people fell ill with tuberculosis (TB) in 2020 (1). Mozambique is one of the countries with the highest TB incidence (368 cases/100,000 population), and faces challenges to detect multidrug-resistant tuberculosis (MDR-TB, resistance to at least isoniazid [INH] and rifampicin [RIF]) and Pre-XDR (MDR plus resistance to at least one fluoroquinolone), and XDR-TB (additional resistance to one World Health Organization Group A drug) (1). In Mozambique, more than 1000 new MDR TB cases are notified every year, however detailed data on drug resistant (DR) determinants are not available. The aim of this study is to characterize the genomic variability of the DR-TB strains circulating in Mozambique from 2015-2021.

Design/Methods: Whole genome sequencing data of 809 DR Mtb strains obtained in years 2015 - 2021 from the National Tuberculosis Reference Laboratory in Maputo were used for a phylogenetic classification, resistance prediction and cluster analysis and linked with phenotypic drug susceptibility testing data.

Results: The majority of strains belonged to lineage 4 (64%), followed by strains of lineage 2 (21%), and lineage 1 (12%). 21% of the rifampicin resistant Mtb

strains were already pre-XDR due to fluoroquinolone resistance, and 2% were XDR. Genome based cluster (5 SNP threshold) revealed a cluster rate of 69% among MDR, of 84% of pre-XDR, and of 92% of XDR strains linked to specific fitness compensate outbreak clones. Furthermore, we document an increasing trend for bedaquiline resistance over the study period (2.5% in 2016 to 15% in 2021).

Conclusions: Pre-XDR, and XDR-TB emerged in alarming numbers in Mozambique. Cluster rates of MDR, pre-XDR, and XDR strains are very high, indicating ongoing transmission of DR TB in the country. Urgent measures to rapidly detect and treat DR TB cases in the country are needed to break transmission chains and avoid the selection of further resistances e.g. bedaquiline.

OA13-291-09 Uncertainty of hospital or community MDR-TB reinfection in patients on TB treatment in high MDR-TB burden setting

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Background: In low resource settings the transmission of the MDR-TB strains might occur not only from a TB patient to a healthy individual in the community, but also among TB patients during hospitalizations. In the present study, we aimed to prospectively assess the risk of nosocomial transmission of the MDR strains of *M. tuberculosis* (Mtb) in a tertiary pulmonology hospital.

Design/Methods: We performed a prospective observational study at the Phthisiopneumology Institute (PPI) in the Republic of Moldova. All patients admitted between 01.07.2014 and 30.06.2015 were enrolled in the study. The study participants were followed up for 2 years upon enrollment.

During the follow up period we looked for any case of culture positive TB confirmed as susceptible on enrollment but in which an MDR strain of *M. tuberculo-*

sis was isolated during the follow up. To investigate putative nosocomial transmission events, we sequenced all culture-confirmed MDR-TB isolates.

Results: During the study period 932 culture confirmed TB patients were admitted to PPI. Of them 293 had MDR-TB at enrollment. Assessing phenotypic DST results of the follow up culture isolates we found 17 patients with susceptible culture positive TB on enrollment in whom follow up cultures shown a MDR Mtb strain (focus patients). By genomic analysis 124/268 (46.3%) of the MDR strains were grouped into 28 clusters. However, we could only link 6/17 focus patients to one of the 28 identified clusters, while the remaining focus patients have no apparent link to the clustered cases in cohort.

However, when phylogenetic analysis is considered and more relaxed genetic distance threshold (12 instead of 5 SNPs) is applied, the genomic data indicate a broad transmission scenario of these strains in the community. **Conclusions:** The genomic analysis did not allow confidently to distinguish between hospital and community MDR-TB reinfection in a high burden MDR-TB setting.

OA13-292-09 Identification of urban areas presenting high incidence of tuberculosis using satellite images allows increasing the yield of active case finding in Kigali, Rwanda

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Background: Tuberculosis (TB) elimination requires enhancing prevention, screening and treatment services in communities presenting high levels of disease. In urban areas, TB is strongly associated with socio-economic determinants, and the poorest populations congregate in neighborhoods which are easily recognizable by a high concentration of small houses. In Africa and elsewhere, such suburbs can be rapidly expanding, making it difficult to precisely identify populations requiring enhanced TB services.

Design/Methods: We applied object contour detection and color filtering on satellite images to grade neighborhoods according to their socio-economic level for the city of Kigali (Rwanda).

Thereafter, we initiated systematic TB screening in the poorest and surrounding areas. To assess the individual risk for TB, participants underwent a digital questionnaire embracing both symptoms and exposure to TB (MediScout, Savics), followed by a laboratory test (Xpert MTB/RIF, Cepheid) for those scoring with a moderate to high score.

Results: In both groups, the initial questionnaire allowed to rule-out TB for over 96% of the participants. When testing was offered, those living the low socio-economic areas were more prompt to take a test (64% versus 58%) and had a higher chance of having a positive PCR test (5.2% versus 3%). 3 out of the 7 people who tested positive for pulmonary TB in the low socio-economic areas had not reported cough for more than 15 days during their initial interview.

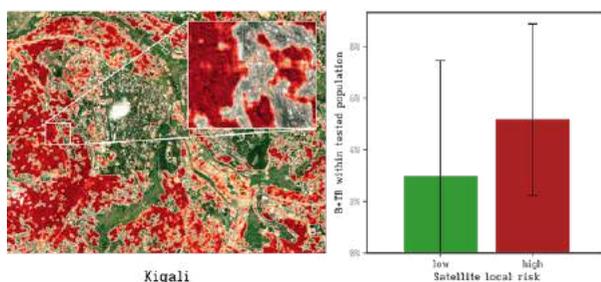


Figure. Left: Grading of suburbs based housing characteristics (red: highest density of small houses); Right: PCR positivity rate among study participants according to grading of suburbs.

Conclusions: In large cities, satellite imagery analysis allows to grade suburbs according to housing size and density. Considering that poverty-related suburbs are often rapidly evolving in size and less covered by TB services, satellite imagery should be considered as a useful tool to guide TB elimination strategies in large cities.

OA13-293-09 High proportion of tuberculosis transmission among social contacts in rural China: a 12-year prospective population-based genomic epidemiological study

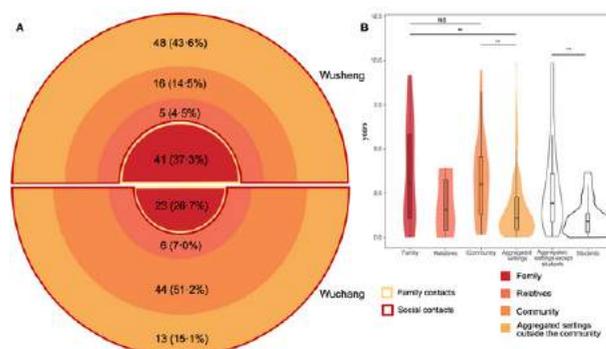
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Background: Tuberculosis (TB) is more prevalent in rural than urban areas in China, and delineating TB transmission patterns in rural populations could improve TB control.

Design/Methods: We conducted a prospective population-based study of culture-positive pulmonary TB patients diagnosed between July 1, 2009 and December 31, 2020 in two rural counties in China. Genomic clusters

were defined with a threshold distance of 12-single-nucleotide-polymorphisms, based on whole-genome sequencing. Risk factors for clustering were identified by logistic regression. Transmission links were sought through epidemiological investigation of genomic-clustered patients.

Results: Of 1517 and 751 culture-positive pulmonary TB patients in Wusheng and Wuchang counties, respectively, 1289 and 699 strains were sequenced. Overall, 624 (31.4%, 624/1988) patients were grouped into 225 genomic clusters. Epidemiological links were confirmed in 41.8% (196/469) of clustered isolates, including family (32.7%, 64/196) and social contacts (67.3%, 132/196). Social contacts were generally with relatives, within the community or in shared aggregated settings outside the community, but the proportion of clustered contacts in each category differed between the two sites. The time interval between diagnosis of student cases and contacts was significantly shorter than family and social contacts, probably due to enhanced student contact screening. Transmission of multidrug-resistant (MDR) strains was likely responsible for 81.4% (83/102) of MDR-TB cases, with minimal acquisition of additional resistance mutations.



Conclusions: This long-term genomic-epidemiological study helped to delineate the patterns of TB transmission in rural China. Transmission appears to occur principally among close contacts, but contact investigation should be extended to include the social interactions that are common in the targeted population. Further improvement and implementation of screening of close contacts are critical to halt transmission and improve TB control in rural areas.

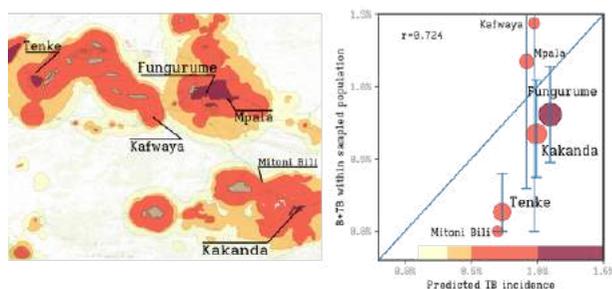
OA13-294-09 Data-driven mapping of tuberculosis incidence allows identifying communities with high circulation of tuberculosis in the Democratic Republic of Congo

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Background: In remote areas of low resource countries, disease notification may underestimate the real burden of TB and therefore lead to inadequate prioritization strategies when it comes to disease prevention and strengthening of health services. To overcome the biases associated with structural under-reporting of disease in such marginalized rural villages, we developed a One-Health approach consisting in complementing official disease notification data with demographic and environmental information such as the dispersal of health facilities and mines.

Design/Methods: We developed algorithms to predict TB incidence at a very granular level based on selected openly available datasets (population distribution, health facility and villages surrounding mines operations) and local disease notification data. This algorithm was ran for the Lualaba province in the Democratic Republic of Congo and resulted in a map predicting disease incidence. To assess the performance of this tool, we performed a prospective multicentric clinical study. Participants from different villages screened for TB using a risk-score questionnaire (MediScout, Savics) followed by a laboratory test (Xpert MTB/RIF, Cepheid) when the risk-score was above a particular threshold.

Results:



Predicted incidence rate and intervention location (left). Comparison to the positive rate in each location (right). The study took place in 6 distinct villages with a predicted TB incidence ranging from 700/100,000 (Tenke) to 1,000/100,000 (Fungurume). In total, 4,776 individuals were enrolled and 458 (9.5%) underwent a laboratory

test following the initial risk assessment highlighting a moderate to high risk of disease. Among these, 33 (7%) were tested positive. The number of people needed to screen to find one case was respectively 752 in Tenke and 124 in Fungurume.

Conclusions: These results indicate that the prioritization of targeted prevention and screening interventions can be data-driven, and should include environmental information. In our experience, the yield of active case finding varied considerably between villages, and followed the estimated incidence.

OA13-295-09 Comparing Mtb transmission risks pre-pandemic to COVID-19 pandemic conditions in a primary care clinic in a TB/HIV high burden setting

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Background: Congregate settings, such as healthcare clinics, play an essential role in airborne transmission. Using patient and environmental data, we studied effects of COVID-19 infection prevention and control (IPC) measures on *Mycobacterium tuberculosis* (Mtb) transmission at a primary care clinic in South Africa.

Design/Methods: During 4 weeks in August 2019 (pre-COVID-19) and in October/November 2021 (COVID-19 alert level 1 of 5), we collected clinical data, patient movements using video sensors, and environmental data including indoor CO₂ levels (parts per million [ppm]), relative humidity (RH), and number of MtbDNA in the air using bio-aerosol sampling devices. Pandemic IPC measures included facemasks for all, physical distancing, increased natural ventilation, additional waiting zone outside, and patient triage.

Results: Compared to pre-COVID-19, the median number of people visiting the clinic per day was lower during COVID-19 (394 interquartile range [IQR] 277-444 vs. 706, 622-823). Density of people remained highest in the waiting room compared to other rooms (Figure), with a distinctive pattern of low-density areas on the benches due to physical distancing during COVID-19.

TB prevalence among patients seen at the clinic was lower during COVID-19 (0.1%, 95%CI 0.01-0.4% vs. 0.5, 0.3-0.7%). Median CO₂ levels were also lower during COVID-19 (444, IQR 426-461 vs. 623ppm, 501-751); although consistently higher in the waiting compared to other rooms. The ventilation rate (air change) was higher during COVID-19 compared to pre-pandemic (52 vs. 11 L/h per person), and the median RH lower (50%,

IQR 48-53 vs. 61%, 57-66%). We are in the process of combining these data with clinical data and *Mtb* DNA in the air to model effects of interventions on TB transmission risks.

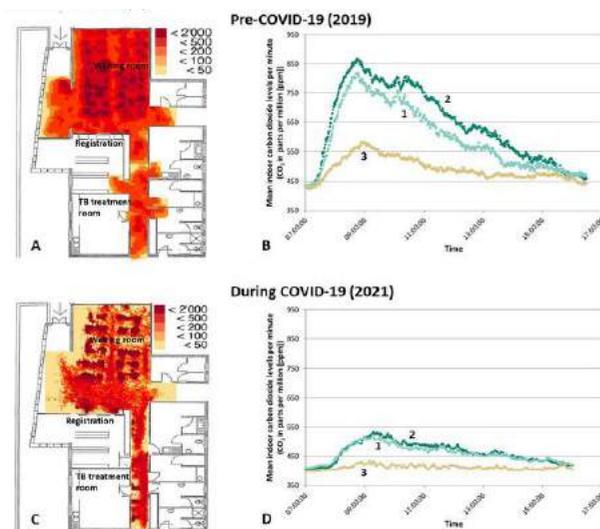


Figure. Density of people visiting a primary care clinic in Cape Town, South Africa, and environment-associated factors for airborne transmission, comparing pre-COVID-19 and under COVID-19 infection control measures.

Panel A and C: Density of visiting people per minute during the study period.

Panel B and D: Mean indoor CO₂ levels during the day at the registration desk (1), waiting room (2) and TB treatment room (3).

Conclusions: Strict implementation of IPC measures to control transmission of COVID-19 at high-risk settings can reduce the transmission other airborne diseases including TB, showing the advantage of sustaining IPC in healthcare settings.

OA13-296-09 Longitudinal transmission of multidrug-resistant tuberculosis in urban China

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Background: China still has a high Tuberculosis disease burden. Currently, the emergence of multidrug-resistant tuberculosis (MDR-TB) makes it more challenging to achieve the goal of ending tuberculosis.

We conducted a retrospective population-based genomic epidemiologic study of MDR-TB in an urban region in China over 15 years with the aim of understanding the extent of MDR-TB transmission and risk factors for new transmission events to inform future efficient disease control.

Design/Methods: Whole-genome sequencing (WGS) was performed on MTBC positive cultures from patients with MDR-TB identified by drug susceptibility testing (DST) in Shanghai, China, between 2004 and 2018. Genomic variants were obtained by using a standardized bioinformatics pipeline and in-house scripts.

We reconstructed the phylogenetic trees, predicted *in-silico* drug resistance profiles, and determined the evolutionary sublineages. We identified transmission clusters and determined the transmission network combined with epidemiological information.

Results: 35% (387/1101) strains were in genomic clusters, of which L2.2.1 was the most prevalent sublineage (876 strains). Among these MDR-TB strains, the genotypic resistance rates of streptomycin (72%) and fluoroquinolones (32%) were relatively high.

The study found two large clusters of transmission of 21 MDR-TB cases, each spanning more than 14 years. We obtained cross-district transmission involving migrant and resident populations despite transmission events in the same residential communities.

The largest cluster of cases spanning 16 years was distributed in six different administrative regions. Heterogeneity of drug resistance mutations was observed during the transmission. The lineage-2 or Beijing family strains were more likely to be clustering compared to L4, as well as the extent in cluster size.

Conclusions: MDR-TB transmission can prolong for a long-term period even with a relatively well-established TB control system. It is crucial that intensive infection control, including aggressive contact tracing or active case findings, be fully implemented to prevent MDR-TB transmission.

OA13-297-09 Manipulation of adult formulations of drug resistant tuberculosis medicine in children diagnosed with drug resistant tuberculosis in eThekweni, KwaZulu Natal, South Africa: a descriptive cohort study

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Background: Optimal drug levels and minimal toxicity are critical success factors in improving treatment outcomes for adults and children with drug resistant tuberculosis. In the absence of child friendly formulations adult formulations are manipulated to achieve the correct dose.

This includes splitting or crushing a number of bitter tasting tablets which may render the medication ineffective and increase rates of resistance.

There is a paucity of data on how the adult formulations are manipulated and the impact of manipulation on treatment outcomes in children.

Design/Methods: A retrospective clinical chart review of children diagnosed with drug resistant tuberculosis initiated on treatment between 2018 and 2020 was conducted. Data on clinical characteristics, regimen, dosage, formulations prescribed, clinical management, adverse events and final treatment outcomes were extracted and analysed.

Results: 142 children were initiated on DR TB treatment between 2018 and 2020. 26.76% were HIV positive initiated on antiretroviral therapy. 95.17% were diagnosed with pulmonary TB and 2.76% extra pulmonary TB. In 83.80% of children the suspected source case was unknown. 18.31% of children presented with positive smears at baseline, 36.62% was culture positive at baseline. 52.11% were initiated on long regimen and 47.89% on short regimen with 100% of children being initiated in hospital. 78.17% of children were initiated on an all-oral regimen with new and repurposed medicine.

Majority of side effects were mild to moderate with some grade 3 side effects being reported. 95.07% children had successful treatment outcomes (cured and completed treatment) and 4.93% had unsuccessful treatment outcomes (lost to follow or died).

Conclusions: Children prescribed adult formulations of drug resistant tuberculosis that are manipulated to achieve required doses in an all-oral DR TB regimen achieve excellent treatment success rates with minimal toxicity.

However, child friendly formulations will simplify administration for caregivers and healthcare workers and make the treatment journey easier to navigate.

OA-14 Prevalence of, risk factors for, mortality due to TB

OA14-298-09 Prevalence of pulmonary tuberculosis among prisons inmates: a case of the Port Harcourt Correctional Centre, Rivers State, Nigeria

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Background: Pulmonary Tuberculosis (PTB) among prisoners is reported as a major public health problem globally, especially in developing countries. USAID-funded KNCV TB LON 1&2 project implemented in 14 states in Nigeria and in collaboration with the NTPLCP, has supported Active Case Finding(ACF) of Tuberculosis in communities; the prison community being one of the high-risk populations. Port Harcourt correctional center is notably the most populated prison in Nigeria with about 4,600 inmates. The study aimed at ascertaining the prevalence of PTB among inmates of the Port Harcourt Correctional center.

Design/Methods: A cross-sectional survey was conducted in the Port Harcourt Correctional Center to determine the period prevalence of bacteriologically positive pulmonary tuberculosis (PTB) between October 2021 to March 2022. Inmates were selected randomly based on availability. Screening for PTB was done using a symptoms checklist and prisoners with cough of 2 weeks or more duration were investigated bacteriologically using GeneXpert test.

Results: The study showed that out of 1,745 inmates screened, 828 presumptive were identified and evaluated bacteriologically, 62 TB cases were diagnosed and placed on treatment with a TB yield of 8%. Three percent of the total diagnosed cases were drug-resistant TB. In other words, it can be deduced that for every 28 inmates in the correctional facility a positive TB case could be diagnosed.

Conclusions: The risk of spread of Tuberculosis especially among prisoners increases every day, suggesting that prisons represent a significant reservoir of tuberculosis. Only comprehensive strategies for tuberculosis and disease control in prisons such as prison decongestion, prison reform, early and efficient diagnosis and treatment of patients would reduce the tuberculosis burden in the prison system.

OA14-299-09 Prevalence of Pre-XDR TB and XDR TB in Indonesia per WHO new definition

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Background and challenges to implementation: Indonesia is among the 27 countries classified as a high-burden country for MDR TB worldwide. It is estimated there were 24,000 drug-resistant TB (DR-TB) cases nationally. In early 2021, WHO updated the definition for pre-XDR TB (MDR/RR-TB with resistance to any fluoroquinolone) and XDR TB (MDR/RR-TB with resistance to any fluoroquinolone and bedaquiline or/and linezolid), which has been adopted in Indonesia promptly.

Intervention or response: There are 14 certified laboratories that are able to conduct tuberculosis phenotypic drugs susceptibility test (DST) and 7 laboratories for second-line LPA test in the country. Since April 2021, Indonesia started to test the susceptibility for bedaquiline (bdq) and linezolid (lzd) for all confirmed RR-TB patients, in addition to other drugs such as moxifloxacin, levofloxacin and clofazimin. The result of DST and LPA can be accessed by the DR-TB treatment facilities through the web-based national TB information system called SITB.

Results/Impact: In 2021, there were 5234 DR-TB patients initiated second-line TB treatment registered in SITB from 34 provinces in Indonesia. There were 3900 patients that were tested for fluoroquinolone resistance with either culture-based DST or second-line LPA, out of which 392 (10%) were found to be resistant with fluoroquinolone (ofloxacin, levofloxacin, or moxifloxacin). Among those with any fluoroquinolone resistant, 3 patients were also resistant to both bdq and lzd, 9 patients resistant to bdq but susceptible/unknown resistance to lzd, and 23 patients resistant to lzd but susceptible to bdq. Total XDR TB patients identified among those tested for DST were 35 (0,9%).

Conclusions: The low prevalence of XDR TB patients brings great hope for the success of the latest DR-TB treatment containing bdq and lzd. However, NTP should increase the effort to ensure that all DR-TB patients starting DR-TB treatment are tested for phenotypic DST or LPA.

OA14-300-09 Prevalence of extrapulmonary tuberculosis in Africa: a systematic review and meta-analysis

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Background: Extrapulmonary tuberculosis (EPTB) can occur alone or together with pulmonary tuberculosis (PTB). EPTB is under-ascertained due to lack of awareness, difficulty in diagnosis, and the greater difficulty in identifying *Mycobacterium tuberculosis* from samples such as urine and cerebrospinal fluid relative to sputum. The burden of EPTB in countries with high HIV prevalence such as sub-Saharan countries is not well understood.

Design/Methods: We conducted a systematic review to estimate the prevalence of EPTB in African countries. We used search databases; PubMed, EMBASE, Web of Science, CINAHL & Scopus. We included 84 study articles published from 1990 to 2020. We conducted meta-analysis using random effects model.

Results: The overall estimate of proportion of EPTB among all TB cases in Africa was (0.24 (95% CI:0.21; 0.28)). To explore the potential sources of heterogeneity, we performed meta-regression analysis. There was a substantial heterogeneity in the prevalence estimate of the five African regions. Eastern region had the highest estimate with 0.31 (95% CI: 0.26;0.36) and the lowest estimate was in Western Africa 0.17 (95% CI: 0.10;0.27).

Conclusions: Our systematic review and meta-analysis gives insight to the burden of EPTB in Africa - an area for which there are few reports. Efforts and strategies aimed at ending the global TB epidemic have centred on PTB. Combined efforts focused on PTB and EPTB are needed to reach global goals and benchmarks for reducing the burden of TB set as part of the Sustainable Development Goals (SDGs) and the WHO's End TB strategy.

OA14-301-09 Sex difference in tuberculosis: Disentangling exposure, access to healthcare, and biological factors

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Background: In most settings, men have a much higher tuberculosis notification rate compared to women. Studies suggest that the sex difference in tuberculosis prevalence exists independently of case reporting and could be explained by a combination of various factors, possibly including a biological difference. We assessed the contribution of addressed factors to the observed sex difference in tuberculosis prevalence.

Design/Methods: A nested case-control study was conducted within the 2017 tuberculosis prevalence survey in Vietnam, in which the case group consisted of all Xpert MTB/Rif *Mycobacterium tuberculosis* positive cases found in the survey, and the control group was randomly selected from the survey participants. We employed structural equation modelling (SEM) to describe pathways to tuberculosis according to an *a priori* conceptual framework, consisting of four domains: socio-economic status (SES), behavioral and environmental risks, access to healthcare, and (to take account of measuring tuberculosis prevalence rather than incidence) clinical symptoms.

Results: There were 1,319 participants included in our analysis, of which 250 were in the case group. Except for SES, men were more disadvantaged than women in all other domains. In the SEM model, sex was directly associated with tuberculosis [adjusted odds ratio for men compared to women 3.1 (95% CI 1.8-5.3)], as well as indirectly through other domains. Clinical symptoms, behavioral and environmental risks, and access to healthcare were also directly associated with tuberculosis. SES affected TB prevalence only indirectly through other domains.

Conclusions: The strong sex difference in TB prevalence found in Vietnam is explained by a complex interplay of factors relating to behavioral and environmental risks, access to healthcare, and clinical presentation, but after controlling for all these factors, there remains a direct sex effect that is likely caused by biological factor(s). Tuberculosis control efforts should include more effective strategies focusing on men to reduce the disease burden, aside from addressing the other controllable factors.

OA14-302-09 Predictors of mortality among patients on tuberculosis treatment in Botswana: a 10-year retrospective cohort study

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Background: Tuberculosis (TB) is one of the leading causes of death by an infectious disease. The aim of this study was to determine the TB mortality rate and its predictors among patients on TB treatment in the Botswana.

Design/Methods: This was a retrospective cohort study utilising program data captured from 2008 to 2017 by the Botswana National TB program (BNTP). All drug-sensitive TB patients aged 16 years or older were included. IBM SPSS statistics software was used for data analysis. Kaplan Meier curves were used to display cumulative survival. The log rank test was used to compare survival between groups. Cox proportional Hazards regression was used to determine the predictors of mortality. A *p* value of <0.05 was considered to signify significant association in the cox multivariate model.

Results: A total of 68,810 TB cases were analysed of which 38,121 (55.4%) were HIV positive, 20,565 (29.9%) were HIV negative and 10,124 (14.7%) had an unknown HIV status. The median age was 37 and 35 years for HIV positive and HIV negative patients respectively. The overall mortality rate was 10.3% disaggregated as 11.5% and 7.1% for HIV positive and HIV negative patients respectively. Being in the 26-35 years (AHR 1.52), 36-45 years (AHR 1.94), 46-55 years (AHR 2.33), 55-65 years (AHR 3.94) and >65 years (AHR 5.63) age groups were all significantly associated with mortality compared to the 16-25 years age group. Other predictors of mortality were positive HIV status (AHR 1.67) unknown HIV status (AHR 1.68), retreatment for loss to follow up (AHR 1.57) and no microscopy diagnosis (AHR 1.21). Having a positive microscopy result was protective (AHR 0.50).

Conclusions: This study confirms a high TB mortality in Botswana especially among HIV positive cases and patients with unknown HIV status. Interventions should target the identified predictors of mortality.

OA14-303-09 Programmatic data over-estimate deaths due to tuberculosis during treatment and under-estimate deaths due to tuberculosis after treatment

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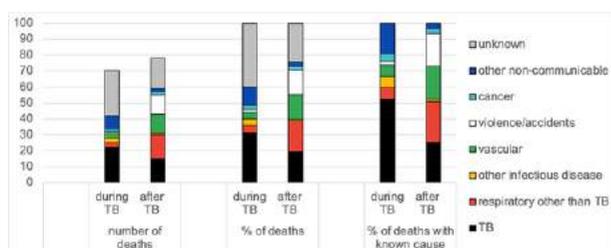
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Background: Reducing deaths due to tuberculosis is the World Health Organization (WHO) End Tuberculosis Strategy first priority. However, determining the cause of death is notoriously difficult.

The aim of this study was to compare routine programmatic mortality data in patients with tuberculosis during and after therapy versus the cause of death (CoD) determined by WHO verbal autopsy (VA).

Design/Methods: After ethical approval, we prospective followed a cohort of 2152 unselected consecutive patients who gave informed consent to be interviewed during and 18-24 months after tuberculosis treatment. We did this between 2016-2022 in 32 community health centers in shantytowns in Callao, Peru. We used WHO definitions of CoD from VA done using the smartVA-Analyze program during face-to-face household visits with members of the households of people who had died.



Results: The overall mortality rate was 6.1% (95% confidence intervals, CI=5.2-7.1, 148/2421). Deaths were more common in men (70%, 95% CI=62-77, 104/148) and people with HIV coinfection (64%, 95% CI=56-72, 95/148). 47% (95% CI=41-49, 70/148) of deaths occurred during TB treatment. VA were completed for 68% (95% CI=60-76, 101/148).

The following data are for those whose CoD was determined. During tuberculosis treatment when deaths are all attributed programmatically to tuberculosis, only 52% (95% CI=36-68, 22/42) of CoD were tuberculosis. After tuberculosis treatment, the CoD was tuberculosis

for 25%, (95% CI=15-38, 15/59) but recurrence had been diagnosed in none of these cases, so none would have been attributed to tuberculosis programmatically.

Thus, there were 43 deaths during tuberculosis treatment that would programmatically be attributed to tuberculosis but only 51% (95% CI=35-67, 22/43) of these were amongst the 37 deaths that VA attributed the CoD to be tuberculosis.

Conclusions: Tuberculosis as the CoD is was over-estimated by tuberculosis programmatic data during therapy and under-estimated after therapy.

OA14-304-09 Subclinical TB in a High TB-incidence country, another call for attention

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Background: Subclinical tuberculosis (TB) is rapidly emerging as a state that warrants attention since it is presumed infectious, yet affected individuals do not present with significant symptoms.

The World Health Organisation recommends the four-symptom screen (W4SS) of cough, fever, weight loss and night sweats when evaluating potential cases. Namibia conducted its first TB prevalence survey in 2018, in which TB cases were defined as those that had bacteriological confirmation with mycobacterial culture or positive Xpert MTB/RIF and a TB-consistent chest radiograph.

We determined the prevalence of subclinical TB, which we defined as screening negative for any of the four symptoms while having bacteriologically confirmed TB and consistent radiographs.

Design/Methods: This was a secondary analysis of the Namibia TB prevalence survey data, where the population was interviewed for symptoms, had chest radiography and were offered bacteriologic testing and statistics, including measures of association, were calculated in STATA version 17.0 (Statacorp LLC).

Results: Of the 29,495 participants from the nationally representative sample (86.8% of target sample size), 123 TB cases were found to meet the survey case definition. The mean age was 45 years and 74 (60%) were male.

Of all the TB cases, 60 (48.8%) reported having a cough of any duration, while 20 (16.3%) reported a fever of any duration; 25 (20.3%) reported weight loss and 26 (21.1%) reported night sweats.

A significant number; 49 (40%) reported negative to any of the four symptoms.

There was no statistically significant difference between the 8 of 19 HIV positive cases who reported no symptoms and the 32 of 83 HIV negative cases who reported no symptoms (p=0.8).

Conclusions: Even when using an inclusive symptom screening system that includes any duration of the W4SS, subclinical TB occurred in 39% of HIV negative cases and 42% of HIV positive, confirming the concern on subclinical TB.

OA-15 Pharmacokinetic studies for better patient care

OA15-305-09 Population pharmacokinetic modeling of linezolid in plasma and cerebrospinal fluid in adults with tuberculous meningitis from the LASER-TBM Study

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Background: Several trials are evaluating novel linezolid-based regimens for tuberculous meningitis (TBM). We described the plasma and CSF pharmacokinetics (PK) of linezolid and investigated the impact of concomitant high-dose rifampicin in a Phase-II trial.

Design/Methods: LASER-TBM investigated safety of intensified antimicrobial and host-directed therapy in adults living with HIV and TBM. Participants were recruited from South African hospitals and randomized to receive standard or experimental regimens containing additional rifampicin (35 mg/kg) plus oral linezolid 1200 mg daily for 28 days, reduced to 600 mg daily for the next 28 days. Intensive plasma sampling up to 24 hours post-dose was performed on day 3, and sparse sampling at day 28. A lumbar CSF sample was obtained at randomly assigned timepoints for up to 24 hours post-dose at each PK visit. Plasma and CSF concentrations were analyzed with nonlinear mixed-effects modelling.

Results: 237 plasma and 28 CSF concentrations from 30 participants in experimental arms were available for PK analysis. Median (min–max) age and weight were 40(27–56) years and 60(30–96) kg, respectively. Linezolid PK in plasma was described by a one-compartment model with first-order elimination and transit compartments absorption. The typical clearance and volume were 5 L/h and 37 L, respectively, allometrically scaled using fat-free mass (FFM).

No statistically significant effect of rifampicin treatment duration was found on clearance or bioavailability. CSF concentrations were linked to the plasma concentrations by a hypothetical effect compartment. The CSF-to-plasma partition coefficient was 29%, while the plasma-to-CSF equilibration half-life was 3.5 hours.

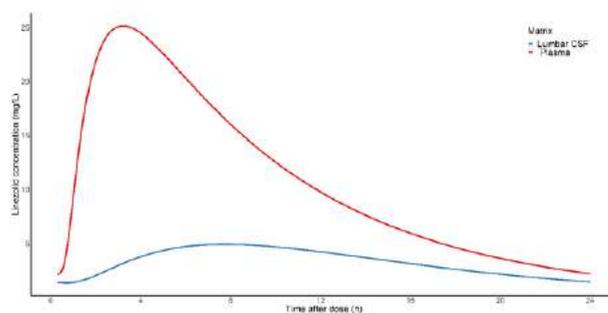


Figure 1: Simulated concentration-time profiles at steady-state for a participant with median FFM (46 kg) on linezolid 1200 mg daily

Conclusions: Linezolid plasma PK was comparable to other populations with non-neurological TB despite co-administration of high-dose rifampicin. CSF concentrations were similar to reports from neurosurgical patients, supporting continued clinical evaluation in efficacy trials for TBM.

OA15-306-09 Pharmacokinetics of isoniazid, rifampicin, and pyrazinamide in Tanzanian children who used WHO recommended dosages

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Background: Tuberculosis is an important public health concern in children. In 2020, the WHO estimated that children represent about 11% of all TB cases worldwide. Studies suggest that the currently recommended dosages of first-line anti-TB drugs are inadequate in children, but data from East-Africa are limited. We conducted a study to describe the steady-state pharmacokinetics of rifampicin, isoniazid, and pyrazinamide. Predictors of exposure to these drugs in Tanzanian children aged 0-14 years were determined.

Design/Methods: Children meeting the eligibility criteria were enrolled and treated using first-line TB drugs according to WHO dosage. Pharmacokinetic sampling was performed at week 3 (21 ± 3 days). Samples taken

were pre-dose and 2, 4, and 8-hours post-dose. Pharmacokinetic parameters in plasma were assessed using standard non-compartmental methods in Phoenix-WinNonlin v.6.3. Total exposure (AUC_{0-24h}) and peak concentrations (C_{max}) were presented descriptively. Effects of gender, age, weight, and HIV status on AUC_{0-24h} and C_{max} were assessed using the Wilcoxon rank-sum test and correlation analyses.

Results: Out of 18 children, 10(56%) were female, 12(67%) were 0-5 years, 5(28%) were HIV positive and 8-11kg (39%) were dominant weight-band. Median AUC_{0-24h} was 18.2h*mg/L, 7.0h*mg/L, 383h*mg/L for rifampicin, isoniazid, and pyrazinamide respectively. Rifampicin and isoniazid AUC_{0-24h} values were much lower than the previously recorded geometric mean in Tanzanian adults (39.9 and 11.0 h*mg/L) Tostmann et al 2013, whereas pyrazinamide AUC_{0-24h} was similar (344h*mg/L in adults). Median C_{max} values were 5.2, 1.7, and 36mg/L for rifampicin, isoniazid, and pyrazinamide respectively. 83% of isoniazid and rifampicin C_{max} concentrations were below the reference range while pyrazinamide is 5%. Strong significant correlation was observed between AUC_{0-24h} and C_{max} for rifampicin, isoniazid, and pyrazinamide.

Conclusions: The current study revealed that Tanzanian children showed more than a half lower total exposure to rifampicin and isoniazid as compared to adults. No clear predictors of exposure were observed. The current WHO dosing guidelines warrant reconsideration.

OA15-307-09 Pharmacokinetics of bedaquiline and delamanid in drug-resistant tuberculosis patients in India

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Background: Pharmacokinetics (PK) studies on Bedaquiline (BDQ) and Delamanid (DLM) in patients with Multi-Drug Resistant Tuberculosis with additional fluoroquinolone resistance (MDR-TB_{FQ+}) is required for optimal use of these drugs for patient management.

Design/Methods: A prospective cohort of adults with MDR-TB_{FQ+} were given combination of BDQ, DLM, clofazimine and linezolid for 24 weeks at 5 sites in India. BDQ was given at 400mg daily for two weeks followed by 200mg thrice weekly for 22 weeks while DLM was

given at 100mg twice daily. An intensive PK study was done in 23 consenting participants at week 8 and 16 of treatment after ensuring drug regularity. Blood was collected at pre-dosing and 2, 4, 5, 6, 8, 12, 24 hours post-dosing.

Results: The mean age and weight was 30 years and 54kg. The median C_{min} and Area under the curve (AUC_{0-24h}) for BDQ was 0.7mcg/ml and 30mcg/ml.h at week 8 and 0.8mcg/ml and 33.8mcg/ml.h at week 16. The C_{min} of BDQ was higher than the average reported (0.36mcg/ml) both at week 8 and 16 while the AUC was comparable with reported values. The median C_{min} and AUC_{0-24h} of DLM was 0.15mcg/ml and 5.2mcg/ml.h at week 8 and 0.18mcg/ml and 6.3mcg/ml.h at week 16 very similar to reported values.

At week 8, 12 patients developed adverse events (QTc prolongation: 2 & liver enzyme elevation: 10) which resolved with symptomatic treatment and did not require treatment interruption. Among these 12 patients, supra-therapeutic levels of BDQ were found in 5, and DLM in 2, and 4 had both.

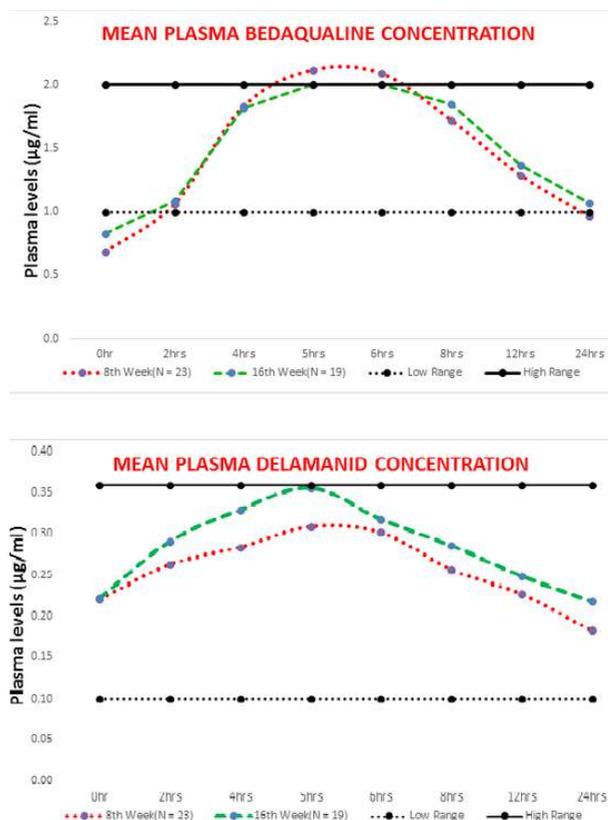


Figure 1: Mean plasma concentration of BDQ and DLM

Conclusions: This is the first study to examine PK parameters of BDQ and DLM in Indian population. Our findings indicate BDQ can safely be combined with DLM in the treatment of MDR-TB_{FQ+}, as the adverse events were manageable in the field setting.

OA15-308-09 Pharmacokinetic-pharmacogenetic-pharmacodynamic analysis of isoniazid and efavirenz for predicting adverse pregnancy outcomes in women with HIV

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Background: IMPAACT P1078 evaluated the safety of isoniazid preventive therapy (IPT) in pregnant women living with HIV. Previously we found that IPT during pregnancy increased the odds of a composite adverse pregnancy outcome (APO). In this analysis, we explored the role of isoniazid (INH) and efavirenz (EFV) pharmacokinetics (PK) and pharmacogenetics (PG) in predicting APOs.

Design/Methods: Women were randomized to initiate 28 weeks of IPT either during pregnancy or at 12 weeks postpartum. PK sampling was done during third trimester of pregnancy. Genetic testing identified NAT2 and CYP2B6 genotypes. The associations of composite and individual APOs with INH and EFV exposure (AUC₀₋₂₄) and PG characteristics were assessed using logistic regression. We considered 3 composite outcomes and the individual outcomes of late perinatal death (<28 days), early perinatal death (<7 days), low birth weight (<2500 grams), and pre-term delivery (<37 weeks gestational age), but focus our report on the primary composite of fetal demise, pre-term delivery, low birth weight or congenital anomaly.

Results: There were 885 women with pregnancy outcome and PK/PG data. At entry, median CD4 count was 497 cells/mm³; 419 women were randomized to receive INH during pregnancy; 749 were taking EFV. Women with missing PK/PG data were more likely to have had a composite APO.

Table 1 shows logistic regression results for the primary composite outcome. Fast NAT2 acetylators were more likely to have a primary composite outcome than inter-

mediate/slow acetylators. Findings were similar for all 3 composite outcomes and low birth weight. No associations between pre-term delivery or perinatal death and PK/PG were identified.

	INH PK/PG				EFV PK/PG				
	N	Adjusted OR (95% CI) ¹	N	Adjusted OR (95% CI) with imputation ^{1,2}	N	Adjusted OR (95% CI) ¹	N	Adjusted OR (95% CI) with imputation ^{1,2}	
INH AUC₀₋₂₄/10	391	1.12 (0.88, 1.42)	447	1.10 (0.88, 1.38)	EFV AUC₀₋₂₄/10	676	0.98 (0.95, 1.01)	694	0.98 (0.95, 1.01)
INH AUC₀₋₂₄ category <5.0 vs. >10.0	391	1.37 (0.69, 2.70)	447	1.16 (0.62, 2.16)	EFV AUC₀₋₂₄ category <50 vs. >100	676	1.92 (1.00, 3.67)	694	1.97 (1.04, 3.72)
5.0-10.0 vs. >10.0		0.89 (0.46, 1.73)		0.63 (0.33, 1.19)	50-100 vs. >100		1.34 (0.69, 2.59)		1.28 (0.67, 2.48)
NAT2 phenotype Intermediate vs. fast	339	0.39 (0.17, 0.89)	447	0.47 (0.21, 1.02)	CYP2B6 phenotype Intermediate vs. fast	575	0.72 (0.41, 1.24)	769	0.78 (0.46, 1.31)
Slow vs. fast		0.36 (0.16, 0.81)		0.49 (0.23, 1.02)	Slow vs. fast		0.54 (0.26, 1.11)		0.65 (0.34, 1.24)

¹Models are adjusted for maternal age at delivery, CD4 quartiles, HIV RNA < LLQ, timing of ART initiation, HBsAg status, MUAC, IGRA status, twin vs. singleton pregnancy, current smoker, noninfectious pregnancy complications, infectious pregnancy complications, and maternal hospitalization. Additionally, EFV models are adjusted for study arm.

²Sensitivity analysis was done using multiple imputation of missing PK/PG variables and covariates.

Table 1: Logistic regression results for composite of fetal demise, pre-term delivery, low birth weight or congenital anomaly.

Conclusions: We found evidence that fast NAT2 acetylators were more likely to experience an APO than intermediate/slow acetylators. Further investigation is needed to understand INH metabolite PK/PG in predicting APOs and underlying mechanisms.

OA15-309-09 Pharmacokinetics of efavirenz co-administered with isoniazid and rifapentine in HIV-infected individuals: a pilot study

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Background: A new one-month regimen of isoniazid and rifapentine 3 times a week (1H₃P₃) has noninferior efficacy compared to the 3HP regimen for TB prevention in China (NCT03900858). However, the use of rifapentine for TB prevention carries a risk of drug-drug interactions with concomitantly used antiretroviral therapy (ART). This study aims to evaluate the interaction of the antiretroviral drug efavirenz in combination with 1H₃P₃ for TB prevention in HIV individuals.

Design/Methods: HIV-positive individuals on efavirenz-containing (600mg) ART received 1H₃P₃ containing rifapentine (450 mg) plus isoniazid (400 mg). Mid-interval efavirenz concentrations were measured during at Weeks 0, 2, 4, 8. Target mid-interval efavirenz con-

concentrations were > 1 mg/L. HIV RNA load were determined on Weeks 0 and 8. The prevention was considered acceptable if $> 80\%$ of participants had mid-interval efavirenz concentrations meeting this target.

Results: Thirty-one participants were enrolled in the pilot study. Two of them were excluded from PK analysis who had a baseline mid-interval efavirenz concentration < 1 $\mu\text{g/mL}$ for the consideration of adherence challenges. Twenty-nine participants had evaluable PK data: 23 (79.3%) of them were male and median (range) age of 42 (22–61) years. The median (interquartile range) efavirenz plasma concentrations were: week 0, 2.37 (2.03–3.37) $\mu\text{g/mL}$; week 2, 2.39 (1.95–3.52) $\mu\text{g/mL}$; week 4, 2.14 (1.87–3.18) $\mu\text{g/mL}$; and week 8, 2.83 (2.20–3.67) $\mu\text{g/mL}$. Median (IQR) rifapentine concentrations were: week 2, 9.69 (6.66–16.89) $\mu\text{g/mL}$; week 4, 11.02 (7.85–16.46) $\mu\text{g/mL}$. All participants had efavirenz concentrations > 1 $\mu\text{g/mL}$ at week 2, 4, 8. What's more, female and patients with body weight < 60 kg had significantly higher mid-dose interval efavirenz concentrations compared with male and those with body weight ≥ 60 kg ($P < 0.05$).

Conclusions: 1H₃P₃ co-administration has limited impact on efavirenz concentration, which was maintained within effective ranges.

OA15-310-09 Isoniazid and pyrazinamide urine colorimetry for evaluation of tuberculosis pharmacokinetics

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Background: Tuberculosis (TB) treatment failure and emergence of drug-resistance can be caused by various factors including adverse pharmacokinetic variability. Typical measurement of serum concentrations of anti-TB medications requires preservation of the cold chain and chromatography or mass spectrometry analyses. Urine colorimetry may provide a low-cost alternative with non-invasive sampling and simple laboratory methods to measure anti-TB drug exposures suitable for on-site dose adjustment in TB endemic areas, or use within pragmatic or operational trials.

Design/Methods: We conducted a prospective, observational study of patients on first-line anti-TB treatment. Serum was collected pre-dose and 1, 2, 4, 6, and 8 hours post dose for measurements of isoniazid (INH)

and pyrazinamide (PZA) concentrations using validated LC-MS/MS methods. Urine was collected between 0-4, 4-8, and 8-24 hour intervals post dose, and pooling was done to determine concentrations at 0-8 and 0-24 hours. Urine concentrations of INH and PZA were measured using colorimetric methods. Non compartmental analysis was performed to calculate serum pharmacokinetics parameters.

Results: We report on the preliminary data from the first 39 participants enrolled. Fifteen (39%) were female, and the average age and BMI for all 39 participants were 44.8 years and 24.3, respectively. The average peak concentration and total area under the time curve during the dosing interval (AUC_{0-24hours}) were 5.9 mg/l and 19.9 mg*h/l for INH, and 48.4 mg/l and 458.1 mg*h/l for PZA. Correlation between serum AUC₀₋₂₄ and amount of drug eliminated in urine was highest during the 0-4 hour interval for INH (correlation coefficient, $r = 0.8$) and during the 8-24 hour interval for PZA ($r = 0.6$).

Conclusions: Urine colorimetry correlated closely with serum INH concentrations and moderately with PZA serum concentration. Colorimetric methods to determine drug concentrations in urine may improve the feasibility of personalized dosing in TB endemic settings following further studies of serum target prediction.

OA15-311-09 Systematic assessment of clinical and bacteriological markers for tuberculosis reveals discordance and inaccuracy of symptom-based diagnosis for treatment response monitoring

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Background: Clinical symptoms are the benchmark of tuberculosis (TB) diagnosis and treatment response monitoring, but not clear how they relate to TB bacteriology, particularly for the novel tuberculosis Molecular Bacterial Load Assay (TB-MBLA).

Design/Methods: Presumptive cases were bacteriologically confirmed for TB by Xpert MTB/RIF assay and smear microscopy (SM) at diagnosis and before start of treatment. Symptom and bacteriological resolution were assessed using SM, culture and TB-MBLA over 6-month treatment course of standard therapy. Kaplan Meier and Kappa statistics were used to test relationship between symptom- and bacteriological-positivity.

Results: A cohort of 59 bacteriologically confirmed TB cases were enrolled for treatment response monitoring over a six-month treatment course. Pre-treatment symptom and bacteriological test positivity concurred in over 70% of the cases. This agreement was lost in over 50%

of cases whose chest pain, night sweat, and loss of appetite had resolved by week 2 of treatment. Cough resolved at a 3.2% rate weekly and was 0.3% slower than the combined bacteriological (average of MGIT and TB-MBLA positivity) resolution rate, 3.5% per week. Drop in TB-MBLA positivity reflected fall in bacillary load, 5.7 ± 1.3 at baseline to 0.30 ± 1.0 \log_{10} CFU/mL at month-6, and closer to cough resolution than other bacteriological measures, accounting for the only one bacteriologically positive case out of 7 still coughing at month-6. Low baseline bacillary load patients were more likely to be bacteriologically negative, HR 5.6, $p=0.003$ and, HR 3.2, $p=0.014$ by month-2 and 6 of treatment respectively.

Conclusions: The probability of clinical symptoms reflecting bacteriological positivity weakens as patient progresses on anti-TB therapy, making symptom-based diagnosis a less reliable marker of treatment response.

OA15-312-09 The first cohort of tuberculosis patients on the BPAL regimen under operational research conditions in the Kyrgyz Republic: preliminary results

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Background: The BPAL regimen with three oral drugs, bedaquiline, pretomanid, and linezolid, and six (extendable to nine) months treatment duration, developed by the TB Alliance (TBA), is recommended by WHO to treat patients with highly resistant TB.

Design/Methods: From August 2021 – to August 2022, 50 patients with pre-XDR-TB or MDR-TB treatment non-response or intolerance will be enrolled in the BPAL treatment under operational research (OR) at the nine TB facilities in the Kyrgyz Republic. TB patients are selected and treated following the national BPAL OR protocol and monitored by TB experts from the NTP, KNCV, WHO Regional Office for Europe, and TBA.

Results: From August 2021 – to March 2022, 32 (66.7%) of 48 screened patients were enrolled into the BPAL OR. Twenty-three (71.9%) of 32 enrolled patients were culture positive at baseline, and 15 (65.2%) of 23 patients had culture conversion after one month of the BPAL

treatment. The first patient enrolled was cured, and two patients were loss-to-follow-up. Twenty-nine patients continue the BPAL treatment.

Adverse events were reported in 11 (34.4%) patients, hepatotoxicity - in one (3.1%), and peripheral neuropathy in 10 (31.3%) patients. Eight (50.0%) of 16 patients screened and not enrolled in the BPAL OR had previous exposure to bedaquiline and linezolid for > four weeks. The national TB expert committee decided not to enroll two (12.5%) patients with relative contraindications (hemoglobin level <8 g/dL and severe peripheral neuropathy). Six (37.5%) patients refused to sign the OR informed consent form.

Screening and enrolment	Number of patients
Number of patients screened	48
Enrolled	32 (66.7%)
Culture positive at baseline	23 (71.9%)
Not Enrolled	16 (33.3%)
Previous exposure to Bdq and Lzd > 4 weeks	8 (50.0%)
Relative contraindications	2 (12.5%)
Refused to sign ICF	6 (37.5%)
Safety monitoring	N=32
Number of patients with AESI	11 (34.4%)
Peripheral neuropathy	10 (31.3%)
Hepatotoxicity	1 (3.1%)
Number of patients with > 1 AESI	3 (9.3%)

ICF, Informed consent form; AESI, Adverse event of special interest

Table 1. Enrolment and safety monitoring of the first patient cohort of the BPAL OR in the Kyrgyz Republic.

Conclusions: Preliminary analysis of the first cohort of TB patients of the BPAL OR in the Kyrgyz Republic showed high rates of culture conversion and the importance of adequate safety monitoring and management. A history of exposure to the BPAL component drugs limits the use of the BPAL regimen in previously treated DR-TB patients.

OA-16 Implementation of TPT

OA16-313-09 Process and contextual factors influencing acceptance and completion of isoniazid-rifapentine (3HP) for tuberculosis prevention by people living with HIV (PLHIV) in Uganda

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Background: Once-weekly isoniazid-rifapentine (3HP) for tuberculosis (TB) prevention is recommended for PLHIV. We explored process and contextual factors influencing acceptance and completion of 3HP among PLHIV enrolled in the 3HP Options Trial, an on-going pragmatic, randomized trial comparing three optimized 3HP delivery strategies: facilitated directly observed therapy (DOT), facilitated self-administered therapy (SAT), or an informed choice between the two using a shared decision-making tool.

Design/Methods: We conducted a qualitative study using semi-structured interviews with PLHIV in each study arm, purposively selected based on demographic and treatment completion characteristics. We used study arm-specific interview guides to understand why PLHIV accepted, completed or stopped 3HP treatment. Interviews were audio-recorded, transcribed and data analyzed using inductive thematic analysis.

Results: We conducted 72 interviews (24 per study arm). Acceptance of 3HP was based on: understanding of TB, previous experience of TB, support from significant others and the shorter duration of 3HP treatment compared to six months of daily isoniazid. PLHIV in the choice arm were motivated to complete 3HP by the ability to choose the delivery strategy which was convenient for them and the ability to switch between DOT and SAT whenever necessary. DOT was convenient for PLHIV who reside near the clinic and for those who had not disclosed their HIV status. SAT was preferred by PLHIV who needed minimal interruptions of their daily

routines. PLHIV stopped 3HP treatment due to adverse events, inability to change delivery strategy (for participants randomized to DOT or SAT without choice), inadequate support from family and significant others, and the disruptive effects of the COVID-19 pandemic and lockdown measures.

Conclusions: 3HP was broadly acceptable for PLHIV. Patient choice of 3HP delivery strategy was a key enabler of treatment completion that should be considered for more effective scale-up.

OA16-314-09 Scale-up of short-course TB preventive treatment (3HP) in high tuberculosis burden countries: the IMPAACT4TB Project

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Background and challenges to implementation: A short TB preventive treatment regimen of rifapentine (RPT) plus isoniazid taken once weekly for three months (3HP) is now available. Unless barriers to its adoption, demand and delivery are removed, implementation may meet the same fate as isoniazid preventive treatment.

We describe approaches used in the IMPAACT4TB project which catalysed 3HP implementation in 12 high burden countries.

Intervention or response: The IMPAACT4TB project has been implemented over 5 years by a consortium to catalyse supply, demand, and uptake of 3HP among people living with HIV (PLHIV) and household contacts (HHC).

Key activities included: generating evidence to support 3HP co-administration with dolutegravir (DTG), negotiating RPT price reductions, addressing barriers to supply and supporting initial scale-up.

The consortium worked with project countries to adopt 3HP, adapt guidelines and recording/ reporting tools, strengthen forecasting and quantification, supply chain management, and delivery of 3HP.

Results/Impact: Between 2018-2022, two generics suppliers, in addition to Sanofi, entered the RPT market. 3HP price dropped from \$72 to \$15/patient-course.

Evidence from the DOLPHIN trial supporting co-administration of DTG and 3HP without requiring dose adjustment, facilitated its adoption. 11/12 countries that committed to rolling out 3HP from 2017 have done so, except for Tanzania. Tanzania, however, introduced 3HP into the TPT guidance update process in 2021. Between June 2019 and December 2021, through the IMP-PAACT4TB project, a total of 67,540 persons started 3HP. Of these 60,382 (89%) were PLHIV and 7,158 (11%) HHC.

Among PLHIV starting 3HP, 22,945 (38%) were newly initiating ART. Commodity security and supply chain were affected by COVID-19 pandemic, nitrosamine contamination and delayed in-country approvals. IMP-PAACT4TB also catalyzed the procurement of 1.4 million 3HP person courses in 2021 across 31 countries from outside funding sources.

Conclusions: Despite the challenges experienced both globally and locally, the IMPAACT4TB project catalyzed the scale-up of 3HP in high burden settings.

OA16-315-09 Evaluation of community-based latent tuberculosis detection using Mantoux tuberculin skin testing (TST) and the QuantiFERON®-TB Gold Plus (QFT-Plus) Interferon-Gamma Release Assay (IGRA) in Vietnam

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Background and challenges to implementation: Approximately 30% of adults in high TB-burden countries have latent TB infection (LTBI). The risk of progression to TB is greatest for certain high-risk populations including people who live with a person with pulmonary TB. The Vietnam NTP introduced TB preventive treatment (TPT) for adult household contacts of people with pulmonary TB, but 2020 data showed unexpectedly low LTBI prevalence using tuberculin skin testing (TST).

Intervention or response: We evaluated community-based LTBI detection among household contacts. TST (positivity thresholds ≥ 10 mm (TST-10) and ≥ 5 mm (TST-5)) was administered using Bulbio’s purified protein derivative (PPD) and compared with QuantiFERON®-TB Gold Plus (QFT-Plus) in the same individual. Using STATA v.17 for analysis, we calculated raw agreement

between TST and QFT-Plus; agreement using Cohen’s Kappa; and concordance using McNemar’s chi-square test to inform national programmatic guidance for LTBI detection.

Results/Impact: From March–December 2020, we administered TST and QFT-Plus during TB community campaigns in 4 provinces of Vietnam among 1,597 household contacts; 1,387 had valid test results for both TST and QFT-Plus and were ruled out for TB disease. QFT-Plus positivity (38.6%) was approximately three times higher than TST-10 positivity (13.0%). TST-5 positivity (37.3%) was closer to expected rates for high-risk groups such as household contacts, although still lower than QFT-Plus positivity. Raw positive agreement, Cohen’s Kappa values, and test concordance were higher for TST-5 versus QFT-Plus compared to TST-10 versus QFT-Plus.

District	TST 5mm compared with QFT-Plus				TST 10mm compared with QFT-Plus			
	% positive test agreement	% negative test agreement	Cohen's Kappa	Chi2, Prob > chi2	% positive test agreement	% negative test agreement	Cohen's Kappa	Chi2, Prob > chi2
Trang Bang	20.95	49.34	0.37		6.90	67.64	0.24	
Ninh Kieu	27.42	25.48	0.06		9.42	43.49	0.12	
Bien Hoa	24.75	38.94	0.26		16.17	51.16	0.29	
Tien Hai	9.25	64.74	0.26		5.49	67.34	0.16	
Total	20.55	44.70	0.26	0.67, 0.41	9.23	57.68	0.20	274.6, 0.00

Analysis of agreement and concordance between TST-5 or TST-10 versus QFT-Plus (n=1387)

Conclusions: TST-5 (Bulbio PPD) has higher agreement with QFT-Plus than TST-10 in this programmatic setting. The NTP used these results, along with WHO recommendations, to change the TST threshold for household contacts from ≥ 10 mm to ≥ 5 mm. Quality assurance checks and additional training were also instituted to address issues with quality of TST injection and interpretation. IGRA cost and quality of TST administration are significant implementation issues for LTBI detection in high TB-burden settings.

OA16-316-09 Completion of IPT among people living with HIV on ART across differentiated service delivery models in Uganda

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Background: Isoniazid Preventive Therapy (IPT) reduces the risk of developing TB disease. Uganda national guidelines recommend delivering IPT and ART together to people living with HIV (PLHIV) across differentiated service delivery (DSD) models (community-based: CDDP and CCLAD; facility-based: FTDR, FBG and FBIM). We determined IPT completion and its associated factors across DSD models.

Design/Methods: We reviewed medical records for PLHIV initiated on IPT between June-September 2019 at TASO Soroti (TS), Katakwi Hospital (KH) and Soroti Regional Referral Hospital (SRRH). IPT completion was defined as completing a 6-month course of IPT within 6-9 months. We compared IPT completion across DSD models using the Chi-square test and utilized modified Poisson regression to determine factors associated with IPT completion in each DSD model.

Results: Data from 2968 PLHIV were reviewed (SRRH: 50.2%, TS: 25.8%, KH: 24.0%); 60.7% were females; 91.7% were on first-line ART; and 61.9% on INSTI-based ART regimen. The median duration on ART at IPT initiation was 6.0 (interquartile range [IQR]: 3.7-8.6) years, and the median age (IQR) at IPT initiation was 43.2 (34.5-52.0) years. IPT completion was 92.8% (95% confidence interval [CI]: 91.8%-93.7%); highest in CDDP (98.1%); lowest in FBG (85.8%); but varied across DSD models ($p < 0.001$; Fig 1).



Figure 1. Number and proportion of PLHIV who completed IPT across the five DSD models.

In CCLAD, males were more likely to complete IPT than females (rate ratio [RR] =1.07, 95% CI: 1.01-1.14). In FTDR, completion was lower among participants on second/third line ART than those on first-line (RR=0.90,

95% CI: 0.83-0.99, $p=0.022$). In FBG, IPT completion was lower among males than females (RR=0.83, 95% CI: 0.70-0.99, $p=0.034$). In FBIM, adults (25+ years) had a higher completion than those <25 years (RR=1.17, 95% CI: 1.01-1.36, $p=0.039$). No factors were associated with IPT completion among participants in CDDP.

Conclusions: IPT completion was high overall; it was highest in CDDP and lowest in FBG. Factors associated with IPT completion differed across DSD models.

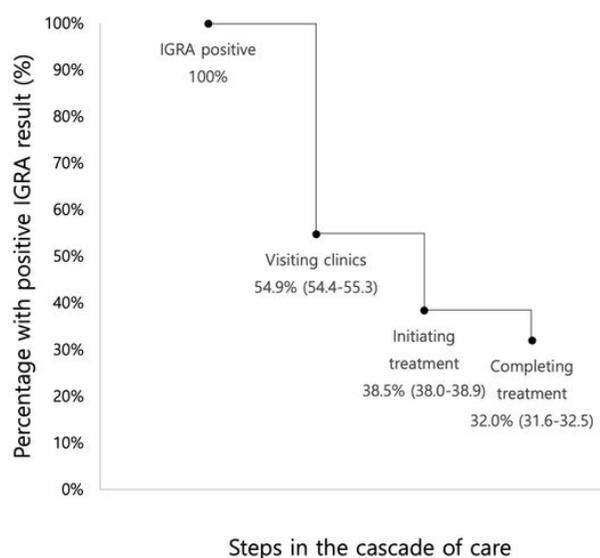
OA16-317-09 Latent tuberculosis cascade of care among healthcare workers: a nationwide cohort analysis in Korea between 2017 and 2018

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Background: In 2017, Korea implemented nationwide latent tuberculosis infection (LTBI) project targeting healthcare workers. We aimed to assess each step of programmatic LTBI management in healthcare workers using the cascade of care model.

Design/Methods: We constructed a prospective observational cohort study based on data were systematically collected from participants of the nationwide screening project for LTBI between March 2017 and December 2018 and included 45,503 employees of medical institutions with positive interferon-gamma release assay result. We described percentages of LTBI participants completing each step in the cascade of care from visiting clinics to completing LTBI treatment. Poisson regression model was conducted to assess individual characteristics and factors associated with not-visiting clinics for further care, not-initiating LTBI treatment, and not-completing treatment. Multivariable analysis was adjusted by sex, age, place of residence, income level, Charlson comorbidity index, and types of occupation.

Results: Proportions of visiting clinics and initiating and completing treatment in healthcare workers were 54.9%, 38.5%, and 32.0%, respectively. Despite of less likelihood of visiting clinics and initiating LTBI treatment, older age ≥ 65 years were more likely to complete treatment (adjusted relative risk [aRR], 0.80; 95% confidence interval [CI], 0.64-0.99), compared to young age < 35 years. Compared to nurse, doctor was less likely to visit clinic; however, was more likely to initiate treatment (aRR, 0.88; 95% CI, 0.81-0.96). Those who visited public health centres were associated with not-initiating treatment (aRR, 1.34; 95% CI, 1.29-1.40). When treated at private hospitals, 9-month isoniazid monotherapy was less likely to complete treatment, compared to 3-month isoniazid and rifampicin combination therapy (aRR, 1.33; 95% CI, 1.16-1.53).



Conclusions: Among employees of medical institutions with LTBI, only one third completed treatment. Age, occupation, treatment centre, and initial regimen were significantly related to LTBI treatment performance indicators. Rifampicin-based short treatment regimens were effective under standard of care.

OA16-318-09 Uptake and completion of TB preventative therapy in people living with HIV: a comprehensive systematic review

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Background: TB is a leading cause of death among People Living with HIV (PLWH) and TB preventative therapy (TPT) is a key intervention to reduce this. Previous research suggests that uptake and completion rates for TPT are low.

Design/Methods: We undertook a systematic review including studies reporting data on any of the defined steps in the TPT cascade of care (CoC). Pooled estimates were calculated at pre-defined points in the CoC.

Results: 301 studies were identified, including data on 2.4 million PLWH excluding those only reporting routinely-collected programmatic data [Table]. 65% of studies were published since 2010; 48% were from Africa and 54% reported data from hospital or outpatient clinics. Where tests for latent TB infection (LTBI) with tuberculin skin tests (TST) or blood IGRAs were used, 81.2% [95%CI 74.8-86.3%] of eligible participants were tested, 5.3% [3.7-7.6%] had indeterminate/unread tests, 18.6% [15.8-21.7%] had a positive TST

result and 12.6% [9.0-17.4%] a positive IGRA result. Overall, 50.1% [40.1-59.4] of participants were eligible for TPT, common reasons for ineligibility were negative TST/IGRA, symptoms suggesting possible TB disease and comorbidities. In cohorts where TPT was available and uptake was reported, 80.7% [73.4-86.3%] of those eligible started TPT. Isoniazid monotherapy was used in 71% of studies. Of those starting TPT, 73.9% [70.2-77.3%] completed. Treatment adherence was reported in 51 (17%) studies, typically by indirect assessments including clinic visit attendance or participant-reported adherence.

Steps in Cascade of Care*	Number of cohorts reporting	Percent point estimate, % [95% CI]
Screening eligible/ total number of PLWH	173	99.6 [99.4-99.8]
Tested/ screening eligible	104	81.2 [74.8-86.3]
Unread or indeterminate/ tested for LTBI	59	5.3 [3.7-7.6]
Positive TST/ tested for LTBI	106	18.6 [15.8-21.7]
Positive IGRA/ tested for LTBI	25	12.6 [9.0-17.4]
TPT eligible/ total number of PLWH	110	50.1 [40.1-59.4]
Started TPT/ treatment eligible	179	80.7 [73.4-86.3]
Adverse events leading to TPT discontinuation/ started TPT	81	2.6 [1.9-3.4]
Completed TPT/ started TPT	150	73.9 [70.2-77.3]

*Point estimate at each step expressed as number with positive result divided by relevant denominator

Conclusions: This systematic review provides an updated, comprehensive and global assessment of the provision of Tuberculosis Preventative Therapy for PLWH, using pooled estimates at multiple steps along the cascade of care. These data highlight opportunities to improve retention within the cascade through changes in policy and practice, as well as a lack of data evaluating TPT adherence.

OA16-319-09 High completion rates of 3HP among household contacts despite COVID-19 in Indonesia

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Background and challenges to implementation: Indonesia is one of the high TB burden countries in the world. TB preventive treatment (TPT) is one of the key interventions recommended by WHO to achieve the

End TB Strategy targets. However, the TPT coverage on under-five household contacts (HHCs) in Indonesia has decreased from 6.2% (2019) to 1.6% (2020). The National TB Program (NTP) in collaboration with Yayasan KNCV Indonesia (YKI) through IMPAACT4TB developed the national LTBI Guideline in 2020. This guideline recommends a 3-month weekly administered TPT containing Rifampentine and Isoniazid (3HP) for all HHCs above 2 years old.

Intervention or response: The NTP took a strategic decision to purchase rifampentine loose drug by domestic budget in Q3 2020 and started the 3HP implementation in December 2020. The implementation of 3HP started in Jakarta Province and involved 5 districts and 41 healthcare facilities. Because of COVID-19, the strategy to find HHCs and delivery of TPT was shifted from contact investigation, requiring home visits, to contact invitation (facility-based) to ensure better infection control. IMPAACT4TB also provided capacity building for healthcare workers and TB program managers, information, education, and communication materials, routine monitoring visits and documenting of challenges and successes to guide national expansion.

Results/Impact: Within the period of December 2020 to June 2021, a total of 503 HHCs were enrolled on 3HP with the highest uptake in the >14-year-old group (300 HHCs). The completion rates across the three age groups were very high (92–97%). There were 30 (6%) participants who did not complete the treatment, which reasons were drug side effects (37%), moving out to another city (10%), discontinuing due to pregnancy (3%), and unknown reasons (50%).

No	Age group	Number of HHCs initiated 3HP	Number of HHCs completed treatment 3HP
1.	< 5 years old	78	76 (97%)
2.	5-14 years old	125	120 (96%)
3.	> 14 years old	300	277 (92%)
Total		503	473 (94%)

Table. Number of HHCs initiated and completed 3HP in Jakarta Province (December 2020 to June 2021)

Conclusions: The first implementation of 3HP shows good acceptance among HHCs and health care workers despite the COVID-19 pandemic. The 3HP implementation should be scaled up to expedite the progress toward TB elimination in Indonesia.

OA16-320-09 Long-term protective effect of preventive treatment for tuberculosis in an upper/moderate incidence rate setting

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Background: Long-term follow-up of randomized clinical trials (RCT) of tuberculosis preventive treatment (TPT) among persons living with HIV shows conflicting results. While incidence increased after the end of the trial in Botswana (incidence rate on study period (2009) =500/100,000/year), it did not in the city of Rio de Janeiro, Brazil (an upper-moderate incidence setting (incidence rate (2010) =87/100,000/year) where TPT is offered for each new exposure in this population. The long-term effect of TPT in household contacts was not evaluated.

Design/Methods: The incidence per 1000 persons per year (ppy) of new tuberculosis up to twelve years after the end of treatment in 997 Brazilian participants of a multicenter RCT that compared 4R to 9H was calculated. Most participants were household contacts of TB index-patients. We searched for participants in the mandatory notification system for tuberculosis until October 2021 (Sinan), using name, sex and date of birth. We calculated the risk difference (RD) between those who completed (80% of doses prescribed) or not TPT and compared regimens.

Results: Overall TB incidence was 1.768 /1000 ppy (95% CI=0.989 to 2.917). The RD of those who did not complete treatment minus those who completed was 1.435/1000 ppy (95% CI=-0.660 to 3.530, Figure 1), and 0.347/1000 ppy (95% CI= -1.449 to 2.143) for those taking 9H minus those taking 4R.

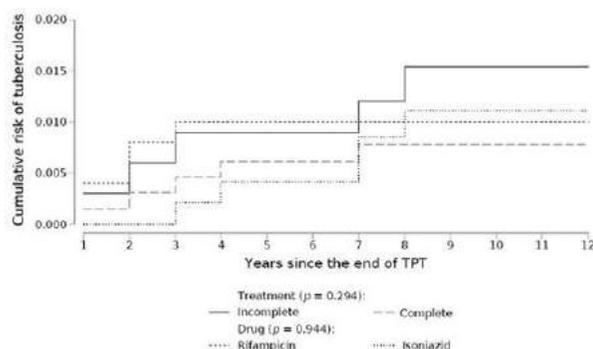


Figure 1. Plot of cumulative risk of tuberculosis for patients who did not complete and completed tuberculosis preventive treatment (TPT) using log-rank test.

Conclusions: The overall incidence rate was low, and the sample power was small for a statistically significant difference. However, in this upper/moderate transmission setting, one course of completed TPT conferred long term protection against TB to mostly non-HIV participants, regardless of the regimen.

OA-17 Active case finding: Impact and Yield

OA17-321-09 The effect of community-wide TB screening and HIV testing with linkage-to-care on TB case notification rates: results from the Zambian HPTN 071 trial sites

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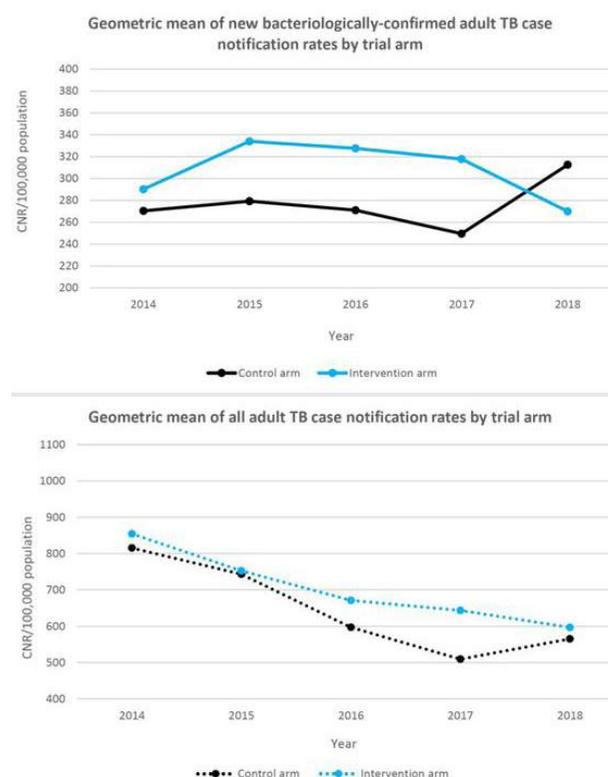
Background: HPTN 071 was a cluster randomised trial, conducted in 21 Zambian and South African communities. In 14 intervention communities, over three consecutive rounds spanning 2014-2017, house-to-house 1) TB symptom screening with sputum collection if symptomatic and linkage-to-care; and 2) HIV testing with linkage-to-care were performed. Seven control communities received standard-of-care through routine services. We investigated the intervention effect on TB case notification rates (CNRs) in the eight intervention and four control Zambian communities.

Design/Methods: Outcomes were

1) new, bacteriologically-confirmed (smear/Xpert positive) adult (≥ 15 years) TB and
2) all adult TB. Community census data provided the population denominator. Geometric mean annual CNRs between 2014-2018 (during and 1 year after the intervention) by trial arm were calculated. CNR ratios (with 95% confidence intervals [95% CI]) in the intervention versus control arms were calculated, using cluster-level summaries. CNRs were adjusted for the 2014 log CNR (as baseline).

Results: During the intervention, the geometric mean of new bacteriologically-confirmed adult CNRs in the intervention arm showed some increase, which was sustained above the control arm (Figure-1). CNRs returned

to baseline following the cessation of the intervention. Adjusted CNR ratios in intervention versus control arms in 2015, 2016, 2017 and 2018 were: 1.17 (95% CI 0.89-1.54), 1.13 (95% CI 0.77-1.66), 1.25 (95% CI 0.77-2.04) and 0.80 (95% CI 0.52-1.22) respectively. Adjusted all adult CNR ratios in intervention versus control arms in 2015, 2016, 2017 and 2018 were: 0.96 (95% CI 0.64-1.44), 1.06 (95% CI 0.70-1.59), 1.20 (95% CI 0.71-2.01) and 1.00 (95% CI 0.63-1.61) respectively.



Conclusions: Although CNRs showed some increase in intervention compared to control communities during the trial, these changes were not statistically significant. Possible explanations include

1. Focus on HIV testing at trial start;
2. TB symptom screening alone insufficient to significantly change CNRs and/or;
3. Universal HIV testing with linkage-to-care changing TB epidemiology among people living with HIV which influenced CNR changes due to screening.

OA17-322-09 The yield of community-based TB services targeting high-risk groups versus facility-based TB services in Gaza and Inhambane provinces in Mozambique in 2021

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Background and challenges to implementation: The low case detection and the barriers to access diagnosis and treatment of TB underpin the continued transmission within communities, particularly among high-risk groups. This study assessed the yields of a community-based active case finding intervention among migrant mineworkers and their communities in two provinces of Mozambique in 2021.

Intervention or response: This is a retrospective cohort study carried out in Mozambique to compare the yields of passive (PCF) at public health facilities versus the active (ACF) case-finding approach developed by IOM in migrant-sending communities. The ACF approach included:

1. Community engagement and awareness-raising
2. Screening for TB symptoms
3. Referral of presumptive cases to TB testing (molecular or smear test)
4. The clinical diagnostic criteria were applied for those unable to provide sputum.

TB case notification rates from January to December 2021 were computed to evaluate the ACF strategy compared to PCF. A chi-square test was applied to compare the incidence proportion of TB cases including demography and the other characteristics of the cases detected.

Results/Impact: Of the 15,123 people screened for TB symptoms, 490 TB cases were detected of which 195 (40%) were miners and ex-miners. There was a significant difference in the incidence proportion of ex-/miners between PCF (880 per 100,000) and ACF (2173 per 100,000) (RR=2.46; 95% CI: 1.8-3.2) during the period of analysis. Significant differences were observed for the following variables: the number of miners/ex-miners detected (ACF, 104 vs PCF, 91); the number needed (12.5 in ACF versus 95.7 in PCF).

Conclusions: Conducting ACF in migrant and mine-workers dense communities with a tailored community engagement approach is a key strategy to finding the missing TB cases among vulnerable populations.

OA17-323-09 Evaluation of TB screening integration into the government of Viet Nam's COVID-19 vaccination campaigns

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Background: Chest X-ray (CXR) screening for TB has been used to expand access to molecular diagnostics in Viet Nam since 2017. However, strict COVID-19 social distancing restrictions severely limited opportunities for TB screening in late 2021 and early 2022. In response, TB screening was integrated into the government's COVID-19 vaccination campaign, which was the only legal mass gathering of people at the time.

Design/Methods: Between October 2021 and March 2022, 90 days of vaccine integrated TB screening events were conducted across Ha Noi and Ho Chi Minh City. People from the general population received their vaccine, and were screened for TB during the observation period. Vaccine event yields were calculated and compared to the yields from community screening events implemented between October 2020 and March 2021, when it was possible to specifically mobilize key populations for TB.

Results: 39,997 people were screened by CXR when they received their COVID-19 vaccine, resulting in the detection of 107 people with TB (268 / 100,000). In comparison, 22,673 participants were screened by CXR during 73 community events one year prior, resulting in the detection of 183 people with TB (807 / 100,000). The incidence rate ratio for vaccine events was 0.33 compared to community events ($p < 0.001$), but the average TB yield at the vaccine screening events was still 1.5x the national TB incidence rate.

Conclusions: Vaccine integrated screening for TB was a feasible approach for ensuring the continuation of TB case finding during a time of unprecedented health system disruption, and the screening events were well received by both the government and participants. Despite achieving lower TB yields, the vaccine screening events detected a substantial burden of TB which would likely have gone undetected, or only detected after significant delays.

OA17-324-09 Impact of active case-finding for tuberculosis on case-notifications in Blantyre, Malawi: a community-based cluster-randomised trial (SCALE)

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Background: Active case-finding (ACF) for tuberculosis can help find the “missing millions” with undiagnosed tuberculosis. We investigated case-notifications during ACF in Blantyre, Malawi, where ACF has been intensively implemented following 2014 national TB prevalence survey estimates of ~1%.

Design/Methods: Following pre-intervention prevalence survey in randomly selected households (May 2019 to March 2020), constrained randomisation was used to allocate neighbourhoods to either door-to-door ACF (sputum microscopy for reported cough ≥2 weeks) or standard-of-care (SOC). Implementation was interrupted by COVID-19.

Cluster-level bacteriologically-confirmed case-notification rate (CNR) ratios within 91 days of ACF was our redefined primary outcome (ISRCTN11400592), calculated using negative-binomial regression.

Secondary outcomes were 91-day CNR ratios comparing all tuberculosis registrations, and all non-ACF registrations, respectively. Investigators, but not participants or field-workers, were masked to allocation until final analysis. Interrupted time series (ITS) analysis of CNRs in SOC clusters examined prevalence survey impact.

Results: 72 clusters served by 10 study-supported tuberculosis registration centres were publicly randomised to ACF (261,244 adults, 58,944 person-years follow-up) or SOC (256,713 adults, 52,805 person-years). Of 1,192 ACF participants, 13 (1.09%) were smear-positive. Within 91 days, 113 (42 bacteriologically-confirmed) and 108 (33 bacteriologically-confirmed) tuberculosis patients were identified as ACF or SOC cluster residents, respectively.

There was no difference by arm, with adjusted 91-day CNR ratios 1.23 (95% CI: 0.73-2.07) for bacteriologically-confirmed tuberculosis (primary outcome); 0.96 (95% CI: 0.72-1.30) for all tuberculosis registrations; and 0.87 (95% CI: 0.63-1.20) for non-ACF (routinely diagnosed).

Of 7,905 (0.15%) ACF and 7,992 (0.21%) SOC pre-intervention survey participants, 12 (0.15%) and 17 (0.21%), respectively, had culture/Xpert-confirmed tuberculosis. ITS analysis showed no survey impact on SOC CNRs.

	Endpoint		Unadjusted			Adjusted**		
	ACF	SOC	Ratio†	95% CI	P-value	Ratio	95% CI	P-value
<i>Adult CNRs (91d)</i>								
Bact-confirmed	42/58944†	33/52805	1.14	0.72-1.80	0.58	1.23	0.73-2.07	0.44
All TB registrations	113/58944	108/52805	0.94	0.72-1.22	0.63	0.96	0.72-1.30	0.80
All routinely diagnosed TB	88/58944	95/52805	0.83	0.62-1.11	0.21	0.87	0.63-1.20	0.39
<i>Other pre-set CNRs</i>								
Bact-confirmed routinely diagnosed	17/58944	20/52805	0.76	0.40-1.45	0.41	0.83	0.40-1.70	0.60

* CNR based on routine notification data

† Ratios obtained by fitting a negative binomial regression model to cluster-levels counts with the number of person years included as an offset.

** Adjusted for variables used to restrict randomisation: Previous CNR, number of adults, mean distance from cluster centres to the nearest health clinic, allocated health centre and longitude and latitude of cluster centre

† Number of notifications within 91 days / person-years follow-up

Table: TB case-notification rates at 91 days*

Conclusions: Despite residual undiagnosed tuberculosis of 0.15%, we saw no increase in tuberculosis registrations from this previously successful approach targeting symptomatic disease. Our sub-District notification system can guide municipal decisions to intensify, continue, or stop ACF.

OA17-325-09 Effect of community active case-finding strategies for the detection of tuberculosis in Cambodia: a pragmatic cluster randomised trial

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Background: Cambodia has adopted active case-finding strategies (ACF) to reach people with tuberculosis (TB). However, their effectiveness in detecting TB has not been systematically assessed. This pragmatic cluster randomised trial evaluated the effectiveness of three ACF interventions in increasing the yield of TB diagnoses and case notifications, their effect on treatment outcomes, and established the number needed to screen and test to detect one person with TB.

Design/Methods: Four clusters, two operational districts per cluster, matched by population size and the number of health facilities, were randomised to receive: 1. ACF using a seed-and-recruit model (ACF SAR), 2. One-off roving ACF (one-off ACF), 3. ACF targeting household and neighborhood contacts, or; 4. Passive case finding (PCF) as the control group between December 2019 and June 2021.

All interventions and PCF were performed according to existing protocols.

The study endpoints were TB case notification rates, the cumulative yield of TB cases, treatment outcomes, and the number needed to screen and test to find one TB case. Twelve months of data for each arm were collected, and analysis was by intention to treat.

Results: The case notification rates (per 100,000 population) in intervention arms 1, 2, and 3 were 208.2, 203.4, and 82.5, respectively, compared with 43.3 in the control arm. Intervention arms 1 and 2 notified more cases than the control arm; rate ratios: 4.8 (95% CI: 1.67,13.8) and 4.7 (95% CI: 1.72,12.9), respectively. ACF SAR needed to screen and test the fewest number of people with presumptive TB (n=9) to identify one all-forms TB (total yield: 210 cases), while one-off ACF needed to screen

and test 26.7 (total yield: 274 cases). The treatment success rates between the intervention and control arms were similar.

Conclusions: Community-based ACF interventions, particularly the SAR and one-off models, effectively increased TB case notifications. ACF SAR was efficient at TB case finding.

OA17-326-09 The impact of self-reported availability on potential yield of household-based tuberculosis contact investigation

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Background: Contact tracing can effectively identify individuals at high risk for TB, but is limited by its ability to reach contacts during the screening process. We investigated the potential effects of expanding the timing of home-based contact investigation on the total proportion and demographic characteristics of index patients and household contacts who may be available to participate in screening.

Design/Methods: Patients diagnosed with TB (index patients) from four health centers and community-based screening events in Kampala, along with their household contacts, were asked about their regular availability at nine different times (weekdays, Saturdays, and Sundays at 9am, 3pm, and 7pm). We calculated the “participant identification gap”, defined as the proportion of index patients and contacts who reported being home <50% of the time, for a base scenario of an intervention conducted only during business hours (weekday mornings and afternoons). We then estimated the incremental reduction in the proportion missed if contact investigation hours were expanded to include weekday evenings, Saturdays, and Sundays, using McNemar’s test.

Results: Nearly half of eligible individuals (42% of index patients and 52% of contacts) would be missed by household interventions conducted only during business hours. Expanding intervention hours to include weekday evenings, Saturdays, and Sundays would reduce the participant identification gap to 15% among index patients and 18% among contacts. More inclusive hours also reduced differences in the participant identification gaps by sex and employment.

Conclusions: Expanding availability of contact investigation hours or other home-based health interventions could reduce the participant identification gap (the number of individuals missed by such interventions) by more than half, with disproportionate effects among harder-to-reach populations.

OA17-328-09 One stop-shop diagnostic package for community active case finding for TB: Findings from a pilot intervention during the 2022 World TB Day celebration in Nigeria

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Background and challenges to implementation: Targeted community active TB case finding interventions using the Delft Light Back (DLB) with CAD4TB Artificial Intelligence (AI) for pre-diagnostic TB screening generates increased number of sputum samples for diagnostic evaluation. To bridge the increasing gap in TB diagnostic evaluation during these community outreach using the DLB, KNCV Nigeria team across supported states coupled the DBL intervention with Truenat or TB LAMP for same day TB diagnosis on site and subsequent linkage to treatment as a pilot intervention. We assessed the impact on TB evaluation rate.

Intervention or response: During the World TB Day community outreach in five states; Kano, Katsina, Delta, FCT, Nasarawa across eight hard-to-reach communities, we deployed DLB with Truenat or TB LAMP as a one stop-shop diagnostic package for TB case finding. We identified communities for the outreach, informed by TB hot spot analytics.

At a selected location for the outreach, clients were assembled, enrolled and screened first using the WHO-recommended clinical symptom checklist and then DLB with CAD4TB AI. Identified presumptive TB provided sputa which were tested on the spot with Truenat or TB LAMP. Presumptive TB with negative results had their DLB x-ray films sent through a virtual platform, the XMAP for Radiologist review. All diagnosed TB cases were linked to DOTS for treatment and notified to the TB program.

Results/Impact: A total of 759 individuals were screened using the WHO-recommended clinical symptom checklist initially, while 92% of them were further subjected to DLB screening. Eighty two presumptive TB were identified and 79 (96%) evaluated on the spot. Twenty one TB cases were diagnosed and linked to care, see Table 1.

State	State	#Patients deployed for outreach	# TB cases screened	# TB cases confirmed	# TB cases not confirmed	# TB cases referred to laboratory for evaluation	# TB cases referred to laboratory for evaluation	# TB cases referred to laboratory for evaluation	# TB cases referred to laboratory for evaluation	# TB cases referred to laboratory for evaluation	# TB cases referred to laboratory for evaluation	# TB cases referred to laboratory for evaluation	# TB cases referred to laboratory for evaluation	# TB cases referred to laboratory for evaluation	# TB cases referred to laboratory for evaluation	# TB cases referred to laboratory for evaluation	# TB cases referred to laboratory for evaluation	# TB cases referred to laboratory for evaluation	# TB cases referred to laboratory for evaluation	
1	Kano	DLB & Truenat	420	420	31	7	10	0	0	0	0	0	0	0	0	0	0	0	0	0
2	Katsina	DLB & Truenat	77	77	3	3	4	0	0	0	0	0	0	0	0	0	0	0	0	0
3	Delta	DLB & Truenat	367	367	24	3	8	0	0	0	0	0	0	0	0	0	0	0	0	0
4	FCT	DLB & Truenat	11	11	2	1	2	0	0	0	0	0	0	0	0	0	0	0	0	0
5	Nasarawa	DLB & Truenat	102	102	5	2	8	0	0	0	0	0	0	0	0	0	0	0	0	0
6	FCT	DLB & TB LAMP	40	40	16	2	20	11 (100%)	0	0	0	0	0	0	0	0	0	0	0	0
7	Nasarawa	DLB & TB LAMP	100	100	0	1	10	100 (100%)	0	0	0	0	0	0	0	0	0	0	0	0
Total			759	759	40	27	73	110 (100%)	0	0	0	0	0	0	0	0	0	0	0	0

Table 1. Results of TB screening and diagnostic evaluation.

Conclusions: Same day diagnosis was achieved for 96% of presumptive TB because Truenat or TB-LAMP was on site to process the samples. This demonstrated the utility of this approach in bridging diagnostic evaluation gap during community TB ACF.

OA-18 Identification and Management of TB Infection

OA18-329-09 Differences in IGRA positivity rates among close contacts exposed to M.tuberculosis lineage 1 and lineage 2 in Thailand

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Background: Thailand is one of the high tuberculosis (TB) burden countries. *M.tuberculosis* lineage 1 and lineage 2 are commonly distributed in the northernmost Thailand. Understanding the pathogenesis and transmissibility of these lineages may contribute to effective TB control. We aimed to assess the interferon-gamma release assay (IGRA) positivity in familial/household contacts to evaluate the transmissibility of lineages.

Design/Methods: We enrolled pulmonary TB patients diagnosed with culture-positive TB between 2017-2020 in Chiangrai province, Thailand. We collected socio-demographic information and performed WGS on Illumina HiSeq 2000 platform after extracting DNA from TB culture samples. We classified lineages using WGS data. TB patients were interviewed to create a list of household/familial contacts of TB patients. We invited household contacts for TB screening by chest X-ray, AFB testing and interferon-gamma releasing assay (IGRA) tests. IGRA was performed using QuantiFERON-TB Gold Plus (QFT) (Qiagen, USA). Positivity of IGRA results was compared between lineage 1 and lineage 2.

Results: Among 101 household contacts who received TB screening, 47 (46.5%) were positive for IGRA and 9 (8.9%) were diagnosed with active TB. 65.0% of contacts were IGRA-positive on TB screening within one month of the index patient's TB diagnosis. The IGRA-positive rate among household contacts was

significantly higher among those who exposed to lineage 2 than lineage 1 (66.0% vs. 27.3%). The odds of IGRA positivity were 5.18 times (95% CI: 1.71-15.64) higher for contacts of lineage 2-infected patients than for those of lineage 1-infected patients. Of the 9 TB patients diagnosed as sputum AFB smear-positive by TB screening, 8 patients were exposed to lineage 2-infected patients.

Conclusions: Close contacts of lineage 2-infected TB patients had a high positivity rate in IGRA. It was suggested that the effect of lineage on the transmissibility of TB might be related to the latent infectious status of TB.

OA18-330-09 Management of latent tuberculosis infection in people experiencing homelessness: a pilot

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Background: People experiencing homelessness have high rates of TB infection, progression to disease, and worse clinical outcomes. Responsible factors include malnutrition, co-morbidity, and difficulty accessing services. Hence the WHO recommendations for systematic screening for LTBI in under-served populations. Find&Treat, an NHS outreach service, conduct active case finding in homeless hostels across London using point-of-care diagnostics for pulmonary tuberculosis, HIV, and viral hepatitis. From September 2021 TB infection testing and treatment was integrated into their activities as a pilot.

Design/Methods: Adults meeting inclusion criteria were offered an interferon-gamma-release-assay (quantIFERON-TB GOLD), and individuals with a positive result underwent a comprehensive medical assessment. Joint decision making on treatment were conducted remotely with a hospital-based TB service, with assessments and follow-up done by the outreach team consisting of doctors, nurses, and peer-workers.

The primary outcome was completion of treatment, with additional outcome measures including proportion passing through the cascade of care, adverse events, and drug-drug-interactions.

Results: 232 people were offered testing for TB infection, 168/232 (72%) agreed and have available results, with 26/168 (15%) having a positive IGRA. The majority were male (23/26), with a median age of 54 years old; a minority were born outside of Europe (4/26). There were high rates of previous incarceration (83%), alcohol misuse (41%), and use of prescribed or illicit opiates (61%). To date, 14/26 completed a medical assessment, with 11/14 deciding to take treatment, 2 of whom have successfully completed so far.

Conclusions: This pilot has successfully diagnosed and treated TB infection in an under-served population with high rates of opiate use. Integration with screening for other diseases and providing the service at the patients place of residence has yielded a progression through the cascade of care similar to the general population. Excellent communication with primary care and drug&alcohol services facilitated the safe management of rifampicin related drug-drug interactions.

OA18-331-09 Short-course rifapentine and isoniazid preventive treatment among people living with HIV in low and middle-income countries is safe and associated with high treatment completion rates

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Background: The World Health Organization recommends tuberculosis (TB) preventive treatment (TPT), including a short regimen of rifapentine and isoniazid taken once weekly for three months (3HP). As part of the IMPAACT4TB project, facilitating the scale-up of 3HP in high TB burden countries, we assessed uptake, treatment completion, occurrence of treatment-limiting adverse events, TB, and deaths in 7 countries.

Design/Methods: We conducted an observational programme evaluation among people living with HIV (PL-HIV) in at least one health facility (sentinel site) per country. Individuals were defined as stable on ART if at the point of initiating TPT they had been on ART

for >90 days and newly initiated ART if they had been on ART for ≤90 days. All clinical procedures including screening for 3HP eligibility, initiating and monitoring treatment were done as part of routine care. Record reviews were done retrospectively and de-identified patient-level data captured into a secure REDCap database. Data was collected from treatment initiation up to completion.

Results: Between July 2020 to December 2021, 3246 persons (66% female, median age; 38.2 years) initiated 3HP and were included in the evaluation. Median follow-up was 81.4 days (interquartile range 21-114days). Of these, 2178(67%) were stable on ART and 1068(33%) newly initiated ART. Overall 2759(85%) persons completed treatment; 1939 (89%) in the ART stable vs 820(77%) in the recent ART initiation group (Table). 2/3246(0.1%) persons were diagnosed with TB while on treatment and 5(0.2%) died. Treatment-limiting adverse events were as follows: 7(0.2%) flu-like reactions, 13 (0.4%) mild hepatotoxicity, 5 (0.2%) systemic hypersensitivity, 2 (0.1%) peripheral neuropathy and 11 (0.3%) other forms of toxicity (Table).

		Initiated on 3HP (n)	Completed 3HP (n)	Completion rate (%)	Treatment discontinuation due to adverse events
A. Newly initiated ART	i. DTG-based regimen	1042	797	77	5 (0.5)
	ii. Other regimen	15	13	87	0 (0)
	*Overall	1068	820	77	5 (0.5)
B. ART stable	i. DTG-based regimen	1715	1520	89	21 (1.2)
	ii. Other regimen	442	405	92	12 (2.7)
	**Overall	2178	1939	89	33 (1.5)

* ART regimen data missing for 11 person and 10 of these completed 3HP; **ART regimen data missing for 21 participants and 14 of these completed 3HP; n-number of persons; %-percentage. The denominator was number of persons initiated 3HP.

Table. Outcomes of people living with HIV initiated on 3HP in the 7 project countries.

Conclusions: The study reported high completion rates, low incidence of treatment-limiting adverse events and TB among PLHIV regardless of whether they were newly initiating or stable on ART, supporting the opportunity of scaling up 3HP among PLHIV in high burden setting.

OA18-332-09 Long-term follow-up for prevention of tuberculosis among contacts receiving 6-month-isoniazid and 9-month-isoniazid: an observation cohort study for effectiveness

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Background: 9-month isoniazid (9H) has been recommended for tuberculosis preventive therapy (TPT) for contacts with latent TB infection (LTBI) in Taiwan since 2008. World Health Organization also recommended 6-month isoniazid (6H) for TPT.

This study was aimed to evaluate whether the effectiveness for prevention of TB was similar for 9H and 6H in a country with HIV prevalence less than 0.2% in general population.

Design/Methods: 32,109 contacts with LTBI who received isoniazid for at least 170 days for TPT were enrolled from April, 2008 to December, 2020. The demographics of index patients and contacts, treatment days and subsequent developing of TB were collected from the National TB Case Management System, linked with Census data and followed-up until the end of 2020. Treatment days was stratified into 2 groups: treatment lasting 170-225 days (6H) and 256 days and up (9H).

Factors	Accumulative incidence (/10,000 person-year)	Adjusted Hazard Ratio (95% CI)	P-value	
Treatment	6H	11.2	1.856 (0.569~6.053)	0.3049
	9H	2.7	1	
Gender of index patient	male	3.3	1.067 (0.589~1.932)	0.8313
	female	2.5	1	
Source patient sputum smear results	Positive	3.3	1.108 (0.55~2.23)	0.7739
	Negative or scanty	2.2	1	
Age of contact	-	-	1.038 (1.027~1.048)	<.0001
Gender of contact	male	3.6	1.408 (0.811~2.445)	0.2236
	female	2.5	1	
Exposure settings	Household	3.8	1.923 (0.95~3.892)	0.069
	Contacts in other settings	1.7	1	
Index from mountainous area	Yes	7.6	4.471 (1.975~10.123)	0.0003
	No	2.8	1	

Table. Characteristics and development of tuberculosis among tuberculosis contacts receiving 6H and 9H with the Cox proportion hazard method.

Results: A total of 806 patients and 31,303 were stratified into 6H and 9H groups according to pills-uptake days. During the study period, 82 out of 32,109 developed active TB but only 50 of the 82 contacts were diagnosed after completion of TPT. The crud rate of devel-

oping TB was 372/100,000 and 150/100,000 for 6H and 9H, respectively ($p=0.114$) with median age of 47 and 18, respectively ($p<0.001$). The accumulative incidence of developing TB among contacts in group 6H and 9H were 11.2/10,000 and 2.7/10,000 person-year, which was not significantly different by Cox proportional hazard methods ($p=0.305$) after adjusted for gender and sputum results of index patients, relationship between index patients and contacts, whether index from mountainous area, gender and age of contacts (Table). Age of contacts and index from mountainous area were associated strongly with developing TB.

Conclusions: Contacts of TB patients may benefit similarly from 6H and 9H. However, the effectiveness could be hampered in elderly and high prevalence regions.

OA18-333-09 A systematic review and meta-analysis of tuberculous preventative therapy adverse events

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Background: Tuberculosis preventive therapy (TPT) is a key part of the WHO's end TB strategy. However, the risk of adverse events (AE) due to TPT is a major concern. We aimed to systematically review AE during TPT with different regimens currently in use.

Design/Methods: Our systemic review (PROSPERO CRD42021269551) included a search of MEDLINE, Health Star, EMBASE and Cochrane from 1952 to April 2021.

We meta-analyzed the cumulative incidence of AE that met different definitions using a generalised linear mixed random effect model, overall, stratified by age and regimen, and AE type.

Results: We included 183 publications, with 277 cohorts, and 186,281 individuals, of whom 71% were from high income countries. Most common regimens were: 6-9H (109170 persons), 3HP (18420 persons) and 4-6R (11933 persons). 34 cohorts were pediatric populations, with 11,226 children. Among adults receiving TPT, the proportion with any AE was 9.3% and the rate of AE leading to drug discontinuation was 3.7%. Hepatotoxicity occurred in 2.9% and the proportion of hepatotoxicity leading to drug discontinuation was 1.1%. In the pediatric population the rate of AE was 2.7% with 0.3% leading to drug discontinuation, and hepatotoxicity occurred in 0.7%.

Pooling the entire included population (adults and pediatric), any AE occurred at a rate of 8.8% in 6-9H regimens, 27% in 3HP regimens and 5.4% in 4-6R regimens. AE leading to drug discontinuation occurred at in 4.1% in 6-9H regimens, 8.1% in 3HP regimens and 2.9% in 4-6R regimens. Grade 3-4 AE occurred at a rate of 2.7% in 6-9H regimens, 3.6% in 3HP regimens and 0.6% in 4-6R regimens. Hepatotoxicity occurred at a rate of 4.0% in 6-9H regimens, 1.5% in 3HP and 0.7% in 4-6R regimens.

Conclusions: Using various definitions, AE leading to drug discontinuation and hepatotoxicity were lowest with 4-6R, and substantially lower in the pediatric population.

OA18-334-09 Determinants of losses in the tuberculosis infection cascade of care among children and adolescent contacts of pulmonary tuberculosis cases in Brazil

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Background: Approximately 10% of the global tuberculosis (TB) burden is in children. Identification, diagnosis, and early treatment of Mycobacterium tuberculosis infection (TBI) is critical to prevent progression to TB in children. The risk of TB, including severe disease, is highest in children <5 years old. We evaluated the cascade of TBI care among child and adolescent TB contacts to identify factors associated with losses in the cascade.

Design/Methods: Close contacts ≤ 18 years old of pulmonary TB patients enrolled between 2015 and 2019 in a multi-center Brazilian cohort were followed for up to 24 months and classified according to age groups: <5 years, 5-9 years, 10-14 years and 15-18 years. Data on clinical investigation, radiographic examination, IGRA testing at baseline and 6 months, initiation and completion of TB preventive treatment (TPT) were collected. Multivariable regression analyses identified factors associated with TBI and losses in the cascade of care in children and adolescents.

Results: Among 1,795 TB contacts initially identified, 530 (29.5%) were ≤18 years old. Losses in the cascade were especially high in children <5 years old (88%). In addition, the lowest percentage (9.8%) of compliance with recommended TPT was observed in children 10-14 years old. Furthermore, multivariable regression revealed that younger age of contacts and TB index cases of contacts who were female, had pulmonary cavities, and persistent cough were independently associated with losses in the cascade of care of contacts.

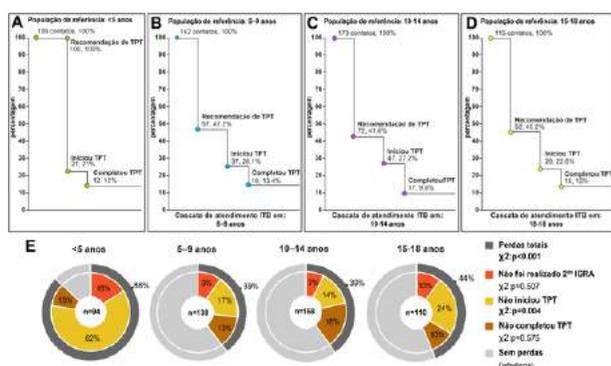


Figure 1. Cascade in TB care in contacts of TB cases and type of losses in the TBI cascade of care according to the age group. Losses and drop-outs at each stage of the TB cascade of care in <5 years old, percentages were calculated among the number of contacts initially identified in (A) <5 years old (B) 5-9 years old (C) 10-14 years old and (D) 15-18 years old. Age categories based on the previous study. Percentages were calculated among the number of contacts initially identified. (E) Distribution of type of losses in the TBI cascade of care (%) by age groups. The comparisons of IGRA results frequencies (%) between the types of losses were made with the chi-square test (χ²).

Abbreviations: TB: tuberculosis; TPT: Tuberculosis preventive treatment; IGRA: interferon Gamma Release Assays.

Conclusions: Losses in the TBI cascade were highest among children <5 years old—the group at highest risk of TB. These observations highlight the need to improve screening and TPT initiation of young children who are close contacts of persons with TB in Brazil.

OA18-335-09 Household costs incurred under two service-delivery models of tuberculosis preventive therapy for children: a survey in Cameroon in Uganda

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Background: Tuberculosis (TB) preventive treatment (TPT) in child household contacts is recommended by WHO but no data has yet been reported on the costs experienced by households of children receiving TPT.

We evaluated the economic impact on households with children receiving TPT in the community-based (intervention) versus facility-based (control) model within the CONTACT cluster randomized control trial that evaluated the impact of child contact TB investigation and TPT management in Cameroon and Uganda.

Design/Methods: The intervention included community health workers led-home-based child-contact screening and TPT monitoring, and referral of children with presumptive TB or side effects. The control was the standard of care with TPT initiation and follow-up done at the facility and the possibility of TB screening in the community for Uganda only. We used a cross-sectional survey with retrospective data collection using a standardized questionnaire adapted from the WHO patient cost generic survey instrument adapted to the local context. Costs are presented in 2021 US\$.

Results: A total of 57 households in Cameroon (intervention, 39 and control, 18) and 47 households in Uganda (intervention, 29 and control, 18) were interviewed. The median estimated household costs were higher in the control (\$245 [IQR; \$11-555] in Cameroon and \$107 [IQR; \$42-312] in Uganda) compared to the intervention (\$55 [IQR; \$0-596] in Cameroon and \$41 [IQR; \$16-246] in Uganda). The distribution of cost drivers is shown in Figure 1. Using a threshold of 20% of household income, 21% of households in Cameroon and 10% in Uganda experienced catastrophic costs in the intervention compared to 28% in Cameroon and 22% in Uganda in the control.

Conclusions: Households with child contacts initiated on TPT incur significant costs, although these are lower than costs expected during tuberculosis treatment. Community-based interventions helped to reduce these costs, however, these were not enough to eliminate catastrophic expenditures.

E-POSTER SESSION (EP)

EP-11 Tuberculosis infection and control in a wider context

EP-11-701 Use of health system strengthening approach improves national TB preventive therapy (TPT) coverage among PLHIV in Malawi

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Background and challenges to implementation: Malawi commenced use of TB preventive therapy (TPT) among PLHIV on ART in 2016 using continuous isoniazid monotherapy (IPT) in 5 high TB/HIV burden districts. 6% of those initiated developed pellagra, uptake stalled. By end 2019, a total of 257,334 ART clients were initiated on IPT (29% national coverage).

From 2020, Malawi will use short course TPT regimens of rifapentine and isoniazid (3HP) and 6 monthly isoniazid monotherapy (6H) and implement strategic interventions to improve coverage from 29% to 85% by 2025. The abstract outlines approach promoted and TPT performance in 2021.

Intervention or response: The national HIV program used health system strengthening approach to improve TPT coverage. In July 2020, 3HP was recommended as preferred regimen for PLHIV newly initiating on ART due to budget constraints. 6H is dispensed to those with rifapentine contraindications. Financial support from Global Fund and UNITAID earmarked for commodity procurement ensured staggered delivery to allow phased national scale up.

Skills development activities to have competent healthcare providers included training, development of wall and desk job aids and regular supportive supervision visits. Screening and dispensing documentation used manual or electronic through TPT module integrated in ART EMR and e-mastercard available in 79% of all ART facilities.

Results/Impact: TPT coverage among eligible PLHIV initiating ART in Malawi increased from baseline of 29% (2019) to 64% (2021). Absolute figures on graph show increasing trend in TPT initiations. 3,212 providers from 512 facilities across the country were trained on TPT administration. 8 cases with moderate flu-like syndromes were reported on 3HP, no pellagra and hepatotoxicity cases reported. None of the cases needed laboratory toxicity monitoring.

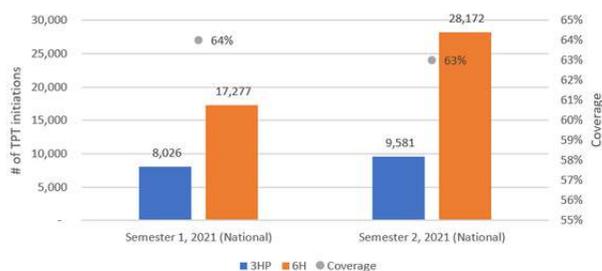


Figure. TPT uptake among eligible clients in Malawi.

Conclusions: Use of health system strengthening approach has improved TPT uptake towards achievement of NSP target. The National HIV program should use quality improvement approach, differentiated TPT dispensing services and enhanced pharmacovigilance to increase TPT coverage.

EP-11-702 TB antigen-based skin tests and QFT-Plus® for the diagnosis of Mycobacterium tuberculosis infection in Brazilian healthcare workers: a cost-effectiveness analysis

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Background: The Brazilian National TB Program (NTP) has defined healthcare workers (HCW) as a priority population for scaling up tuberculosis preventive treatment (TPT) in its 2021-2025 Plan to End TB. Intermittent shortage of PPD Rt-23 and the low specificity of the test in BCG-vaccinated populations have encouraged the NTP to search for newer, more specific tests. We evaluated the cost-effectiveness of two TB antigen-based skin tests (TBST) and QuantiFERON-TB-Gold-Plus (QFT-Plus®, Qiagen, Germany) versus tuberculin skin test (PPD-TST) in Brazilian HCWs.

Design/Methods: We developed a cohort-based Markov model to estimate the incremental cost-effectiveness ratio of two TBST [Diaskintest® (Generium, Russian Federation) and C-TST® (Anhui Zhifei Longcom, China)] and QFT-Plus® versus PPD-TST (standard-of-care) for the annual evaluation of HCWs for TBI under the Brazilian health system perspective, over a 5-year time horizon.

If TBI was detected, treatment with 3HP (US\$ 50.78) was recommended, as per national guidelines. Effectiveness was the number of TB cases averted. Costing data

was sourced from previous studies and the NTP (2021 US\$). Costs and effectiveness were discounted at a 5% fixed annual rate. We performed probabilistic and deterministic sensitivity analyses. Global Drug Facility (GDF) costs by combined weekly dose of 3HP were used in the sensitivity analysis (US\$ 46.44).

Results: Diaskintest® strategy was cost-saving for TBI diagnosis (US\$ 20.672 per averted TB case, Table). Despite the strategy using the QFT-Plus® having slightly higher effectiveness, it had an incremental cost-effectiveness ratio of US\$ 58.384 per TB case averted, mostly driven by equipment and human labor costs. In sensitivity analyses, the Diaskintest® remained cost-saving compared to PPD-TST.

Strategy (cost per test)	Cost per 100,000 HCWs	95% UR		Incremental cost per 100,000 HCWs	TB cases	95% UR		TB cases averted	ICER
		Low	High			Low	High		
TST PPD Rt-23 (US\$ 2.96)	5,821,360	4,482,439	7,374,603	-	592	239	1217	-	-
Diaskintest® (US\$ 3.59)	4,581,827	3,610,564	5,716,591	-1,239,533	532	286	963	60	-20,672
C-TST® (US\$ 7.79)	5,844,782	4,598,652	7,283,774	23,422	547	285	1003	46	512
QFT-Plus® (US\$ 20.27)	9,502,050	7,166,970	12,288,814	3,680,690	529	284	955	63	58,384

Abbreviations: 3HP - 3 months of weekly doses of rifampentine (900 mg/dose) and isoniazid (900 mg/dose); ICER - incremental cost-effectiveness ratio, QFT-Plus® - QuantiFERON-TB-Gold-Plus; TST - tuberculin skin test; PPD - purified protein derivative; US\$ - US dollars; UR - uncertainty ranges.

Table. Strategy rankings - all referencing a common baseline (in US\$ 2021).

Conclusions: In the Brazilian scenario, Diaskintest® is the least costly and most effective test for sequential testing of HCWs, mainly due to the higher costs of QFT-Plus® and lower specificity of PPD-TST.

EP-11-703 Closing the science-to-service gap by increasing TB preventive therapy (TPT) uptake using the choice architecture tuberculosis preventive therapy (CAT) prescriptive stickers

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Background and challenges to implementation: Tuberculosis (TB) accounted for 30% of deaths among people living with HIV (PLHIV) worldwide in 2019.¹ A 54% TB/HIV co-infection rate contributes to Zimbabwe's considerable TB burden - incidence of 193 per 100,000.¹ In PLHIV, TPT reduces TB incidence by 62% and death by 39%.²

A global science-to-service gap of <20% eligible PLHIV starting TPT was reported.³ Moreover, in Zimbabwe only 38% of PLHIV were initiated among them 26% completed in 2019. Health worker challenges contributing to the 38% science-to-service gap include inadequate understanding of the TPT benefits; high TPT prescriptive cognitive burden due to integrated service provision; TPT initiation skepticism and many reporting tools.

Intervention or response: The Clinton Health Access Initiative and the Ministry of Health and Child Care are implementing a two-pronged choice architecture intervention study. The choice architecture TPT (CAT) prescriptive sticker intervention shifts clinician decision-making from prescribing TPT to identifying people who should not receive TPT, making TPT delivery the default. The intervention included healthcare worker training, printing, and distribution of CAT prescription stickers. The intervention's purpose was to see if prescribing TPT using a "default" CAT prescriptive strategy would dramatically increase TPT prescribing.

Results/Impact: Preliminary results reveal that the CAT prescriptive sticker is attributable to an increasing TPT initiation among newly PLHIV clients from 52% to 61%. Intervention sites have reported a huge increase in Rujeko from 18% to 93%, Highfield 18% to 64%, Northern Suburbs from 0% to 100% as compared to control sites St Luke's from 30% to 33%, Beitbridge from 41% to 25% Pumula 0% to 9%.

Conclusions: As a result of the CAT-prescriptive sticker, TPT initiation among PLHIV has increased from 52% to 61%. Other services including ART, Cotrimoxazole, cervical cancer, and other drugs provided to PLHIV are integrated into the CAT-prescriptive sticker, ensuring that PLHIV receive a quality, holistic and comprehensive package.

EP-11-704 Features of symptomatic and asymptomatic tuberculosis diagnosed through community-based symptom-agnostic screening in an HIV-TB endemic rural South African population

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Background: We characterized prevalent tuberculosis in an HIV-TB-endemic rural South African population with wide-scale ART uptake.

Design/Methods: Between 2018-2020, adolescent and adult residents of a rural demographic surveillance area in KwaZulu-Natal, South Africa were offered multi-disease screening, including TB symptom screening and digital chest x-ray. People with symptoms or CAD4TB score ≥ 25 had sputum collected for GeneXpert Ultra and MGIT liquid culture. Individuals not on TB treatment with evidence of Mtb in the sputum were considered to have undiagnosed TB. We compared people with undiagnosed TB to those without TB and to those on TB treatment, and asymptomatic undiagnosed TB to symptomatic.

Results: 0.4% of enrolled participants (41/18041) were on TB treatment. 1% (174/18041) had undiagnosed TB. Compared to people without TB, people with undiagnosed TB were more likely to be male (OR 1.81, $p < 0.001$), smokers (OR 2.69, $p < 0.001$) and HIV positive (OR 2.32, $p = 0.004$).

	Asymptomatic TB N = 143	Symptomatic TB N = 31	OR	95% CI	p-value
Female sex	80 (56%)	14 (45%)	0.65	0.29, 1.41	0.3
Age	41 (31, 62)	54 (43, 66)	1.02	1.00, 1.04	0.11
HIV status	59 (41%)	17 (55%)	1.73	0.79, 3.83	0.2
Wellness index	98 (80, 100)	80 (70, 95)	0.97	0.95, 0.99	0.011
Underweight (BMI < 18.5)	9 (6.3%)	6 (20%)	3.47	1.03, 11.1	0.038
Current smoker	19 (13%)	10 (32%)	3.16	1.25, 7.71	0.012

Compared to those on treatment, the undiagnosed were more likely to be HIV negative (OR 2.32, $p = 0.003$). 82% (143/174) of people with newly diagnosed TB reported no symptoms, and their self-reported health score (me-

dian 95 [IQR 80-100]) was similar to those without TB (90 [80-100]). Compared to the symptomatic, the asymptomatic were similar in age, sex and HIV status, and less likely to have a BMI < 18.5 or smoke tobacco. 12% (21/174) of undiagnosed TB was drug resistant, of which 86% (18/21) were asymptomatic.

Conclusions: There is a high prevalence of undiagnosed tuberculosis – predominantly asymptomatic – in rural KwaZulu-Natal. Although 80% of clinically-diagnosed TB in this setting is among PLWHIV, more than half of undiagnosed TB is among the HIV-negative, suggesting enhanced screening in the HIV-negative population is needed. People with asymptomatic and symptomatic TB were demographically and clinically similar. Further research is needed to understand the progression and transmission of asymptomatic TB, which dominates active disease in the region.

EP-11-705 Resistance to Mycobacterium tuberculosis infection among highly TB exposed, HIV infected goldminers in South Africa

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Background: Despite high rates of HIV and prolonged exposure to TB, a small proportion of goldminers in South Africa resist *Mycobacterium tuberculosis* infection. Among long-service goldminers who were HIV-infected, we determined: i) the proportion who were TB uninfected and ii) epidemiological factors associated with being uninfected.

Design/Methods: We enrolled HIV-positive goldminers who were on antiretroviral treatment (ART), aged 33-60 years, with ≥ 15 years' service, no prior or current TB, no silicosis, and with body mass index (BMI) > 18.5. TB infection status was assessed using QuantiFERON-TB-Gold-Plus (QFT-Plus) and tuberculin skin test (TST). Miners were considered TB uninfected if they had a negative TST (induration < 5mm) and negative QFT-Plus (response < 0.35 IU·ml⁻¹ on both TB1 and TB2 antigen tubes) and resisters if they were of Black/African ethnicity with negative QFT-Plus and zero TST response. Logistic regression was used to identify epidemiological factors associated with being TB uninfected.

Results: We enrolled 245 miners with median age of 48 years (interquartile range [IQR]: 44, 52 years) and median CD4 count of 506 (IQR: 372, 677). Overall, 98% (239) were males and 99% (243) Black/African with a median time of 24 years (IQR: 18, 29 years) in the workforce. Of this, 48% (117/245) were TB uninfected and this was associated with having BMI of ≥ 30 kg/m² (aOR 0.26; 95% confidence interval [CI]: 0.07 - 0.93; $p = 0.038$).

Among the 243 participants that were of Black/African ethnicity, 114 (46%) had a negative QFT-Plus and a zero TST response. Participants with a CD4 count ≥ 500 (aOR 0.41, 95% CI: 0.18 - 0.93, $p=0.033$) were less likely to be TB uninfected (Table).

Variable (N=114)	QFT-Plus Negative/TST=0mm n/N (%)	Univariate analysis			Multivariable analysis		
		Crude OR	95% CI	p-value	Adjusted OR	95% CI	p-value
Age group, years							
<45	34 (84.1)	1	Reference	Reference	1	Reference	Reference
45-49	36 (81.8)	0.96	0.36 - 2.56	0.939	0.98	0.28 - 3.41	0.974
≥ 50	45 (76.3)	0.59	0.25 - 1.41	0.233	0.80	0.23 - 2.81	0.728
Mine house vs non-mine house							
Mine house vs non-mine house	77 (68.1)	0.40	0.16 - 0.99	0.049	0.51	0.18 - 1.42	0.198
Years worked in mines 15 - 20 years vs ≥ 20 years							
15 - 20 years vs ≥ 20 years	80 (69.6)	0.54	0.23 - 1.28	0.161	4.17	0.27 - 64.55	0.304
Years worked underground 15 - 20 years vs ≥ 20 years							
15 - 20 years vs ≥ 20 years	74 (67.9)	0.42	0.18 - 1.00	0.050	0.13	0.01 - 1.84	0.131
CD4 count 200 - 500 vs ≥ 500							
200 - 500 vs ≥ 500	46 (63.9)	0.44	0.22 - 0.91	0.026	0.41	0.18 - 0.93	0.033

Table.

Conclusions: We found an unexpected high proportion of HIV-infected goldminers who resisted TB infection despite high exposure. The association with CD4 count is unclear and might be reflective of loss of responsiveness in those with lower counts.

EP-11-706 The impact of the COVID-19 pandemic in tuberculosis preventive treatment in Brazil: a retrospective cohort study

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Background: Disruptions in Tuberculosis (TB) services have been observed around the world since the emergence of the COVID-19 pandemic. However, the pandemic effect on TB preventive treatment (TPT) was poorly explored. We compared TPT notified prescriptions and outcomes in the national information system before and during the COVID-19 pandemic in Brazil.

Design/Methods: We analyzed a retrospective cohort using secondary data from the Brazilian TPT information system (IL-TB) for five cities with over 1,000 no-

tifications in the study period. Successive trainings of healthcare workers on TPT followed the implementation of the IL-TB, in 2018. The number of TPT prescriptions was analyzed from 6 months after training to July 2021.

The proportion of TPT outcomes was analyzed by date of treatment initiation up to the end of 2020, as most outcomes of the TPT started in 2021 were still open by the time of analyses. TPT data were contrasted with the notifications of new cases of COVID-19 in Brazil, available from health surveillance department. Joint point models were used to evaluate changes.

Results: Out of 16,909 TPT prescriptions in the database, 14,014 were included, of which 8,032 in São Paulo and 3,187 in Rio de Janeiro. Isoniazid was prescribed for 97%. In 2020, the number prescribed TPT increased due to a 60% increase in Rio de Janeiro.

In São Paulo, prescriptions remained stable, while in the other cities, there was a reduction. In 2021, there was a 93% reduction in TPT prescriptions in all cities. The proportion of completed TPT remained constant (median=74%).

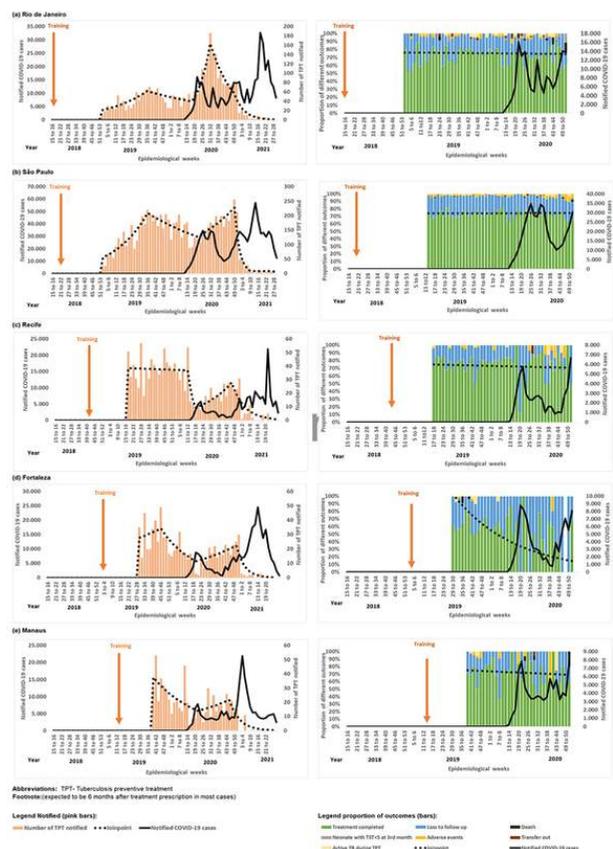


Figure. Notified (pink bars) and proportion of outcomes (bars) of TPT and number of notified COVID-19 cases (black line), by two-week periods (2018-2021)

Conclusions: The COVID-19 pandemic in Brazil was associated with a dramatic decrease in TPT prescriptions in 2021. Treatment adherence remained constant, sug-

gesting that health services were able to keep people on treatment, but did not perform well for people entering care. Efforts are needed to expand access to TPT.

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EP-11-707 Behavior change intervention promotes uptake and completion rates of IPT among HIV-infected adults initiating antiretroviral therapy at a tertiary referral hospital in Johannesburg, South Africa

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Background: In December 2019, South Africa started rolling out tenofovir disoproxil fumarate-lamivudine-dolutegravir (TLD) to PLHIV, and implemented a policy of same-day ART and TB Preventative Therapy (TPT) initiation (if eligible).

We used routine programmatic data to describe changes in uptake and completion rates between 01/2018-12/2020.

Design/Methods: Retrospective analysis of adults (≥ 18 yrs) initiating ART at the Themba Lethu Clinic, Johannesburg, South Africa. We excluded patients on TB treatment at ART initiation.

We defined three cohorts:

01/2018–12/2018 (cohort 1),

01/2019–12/2019 (cohort 2), and;

01/2020–12/2020 (cohort 3—same-day initiation of TLD and TPT with a prompt to remind pharmacists to dispense TPT).

We describe isoniazid prophylaxis therapy (IPT) uptake and completion for these cohorts.

Results: 3602 patients initiating ART (46.2% male, median age 38 years IQR 30–46) were eligible to receive IPT. Records showed that less than a third initiated IPT (26.1% 95% CI 22.8–26.3), and of these 42.2% (95% CI 38.2–46.3) completed treatment.

Of note, cohort 3 had significantly fewer eligible patients due to the reduction in ART initiations in South Africa during the COVID-19 pandemic.

Rates of IPT initiation were similar for cohorts 1 and 2 ($p > 0.05$). In 2018 the duration of IPT was standardized so that all adults with HIV would receive and complete TPT for a duration of 12 months. This change may have contributed to an improvement in adherence and IPT completion rates in 2018.

Compared to the previous year, same-day TLD and TPT initiation along with prompts significantly improved IPT initiation (73.8% vs. 20.1%) and the documentation of IPT completion 66.4% vs. 37.1%; $p < 0.05$

	Cohort 1	Cohort 2	Cohort 3	Total
TPT (isoniazid monotherapy – not TB treatment)	January – December 2018	January – December 2019	January – December 2020	January 2018 – December 2020
Eligible for IPT	1066	1142	202	2410
Initiated on IPT	212/1066 (19.9% 95% CI 17.5–22.4)	229/1142 (20.1% 95% CI 17.8–22.5)	149/202 (73.8% 95% CI 67.1–79.7)	590/2410 (24.5% 95% CI 22.8–26.3)
Completed course of IPT	65/212 (30.7% 95% CI 24.5–37.3)	85/229 (37.1% 95% CI 30.9–43.7)	99/149 (66.4% 95% CI 58.3–74.0)	249/590 (42.2% 95% CI 38.2–46.3)

Conclusions: Documentation of IPT uptake and completion rates for 2018 and 2019 were consistent with previous reports for South Africa. Results suggest that same-day TLD and TPT initiation and a prompt or “behavior change intervention” that reminds pharmacists to dispense TPT improve IPT uptake and completion.

EP-11-708 Patients' experiences with video directly observed therapy for tuberculosis care in Kampala, Uganda: a qualitative exit study

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Background: Digital adherence technologies (DATs) are emerging as alternative methods of monitoring treatment adherence for patients with tuberculosis (TB). Asynchronous video observed therapy (VOT) has been shown to be effective, but few studies have evaluated its use in Africa. Our study aimed to assess the acceptability and experiences of patients who used VOT during their TB treatment.

Design/Methods: Cross-sectional qualitative in-depth interviews were conducted with 30 patients at the exit of a randomized control trial of VOT conducted in Kampala, Uganda, from July 2020 to December 2021. Questions were guided by the technology acceptance model for resource-limited settings (TAM-RLS) framework developed based upon end-user experiences in rural Uganda. This framework incorporates both classic technology acceptance model categories as well as novel factors affecting use in this setting. The interviews were audio-recorded, transcribed, and analyzed using the Dedoose software. We used inductive and direct content analysis to derive categories describing perceived ease and usefulness, use behaviors, facilitators and barriers to acceptability of VDOT use.

Results: The mean age of participants was 35.2 years (SD, 12.0), 50% were female. Majority (73%) owned cellphones, with 46% being smartphones. Majority of

patients perceived VOT as ease to use and beneficial. Facilitators to VOT acceptability were text reminders, the easy-to-use application, the supportive training on technology use by the health workers and the ability to get family members' support.

Barriers to acceptability and use of VOT were mostly technology-related including phone malfunctioning, lack of electricity, intermittent network services and privacy and stigma concerns within the sociocultural context.

Conclusions: Overall, participants reported positive experiences with using VOT. Acceptability was mostly facilitated by the ease-to-use mobile app, the training support from health workers and social support from family members. However, technological and some social cultural issues remain barriers that must be addressed for the future adoption of VOT.

EP-11-709 A qualitative inquiry into barriers against the public-private mix for TB control in Ghana

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Background: The Public-Private Mix (PPM) TB control initiative was implemented in 2003 in the Accra and Kumasi Metropolitan areas of Ghana to improve TB control in the country. Despite efforts, health providers' interest in the scheme has waned hence the initiative has not been scaled up nationally. Consequently, outcome measures are sub-par e.g., a low TB case notification in Ghana. Hence, this implementation research explored barriers affecting the PPM initiative in Ghana.

Design/Methods: After purposive selection with maximum sampling variation, we interviewed 23 public and private sector TB focal persons involved in the PPM initiative in the Accra and Kumasi metropolitan areas between May and June of 2019. A semi-structured guide was used to explore their experiences which were digitally recorded and transcribed. Thematic content analysis was then done aided by NVivo-12.

Results: PPM implementation has been negatively affected by several factors related to a general inadequacy of funds for TB control amidst low political will. These include the suspension of the *Enablers Package* which generally led to reduced commitment of patients and providers to the program, and a high attrition rate of trained staff and volunteers especially in the private sector.

Additionally, training, monitoring, and supervision activities by the national TB program (NTP) were deemed insufficient and irregular. Logistical challenges such as

equipment malfunction, shortages of consumables, and occasional stock-out of TB medications were also reported.

Conclusions: The PPM initiative in Ghana is generally on the decline stemming from multiple factors which are mostly linked to insufficient funding. Concurrently with strategies to heighten political commitment, the NTP must devise innovative funding mechanisms to curb attrition and improve support to facilities by way of equipment provision, reliable drug supply, and more frequent training. Overall, these efforts should be geared towards a nationwide scale-up of PPM to promote the attainment of TB control targets.

EP-11-710 Increased child contact investigation and tuberculosis preventive treatment management through a community-based intervention in Cameroon and Uganda: results of the contact cluster randomized trial

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Background: In tuberculosis (TB) endemic countries, the screening and management of household contacts remains low including the uptake of TB preventive treatment (TPT). One of the challenges is the necessity for parents to bring children to the health facility for TB screening and TPT initiation. This study evaluated TPT initiation and completion in a community-based intervention (intervention) compared to the facility-based standard of care (control) among eligible household child contacts in Cameroon and Uganda.

Design/Methods: This is a multicentre cluster randomized controlled trial with twenty TB diagnostic and treatment facilities and catchment areas randomized between intervention and control arms. Bacteriologically confirmed index cases were asked to declare household contacts.

The intervention included screening for TB in household contacts by community health care workers with referral of symptomatic child contacts to a facility for TB diagnostic investigations; TPT initiation for child

contacts—a negative symptom screen and <5 years irrespective of HIV status or 5-14 years for children living with HIV (CLHIV); and TPT follow-up through home visits. TPT completion was defined as $\geq 90\%$ drug intake within 120 days. We compared the proportion of declared child contacts <5 years or CLHIV (5-14 years) who initiated and completed TPT between the two arms using a generalized linear mixed model.

Results: Between November 2019 and December 2021, a total of 562 and 342 index cases were enrolled in the intervention and control arms, declaring 1,895 and 1,005 child contacts, respectively. Of them, 941 (49.7%) and 459 (45.7%) were <5 years or CLHIV aged 5-14 years. In the intervention arm, 752/941 (79.9%) children initiated and completed TPT compared to 280/459 (61.0%) in the control arm, adjusted OR=3.13 (95% CI 1.28, 7.80), $p=0.009$ (Table).

Steps	Control	Intervention
Declared child contacts < 5 years old and 5-14 years CLHIV, N	459	941
Child contacts screened for TB, n (%)	372 (81.0)	837 (88.9)
Asymptomatic child contacts, n (%)	367 (80.0)	805 (85.5)
Child contacts eligible to TPT, n (%)	365 (79.9)	805 (85.5)
Child contacts initiated on TPT, n (%)	365 (79.9)	798 (84.8)
Child contacts who completed TPT, n (%)	280 (61.0)	752 (79.9)

Table. Cascade of care per arm

Conclusions: Scaled-up, community-based interventions have the potential to improve TPT coverage and outcomes among child contacts in resource-limited settings.

EP-12 TB and vulnerable population

EP-12-711 Pregnancy outcomes among South African women with tuberculosis in the context of HIV

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Background: The incidence of tuberculosis (TB) in South Africa was ~554/100,000 population in 2020 with an antenatal maternal HIV prevalence of ~30%. Maternal TB increases the risk of adverse pregnancy outcomes especially in the context of maternal HIV co-infection. We describe TB and pregnancy outcomes in women with and without HIV routinely diagnosed with TB in a programmatic setting in South Africa.

Design/Methods: We identified all pregnant women routinely diagnosed with TB in 2 high-burden sub-districts (Tygerberg and Khayelitsha) in Cape Town, South Africa, October 2018 to March 2020, through the Western Cape Provincial Health Data Centre.

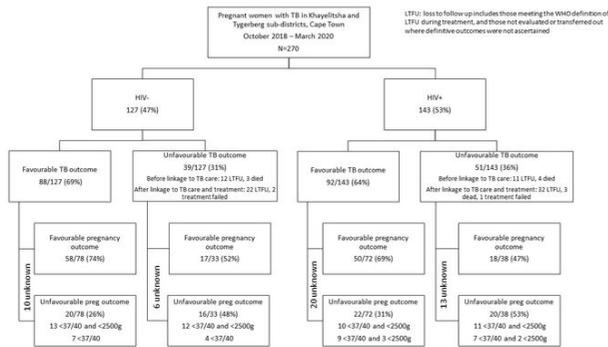
We distinguished between favourable (successfully completed TB treatment) and unfavourable TB outcomes (WHO TB reporting outcomes and loss to follow up (LTFU) prior to linkage to care and death, irrespective of TB treatment completion).

Favourable pregnancy outcome was defined as a pregnancy that resulted in an infant alive at 28 days, with a birth weight ≥ 2500 g and gestational period ≥ 37 weeks.

Results: Overall, 270 pregnant women with TB were identified, median age 27.9 years (IQR:23-32), 211/270(78%) bacteriologically confirmed, 50/270(19%) with previous TB, and 143/270(53%) living with HIV, all on ART. The median CD4 count (closest to TB diagnosis) was 235.5 (IQR:118-444).

Overall, 90/270(33%) had unfavourable TB outcomes; 30/90(33%) were LTFU prior to linkage to care, of which 7/30(23%) died. 39/127(31%) HIV-negative women, and 51/143(36%) HIV-positive women had unfavourable TB outcomes.

Almost half of the women with unfavourable TB outcomes had an unfavourable pregnancy outcome (48% in HIV-negative and 53% in HIV-positive TB women, respectively).



Conclusions: TB outcomes were poor in pregnant women, irrespective of HIV status. Women with poor TB outcomes were at very high risk of unfavorable pregnancy outcomes. Pregnant women with TB are an extremely vulnerable group and require prioritized TB care to ensure good TB and pregnancy outcomes.

EP-12-712 Treatment outcomes of pregnant women with multidrug-resistant tuberculosis

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Background: The management of multidrug-resistant tuberculosis (MDR-TB) is particularly challenging during pregnancy, yet no systematic synthesis of evidence accurately measures treatment outcomes.

Design/Methods: We conducted a systematic review and meta-analysis to quantify treatment outcomes of MDR-TB in pregnant women. The primary outcome of interest was treatment success, and secondary outcomes included pregnancy outcomes and adverse events. Meta-analysis was performed to estimate the pooled proportion of each of the outcomes of interest using random-effects models. The sources of heterogeneity were explored through meta-regression.

Results: Of 487 records screened, 10 relevant studies consisting of 275 pregnant women with known MDR-TB treatment outcomes were included. The overall pooled estimate was 72.5% (95% CI: 63.3, 81.0) for treatment success, 6.8% (95% CI: 2.6, 12.4) for death, 18.4% (95% CI: 13.1, 24.2) for loss to follow up, and 0.6% (95% CI: 0.0, 2.9) for treatment failure. Treatment success was significantly higher in studies where the

proportion of women taking linezolid was greater than the median (20.1%), compared with studies where this proportion was lower than the median (OR:1.22; 95% CI: 1.05, 1.42). More than half of the pregnant women (54%) experienced at least one type of adverse event, most commonly liver function impairment (30.4%), renal function impairment (14.9%), hypokalaemia (11.9%), hearing loss (11.8%), gastrointestinal disorders (11.8%), psychiatric disorder (9.1%) or anaemia (8.9%). The pooled proportion of favourable pregnancy outcomes was 73.2% (95% CI: 49.4, 92.1); and the most common types of adverse pregnancy outcomes were preterm birth (9.5%; 95% CI: 0.0, 29.0), pregnancy loss (6.0%; 95% CI: 1.3, 12.9), low birth weight (3.9%; 95% CI: 0.0, 18.7), and stillbirth (1.9%; 95% CI: 0.1, 5.1).

Conclusions: High treatment success and favourable pregnancy outcomes can be achieved when pregnant women with MDR-TB are treated with effective regimens. Further research is needed to design shorter, more effective, and safer treatment regimens for pregnant women.

EP-12-713 Increasing trend of bacteriologically confirmed TB cases among pediatric TB cases: experience of Ethiopia

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Background and challenges to implementation: Laboratory confirmation is the mainstay of TB diagnosis. To ensure this, there are globally approved diagnosis mechanisms which include microscopy and molecular tests like GeneXpert. Due to challenges related to obtaining samples, there is increased focus to ensure children (younger than 15 years of age) access laboratory services. The National TB Program (NTP) of Ethiopia has included the use of highly sensitive TB diagnostic tools like GeneXpert as a primary testing tool for children.

Intervention or response: The USAID Eliminate TB project supports the NTP technically and financially through comprehensive TB services. The project is involved in the inclusion of child-focused TB programming in the national TB and TB/HIV guidelines and standard operating procedures. There has also been an expansion of laboratory diagnosis tools. Health workers are trained on childhood TB-- specifically on the means of collecting sputum samples for GeneXpert. Support, mentorship, and supportive supervision is provided at the district level. We used the national District Health

Information System to analyze trends in the percentage of bacteriologically confirmed TB cases among children from January 2019 to December 2021.

Results/Impact: Since January 2019, a total of 25,792 children with TB cases were diagnosed and treated at health facilities in the project-supported regions, which is 10.4% of all the TB cases in the regions. Among the 25,792 TB cases in children, 35% of the patients were bacteriologically confirmed TB cases. The percentage of bacteriologically confirmed TB cases increased from 32.8% in 2019 to 35.8% in 2021 annual reporting period.

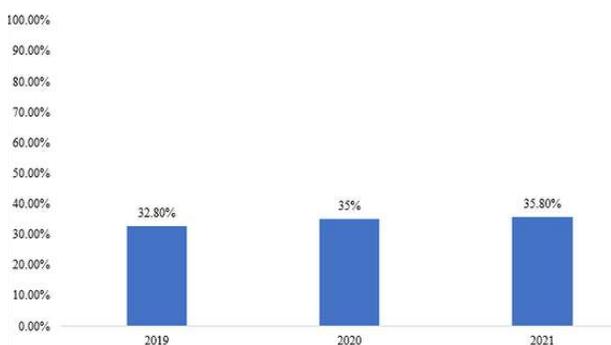


Table. Trend of bacteriologically confirmed TB cases (%) among children, 2019-2021

Conclusions: There was a 2-3% annual increment in the proportion of bacteriologic confirmed TB cases among children using GeneXpert. The use of highly sensitive TB diagnostics using alternative specimen among children needs to be emphasized to further increase the identification of infectious patients and treat them early.

EP-12-714 Spiritual holy water sites: Unrecognized congregate settings for pulmonary TB transmission in Ethiopia

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Background: In Ethiopia, several TB patients have different healthcare-seeking behaviour. They commonly visit spiritual places such as holy water sites (HWSs) and traditional healers before seeking treatment in health facilities. This study aims to assess the prevalence of TB among individuals with symptoms of pulmonary TB (PTB) attending spiritual HWSs in the Amhara region, Ethiopia.

Design/Methods: Between June 2019 and March 2020, a cross-sectional study was conducted at nine selected HWSs. During the study period, among 10,313 holy water attendees (≥ 18 years of age) who were screened, 560 showed PTB symptoms. The sputum samples were collected using leak-proof sterile collection containers. The mycobacterial culture was processed using a solid LJ culture. Descriptive statistical analyses were performed using STATA 15. Statistical significance was declared at $p < 0.05$.

Results: Of 560 PTB symptomatic participants, 122 (21.8%) (95% CI: 18.4-25.2%) were culture-positive cases, resulting in a point prevalence of 1183/100,000 holy water attendees. Males and females had an equal proportion of culture-positive TB. Culture-positive TB was higher among participants aged 18-33 years, with a rate of $28.52\% \pm 2.78\text{SE}$ (95% CI: 23.38-34.28%). Rural residents (aOR=2.65; 95% CI: 1.38-5.10), married participants (aOR=2.43; 95% CI: 1.28-4.63), family size >5 per household (aOR=1.84; 95% CI: 1.04-3.24), sharing living space (aOR=10.57; 95% CI: 3.60-31.13) and drinking cups at HWS (aOR=10.59; 95% CI: 3.60-31.13), and never having an HIV test (aOR=2.69; 95% CI: 1.50-4.84) were factors significantly associated with culture-positive TB (Table 1). A prospective follow-up study on 438 participants who had culture-negative test results revealed that 30 (6.8%) (95% CI: 4.40-9.40%) individuals developed TB post-exposure to HWSs.

Characteristics	Prevalence of culture-positive TB		aOR (95%CI)	p-value	
	Positive (n)	Negative (n)			
Residence	Urban	46	212	ref	0.003
	Rural	76	226	2.65 [1.38-5.10]	
Marital status	Married	85	271	2.43 [1.28-4.63]	0.007
	Single*	37	167	ref	
Household size	1-5	57	237	ref	0.036
	>5	65	201	1.84 [1.04-3.24]	
Sharing a living space at the HWS	Yes	118	320	10.57 [3.60-31.13]	0.00
	No	4	118	ref	
Sharing drinking cups at the HWS	Yes	91	268	10.59 [3.60-31.13]	0.00
	No	31	170	ref	
Do you know your HIV status?	Yes	34	179	ref	0.001
	No	88	259	2.69 [1.50-4.84]	

*single, divorced & widowed; ref, reference; aOR, adjusted odds ratio; CI, confidence interval; HIV, human immunodeficiency virus; HWS, Holy water sites; n, number; TB, tuberculosis.

Table 1: Multivariate logistic regression analysis of potential risk factors for culture-positive TB among symptomatic holy water attendees, Amhara region, Ethiopia, 2019-2020 (n=560).

Conclusions: The prevalence of culture-positive PTB among spiritual HWS attendees was 4.3 fold higher than the general population. To effectively prevent and control TB in the country, the national TB preventive programs should recognize HWSs as potential congregate

sites for TB transmission and implement regular systematic TB screening and health education for individuals at HWSs.

EP-12-715 Genetic diversity and drug resistance patterns of *M.tuberculosis* strains isolated from pulmonary TB symptomatic individuals attending spiritual holy water sites in the Amhara region, Ethiopia

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Background: Investigating *M.tuberculosis* (*Mtb*) genetic diversity in high TB burden countries like Ethiopia is important in understanding disease transmission and dominant strains, as well as strengthening regional TB prevention and care programs. We aimed to investigate the genetic diversity and drug resistance patterns of *Mtb* strains isolated from pulmonary TB (PTB) symptomatic holy water site (HWS) attendees in the Amhara region, Ethiopia.

Design/Methods: Sputum samples were collected from PTB symptomatic individuals (≥ 18 years of age). The mycobacterial culture was processed at the Amhara Public Health Institute, Bahir Dar, using a solid LJ culture. Mycobacterial suspensions were prepared from colonies grown on LJ culture, transferred to 1.5ml PrimeStore Molecular Transport Medium, and transported to South Africa for genotyping. Drug-resistance detection was done using GenoType®MTBDR*plus* v2 and GenoType®MTBDR*sl* v2 assays. *Mtb* isolates were genotyped using the spoligotyping method.

Results: Of 560 PTB symptomatic participants, 122 (21.8%) were culture-positive cases. Spoligotyping identified 116 isolates with interpretable spoligo-profiles comprising 31 different spoligo-patterns. About 101 (87.1%) isolates were grouped into 16 clusters (with a clustering rate of 73.3%). The predominant lineages were CAS1-Delhi (30.2%), T3-ETH (14.7%), T2 (10.3%), T1 (8.6%), CAS1-Kili (6.9%). About 11.2% (13/116) of isolates were “new” (Figure 1).

Most strains (55.2%) are Euro-American, while 42.2% belong to East African Indian lineages. Of 122 isolates tested, INH and RIF resistance was detected in 16.4% and 12.3% of isolates, respectively. MDR-TB was de-

tected in 12.3% (15/122) of isolates, and five were pre-extensively drug-resistant (pre-XDR). SIT149 (T3-ETH) and SIT21 (CAS1-Kili) genotypes were associated with drug resistance.

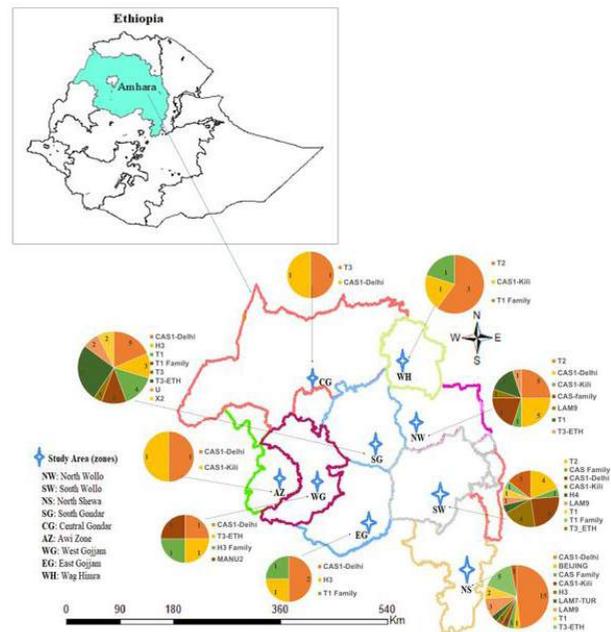


Figure 1. Geographical location of the study area, as well as the distribution of *M. tuberculosis* lineages/sublineages in each study zone.

Conclusions: Diverse *Mtb* genotypes were found, with the most prevalent lineages being CAS1-Delhi and T3-ETH. The high strain clustering indicates recent TB transmission among HWS attendees. This underlines the significance of strengthening TB prevention measures, enhancing case detection, and TB screening in the HWS to halt the transmission.

EP-12-716 Alcohol exposure group classification using self-reported and biomarker measures in a South African cohort of persons with tuberculosis: a latent class analysis

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Background: Alcohol's impact on tuberculosis (TB) treatment response is unknown. Self-reported alcohol measures are vulnerable to underreporting and biomarkers have limitations. We group individuals into alcohol exposure classes from a combination of self-reported acute consumption and chronic use, and an alcohol biomarker.

Design/Methods: We analyzed data from 278 participants initiating TB treatment in South Africa. The Alcohol use disorders identification test (AUDIT) and Timeline follow-back (TLFB) were administered to capture past-year alcohol use behaviours and past two-week consumption, respectively. The biomarker, Phosphatidylethanol (PEth), was utilized to avoid underreporting of self-reported alcohol use. We conducted a latent class analysis to identify subgroups of alcohol use using three ordinal variables: AUDIT (low risk/abstinence, harmful to hazardous, dependence); recent alcohol consumption from TLFB categorized as heavy alcohol use (defined as 3+/4+ standard drinks for women/men consumed in one sitting or 14+/28+ drinks for women/men consumed in two weeks), non-heavy alcohol use, or abstinence; and PEth (<50, 50-200, >200; ng/mL). Class membership probabilities were estimated and the frequency of predicted class assignments was calculated. The association between participant demographics, TB severity, alcohol measures and class assignment was examined.

Results: Three classes were constructed to describe the latent variable of alcohol exposure. 145 (52.2%) participants were classified as low, 72 (40.4%) as moderate, and 61 (21.9%) as high. Participants with high exposure

were older (42(36.49), p-value=0.013), less likely to use smoked substances (26(42.6%), p-value=0.005), and more likely to use tobacco (53(86.9%), p-value<0.001). 16 (26.3%) participants were classified as high exposure and 20 (27.8%) as moderate exposure that reported no recent alcohol use. 16 (5.8%) participants with PEth <50 ng/mL were classified as high or moderate exposure.

	Total (N=278)	Low (N=145)	Moderate (N=72)	High (N=61)	p-value
Age (years)	38 (27.49)	33 (25.48)	41 (31.49)	42 (36.49)	0.013
Male sex	167 (60.1%)	81 (55.9%)	44 (61.1%)	42 (68.9%)	0.216
Living with HIV	79 (28.5%)	45 (31.2%)	19 (26.4%)	15 (24.6%)	0.563
Tobacco Use	190 (68.3%)	78 (53.8%)	59 (81.9%)	53 (86.9%)	<0.001
Smoked Drug Use	153 (55.0%)	93 (64.1%)	34 (47.2%)	26 (42.6%)	0.005
History of TB	104 (37.4%)	52 (35.9%)	29 (40.3%)	23 (37.7%)	0.817
Sputum culture TTP	7 (5.11)	7 (5.10)	8 (6.11)	9 (5.13)	0.276
Sputum smear positivity	221 (79.5%)	118 (81.4%)	52 (72.2%)	51 (83.6%)	0.193
Lung cavitation	86 (35.4%)	38 (30.9%)	23 (41.8%)	25 (38.5%)	0.214

Conclusions: Self-reported measures combined with a biomarker captured different alcohol exposure levels. Longer-term use not captured by the biomarker, potentially due to reduced consumption at peak TB disease, was classified more appropriately.

EP-12-717 Interventions to address the global underreporting of pediatric and adolescent tuberculosis: a systematic review

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Background: The WHO estimates that at least a third of pediatric and adolescent tuberculosis cases go untreated or incompletely treated each year. Many cases are detected but lost to follow-up due to underreporting to national or private surveillance systems.

Design/Methods: We conducted a systematic literature review to better understand the global reporting gap of pediatric tuberculosis as well as current interventions. Following PRISMA guidelines, the review included articles published in English within the past 30 years. Studies were included if they discussed underreporting of tuberculosis in pediatric and adolescent patients. Studies were excluded if they did not include these populations or focused on challenges with diagnosis or loss to follow-up rather than underreporting. In May and June 2021, we searched PubMed and Ovid databases along with reference lists of included works. Multiple reviewers and further assessments of heterogeneity and bias will be implemented in the next steps of the project.

Results: Of 458 records identified, 420 were screened and 19 met inclusion criteria in the preliminary search. Of included studies, 14 described the gap in reporting of pediatric tuberculosis and 5 described interventions to close this gap. The estimated gap in reporting ranged from 16% to 98% and was described in 23 countries. Larger gaps were described in rural areas, in areas with higher disease burden, in patients with disseminated disease, and in those under age 5 years. Effective interventions are limited and include strengthening linkage systems between facilities, increasing communication following initial diagnosis, utilizing electronic systems for ongoing monitoring, improving death registration, and using implementation science for quality improvement.

#	Paper	Year	Country/Countries	Age Range (yrs)	Reported Gap
1	Berman S et al.	1992	South Africa	0-14	44%
2	du Preez et al.	2011	South Africa	0-13	38%
3	Lestari T et al.	2011	Indonesia	0-14	98%
4	Coghlan R et al.	2012	Indonesia Nigeria Pakistan	0-14*	Varied
5	Ade S et al.	2013	Benin	0-14	16%
6	Rose PC et al.	2013	South Africa	0-14	36%
7	Dodd PJ et al.	2014	22 high burden countries	0-15	65%
8	Tollefson D et al.	2016	Kenya	0-55+ (0-24)	20.8%
9	Fatima R et al.	2019	Pakistan	0-14	78%
10	Li T et al.	2019	China	0-65+ (0-15)	19.3%
11	Siddaiiah A et al.	2019	India	1-65+ (0-14, 15-24)	76.8%
12	Nzombe P et al.	2020	Zimbabwe	0-14	37%
13	Yaqoob A et al.	2021	Pakistan	0-14	97%
14	Arscott-Mills T et al.	2021	Botswana	0-15	35%
#	Paper	Year	Country/Countries	Age Range (yrs)	Reported Intervention
15	Edginton ME et al.	2006	South Africa	0-55+ (0-14, 15-34)	Establishment of TB care center with registration in hospital, death registration, education and referral
16	Safdar N et al.	2010	Pakistan	0-14	Implementation of standard policy guidelines for childhood TB
17	Joshi B et al.	2015	Nepal	0-14	Intensified early TB case detection with direct registration
18	Wobudaya E et al.	2017	Uganda	0-14	Appointment of national pediatric TB focal person, mentorship in childhood TB care, recording and reporting
19	du Preez K et al.	2020	South Africa	0-14	Dedicated TB referral service within pediatric ward

Yrs, years; *Indicated pediatric population but did not specify age

Background and challenges to implementation: The WHO estimates that at least a third of pediatric and adolescent tuberculosis cases go untreated or incompletely treated each year. Many cases are detected but lost to follow-up due to underreporting to national or private surveillance systems.

Conclusions: Underreporting of pediatric and adolescent tuberculosis is a significant global problem. Few evidence-based effective strategies exist to close this gap. Future research should assess the ability of creative, pragmatic solutions to mitigate this with an emphasis on pediatric populations in high-TB burden countries.

EP-12-718 Where are the missing people affected by tuberculosis? Patient-pathway and cascades of care analyses to optimize tuberculosis care in Cambodia

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Background: Cambodia has achieved great success in TB control in the past decade. Nevertheless, progress toward ending TB was impeded by persons missed by the health systems. We aimed to corroborate the care-seeking behaviors of people with TB and TB services availability and estimate the number of people completing each step of the TB disease care cascade.

Design/Methods: We conducted the patient pathway analysis and the care cascade for TB disease, mainly using data from 2019. Data were drawn from the national TB prevalence survey 2011, surveillance data, the global TB database, and published studies. We randomly selected TB survivors in the 2019 cohort to assess recurrence-free survival 1-year after post-treatment to conclude the cascade.

Results: Nationally, 54% of those who exhibited TB symptoms sought initial care in the private healthcare sector, followed by the public (42%) and non-medical sectors (4%). Most public hospitals (85%) and a small fraction (9%) of the public health centers are equipped with TB diagnostics.

Overall, 7% of people with presumptive TB accessed a facility with TB diagnostic services at the first point of care-seeking. TB treatment was available at all health centers in Cambodia. The private and non-medical sectors do not provide TB diagnostic and treatment services.

Overall, 63% of the estimated TB cases were notified by the public sector in 2019, and 96% achieved treatment success (*Figure 1a*). Of the 47000 estimated TB cases (all forms) in 2019, we estimated that 84% accessed public

health facilities. Approximately 80% were diagnosed with TB, of which 95% were registered in treatment, and 94% of the survivors remained recurrence-free 1-year post-treatment (Figure 1b).

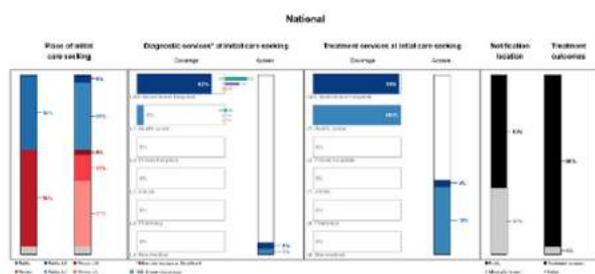
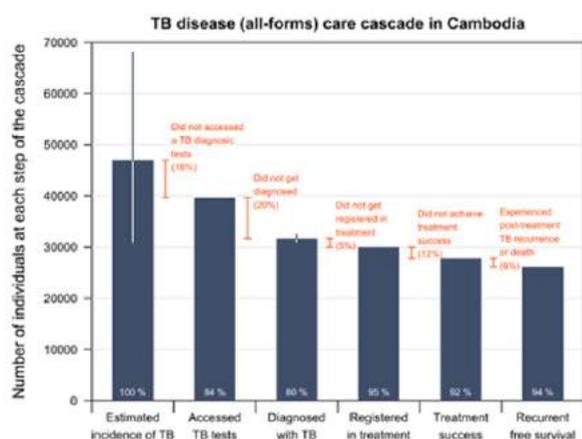


Figure 1a. Patient pathway analysis.



The treatment success rate was 92% based on the number of people notified and registered in treatment as the denominator. The rate would be 96% (as per PPA) when we considered the people who were evaluated in the same year as the denominator.

Figure 1b. TB disease care cascade.

Conclusions: We illustrated gaps in care-seeking, coverage, and access to TB services. Efforts should be concerted in formulating policies and programs to address barriers and improve access and retention throughout the care cascade.

EP-12-719 Access to TB care services among vulnerable populations in Kampala, Mukono and Wakiso districts in Uganda; a descriptive study

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Background and challenges to implementation: Marginalized and vulnerable populations- prisoners, people living with HIV (PLHIV), refugees, adolescents/youth and people with substance abuse are at increased risk of tuberculosis (TB) infection and disease. We aimed to identify the gaps in access to TB care services among vulnerable and marginalized populations in three districts of Uganda.

Intervention or response: We abstracted data and conducted descriptive analysis on TB screening and treatment cascades from the district health information system II (DHIS II) for the period October 2020 to September 2021. We constructed the TB screening cascade for all patients disaggregated by age and sex. We compared the proportions of patients screened, those with presumptive TB and presumptive TB patients diagnosed with TB. In addition, we compared TB treatment outcomes of vulnerable populations to those in the general population.

Results/Impact: The proportion of patients screened for TB in the outpatient department (OPD) was fairly constant among all age-groups (33%), while the proportion diagnosed with TB was markedly lower among adolescents aged 10-19 years at 6% compared to 12% for the general population. A focused analysis among other vulnerable populations showed that only 20% of all registered refugees accessed the public health system. However, among those that sought care, the proportion of patients diagnosed with TB was higher than other groups (17.5% compared to the general population -14%). Treatment success amongst PLHIV, prisoners and refugees were 80%, 82% and 85% respectively which were below the 90% End TB target. Suboptimal treatment success rates among vulnerable groups were driven by high death rates among PLHIV and refugees (13% and 12% respectively) and loss to follow up (LTFU) rates among prisoners (6%).

Conclusions: There is need to design interventions that enhance TB case identification and retention in care for vulnerable groups.

EP-12-720 TB case finding and treatment of missing cases among women in selected districts of Sindh through improved access of rural women to TB care services

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Background and challenges to implementation: The low case notification rate in women remains the main challenge to ending TB in Pakistan. In the rural districts of Sindh females' contribution is less than 45% of the total TB case notification.

Due to the dearth of female health care providers (FHCP) offering TB care both in public and private sectors and cultural barriers, in rural Sindh women face added barriers to access TB care, diagnostic, and treatment services and often remain unnotified.

Intervention or response: The project was implemented from Feb 2020 to Jun 2021 through the TB REACH grant in four districts of Sindh province. We trained 96 Female FHCPs, (who were previously managing only mother and child health) and their paramedics' National TB Control program guidelines.

Women and children who visited clinics of these FHCPs were verbally screened for TB. Sputum specimens of TB presumptive were collected and tested on WHO Diagnostic Tools (WDT) including gene-Xpert in designated labs. Diagnosed TB patients were registered for TB treatment at project FHCP clinics. Chestcamps were organized in the community at hot spots. The project organized advocacy sessions in the community. These sessions empowered women in the community to recognize and refer to TB presumptive.

Results/Impact: A total of 268640 (242237 women, 26027 Men) were screened, Total of 15505 (women 14259, Men 1247) were identified as presumptive. A total of 1177 TB cases were diagnosed and registered for ATT. The project contributed 17% of the overall notification and 32% to women's notification in these districts.

Conclusions: The engagement of FHCPs made it more comfortable for women to seek TB care. Male treatment supporters from the family improve follow-ups and complete treatment. The training of FHCPs and the awareness created in the community are long-lasting and will continue to reap benefits by finding the missing women TB patients even after the project ends.

EP-13 TB and COVID

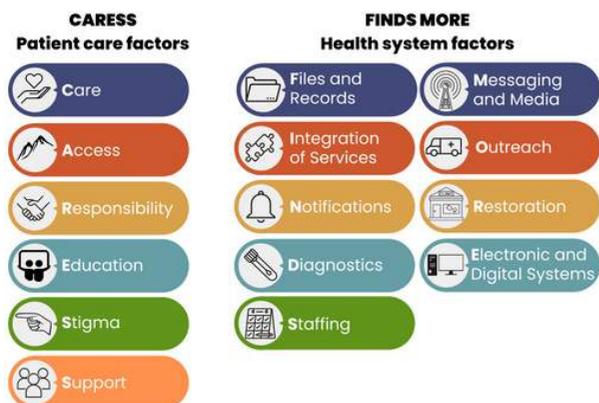
EP-13-721 'It's like they didn't come at all' health worker perspectives on TB care during the COVID-19 pandemic in the Western Cape, South Africa

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Background: The COVID-19 pandemic has had a devastating impact on TB care. Between 2019 and 2020 global TB mortality rose and TB diagnosis notifications fell by almost one fifth. South Africa reported over 25% fewer TB notifications. Even prior to the COVID-19 pandemic, care cascade analyses from South Africa demonstrate a further 25% of people with TB are lost between evaluation and TB treatment initiation. We conducted a qualitative study to explore explanatory factors for widening gaps in the TB care cascade during 2020-2021 and inform interventions for TB service restoration from the perspectives of health workers (HWs) in George sub-district, Western Cape, South Africa.

Design/Methods: Using purposive sampling we conducted thirteen in-depth interviews with community HWs, TB nurses, primary care and emergency physicians, TB specialists, communicable disease coordinators and clinical managers. Open coding of participant responses and inductive thematic analysis identified two sets of emergent intervention themes, with selective coding to identify relevant citations.

Results: Analysis of HW suggestions regarding interventions yielded two thematic frameworks for the restoration of TB care services: CARESS (patient-level factors) and FINDS MORE (health-system factors). Within CARESS, while access issues related to COVID-19 isolation, migration and economic factors were commonly identified, HWs emphasised the need for increased patient support, along with education and stigma reduction. Within FINDS MORE, HWs highlighted fragmentation of care due to staff redeployment, the lack of electronic records to facilitate care linkage, and the need for community outreach TB services, including access to rapid diagnostics facilitating same-day treatment initiation.



Conclusions: Efforts to mitigate the impact of the COVID-19 pandemic on TB care can benefit from leveraging innovations used to combat COVID-19 such as electronic data notification systems and integrated disease testing. Yet, ultimately improving TB outcomes requires a fundamental reimagining of TB services with a focus on delivering high-quality person-centred care and support.

EP-13-722 The drug-susceptible and drug-resistant TB care cascades prior to and during the COVID-19 pandemic in Lima, Peru

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Background: The COVID-19 pandemic has disrupted TB programs globally, with an estimated 1.4 million fewer people accessing TB care in 2020 vs. 2019. Mitigating the impact of COVID-19 on TB care is urgent in Peru, which has a high burden of drug-resistant (DR) TB and the highest COVID-19 death rate per capita worldwide. We are therefore constructing drug-susceptible (DS) and DR-TB care cascades (representations of the proportion of patients reaching milestones in TB care) prior to and during the COVID-19 pandemic in Peru and identifying predictors of treatment completion.

Design/Methods: We collected data from patient registries in TB clinics in San Juan de Lurigancho (S JL), Peru's most populous district. Predictors of cascade completion will be identified using logistic regression,

adjusting for relevant covariates, with the primary predictor of interest being TB treatment pre- vs. during the COVID-19 pandemic (before/after 16.03.2020).

Results: We collected data from n=1,519 patient records (n=1,071 DS-TB, n=448 DR-TB) from 25 clinics in S JL (mean age: 32.4 years (SD=16.2), n=937 (61.7%) male, n=72 (4.7%) with HIV co-infection, n=89 (5.9%) with diabetes).

Preliminary data show that, excluding n=50 patients transferred to other centres, of the remaining n=1,469, n=1,092 have completed treatment, n=103 were lost to follow-up/hospitalized/incarcerated, n= 35 died, and n=239 remain on treatment.

Excluding transfers, for patients receiving TB treatment prior to the COVID-19 pandemic, 93.3% (95% CI:90.7-95.3%) of DS-TB patients and 70.5% (95% CI:61.9-78.2%) of DR-TB patients reached the end of the care cascade. For those receiving some or all of their treatment during COVID-19, 76.5% (95% CI:72.6-80.0%) of DS-TB patients and 38.7% (95% CI:33.2-44.5%) of DR-TB patients have completed the cascade (17.3% and 48.3% still on treatment, respectively). (Full cascade and predictors of completion to be presented at the conference).

Conclusions: Understanding the impacts of COVID-19 on TB care through constructing care cascades is critical to getting back on track towards TB elimination.

EP-13-723 Sustaining gains in TB awareness and infection prevention in a post-pandemic world: the KNCV Nigeria experience

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Background and challenges to implementation: In the campaign to end TB, awareness is a vital tool, as it facilitates increase in knowledge about the disease and strategies to prevent transmission. The advent of Covid-19 disease in 2020 was a crossroad moment for the TB program. Being symptomatically similar to COVID-19, the tuberculosis programme suffered a setback due to stigma and knowledge gaps.

Intervention or response: The USAID TB LON 1 and 2 regions project is implemented in 14 states in Nigeria, including Akwa Ibom, Crossriver, Delta, Rivers, Anambra, Imo, Kaduna, Kano, Katsina, Bauchi, Nasarawa, Benue, Taraba, and Plateau by KNCV Nigeria. To overcome the challenge imposed by Covid -19 to TB programming, intensified awareness campaigns and infection prevention control measures were implemented in a

multi-facet approach. These approaches include security and health information support to frontline workers on covid-19 case updates, provision of information, education and communication materials in local languages to enlighten people on TB – Covid -19 distinctions, capacity building of frontline workers to close the knowledge-gap, PPE supply to frontline workers and intensified community active TB case finding.

This strategy was implemented throughout the Covid-19 pandemic and results were tracked in the weekly TB Case finding reports.

Results/Impact: A review of KNCV Nigeria to TB case finding in supported states during the pandemic showed that in Q2 2020, the LON project contributed 1,866 TB cases (14% of TB case notification) in supported states and through sustained strategies in Q2 2021 contributed 11,368 TB Cases (47% of TB case notification) in supported states, indicating a 609% increase.

Conclusions: The strategy employed in increasing TB awareness and infection control was successful in increasing case detection and notification and if sustained could be instrumental to reaching end TB goals.

EP-13-724 Internally displaced people and COVID-19 patients are emerging vulnerable populations for TB in Ethiopia

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Background and challenges to implementation: Conflict and COVID-19 posed significant public health threats in Ethiopia. A decrease in TB incidence during the conflict and COVID-19 pandemic is likely the result of impacts to the health system and delayed diagnosis. Evidence shows that patients with COVID-19 and people displaced due to conflict are susceptible to developing TB. This was one of the reasons why a nationwide campaign to identify missed TB cases in Ethiopia targeted internally displaced people (IDP) and COVID-19 patients for TB screening.

Intervention or response: The USAID Eliminate TB Project supported the national campaign to identify missed TB cases. The campaign targeted key affected populations (KAP) for TB. The project provided an orientation to TB focal persons and clinicians on TB screening with KAP, recording, and reporting. They conducted the screening with selected KAP during January-March

2022. The proportion of TB cases among screened KAP and the TB case notification rate (CNR) per 100,000 screened KAP was computed and compared with the national estimate.

Results/Impact: Fifteen groups of KAP were identified and screened. About 58% of the estimated KAP (470,825 of 809,596) were screened, with the highest percent screened of missionary of charity residents (100%), urban slum residents (99.3%), household contacts (94.4%), and HIV patients (98%); and the lowest percent screened of refugees (21.3%), diabetic patients (11.1%), and malnourished patients (36.1%). The proportion of identified presumptive TB cases was higher among IDPs (34.1%), COVID-19 patients (23%), missionary residents (19.1%), and malnourished patients (16.1%). The point prevalence of TB was detected among missionary of charity residents (3.3%), IDPs (3.3%), and COVID-19 patients (2%).

Conclusions: The CNR among missionary residents, IDPs, and COVID-19 patients is at least fourteen times greater than the national prevalence of 132/100k. Routine screening for TB should be established among suspected or confirmed cases of COVID-19, missionary residents, and IDPs in Ethiopia.

EP-13-725 Mental health among COVID-19 healthcare workers

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Background: Healthcare workers involved in the COVID-19 response are at increased risk of physical and psychological stress. They experience extreme working conditions and traumatizing events while caring for COVID-19 patients. We conducted a qualitative study to gain in-depth understanding of the factors negatively influencing the mental well-being of COVID-19 HCWs in The Netherlands, Ireland, Nigeria, Pakistan, and Philippines. These insights can inform the development and implementation of effective tools to improve the mental wellbeing of COVID-19 HCWs and therewith the quality of care, which is so essential in the response to the COVID-19 pandemic.

Design/Methods: We conducted a qualitative study for which we purposively recruited 53 HCWs for online semi-structured in-depth interviews (13 in Ireland; 15 in Nigeria; 6 in The Netherlands; 6 in Pakistan; and 13 in The Philippines). We transcribed all interviews verbatim transcribing interviews and used a thematic approach for data analysis.

Results: Almost all HCWs reported comprised mental well-being as a result of their work caring for COVID-19 patients. HCWs reported feelings of anxiety, loneliness, depression, exhaustion, fear, guilt, and stress.

These feelings and consequently their mental wellbeing were rooted in high workload, the feelings of powerlessness in the care of COVID-19 patients, the experience of sudden death of COVID-19 patients, and the feeling of being unappreciated and avoided by hospital management and sometimes government and society.

Conclusions: Improved support mechanisms and effective interventions improving the mental wellbeing of COVID-19 HCWs are needed to ensure continuation of good quality care.

EP-13-726 Inequalities in the impact of COVID-19-associated disruptions on tuberculosis diagnosis by age and sex in 49 high burden countries

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Background: Globally, and in most countries, men and older people have a disproportionately high burden of TB, and case detection rates are unacceptably low, especially for children. Disruptions in TB services due to the COVID-19 pandemic may have exacerbated these inequalities.

Design/Methods: We modelled trends in age- and sex-disaggregated notifications for all forms of new and relapse TB cases reported to the World Health Organization (WHO) for 49 high TB, TB/HIV and MDR/RR-TB burden countries from 2016 to 2019, estimating the number of people with TB likely to have missed or delayed their diagnosis in 2020 by comparing trend predictions and actual notifications.

We estimated the odds that disruptions had affected children (aged <15 years) or older adults (aged ≥55 years) more than younger adults (aged 15-55 years), and women more than men (both aged ≥15 years).

Results: An estimated 169,000 (32.1%, 95% confidence interval, CI:-20,800-372,900) children, 873,400 younger adults (19.9%, CI:-123,200-1,825,300) and 460,100 older adults (26.6%, CI:-106,200-1,001,00) were likely to have had their diagnosis missed or delayed as a result of the pandemic. This included 517,300 women (21.9%, CI:-101,700-1,117,300) and 823,800 men (21.4%, CI:-126,700-1,747,000).

The odds of having diagnosis missed or delayed were higher for children than younger adults globally (odds ratio 1.49 [CI 1.32-1.69]) and in the WHO African Region. The odds were also higher for older adults than younger adults globally (OR 1.54 [1.35-1.75]) and in the South-East Asia and Western Pacific Regions. The odds of missed or delayed diagnosis were higher for women than men in the African Region, while they were higher for men than women in the Eastern Mediterranean Region. Heterogeneity was high in most analyses.

Conclusions: Some populations with TB, particularly children and older adults, have been disproportionately affected by the COVID-19 pandemic, and should be prioritised for catch-up campaigns. However, these disruptions are highly setting-specific.

EP-13-727 Sequential infection between Mycobacterium tuberculosis and severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in East Java, Indonesia

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Background and challenges to implementation: From January 2020 to April 2022, in East Java Province, 105,349 newly diagnosed TB and 687,121 COVID-19 notified patients. TB notification rate was sharply reduce during the peak of COVID-19 outbreak.

This study aims to compare the risk of being notified as COVID-19 infection among TB patients and the risk of being notifying TB infection among COVID-19 patients.

Intervention or response: Main data sources are registries for COVID-19 and TB developed by Ministry of Health, Indonesia. District age group-specific populations were obtained from National Statistics Office. Identification variables of patients registered in these two data sets were encrypted using the same encryption algorithm. Age-standardized morbidity (and mortality) ratios (SMR) of getting COVID-19 among newly diagnosed TB patients and those of getting TB among COVID-19 patients were computed.

Results/Impact: Among newly diagnosed 105,349 TB patients, 2,413 were subsequently infected with COVID-19 during the study period against 2,043 expected. SMR (95%CI) was 118.1% (113.5%, 122.9%). Among 687,121 newly diagnosed COVID-19 infected patients, 960 were subsequently diagnosed as having active TB during the study period against 2,043 expected. The SMR was 46.9% (44.1%, 50.0%).

In a similar way, 218 of the first group subsequently died from COVID-19. Standardized Mortality Ratio was 215.4% (188.6, 246.0). 62 patients in the second group died; SMR equals 70.3% (54.5, 89.7).

Conclusions: The chances of a COVID-19 patient subsequently notified as a TB case or dying from TB was significantly decreased compared to the general population. TB patient was, however, more likely to be subsequently notified as a COVID-19 and died from COVID-19.

The opposite direction of these changes in risk may be explained by the difference of completeness between TB and COVID-19 notification systems during the pandemic period.

EP-13-728 A quarterly trend analysis of TB case finding in Liberia: before and after COVID-19 pandemic

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Background and challenges to implementation: Globally, there has been documented gap in TB case finding especially in 2020 due to COVID-19 pandemic. We analyzed Liberia's TB case notification trend from its National Tuberculosis Program (NTP) one year before and after the pandemic to identify existing pattern and lessons learnt.

Intervention or response: Secondary data from the NTP's quarterly report on the DHIS from Q1 of 2019 to Q4 of 2021 were retrieved. These include total cases notified every quarter disaggregated by sex and age-group for 2019, 2020 and 2021. A simple trend analysis was done to note dips and spikes. Results of the analysis was followed by Key Opinion Leaders' consultation and review of narrative reports from the NTP to better understand possible causes of any fluctuation.

Results/Impact: Over the three-year period a total of 22,925 TB cases were notified in Liberia; (2019 = 8,391; 2020 = 7,180 and 2021 = 7,354). These include 9,631 (58%) males and 3,702 (16%) 14 years and below.

There was decline in case finding from Q1 '19 till Q1 '20 where the case notification improved. Of special interest is the all-time dip (first arrow) in Q2 '20 which was largely attributed to the effect of COVID-19 pandemic. Childhood TB suffered the largest decrease. The

proceeding early recovery (Q4 '20) shows the resilience of the system after recovery from other historical outbreaks in recent time like Ebola. The program's efforts to sustain the gains experienced a decline notably at Q3 and Q4; attributed majorly to non-verification of data as at the time of this study, intrinsic challenges with program funding mechanism and seasonal commodity stock outs.



Conclusions: Lessons learnt from combating Ebola outbreak was transferred to aid recovery from COVID-19. Non-verification of data, disruption in funding structure and gap in supply chain amongst other programmatic issues negatively impacts TB case finding.

EP-13-729 COVID-19 lockdowns resulting in household income decline for people with TB in Ho Chi Minh City: interrupted time series analysis of household income changes

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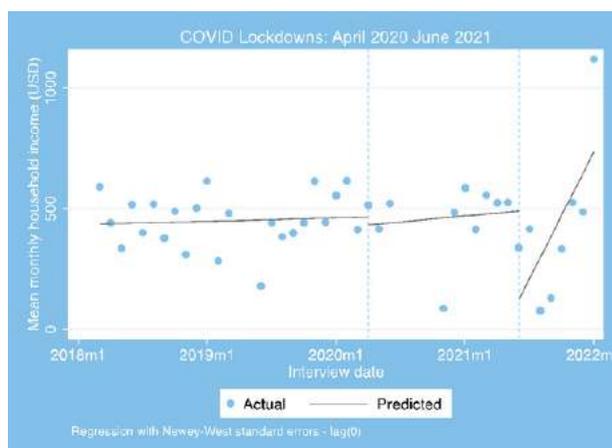
Background: There is little understanding of the economic impact of the COVID-19 lockdowns on TB-affected households. Vietnam imposed one of the world's most stringent 'Zero COVID-19' policies, including strict lockdowns followed by periods of social mobility. Ho Chi Minh City (HCMC) was the epicenter of the pandemic in the country at two timepoints, resulting in lockdown periods. The first lockdown was instituted for approximately two weeks upon the arrival of COVID-19 in April 2020 and the second came with the B.1.617.2 Delta variant in June 2021. This lockdown was more stringent and lasted four months.

Design/Methods: A quasi-experiment design using a prospective longitudinal cohort consisting of 385 TB-affected households assessed differences in household in-

comes and coping strategies of the COVID-19 lockdown periods. People with TB >18 years, living in HCMC were included for analysis. People with MDR-TB and those using private health care facilities were excluded. An interrupted time series regression was conducted with patient cost data from 2018-2022.

Results: The lockdown in April 2020 led to an insignificant decrease in household income (-31 USD, $p=0.690$), the lockdown in June 2021 led to a significant decrease (-368 USD; $p=0.037$). After both lockdowns, an insignificant recovery in household income occurred. No statistically significant increase in the deployment of coping strategies was seen.

There was, however, a shift in the mechanisms used: Money was borrowed from friends ($p=0.00$) and family ($p=0.02$) less frequently and gold was sold ($p=0.00$) more frequently following the lockdowns.



Conclusions: The strict COVID-19 lockdowns have further impoverished the households of people with TB, a population already at high risk for catastrophic costs. More research is needed to assess the long-term impact of lockdowns on catastrophic cost and health outcomes of people with TB. Expansion of social protection should be considered to protect vulnerable households from future financial shocks.

EP-13-730 The long term effect of BCG-vaccination on the risk of a COVID-19 infection and the severity of symptoms. A prospective cohort study

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Background: At the start of the coronavirus (COVID-19) outbreak in 2020, it was suggested that the vaccine against tuberculosis, the BCG vaccine, might provide protection against the SARS-CoV-2 virus.

The aim of this study is to assess whether a BCG vaccination, administered prior to the pandemic, has an effect on the risk of contracting COVID-19. As secondary

outcome the severity, type and duration of symptoms in confirmed COVID-19 cases was examined. This can provide information about the long-term effects of the vaccine against COVID-19.

In addition, it may provide new insights in the side effects of BCG-vaccination and can play a role in the use of BCG-vaccination as a protective agent during future pandemics.

Design/Methods: A prospective cohort study was performed by the municipality health service of the Hague, the Netherlands. The BCG-vaccination status of 676 COVID-19 patients and 229 contacts was evaluated using online questionnaires. Contacts of a COVID-19 index (including 'household contacts' and 'close contacts') were monitored for signs of transmission for a duration of 14 days after exposure.

In a second questionnaire, participants with a confirmed COVID-19 infection were assessed on severity of illness, duration and type of symptoms.

Results: The first questionnaire included 947 respondents. The risk of contracting COVID-19 after exposure did not differ between individuals with BCG vaccination and those without (OR 1.5 95% CI 0.7-3.1). Among household contacts the risk of transmission was 3.7 times lower for BCG vaccinated respondents compared to those without vaccination.

However, this difference was not significant (OR 3.7, CI 95% 0.95-14.78 $p=0.06$). Among the 303 COVID-19 patients who completed the second questionnaire, no difference was found in type or duration of symptoms between participants with BCG vaccination and those without.

Conclusions: No clinically relevant long-term effects of the BCG-vaccination were found on the risk of COVID-19 infection or the severity of symptoms.

EP-14 Epidemiology of TB and DR-TB

EP-14-731 Subclinical tuberculosis: Infectious or not?

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Background: Subclinical tuberculosis is a disease state caused by viable *Mtb* detected using radiology or microbiology tools but without typical symptoms. Studies have suggested that subclinical tuberculosis could contribute to *Mtb* transmission, however, the infectiousness of subclinical tuberculosis is still unknown.

Design/Methods: We analysed the data from the 2007 national tuberculosis survey in Vietnam, in which children living with eligible adults underwent TST to examine if they were infected with *Mtb*. We used a TST positive threshold of 15 millimeters to optimize specificity, thus reducing bias in the analyses.

We categorized households into three types: type A (no prevalent tuberculosis case found in the household), type B (having a clinical tuberculosis case), and type C (having a subclinical tuberculosis case).

Multivariable logistic regression adjusting for differences in tuberculosis treatment history and smear status of the household case, and household socioeconomic status was done to compare the odds of being TST positive among children living in the three household types.

Results: There were 21,487 children included in the analysis. Among them, 189 lived with at least one prevalent tuberculosis case, 88 of which lived with a subclinical tuberculosis case. 1,556 children were TST positive: 1,528 (7.2%) in household type A, 20 (19.8%) in household type B, and 8 (9.1%) in household type C.

The odds of being TST positive among children living in household type C was not significantly different from household type A (adjusted OR= 1.5, 95% CI: 0.7-3.3). For household type B compared to A the adjusted OR was 3.6 (95% CI 2.1-6.1).

Conclusions: We found no evidence that *Mtb* transmission is higher in households with a subclinical tuberculosis case compared to background transmission. Further studies are needed with a larger sample size and prospective follow-up of households with subclinical tuberculosis patients to confirm the infectiousness of subclinical tuberculosis in community settings.

EP-14-732 Quantifying incidence and pathways across TB disease states following *Mtb* infection

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Background: As the conceptualisation of tuberculosis (TB) shifts from a binary division between *Mycobacterium tuberculosis* (*Mtb*) infection and TB disease towards a spectrum of presentation, axioms about disease progression following *Mtb* infection must be revisited. We used historical data and mathematical modelling to estimate incidence across different TB disease states and to quantify pathways following *Mtb* infection.

Design/Methods: We developed a deterministic modelling framework of *Mtb* infection and minimal (pathological damage but not infectious), subclinical (pathological damage and infectious) and clinical (infectious and symptomatic) TB disease.

We used a Bayesian approach to calibrate the model to data from historical cohorts that followed tuberculin-negative individuals to tuberculin conversion and subsequent TB disease, as well as data on progression and regression between disease states, disease state prevalence ratios, and disease duration. We assumed uninformed priors for all transition rates (U(0,3)) except mortality (N(0.39,0.03)). We used posterior parameters to estimate incidence and pathways following infection for a cohort of infected individuals.

Results: We found data on progression following *Mtb* infection cannot be explained without allowing heterogeneous pathways to disease (see Figure for structure and posterior parameter values).

Our findings indicate 7.9% (95% credible interval, CrI, 6.2-9.7), 3.8% (95% CrI 2.7-4.9), and 1.0% (95% CrI 0.5-1.7) of individuals infected with *Mtb* will develop incident minimal, subclinical, and clinical disease, respectively, within 2 years, and 8.8% (95% CrI 7.1-10.8), 6.8% (95% CrI 5.3-8.3), and 3.1% (95% CrI 2.1-4.2), respectively, within 10 years.

We estimate 90.9% (95% CrI 89.2-92.8) of individuals infected with *Mtb* self-clear within 2 years and 96.9% (95% CrI 95.8-98.1) within 10 years, in the absence of treatment.

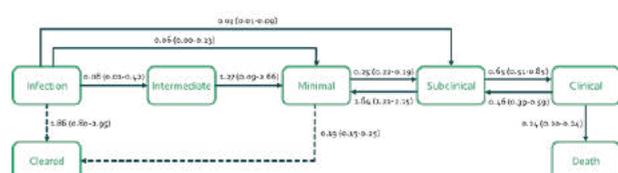


Figure.

Conclusions: Our findings show diverse pathways with different trends in incidence following *Mtb* infection across disease states, building evidence for more effective prevention and treatment efforts within this novel paradigm of TB.

EP-14-733 Molecular epidemiology and drug resistance pattern of *Mycobacterium tuberculosis* isolates from Amhara, Gambella and Benishangul-Gumuz regions of Ethiopia

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Background: Globally, emergence of drug-resistant tuberculosis has been a major obstacle to control the disease, especially in developing countries including Ethiopia. We investigated genetic diversity and drug resistance pattern of *Mycobacterium tuberculosis* circulating in Amhara, Gambella and Benshangul-Gumuz regions.

Design/Methods: A cross-sectional study was conducted using 128 *Mycobacterium tuberculosis Complex* (MTBC) isolates that were obtained from presumptive TB/MDR-TB patients. A total of 127 isolates were recovered successfully and were used to investigate drug resistance patterns with the indirect proportion method using the MGIT 960 system and the genotypic method at the Ethiopian Public Health Institute. Further, identification of mycobacterial strain types and mycobacterial lineages were done using spoligotyping. Data were managed using the Epi-info, SPSS version 25, SITVIT2, MIRU-VNTRplus and TBInsight databases.

Results: Of 127 recovered mycobacterial isolates, 100 (78.7%) were sensitive to four first-line anti-TB drugs, but 27 (21.3%) were resistant to at least one anti-TB drug, 20 (15.7%) were poly-resistant, 17(13.4%) were multi-drug resistant and 2 (10.5%) were Pre-XDR.

Highest gene mutations associated with INH and RIF resistance were observed in *katG MUT1* gene (S315T1) [20 (76.9%)] and *rpoB* gene (S531L) [10 (52.6%)], respectively. Furthermore, two pre-XDR cases showed mutations in *gyrA* gene.

Among 127 spoligotyped isolates, 119 generated 43 different spoligotyping patterns; 87 (73.1%) generated 26 distinct spoligotype patterns; and 31 (26.0%) generated 17 different spoligotype patterns. The predominantly identified strains, family, lineages and sublineages were

SIT149 (19, 15.9%), T family (54, 45.4%), Euro-American (72, 60.5%) and CAS1-Delhi (24, 20.2%), respectively.

Additionally, *Mycobacterium africanum* was identified from 12 (10.1%) isolates. Furthermore, drug resistance was significantly associated with previous TB history ($X^2=46.59$; $p<0,001$) and previous TB treatment outcome ($X^2=47.677$; $p<0.001$).

Conclusions: The study identified significant proportion of Euro American lineage and East-African-Indian lineages that are strongly associated with drug-resistant TB, which could imply that drug-resistant TB is major public health problem in Ethiopia.

EP-14-734 Incidence and epidemiology of active tuberculosis in a healthy, HIV vaccine trial cohort in South Africa

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Background: The incidence of TB in South Africa in 2020 was 554 per 100,000 person-years, and much of the burden of TB is driven by HIV/TB coinfection. We evaluated the incidence and epidemiology of TB in a cohort of healthy adults without HIV participating in the HVTN 702 HIV vaccine trial in South Africa.

Design/Methods: Participants were healthy volunteers enrolled between 10/26/16-6/21/19 into HVTN 702. Median follow-up time in the study was 2.57 years. Participant ages ranged from 18-35; diabetes, HIV, and active tuberculosis were all exclusion criteria from the parent study. No TB testing was performed as part of study procedures. We reviewed adverse event and medication logs for evidence of incident TB reported during study follow-up. We evaluated possible predictors of incident TB using univariate logistic regression.

Results: 26 participants reported TB diagnoses after enrolling. The mean time to diagnosis from enrollment was 1.16 years, an incidence of 196.1 cases per 100,000

person years. 2 participants were diagnosed with TB within 12 weeks after enrollment and represent prevalent cases. All TB cases identified remained HIV negative until the end of the study period. No statistically significant demographic or clinical predictors of incident TB were identified.

There was a trend towards higher odds of TB among participants who were male, OR 1.61 (95% CI 0.53-5), had lower BMI (OR 1.05 (95% CI 0.98-1.15) and lived in an informal dwelling (OR 1.82 (95% CI 0.30-3.48)).

	TB Cases N=26	Non-TB Cases N = 5410	Odds Ratio (95% CI)	P value
Age (median, IQR)	25 (23.25-27.75)	24 (21-28)	1.05 (0.96-1.15)	0.28
Male sex at birth	11 (42.3%)	1624 (30.0%)	1.61 (0.53-5)	0.39
BMI (mean, sd)	24.08 (18.11-30.05)	26.07 (19.36-32.78)	0.95 (0.87-1.02)	0.17
ANC/ALC ratio at baseline (mean, sd)	1.79 (0.93-2.62)	1.79 (0.83-2.75)	1.01 (0.72-1.59)	0.98
Hgb g/dL at baseline (mean, sd)	13.83 (12.79-14.82)	13.78 (12.25-15.31)	1.15 (0.84-1.54)	0.36
Population density of residence N (%)	4 (16.0%) 21 (84.0%)	773 (15.0%) 4387 (85.0%)	1.23 (0.30-2.63)	0.99
Rural/countryside Urban/City				
Dwelling type N (%)	19 (76.0%)	4202 (81.4%)	N/A	0.49
Brick/concrete (Ref)	0 (0%)	1 (0.0002%)	1.82 (0.30-3.48)	
Tent/caravan	6 (24.0%)	787 (15.3%)	N/A	
Corrugated metal/scrap wood	0 (0%)	170 (3.3%)		
Mud/grass/reed				

BMI = Body Mass Index
ANC = Absolute Neutrophil Count
ALC = Absolute Lymphocyte Count
Hgb = Hemoglobin

Conclusions: Passive case-detection identified a measurable incidence of TB in this cohort of healthy, young persons without HIV. Two participants may have been enrolled with undetected active tuberculosis. In settings with a high incidence of TB, systematic screening for TB at study visit prior to enrollment or at follow-up visits may provide an opportunity for earlier diagnosis of active TB than afforded by passive case-detection.

EP-14-737 Implementation of active drug safety and monitoring (aDSM) in the programmatic management of drug resistant tuberculosis (PMDT): early learning from Uganda

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Background and challenges to implementation: Since 2012 WHO has been promoting aDSM for new and repurposed drugs in the treatment of drug resistant tuberculosis. Uganda rolled out use of novel regimens for multidrug-resistant Tuberculosis (MDR TB) treatment albeit with inadequate clinical and laboratory resources for detecting, managing, and reporting adverse drug reactions (ADRs).

We share lessons from the use of aDSM for MDR TB under program conditions in Uganda.

Intervention or response: The USAID Defeat TB in collaboration with the AIDS control program, ministry of health, National TB and leprosy program and National Drug authority (NDA) conducted an aDSM training targeting health care workers from the 17 MDR TB treatment sites. During the training, an adverse event (AE) screening tool and aDSM health worker desk guide to aid clinical decision were developed and disseminated to all the treatment sites.

In 2021, the project also provided Snellens charts, Ishihara color vision charts, Hemoglobin point of care machines, ECG paper and supported quarterly aDSM mentorships at 15 MDR TB sites.

Patient files were reviewed for AE screening, accurate recording, and management of AEs. Filled NDA reporting forms were also reviewed to corroborate the file review. Mentors also looked out for performance of basic lab and non-lab aDSM monitoring tests (ECGs, chest X-ray, visual acuity).

Results/Impact: A total of 299 people with MDR TB (96 female and 203 male) were screened, 78 (26%) of whom had ADRs; peripheral neuropathy 38 (49%), anemia 11 (14%), Musculo skeletal pain 9 (12%) and visual impairment 9 (12%) as seen in the figure on the following page. All the registered ADRs were managed in accordance with the national guidelines.

Conclusions: Under programmatic settings aDSM enabled prompt identification, management, and reporting of ADRs. We recommend strengthening these efforts across sites including electronic data capture methods for AEs.

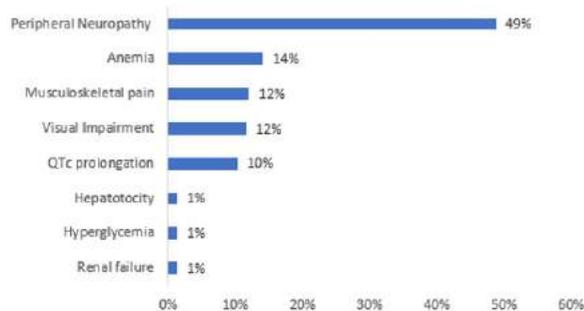


Figure. Distribution of ADRs (N=78)

EP-14-738 No association between HIV status and MDRTB treatment outcome in Lesotho

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Background: Studies have shown that HIV is a risk factor for unfavorable treatment outcome among patients treated for rifampicin-resistant (RR) or multidrug-resistant (MDR) tuberculosis (TB). Lesotho has a high prevalence of HIV (25.6%). Yet, the extent to which those with HIV experience worse RR/MDR treatment outcomes is unknown.

Design/Methods: This is a secondary analysis of data from the endTB observational study (a prospective cohort of patients initiating a bedaquiline and/or delamanid containing regimen for RR/MDR-TB between 2015 and 2018). Unfavorable treatment outcomes included death, loss to follow-up, and treatment failure.

Results: Of 264 patients, 79% (208) were living with HIV, in whom median CD4 cell count was 155 cells/mm³ [IQR: 51 to 281; N=181]. Of those with HIV, 71% experienced a favorable outcome, 22% died, 1% experienced treatment failure, 1% was lost and 5% were not evaluated.

Among patients without HIV, these frequencies were 67%, 25%, 4%, 0% and 4%, respectively. Individuals with and without HIV were similar with regard to drug resistance, alcohol use, low BMI, diabetes, and extent of disease (as defined by 3+ smear and cavitary disease). Those with HIV were younger and more likely to have anemia, impaired activities of daily living, and be hospitalized.

In adjusted analyses, there was no association between HIV status and unfavorable treatment outcome [RR: 0.88; 95% CI: 0.57, 1.35]. Unfavorable outcomes among participants without HIV tended to occur among older individuals as compared to deaths among those without HIV [median age: 61 versus 42 years, p=0.0004].

Conclusions: Outcome was not associated with HIV status; this may be due to a high frequency of death among individuals without HIV. Early diagnosis and initiation of antiretroviral therapy should be prioritized for those living with HIV. High mortality among those without HIV should be explored.

EP-14-739 Increasing drug resistant tuberculosis (DR-TB) case finding through intensified DR-TB case search activities after peak incidence of COVID-19 pandemic in Ogun State Nigeria

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Background and challenges to implementation: Tuberculosis (TB) is a leading killer infectious disease after Covid-19. Drug resistant tuberculosis (DR-TB) appears as a huge monster in control of TB.

Ogun state is one of the states in Nigeria with huge DR-TB burden. The National Tuberculosis Control Programme has annual set target of 268 DR-TB case diagnosis (67 per quarter) for the state. In 2020, the state diagnosed only 74 DR-TB cases (28%) of the set targets.

Intervention or response: Intervention

USAID TB LON 3 Project implemented by the Institute of Human Virology Nigeria (IHVN) identified challenges for diagnosis gap and carried out various strategic activities with the state TB programme from quarter 1 to 4 2021 to improve the situation. These included:

1. Awareness emphasizing symptoms and signs of DR-TB during clinical and community outreaches.
2. Provision of Information, Education and Communication materials in language understood by users.
3. Printing and distribution of work-aid to guide management of RIF-Resistant indeterminate results.
4. Guide on active management of month 2 positive smear results – need to run genotypic and phenotypic TB test.
5. Active work with state and Community Based Organisations (CBOs) to improve identification, tracking and care of diagnosed DR-TB cases and also improve contact tracing of index DR-TB patients.
6. Technically support the state consilium of experts
7. Support Monthly DR-TB Out Patient Department (OPD) clinics.
8. Inclusion of laboratory and DOT staff in cascade management team (CMT) review meetings to enhance capacity building and improve programme performances.

Results/Impact: DR-TB cases moved from 74 (28% of set target) in 2020 to 141 (53% of set target) in 2021. Percentage of DR-TB case diagnosed (versus targets) per quarter moved from 31% in Q1 2020 (prior intervention) to 72% in Q4 2021 (with intervention).

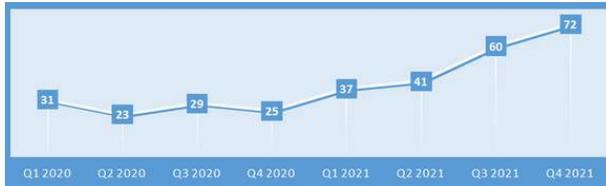


Figure. % achieved per quarter in relation to set target.

Conclusions: Focused and enhanced interventions could improve DR-TB case finding in a state and country especially when the right activities and support are targeted and provided.

EP-14-740 Addressing loss to follow up and mortality among patients receiving treatment for drug resistant TB: lessons from Uganda

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Background and challenges to implementation: According to the Global TB report 2021, the treatment success rate for drug resistant tuberculosis remains suboptimal at 59% due to high loss to follow up and mortality ranging between 15- 20%. Uganda applies a mixed model (ambulatory and hospital based) of DR-TB care that is decentralized across 17 treatment facilities in the country. The average TSR for 2016-17 cohorts was 66% with high loss to follow at 15% and mortality at 20%.

We evaluated the effect of a package of interventions implemented to reduce loss to follow up and mortality over a 4-year period.

Intervention or response: Using a quality improvement approach we applied a root cause analysis to determine reasons for loss to follow up, conducted mortality audits and developed a package of interventions including engagement of CSOs, VHTs and linkage facilitators to support treatment adherence, appointment keeping, medicine deliveries & DOT, clinical decision support through mentorship, coaching and panel meetings, quality improvement projects and monthly appointment/retention monitoring.

Patient enablers were provided and WHO approved shorter and injection free regimens were adapted under programmatic settings. Interim and final treatment outcomes were tracked on a quarterly basis using standard MOH tools

Results/Impact: Out of about 500 DR-TB patients notified annually, there was a 60% and 27% reduction in Loss to follow up and mortality respectively for the cohorts notified during the period Oct 2017 – Sept 2018 and Oct 2020 – Sept 2021. The national DR-TB TSR improved from 67% to 80% as illustrated in figure 1.

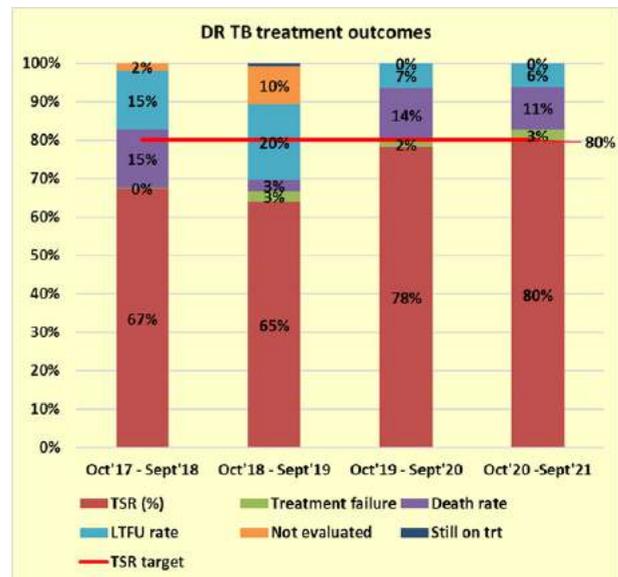


Figure 1: Trend of DR-TB treatment outcomes.

Conclusions: The package of interventions implemented in Uganda greatly reduced the loss to follow up and mortality. We recommend replication of the package in similar settings with high DR-TB loss to follow up and mortality. More work remains to reduce the mortality further in order to make more gains on DR-TB TSR.

EP-15 Access to quality TB care and services

EP-15-741 Effects of zinc and vitamin A supplementation on tuberculosis treatment outcomes and its prognostic markers: a systematic review and meta-analysis

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Background: Undernutrition is a major and under-appreciated risk factor for TB, which is potentially responsible for 2.2 million cases of TB per year globally. The effectiveness of micronutrient supplementation on TB treatment outcomes and its prognostic markers such as sputum conversion and serum zinc, retinol and hemoglobin levels has been poorly understood.

This systematic review and meta-analysis aimed to determine the association between zinc and vitamin A supplementation and TB treatment outcomes and its prognostic markers.

Design/Methods: A systematic literature search for randomized controlled trials (RCTs) was performed in PubMed, Embase and Scopus databases. Meta-analysis with a random effect model was performed to estimate risk ratio (RR) and mean difference (MD), with 95% confidence interval (CI), for dichotomous and continuous outcomes respectively.

Results: Our search identified 2,195 records. Of these, nine RCTs consisting of 1,375 participants were included in the final analyses. Among people being treated for TB, zinc (RR: 0.94, 95%CI: 0.86, 1.03), vitamin A (RR: 0.90, 95%CI: 0.80, 1.01), and combined zinc and vitamin A (RR: 0.98, 95%CI: 0.89, 1.08) supplementation was not significantly associated with TB treatment success. Combined zinc and vitamin A supplementation was significantly associated with increased sputum smear conversion at 2 months (RR: 1.16, 95%CI: 1.03, 1.32), serum zinc levels at 2 months (MD of 0.86µmol/l, 95% CI: 0.14, 1.57), serum retinol levels at 2 months (MD: 0.06µmol/l, 95 % CI: 0.04, 0.08) and 6 months (MD: 0.12µmol/l, 95 % CI: 0.10, 0.14), and serum hemoglobin level at 6 months (MD: 0.29 ug/dl, 95% CI: 0.08 to 0.51), among adults living with TB.

Conclusions: Providing zinc and vitamin A supplementation during TB treatment may increase early sputum smear conversion, serum zinc, retinol and hemoglobin levels. However, the use of zinc, vitamin A, or both was not associated with TB treatment success, compared with placebo.

EP-15-742 Acceptability and feasibility of integrating tuberculosis services into pediatric care in Cameroon and Kenya: a qualitative analysis

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Background: This qualitative study sought to explore acceptability and feasibility of integrated pediatric tuberculosis (TB) services provided through the Catalyzing Pediatric TB Innovations (CaP-TB) project in selected sites in Cameroon and Kenya.

Design/Methods: In-depth interviews (IDIs) were conducted with caregivers of children under five years old whose child had gone through TB investigations and program managers overseeing the CaP-TB project.

Focus group discussion (FGDs) were conducted with health care workers (HCWs) providing integrated CaP-TB services. In Kenya, additional FGDs were conducted with community workers (CWs) supporting the sites.

All interviews and FGDs were audio-recorded at the health facilities and. Recordings were transcribed, translated, then analyzed with MAXQDA, using thematic analysis.

Results: Many caregivers were not aware TB could affect children. Caregivers were generally accepting of the pediatric TB services, but providing free services was key to ensure acceptance. Some caregivers still rejected the TB investigations due to lack of awareness, dislike of the sample collection procedures (gastric aspirate), length of treatment time, fear of stigma and not wanting to believe the child could have TB.

HCWs and CWs reported the integrated TB services brought additional awareness to HCWs and facility staff about pediatric TB screening and diagnostic services and generally improved children's health outcomes. Challenges at the facilities included an insufficient supply of pediatric TB medications, insufficient staff, and the occasional lack of motivation among HCWs.

Study participants recommended increasing knowledge of pediatric TB in the communities, increasing staff and making the location of TB diagnosis more accessible.

Conclusions: CaP-TB increased provider knowledge and caregiver awareness about pediatric TB. There is still considerable need to shift the paradigm surrounding pediatric TB, to increase HCW awareness of pediatric TB and knowledge on pediatric TB diagnosis and management as well as to help communities understand children are at risk of TB and TB is curable.

EP-15-743 Improving sputum follow-up and TB cure rate using quality improvement approaches. Lessons from Namutumba HCIII in Namutumba district

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Background and challenges to implementation: Tuberculosis (TB) cure rate is an important measure of performance of quality TB programs. In July, 2021, MoH (NTLP) with support from partners (USAID Defeat TB) rolled out a national TB/HIV cascade improvement collaborative to address the bottle necks affecting performance of different elements in these cascades. Namutumba HCIII located in Namutumba district in East-Central Uganda, was one of the collaborative sites selected. The district has Seven TB diagnostic and treatment units (DTUs), with a cure rate of 55.2% for July-September 2021, while Namutumba HCIII had cure rate of 11% (same cohort).

Gaps identified included: no gazette space, day and healthcare worker to receive and attend to TB patients returning for TB care services, no system to effectively track patient due for drug refill, sputum follow up and those who miss appointments / loss to follow up.

Intervention or response: Teams identified TB clinic space and specific clinic day, staff duty allocation was developed, patient's appointment system (improvised book) was established, persons with TB disease given clinic appointments indicating services to be received. Sputum mugs given to patients prior to their next visit, pre-appointment reminder phone calls made and immediate follow -up for missed appointments done by either phone call/through community actor to understand their challenges and plan/re-schedule their appointment.

Results/Impact: TB cure rate progressively improved from 11% for cohort completing treatment in Jul – Sept 2021 quarter to 50% (Oct – Dec2021) and to 91% in Jan – Mar2022 for Namutumba HC III. whereas Cure rate for Namutumba district improved from 55.5% to 59% and to 79.3% in the same periods.

Conclusions: Using QI collaborative approach and focusing on establishing systems to track patient's retention in care improved TB Cure rate. To improve and sustain TB cure rate (TSR) nationally and globally, we recommend the adaption of this approach at similar settings.

EP-15-744 Training peripheral health staff and monitoring quality of chest X-ray interpretation for TB diagnosis in children through quality assurance

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Background and challenges to implementation: Chest X-ray (CXR) plays an important role in the process of TB diagnosis in children. Quality assurance (QA) on CXR interpretation aims at improving clinician's skills to interpret CXRs in children.

Intervention or response: In the TB-Speed-Decentralization study (2020-2021), we implemented an optimized childhood TB CXR diagnostic approach in two district hospitals and four primary health centres per country in Cambodia, Cameroun, Cote d'Ivoire, Mozambique, Sierra Leone, and Uganda.

It included site equipment with digital radiology plates and tablets, a 1.5-day training course on CXR interpretation based on a simplified classification considering six TB suggestive lesions (*enlarged lymphadenopathies; alveolar opacity; airway compression; cavitation; pleural/pericardial effusion; miliary*), QA on CXR based on blind quarterly review of 10% randomly selected normal CXR, all not readable and all TB suggestive CXR, by national re-readers using the same classification, and use of re-reading reports in onsite supervision and continuous training.

We present preliminary data on *sensitivity and specificity of CXR reading by site clinicians, assessed against the reading by national re-readers who were themselves assessed by an international re-reader.*

Results/Impact: Overall, 219 participants from 59 health facilities attended training. During the study, of 1,660 CXR performed, 239 (14%) were reviewed by local re-readers (132 normal and 94 TB suggestive). Overall, CXR reading sensitivity reached 91% [95% CI 64-100%], and specificity reached 50% [26-73%],

with a trend toward improvement over time (see details in figure). Sensitivity and specificity between national and international re-readers were 90% and 88%, respectively.

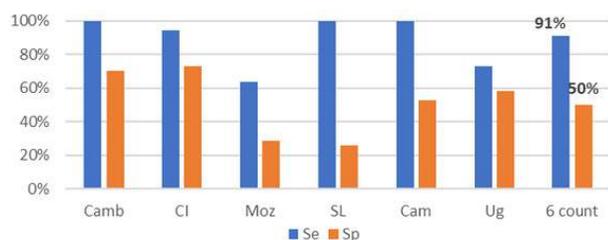


Figure. Sensitivity-specificity of CXR re-reading btw readers and national re-readers.

Conclusions: Most sites clinicians were able to adequately identify TB suggestive CXR, which may lower risk of missing TB cases. The low specificity is a concern however and can result in overdiagnosis. QA on child CXR interpretation is an essential tool to monitor clinicians' skills on CXR interpretation and reinforce training and mentoring when needed.

EP-15-745 Standard of care-based technical support improves data quality: experience from Ethiopia

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Background and challenges to implementation: Data quality is the cornerstone of any program to ensure proper monitoring and decision making. Regular support and follow up is needed to establish a strong monitoring and evaluation (M&E) system in the health program. Data quality problems are often observed.

Intervention or response: The USAID Eliminate TB Project supports the Ministry of Health of Ethiopia in comprehensive TB and TB/HIV services. One of the project's activities is supporting the M&E system. In line with this, the project introduced Standard of Care (SoC)-based support, a model where a data quality assurance system for major TB indicators is incorporated. Project and government staff are trained on this tool and deployed to health facilities to assess performance. The indicators evaluated include the number of all forms TB, number of TB patients tested for TB, number of household contacts initiated on TPT, and number cured. Values are recounted from registers and compared with the reported values. The discrepancy rate is calculated for each indicator and those with less than +5% discrepancy are rated as an acceptable level of data quality. In

average, a total of 743 health facilities were evaluated in four regions of Ethiopia from October 2020 to December 2021.

Results/Impact: After the activities were implemented, the percentage of health facilities with acceptable data quality improved for key TB program indicators, among which the major improvement observed was in the number of TB patients tested for HIV (from 72.3% in the baseline to 93.1% in October-December 2021). The all forms of TB indicator showed a 13.4% improvement from the baseline (Graph).

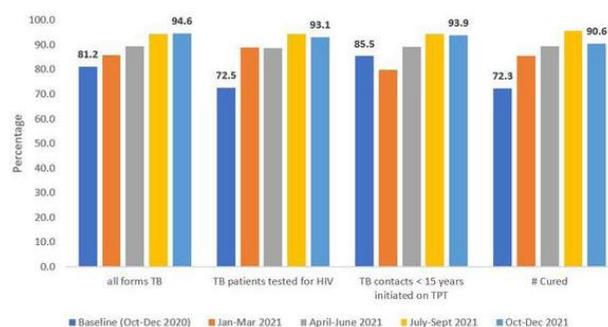


Figure. Trend in percentage of health facilities with acceptable data quality, Oct 2020-Dec 2021, Ethiopia.

Conclusions: SoC-based support to health facilities improved the performance of data quality in intervention areas. Sustaining and scaling up the SoC-based support in the national level is recommended.

EP-15-746 Interventions to improve adolescent and young adult TB service provision from the perspectives of adolescents, healthcare workers and policy stakeholders

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Background and challenges to implementation: The management and clinical care of adolescents and young adults (AYA) with TB requires tailored approaches, however existing youth-specific approaches to TB care are lacking. This study used a qualitative and participatory approach to explore specific AYA needs and challenges in TB care. A triangulation of perspectives from AYAs affected with TB, their healthcare providers and policymakers were employed to identify interventions that optimize AYA engagement in TB care.

Intervention or response: Sixteen adolescents and young adults (AYA; aged 10-24) diagnosed with TB and living in Harare, Zimbabwe were enrolled to participate in two participatory workshops and semi-structured in-depth interviews.

The study also enrolled eleven healthcare workers (HCW) and nine policymakers for in-depth interviews. Key themes explored AYAs experiences with TB disease and treatment, psychosocial challenges, youth-friendly services, and specific policies for AYAs affected with TB. Data were organized, coded, and analyzed using grounded theory approach to thematic analysis. A socio-ecological conceptual model was employed to frame the resultant findings.

Results/Impact: Needs and challenges were identified across socio-ecological levels. Developmental needs included family support, attending school or work, building trust with HCWs, TB awareness and education, and adherence support. Proposed interventions included the implementation of youth-friendly services, HCW training in AYA care, peer support, and stigma reduction TB education and awareness, in addition to health system strengthening and developing adolescent-specific TB policies.

Conclusions: Findings suggest that existing models of care for AYAs with TB do not meet their needs. Interventions were identified across socio-ecological levels and were supported by stakeholders involved in TB care, including AYAs. Further work is needed to study the implementation of interventions and evaluate youth-friendly policies and programs.

EP-15-747 Diagnostic outcomes and pattern of rifampicin resistance in the three senatorial zones of Benue state: retrospective study from April 2020 to August 2021

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Background and challenges to implementation: MDR-TB/RR-TB has been an area of growing concern to human health worldwide and poses a threat to the control of TB. Rifampicin-resistant tuberculosis is a form of TB that is resistant to Rifampicin and this form of TB can be diagnosed using the Genexpert machine.

Intervention or response: Aim: We seek to determine the diagnostic outcomes and pattern of Rifampicin Resistance TB in the three senatorial zones of Benue state – Zone A, B, and C.

Method: Data generated from the investigation of sputum samples of presumptive pulmonary TB patients using Genexpert in the 3 senatorial zones were collated and retrospectively analyzed for the period between October 2020 – September 2021

Results/Impact: Rif resistance distribution by zone showed that Zone A recorded 54 RRTB cases giving us a yield of 3% amongst diagnosed cases, Zone B recorded 35 RRTB cases with a yield of 3% amongst TB cases diagnosed, and Zone C 25 DRTB cases with a yield of 5%.

	Presumptive Evaluated	TB Cases Diagnosed	RR-TB Diagnosed	RR-TB Yield
Zone A	19,114	1833	54	3%
Zone B	20,902	1222	35	3%
Zone C	6,646	555	25	5%

Conclusions: Zone A recorded the highest number of RR-TB, but Zone C had the highest yield for RR-TB. Zone C has only 5 Genexpert machines compared to the 14 and 9 in Zone A and B respectively. Therefore, the state may be missing opportunities for closing the gap in RRTB diagnosis in the state. In ensuring that we close

the gap in diagnosing Rif Resistance in Benue State more methodical analysis must be employed to ensure that we are investing in the right places. Also, TB Programs and interventions may have to scale up resources in Zone C as part of the larger effort in ending Rif Resistant TB.

EP-15-748 Data-to-action continuum: introduction to the D2AC model and toolkit

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Background: A strong tuberculosis (TB) monitoring and evaluation (M&E) and surveillance system is vital for countries to end TB and rapidly adapt to global pandemics, such as COVID-19. The Data-to-Action Continuum (D2AC) can assess an implementing country's TB M&E and surveillance systems and help identify areas of improvement, and priority actions. This is critical to support equitable and quality services for TB and other infectious diseases.

Design/Methods: The D2AC Toolkit was developed through a phased development and review process. The framework incorporates domains and subdomains across a continuum of five levels. The Toolkit was field tested in Ghana and Nigeria using a mixed methods approach with a total of 67 participants. Participants first completed an individual assessment, and then gathered in groups to reach a consensus score. Groups were reformed based on subdomain interest to identify priority actions for an implementation plan.

Results: Both Ghana and Nigeria presented overall scores at the "established" level. Ghana's highest domain score was "Leadership, Governance, and Accountability"; in Nigeria, both domains, Data Collection and Reporting and Leadership, Governance, and Accountability scored the highest. In both countries, Information and Communications Technology scored the lowest. Based on these findings, the implementation plan focused on five and seven subdomains, respectively, including the following subdomains in common for both countries: Hardware, Data Quality, Data Integration and Exchange, and Skill and Knowledge Development.

Conclusions: D2AC is an effective tool to gauge a country's TB M&E and surveillance systems current capability level. It helps identify specific areas of improvement and next steps through an improvement plan. Moreover, it serves as baseline data for future assessments and as a funding resource, and advocacy tool. The toolkit is for TB, but it can potentially be applied to other infectious disease M&E and surveillance systems.

EP-15-749 Contribution of a virtual community of practice using the Project ECHO (Extending Community Healthcare Outcome) model to clinical management of DR-TB patients in Afghanistan

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Background and challenges to implementation: Urban Health Initiative (UHI) is a five-year USAID-supported project in Afghanistan focusing on strengthening the national tuberculosis response. Afghanistan's TB prevalence is 340/100,000 and incidence of 193/100,000 population. The UHI project adapted the Project ECHO virtual case-based community of practice model to help strengthen tuberculosis care in Afghanistan through continuous tele-mentoring during a challenging period of conflict.

Intervention or response: The TB ECHO program launched in February 2022 with the National TB Program selected as the tele-mentoring hub with 15 spoke sites in Kabul, Herat, Kandahar, Jalalabad, and Mazar cities for properly managing complicated DR-TB cases. Between February-April 2022, six ECHO sessions conducted; three theoretical sessions and three focused on DR-TB cases presented by spoke sites. This evaluation reflects the outcomes of ECHO in the clinical management of three DR-TB complicated cases:

1. A DR-TB patient with anemia, neuropathy, and tachycardia
2. A 30 years woman, failing standard DR-TB treatment
3. A patient with peripheral numbness, arthritis, and vision problems.

We collected patient data from training reports and patient files on these three cases.

Results/Impact: The clinical issues of the patient suffering from anemia, neuropathy, and tachycardia resolved after recommendations made during the ECHO session; for case 2, the regimen was changed to pre-XDR TB as a result of the discussion, and the patient clinically improved; and for case 3, the numbness, arthritis, and vision problems resolved by the care and treatment recommended during the ECHO session.

Conclusions: The UHI TB ECHO program provided a platform for clinical capacity strengthening and successful case management of complex DR-TB patients at the facilities level. Given the favorable patient outcomes related to the patients discussed during the ECHO sessions, we recommend the adoption and expansion of the ECHO model across Afghanistan to help strengthen the management of DR-TB and other priority public health challenges.

EP-15-750 Patient characteristics associated with non-adherence to tuberculosis treatment: a systematic review

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Background: Patient characteristics associated with non-adherence to Tuberculosis treatment: a systematic review.

Design/Methods: A Systematic review of 53 studies addressing the patient characteristics associated with TB medication non-adherence was performed. The publications were identified by searching the PubMed, World Health Organization (WHO), and Centers for Disease Control and Prevention (CDC) database, EmBase, Scopus database Arts, humanities, Social Science database and Google scholar. Only English language publications were eligible. Potentially eligible studies were retrieved and the full articles were assessed. The potentially eligible studies were included if they concerned patients treated for tuberculosis, reported non-adherence and reported on potential risk factors associated with non-adherence.

Results: Factors that were most frequently consistently and statistically significantly related to non-adherence to tuberculosis treatment were: family income, patient movement and changing address or giving wrong address, tuberculosis relapse or multidrug-resistant TB (MDRTB), during intensive phase of treatment, history of default, treatment regimen(long course), response to treatment, homeless, stigma, seeking traditional healers, staff receptiveness, lack of directly observed therapy short course (DOTS), poor knowledge or lack of health education, side effects of drugs, feeling better, alcohol intake and lack of family and social support.

Conclusions: Non- adherence to tuberculosis treatment was influenced by several factors

EP-16 Treatment selection and patient support opportunities to improve treatment outcomes

EP-16-751 Feasibility and acceptability of a peer-led socioeconomic intervention for tuberculosis-affected households in Peru: feedback from the CRESIPT trial

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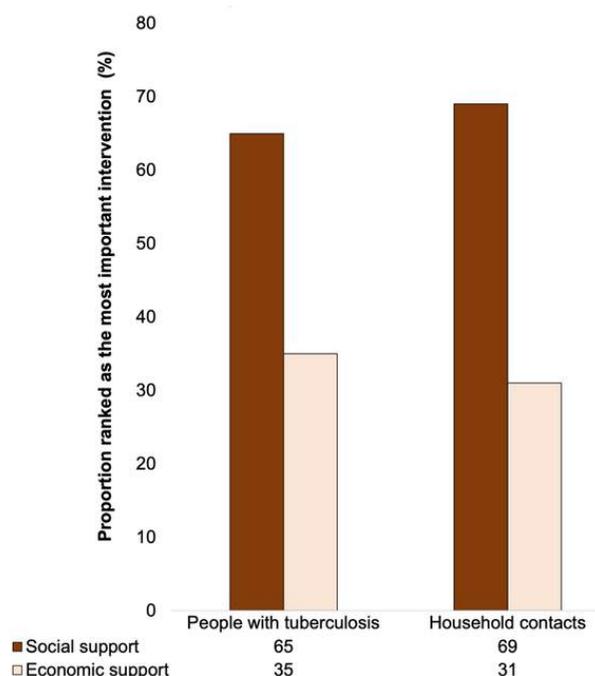
Background: The WHO End Tuberculosis Strategy emphasises the need to address inequalities in tuberculosis care through provision of socioeconomic interventions. However, evidence is limited on the feasibility and acceptability of these interventions for tuberculosis-affected households, and on which aspects are most highly valued.

Design/Methods: The CRESIPT trial was a community-randomised trial undertaken in 32 impoverished communities in Lima, Peru between 2016 and 2021. In 16 randomly selected supported communities, tuberculosis-affected households (people with tuberculosis and their household contacts) were offered a socioeconomic intervention for the duration of treatment, principally led by peer mentors (tuberculosis survivors).

This consisted of integrated social support (household visits and tuberculosis clubs providing information and peer support); and economic support (monthly conditional cash transfers). People with tuberculosis were interviewed after six months to collect feedback on intervention activities.

Results: 813 people with tuberculosis were recruited, of whom 741 (91%) provided feedback. 98% participated at least partially with intervention activities, and 97% said they would participate again.

Among people who participated, 77% said that the interventions helped them “a lot” to complete treatment and 19% said they helped “a little”, versus only 4% who said the interventions didn’t help. 65% said that social support most helped them to complete treatment, versus 35% who said economic support; and 69% said that social support most helped their household contacts to complete tuberculosis screening and preventive treatment, versus 31% who said economic support (Figure).



Conclusions: A socioeconomic intervention for tuberculosis-affected households was feasible and acceptable. Although global tuberculosis policy focuses on economic support to reduce catastrophic costs, participants in our study reported that social support was more valuable. This highlights the importance of meeting social as well as medical and economic needs of people living with tuberculosis, and of research assessing the impact and cost-effectiveness of social versus economic versus socioeconomic support.

EP-16-752 Rethinking how we define treatment effects for TB trials using estimands

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Background: In randomised clinical trials evaluating TB treatments, choice of outcome definitions and approaches to handling intercurrent events (ICEs) change the treatment effect being estimated (ICEs are post-randomisation events which affect interpretation or preclude measurement of the intended final outcome). However, ICEs are often inconsistently described, thus inhibiting clear interpretation and comparison across trials.

Design/Methods: Using latest ICH guidelines (E9(R1) addendum), our experience of conducting large phase III TB treatment trials, and our understanding of the estimand framework, we discuss key decisions regarding how different ICEs could be handled in the primary outcome definition. We use two completed trials (REMoxTB and STREAM Stage 1) as illustrative examples.

Results: We consider common ICEs including treatment changes and treatment extension, poor adherence to randomised treatment, re-infection with a new strain of TB which is different from the original infection, and death.

First, changes to allocated regimens should not necessarily be viewed as an unfavourable outcome; from the patient perspective, the potential harms associated with a change in the regimen should instead be directly quantified.

Second, handling poor adherence to randomised treatment using a per protocol analysis does not necessarily target a clear estimand; instead, investigators should develop ways to estimate the treatment effects more relevant to programmatic settings.

Third, re-infection with a new strain of TB could be handled with different strategies, depending on whether the outcome of interest is the ability to attain culture negativity from infection with any strain of TB, or specifically the presenting strain of TB.

Fourth, where possible, deaths could be separated into TB-related and non-TB-related and handled using appropriate strategies.

Conclusions: The estimand framework clarifies many issues in TB trials but also challenges TB trialists to justify and improve their outcome definitions. Future TB trialists should consider all the above points in defining their outcomes.

EP-16-753 Highly favorable outcomes of the practical implementation of new treatment regimens in the operational research context in Tajikistan

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Background: In 2019, drug resistant (DR) tuberculosis (TB) 713 cases were registered in Tajikistan, including 22% with extensively drug-resistant TB (XDR-TB). Prior to the introduction of new all-oral regimens, XDR-TB was treated with a difficult-to-maintain 18-20 month regimen of 7-8 antibiotics, including an injectable.

Design/Methods: An operational research study to evaluate the efficacy and safety of the BPaL regimen started in in Tajikistan in November 2020. The regimen

was prescribed in standard doses for 26 weeks, with the option for an extension for additional three months in case of late culture conversion or lack of clinical improvement.

Results: Out of 46 registered participants in the study, 25 were women, 42 had pulmonary TB, and 29 were newly diagnosed cases. Forty-four participants tested resistant to rifampicin and fluoroquinolone (FQ), while two had negative culture but were symptomatic contacts of XDR-TB cases.

Out of 46 individuals enrolled, 22 has finished 6 months course of treatment, out of them fifteen had favorable outcomes, one died due to heavy bleeding, and two were switched to individualized regimens due late-arriving baseline culture showing resistance to BDQ and LZD. For four participants, the regimen was extended by 3 months due to comorbidities.

Among the remaining 33 participants, 16 (48.5%) experienced culture conversion after the first month of treatment and 11 (33.3%) after the second month. Culture conversion among 81.8% of XDR cohort in the first two months demonstrates the rather high efficacy of this treatment regimen.

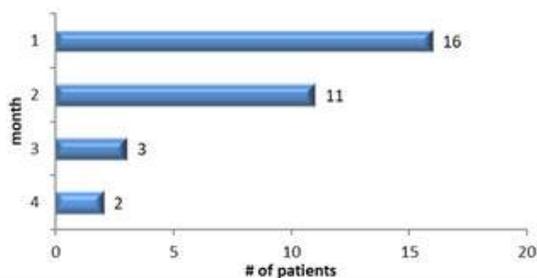


Figure. Time to culture conversion, month.

Two participants in the cohort experienced neuropathy linked to LZD, one at 5 months and one at 6 weeks.

Background and challenges to implementation: In 2019, drug resistant (DR) tuberculosis (TB) 713 cases were registered in Tajikistan, including 22% with extensively drug-resistant TB (XDR-TB). Prior to the introduction of new all-oral regimens, extensively drug-resistant TB (XDR-TB) was treated with a difficult-to-maintain 18-20 month regimen of 7-8 antibiotics, including an injectable.

Intervention or response: An operational research study to evaluate the efficacy and safety of the BPaL regimen started in in Tajikistan in November 2020. The regimen was prescribed in standard doses for 26 weeks, with the option for an extension for an additional three months in case of late culture conversion or lack of clinical improvement.

Results/Impact: Out of 46 registered participants in the study, 25 were women, 42 had pulmonary TB, and 29 were newly diagnosed cases. Forty-four participants tested resistant to rifampicin and fluoroquinolone, while two had negative culture but were symptomatic contacts of XDR-TB cases.

Out of 46 individuals enrolled, 22 has finished 6 months treatment course, out of them fifteen had favorable outcomes, one died due to heavy bleeding, and two were switched to individualized regimens due late-arriving baseline culture showing resistance to Bedaquiline and Linezolid. For four participants, regimen was extended by 3 months due to comorbidities.

Among the remaining 33 participants, 16 (48.5%) experienced culture conversion after the first month of treatment and 11 (33.3%) after the second month. Culture conversion among 81.8% of XDR cohort in the first two months demonstrates the rather high efficacy of this treatment regimen.

Two patients in cohort experienced neuropathy linked to Linezolid, one at 5 months and one at 6 weeks.

Conclusions: Analysis of final and interims outcomes of BPaL regimen piloted in Tajikistan allows us to predict a rather high effectiveness of the BPaL regimen for XDR cases compared to long-term individual treatment regimens and supports future use of this regimen in program conditions.

EP-16-754 Effectiveness of a bedaquiline, linezolid, clofazimine "core" when fluoroquinolones are unlikely to be active

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Background: Treatment outcomes may be compromised among individuals with rifampicin- or multidrug-resistant tuberculosis with additional resistance to a fluoroquinolone (FQ). Among individuals in whom a FQ was unlikely to be effective, we compared the effectiveness of longer individualized regimens comprised of bedaquiline (Bdq) for < 9 months, linezolid (Lzd), and clofazimine (Cfz) to those reinforced with ≥ 1 group C drug and/or longer duration of Bdq.

Design/Methods: We emulated a target trial using data from the prospective, multi-country endTB observational cohort and compared the effectiveness of initiating, and remaining on, one of 5 reinforced regimens: (1) Bdq (> 9 months), Lzd, Cfz; (2) Bdq (> 9 months),

Lzd, Cfx, delamanid (Dlm); (3) Bdq, Lzd, Cfx, imipenem (Imp); (4) Bdq, Lzd, Cfx, second-line injectable; (5) Bdq (> 9 months), Lzd, Cfx, Dlm, Imp, to a core regimen of Bdq (<9 months), Lzd, Cfx. We included individuals in whom a FQ was unlikely to be effective based on drug susceptibility testing and/or prior exposure, and who received a regimen of interest by the second week of treatment (time zero). To account for immortal time bias, we assigned clones of each person to regimens of interest that aligned with their observed data at time zero and censored clones if treatment deviated from the initial regimens. We estimated the relative risks of treatment success using inverse probability weighting to adjust for time-varying confounding.

Results: Among 454 individuals, treatment success was high, ranging from 75% to 89% across regimens. In analyses adjusting for baseline and time-varying confounding, we found no evidence that reinforced regimens improved the core regimen, with relative risks ranging from 0.91 (95% CI: 0.81-1.01) to 1.01 (95% CI: 0.91-1.11; Table).

Regimens of interest	Relative risks (95% CI)
Bdq (<9 m), Lzd, Cfx	Reference
BDq (≥9 m), Lzd, Cfx	0.93 (0.81-1.06)
BDq (≥9 m), Lzd, Cfx, Dlm	0.91 (0.81-1.01)
BDq, Lzd, Cfx, Imp†	1.00 (0.81-1.24)
BDq, Lzd, Cfx, Km/Cm/Am†	1.01 (0.91-1.11)
BDq (≥9 m), Lzd, Cfx, Dlm, Imp	0.93 (0.83-1.04)

Notes:

m: months, Bdq: bedaquiline. Lzd: linezolid, Cfx: clofazimine. Dlm: delamanid. Imp: imipenem. Km: kanamycin. Cm: capreomycin. Am: amikacin.

Adjusted for year of enrollment, Armenia, Belarus, Peru, baseline HIV infection, baseline culture result, and monthly culture result.

† Duration of Bdq was not examined due to small sample size.

Table. Relative risk of treatment success, as compared to a regimen comprised of Bdq (< 9 months), Lzd, Cfx, among individuals in whom a fluoroquinolone was unlikely to be effective.

Conclusions: High treatment success underscores the need for expanded access to these drugs. Future evaluations should consider safety/tolerability and subgroup heterogeneity.

EP-16-755 A phase 2A trial of the safety and tolerability of increased dose rifampicin and adjunctive linezolid, with or without aspirin, for HIV-associated tuberculous meningitis

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Background: Tuberculous meningitis (TBM) is the most severe form of tuberculosis with mortality up to 50% in those who are HIV-1 co-infected. Standard antibiotic regimens are not designed for use in TBM. Regimens which include intensified antibiotics alongside effective host directed therapies may improve outcomes. Safety data on the use of such drugs in combination and in the context of HIV-1 are needed to inform clinical trial design.

Design/Methods: We conducted a phase 2 open-label randomised controlled trial to assess the safety of high-dose rifampicin, linezolid and aspirin in HIV-associated TBM. Participants were randomised (1.4:1:1) to one of three treatment arms ((1), standard of care (SOC); (2) SOC + additional rifampicin (up to 35mg/kg/day) + linezolid 1200mg/day (600mg/day after 28 days); (3), as per arm 2 + aspirin 1000mg/day). The primary outcome of adverse events of special interest (AESI) or death was assessed at day 56.

Results: 52 participants were randomised. Most participants had mild disease (MRC Grade 1, 59%; 2, 39%; 3, 2%). A higher number of events (AESI or death) occurred in arm 3 (10/16) compared with arm 1 (6/20) and 2 (4/14) although this was not statistically significant ($p=0.083$).

Kaplan Meier analysis of cumulative incidence of AESI or death demonstrated worse outcomes in arm 3 vs arm 1 ($p=0.04$).

Toxicity attributable to the experimental treatments was mild and infrequent (number of attributed events: melena(1); transaminitis(2); haematological(3)).

There was no difference in efficacy assessed by Modified Rankin Scale at day 56 between the three arms.

Conclusions: High dose rifampicin (35mg) and adjunctive linezolid can safely be added to SOC in HIV-associated TB. The higher number of events in arm 3 were not attributed to aspirin use however larger studies are required to evaluate whether any potential toxicity associated with high dose aspirin is outweighed by a mortality or morbidity benefit.

EP-16-756 Risk factors for unfavorable outcomes of MDR-TB regimens using bedaquiline, linezolid and clofazimine in Peru

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Background: Peru is home to the largest percentages of RR/MDR-TB (28%) and of TB resistant to fluoroquinolones and injectables (64.4%, "old XDR-TB") in the Americas. In patients that started treatment in 2015, 53.7% of MDR-TB and 71.4% of old XDR-TB patients experienced treatment success. Here, we explore the effectiveness of treatment regimens containing bedaquiline, linezolid, and clofazimine (Bdq-Lzd-Cfz) and risk factors associated with unfavorable outcomes.

Design/Methods: Through the endTB project, the Peruvian National Tuberculosis Program introduced regimens containing Bdq-Lzd-Cfz for MDR-TB from 2016-2020. We report on a prospective cohort of patients who were systematically supported and followed during treatment in Lima.

We describe patient characteristics. Chi-squared test was used to examine association between variables. Factors associated with unfavorable treatment outcome were identified using logistic regression.

Results: We included 248 patients, 65.3% were male. Median age was 29 (interquartile range: 23 to 39); 22 (8.9%) had diabetes, 10 (4.0%) had HIV infection, 234 (94.4%) had prior exposure to second-line drugs. Additional resistance to fluoroquinolones was present in 148 (60.2%). Cavitation was observed in 161 (70.0%). All patients received Bdq-Lzd-Cfz as part of their regimens; 35.1% (87) of which were all oral.

Success was reported in 89.5%: 87.3% among old XDR-TB patients and 91.5% among other MDR-TB. Age over 40 years ($p=0.031$; AOR=2.75), male gender ($p=0.014$; AOR=4.94) and HIV coinfection ($p=0.020$; AOR=5.52) were independently associated with unfavorable outcomes.

Variable	AOR	95% CI	p value
Age > 40	2.75	1.10 - 6.91	0.031
Male	4.94	1.39 - 17.57	0.014
BMI < 18.5	2.46	0.78 - 7.79	0.125
HIV coinfection	5.52	1.31 - 23.22	0.020
Hb < 12.5	1.98	0.70 - 5.59	0.197
Previously treated for TB	0.27	0.04 - 1.82	0.180

AOR: Adjusted Odds ratio, CI: Confidence Interval, BMI: body mass index, HIV: human immunodeficiency virus

Table 1. Risk factors for unfavorable treatment outcomes among endTB observational study participants who received regimens containing at least bedaquiline, linezolid and clofazimine in Peru (N=248)

Conclusions: Success is high in Peru using this 3-drug nucleus in patients with MDR-TB and old XDR-TB. If used more widely, regimens containing these drugs, complemented by treatment support, could dramatically improve care for MDR-TB. For TB also resistant to fluoroquinolones (and injectables), this all-oral core could replace the current Peruvian standard which requires IV therapy, without compromising outcomes. Optimization is required to improve outcomes for older, male patients and/or those living with HIV.

EP-16-757 Effectiveness and safety of bedaquiline-based, modified shorter treatment regimen for rifampicin resistant tuberculosis in Vietnam

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Background: Vietnam is a high tuberculosis (TB) and rifampicin-resistant TB (RR-TB) burden country. The WHO recommended a 7-drug standardized all-oral shorter regimen (STR) with bedaquiline replacing the injectable drug for RR-TB. To address concerns with regards to the pill burden of this 7-drug STR, a novel modified STR (mSTR) was piloted in Vietnam under operational research conditions, to assess the safety and effectiveness of this mSTR and inform RR-TB treatment guidelines in Vietnam.

Design/Methods: A prospective cohort study of a 9-11 months all-oral STR (comprising bedaquiline, levofloxacin, linezolid 600mg, clofazimine and/or pyrazinamide) for RR-TB patients without confirmed additional resistance to fluoroquinolone, in Vietnam from July 2020 to February 2021.

Results: Among 106 RR-TB patients enrolled, 66 (62%) were new cases. One (1%) was previously exposed to second-line TB drugs. About 40% had cavities and/or extensive lesions on chest X-ray. Culture conversion at 2 months was achieved in 63 of 74 (85%) patients with a positive baseline culture. Of 106: 95 (90%) were successfully treated, 6 (6%) were lost-to-follow-up, 1 (1%) died and 4 (4%) were reported with treatment failure, including 3 because of permanent regimen change due to adverse events (AE) and 1 because of reversion on culture. Thirty-two (30%) patients encountered at least one AE. A total of 45 AEs were recorded. Of those, 13 (29%) were serious (hospitalization, life threatening (grade 4) or death). The median time to AE was 3 months (IQR:2-5). Twenty-six AEs led to an adaptation of the prescribed regimen: either dose reduction (N=1), drug interruption (N=19), or drug withdrawal (N=6, 4 due to linezolid).

Treatment outcomes	106	%
Cured	88	83
Treatment completed	7	6.6
Failure/ culture reversion	1	0.9
Failure due to adverse events	3	2.8
Lost to follow up	6	5.7
Died	1	0.9
Adverse events	45	%
Grade 3	10	22.2
Grade 4	2	4.4

Conclusions: The mSTR resulted in high 2-month culture-conversion and high treatment success in Vietnam. Adverse events were frequent, but manageable in most patients. Active drug safety monitoring and management (aDSM) is still essential, particularly when linezolid is used throughout treatment.

EP-16-758 Linezolid resistance among MDR-TB patients from metropolitan cities of Pune and Mumbai, Western Maharashtra, India

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Background: Linezolid is one of the most effective and frequently used 'Group A' drugs for multi-drug resistant tuberculosis (MDR-TB) treatment, especially in India with high Fluoroquinolone (FQ) resistance (16-30%). While low prevalence of Linezolid resistance in MDR-TB patients has been reported, emergence of baseline resistance to Linezolid has not been studied. "endTB" and "endTB-Q" phase III clinical trials in Mumbai and

Pune, India aims to evaluate efficacy and safety of shortened regimens containing new and repurposed drugs for MDR-TB.

This study highlights existing baseline resistance patterns among participants screened for these trials, focusing on Linezolid resistance.

Design/Methods: Cross-sectional study analyzed baseline drug sensitivity tests (DST) of 182 participants, screened between October 2020 to March 2022. Mycobacterium Growth Indicator Tube (MGIT) based DST at WHO recommended critical concentrations for 11 drugs including Linezolid (1.0 µg/ml) was performed for all participants at JJ Group of Hospitals, Mumbai.

Results: Among 182 participants, baseline linezolid resistance was found in 5.5% (n=10). [Fig 1] The median age was 28.5 (18-37) and mean BMI was 18.15 (14.71-21.07). Five were females. Two were diabetic and 4 were anemic.

No patient had history of MDR-TB or exposure to 2nd line drugs. Four had history of Drug sensitive TB treatment (DS-TB). Six had family history of TB [DS-TB=5, MDR-TB=1]. Sputum grading was at least 1+ in 40% and scanty in 30%. Chest X-ray revealed bilateral disease in 80% and 50% had cavities.

There is higher odds of baseline Linezolid resistance in patients, who are resistant to any FQs and any second line injectables (SLIs) [OR=14.64, 95% CI (3.68-58.29)] compared to those who are not resistant to any FQs and any SLIs, a statistically significant association [p<.00001].

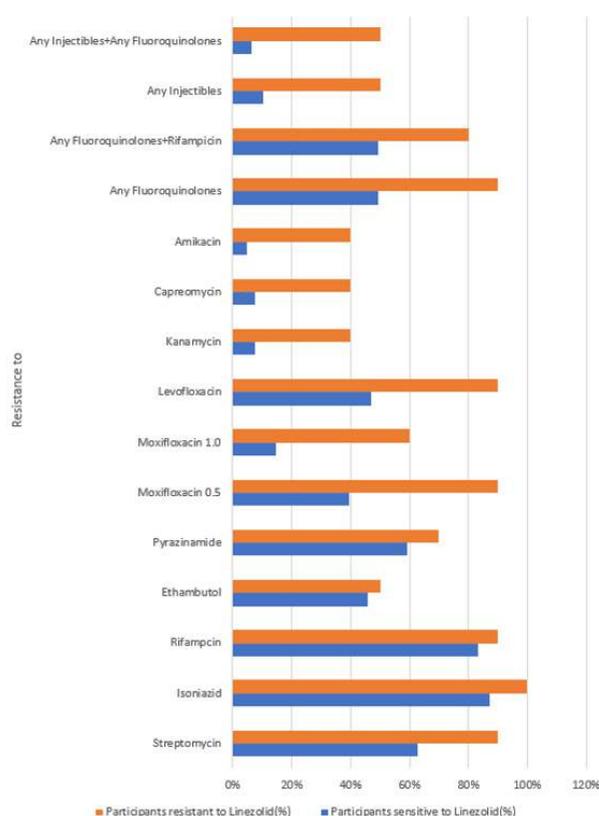


Figure 1.

Conclusions: This analysis draws attention towards growing concern of dual baseline resistance to Linezolid and Fluoroquinolones in India. This result underscores needs of universal DST and novel regimens for MDR-TB.

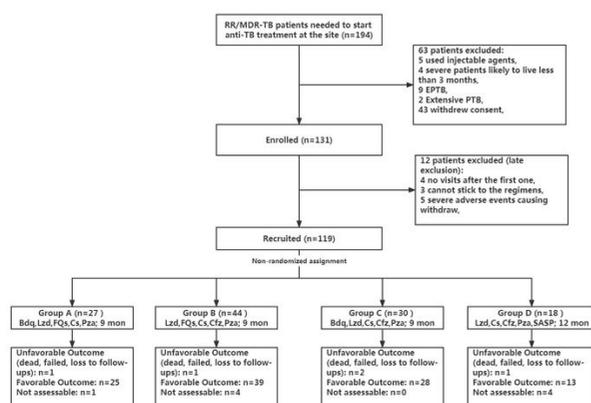
EP-16-759 MDR-TB All-Oral Short-Course Regimens in China (MDR-Chi): A multi-centre open-labeled non-randomized controlled trial

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Background: WHO recommended using a lower number of agents for a shorter period for improving treatment outcomes in patients with MDR-TB; yet, there is still a lack of evidence in various real-world settings, and even less for those with extra resistance to fluoroquinolones (FQs) (pre-XDR-TB).

Design/Methods: In this multi-center open-labeled non-randomized controlled trial, for FQ susceptible MDR-TB (FQ(S)MDR-TB), we had regimen A (bedaquiline/linezolid/moxifloxacin/cycloserine/pyrazinamide) and regimen B (linezolid/moxifloxacin/cycloserine/clofazimine/pyrazinamide) of nine months, based on the patients' will to use bedaquiline. For FQ resistant MDR-TB (FQ(R)MDR-TB), we had regimen C (bedaquiline/linezolid/cycloserine/clofazimine/pyrazinamide) of 9 months and regimen D (linezolid/cycloserine/clofazimine/pyrazinamide/sulfasalazine) of 12 months. As an adjunctive therapy, sulfasalazine was to address the under-strength of this regimen.

The primary outcome was unfavorable outcome defined as the incidence of bacteriologic failure or relapse or clinical failure through follow-up (until 6 months after the end of treatment).



Results: 119 participants were finally enrolled for analyses. There were 27 in regimen A and 44 in regimen B. Excluding not assessable cases, the unfavorable outcome was 3.8% and 2.5% ($P<0.05$). The culture conversion

rate at 2 month was 73% and 48% ($P=0.12$). The culture conversion rate at 6 month was 100% for both ($P>0.9$). AEs of grade 3 and 4 was 13 (48%) and 15 (34%), with peripheral neuropathy and liver injury being the most common reason for drug discontinuation. QTcF >500 ms was 1 (3.7%) and 4 (9.3%). There were 30 in regimen C and 18 in regimen D. The unfavorable outcome was 6.7% and 7.1% ($P<0.05$). The culture conversion rate at 6 month was 86% and 92% ($P>0.9$). AEs of grade 3 and 4 was 7 (23%) and 6 (35%).

Conclusions: In this trial, we demonstrated all-oral short-course regimens of five drugs across 9-12 months and gained a satisfying outcome with enduring and manageable adverse effects, thus providing options for patients with different needs.

EP-16-760 Impact of a mobile phone-based interactive voice response software on tuberculosis treatment outcomes at public facilities in Uganda

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Background: Tuberculosis (TB) is the leading infectious cause of death. Treatment success rate for TB in Uganda is 77% and barriers to optimal results include inadequate engagement and empowerment of patients, sub-optimal screening of presumptive TB cases and high attrition. Digital health innovations (DHIs) may address operational barriers and improve treatment. This study investigated the effect of an interactive voice response system (CFLTb) on TB treatment success among drug-susceptible TB patients at five public health facilities in Uganda.

Design/Methods: An open-label randomized controlled trial; participants with TB randomized (1:1) to CFL-TB or standard of care (SOC). CFL-TB is an interactive voice response (IVR) software providing daily adherence call reminders, health tips, appointment reminders, and allows remote symptom reporting. Participants interviewed at months 0 (baseline), 2, and 6. Data collected on socio-demographics and TB knowledge. TB treatment response and appointment data taken from Ministry Of Health and CFL-TB records. Follow-up continued until completion of treatment (six months), or lost to follow-up, if earlier. Treatment success, missed visits rates were compared using chi-square.

Results: By December 2021, 260/274 participants had been enrolled, 113 completed 6 months' treatment (CFL-TB 129; SOC 131). Median (IQR) age, body mass index and distance from health facility were 34.4 (26.6-45.3) years, 19.6 (17.4-21.4), and 30 (25-60) kilometers, respec-

tively. Overall, 165(63.5%) were male and 90(34.6%) had HIV. At baseline, 84/260(32%) not aware that TB treatment halts transmission, 72/260(27.7%) not aware of TB vaccination, 112/260(43.1%) not aware of TB resistance arises from poor treatment adherence. TB treatment success rate higher in the CFL-TB arm 51/54 (94.4%) than SOC 52/59(88.1%) [crude RR 0.47, 95% CI 0.13-1.72, $p=0.326$]. Fewer missed visits noted in the intervention arm (3/129) vs SOC(6/131) [Crude RR =0.51, 95% CI 0.13-1.99, $p=0.320$].

Conclusions: There was a trend towards higher treatment outcomes and fewer missed visits in TB patients who received software-enhanced support compared to SOC. DHIs may be helpful especially during epidemics that preclude physical facility visits.

EP-17 Screening and preventive interventions finding the correct balance

EP-17-761 Prevalence of latent tuberculosis infection among household contacts of persons with pulmonary TB – Mumbai, India

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Background: Household contacts (HHC) of persons with pulmonary tuberculosis (PTB) are at greater risk of latent TB infection (LTBI) and PTB. TB preventive treatment (TPT) can reduce progression from LTBI to TB disease but is not widely implemented in India. PTB prevalence is high in Mumbai (276 cases per 100,000 population); however, among HHCs in Mumbai, the burden of LTBI and acceptability of TPT is unknown.

Design/Methods: During September 2021–December 2021, we selected, by simple random sampling, 158 microbiologically-confirmed, drug-sensitive, PTB in-

dex cases registered for TB treatment in Mumbai. All consented and enrolled HHCs age ≥ 5 years were interviewed (or by parental proxy) with a structured questionnaire to obtain demographic and clinical information and screened for TB-related symptoms. All HHC were offered chest radiographs and interferon-gamma release assay (IGRA) (QuantiFERON-TB Gold Plus) tests.

IGRA-positive HHC with no evidence of PTB were considered to have LTBI and referred for TPT as per national guidelines. We calculated stratified prevalence and 95% confidence limits (95% CL) to describe the burden of LTBI. (Figure.)

	N	QFT+	QFT-	LTBI Prevalence	95% confidence limits		p-value**
					LL	UL	
Age in years 5–18	158	66	92	41.8%	40.2%	43.3%	0.009
≥ 19	344	188	156	54.7%	53.6%	55.7%	
Sex Male	257	135	122	52.5%	51.3%	53.8%	0.425
Female	245	119	126	48.6%	47.3%	49.8%	
Clinical Conditions Immunocompromised*	36	15	21	41.7%	33.5%	49.8%	0.348
Not immunocompromised	466	239	227	48.7%	50.4%	52.2%	
Overall	502	254	248	50.6%	49.7%	51.5%	

*Conditions included: cancer (all forms), diabetes mellitus, HIV, and thyroid dysfunction
LL=lower limit, UL=upper limit, QFT=QuantiFERON-TB Gold Plus
**Yates-corrected chi square

Figure. Stratum-specific latent tuberculosis infection (LTBI) prevalence estimates among household contacts of pulmonary tuberculosis index-cases - Mumbai, India.

Results: Among 558 identified HHC, 502 (90%) were enrolled. Overall, 120(76%) index cases had at least one HHC with LTBI; LTBI prevalence was 50.6% (95% CL: 49.7–51.4%). Persons aged 5–18 years had significantly lower prevalence (41.8%; 95% CL: 40.2–43.3%) than other age strata. HHC with at least one concurrent immunosuppressive medical condition (e.g., cancer, diabetes, HIV, or thyroid dysfunction) had a lower prevalence (41.7%; 95% CL: 38.4–44.9%) of LTBI than those without (51.3%; 95% CL: 50.4–52.2%) but this difference was not significant. Among 254 eligible HHCs with LTBI, 215(84%) initiated and 144 (67%) completed TPT.

Conclusions: We observed a high LTBI prevalence among HHCs. HHCs with LTBI were willing to initiate and complete TPT. Screening HHCs for LTBI using IGRA and referral for TPT appears to be feasible. A comprehensive strategy for programmatic management of LTBI will be important.

EP-17-762 Implementation of an integrated care strategy for children household contacts of patients with pulmonary tuberculosis, Colombia, 2021-2022

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Background: This study aims to evaluate an integrated care strategy for children under five years who are household contacts of persons with tuberculosis (TB) in Colombia.

Design/Methods: Quasi-experimental study, including children under five years, household contacts of persons with smear-positive pulmonary TB from Medellín, Bello, and Itagüí, Colombia. Sample size estimated for treatment completion outcome: 85 children who require TB preventive treatment (considering 59% isoniazid treatment completion in a 2015-2018 comparison cohort, expected completion of at least 80%, 95% confidence, 80% power).

Recruitment started in July 2021; preventive TB treatment is offered under an integrated care strategy, including diagnosis with clinical assessment, Tuberculin Skin Test (TST), Interferon Gamma Release Assay (IGRA), and chest X-ray with standardized reading. Children with latent TB infection (LTBI) or recently exposed (less than 3 months) are offered rifampicin (four months), multidisciplinary care with a nurse, general practitioner, pediatrician, infectious disease specialist, social worker, psychologist, nutritionist, and the provision of incentives (transport and food assistance); person-centered care, active follow-up, education, and information materials. The study has the UPB Research Ethics Committee's approval.

Results: Until March 2022, 74 children have been recruited. Mean age 2 years (SD 1.3 years), 8 children under 1 year (10.8%); 33 female (44.6%), 21 migrants (28.4%),

11 have no health system affiliation (14.9%), 23 negative TST (<5 mm) and were recently exposed (31%), 34 children completed 4 months of rifampin (45.9%), 16 children suspended, 10 with a negative second TST (13.5%), and 6 because of guardian decision (8.1%), 4 children were lost of follow (5.4%), 21 children are still on treatment (28.4%), 7 children presented mild adverse events (9.5%).

Conclusions: A comprehensive care strategy for TB contact children, including person-centered care, with a multidisciplinary approach, a less extensive treatment, and the provision of incentives, seems to improve the completion rates, supporting the World Health Organization recommendations.

EP-17-763 Efficacy of tuberculosis preventive therapy in a national cohort of people with HIV

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Background: Tuberculosis Preventive therapy (TPT) is a recognized intervention to reduce the burden of TB in people living with HIV. Namibia has implemented TPT using isoniazid since 2005. We analysed the national cohort of people registered for HIV care to determine the risk of TB disease and the risk of death among those who received TPT compared to those who did not.

Design/Methods: This was a secondary analysis of electronic records kept by the Ministry of Health from HIV care clinics as well as electronic TB registers. Linkplus® software (CDC) was used for the probabilistic linkage of records between the HIV database and the TB database using the first names, surname, dates of birth, sex and resident district. Risk ratios, incidence ratios and Kaplan-Meier survival statistics were calculated in STATA version 17.0 (Statacorp LLC).

Results: Of the 396,791 complete records that could be found in the HIV database, 64% (253,084) were female and (143,475) were male. The mean age was 42 years and a total of 227,877 (57%) received a form of TPT. The mean follow-up time was 6.2 years with a total of 2,243,607 person-years analysed. Only a minority, 39,423 individuals could be linked to the TB registers. The risk of having TB was 6.4% in the TPT group vs 14.6% in the non-TPT group (RR=0.44; 95% CI 0.43-0.45). The risk of death was 2.4% vs 12.1% respectively (RR=0.20; 95% CI 0.19-0.21).

Conclusions: Provision of TPT in a national HIV programme was associated with an over 50% lower risk of active TB among people registered for HIV care.

EP-17-764 Multi-drug resistant tuberculosis (MDR-TB) diagnosis to treatment gap in Cameroon: lessons from clinic audits in five regions

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Background: Multi-drug resistant tuberculosis (MDR-TB) continues to be a global public health threat. In 2020, 26% of patients diagnosed with MDR-TB in Cameroon did not initiate treatment. The objective of this study was to identify gaps in the implementation of the national MDR-TB treatment guidelines.

Design/Methods: In April 2021, a clinic audit was conducted by trained external research assistants in five regional MDR-TB treatment centers in Cameroon, including regions with the highest and lowest diagnosis to treatment gap in 2019/2020. Elements of the audit checklist were extracted from the Cameroon national MDR-TB treatment guideline including: knowledge and use of the national MDR-TB treatment guidelines in health-staff; patients' sample transport and results circuits; treatment initiation procedures, follow-up of patient not initiated on treatment.

Results: The MDR-TB diagnosis to treatment gaps were: Littoral (30/106; 28.3%), Center (20/89; 22.5%), Far North (4/35; 11.4%), North-West (0/5; 0%) South-West (0/12; 0%). The clinic audit revealed a generally good implementation of the national MDR-TB treatment guidelines across the five MDR-TB clinics. However, sample transport and communication systems were not harmonized across the MDR-TB treatment centers. While the TB clinics had direct communication link (shipment of samples/results and telephone calls) with the GeneXpert laboratories for three of the sites, the Regional TB Technical Groups (RTG) served as intermediary in the Centre and Littoral, the two regions with disproportionately higher MDR-TB diagnosis to treatment gap.

Conclusions: MDR-TB diagnosis to treatment gap varied across the five regions. The existence of an intermediary between the MDR-TB clinic and GeneXpert laboratory could have introduced a communication gap between the health systems and the MDR-TB patients.

Replicating practices across all the sites could reduce the number of MDR-TB patients not initiating treatment. Further research is needed to understand the patient-level determinants of the gap.

EP-17-765 Operational Implementation of three-month rifampicin and isoniazid for household contacts in Indonesia

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Background and challenges to implementation: In 2020, the National Tuberculosis Program (NTP) recommended a 3-month daily administered treatment course of rifampicin with isoniazid (3RH) as tuberculosis preventive treatment (TPT) in alternative to 6-month isoniazid (6H). There is no data regarding the acceptability and feasibility of using 3RH in Indonesia yet.

We presented our experience of using the 3RH as TPT for household contacts of all ages, funded by TB REACH wave 7.

Intervention or response: Three primary health care (PHC) facilities in Yogyakarta Province were selected for the initial 3RH implementation. HHCs of microbiologically confirmed TB cases were screened for TB symptom, underwent chest x-ray (CXR) and sputum collection as indicated. TST was performed for HHCs aged above five. 3RH was offered for those meeting eligibility criteria for TPT.

Under the coordination of district TB programmer, we conducted training for the PHC TB teams and provided two dedicated nurses to assist the TB programmers in conducting contact investigation, including treatment initiation, follow-up, and evaluation post treatment completion. All data was reported in the national TB information system.

Results/Impact: Of 54 index cases screened, 198 HHCs were screened for TB. Of this, 64 (32.3%) were eligible for TPT and 56 (87.5%) commenced TPT. 8 (12.5%) refused TPT as they reported not feeling ill.

Of all HHCs commenced TPT, 52 (92.8%) completed, and 4 (7.2%) did not for reasons: drug adverse reaction and died of other causes.

Of the HHCs commenced TPT, 43 (76.7%) and 28 (50%) were screened for TB 6 and 12 months after TPT completion. No TB case was found in both events.

Conclusions: The use of 3RH was overall feasible, acceptable, effective in preventing TB. Yet, additional efforts to raise TB awareness, also improvement in PHC's ability to adequately manage adverse drug reactions, were keys to having higher coverage of completed TPT.

EP-17-766 Comparison of yield from symptomatic W4SS screening and mass mobile X-ray in schoolchildren in Lagos, Nigeria

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Background and challenges to implementation: Globally, tuberculosis causes significant morbidity and mortality among school age children, many of which may go undetected. There is a crucial need to develop effective strategies to improve case detection in this group. This study compared the yield from symptomatic (W4SS) and mass mobile X-ray screening in similar groups of schoolchildren during an active case finding activity in Lagos, Nigeria.

Intervention or response: Schoolchildren between the ages of 6-15 were randomly assigned to either a symptomatic screening using the WHO 4 symptom screening checklist, administered by trained community volunteers or a CAD enabled chest X-ray fitted in a mobile van. This study was over a period of 6 months. Presumptive TB cases were identified and sputum samples were then taken from them to be analyzed using the GeneXpert MTB Rif assay. The presumptive TB cases who couldn't produce samples or returned negative from GeneXpert had their chest X-ray films reviewed and then sent for a clinical assessment. Children who are already on TB treatment were exempted. Consent were taken from their parents through the school and assent was given by the participants prior to the activity. The yield, number needed to screen and number to test were calculated for both groups.

Results/Impact: A total of 13,384 schoolchildren were screened over the 6 months period. 2,287 of them were screened by the CAD mobile X-ray while 11,097 had the W4SS checklist administered on them. The W4SS group identified 1143 presumptives while the CXR group identified 129 with active TB yield of 70 and 15 respectively. The W4SS recorded (NNS 158, NNT 16) while the CXR group had (NNS 152, NNT 9).

Group	Screened	Presump	evaluated	TB cases	NNS	NNT
W4SS	11097	1143	1143	70	158	16
CXR	2287	129	129	15	152	9

Conclusions: Active case-finding based on CXR was preferable as the yield was better than the W4SS. Therefore, less cases would be missed and would be worthwhile to invest more in the mobile CXR.

EP-17-767 The negative and positive predictive value of IGRA for development of TB disease among a TST positive population

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Background: In the Netherlands, Tuberculosis (TB) infection (TBI) screening guidelines recommends using a two-step screening approach (tuberculin skin test (TST), with confirmatory interferon-gamma release assay (IGRA)) to identify persons with TBI. However, the sensitivity and specificity of both TST and IGRA are suboptimal. To evaluate the accuracy of the two-step approach, we assessed the risk and associated factors of developing TB disease among TST-positive individuals with negative and positive IGRA test results.

Design/Methods: We used retrospective cohort data from persons screened for TBI by both TST and IGRA (2007-2010). We matched the cohort data, including demographics, TBI screening results, and follow-up actions, to data from the National TB Register (NTR)-Osiris to identify persons who developed TB disease post-TBI screening (until 2019). We excluded persons receiving TPT following TBI screening (n = 556). We first determined the overall negative predictive value (NPV) and positive predictive value (PPV) of IGRA and used Cox regression analysis to assess factors (gender, age, Dutch- or foreign-born, BCG vaccination status, TB risk profile and time in endemic area) associated with the development of TB disease.

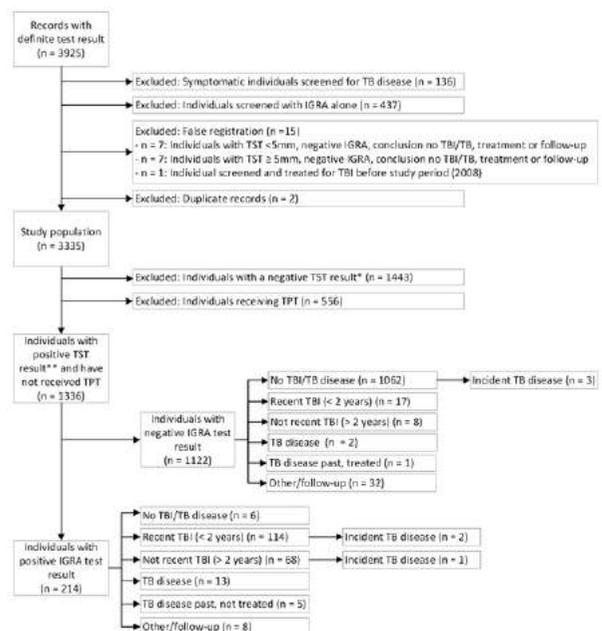


Figure 1. Study population.

*TST < cutoff for TBI following TST guidelines 2005;

**TST ≥ cutoff for TBI following TST guidelines 2005.

TB = tuberculosis; IGRA = interferon-gamma release assay; TST = tuberculin skin test; TBI = tuberculosis infection; TPT = tuberculosis preventive treatment.

Results: Of persons screened for TBI, 1336 (40.1%) had a positive TST, of whom 214 (11.3%) and 1122 (59.3%) had a positive and negative IGRA test result, respectively. In total, 6 (0.2%) persons developed TB disease during follow-up (Figure 1). The PPV and NPV of IGRA were 1.4% (95% CI = 0.4 – 3.6) and 99.7% (95% CI = 99.3 – 99.9), respectively. Furthermore, persons with a positive IGRA test result have a higher risk of developing TB disease compared to IGRA negative persons (Hazard ratio: 5.58 (95% CI: 1.13 – 27.6)).

Conclusions: The preliminary findings of this study show that using the two-step approach for TBI screening identifies those TBI patients that are at the highest risk of progressing to TB disease.

EP-17-768 Improving uptake of tuberculosis preventive therapy among contacts of TB patients in Nigeria

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Background and challenges to implementation: Nigeria still maintains her position of being 6th among high Tuberculosis burden countries globally. The country is high burden for TB, MDR-TB, TB/HIV. Efforts driven by the National programme (NTP) to improve case finding yielded results as treatment coverage rate gradually increased from 24% in 2018 to 45% in 2021 (207,785 cases).

Despite the achievements with case detection, the NTP lagged in the aspect of identifying and placing contacts of index TB cases on TB preventive therapy (TPT) with only 25% of the UNHLM target achieved in 2020, this is because the activity is majorly passive and depends on bringing the clients to facility for TPT initiation. The NTP in addressing low TPT uptake in 2021 integrated TPT into active contact tracing activities, this study describes the results of this intervention.

Intervention or response: By the end of 2020 the NTP operationalised active contact tracing by providing transportation allowance (stipends) for visitation of bacteriologically diagnosed index TB patients at home for contact evaluation. Health workers conducting the contact tracing were trained to provide TPT using programme tools. Contacts eligible for TPT are identified during home visits and are placed on TPT.

Results/Impact: A gradual increase in total number of contacts placed on TPT was observed as a 7year quarterly trend of contacts placed on TPT shows 522% increase from Q1 2021 (2497) to Q1 2022 (15,539).

At the end of 2021 about 17,519 were placed on TPT, which is about 80% increase when compared to the baseline of 9730 in 2020.

Conclusions: Integrating TPT into active contact tracing interventions eliminates the indirect cost incurred by clients while receiving TPT services in the health facilities, it increases TPT uptake and additionally improve capacity within the community for TPT delivery. Programmes with low TPT uptake can significantly drive uptake by integrating TPT into active contact tracing.

EP-17-769 Efficacy and safety of a new one-month regimen of rifapentine plus isoniazid to prevent tuberculosis in Chinese silicosis patients: a pilot study

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Background: Tuberculosis preventive treatment (TPT) is now a critical component of the End TB Strategy. In this pilot study (NCT03900858), an innovative one-month, three-times-weekly rifapentine and isoniazid (1H3P3) regimen was designed to be evaluated for its efficacy, safety and completion rate among Chinese silicosis patients.

Design/Methods: Male silicosis patients without HIV infection, aged 18 years to 65 years, with or without latent TB infection, were received 1H3P3 regimen (400mg isoniazid and 450mg rifapentine 3 times a week for 4 weeks). All enrolled individuals will be actively followed up for active diseases, adverse events of TPT and completion of regimen for 3 years. The safety and efficacy were compared with 3RPT/INH group and observation group in our previous trails in silicosis patients (NCT02430259).

Results: A total of 452 adults with silicosis were screened; 279 eligible participants were enrolled and 241 provided informed consent. All eligible participants had media age of 56 (IQR 52-60) years. Of the included participants, 57 (23.7%) in silicosis stage 1, 84 (34.8%) in stage 2 and 100 (41.5%) in stage 3. A total of 151 (62.6%) had BCG scar and 72 (29.9%) had positive QuantiFeron Gold. There were 82 adverse events from 66 (27.4%) participants and only one (0.4%) participant had Grade 3 or 4 adverse event. Two (0.8%) participants had flu-like systemic drug reactions; three (1.2%) experienced hepatotoxicity. The completion rate of the 1H3P3 was 92.1% (222/241). Four (1.7%) participants were diagnosed with active TB, three of them were bacterial confirmed cases. In the intention-to-treat analysis, the cumulative active TB rate was 1.7% (4/241). The safety profile and completion rate of 1H3P3 was significantly superior to 3RPT/INH and the efficacy was similar.

Conclusions: This innovative short-course 1H3P3 TPT regimen is both safe and efficacy among silicosis patients. Further work is necessary to test the regimen in other high-risk population.

EP-18 Tuberculosis laboratory services: challenges and solutions

EP-18-771 TB-LAMP for expansion of diagnostic access: planned and purposeful implementation

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Background and challenges to implementation: No single diagnostic test currently satisfies a country's demand for a rapid, affordable, and user-friendly platform. Given the vast population and endemic nature of TB in Nigeria, it became imperative to expand the diagnostic platforms. Accordingly, TB LAMP was piloted and rolled out by the National TB Control Program in collaboration with KNCV Tuberculosis Foundation Nigeria to close testing gap and complement the GeneXpert. We aimed to assess the impact of the roll out of TB-LAMP in Nigeria.

Intervention or response: A pilot study was conducted prior to roll-out to ascertain the appropriateness of the platform for TB diagnosis in Nigeria. Eleven TB LAMP platforms were rolled out across 11 states by KNCV in February 2021. Site selection and machine installation was guided by the magnitude of unmet needs, including power issues and absence of alternative diagnostic tools in the community.

Ad hoc staff were recruited and trained in human resource challenged sites on the use of equipment to provide additional support. Awareness creation among clinicians on the new technology and need for sample referral was done.

Results/Impact: Between February 2021 and March 2022, a total of 37,354 samples were tested and 2,554 MTB positive cases were diagnosed. Samples that were positive for MTB were tested using Xpert to determine the RIF status of the detected strain. A total of 26 RIF resistant TB was recorded representing a 7% TB yield.

Conclusions: TB-LAMP has been very useful in prompt processing of large numbers of samples from community intervention due to its high throughput of 70 samples per day.

Prompt referral of positive results from TB-LAMP to Xpert to confirm the RIF status of samples highlighted the complementarity of two equipment for the Community outreaches in DR-TB endemic locations.

EP-18-772 Strengthening institutional capacity for improved TB diagnostics laboratory services in the Kyrgyz Republic

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Background: Kyrgyzstan is among the 30 countries with the highest rates of multidrug-resistant TB (MDR-TB). According to the 2020 Global TB Report, the estimated MDR-TB rates for new and retreatment cases are 29 percent and 60 percent, respectively. The country faces several challenges that hinder improving TB case detection and addressing the root causes of MDR-TB in the country.

Design/Methods: The USAID Cure Tuberculosis project, led by JSI and in partnership with USP, is providing technical assistance to build the capacity of TB laboratory networks in the Kyrgyz Republic to meet its TB reduction targets. As part of the intervention, the project conducted quantitative lab assessments and qualitative interviews of 60 national, regional, and district level TB stakeholders.

Results: Critical findings include gaps in line-item costing which prevent the government from having visibility to fully fund all the elements of a sustainable TB program. More than 60% of key informant interviews indicated lack of proper funding and appropriate funding methods as underlying challenges within the TB network.

Conclusions: Critical systems strengthening interventions including developing a National Laboratory Strategic Plan that contains detailed cost of ownership information is critical to securing and sustaining funding for the TB diagnostic network.

EP-18-773 Comparing customized workshop-based and facility-based models of TB SLMTA approach for mentoring labs towards ISO-15189 accreditation: experiences of mentoring 6 TB labs in India

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Background: FIND in collaboration with India's National TB Elimination Programme (NTEP), under CDC project, provided technical assistance to TB laboratories for improving quality management systems (QMS) and achieve ISO-15189 accreditation through National Accreditation Board for Testing and Calibration Laboratories (NABL) in India.

TB laboratories mentored using a customized Strengthening TB Laboratory Management Towards Accreditation i.e. TB SLMTA approach.

Five labs were mentored during Feb-Nov'2019 using workshop-based model. In Feb'2020, one more laboratory was included in the project. However, due to Covid-19 pandemic and associated challenges, this lab was mentored using facility-based model from Mar-Dec'2020 period.

Design/Methods: Workshop-based TB SLMTA model included stakeholders meeting to explain needs, mentoring process and challenges, prior to mentoring. Mentoring included three workshops, onsite visits and offsite support.

In customized facility-based model, site was explained the process and mentoring was done remotely through weekly online sessions, monthly virtual site visits and offsite support. Staff was trained onsite to perform in-house calibration of equipment.

In both the approaches, staff underwent upfront Internal auditors' and QMS training. They underwent baseline assessment using FIND's TB QMS Harmonized Checklist.

Gaps identified in assessment were converted into simple/complex improvement projects. Progress was monitored for various quality parameters. Documentation was strengthened including for risk management and contingency plans.

All sites were guided for conducting Internal Audits, Management Review Meeting, NABL application and resolving non-conformities from NABL assessments till accreditation.

End line assessment was done prior to submitting NABL application.

Results: Overall, baseline scores were low i.e. 36% for workshop and 48% for facility based models. With mentoring, in both models, endline scores improved significantly to >85%. (Fig:1)

This helped all six sites to achieve ISO-15189 accreditation.

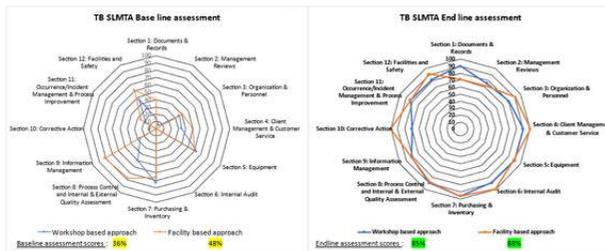


Figure. Comparison of baseline and end line assessment scores for different quality system essentials between workshop and facility-based models of TB SLMTA approach.

Conclusions: Both workshop-based and facility-based models of customized TB SLMTA approach are equally effective for mentoring TB labs towards ISO 15189 accreditation under different circumstances.

EP-18-774 Improving quantification of tuberculosis laboratory supplies by using standardized quantification tool in Ethiopia

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Background and challenges to implementation: A well-functioning laboratory system is essential for the programmatic and clinical management of tuberculosis (TB). However, TB laboratory service in Ethiopia has several challenges that affect the quality and quantity of services at various levels of the laboratory network. One of these challenges is laboratory supply chain management which is unresponsive to the unique features of TB laboratory services. Due to the lack of standardized tools and the complexity of lab commodities, there was difficult of conducting supply quantification. There were no exhaustive product lists available and those available were not standardized. This caused extended delays in finalizing the quantification process.

Intervention or response: In response to this, USAID funded Global Health Supply Chain Program-Procurement and Supply Management (GHSC-PSM) project in collaboration with Ethiopian Public Health Institute (EPHI) supported the development of a standard excel-based quantification tool for all TB laboratory products. The activity began by organizing a series of workshops to standardize the list of products by category of tests and determine the quantity of supplies/reagents per test/parameter.



Results/Impact: The quantification tool enabled TB supplies to have a comprehensive list of products in each category of test, helped to minimize missing supplies during quantification, simplified the overall quantification and process and improved the quality of data. It also shortened the lengthy process of quantification and write-up which was the main challenge during previous years. Currently, the data generated by the tool is used for supply planning and ordering TB laboratory supplies.

Conclusions: The quantification tool has improved the process overall TB laboratory supplies quantification process in Ethiopia. Therefore, further devolvement using an advanced tool with a supply plan is recommended to scale up the use of the tool for other laboratory programs.

EP-18-775 TB diagnostic network assessment: a critical input to achieve TB goals and targets in Tanzania

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Background and challenges to implementation: Tanzania is among the 30 high-burden TB countries globally. A major challenge has been the Tanzania TB diagnostic network's ability to meet the National Strategic Plan (NSP) goals and targets: only 37,312 (44%) among 84,800 pulmonary TB cases were bacteriologically confirmed in 2020, and systems delays prevent timely diagnosis and results feedback.

Intervention or response: IDDS and Tanzania's National TB and Leprosy Program performed a Tuberculosis Diagnostic Network Assessment (TB DNA) in 2021. The TB DNA reviews ten core competencies for TB di-

agnostic networks. Government and NGO stakeholders participated in the TB DNA's self-assessment process to review the program. Findings from the self-assessment were then verified by an external team, which then visited 35 diagnostic and clinical facilities in 12 regions. The TB Net tool was used to apply semi-quantitative scoring to different aspects of the diagnostic network, describe current capabilities, and identify key improvement areas.

Results/Impact: The findings were categorized by the ten core capacities of the TB Net tool. The assessment noted the availability of an organized and structured TB diagnostic network with clearly defined roles for each level, strong collaboration between HIV and TB programs, and relevant, up-to-date laboratory network policies and guidelines. However, these policies and guidelines, including the integrated sample referral guidelines, were not fully implemented at all levels. There were also challenges in providing free TB diagnostic services for chest X-ray. Although TB diagnostic data were collected in standardized tools, there was no evidence of data review and analysis. Biosafety and safety practices scored lowest of all core capacities.

Conclusions: The Tanzania TB diagnostic network can perform essential clinical and public health functions and link those affected by TB to testing and care. However, operational and coordination challenges must be addressed for the TB diagnostic network to support achievement of all NSP goals and targets.

EP-18-776 Rapid drug susceptibility testing for fluoroquinolone resistance in rifampicin-resistant TB patient using MTB/XDR assay

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Background and challenges to implementation: Pakistan is 5th among high TB and DRTB burden countries. RR-TB patients are offered ambulatory treatment, and fluoroquinolone (FQ) resistance is high among RRTB patients. A fresh specimen is transported for LPA/DST to the laboratory on the day of enrollment. The patient is started on second-line treatment based on clinical judgment. In routine, treatment sites receive an LPA report within 10-14 days and the patient is advised to return to the treatment facility if treatment modification is required.

In 2021, WHO endorsed a cartridge-based, fully automated real-time PCR assay to detect FQ and isoniazid (INH) resistance. The test is recommended as a reflex test to diagnose resistance in MTB-positive specimens.

We conducted this prospective study to compare interpretable results of FQ and INH resistance by MTB/XDR and LPA.

Intervention or response: After informed consent, the specimen was collected from TB patients diagnosed on MTB/RIF. Specimens were sent to the national TB reference laboratory. Only samples, 4ml or more in volume, were processed further. The samples were homogenized and divided into three aliquots. One aliquot was used for Xpert MTB/RIF only if MTB was detected with interpretable RIF results, MTB/XDR was tested on the second aliquot, and the third aliquot was processed for LPA and culture. Phenotypic DST was performed on MTB isolates.

Results/Impact: Of patients enrolled, 499 samples submitted had adequate volume, and MTB was detected in 412 (82.6%). Of specimens tested by MTB/XDR (n=412) and LPA (n=356) respectively, MTB was detected in 96.8% compared to 94.4% ($P=.103$), interpretable results for FQ were reported in 94.9% and 83.4% ($P=.001$), for INH in 95.1% and 94.1% ($P=.540$). Results were consistent in rifampicin-sensitive and resistant groups (Figure 1).

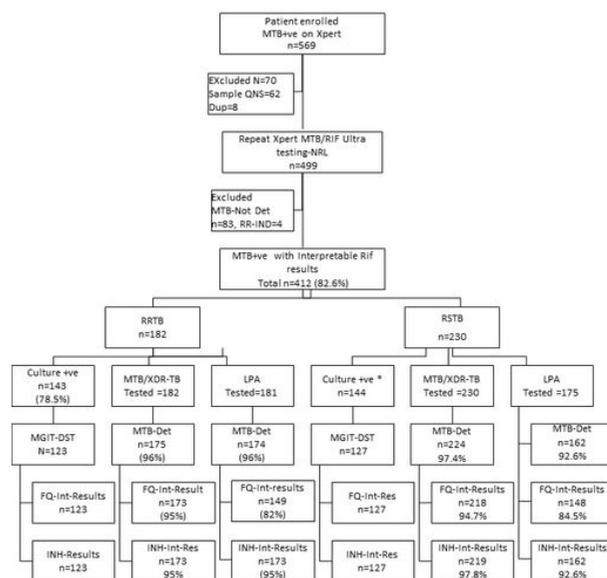


Figure 1. Flow diagram showing TB patient tested by MTB/XDR, Line Probe assay, and Phenotypic DST (MGIT 960).

Conclusions: MTB/XDR assay reported significantly higher FQ results than LPA. Effective treatment based on rapid FQ results will be possible when testing is offered close to the point of care.

EP-18-777 Scaling up access to rapid tuberculosis diagnosis in Uzbekistan to support National TB Program (NTP) strategy of shifting to genexpert as the primary diagnostic test

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Background and challenges to implementation: According to WHO (2019), RR/MDR-TB prevalence among new cases is 12%, and among previously cases is 22%. Only 2,060 RR/MDR-TB were treated against estimated 3200(64.4%). With 220 GX modules the total testing capacity in 2019 was about 94% compared to testing needs. Nevertheless, the percentage of TB suspects tested with Xpert MTB/Rif as the initial diagnostic test was only 63%.

Intervention or response: USAID Eliminating Tuberculosis in Central Asia (Activity) helped NTP to identify gaps with access to Xpert MTB/Rif testing through TB laboratory network assessment. Testing capacity to cover diagnostic needs was estimated as 110000 tests annually and potentially could be covered by 94% with existing modules. Due to limited geographic accessibility of available instruments, it was challenging to increase diagnostic coverage for some remote districts. Assessment included analysis of diagnostic demand, testing capacity and access which resulted in “GeneXpert Network Optimization Roadmap.”

The document provides an estimate of the number of modules and cartridges required for universal coverage. To close the gaps with testing access in several remote areas, Activity procured and installed additional 46 modules.

Results/Impact: Spatial analysis identified that testing access could be sustained if GeneXpert testing facility is situated within 50 km of driving distance. New 46 modules were strategically placed to avoid traveling distance more than 50 km from PHC facility. Some of already available 68 modules were rearranged accordingly to enable universal access for country’s population of 35 million to rapid TB diagnostics.

As a result of this reorganization, over 100 inefficient microscopy laboratories were transformed to sputum collection points.

Conclusions: Thoroughly planned lab assessment is an essential precursor for lab network expansion and rational deployment of technologies. The Activity and NTP

will continue improving the access to and appropriate use of the molecular testing network in line with country strategy and needs.

EP-18-778 Impact of GeneXpert sites optimization strategy on diagnostic error rates in Nigeria

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Background and challenges to implementation: In 2016, Xpert MTB/RIF testing was adopted as the first point of diagnosis for Tuberculosis (TB) in Nigeria. However, varying environmental conditions such as high temperature and pervasive power issues impact the functionality of the machine resulting in increased errors and invalid test results, negatively contributing to low detection of TB Cases in Nigeria. KNCV Tuberculosis Foundation Nigeria, through funding from the United States Agency for International Development (USAID) optimized GeneXpert sites in the 14 TB LON 1 and 2 states. The aim of this study is to showcase the impact of GeneXpert Optimization strategy on the error rate across optimized facilities.

Intervention or response: In this study, we analyzed the proportion of GeneXpert errors recorded in health facilities between February 2020 and June 2021. Optimization strategies, implemented from August 2020 to June 2021, included provision and maintenance of High-capacity solar Panels System (HCSPs), Inverters and Inverter batteries, and air conditioners. 84 out of 185 health facilities with functional GeneXpert machines were optimized (45% coverage).

Results/Impact: Prior to optimization, the monthly error rate across the facilities rose as high as 6% in some months, exceeding the acceptable limit of 5%. However, with the implementation of GeneXpert optimization, the error rate dropped to 3% in some months (averaging at 3.9%) and never exceeded the 5% upper limit throughout the implementation period.



Figure. geneXpert monthly error rate across selected facilities in TB LON 1 & 2 regions.

Conclusions: There was reduction in the error rate, and it was sustained throughout the implementation period. This demonstrated that Continuous optimization and maintenance of GeneXpert facilities will yield lower error rates, which will reduce cartridge wastages and ultimately improve the efficiency of TB diagnosis.

EP-18-779 GeneXpert devices module failure and underutilization: the major changes in Ethiopia GeneXpert MTB/RIF assay rollout: a retrospective study

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Background: In Ethiopia, GeneXpert MTB/RIF assay was adopted in 2014, following WHO policy recommendation for eligible groups of patients and expanded to Xpert for all presumptive TB cases. Xpert machines module failure and underutilization has been a long-standing challenge in Ethiopia. The root cause of these challenges was not well studied.

This study aimed to determine the utilization rate and associated factors for Xpert module failure and underutilization.

Design/Methods: A retrospective study design was conducted to determine the utilization rate and the associated factors. Out of the total 281 Xpert testing hubs, 145 of them were enrolled in this study.

Retrospective Xpert program data were collected from 2018 to 2021 through GxAlert connectivity solution and verified from health facility GeneXpert registration book. Trained laboratory professionals, clinicians and postal courier were filled the self-administered questionnaire.

Data was double entered and exported into IBM statistical package for social sciences (SPSS) version 20.0 for the analysis. Utilization was categorized as underutilized ($\leq 50\%$ performance), and well utilized ($\geq 51\%$).

Descriptive statistics were calculated for Xpert sites distribution and their performance. Chi-squared tests and multiple logistic regression model were conducted to determine factors associated with Xpert MTB/RIF assay utilization and its independent association, respectively.

Results: In this study 54.5% (79) of them were underutilized, while 45.5% (66) of them were well utilized. The four years calculated positivity, unsuccessful testing and modules failure rates were 11.4%, 9.5% and 25.4%, respectively. Lack of clinician's awareness on Xpert for all approach (AOR = 2.1; 95% CI (1.1 - 4.2), $p = 0.035$) was significantly associated with Xpert machine utilization. Delayed calibration and irregular preventive maintenance were significantly associated with module failure rate.

Conclusions: Health care providers sensitization on TB diagnostic algorithm, and timely calibration and regular maintenance need to be considered to address underutilized and frequent modules failure, respectively.

EP-18-780 Gloom and boom - the real impact of COVID-19 on GeneXpert TB testing volumes

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Background: The COVID-19 pandemic in 2020 focused global attention on a single disease entity, raising fears that health service disruptions could result in reversal of progress made in the fight against TB. Health centers, laboratories, and diagnostic instruments were diverted to the COVID-19 response and lockdowns made it difficult to access TB testing services. Some countries reported drastic decreases in GeneXpert TB testing volumes. It is assumed that these declines will be seen across all countries.

We look at the actual impact of COVID-19 on GeneXpert TB test volumes across 6 countries to counterbalance widely-held fears with a real-world perspective.

Design/Methods: GxAlert (SystemOne) was used to extract 2019 and 2020 TB testing data from GeneXpert instruments in 6 randomly chosen countries: 3 African/1 European/2 Asian. Data was imported into excel for descriptive analysis.

Results: Analysis included 1,396 GeneXpert instruments in 2019 and 1,554 instruments in 2020 across 6 countries. TB test numbers increased from 1,382,270 in 2019 to 1,554,753 in 2020. Average instrument utilization rates were 31.6% and 29.4% for 2019 and 2020 respectively. 2/6 countries showed a decrease in 2020 (-9%;-29%) compared to 2019 test volumes; 4/6 countries, 3 African, 1 Asian, showed an increase in TB test volumes (average 45%)(Figure 1).

Stratified by quarter for 2020, 5/6 countries showed an average decline of 35% in testing volumes in Q2. All countries showed improvement in test volumes in Q3.

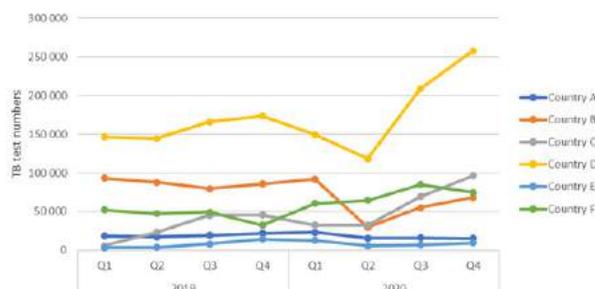


Figure 1. TB testing numbers per Quarter for 2019 and 2020.

Conclusions: Compared with 2019, COVID-19 did not result in the touted “irreparable” declines in overall TB testing numbers ubiquitously. Declines in TB numbers were seen in Q2 2020, as the pandemic boomed, for 5/6 countries, but numbers rebounded in Q3 and virtually returned to normal by Q4.

Unexpectedly, African countries assessed showed an overall increase in TB numbers between 2019 and 2020, probably due to differences in intensity of COVID-19 outbreaks and response strategies.

EP-19 TB diagnostics speed and availability

EP-19-781 Performance of the TB-LAMP assay for the rapid diagnosis of pulmonary tuberculosis in Tunisia

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Background: Rapid diagnosis of pulmonary tuberculosis (PTB) is challenging.

The aim of this study was to evaluate the performance of the LoopampTM MTBC detection kit (Eiken Chemical Co, Japan) for diagnosing PTB in Tunisia, a middle TB incidence country, in comparison with conventional and molecular methods.

Design/Methods: One-hundred-twenty-three pulmonary samples collected from presumptive PTB cases in the National Reference Laboratory for mycobacteria, Tunisia, during the period December 2021 -February 2022, were included in this study.

All pulmonary samples were tested by smear microscopy using auramine staining, solid (on Lowenstein Jensen medium) and liquid culture (on Mycobacteria Growth Indicator Tube : MGIT960), Xpert MTB/RIF ultra (Cepheid, US) and TB-LAMP.

Statistical analysis was performed using OpenEpi Version 3.01 software.

Results: TB-LAMP presented a sensitivity and a specificity of 89.30% (CI 95%: 72.8-96.30) and 96.84% (CI 95%: 91.12-98.92), respectively to detect PTB in comparison with culture.

Smear microscopy had a sensitivity of 71.43% (CI 95%: 52.94-84.75) and a specificity of 97.90% (CI 95%: 92.65-99.42) in comparison with culture for diagnosing TB.

In this study, 28.57% of PTB cases detected by TB-LAMP had a negative smear microscopy.

The sensitivity of TB-LAMP for smear positive samples with TB culture positivity was 100.00% (CI 95%: 83.90-

100.00). For smear negative samples with a positive TB culture, the sensitivity of TB-LAMP was 62.50% (CI 95%: 30.57-86.32).

The GeneXpert MTB/RIF ultra presented a sensitivity of 96.43% (CI 95%: 82.30-99.37) and a specificity of 95.80% (CI 95%: 89.67-98.35) compared to the culture. The overall agreement between TB-LAMP and Xpert MTB/RIF ultra was very good in this study (K=0.89).

Conclusions: Our results showed that TB-LAMP could replace smear microscopy for diagnosing PTB patients or could be used as add on testing following negative smear microscopy cases in Tunisia.

EP-19-782 Validating proficiency testing panels for the new TruenatTM TB assays in India using CDC's dried tube specimen technology

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Background: For any diagnostic technology, External Quality Assurance (EQA) program is critical to confirm that the entire testing process (pre-analytical, analytical, post-analytical) is quality assured.

In India, FIND supported introduction of a EQA program for GeneXpert[®] TB testing under National TB Elimination Program (NTEP) leveraging Proficiency Testing (PT) panels manufactured using CDC's Dried Tube Specimen (DTS) technology.

NTEP has incorporated TruenatTM, recommended by WHO for detection of MTB and Rif resistance, into its diagnostic algorithm which has been deployed at >1500 sites across the country.

FIND validated PT panels for TruenatTM assays using CDC's DTS technology at International Center for Excellence in Laboratory Training (ICELT) lab located in National TB Institute, Bangalore.

Design/Methods: Six well characterized M.tb isolates were selected, sub-cultured and chemically inactivated in Aug' 2019. Non-viability was confirmed by sub-culturing the isolates in liquid culture (MGITTM) for two negative cycles (84 days) in Nov' 2019. Inactivated stocks were stored at 4°C.

They were aliquoted in 1:50 & 1:100 dilutions in Apr' 2021 and 10 aliquots of each were subjected to testing on TruenatTM machines using MTB and MTB Plus assays.

Qualitative & quantitative analyses was done, and their mean & standard deviations (SD) were derived for positive specimens. SD within 3 & Coefficient of Variation (CV) within 10- were considered as statistically significant for panel preparation. Further, M.tb positive isolates were tested with MTB-RIF Dx assay and analysed for concordance.

Results: Qualitative results of all six isolates were concordant with expected results. Quantitative results for both dilutions were statistically significant for MTB and

MTB plus assays i.e. SD value ranging from 0.22 to 2.43 and CV ranging from 1.10 to 9.27 (Fig.1).

Conclusions: DTS technology can be used for manufacturing PT panels for Truenat™ TB assays.

EP-19-783 Effectiveness of TB-LAMP in diagnosis of tuberculosis in persons affected by HIV in Cameroon

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Background and challenges to implementation: The diagnosis of tuberculosis (TB) is still challenging in primary care settings particularly in person living with HIV. Currently, the Xpert MTB/Rif assay is the point of care WHO recommended rapid diagnosis (WRD) test for TB diagnosis in person living with HIV.

However, this test remains difficult to implement in resource limited settings. Hence, the loop-mediated isothermal amplification (TB-LAMP) that is another WRD test in non-HIV person is applicable in peripheral laboratories. The aim of this work is to evaluate the performance of TB-LAMP test to diagnose TB in HIV-presumptive TB cases.

Intervention or response: We conducted a retrospective cohort study using 668 files of persons who were found HIV positive or negative from May 2021 to October 2021 in Jamot Hospital, Baptist Hospital of Mutenguene and Centre Pasteur of Cameroon.

Relevant information from HIV and TB status were collected. Identification was performed retrospectively with TB-LAMP assay, smear microscopy, culture and the Xpert MTB/Rif. Multivariate analysis was performed by R software.

Results/Impact: Performance evaluation among persons affected with HIV shows that TB-LAMP has a good sensitivity (80%, 95% CI: 68-89 and specificity (88%, 95% CI: 81-93). Microscopy presented a sensitivity of 52% (95% CI: 39-64) and a specificity of 94% (95% CI: 89-98) while Xpert MTB/Rif has a sensitivity of 91% (95% CI: 81-96) and a specificity of 91% (95% CI: 85-95). TB-

LAMP has a higher sensitivity compared to microscopy but a similar specificity. There was no significant difference between TB-LAMP and Xpert MTB/Rif. The sensitivity (89%, 95% CI: 79-96) and specificity (98%, 95% CI: 92-100) of TB-LAMP among non-HIV persons were similar to those of persons affected with HIV.

Conclusions: TB-LAMP test displayed good performance in TB diagnosis for persons living with HIV. This test could be therefore recommended for the diagnosis of TB in HIV positive person.

EP-19-784 Roll out of Truenat assay in Nigeria: early experiences and lessons learned

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Background and challenges to implementation: Early and improved tuberculosis (TB) case detection as well as expanded capacity to diagnose drug resistant TB are global priorities for TB control. High mortality of DR-TB highlighted the urgency for rapid diagnostic methods. Through concerted efforts of USAID and Stop TB partnership, Nigeria successfully introduced 38 Truenat testing platforms for expansion of TB and RR-TB diagnostic access particularly in underserved rural communities. This abstract describes the implementation processes and lesson learned for other countries to emulate. **Intervention or response:** Pre-implementation activities entailed getting the buy-in of NTP and other stakeholders followed by site assessment, selection, and infrastructural upgrade. Thereafter, trainings and machine installations were conducted. During the implementation stage, health care workers and TB stakeholders were sensitized to create demand for the test and facilitate sample logistic, prompt result retrieval across facilities as well as linkage to treatment. Testing across few sites commenced in December 2022. Mentoring and supervisory visit was also part of the hand-holding activities for continuous quality improvement. Molbio local agents provided service support to sites as needed.

Results/Impact: A total of 11,661 sputum samples were processed between January and -March 2022 using 38 Truenat Duo platforms, giving an average utilization rate of 52%. Out of these, 1,147 (10%) was positive for MTB. Utilization rate after sensitization of HCW (from 25th Jan to 28th February) was 44%, 50% and 64% in January, February and March respectively. The average rate of unsuccessful tests was 4% (452/11,661), which was largely due to incomplete liquefaction of samples.

Conclusions: Involvement of NTP from onset played a remarkable role in the successful implementation of Truenat test. Intensive training of lab staff including mentoring and supervisory visit contributed to the seamless implementation especially the low rate of unsuccessful tests, while health care workers sensitization workshop improved utilization rate.

EP-19-785 Support package for Truenat™ MTB-RIF Dx assay implementation at the peripheral level

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Background and challenges to implementation: Truenat™ MTB-RIF Dx assay is being implemented for the first time at the peripheral level in nine countries led by the Stop TB Partnership and supported by USAID's Infectious Disease Detection and Surveillance (IDDS) project with the aim to decentralize and provide rapid molecular diagnostic testing near the point of care. End-user training for Truenat™ has been provided to laboratory technicians with minimal expertise using rapid molecular diagnostic tools. Additional support for the end users is critical to ensure successful implementation.

Intervention or response: IDDS developed a support package with key objectives to identify low performing labs and provide ongoing technical support and mentorship. The package includes two components: External Quality Assessment (EQA) to assess proficiency of laboratories; and recruitment of TB rapid molecular diagnostic subject matter experts (superusers) to provide mentorship and supervision through supportive visits.

Results/Impact: The Truenat™ support package was piloted in Zimbabwe in Q1 2022. All 20 sites were enrolled in three cycles of MTB-RIF EQA (SmartSpot Quality). In addition, 14 superusers were recruited and trained during a three-day workshop that included theoretical and practical hands-on Truenat™ training. Feedback was solicited from the participants at the end of the workshop. Recommendations included: extend the time for the practical lab workshop; host a practice session for EQA reporting; create job aids and standard operating procedures; and provide a channel for end users to share challenges and best practices.

Conclusions: Ongoing support for the introduction of new tools is important to ensure success. The effectiveness of the Truenat™ support package to improve performance is monitored through collection of key performance indicator data and performance reports.

Based upon the pilot feedback in Zimbabwe, the implementation support package was modified and was useful to identify low performing labs and help them overcome challenges.

EP-19-786 PCR-ELISA technique for rapid and simple detection of Mycobacterium tuberculosis rifampicin resistance in sputum: a proposal for use in high prevalence countries

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Background: Drug-resistant TB remains a public health problem due to simultaneous resistance to isoniazid (INH) and rifampicin (RIF). Peru has a high prevalence of MDR-TB incidence cases in America (2016-2020). Molecular methods to detect drug resistance need special infrastructure and highly trained personnel. The development of a rapid and low-cost technique is necessary to use.

We present the PCR-ELISA technique as an alternative that will detect resistance to RIF quickly, easily, and economically. This work presents the standardization and evaluation of a PCR-ELISA for the detection of rifampicin resistance mutations.

Design/Methods: A PCR-ELISA was standardized to detect the following changes: H445Y, H445D, and S450L, which are of high frequency in Peru generating resistance to RIF. Different parameters were optimized: hybridization temperatures, hybridization buffer stringency, and probe concentration, among others. The sensitivity, specificity, and Cohen's Kappa index (k) of the technique against GenotypeMDRTBplus v2 (reference method) were evaluated using 20 sputum samples in a pilot assay. The k-value was calculated with the SPSSv25 software.

Samples	No. of crossings per BK	Concentration of DNA	Absorbances (O.D.=450nm)			Resistance profile	
			H445D	H445Y	S450L	GENOTYPE	PCR-ELISA
M2	3+	1.60 ng/µL	0.05	0.177	0.486	Sensible	Sensible
M4	2+	3.26 ng/µL	0.016	0.087	0.211	Sensible	Sensible
M6	3+	1.58 ng/µL	0.075	0.233	0.844	Resistant	Resistant
M8	3+	1.35 ng/µL	0.085	0.22	0.696	Resistant	Resistant
M10	2+	0.085 ng/µL	0.032	0.101	0.488	Resistant	Sensible
M12	2+	3.03 ng/µL	0.058	0.172	0.795	Resistant	Resistant
M14	1+	3.40 ng/µL	0.03	0.127	0.147	Resistant	Sensible
M16	2+	4.04 ng/µL	0.041	0.152	0.646	Resistant	Resistant

* Controls (+): Absorbance of the probes (450 nm): H445D (0.321), H445Y (0.651) and S450L (1.118)

Table. PCR-ELISA results of 8 selected samples analyzed by pilot assay. The results of smear microscopy, DNA concentration, absorbance of the 3 probes and resistance profile between PCR-ELISA vs GenotypeMDRTBplus are shown.

Results: PCR-ELISA was optimized for the detection of resistance mutations, achieving a detection limit of 400 pg for H445D and H445Y probes and 40pg for the S450L probe. The technique had a specificity of 100% and a sensitivity of 86.7%. Two mutations S450W and L452P were found, which were not detected by the system. In the pilot assay, a “good agreement” ($k=0.737$) was obtained between both techniques.

Conclusions: A PCR-ELISA was standardized for the detection of the 3 more frequent mutations associated with resistance to RIF simultaneously, the most frequent change detected was S450L.

It is necessary to validate the PCR-ELISA using a large number of samples in order to determine the performance of the test with greater accuracy so that in the near future the test can be used by health laboratories at the first level of care centers.

EP-19-787 Impact of gaps in accessing second line-line probe assay (SL-LPA) testing on enrollment in drug-resistant (DRTB) treatment for rifampicin resistance (RR TB) confirmed cases

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Background: Bangladesh National TB Control Program (NTP) introduced the Line Probe Assay (LPA) to detect the mutations for first line (Isoniazid and Rifampicin) and second line (fluoroquinolones and injectable) anti TB drugs in 2012 and 2017, respectively. As per NTP policy, all the rifampicin resistant (RR) TB cases need a second line-line probe assay (SL-LPA) result to start the Shorter Treatment Regimen (STR). Currently, the SL-LPA is available at five reference laboratories located at national or divisional level.

The objective of this study was to assess the gap in accessing SL-LPA before enrolling on STR in programmatic conditions.

Design/Methods: SL-LPA data from 2017 to 2021 was extracted from the NTP and World Health Organization (WHO) TB annual report and analyzed to determine the percentage of RR TB cases tested by SL-LPA.

Results: A total of 6,156 RR TB cases were detected through GeneXpert™ from 2017 to 2021, but only 3,953 (64.2%) were further tested by SL-LPA. During this period, the rate of SL-LPA for RR TB cases varied from 38.3% in 2017 to 90.9% in 2019. The testing figures declined to 66.1% in 2020 and 50.3% in 2021 presumably due to the COVID-19 pandemic. The remaining RR TB patients enrolled for STR based upon the previous history of treatment.

Conclusions: Despite having five LPA laboratories across the country, the gaps in the SL-LPA test persist possibly due to poor implementation of the diagnostic algorithm, and difficult access due to a weak specimen referral system. NTP should reorient the clinicians, strengthen the specimen referral system, and ensure drug susceptibility testing for at least fluoroquinolones to construct the right regimen for effective treatment. In addition, the decentralization of DST should be considered through the GeneXpert MTB/XDR test.

EP-19-788 Diagnostic performance of the GenoType MTBDRplus VER 2.0 line probe assay for the detection of isoniazid resistant Mycobacterium tuberculosis in Ethiopia

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Background: Isoniazid (INH) resistant *M tuberculosis* (Hr-TB) is the most common type of drug resistant TB and is defined as *M tuberculosis* complex (MTBC) strains resistant to INH but susceptible to rifampicin (RIF). Resistance to INH precedes RIF resistance in almost all MDR-TB cases, across all MTBC lineages and in all settings.

Therefore, early detection and management of Hr-TB is critical to ensure rapid initiation of appropriate treatment, helping to prevent treatment failure, the emergence of additional drug resistance, and progression to multidrug resistant TB (MDR-TB).

Design/Methods: We assessed the performance (sensitivity, specificity, positive predictive value, and negative predictive value) of the GenoType MTBDR *plus* VER 2.0 line probe assay (LPA) in detecting INH resistance among 137 *M. tuberculosis* complex (MTBC) clinical isolates and compared to phenotypic drug susceptibility testing (DST) using the Mycobacteria Growth Indicator Tube (MGIT) system. A total of 62 Hr-TB, 35 MDR and 40 INH susceptible MTBC isolates were evaluated. All isolates were obtained from national drug resistance survey (DRS), which enrolled 2560 TB cases.

Results: The sensitivity of the GenoType MTBDR *plus* VER 2.0 for detecting INH resistance was 77.4% among Hr-TB isolates and 94.3% among MDR-TB isolates. The specificity of the assay for detecting INH resistance was 100%. The *katG* 315 muta-

tion was observed in 71% (n=44) of Hr-TB phenotypes and 94.3% (n=33) of MDR-TB phenotypes. Mutation at position-15 of the *inhA* promoter region was detected alone in four (6.5%) Hr-TB isolates, and concomitantly with *katG* 315 mutation in one (2.9%) MDR-TB isolate.

Conclusions: GenoType MTBDR*plus* VER 2.0 demonstrated superior performance in detecting INH resistance among MDR-TB cases compared to Hr-TB cases. The *katG*315 mutation is the most common INH resistance conferring gene among Hr-TB and MDR-TB isolates.

Additional INH resistance conferring mutations should be evaluated to improve the sensitivity of the assay for the detection of INH resistance among Hr-TB cases.

EP-19-789 Alignment of care seeking behavior with diagnostic availability in health facilities in Nigeria

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Background: Access to TB diagnosis and treatment is key to TB control. A good understanding of care seeking behavior with diagnostic availability is critical to improve TB care. The current study aims to identify the gaps between first point of seeking TB care and location of TB diagnostic services by patients in some states in Nigeria.

Design/Methods: This was a cross sectional study under programme implementation in 14 states, 92 facilities in both public and private sectors as well as primary, secondary and tertiary levels of care from June 2020 to December 2021. These were states and facilities supported under the USAID funded KNCV TB Foundation Nigeria TB LON 1 and 2 project. Proforma was used to collect data on diagnostic availability and questionnaire for where clients first sought care for TB complaints.

Results: For Public facilities: 8 of 14 states (57%) had GeneXpert at the tertiary levels and approximately 2% of primary facilities; 11 of the 14 (79%) states have Smear Microscopy in either secondary or tertiary facilities as well as about $\leq 20\%$ in primary facilities; TB LAMP- tertiary (2, 14%), secondary (4, 29%) and none in primary.

However, respondents often first sought care in the secondary and primary facilities - 12 of 14 states (86%). Only 4 (29%) states had tertiary facilities as the place

where respondents first sought for care. However diagnostics are more at tertiary facilities. More respondents (>50%) first sought care in the private sector. However, there is a lower availability of diagnostics in private sector compared to the public. See Fig 1 and 2.

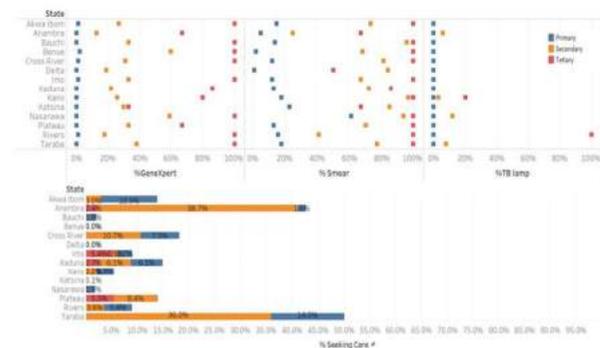


Figure 1: Alignment of diagnostics and where patients first seek care in the public sector

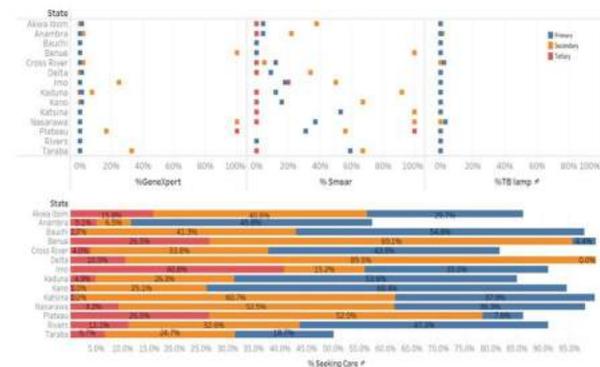


Figure 2: Alignment of diagnostics and where patients first seek care in the private sector

Conclusions: There is a poor alignment of diagnostic services across health sectors and levels of care with patient health care seeking behavior. Addressing this will promote access to TB services, improve TB treatment outcome and control in Nigeria.

EP-19-790 EFFECT of continuous mentorship at TB diagnostic and treatment units in the national HMIS reporting system in Kampala, Wakiso and Mukono

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Background and challenges to implementation: In 2017, the Uganda National TB and Leprosy Program (NTLP) was using Microsoft excel and access for reporting. Confined to a few people involved in its collection at program level, it was difficult to access tuberculosis data

by stakeholders. In October 2017, the USAID Defeat TB activity started strengthening TB care service delivery in Uganda focusing on select central districts of Kampala, Wakiso and Mukono. Reporting submission rate stood at 82% as it was limited to District tuberculosis and leprosy supervisors (DTLS's) who prepared independent reports to NTLP, this resulted in lower reporting rates. Defeat TB activity together with NTLP strengthened national TB reporting in DHIS2 platform and addressed the existing reporting challenges.

Intervention or response: To address these challenges, NTLP streamlined national reporting in DHIS2 by supporting DTLS's, health sub district TB focal persons to train TB focal persons to report into DHIS2, conducted TB data quality assessments, data validation, DHIS2 entry skilling and performance review meeting processes.

Results/Impact: By March 2022, there was a 13% increase (from 82% to 95%) in Oct-Dec 2017 to Jan - Mar 2022 submission of reports as shown below.



Conclusions: Efforts to use one national DHIS2 reporting system together with implementation of different activities directed towards improving health worker knowledge for TB data report compilation plus regular data review improves report submission rates. It is very critical to adopt a single national reporting system for the best system strengthening results.

EP-20 Access to rapid testing for TB

EP-20-791 Access to GeneXpert testing and yield of TB across different outpatient department settings in Ethiopia

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Background and challenges to implementation: TB is one of the deadliest infectious diseases in the world. Integrating TB screening at all health service outlets is a major strategy to ensure early diagnosis, treatment, and curbing of TB transmission. We evaluated access to GeneXpert testing service and yield of TB across different service outlets in Ethiopia.

Intervention or response: The USAID Eliminate TB Project supported the National Tuberculosis and Leprosy Program (NTLP) of Ethiopia to implement screening of all TB patients coming to outpatient departments (OPD). this included working with the NTLP to prepare and develop national guidelines, standard operating procedures, and recording and reporting materials, as well as to provide routine mentorship and training to health workers. The percentage of those tested with GeneXpert and yield of TB was computed July-September 2021 for different OPDs including: adult OPDs, diabetes mellitus (DM) clinics (DM), non-DM non-communicable diseases (NCD) units, and OPDs for children under five years of age. Percentages, number needed to screen (NNS), and number needed to test (NNT) were calculated.

Indicator	Service outlets				Total
	Adult OPD	DM clinics	Non-DM NCD	Under 5 years OPDs	
# of OPD visits	1,962,204	20,953	83,651	437,726	2,504,534
# screened for TB	1,791,335	17,220	65,020	359,146	2,232,721
# of presumptive TB cases tested for TB	23,921	303	363	1,150	25,737
# of presumptive TB cases tested by GeneXpert (%)	9,808 (24.9%)	210 (32.7%)	291 (53.9%)	771 (30.1)	11,080 (43.1%)
# of presumptive TB cases tested by AFB	14,113	93	72	379	14,657
# of TB cases diagnosed	3,467	35	43	229	3,774
NNS	517	492	1,512	1,568	593
NNT	7	9	8	5	7

Table. Yield of TB and GeneXpert access by type of OPD, July-September 2021, Ethiopia.

Results/Impact: Cumulatively, 2,232,721 (89%) of OPD clients were screened, among which 1.2% were presumptive TB cases. Overall access to GeneXpert testing was 43.1%, highest in non-DM NCD (53.9%) units and

lowest in adult OPDs (24.9%). The higher burden of TB was among DM clinics (NNT, 492) and lowest among under 5 years (NNS, 1,568).

Conclusions: Disaggregation of data to show access to GeneXpert testing and yield of TB by type of OPDs shows the need for targeted interventions to expand quality diagnostics. Fewer than half of eligible patients had access to GeneXpert testing, highlighting the need for advocacy to promote universal testing using GeneXpert.

EP-20-792 Evidence of active TB among individuals with a trace result on Gene Xpert MTB /RIF Ultra during community-based TB screening in Kampala, Uganda

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Background: Xpert MTB/RIF Ultra is a highly sensitive, WHO-recommended rapid diagnostic test for tuberculosis (TB). The assay's lowest semi-quantitative result level, 'trace MTB detected', occurs often during community-based TB screening and may provide an opportunity to detect TB at an early stage, but may also be associated with false positive results. We sought to determine the prevalence of active TB among individuals who had trace Xpert MTB/RIF Ultra sputum results during community-based TB screening.

Design/Methods: We conducted community-based Xpert MTB/RIF Ultra sputum screening of individuals age ≥ 15 years in Kampala, Uganda. Participants with trace results underwent extensive microbiological, radiological, and clinical evaluation. Study physicians reviewed results to identify participants warranting TB treatment versus close follow-up. We quantified the prevalence of culture-positive TB, any positive bacteriologic result (culture, Xpert MTB/RIF Ultra testing of a second sputum specimen, or positive urine LAM if HIV positive), and clinical presentation sufficiently consistent with TB that treatment was recommended by study physicians after review of all baseline data.

Results: Of 62 participants with trace screening results, 34 (55%) were female, median age was 32 (IQR 24-38), six (10%) were living with HIV, six (10%) reported previous treatment for TB, and 43 (70%) had at least one TB symptom. Of 51 participants whose culture status could be evaluated, eight (16%) had a positive result. Fourteen participants (23%) had at least one positive

bacteriologic result on follow-up testing, and 16 (26%) were recommended for treatment based on the baseline evaluation.

	Overall	Culture positive	Culture negative	Culture in progress or not evaluable
N	62	8	43	11
Positive follow-up Xpert	7/62 (11%)	3/8 (38%)	2/43 (5%)	2/11 (18%)
Trace-positive follow-up Xpert	1/62 (2%)	0/8 (0%)	0/43 (0%)	1/11 (9%)
TB LAM positive*	1/6 (17%)	0/1 (0%)	1/5 (20%)	0/0 (0%)
CT highly consistent with active TB	13/62 (21%)	3/8 (38%)	8/43 (19%)	2/11 (18%)
Recommended for treatment by physician consultants	16/62 (26%)	8/8 (100%)	5/43 (12%)	3/11 (27%)

Table. Results. *Urine LAM test only done if HIV Positive

Conclusions: Most people with trace-positive results in community-based screening do not have active TB. About one-quarter of trace-positive results reflect TB disease, but multiple follow-up modalities are required to identify these individuals.

EP-20-793 Outcome of culture and DST on Xpert® MTB/RIF Ultra MTB trace rifampicin indeterminate at National Tuberculosis Reference Laboratory (NTBRL) Zimbabwe (January 2019 to December 2021)

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Background: The END-TB strategy recommends initial Drug susceptibility testing (DST) for all presumptive Tuberculosis patients diagnosed with Tuberculosis (TB) so that they are started on the correct regimen. Despite Zimbabwe adopting WHO recommended Rapid diagnostics (WRD), initial Rifampicin Indeterminate result is a challenge to patient management. The aim of the study was to check culture growth and DST of Xpert® MTB/RIF Ultra Rifampicin indeterminate samples.

Design/Methods: A cross-sectional study was conducted on secondary data of Rifampicin Indeterminate samples referred to NTBRL for routine analysis between 01 January 2019 and 31 December 2021. Culture was done on both liquid and solid media. DST was done on *M. tuberculosis* positive samples. Results of the culture and DST tests were recorded and entered into a Microsoft Excel spreadsheet. Data was analyzed using STATA v.12 and presented in the form of descriptive statistics.

Results: MTB 'Trace' Rifampicin Indeterminate samples were collected from 73 females and 98 males, totaling 171 (139 sputum and 32 extra pulmonary samples). The mean age of the patients was 36.41, 95% CI [33.42, 39.41]. There was growth in 19% (32 of 171 Xpert® MTB/RIF Ultra MTB Trace Rifampicin Indeterminate Samples), (25 *M. tuberculosis* (18 sputum and 7 extra pulmonary). This translates to 15789 MTB cases per 100000 Xpert® MTB/RIF Ultra Rif Indeterminate samples. 7 (sputum and 1 extra-pulmonary) had mycobacteria other than tuberculosis (MOTT), while 139 (115 sputum and 24 extra-pulmonary) showed no growth. Rifampicin sensitivity was 100 percent in phenotypic DST on MTB isolates.

Conclusions: Although the prevalence of Xpert® MTB/RIF Ultra Indeterminate Trace Results is very low, Culture and DST of Xpert® MTB/RIF Ultra MTB trace Rif Indeterminate samples can be used to establish DST status so that patients are put on the correct TB treatment regimen for favorable treatment outcomes. Further studies need to be conducted on the significance of MOTT

EP-20-794 Role of repeat GeneXpert Ultra test after trace results: an experience from Vietnam

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Background and challenges to implementation: Following the recommendations of the WHO, Vietnam is gradually replacing the Xpert®MTB/RIF test with the Xpert® MTB/RIF Ultra test (Xpert-Ultra) to support early detection and increase bacteriological confirmation due to its higher sensitivity. The Xpert-Ultra uses the same semi-quantitative categories used in the Xpert®MTB/RIF assay, with an additional semi-quantitative category, "trace call," that corresponds to the lowest bacillary burden for *Mycobacterium tuberculosis* (MTB) complex detection.

As per Vietnam's national guidelines, all Xpert-Ultra trace results need to be repeated before confirmation and treatment enrollment.

Intervention or response: We evaluated the practice of either re-testing or not re-testing after a trace result at the pilot health facilities when applying Xpert-Ultra in the detection and treatment of pulmonary TB.

This assessment reviewed the records and reports of data routinely collected under the National TB Program (NTP) between October 1, 2020, and June 30, 2021. We reviewed the diagnostic outcome and analyzed records for patterns of association.

Results/Impact: 404 children and adults from Can Tho, Tien Giang, Tay Ninh, and An Giang provinces had initial trace result from Xpert-Ultra tests. According to NTP data, 230 (56.9%) received a second Xpert-Ultra test. Among those re-tested, 102 were MTB negative, 74 were MTB positive (7 with RIF resistance), 52 had a second trace result, and 2 returned errors.

Of the 404 persons with an initial trace result, 198 people were initiated on TB treatment: 31.3% (62) who received only a first test, and 68.7% (136) who were retested.

Predictive factors for TB treatment [1][CD2] included: having a second Xpert Ultra test, age group <35 years, regular medical examination, and health insurance.

Conclusions: Repeated testing of patients with Xpert Ultra trace may identify additional TB cases and increase number of those starting treatment.

EP-20-795 The simple one-step (SOS) stool processing method for Xpert MTB/RIF Ultra is robust: results from an optimization study in Ethiopia

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Background: Simple One-Step (SOS) stool processing method is simplified way of using stool as alternative specimen for tuberculosis (TB) diagnosis, but its robustness was not assessed. Our objective was to determine robustness of SOS for Xpert MTB/RIF Ultra in patients with confirmed TB.

Design/Methods: In cross-sectional study that took place between January 2020 to December 2021, we assessed sample processing steps, stool volumes, storage temperatures and sampling from stool-sample reagent mixture using Xpert MTB/RIF Ultra. EpiData and STATA were used for data entry and analysis respectively.

Mycobacterium tuberculosis (MTB) positivity rate and proportion of unsuccessful Xpert-Ultra test results were compared between different experiments.

Results: We enrolled 48 patients and 16 (33.3%) were children. Stool storage conditions showed; highest MTB positivity (69, 82.1%) for stool stored in refrigerator (2-8°C) for 5 and 10 days, lowest unsuccessful results (8, 9.5%) for stools stored in refrigerator for 2 days, and highest unsuccessful results (24, 28.6%) for stools stored in incubator (37°C) for 3 days. Varying incubation and sedimentation time resulted in highest MTB positivity (103, 82.4%) and lowest unsuccessful results (14, 10.4%) with a 10'+10' handshake, and highest unsuccessful results (19, 15.2%) with 10'+10' vortex method. From storage of stool/sample reagent mixture we found; highest MTB positivity (100, 80%) for mixtures stored in refrigerator for 12 hours, lowest unsuccessful results (15, 12.1%) for mixtures stored in refrigerator for 5 hours, and highest unsuccessful results (32, 25.8%) for mixtures stored at room temperature for 24 hours. MTB positivity rate was highest (74, 90.2%) with 0.3g stool sample, unsuccessful results were lowest (4, 4.7%) with 0.5g stool sample and highest unsuccessful (20, 23.3%) with 1.2g stool sample.

Conclusions: SOS stool processing method is robust method that provides valid results under a range of storage conditions requiring no vortex, and gives better results with smaller stool amounts.

EP-20-796 Prevalence of Xpert Ultra trace among presumptive TB patients in Tunisia, 2018-2021

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Background: The GeneXpert MTB/Rif ultra (Cepheid, USA) presents an increased sensitivity to detect *M. tuberculosis* complex compared to the Xpert MTB/Rif due to the inclusion of multicopy amplification targets and a novel "Trace call".

The aim of this study was to determine the prevalence of "Xpert Ultra trace" among presumptive TB patients in Tunisia, a middle TB incidence country with a very low prevalence of HIV infection, over 4 years.

Design/Methods: During the period 2018-2021, 3628 samples: 2504 pulmonary and 1124 extrapulmonary (EP) specimens were collected from presumptive TB patients.

All these samples were subjected to acid fast bacilli staining using auramine, a solid and liquid culture and a molecular diagnosis using Xpert MTB/Rif ultra.

Results: Xpert ultra showed the presence of *M. tuberculosis* complex DNA (high, medium, low, very low and trace) in 46.1% (n=1673) of the samples tested. In

fact, Xpert was positive in 49.8% of pulmonary samples (n=1249) and detected *M. tuberculosis* complex in 37.7% (n=424) of EP specimens.

A "Trace call" was found in 6.3% (n=229) of the samples tested. In our study, 5.6% (n=13) of the samples presenting a "trace call" were collected from patients with a prior or recent TB history.

For the pulmonary samples, 4.4% of the specimens tested (n=112) had a "Trace call" result. The presence of *M. tuberculosis* complex was confirmed in 17.0% (n=19) of pulmonary samples that showed a "trace call" by microscopy and/or culture.

Regarding EP specimens, "Trace call" result was found in 10.4% (n=117) of the samples tested.

M. tuberculosis complex detection was confirmed in 31.6% (n=37) of EP samples presenting a "trace call" by microscopy and/or culture.

Conclusions: An important minority in this study (6.3%) had an "Ultra trace" result. This result should be interpreted carefully especially in patients with a prior or a recent TB history.

EP-20-797 Addressing the social determinants and consequences of tuberculosis (ASCOT): interim findings from the ASCOT pilot randomised-controlled trial in Nepal

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Background: WHO policy advocates reducing stigma and eradicating catastrophic costs of people with TB. Evidence on the optimal socioeconomic interventions to achieve these aims is minimal, especially in low-income, high-burden settings. We did a pilot randomised-controlled trial (RCT) with mixed-methods process evaluation to evaluate the feasibility and acceptability of socioeconomic support for TB-affected households in four districts of Nepal.

Design/Methods: The pilot aimed to recruit and randomly allocate 128 people with drug-sensitive TB notified to the Nepal National TB Program into four study arms: control, social, economic, and combined social and economic (socioeconomic) support arms. Social support consisted of: enhanced TB information, education, and counselling (IEC) at household visits and with an illustrated wall calendar to increase knowledge; and TB Community Get-Togethers led by TB Champions/Survivors, which used group-counselling and a locally-made animated video to reduce stigma. Economic support consisted of six unconditional cash transfers of 3000 Nepalese Rupees each (~30USD) monthly throughout TB treatment. Fidelity to recruitment, follow-up, and ASCOT intervention activities, and participant feedback were collated.

Results: Of 131 people with TB invited to participate, 128/131 (98%) were recruited of whom 126/128 (98%) were still participating in May 2022 (Table). Cash transfers were received by 27/32 (84%) and 26/32 (81%) eligible participants in the economic and socioeconomic arms, respectively. IEC was received by 24/32 (75%) and 25/32 (78%) and Get-Togethers attended by 14/32 (44%) and 14/32 (44%) participants in the social and socioeconomic arms, respectively. Most (32/41, 78%) participants rated Get-Togethers as good/very good and reported they would participate in ASCOT again if the opportunity arose.

Conclusions: Interim findings from the ASCOT pilot trial suggest that social, economic, and socioeconomic support for TB-affected households in Nepal is feasible, acceptable, and suitable for scale-up into a well-powered RCT to evaluate their effectiveness to mitigate catastrophic costs and reduce stigma.

EP-20-798 Finding tuberculosis among HIV +ve clients: use of lateral flow urine lipoarabinomannan assay (LF-LAM) test kit to find the missing TB cases

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Background and challenges to implementation: Tuberculosis (TB) and HIV are closely linked since the emergence of AIDS. TB is the most common opportunistic infection and cause of death in patients with HIV. Although HIV-related TB is both treatable and preventable, incidence continues to climb in developing countries wherein HIV infection and TB are endemic, and resources are limited. LF LAM is recommended for

TB diagnosis in Advanced HIV Disease (AHD) among HIV-positive adults and adolescents, and children older than five years with CD4+ lymphocyte count <200cells/mm³.

Intervention or response: The study was carried out across 14 ART sites in the three states – Akwa Ibom, Cross Rivers, and Rivers. In line with the AHD package of care all newly diagnosed HIV clients, clients with suspected treatment failure and those who interrupted treatment and returned to care had same-day urine LF LAM test to rule out the presence of tuberculosis (TB), with or without the presence of symptoms pathognomonic of the disease.

Results/Impact: Data analyzed from Commcare for the 14 ART study sites between October 2021 to March 2022 revealed the following: TB screening cascade (Screened for TB 11172, presumptive 1104, evaluated 1092, diagnosed 211, enrolled on treatment 194). 4% of the evaluated and 18% of diagnosed TB cases were attributed to the use of LF LAM. Also, the LF LAM test had a high positivity rate of 88%. The enrollment rate of 97% for clients diagnosed through LF LAM.

Conclusions: The LF LAM test has proven to be very efficient in diagnosing TB among HIV-positive clients despite the low testing coverage due to the availability of test kits. Its high positivity rate and reduced time-to-treatment are key to finding and controlling TB among seropositive clients. An adequate supply of test kits and scale-up to all ART service points will bridge a major gap in TB case finding.

ABSTRACT PRESENTATIONS THURSDAY 10 NOVEMBER 2021

ORAL ABSTRACT SESSION (OA)

OA-19 Application of the GeneXpert platform new developments

OA19-336-10 Xpert MTB/XDR to increase conclusive, rapid fluoroquinolone resistance test results to inform MDR/RR-TB treatment

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Background: Screening for fluoroquinolone (FQ) resistance in the endTB/Q trials depends on the direct application of Genotype MTBDR *sl* assay. However, in these trials, inconclusive FQ resistance results by this assay were common, affecting ~50% of all screened and ~80% of smear-negative screening samples, frequently resulting in screen failure. The Xpert MTB/XDR is a rapid molecular assay that can detect resistance to FQ, isoniazid, ethambutol, and second-line injectables. Early studies report a sensitivity of 88.5-100%, a specificity of 97.3%-100% for resistance detection, and a similar limit of detection (71.9 CFU/ml) to Xpert MTB/Rif (86.9 CFU/ml).

Design/Methods: In the endTB/Q trials, sputa collected at screening were tested in parallel with Xpert MTB/Rif or MTBDR plus and Genotype MTBDR *sl* in a site study reference laboratory. In this analysis, we compared the proportion of conclusive drug resistance results by Xpert MTB/Rif with that of Genotype MTBDR *sl* on

confirmatory sputa collected for screening in India, Pakistan, and Kazakhstan. We stratified by the semi-quantitative microscopy result to predict the potential increase in conclusive fluoroquinolone results if Genotype MTBDR *sl* assay was replaced by Xpert MTB/XDR.

Results: The proportion of conclusive drug resistance results produced by Xpert MTB/Rif [248/289 (85.8%)] was significantly higher than that generated by Genotype MTBDR*sl* assay [202/289 (69.9%)], with an average increase of 15.9%. In smear-negative and scanty-positive samples, this gain was above 25%.

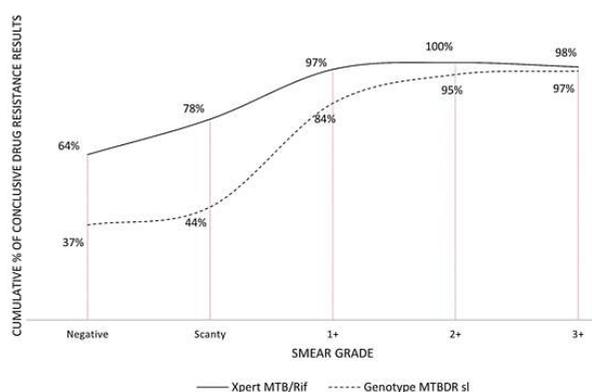


Figure 1. Cumulative percentage of valid drug resistance results by Xpert MTB/Rif and Genotype MTBDR plus assays by smear grade.

Conclusions: If the LOD for Xpert MTB/XDR is comparable to that of Xpert MTB/RIF, use of Xpert MTB/XDR could improve the yield of FQ-resistance testing (compared to Genotype MTBDR *sl*), especially among patients with negative and scanty smears. In settings with high burdens of MDR/RR-TB, scaled-up use of the Xpert MTB/XDR assay is essential. In light of the substantial public funding used to develop the Xpert platform, further price reductions should be assured to promote uptake.

OA19-337-10 Performance assessment of four stool processing methods using Xpert-Ultra to detect tuberculosis in children

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Background: Stool samples were recently recommended by WHO for Xpert tuberculosis testing in children. We assessed the performance, feasibility and acceptability of a centrifuge-based method, the Classical Sucrose Flootation method (CSF) and 3 centrifuge-free methods for use in resource-limited settings, the Optimized Sucrose Flootation method (OSF; TB Speed), Simple One Step stool method (SOS; KNCV) and Stool Processing Kit (SPK; FIND).

Design/Methods: Children <15 years with presumptive TB were enrolled at 3 tertiary hospitals in Uganda and Zambia in a prospective diagnostic accuracy study. Each participant gave at least one respiratory sample (RS) and two stools on two consecutive days. For each method we assessed the sensitivity and specificity of Ultra on stool against culture or Ultra on RS as the reference standard. Also we determined the proportion of non-determinate results and agreement across methods, as well as laboratory technician’s perceptions using a self-administered questionnaire.

Results: Between January 2020 and December 2021, we enrolled 216 children of whom 196 had a stool sample tested with at least one method and at least one RS result available (negative or positive). Sensitivities of CSF, OSF, SOS, and SPK, were respectively 56% (95% CI 38 – 72), 69% (95% CI 52 – 84), 56% (95% CI 38 - 72) and 58% (95% CI 41 – 74). Specificities were > 95% for all methods (Table).

	Ultra/CSF	Ultra/OSF	Ultra/SOS	Ultra/SPK
Sensitivity (%; n/N)	56% (38-72); 20/36	69% (52-84); 25/36	56% (38-72); 20/36	58% (41-74); 21/36
Specificity (%; n/N)	97% (93-99); 136/140	96% (92-99); 131/136	97% (93-99); 135/139	95% (90-98); 125/131
Invalid (%; n/N)	3.6%; 7/195	6.6%; 13/196	5.1%; 10/195	10.8%; 21/194
Error (%; n/N)	2.1%; 4/195	2%; 4/196	1.5%; 2/195	1.5%; 3/194

Table.

Amongst 197 children having a stool tested with all the methods, the percentage of agreement was 53% and 73% on samples with positive and negative culture results, respectively. The 7 laboratory technicians reported that all three methods were easy-to-perform, with more favorable attitudes towards the SOS method.

Conclusions: Simplifying stool processing, regardless of the method used, did not decrease its performance when compared with the CSF. All centrifuge-free methods were feasible and well accepted by laboratory technicians.

OA19-338-10 Pooling sputum samples to extend reagent availability for Xpert MTB/RIF and Xpert MTB/RIF Ultra testing for TB in Cameroon: a retrospective evaluation

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Background: The coverage of molecular testing can be increased by pooling samples from multiple persons to reduce the number of tests needed. Specimen pooling has been adopted for various diagnostic procedures, though it is not yet widely used for TB. In 2020, during a shortage of reagents caused by supply chain issues, some laboratories in Cameroon adopted specimen pooling to extend the availability of Xpert and Ultra testing for TB. Here we evaluate the effect of specimen pooling on testing efficiency and sensitivity.

Design/Methods: Data from specimens tested from July 2020 to September 2021 were collected retrospectively. Specimens sent for TB testing were individually processed and tested in pools of 3 with the Xpert or Ultra assay. Samples from pools with TB not detected were each reported as not detected; samples from positive pools were re-tested individually from the initial specimen, and individual results were reported. The efficiency was evaluated as the number of samples with results per Xpert or Ultra test used. We compared the pooled cycle threshold (Ct) with the individual Ct for pools containing only a single positive specimen to estimate the reduction in sensitivity due to pooling.

Results: We tested samples from 9,024 people using 4,828 cartridges, giving an efficiency of 1.87 and saving 4,196 (46%) tests. Overall, 596 people (6.6%) had a result positive for TB. The average increase in pooled vs individual cycle threshold (Ct) value was similar to

the theoretical value of +1.6 Ct for a pool size of 3 for Xpert and significantly lower than this theoretical value for Ultra.

Conclusions: Using specimen pooling, many more people were able to benefit from an Xpert or Ultra test, with only a small estimated reduction in sensitivity.

OA19-339-10 Diagnostic accuracy of the simple one-step (SOS) stool processing method with Xpert MTB/RIF Ultra testing of children with pulmonary tuberculosis in Ethiopia

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Background: Stool samples can be tested with GeneXpert system for diagnosis of Tuberculosis (TB) in children using various stool processing techniques. Simple One-step (SOS) method is recently developed, relatively simple stool processing method and can be performed in any GeneXpert laboratory, but its diagnostic performance is not well evaluated. We evaluated diagnostic accuracy of SOS stool processing method for Xpert MTB/RIF Ultra testing of children visiting selected health facilities in Addis Ababa and Oromia, Ethiopia.

Design/Methods: A cross-sectional study was conducted on children (≤ 10 years) with presumptive TB from December 2018 to August 2021. Participants were recruited in 38 health facilities and submitted respiratory and stool samples. GeneXpert testing of stool (using the SOS method) and respiratory samples was carried out at health facilities. The remaining sputum/NGA samples were transported to EPHI for liquid and solid culture testing. Paper-based data were collected, entered with EpiData and analyzed using Stata version 15.1. We calculated sensitivity, specificity, positive predictive value, and negative predictive value.

Results: A total of 898 children were enrolled and 74 were diagnosed with TB. Of these, 58 had bacteriologically confirmed TB (49 by Xpert Ultra (11 on sputum/GA, 1 on stool and 37 on both sputum/GA and stool) and 9 only by MGIT). Four children tested MTB-positive with only stool Xpert. The sensitivity of SOS stool with Xpert Ultra was 68.5% (95% confidence interval (CI), 54.4-80.5%) when compared to MGIT culture, 76.8% (95% CI, 63.6 – 87.0%) compared to Xpert Ultra on sputum/GA, and 67.2% (95% CI, 54.6 - 78.2%) compared to TB treatment initiation. Specificity of SOS

stool with Xpert Ultra was 98.5% or higher, with narrow confidence intervals. PPV and NPV were 78.7% and 97.5% against MGIT culture.

Conclusions: The SOS stool processing method has good diagnostic accuracy and sensitivity compared to Xpert Ultra on sputum/NGA and provides minimal unsuccessful Xpert results.

OA19-340-10 Xpert MTB/RIF Ultra: rapid and improved diagnosis of extrapulmonary tuberculosis in a clinical setting

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Background: Diagnosis of extrapulmonary tuberculosis (EPTB) remains a challenge due to its paucibacillary nature, subclinical or nonspecific clinical symptoms, and difficulties in obtaining appropriate specimens. The Xpert MTB/RIF Ultra (Xpert Ultra) has been developed to overcome the challenge of paucibacillary specimens. This study aimed to compare the diagnostic accuracy of Xpert Ultra and Xpert against solid culture and composite microbiological reference standard (CRS) in diagnosing EPTB in a routine diagnostic setting at the TB Screening and Treatment Centre of icddr, b.

Design/Methods: In this prospective study, a total of 240 EPTB presumptive participants with median age of 36 years were enrolled between July 2021 and January 2022. The specimens were tested with Xpert Ultra, Xpert, and Culture.

Results: Out of 240 specimens, 86 (35%), 50 (20%), and 27 (11%) were identified as positive by Xpert Ultra, Xpert, and culture respectively. Among the Ultra positive cases, 28 (32.5%) were detected as 'trace call'. Compared with culture, the sensitivities of Xpert Ultra, and Xpert were 100% (27/27, 95% CI 87.2-100), and 92.6% (25/27, 95% CI 75.71-99.09); and specificities were 72.3% (154/213, 95% CI 65.7-77.2), and 88.3% (188/213, 95% CI 83.2-92.3) respectively. In comparison with CRS, the sensitivities of Xpert Ultra and Xpert were 98.9% (86/87, 95% CI-93.8-99.9) and 57.5% (50/87, 95% CI 46.4-68.0) respectively, with a specificity of 100% for all tests. The diagnostic accuracy of Xpert Ultra was 75.4% (95% CI 69.5-80.7) and 99.6% (95% CI 97.7-99.9) compared with culture and CRS, respectively.

Conclusions: In conclusion, we found improved sensitivity for Xpert Ultra compared to Xpert and lower specificity due to the higher number of 'trace call' results in diagnosing EPTB.

OA19-341-10 The accuracy of tuberculosis molecular bacterial load assay, Xpert MTB/RIF Ultra, smear microscopy and culture for tuberculosis treatment response monitoring: a comparative longitudinal study

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Background: Tuberculosis (TB) takes long to treat, and thus requires effective tools to monitor treatment response and guide clinical decision making. We evaluated the utility of Tuberculosis Molecular Bacterial Load Assay (TB-MBLA) for monitoring TB treatment response.

Design/Methods: Sputa from presumptive TB cases were tested at baseline and monitored for treatment response from week 2 to 26, and then at 3 months after TB treatment course using TB-MBLA in comparison to smear microscopy (SM), Xpert MTB/RIF Ultra (Ultra), and Mycobacteria Growth Indicator Tube (MGIT) as the reference. Test positivity rates, sensitivity, specificity, and reduction in bacterial load were measured.

Results: 210 participants, median age 35 years (Q1-Q3: 27-44); 64% male were tested at baseline. 129(61%) of the participants tested positive by Ultra and were enrolled for treatment follow-up.

During treatment follow-up, positivity rates reduced for all tests but at a remarkably slower pace for Ultra, 4-fold less than TB-MBLA. At week 26 (n = 95), positive results were 31(33%) for Ultra, 6(6%) for SM, and none for TB-MBLA and MGIT culture (Figure 1).

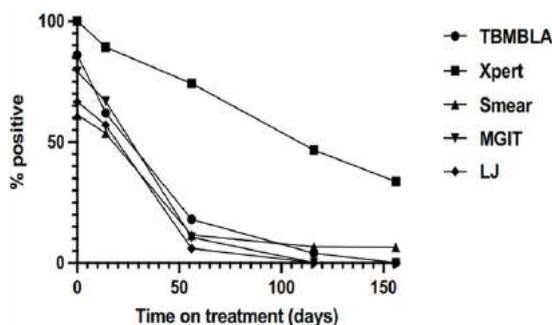


Figure 1. Qualitative data for follow-up visits.

While Ultra remained highly sensitive at 90% during treatment follow-up, TB-MBLA was more specific at 93% and 94% in agreement with MGIT. Post-treatment

follow-up (at month 9) revealed that all 31 Ultra positive and six SM positive participants were clinically well with only two cases still Ultra positive but negative on all other tests.

There was no difference in TB-MBLA-measured bacillary load among SM positive and SM negative cases at 2 months despite the former having an extra month of intensive phase of treatment.

Conclusions: The findings show that both Xpert MTB/RIF Ultra and SM have weakness as treatment monitoring tools. MGIT culture and TB-MBLA provide a similar quantitative read out of patient's TB bacterial load in time to guide patient management.

OA19-342-10 Discrepant genotypic/phenotypic rifampicin resistance results in patients tested with Xpert MTB/RIF at the Singapore Tuberculosis Control Unit

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Background: Xpert is a rapid genotypic test that detects Mycobacterium Tuberculosis complex (MTB) and RIF resistance. However, discrepancies between Xpert and phenotypic drug sensitivity testing (pDST) may occur.

Design/Methods: All sputum specimens subjected to Xpert point-of-care testing at the Singapore Tuberculosis Control Unit between December 2018 to March 2022 were reviewed.

Results: Of the 15,427 sputum specimens tested, 1,786 (11.6%) were positive for MTB of which 33 (1.8%) showed RIF-resistance. These 33 samples belonged to 29 unique patients: 26 had pDST and whole genome sequencing (WGS) information available. 12 (46.1%) patients had Xpert RIF-resistant /phenotypic-susceptible results. 2 patients had an Xpert RIF-susceptible/phenotypic resistant result.

Nine patients with Xpert RIF-resistant /phenotypic-susceptible results had *norpoB* gene mutation detected on WGS. All had specimens with very low bacterial load which likely caused false-positive RIF resistance results on Xpert due to absent probes from insufficient mycobacterial DNA in the sample.

In the remaining three patients with RIF genotypic-resistant/phenotypic-susceptible results, WGS detected a silent mutation *rpoB* T444T (detected on Xpert probe D); the disputed *rpoB* L452P conferring low level RIF-resistance (detected on Xpert probe E), and *rpoB* N438- (detected on Xpert probe C).

1 patient with Xpert RIF-susceptible/phenotypic resistant result had mutation *rpoB* V170P which was outside of the rifampicin resistance determining region. WGS detected *rpoB* S450L mutation for the other patient with Xpert RIF-susceptible/phenotypic resistant result. The cause of this discrepant result was unknown.

Conclusions: Among samples tested with Xpert at the TB Control Unit in Singapore, a low MDRTB prevalence country, the most common reason for discrepant RIF genotypic-resistant/phenotypic-susceptible results was false positive results in paucibacillary samples.

OA19-343-10 Improving uptake of stool based GeneXpert test for childhood TB diagnosis. The Imo State experience

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Background and challenges to implementation: Diagnosis of Tuberculosis in children is challenging as children tend to swallow their sputum sample making it difficult to collect. Gastric aspirate as an alternative requires highly skilled healthcare workers to collect it. Chest X-ray though useful, is subject to bias of the clinician interpreting the X-ray film. This has led to a steady decline in childhood TB notification. KNCV TB Foundation Nigeria in collaboration with NTBLCP and with USAID funding under the TB LON 1 and 2 project introduced the use of stool specimen for TB diagnosis in Children in Imo State and other supported states. This study evaluates the impact of strategies taken to increase uptake of Stool based GeneXpert testing in Imo state.

Intervention or response: First, Lab Staff across 10 GeneXpert facilities were trained to use stool sample to run MTB/RIF Assay test. This was done in 2 batches (August 2020 and March 2021). Afterwards targeted sensitization on the availability of the new diagnostic method was done for healthcare workers and clinicians across target facilities. This sensitization was a mixed model of facility-based sensitization, one-on-one engagement, and online webinars with weekly reminders via WhatsApp.

This took place in June 2021. Data was collected 2 months before sensitization and 9 months after the sensitization to show the impact of the intervention on case finding in the state (April 1, 2021, to March 31, 2022). Results from 10 GeneXpert facilities was used for this study.

Results/Impact: Sensitization had an immediate positive impact on number of samples generated, TB cases diagnosed, and contribution to Imo state Childhood TB Diagnosis. This later declined but not to pre intervention levels.

Quarter/ Year	Before Sensitization					
	Number of Stool Samples Referred	Number of Stool Samples Tested	Number of positive TB cases	TB Case yield from samples tested	Total Number of Childhood TB Cases in Imo State	% Contribution to Childhood TB Diagnosis in Imo state
Q2 2021	91	91	8	9%	63	13%
After Sensitization						
Q3 2021	260	260	16	6%	98	16%
Q4 2021	269	269	9	3%	103	9%
Q1 2022	218	218	18	8%	107	17%

Conclusions: Training and retraining of lab staff on stool sample testing should be followed with awareness creation amongst the healthcare workers to raise demand for the test. The awareness creation should be consistent for sustainability purposes.

OA-20 Developments in tuberculosis imaging

OA20-344-10 Point-of-care thoracic ultrasound for the detection of pulmonary tuberculosis: intermediate analysis of a prospective cohort in Benin

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Background: In Sub-Saharan Africa, tuberculosis (TB) is a leading cause of mortality. There is a need to integrate sustainable triage and management strategies into standard care. We investigate the diagnostic performance of thoracic point-of-care ultrasound (POCUS) in the outpatient consultation of a referral hospital in urban Benin.

Design/Methods: This prospective cohort study includes adult patients presenting with a clinical lower respiratory tract infection (LRTI) according to the treating physician since October 2021. Standardized ultrasound images and videos in 14 lung zones including 4 apical views, and subxyphoid (pericardium) videos are collected. A blinded expert reviewed all recorded images of the lungs and the pericardium according to pre-specified descriptive categories. We evaluate the predictive value of these ultrasound categories for TB according to GeneXpert MTB/RIF® assay on sputa using univariate logistic re-

gression. We conducted a multivariate logistic regression using ultrasound findings to derive a diagnostic score. All patients had an Alere Determine® HIV-1/2 test and a Sars-CoV-2 XPRESS® on naso-pharyngeal swab.

Results: Out of 111 patients included, 40 (36%) were TB positive according to GenXpert MTB/RIF® assay on sputum (TB+) and 71 (64%) TB negative (TB-). TB+ was associated with consolidations larger than 1 cm in any quadrant ($p < 0.01$, odds ratio [OR] 4.9 95%CI 2.0-12) and any type of apical lesion ($p = 0.01$, OR 3.2 95%CI 1.3-7.6). Combining thoracic ultrasound features in a multivariate logistic regression score showed an area under the receiver-operating curve of 68% to detect TB. The optimal cut-point chosen with Youden's index had a sensitivity of 100%, a specificity of 61%, a NPV of 100 and a PPV of 38.5.

Conclusions: With its high NPV, thoracic POCUS is a promising triage tool to exclude TB in the outpatient setting for patients with LRTI symptoms in a TB endemic region. Further multicentric data are necessary to validate these preliminary findings.

OA20-345-10 Clinical outcomes over time in participants from a TB prevalence survey with a high CAD score without microbiological confirmed TB in Zambia and South Africa

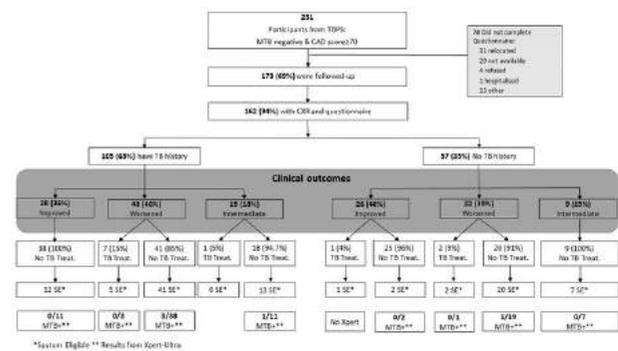
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Background: Latest WHO TB guidelines recommend computer-aided detection (CAD) in chest X-ray (CXR) for systematic screening of TB. Scale-up will identify more individuals with high CAD-score but without diagnostic evidence of TB, requiring guidance on their clinical management. We followed participants of the TREATS TB prevalence survey (TBPS) in Zambia and South Africa with high CAD-score but no microbiologically confirmed TB over 6-12 month to assess their clinical outcomes.

Design/Methods: Microbiologically-negative participants with CAD-score ≥ 70 were followed-up after 6-12 months. At follow-up they were asked about TB symptoms and had a repeat CXR with CAD. Participants with TB symptoms or a CAD-score ≥ 70 at follow-up were asked to submit a sputum sample for testing with Xpert-Ultra. We used a composite 'clinical' outcome combining changes in CAD-score and TB symptoms from TBPS to follow-up. Presence of symptoms, increase of $\geq 10\%$ points in CAD-score or persistent CAD-score of ≥ 85 at follow-up was defined as a 'worsened' clinical outcome. Conversely, an 'improved' clinical outcome was defined as a reduction of $\geq 10\%$ points in CAD-score and being asymptomatic at follow-up. All other outcomes were classed as 'intermediate'.

Results: 251 individuals had a CAD-score ≥ 70 without microbiological confirmation of TB at the TBPS, 162 (65%) had complete follow-up results of whom 65% (105/162) self-reported previous TB. Overall, 43% (70/162) participants had a 'worsened' clinical outcome, 69% (48/70) reported previous TB. Among individuals who had a 'worsened' clinical outcome 87% (61/70) were tested with Xpert-Ultra and only 4 (7%) had a positive result.



Conclusions: Many individuals with high CAD-score and no microbiological evidence of TB had 'worsened' clinical outcomes over time despite having a repeatedly negative Xpert. A high proportion had a history of TB, possibly leading to persistent symptoms and lung damage. Further investigations will be needed to understand poor clinical outcomes in those with no TB history.

OA20-346-10 Pulmonary tuberculosis screening from radiological signs on chest X-ray images using deep models

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Background: The World Health Organization has recently recommended the use of computer-aided detection (CAD) systems for screening pulmonary tuberculosis (PTB) in Chest X-Ray images. Previous CAD models are based on direct image to probability detection techniques – and do not generalize well (from training to validation databases). We propose a method that overcomes these limitations using radiological signs as intermediary proxies for PTB detection.

Design/Methods: We developed an **open-source** multi-class deep learning model, mapping images to 14 radiological signs such as cavities, infiltration, nodules, and fibrosis, using the NIH CXR14 dataset, which contains 112,120 images. Using three public PTB datasets (Montgomery County–MC, Shenzhen–CH, and Indian–IN), totalizing 955 images, we developed a second model mapping radiological finding probabilities to PTB diagnosis (binary labels). We evaluated this approach for its generalization capabilities against direct models, learnt directly from PTB training data or by transfer learning via cross-folding and cross-database experiments. The performance of each approach was evaluated by the area under the specificity vs. sensitivity curve (AUC).

Results: The AUC for intra-dataset tests baseline direct detection deep models achieved 0.95 (MC), 0.95 (CH) and 0.91 (IN), with up to 35% performance drop on a cross-dataset evaluation scenario.

Our proposed approach achieved AUC of 0.97 (MC), 0.90 (CH), and 0.93 (IN), with at most 11% performance drop on a cross-dataset evaluation (Table). In most tests, the difference was less than 5%.

Conclusions:

AUC	MC test	CH test	IN test
Direct (best overall)	0.95	0.95	0.91
Indirect (train: MC)	0.97	(-11%) 0.87	(-4%) 0.93
Indirect (train: MC+CH)	0.96	(-6%) 0.90	(-3%) 0.93
Indirect (train: MC+CH+IN)	0.95	(-5%) 0.90	(-3%) 0.92

Table: AUC for indirect detection via radiological findings. Values in parentheses are drops of performance compared to best performing test (in bold). Values with gray background are cross-database evaluations.

A two-step CAD model based on radiological signs offers an adequate base for the development of PTB screening systems and is more generalizable than a direct model. Unlike commercially available CADs, our model is completely reproducible and available open-source at <https://pypi.org/project/bob.med.tb/>.

OA20-347-10 Automatic classification of pulmonary abnormalities from chest X-ray images: a multi-task deep learning model

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Background: Chest X-ray radiography (CXR) is commonly used to detect different lung abnormalities or diseases. However, interpretation of CXR remains a challenging task for radiologists. In order to overcome this clinical challenge, we develop and test a new Multi-Task Optimal-Recommendation Max-Predictive Chest X-Ray Classification and Segmentation (MOM-ClaSeg) system that can detect and delineate 65 different abnormal regions of interest (ROI) on CXR images.

Design/Methods: The MOM-ClaSeg System is built based on a Mask R-CNN and Decision Fusion Network that is trained using a dataset involving 310,333 adult CXR images, which contains 243,262 abnormal images depicting 307,415 confirmed ROIs depicting 65 different abnormalities and 67,071 normal images. Another independent testing dataset containing 22,642 images collected from 54 hospitals is used to evaluate detection performance of MOM-ClaSeg system where each ROI has one recommended abnormality. Performance of detecting different diseases are evaluated using ROC method under 3 scenarios to divide images into positive and negative classes namely, diseases vs. normal cases (clinical scenario), the targeted one disease vs. other disease cases (differential diagnosis scenario), and the targeted disease vs. all other disease and normal cases (screening scenario).

Results: The number of testing diseased cases vary from a few to thousands. To detect most abnormalities, AUC > 0.9. For the 8 most popular pulmonary diseases in the testing dataset, including pneumonia, secondary pulmonary tuberculosis, bronchitis, fibrous calcification, nodule, calcification, mass and rib fracture (old), AUCs range from 0.880 to 0.988, in which the lowest AUCs (0.880-0.914) and the highest AUCs (0.970-0.988) are

yielded in detecting nodules and calcifications, respectively. For detecting the secondary pulmonary tuberculosis, AUCs range from 0.958 to 0.987 in three detection scenarios.

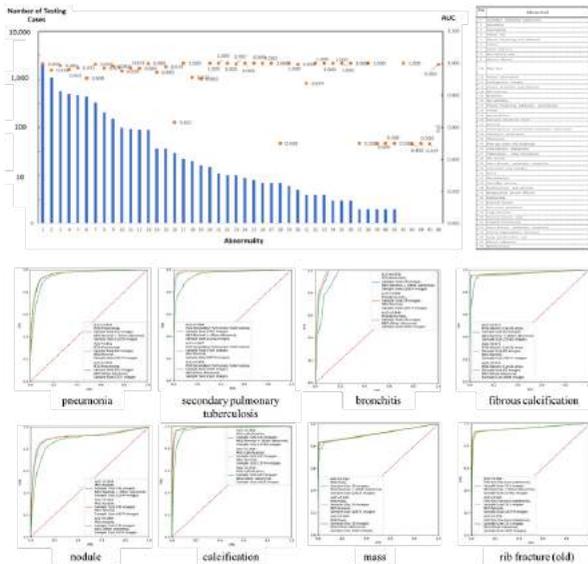


Figure 1. Detection performance for each individual abnormality and ROC curves of 8 types of pulmonary diseases by using MOM ClaSeg system for single individual abnormality detection in different scenarios.

Conclusions: This study demonstrates a unique deep learning trained MOM-ClaSeg System that enables to detect multiple abnormalities using CXR images with high AUC values under 3 common scenarios.

OA20-348-10 Computer-aided detection of tuberculosis using chest X-ray: clinical validation of the CAD4TB v7 system

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Background: As the use of artificial intelligence systems to aid the detection of abnormalities consistent with Tuberculosis on chest X-rays becomes increasingly available, local data is needed to determine optimal threshold scores for use in specific geographical settings. We aimed to validate the CAD4TB v7 software and produce a threshold score predictive for pulmonary tuberculosis in Uganda, a resource limited high TB and TBHIV burden setting.

Design/Methods: Patients presenting to the outpatient and HIV clinics of two hospitals were screened for TB using the WHO symptom screen and offered an HIV test (if HIV status was unknown). Patients were enrolled

into the study if they were HIV-ve, had cough (of any duration) with at least one other TB symptom or if they were HIV+ and had cough (any duration) +/- any of the other TB symptom. All patients received both a chest X-ray and a sputum examination using Xpert Ultra[®]. X-rays were interpreted by the CAD4TBv7 system and a score between 0-100 was generated. We calculated the sensitivity and specificity of different CAD4TB scores for the diagnosis of bacteriologically confirmed TB using Xpert Ultra[®] as the reference standard.

Results: From July 2021- April 2022, we enrolled 1321 patients with presumptive TB. Of these 440 (33.3%) were male; 615 (46.6%) were HIV positive and 157 (11.9%) had previous history of TB. Fifty-nine patients were diagnosed with TB.

Overall, the area under receiver operating curves (AUC) was 0.93 95% CI 0.91-0.94) The AUCs were comparable for HIV + and HIV -ve patients 0.902 (95% CI 0.84-0.96) vs 0.944 (95% CI 0.89-0.99) p=0.27. A CAD4TB score >47 gave the optimum sensitivity 81.9% (95% CI 70.0% – 90.6%) and specificity 91.3 (95% CI 89.7%-92.8%).

Conclusions: A threshold score of 47 gave the optimum cut off point for detection of Tuberculosis in Uganda, a high TB/TBHIV burden setting.

OA20-349-10 Chest X-ray features of non-severe pulmonary tuberculosis in children enrolled on the SHINE trial

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Background: SHINE was a phase-3 randomised controlled trial of treatment shortening in Zambian, Indian, South African and Ugandan children with non-severe pulmonary tuberculosis (PTB) and/or peripheral lymphadenitis. We present baseline chest x-ray (CXR) results as classified by central expert review.

Design/Methods: Baseline CXRs were interpreted by on-site clinicians to exclude severe disease and determine trial eligibility. CXRs were additionally interpreted retrospectively by a panel of paediatric specialists, to provide final CXR classification for the adjudication of TB disease status using standard clinical case definitions.

For central expert review, each CXR was interpreted independently by two specialists blinded to all other information; a third specialist independently reviewed where there was lack of consensus. CXRs were classified by technical acceptability, as normal or abnormal and, if abnormal, for features “typical of TB” and for radiological disease severity. Children without PTB were excluded from this analysis.

Results: All 1157 CXRs from children enrolled with PTB were interpreted by on-site clinicians as technically acceptable and non-severe. 1127/1157 CXRs were available for expert review (Table 1). Overall, 210 (18.6%) CXRs were normal, 373 (33.1%) were abnormal but not typical of TB and 341 (30.3%) were typical of TB. Children with bacteriologically confirmed PTB were more likely to have typical CXR features (odds ratio: 2.63; 95% confidence interval: 1.82-3.80). After central expert review 71/1127 (6.3%) CXRs were classified as severe.

	All N=1127	Bacteriologically unconfirmed N=991	Bacteriologically confirmed ⁴ N=136	OR and 95% CI	P value
Median age	3.4 (1.4, 6.8)	3.3 (1.4, 6.5)	5.1 (1.6, 8.7)	.	<0.01
Living with HIV	118 (10.5)	112 (11.3)	6 (4.4)	0.36 (0.16, 0.84)	0.01
Final CXR classification¹					
Unacceptable quality	170 (15.1)	148 (14.9)	22 (16.2)	1.10 (0.67, 1.80)	0.70
Normal	210 (18.6)	188 (19.0)	22 (16.2)	0.43 (0.51, 1.34)	0.43
Abnormal, typical of TB ²	341 (30.3)	273 (27.6)	68 (50.0)	2.63 (1.82, 3.80)	<0.01
Abnormal, not typical of TB	373 (33.1)	349 (35.2)	24 (17.7)	0.39 (0.25, 0.63)	<0.01
Abnormal, severe disease ³	71 (6.3)	55 (5.6)	16 (11.8)	2.27 (1.26, 4.10)	<0.01

¹33 CXRs classified as ‘no consensus after 3 reads (these CXRs were all interpreted by 3 readers and classified as normal by one reader, not typical of TB by one reader and typical of TB by one reader); ²Patterns classified as ‘typical of TB’ were: lymph node disease, pleural effusion, cavitary disease, miliary infiltrates and expansile pneumonia; ³Severe disease was classified as complicated lymph node disease, miliary infiltrates, cavitary disease, expansile pneumonia, complicated pleural effusion and the presence of any lung opacification involving ≥1 lobe; ⁴Bacteriologically confirmed included confirmation on GeneXpert and/or culture

Table 1. Baseline chest X-ray classification after central expert review, by bacteriological confirmation status.

Conclusions: On-site clinician and central expert review of CXRs was successfully undertaken on the SHINE trial. Only 6.3% of CXRs classified as non-severe by on-site clinicians were classified as severe by the expert panel. The radiological disease spectrum included a high proportion of normal and non-typical CXR features. This proportion was higher in children without bacteriological confirmation, where the diagnostic challenge is greatest, highlighting the urgent need for better tools to diagnose tuberculosis in children.

OA20-350-10 CAD4TB y Lunit INSIGHT CXR to identify pulmonary tuberculosis among COVID-19 survivors, Peru

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Background and challenges to implementation: The prevalence of TB among patients with COVID-19 has been described in the range of 0.5-4.5%. However, there have been few studies of TB prevalence among COVID-19 survivors, and even fewer that have evaluated artificial intelligence radiography systems for this population.

Intervention or response: We conducted TB screening for COVID-19 survivors, defined as people who had received a positive SARS-CoV-2 PCR or antigen test at least 8 weeks prior. TB screening was performed using digital chest radiography with computer-aided detection via an artificial intelligence system during two periods: January-June 2021 using the CAD4TB system, and January-April 2022 using the Lunit INSIGHT CXR system. Those with abnormal radiographs (score >50) were evaluated with Xpert Ultra.

Results/Impact: We screened 1127 COVID-19 survivors, 882 (78%) of whom had COVID-19 symptoms at the time of their positive test; the other 245 (22%) had asymptomatic COVID-19 infections. Screened survivors had a median age of 50 years (interquartile range 37-51), and 650 (58%) were women. Of those screened, 241 (21%) had an abnormal radiograph, of whom 7 (3%) had a positive Xpert test (prevalence of 621 per 100,000), all rifampin-sensitive. Five of the 7 positive Xpert tests were trace positive results.

Among survivors of symptomatic COVID-19, the number needed to test (NNT) was 17 using Lunit INSIGHT CXR and 39 using CAD4TB. For survivors of asymptomatic COVID-19 the NNT was 48 using CAD4TB.

Conclusions: The prevalence of cases in this cohort is higher than the national average, even in people who experienced asymptomatic COVID-19. The algorithm with Lunit INSIGHT CXR had the highest yield. It is important to consider people with prior COVID-19 as a risk group for TB.

OA-21 Susceptibility resistance

OA21-351-10 The thin-layer agar method allows a fast determination of the minimal inhibitory concentration for Bedaquiline

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Background: Since 2018, WHO guidelines recommend bedaquiline (BDQ) for the treatment of MDR-TB. The genotypic background of BDQ resistance and its association with the resistance phenotype and treatment outcome remain however unclear.

Therefore, phenotypic drug-susceptibility testing (pDST), especially determination of the minimal inhibitory concentration (MIC) is indispensable. Unfortunately, the long turnaround time and the need for primary culture and biosafety level 3 infrastructure complicate pDST and delay results. We aim to validate the ability of thin-layer agar (TLA) testing directly from sputum to establish the MIC for BDQ.

Design/Methods: As a first step we evaluated TLA as indirect pDST method, inoculating 40 replicates of the H37Rv reference strain by two operators on different days, with and without CO₂ incubation, along with a panel of *Mycobacterium tuberculosis* isolates with a known pattern of resistance, which were tested 8 times each. Results were compared against the indirect 7H11-polystyrene(PS)-tube testing with 3 weeks incubation.

Results: The pooled MIC for H37Rv ranged from 0.03 to 0.125mg/L with a mode of 0.06mg/L, similar to previously reported 7H11 results, and all below the proposed breakpoint.

Regarding the first 6 clinical isolates (Table 1), their MIC values are identical to 7H11-PS in a 81.3% of the cases, with only a 1-dilution difference in the rest and with a better accuracy without the presence of CO₂ (70.8% CO₂ incubator vs 91.7% CO₂-free). TLA results for all isolates were obtained at day 7.

Isolate number	Origin	7H11-PS MIC	MIC MIC (mg/L) by indirect TLA																	
			CO ₂ incubator							CO ₂ free										
			0.006	0.015	0.03	0.06	0.125	0.25	0.5	1	2	0.006	0.015	0.03	0.06	0.125	0.25	0.5	1	2
H37Rv	clinical	0.03			54	0							4	55	1					
05-01899	clinical	0.25					2	1								4				
12-00594	clinical	0.03			1	3							4							
14-01268	clinical	1						4										1	3	
15-02136	clinical	0.03			1	1	2						1	3						
15-02119	clinical	0.03					4							4						
15-02150	clinical	0.03					2	2						4						

Table 1.

Conclusions: These results strengthen our hypothesis that TLA could be a fast and reliable technique for pDST for BDQ, accessible to low-resource settings in a biosafety level 2 without CO₂ incubators. The accuracy for direct-on-sputum testing needs to be evaluated.

OA21-352-10 Phenotypic drug susceptibility profile, genetic determinants of drug resistance and treatment outcomes of newly diagnosed pulmonary tuberculosis patients in two TB Centers, Myanmar

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Background: Myanmar is one of the 30 highest burden countries for tuberculosis (TB) and multidrug resistant (MDR-TB) worldwide. Phenotypic anti-TB drug susceptibility and genetic determinants such as lineage and resistance-associated gene mutations play a role in determining the treatment outcomes.

Design/Methods: A prospective observational study was carried out on newly diagnosed pulmonary TB patients registered for drug susceptible TB treatment (DSTB) and rifampicin (RIF) resistant (RR)/MDR-TB treatment at two Township TB Centers, Yangon, Myanmar during 2020-2021. Routine diagnostic GeneXpert MTB/RIF was carried out at the enrolment.

Sputum microscopy and/or culture were conducted at the enrolment and at seven follow-up visits up to 18 months. Phenotypic drug susceptibility testing (DST) was performed by Mycobacterial Growth Indicator Tube (MGIT) method.

Whole genome sequencing (WGS) using Illumina Miseq platform were conducted on a sub-set of *Mycobacterium tuberculosis* (MTB) isolates. Treatment responses and outcomes of patients were evaluated.

Results: A total of 126 patients (76 enrolled for DS-TB and 50 enrolled for RR/MDR-TB treatment) were eligible in the outcome analysis. Phenotypic DST (n=126) revealed 2 (1.6%) pre-extensively drug-resistant TB (pre-XDR-TB), 49 (38.9%) MDR-TB, 11 (8.7%) poly-resistance other than MDR and 9 (7.1%) mono-resistance.

Genome sequencing of 45 MTB isolates showed 22 (48.9%) were harboring drug resistance-associated mutations and Beijing genotype was most frequent among drug-resistant isolates.

Successful treatment outcomes were observed in 74 (97.4%) among 76 DSTB patients and 39 (78.0%) among 50 RR/MDR-TB patients. Minimum confident rifampicin resistance-conferring *rpoB* I491F mutation was found to be associated with misdiagnosis of RR-TB and failed DS-TB treatment.

Conclusions: Uncommon drug resistance–conferring mutations missed by routine diagnostic assays may result in poor treatment outcomes and can lead to continued amplification of drug resistance and concurrent silent transmission in the community. Comprehensive analysis of genetic determinants of drug resistance by genome sequencing provides advanced approach towards successful TB treatment.

OA21-353-10 Evaluation of Meltpro® MTB/PZA to detect susceptibility of pyrazinamide among rifampicin-resistance tuberculosis patients

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Background: Drug-resistant tuberculosis (TB) continues to be a public health problem. Pyrazinamide (PZA) is one of the important drugs in tuberculosis chemotherapy. PZA resistance is significantly associated with longer treatment duration and poor outcomes. The Meltpro® MTB/PZA (Zeesan Biotech, Xiamen, China) is a novel assay for the diagnosis of tuberculosis and rapid detection of PZA resistance in clinical specimens. The aim of this study was to evaluate the performance of the Meltpro® MTB/PZA among rifampicin-resistance TB (RR-TB) patients in China.

Design/Methods: The Meltpro® MTB/PZA was evaluated using clinical specimens from RR-TB patients. Next generational sequencing (NGS) served as a reference standard. When the results are uncertain and specimens are available, the test is repeated once, and the second test results are used for analysis. When the results of the second test are still inconclusive, the results of the survey analysis are listed. The sensitivity, specificity and accuracy of the assay were evaluated. The study received ethical approval from the Ethics Advisory Group of Huashan Hospital, Fudan University.

Results: The Meltpro® MTB/PZA was used to directly test 232 specimens. *Mycobacterium tuberculosis* (MTB) was detected in 195 (84.0%) of the patients by the assay. The assay showed good diagnostic accuracy for pyrazinamide (89.1%, 84.3%–93.8%).

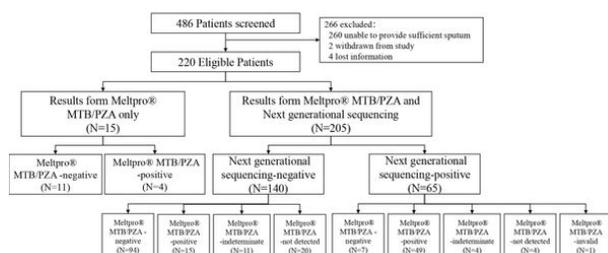


Figure. Flowchart of patient enrollment and outcomes, 15 patients without Next generational sequencing results: 13 culture negative and 2 with insufficient data, PZA, pyrazinamide.

The sensitivity and specificity, respectively, of the Meltpro® MTB/PZA for the detection of resistance were (88.3%, 76.8%–94.8%) and (89.5%, 81.6%–94.4%) for pyrazinamide against NGS.

Conclusions: The Meltpro® MTB/PZA assay is a simple and low-price method, and grass-roots medical staff with minimal training can use the system. The assay can obtain pyrazinamide resistance in a relatively short period of time, which can be used as the initial screening for tailoring the treatment regimen.

Overall, the test demonstrated good performance for detection of PZA-resistance, with a sensitivity of 88.3%. However, we can still wait for the clinical specimen culture to be positive for Next generational sequencing.

OA21-354-10 Isoniazid resistance-conferring mutations are associated with highly variable phenotypic resistance

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Background: High-dose isoniazid is recommended in drug-resistant tuberculosis. However, there is insufficient evidence supporting its use in the presence of isoniazid resistance-conferring mutations. This study aimed to identify the genetic mutations associated with high level phenotypic isoniazid resistance.

Design/Methods: Isoniazid resistance-conferring mutations in whole genome sequences, and the isoniazid minimum inhibitory concentrations (MICs) of 94 isolates was examined. MICs were performed in different concentration ranges based on the mutation present: INH susceptible and H37Rv (0.016–0.256) µg/ml, *inhA* (0.256–4.0) µg/ml, *katG* (1.0–16.0) µg/ml and *inhA* plus *katG* (4.0–64) µg/ml. Isolates showing resistance throughout tested concentrations within their range were tested at a higher concentration.

Results: A total of 58 clinical isolates from 55 patients were included in this analysis after excluding 36 clinical isolates (11 negative MPT64 antigen and non-roping acid-fast bacilli, 23 non-growers, and two contaminated). *InhA* mutants demonstrated a highly variable range of MICs from low to high-level resistance (0.256 to >64 µg/ml), similarly *katG* mutants ranged from low to high-

level resistance (1 to 32 µg/ml), and *inhA* and *katG* mutants demonstrated exclusively high-level resistance (>16 µg/ml). Furthermore, the median MIC demonstrated by these mutants were 8 µg/ml (*inhA*), 4 µg/ml (*katG*) and 64 µg/ml (*inhA* plus *katG*).

Conclusions: *InhA* mutants demonstrated unexpectedly high MICs raising concern for the ongoing use of the high-dose INH in our setting. Our findings suggest that the use of high-dose INH in DR-TB requires urgent review.

OA21-355-10 Genotype-phenotype profiling of serial isolates in patients receiving bedaquiline for drug-resistant TB

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Background: Genetic determinants of bedaquiline (BDQ) resistance are still poorly understood. Studies characterizing genetic changes in serial isolates, obtained from patients receiving BDQ, can improve our understanding of BDQ resistance determinants.

Design/Methods: PROBeX was an observational cohort study of pulmonary DR-TB patients from three South African provinces who received BDQ-containing regimens. We obtained serial *M. tuberculosis* isolates while participants were on TB treatment. All isolates underwent phenotypic BDQ resistance testing. In this analysis, we included participants with a BDQ mini-

mum inhibitory concentration (MIC) >1 mcg/mL at any time during treatment. We performed whole genome sequencing (WGS) on all isolates and examined genetic mutations and changes in BDQ susceptibility over time. We used the WGS data to characterize *M. tuberculosis* within-host diversity.

Results: 73 serial isolates from 22 participants had WGS and BDQ MIC data (range: 1-9 isolates per patient). All 23 isolates with *Rv0678* frameshift mutations had elevated BDQ MIC values >1 (range: 4 or 8 mcg/mL); 80% of isolates (4 of 5) with non-frameshift *Rv0678* mutations and 6.7% (3 of 45) with wild-type *Rv0678* had BDQ MICs >1 mcg/mL. 2 of 16 participants with ≥ 2 total isolates had baseline BDQ MICs ≤ 1 and wild-type *Rv0678*, then subsequent isolates with elevated BDQ MIC, *Rv0678* mutations, and low between-isolate single nucleotide polymorphism differences (<10), consistent with acquisition of *Rv0678*-mediated BDQ resistance while on treatment. 3 of these 16 participants had BDQ MICs > 1 at baseline. 6 of these 16 participants had highly diverse infections involving distinctly unrelated isolates, including those with different BDQ MICs and either wild-type or mutant *Rv0678*, at different time points.

Conclusions: Diverse *M. tuberculosis* within-host subpopulations, and differential clinical sampling of these populations, may pose challenges for the management of patients with BDQ-resistant TB. WGS data can distinguish evolution of BDQ-resistance mutations from polyclonal infections with different strains.

OA21-356-10 The simple one step stool processing method to diagnose tuberculosis in children: data from a pilot study in general hospitals in Southern Ethiopia

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Background and challenges to implementation: Lack of simple diagnostic tools is one of the main contributors to the low childhood TB detection rate in high TB burden countries. The introduction of stool as a readily obtainable sample and the recently developed simple-one-step (SOS) stool processing method offers an opportunity for TB diagnosis in younger children.

Our objective was to determine the rate of agreement between sputum and stool sample results on Xpert MTB/RIF Ultra in four hospitals in Southern Ethiopia.

Intervention or response: Across-sectional study was conducted among children 0-14 years with presumptive pulmonary TB in 4 hospitals in Southern Ethiopia. Eligible children were asked to provide stool sample in addition to routinely requested sputum samples. Stool

and sputum samples were tested using Xpert MTB/RIF Ultra. We computed test agreements between sputum and stools using kappa statistic.

Results/Impact: 373 children included in the study, 61% were < 5 years of age and 56% were male. Most patients reported chronic cough, followed by fever and weight loss or failure to thrive as presenting symptoms, and 21% had contact history with a known TB patient. Thirty-six children (9.7%) were diagnosed to have TB and all started treatment. Of 368 children with valid test result for both stool and sputum, 360 (96.5%) were concordant. The rate of concordance between stool and sputum was high with kappa value of 0.83 ($P < 0.001$) which shows a very good test concordance rate. The rate of unsuccessful test results was higher for stool samples (9/373, 2.4%) than respiratory samples (1/371, 0.27%); however, repeating the test on the remaining stool mixture led to valid results.

Conclusions: The rate of concordance between sputum and stool results was very good when done under routine care conditions highlighting that stool Xpert testing is a feasible option to expand childhood TB services at primary and secondary care levels.

OA21-357-10 Implementation and comprehensive molecular drug resistance profile analysis derived from whole genome sequencing of *Mycobacterium tuberculosis* in Kazakhstan

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Background: TB diagnosis at early stages and identification of drug resistance patterns of TB are crucial parts that increase treatment success. Whole Genome Sequencing (WGS) rapidly provides high-level information about the *Mycobacterium tuberculosis* complex (MTBC) using just one test. Also WGS helps in overcoming disadvantages of other molecular assays such as the indirect identification of MTB and a limited set of resistance mutations. Therefore, the aim of this study is to provide WGS perspectives in TB diagnosis in Kazakhstan.

Design/Methods: We evaluated the performance of a whole genome sequencing to detect MTBC and mutations associated with drug resistance to 10 drugs. Illumina™ MiSeq NGS sequencer was used in the study with the Nextera XT™ library prep kit. DNA libraries were prepared from 19 *Mycobacterium tuberculosis* isolates with known drug resistance determined by WHO approved molecular DST methods plus one NTM. Obtained data was analyzed with PhyResSE and MTBseq bioinformatic pipelines.

Results: WGS detected MTBC DNA in 19 MTBC and 1 non-tuberculous mycobacteria (NTM) isolate. Drug resistance patterns of 18 out of 19 (95%) MTBC samples

obtained through WGS matched with data from the current molecular diagnostic test. Interestingly, 4 out of 19 MTBC samples had isoniazid resistance-associated mutations but were phenotypically susceptible to the drug.

Conclusions: WGS is a useful tool in TB diagnosis with promising perspectives in Kazakhstan. Because WGS can replace different diagnostic tools by providing full and reliable information about MTBC strains. However, uptake of these technologies is limited by the cost of reagents and availability of qualified engineers in the country.

OA-22 Tuberculosis sequencing and resistance

OA22-358-10 Baseline and acquired resistance to bedaquiline, linezolid and pretomanid, and impact on treatment outcomes in four pretomanid-containing clinical trials

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Background: Bedaquiline (BDQ), linezolid (LZD) and pretomanid (PMD) are key components of regimens for treating drug-resistant (DR) forms of tuberculosis (TB). However, there is limited information on the global prevalence of resistance to these drugs and the impact of resistance on treatment outcomes.

Design/Methods: *Mycobacterium tuberculosis* drug susceptibility testing and whole genome sequence (WGS) data, as well as patient clinical profiles from 4 pretomanid-containing trials – STAND, Nix-TB, ZeNix and SimpliciTB – were used to investigate the rates of baseline resistance (BR) and acquired resistance (AR) to BDQ, LZD and PMD, in addition to their impact on treatment outcomes.

Results: Data from >1,000 TB patients enrolled over 7 years in 12 countries (Table) was assessed. We identified only two cases of LZD BR, both ZeNix participants from Russia (1.4%) who exhibited additional BDR BR. PMD BR was also rare, with no marked variation in

rates by TB type or enrollment period (0-2.1%). In contrast, BDQ BR was more prevalent among patients with pre-extensively drug resistant (pre-XDR) or multidrug resistant (MDR) TB than those with drug susceptible (DS) or DR-TB (5.2-6.3% vs. 0-0.3%). This cannot be fully attributed to prior exposure to BDQ or clofazimine. BDQ BR was a risk factor for bacteriological failure or relapse; 3 out of 9 ZeNix participants with vs. 4 out of 134 without BDQ BR. LZD AR was not observed in any trial. BDQ AR was rare across trials (0.4-1%). PMD AR was also rare (0-4%), except in patients with BDQ BR (4 out of 9 cases). WGS analyses revealed new resistance-conferring mutations.

Study, countries (reference)	Enrollment period	TB patient population*	Regimens**	Number of patients enrolled	Number of patients with MTB isolates analysed	Drugs MIC tested (Y/N)
					Baseline	Post-baseline
					B	Pz
SIAMU Sri Lanka, Kenya, Malaysia, South Africa, Tanzania, Thailand, The Philippines, Uganda, Ukraine (Wend et al. 2021)	February 2015 to September 2015	DS-TB	4PZA/4E/4F or 4PZA/4E/4F or 2HRZE/4E/4F or 4PZA/4E	771	201	16
		RR-TB	4PZA/4E	13	9	
ZeNix S. Africa (Korostoff et al., 2020)	April 2015 to November 2017	Pre-XDR-TB, MDR-TB	4PZA	109	58	5
ZeNix Georgia, Moldova, Russia, S. Africa (ClinicalTrials.gov id: NCT03086484)	November 2017 to December 2019	Pre-XDR-TB, MDR-TB	4PZA/1300A1/4F or 4PZA/1300A1/4F or 4PZA/1300A1/4F	181	163	9
SIAMU/ZeNix South Georgia, Malaysia, Russia, S. Africa, Tanzania, The Philippines, Uganda (ClinicalTrials.gov id: NCT03338622)	July 2018 to June 2020	DS-TB, DR-TB	4PZA/4E/4F or 2HRZE/4E/4F	308	302	9
			4PZA/4E	152	145	

*B = BCG, F = rifabutin, H = isoniazid, I = islatravir, M = moxifloxacin, Pz = PMZ, R = rifampicin, Z = pyrazinamide
**For regimen details such as dose and duration, see references

Conclusions: BR rates in PMD-containing TBA trials were from highest to lowest: BDQ>PMD>LZD. AR to the three drugs was low, suggesting that regimens based on BDQ+PMD plus either LZD or moxifloxacin+pyrazinamide are effective in protecting those core drugs.

OA22-359-10 Identification and drug resistance prediction of Mycobacterium tuberculosis directly from sputum samples

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Background: Global increases in *Mycobacterium tuberculosis* (MTB) drug resistance highlights the need for rapid detection of drug resistance as current culture-based methods are slow and labour-intensive. We aim to develop a method of mycobacterial DNA extraction directly from sputum for the purpose of whole genome sequencing to identify species and predict drug resistance. Validation will be done in 2 phases:

1. Negative sputum spiked with *Mycobacterium bovis* BCG,
2. MTB positive sputum. This rapid detection could reduce turn-around-times and prevent costly, ineffective treatments.

Design/Methods: Sputum is decontaminated using standard methods to liquefy and remove contaminating microflora and host DNA. Samples are enzymatically-

treated to deplete host DNA before bacterial genomic extraction. Prior to sequencing, extracts are subject to two amplification methods: an in-house developed multiplex-PCR targeting known resistance genes and a random approach using GC-rich primers.

Following Illumina and Nanopore sequencing, sequences are subject to quality checks before submission to our bioinformatics pipelines: BioHansel, Kraken and Mykrobe Predictor which are used to assess sequence classification and resistance prediction, respectively.

Results: Phase 1 (n=72) tested 12 different conditions for sample decontamination and DNA extraction. We determined an optimal protocol that reduced host DNA by an average of 54% (0.3% to 95%). Post genome-sequencing, this protocol recovered the highest concentrations and increased mapped reads while decreasing non-covered bases. Random amplification increased DNA concentrations over 100-fold and the addition of GC-rich primers improved coverage while reducing non-covered bases.

When pooled with multiplex-PCR reaction, all showed reduction in the relative abundance of host DNA with an increase in mycobacterial DNA. Simultaneously, this reduced incorrect drug resistance predictions over un-amplified DNA.

Conclusions: The optimized protocol was able to improve mycobacterial DNA quantity and quality while also improving drug resistance predictions using both targeted and random amplification. This could allow for rapid identification and drug resistance predictions.

OA22-360-10 A bioinformatics and artificial intelligence algorithm for determining sequencing based drug resistance for Mycobacterium tuberculosis

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Background: Rapid drug susceptibility testing (DST) using genotypic methods for most anti-tubercular drugs is central towards ending TB. Genome sequencing has huge potential as an alternative drug resistance detection tool, however, its use is limited by complicated and insensitive analytical tools.

AarogyaAI® TB is AI bio-informatics pipeline, that has been developed for MTB gDST analysis. Present study explores the preliminary performance of AarogyaAI® TB platform against well-established Mykrobe platform.

Design/Methods: Present study was carried out at Tuberculosis National Reference Laboratory in India. 112 MTB isolates were subjected to sequencing using MiSeq platform. Raw sequences obtained were processed simultaneously on AarogyaAI and Mykrobe 10.0 pipeline. All SNPs and indels obtained were compiled for both pipelines and concordance and discordance was calculated.

Results: Total of 103 sequences were obtained of which 97 were comparable by both pipelines (table); 6 samples failed quality checks for Mykrobe. AarogyaAI® detected mutations missed by Mykrobe including D435G & L430P in *rpoB* (Rifampicin); 1 indel and SNPs; W91R, S315T in *katG* (Isoniazid); single indel c.-11C>A and SNP M306V in *embA* (Ethambutol). In *pncA* gene (Pyrazinamide), five different mutations including 2 indels and 3 SNPs were detected and in *gid* (Streptomycin) 5 indels and 10 SNPs were found only by AarogyaAI®.

Complete concordance was observed for Amikacin and Capreomycin, however for Kanamycin, concordance was 93.8% as *ineI* gene, mutations c-37G>T in 1 sequence & c-12C>T led to resistance prediction in 5 sequences using AarogyaAI®. Only for fluoroquinolones, G88A in *gyrA* was missed by AarogyaAI®, picked by Mykrobe.

Drug	Discordance		Concordance		Total Percent Concordance (%)
	Positive (R)	Negative (S)	Positive (R)	Negative (S)	
Pyrazinamide	15	0	16	66	84.53
Rifampicin	2	1	44	50	96.9
Isoniazid	3	0	49	45	96.9
Ethambutol	4	0	37	56	95.8
Streptomycin	22	0	29	46	77.3
Amikacin and Capreomycin	0	0	3	94	100
Kanamycin	6	0	6	85	93.8
FQs (MOX, OFX, LEVO, CIPRO)	0	1	45	51	98.9

Conclusions: In this preliminary evaluation, AarogyaAI® was found to be more sensitive computational tool than Mykrobe as it identified 29 additional mutations, of which 10 are established as associated with resistance as per WHO. The pipeline is being further expanded to include newer drugs bedaquiline, delamanid, clofazamine, linazolid.

OA22-361-10 Development and assessment of a targeted next-generation sequencing assay for detecting susceptibility of *Mycobacterium tuberculosis* to 14 drugs

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Background: Targeted next-generation sequencing (tNGS) has emerged as an alternative for detecting drug-resistant tuberculosis (DR-TB). To provide comprehensive drug susceptibility and to circumvent mutations missed by available commercial molecular diagnostics, we developed and evaluated a tNGS panel to detect susceptibility of 14 TB drugs.

Design/Methods: We selected 50 *Mycobacterium tuberculosis* complex (MTBC) isolates with various DR profiles as the training set. A targeted NGS assay was designed and performed using the Ion Torrent platform to predict drug resistance to 14 drugs including RIF (*rpoB*), INH (*katG*, *fabG1* and *inhA*), EMB (*embB*), PZA (*pncA*), FQs (*gyrA* and *gyrB*), SM and SLIDs (*rrs*, *eis* and *rpsL*), BDQ and CFZ (*atpE*, *Rv0678*, *pepQ* and *Rv1979c*), LZD (*rhl* and *rplc*), and DLM (*ddn*, *fgd1*, *fbiA*, *fbiB* and *fbiC*).

Comparative variants analyses of DR gene were performed using Sanger sequencing and whole genome sequencing (WGS). Phenotypic drug susceptibility testing (pDST) results were used as gold standards.

Results: We assessed a comprehensively designed tNGS assay with 22 whole-gene targets of 14 drugs. Regarding the limit of detection (LOD), the tNGS assay detected 3.4% RIF *rpoB*, 3.4% INH *katG*, 3.2% EMB *embB*, 2.7% PZA *pncA*, and 3.4% FQs *gyrA* mutations in a mixture containing 4% mutants.

The sensitivity of tNGS, WGS and Sanger sequencing was 96.6% (71.4-100.0%), 96.1% (50.0-100.0%) and 91.4% (50.0-100.0%), respectively; the specificity was 98.9% (75.0-100.0%), 99.1% (75.0-100.0%) and 99.2% (75.0-100.0%), respectively; the concordance was 98.2% (91.8-100.0%), 98.3% (93.9-100.0%) and 97.0% (88.0-100.0%), respectively.

Overall, the tNGS results demonstrated substantial to perfect agreement (kappa values ranging from 0.791 to 1.000) with the pDST results for all 14 drugs.

Furthermore, we identified 17 uncharacterized novel or rare variants in pDST-resistant MTBC isolates.

Conclusions: We demonstrated that a tNGS assay with a flexible novel panel has high concordance with pDST and could facilitate better DR-TB treatment.

OA22-362-10 Routine Mycobacterium tuberculosis drug susceptibility prediction by whole genome sequencing supplemented by phenotypic testing

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Background: The Tuberculosis Reference Laboratory in the Netherlands has routinely applied WGS to all *M. tuberculosis* complex isolates since 2016. In 2020 WGS became the main tool for the secondary routine diagnostics. In our diagnostic algorithm WGS is only supplemented by phenotypical drug susceptibility testing for a small number of isolates.

Design/Methods: The RIVM reference laboratory receives all positive cultures from the laboratories responsible for the first line diagnostics. To reduce human DNA all positive cultures are recultured then subjected to Illumina WGS. The WGS data is run through an in-house pipeline and the data is reported in a web based database. Data are screened for sequence depth, purity and mixed genotypes to ensure quality.

Resistance associated mutations are flagged using two lists, one SNP-list based on genome position and one gene based for INDELS. Mutations are characterized as high, medium, low confidence or new mutations, with defined follow up actions.

The lists are updated based on the targeted phenotypical drug susceptibility testing and international literature including the WHO "Catalogue of mutations in *Mycobacterium tuberculosis* complex and their association with drug resistance" of 2021.

Results: The routine diagnostic workflow based mainly on WGS reduces the culture workload. For about 85% of the isolates phenotypic testing was not performed. The DST that is performed is monitored to control the WGS susceptibility prediction performance.

Conclusions: A routine workflow mainly based on WGS is an effective accurate and precise method for first line drugs due to the pre-existing dataset of (first line) genetic markers and resistance profiles.

DST is required for novel or uncertain mutations and highly resistant isolates only, as the data on second line and newer drugs is less extensive. International initiatives and collaborations are rapidly expanding the knowledge base increasing the confidence of WGS for susceptibility prediction.

OA22-363-10 Sequencing reveals a high proportion of PZA resistance among presumed multidrug-resistant TB patients in India

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Background: Pyrazinamide (PZA) is indispensable for effective treatment of tuberculosis due to its unique bactericidal effect on persisting bacilli *in vivo*. PZA phenotypic drug susceptibility testing (pDST) is technically difficult, insufficiently reproducible, prone to false positivity and being scaled-up in India. Despite historical reports highlighting similar prevalence of PZA-resistant (PZA^R) and multidrug-resistant TB (MDR-TB) in India, little is known about its current prevalence and mutational diversity.

Design/Methods: In a nationally representative survey across India from 2018-2020, we collected *Mycobacterium tuberculosis* isolates from 1644 patients presumed to have MDR-TB. Isolates underwent MGIT 960 pDST and whole genome sequencing (WGS) genotypic DST (gDST). We compared pDST and gDST PZA^R resistance results to determine diagnostic accuracy of gDST in the Indian setting, identified polymorphisms in four PZA^R-associated genes (*pncA*, *rpsA*, *panD* and *ClpC1*), and correlated PZA^R with pDST-based resistance profiles for 13 other antituberculosis drugs.

Results: Among 1644 MDR-TB isolates, the prevalence of phenotypic PZA^R was 59%, while that of genotypic PZA^R was 48%. We found substantial co-resistance with the first-line TB drugs (72%), fluoroquinolones (62%), aminoglycosides (65%), and linezolid (78%).

Overall, 171 known resistance mutations were dispersed throughout *pncA*. *ClpC1* mutations did not independently impart resistance at the critical phenotypic concentration (100 µg/ml). Only one susceptible isolate carried a *rpsA* mutation whereas two susceptible and resistant isolates carried a *panD* mutation. Dismissing *rpsA* and *ClpC1*, concurrent assessment of *pncA* and *panD* showed similar sensitivity and specificity to *pncA* alone (77% and 95%, respectively). Moreover, two novel, independent *pncA* mutations were significantly associated with PZA^R.

Conclusions: Considering overall prevalence of PZA mono- and co-resistance among MDR-TB patients in India, and the moderate sensitivity, high specificity, and reproducibility of WGS-based PZA^R detection in the context of known pDST challenges, sequencing of *pncA* could prove reliable to hasten decisions on use of PZA in TB treatment regimens of India.

OA22-364-10 Evolution of *Mycobacterium tuberculosis* from people with drug-resistant tuberculosis failing treatment

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Background: Full characterization of within-host drug resistance evolution of *Mycobacterium tuberculosis* (*Mtb*) will enable more effective treatment of drug-resistant tuberculosis (DR-TB). Currently, limited deep sequencing data describing *Mtb* genomic heterogeneity and low frequency variants, exists. This study aimed to characterize acquisition of mutations and low frequency variants associated with *Mtb* drug resistance in longitudinal clinical isolates obtained from people failing TB treatment.

Design/Methods: We retrospectively analyzed 23 clinical isolates obtained longitudinally at nine timepoints from five participants failing DR-TB treatment enrolled in the InDEX study. Deep Whole Genome Sequencing was performed on all 23 isolates. The Minimum Inhibitory Concentrations (MICs), evaluated at varying concentrations on the BACTECTM MGIT 960TM system, were established on 15/23 longitudinal clinical isolates against eight TB drugs (rifampicin, isoniazid, ethambutol, levofloxacin, moxifloxacin, linezolid, clofazimine, bedaquiline).

Results: In total, 32 resistance associated mutations/variants were detected by an average sequencing depth of 159× coverage. We observed 30 mutations present at baseline and two acquired mutations/variants emerging at months seven and eight in two participants, both observed two months after the detection of microbiological failure. Emerging resistance to fluoroquinolones was associated with the D94G mutation and A90V variant at 25% frequency in the *gyrA* gene, and with elevated levofloxacin and moxifloxacin MICs. In addition, an *Rv0678* variant, with unknown resistance association (491_492insCG), emerged at month four (23%) and became fixed in the population by month seven (100%) in one participant conferring acquired phenotypic BDQ resistance.

Conclusions: *Mtb* is an adaptable pathogen capable of acquiring genotypic and phenotypic drug resistance. Deep sequencing combined with multiple longitudinal

isolate sequencing and phenotypic MIC quantification demonstrated within-host *Mtb* evolution and emergence of fluoroquinolone and bedaquiline resistance. Proper adherence to treatment will aid in limiting emerging resistance and failed treatment.

OA-23 Innovation in tuberculosis diagnostics

OA23-365-10 A nine-gene blood-based signature meets the World Health Organization target product profiles for diagnosis of active tuberculosis and predicting progression from latent to active disease

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Background: The WHO End TB strategy describes a target product profile (TPP) for a non-sputum-based triage test with at least 90% sensitivity at 70% specificity for diagnosis of active tuberculosis (ATB), and at least 75% sensitivity and specificity for predicting progression from latent tuberculosis (LTB) to ATB. The translation of a 3-gene blood-based signature, identified using diverse datasets, into a prototype point-of-care diagnostic that meets the WHO TPP, has demonstrated the power of integrating large amounts of heterogeneous data to identify generalizable disease signatures.

We hypothesized that integrating more diverse datasets, comprising individuals with ATB or other inflammatory lung diseases, e.g., COPD, viral infections, sarcoidosis, etc., would identify novel, robust signatures that meet the WHO TPP.

Design/Methods: By integrating data from 3615 peripheral blood samples across 49 publicly available transcriptomic datasets, we identified a 9-gene signature for diagnosing ATB patients from healthy controls, or individuals with LTB or other diseases.

Results: The 9-gene signature achieved 90% sensitivity and 82% specificity for ATB diagnosis in retrospective validation (Figure 1A) and maintained performance in

samples with HIV coinfection (Figure 1B). We prospectively profiled the 9-genes in a household contact study in Moldova and an active screening study in Brazil, using NanoString and Fluidigm, respectively. The signature achieved 90% sensitivity at 69% specificity in the novel Moldova cohort (Figure 1C), and 92% sensitivity at 88% specificity in the High/Medium bacterial load samples from the novel Brazil cohort (Figure 1D). In a longitudinal cohort of adolescents, the 9-gene signature predicted progression from LTB to ATB up to 1 year before sputum conversion with 76% sensitivity and 83% specificity (Figure 1E). Finally, the signature predicted prolonged lung inflammation post-treatment in the Catalysis Treatment Response Cohort (Figure 1F).

OA23-366-10 Point-of-care C-reactive protein-based tuberculosis triage testing for people with and without HIV: a multi-country diagnostic accuracy study

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Background: An effective tuberculosis (TB) triage test could improve the efficiency of case finding by identifying symptomatic individuals who require confirmatory testing. C-reactive protein (CRP) was recently endorsed by the WHO for TB screening among PLHIV.

However, there are limited data in other populations or settings outside of Africa. In a multi-country diagnostic trial, we evaluated whether POC CRP meets the WHO target product profile accuracy thresholds for a TB triage test.

Design/Methods: We screened patients presenting to clinics in Uganda, South Africa, Vietnam, the Philippines and India and enrolled adults with cough ≥ 2 weeks. We performed POC CRP testing (Boditech, iCHROMA II) from capillary blood and collected sputum for TB testing (Xpert MTB/RIF Ultra [Xpert]; liquid culture x 2 if Xpert-negative).

We determined the diagnostic accuracy of POC CRP (5 mg/L cut-point) using a microbiologic reference standard (MRS) incorporating sputum Xpert and culture results, and a sputum Xpert reference standard (SXRS) including Xpert results only.

Results: Of 1006 outpatients with cough ≥ 2 weeks (439 [44%] female, median age 41 years [IQR 28-54], 150 [15%] living with HIV and 111 [11%] living with diabetes), 245 (24%) had confirmed TB, of whom 219 (89%) were sputum Xpert-positive. POC CRP levels were elevated (≥ 5 mg/L) in 431 (43%) patients including 193/245 patients with confirmed TB (sensitivity 79%, 95% CI: 73-84%) and 222/723 patients without TB (specificity 69%, 95% CI: 66-73%) by the MRS (Table 1). Sensitivity was higher (84%, 95% CI: 79-89%) and specificity similar (69%, 95% CI: 65-72%) when using the SXRS. Sensitivity and specificity varied across countries and by HIV status (Table 1).

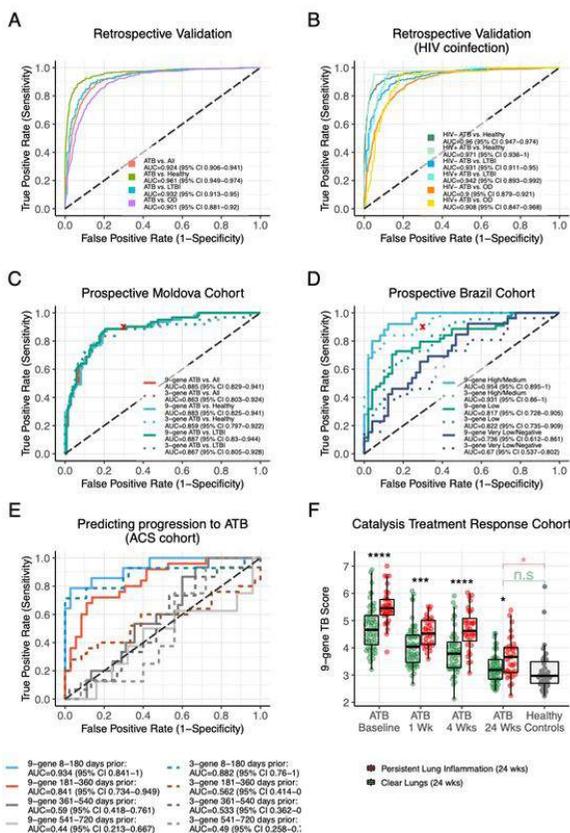


Figure 1. 9-gene signature validates in independent retrospective and prospective cohorts. (A) ROC curves for comparing ATB vs. all other samples (All), or individually comparing ATB vs. Healthy, LTB or Other Disease (OD) samples in retrospective validation and (B) comparing the performance for diagnosing ATB with or without HIV coinfection. (C) ROC curves diagnosing ATB in a prospective Moldova cohort and (D) a prospective Brazil cohort with active TB samples stratified by bacterial load. Red cross shows the WHO TPP of 90% distribution at 70% specificity. 9-gene signature performance shown in solid lines and previous 3 gene signature in dotted lines. (E) ROC curves comparing progressor and non-progressor samples collected at different time points in the Adolescent Cohort Study (ACS). (F) Distribution of the 9-gene score at different time points post-treatment in the Catalysis Treatment Response Cohort Study, for individuals with persistent lung inflammation at 24 weeks compared with those who had clear lungs at 24 weeks.

Figure 1. 9-gene signature validates in independent retrospective and prospective cohorts.

Conclusions: Overall, the 9-gene signature meets the WHO TPPs required for the End TB strategy.

	Microbiologic Reference Standard (MRS) ²		Sputum Xpert Reference Standard (SKRS)	
	Sensitivity n/N, % (95% CI)	Specificity n/N, % (95% CI)	Sensitivity n/N, % (95% CI)	Specificity n/N, % (95% CI)
Overall	78.8% (73.1%, 83.7%)	69.3% (65.8%, 72.6%)	84.0% (78.5%, 88.6%)	68.6% (65.2%, 71.8%)
Country				
Uganda	97/111 87.4% (79.7%, 92.9%)	133/208 63.9% (57.0%, 70.5%)	95/105 90.5% (83.2%, 95.3%)	139/221 62.9% (56.2%, 69.3%)
Philippines	13/24 54.2% (32.8%, 74.4%)	181/207 87.4% (82.1%, 91.6%)	32/19 63.2% (38.4%, 83.7%)	203/232 87.5% (82.5%, 91.5%)
Vietnam	54/76 71.1% (59.5%, 80.9%)	75/114 65.8% (56.3%, 74.4%)	51/66 77.3% (65.3%, 86.7%)	83/128 64.8% (55.9%, 73.1%)
India	8/11 72.7% (39.0%, 94.0%)	76/123 61.8% (52.6%, 70.4%)	7/10 70.0% (34.8%, 93.3%)	77/129 59.7% (50.7%, 68.2%)
South Africa	21/23 91.3% (72.0%, 98.9%)	36/71 50.7% (38.6%, 62.8%)	19/19 100% (82.4%, 100%)	38/77 49.4% (37.8%, 61.0%)
Risk group				
Persons with HIV	28/34 82.4% (65.5%, 93.2%)	65/112 58.9% (49.2%, 68.1%)	24/28 85.7% (67.3%, 96.0%)	69/122 56.6% (47.3%, 65.5%)
Persons with diabetes	23/29 79.3% (60.3%, 92.0%)	54/80 67.5% (56.1%, 77.6%)	21/25 84.0% (63.9%, 95.5%)	56/86 65.1% (54.1%, 75.1%)

¹ Cohort includes participants enrolled from 14 April 2021 through 28 February 2022 with a CRP result available.
² 38 participants were excluded: 9 with two contaminated cultures and 29 with pending culture results. Most patients classified as not having TB had two negative culture results: 84 participants had only one negative culture result (in addition to a negative sputum Xpert result): 43 in India, 17 in Vietnam, 12 in the Philippines, 9 in South Africa, and 4 in Uganda.

Table 1. Sensitivity and specificity of C-reactive protein by key sub-groups (CRP ≥ 5 considered positive)¹

Conclusions: Overall, POC CRP did not meet the recommended sensitivity and specificity targets for a TB triage test. However, diagnostic accuracy was variable and POC CRP may be a useful triage test in some settings and populations.

OA23-367-10 Field experience of nasopharyngeal aspirate and stool sample collection for the detection of tuberculosis in children in six low-income and high tuberculosis incidence countries

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Background: WHO recommends stool and nasopharyngeal aspirate (NPA) as alternative samples to be collected for TB diagnosis in children. The objective is to describe the implementation of NPA and stool sample collection for Xpert MTB/RIF Ultra testing at district hospitals (DH) and primary health centres (PHC) in low-income countries with high TB incidence.

Design/Methods: Children <15 years with presumptive TB were enrolled in the TB Speed decentralization study from March 2020 to September 2021 to assess the im-

port of an innovative childhood TB diagnostic approach in 6 countries (Cambodia, Cameroon, Côte d'Ivoire, Mozambique, Sierra Leone, Uganda). As part of the diagnostic approach, at PHC level, NPA was tested on site and stool sent to DH for testing while at DH level, NPA and stool were tested on site. We describe the feasibility (percentage of children with sample tested with Ultra among children with presumptive TB) and TB detection yield of Xpert MTB/RIF Ultra (MTB detected among children with samples tested) for NPA and stool samples at DH and PHC levels.

Results: Of 3106 children with presumptive TB, 2992 (96%) had a NPA sample and 2241 (72%) a stool sample collected. For 1189/2172 (55%) children, the stool sample could not be collected at the same visit as the NPA and was collected at an additional visit. The feasibility was 90.4% (IC₉₅89.4-91.5%) (2808/3106) for NPA and 68.9% (IC₉₅67.3-70.5%) (2141/3106) for stool. The TB detection yield was 1.7% (IC₉₅1.2-2.2%) (47/2808) for NPA and 1.5% (IC₉₅1.1-1.9%) (32/2141) for stool. Results by type of health facilities are presented in the table.

Sample type	District Hospital		Primary Health Centre	
	NPA	Stool	NPA	Stool
Sample collection attempted, N (%)	1845/1938 (95.2%)	1710/1938 (88%)	1155/1168 (99.9%)	916/1168 (78%)
Sample collected, N (%)	1838/1938 (95%)	1527/1938 (79%)	1154/1168 (99%)	714/1168 (61%)
Sample collection needing additional visit N, (%)		776/1467 (51%)		413/705 (58%)
Sample tested with Xpert Ultra, N (%)	1783/1938 (92%)	1456/1938 (75%)	1025/1168 (88%)	685/1168 (59%)
TB detection yield, N (%)	39/1783 (2.19%)	27/1456 (1.85%)	8/1025 (0.78%)	5/685 (0.73%)

Table. Uptake of specimen collection and Xpert MTB/RIF Ultra testing per facility level.

Conclusions: The implementation of NPA and stool sample collection methods is feasible at low level health facilities with a lower uptake for stool. The overall TB detection yield of Ultra on NPA and stool sample is lower than that observed in clinical studies in similar setting.

OA23-368-10 Novel urine specimen processing technology improves the sensitivity of a lateral flow urine lipoarabinomannan assay

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Background: The Determine TMTB LAM Ag (Alere LAM) lateral flow test has a low sensitivity in HIV-negative people, possibly because the concentration of lipoarabinomannan (LAM) in the urine of these people is below the assay's detection limits. We evaluated whether magnetic Nanotrap particles (Ceres Nanosciences) could increase LAM concentrations enough to improve Alere LAM's sensitivity.

Design/Methods: 100 participants with Xpert-positive, pulmonary TB gave a full-stream urine specimen prior to starting TB treatment. Unprocessed urine specimens were used to perform AlereLAM tests, and the remaining urine was processed using Nanotrap particles. Processed urine was then used to perform a second AlereLAM test for each participant.

The sensitivity gain from using Nanotrap-processed urine was measured with McNemar's test, and a multivariate logistic regression identified risk factors for a negative-to-positive AlereLAM test conversion.

		Unprocessed Urine		Total
		LAM(+)	LAM(-)	
Nanotrap-Processed Urine Confirmed (+) Only	LAM(+)	12	16	28
	LAM(-)	0	72	72
	Total	12	88	100

		Unprocessed Urine		Total
		LAM(+)	LAM(-)	
Nanotrap-Processed Urine Confirmed & Possible (+)	LAM(+)	12	24	36
	LAM(-)	0	64	64
	Total	12	88	100

	Sensitivity	Sensitivity Gain	P-Value
Unprocessed urine	12.0%	-	-
Nanotrap-processed urine Confirmed positives only	28.0%	+133.3%	<0.001
Confirmed & possible positives	36.0%	+200.0%	<0.001

Results: AlereLAM testing with fresh / unprocessed urine achieved a sensitivity of just 12.0%. The assay's sensitivity increased to 28.0% (+133.3%, p<0.001) when using Nanotrap-processed urine and further increased to 36.0% (+200.0%, p<0.001) when possible positive results were included.

Testing the first urine of the day, sex and age were not associated with negative-to-positive conversions. However, participants with lower smear grades were significantly more likely to convert (aOR 8.9 [p=0.014] for smear-negative and aOR 7.0, [p=0.017] for 1-9 AFB/1+), indicating participants with higher smear grades (2+/3+) were more likely to have a positive result using fresh/unprocessed urine.

Conclusions: We demonstrated a significant sensitivity gain when using Nanotrap-processed urine to conduct AlereLAM tests. However, the assay's new sensitivity still remains too low for it to be a clinically useful tool. Further Nanotrap evaluations should be conducted with next-generation LAM assays, which purport to have lower LAM detection limits and higher sensitivity than AlereLAM.

OA23-369-10 Identification of host protein biomarker signatures for diagnosis and treatment monitoring of tuberculosis infection in Madagascar using a multiplex assay

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Background: There is an urgent need for rapid non sputum based test to identify and treat patients infected by *Mycobacterium tuberculosis*.

We aimed in this study to develop and evaluate a monitoring tool based on a multiplex assay for the detection of host plasma protein biomarkers for tuberculosis treatment monitoring and diagnosis.

Design/Methods: The technique used is based on Luminex xMAP technology. Biomarkers measurement were performed in multiplex and the assay was evaluated on 42 Tuberculosis patients (ATB) followed up during 6 month, 26 Latent TB (LTBI) and 23 healthy donors (HD) from Madagascar. Seven biomarkers were analysed separately and in combination as biological signatures using CombiROC algorithm.

Results: A total of 120 biomarker combinations have been identified. They were rank by performance. A 3 biomarker signature (C1Q-IP10-CD14) had 100% of sensitivity and specificity to discriminate ATB from HD, reaching WHO target product profile (TPP) for triage test. A 5 marker signature was able to distinguish treated from untreated patients, AUC = 0.73 (sensitivity=67%, specificity=74%).

Another 3 biomarker signature that reached also TPP for treatment monitoring, by comparing between Fast and Slow culture converters, is the combination of C1Q, IP10 and CD14 with an AUC=0.92 (sensitivity=100%, specificity=82%).

	Combination	Marker signature	AUC	SE	SP	Cutoff	ACC	NPV	PPV
TB vs HD	Combination 25	C1Q-CD14-IP10	1	1	1	0.5	1	1	1
	Combination 26	C1Q-CD14-SELL	1	1	1	0.5	1	1	1
	Combination 60	C1Q-CD14-CLEC3B-SELL	1	1	1	0.5	1	1	1
ATB vs Cured	Combination 116	C1Q-CD14-CLEC3B-IGFBP3-IP10-SELL	0.73	0.5	0.92	0.64	0.70	0.63	0.87
	Combination 92	C1Q-CD14-CLEC3B-ECM1-IGFBP3	0.73	0.67	0.74	0.57	0.70	0.67	0.73
	Combination 114	C1Q-CD14-CLEC3B-ECM1-IGFBP3-SELL	0.73	0.59	0.79	0.58	0.69	0.64	0.76
	Combination 72	C1Q-CLEC3B-IP10-SELL	0.93	1.00	0.82	0.19	0.86	1.00	0.57
Fast vs Slow	Combination 36	C1Q-IP10-SELL	0.92	1.00	0.82	0.19	0.86	1.00	0.57
	Combination 75	C1Q-ECM1-IP10-SELL	0.92	1.00	0.79	0.19	0.83	1.00	0.53

Table 1: Identification of biomarkers showing the strongest association using combination of proteins, for triage and treatment monitoring. AUC, Area under the ROC curve; SE, sensitivity; SP, specificity; PPV, Positive predictive value; NPV, Negative predictive value; ACC, Accuracy.

Conclusions: Our data demonstrate that host biomarker signatures identified are promising alternative for TB treatment monitoring and TB diagnosis, as they reached WHO TPP profile for triage test.

OA23-370-10 Yield of bacteriologically confirmed pulmonary TB in the private sector in a high-TB burden district of South Africa

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Background: While tuberculosis (TB) is primarily addressed in South Africa's public sector, recent evidence suggests people presenting with typical pulmonary TB

symptoms in the private sector may be delayed or lost in the TB care cascade. We undertook a pilot study to connect symptomatic clients of private General Practitioners (GPs) to TB testing by Xpert MTB/RIF Ultra (Xpert) through National Health Laboratory Services in eThekweni District, South Africa. We aimed to determine testing uptake and diagnostic yield.

Design/Methods: We approached registered GPs in eThekweni District for consent to participate. Participating GPs were provided with specimen jars and transport between May 2021-March 2022. The Department of Health covered the cost of Xpert testing.

To encourage GP participation, the TB testing algorithm differed from national TB guidelines:

- Cough >2 weeks or any length among people living with HIV (PLHIV) or;
 - Cough (any length) with night sweats or weight loss.
- The national guidelines recommended testing clients with any one of: cough >2 weeks or any length in PLHIV, fever >2 weeks, weight loss, or night sweats.

We report study uptake, diagnostic yield, and specimen-quality amongst private GPs, comparing yield and quality of specimens in eThekweni's public sector using a two-sample test of proportions in Stata 17.

Results: Of 313 GPs approached, 158 (50.5%) consented to participate. Fifty-nine GPs (37.3%) submitted at least one sputum specimen for Xpert testing (median=5.5, range=1-97), among whom, 34 diagnosed at least one client with TB (median=2, range=1-22).

Sector	Xpert tests performed n	Unsuccessful specimens n (%)	p-value	Pulmonary TB detected n (%)	p-value
Private GPs	571	2 (0.4)		102 (17.9)	
Public clinics	183 434	3125 (1.7)	0.02	14 538 (7.9)	<0.0001

Conclusions: Engaging private sector GPs in eThekweni led to the early diagnosis of >100 people with pulmonary TB who might have otherwise been lost or delayed in the TB care cascade. Reasons for the comparatively high yield of private sector specimens may include a higher sensitivity of the screening algorithm, efficient transport, good quality sputum, and potential under-screening of private clients.

OA23-371-10 Feasibility and performance of the PAANTHER treatment decision algorithm in HIV-infected children with presumptive tuberculosis: the prospective multicentre TB-Speed HIV study

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Background: TB is the leading cause of death and is challenging to diagnose among children living with HIV (CLHIV). Prompt and accurate TB diagnosis is key for reducing mortality.

We assessed the feasibility and performance of the PAANTHER TB treatment decision algorithm in CLHIV with presumptive TB.

Design/Methods: In an external validation study in Côte d'Ivoire, Mozambique, Zambia and Uganda, CLHIV aged <15-year-old with presumptive TB were enrolled in seven hospitals.

Assessments planned in the PAANTHER score/algorithm were: Xpert MTB/RIF Ultra (Ultra) on respiratory and stool samples, history of contact, symptoms (fever >2 weeks, unremitting cough, haemoptysis, weight loss in previous 4 weeks, tachycardia), chest radiography (CXR) and abdominal ultrasound features. A score ≥100 was diagnostic of TB and prompted treatment initiation. Children were followed-up for 6 months.

We assessed the time to treatment initiation in those scoring ≥100 and the proportion of missed TB cases (children scoring <100 initiated on TB treatment) and compared the negative predictive value (NPV, 1 - rate of false negative) to a 75% pre-established minimal acceptable lower CI limit.

Results: Of 277 CLHIV enrolled in the study (See characteristics in table), 272 (98.2%) had a complete evaluation; 210 (75.8%) scored ≥100, including 22 (10.5%) with positive Ultra results. Among children scoring ≥100, 182 (86.7%) were initiated on TB treatment, at a median of 1 (IQR: 0-3) day after inclusion.

Additionally, 12 missed TB cases were diagnosed in children scoring <100, for a NPV of 55/67 (82%; 95%CI: 71.3-89.4).

	Score <100 (N = 67)	Score ≥100 (N = 210)
Gender female – n (%)	34 (50.7%)	108 (51.4%)
Age – median [IQR]	4.67 [2.02, 10.0]	5.17 [1.92, 9.81]
Weight-for-age Z score <-2SD – n (%)	25 (37.3%)	81 (38.6)
CD4 percentage -median [IQR]	17.0 [12.9, 29.0]	21.0 [10.2, 29.8]
Xpert Ultra positive – n (%)	0 (0%)	22 (10.5%)
History of contact smear or Xpert + TB case - n (%)	0 (0%)	41 (19.5%)
CXR lesions evocative of TB – n (%)	15 (22.4%)	171 (81.4%)
Lymphadenopathies on abdominal ultrasound – n (%)	2 (3.0%)	34 (16.2%)
Initiated on TB treatment – n (%)	12 (17.9%)	182 (86.7%)

Conclusions: The PAANTHER algorithm was highly feasible in this population. It allowed most children with detected TB to initiate treatment within a day. Few TB cases were missed by the score, although the NPV was not significantly higher than 75%. The use of this algorithm should allow a rapid treatment decision and thus could reduce mortality in CLHIV.

OA-24 Person-centred care: how new technologies can support

OA24-372-10 Client-centered interventions to reach persons at high risk of TB: lessons from Kampala, Uganda

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Background and challenges to implementation: Tuberculosis (TB) disproportionately affects males in many high TB burden settings. However, access to TB care services is low among men, and those who present at health facilities present late leading to high mortality rates. The transport sector is male-dominated and these men are often unreached by the healthcare system due to their long working hours. We set out to implement a differentiated care approach that extended TB care services to these men at their work places.

Intervention or response: As part of the national drive to raise community awareness, improve TB screening, testing and treatment to end TB in Uganda and thus contribute to finding of the missing TB patients, USAID Local Partner Health Services TB project partnered with the Ministry of Works and Transport and the United Bus Operators' Association to reach men in three major bus terminals in Kampala City. From March 14th to 18th 2022, TB sensitization, screening, and diagnosis us-

ing CAD4TB mobile digital X-rays and GeneXpert were carried out. Patients diagnosed with TB were initiated on TB treatment at their workplace by health workers from the nearest public health facility.

Results/Impact: A total of 1,858 people was screened for TB during this period. Of these, 92% (1709/1858) were men and 1,131/1,858 (66%) were bus operators. Out of the persons screened, 867/1,858 (47%) had presumptive TB and 15 were diagnosed with TB using both the GeneXpert and CAD4TB. Majority of those diagnosed (13/15) were men. The number of TB cases diagnosed translated into a TB prevalence rate of 807/100,000 population which is three times higher than the national average (253/100,000 population).

Conclusions: This activity demonstrated the more people can be reached with TB services through interventions that bring health services closer to the people. This initiative should be replicated and scaled up among other high-risk groups for TB in Uganda.

OA24-373-10 Improved TB treatment outcomes through buddying TB patients with CBVs in 24 high-TB burden districts, Zambia

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Background and challenges to implementation: A patient's tuberculosis (TB) treatment outcome is directly dependent on their treatment adherence. In six Eradicate TB (ETB) project-supported provinces in Zambia, treatment success rates were less than 80%. Community-based volunteer (CBV)-supported directly observed therapy (DOT) was not working effectively. CBVs were demotivated, inadequately trained, and had limited support and enablers to provide care to patients.

Intervention or response: In 2018, ETB trained 500 CBVs from 24 high-TB burden districts and provided them with enablers to conduct routine TB awareness raising, active case finding, treatment adherence counseling, DOT, and patient follow-up. CBVs were also given a stipend for transport costs. ETB and facility TB focal point persons (TBFPPs) assigned or "buddied" each CBV with one to six patients, based on location. CBVs provided buddies with DOT and follow-up appointment reminders to ensure sputum smear examination at 2, 5, and 6 months of treatment to reduce patients lost to follow-up (LTFU). ETB and TBFPPs jointly provided supervision and mentorship to facility-based CBV supervisors.

Results/Impact: There was a noticeable rise in the proportion of TB patients successfully treated (completed and cured) after CBVs buddyed with them in these high-burden districts: treatment success in 2018 was 79%, 87% in 2019, 91% in 2020, and 92% in 2021. There was also a steady increase in the proportion of TB patients

cured from 68% in 2018 to 85% in 2021, compared to 66% to 70% during the same period in districts without CBV support. Additionally, patients LTFU reduced from 6% in 2018 to 3% in 2021 in project-supported districts.

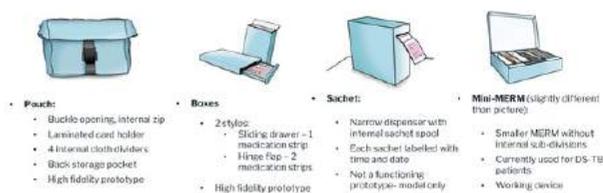
Conclusions: Buddying CBVs with TB patients for DOT management has demonstrated enhanced treatment adherence, improving TB treatment success rates. CBVs are well positioned to provide patient education, support adherence, and reduce disengagement during treatment if paired with TB patients. We recommend scaling up CBV buddies nationwide in Zambia.

OA24-374-10 Designing for diversity in patient preferences for digital adherence products across urban and rural India

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Background: Digital adherence technology (DAT) product (99dots, MERM, VoT) uptake among TB patients has been limited by factors including stigma, user burden, low digital access and portability.

Preferences for novel prototypes among patients, providers, and caregivers were studied in India to develop user segments based on specific form factor and feature needs.



Design/Methods: A purposively sampled study was conducted with 203 current TB patients in a rural northern district (Darbhanga, Bihar) and a metropolitan Southern city (Chennai, Tamil Nadu). Product preferences were captured through a standardized patient walkthrough survey.

Latent cluster analysis (LCA) was used to derive patient clusters. A logistic regression model was used to profile clusters by identifying significant psychosocial differences across segments.

Subsequently, a longitudinal usability study was conducted with 23 patients over 3 weeks. In-depth interviews were thematically analyzed.

Results: Overall, a majority of patients preferred the pouch design, followed by the MERM. Cluster analysis yielded three segments with different preferences. The first segment (42%) of “homebound agnostics“ were open to using multiple products. This group tended to be older, more rural, less literate and take medicines at home. The second segment (37%) were identified as “low burden seekers“ and preferred the easily operable and spacious MERM device and pouch. This group tended to be younger, less likely to travel and face lower levels of self-reported TB stigma. The third segment (21%) faced self-reported TB stigma and traveled frequently. This group identified significant adoption challenges for all devices except the pouch, valued for portability and discretion. They were wealthier, more urban, and disproportionately female.

Conclusions: Given varying levels of digital access, and adoption challenges, patient preferences around adherence products should be a key factor directing product development, and targeting within large-scale DAT programs, such that acceptance of these tools can be optimized.

OA24-375-10 Decentralization of ECG monitoring using a mobile device (KardiaMobile-6L) for patients on drug-resistant tuberculosis (DR-TB) treatment in an outpatient setting

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Background and challenges to implementation: Drug resistant TB Patients receiving new drugs or novel treatment regimens with QT prolonging effect required Electrocardiogram (ECG) monitoring throughout the treatment period. ECG is an integral part of active TB drug-safety monitoring and management (aDSM) to ensure timely identification and management of QT prolongation. Access to ECG is mostly limited to centralized settings, which would mean patients have to stay admitted in hospitals or frequently travel long distances to healthcare facilities. Decentralization of ECG monitoring is essential.

Intervention or response: Innovations in medical technology prompted the use of mobile ECG devices designed for personalized care in ambulatory settings thereby providing a valuable patient-centered approach to decentralized ECG monitoring and minimizing unnecessary patient visits to the healthcare facilities. The AliveCor KardiaMobile 6L device wirelessly transmits

ECG data to a smartphone or tablet. KardiaMobile 6L was approved for ECG monitoring of QT prolongation on coronavirus patients (SARs-COV 2)-COVID-19, treated with cardiotoxic drugs. KardiaMobile 6L is a simple and easy to use device by patients themselves to record ECG and transfer via the internet for clinical evaluation.

Results/Impact: KardiaMobile 6L device has been implemented as a pilot study to decentralize ECG monitoring for patients on drug-resistant tuberculosis (DR-TB) treatment in an outpatient setting in Kazakhstan. Between December 2021 and April 2022, 66 patients were screened and 64 enrolled. Safety monitoring of patients using the device is recognized as being satisfactory.

Conclusions: With more innovation of medical technology being discovered and the expansion of the digital health interventions in TB care, there is a need to continue studying new devices in the management of DR-TB not only to improve patient’s safety monitoring and care but, to reduce the burden of in-patient hospital stay and minimize frequent healthcare visits by introducing decentralization method of care.

OA24-376-10 Patient acceptability of using medication monitors and experience of a differentiated care approach for TB treatment adherence in South Africa

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Background: The introduction of digital adherence technologies (DATs) in tuberculosis (TB) programmes supports treatment completion among people with tuberculosis (PWTB). However, adoption of DATs relies on understanding end-user insights to refine implementation. We evaluated the acceptability of using medication monitors (Wisepill evriMED 1000 device) prompting a differentiated care approach (DCA), involving short message service - SMS, phone calls, home visits and motivational counselling, among PWTB in South Africa.

Design/Methods: We conducted 60 in-depth interviews with PWTB in local languages across three provinces (January - October 2020). PWTB were purposively selected by treatment month, adherence history and gen-

der. Interviews were audio recorded, transcribed verbatim and translated. Saturation was assessed during data collection. Using a deductive approach and the Theoretical Framework for Acceptability (TFA), we explored prospective, concurrent, and retrospective acceptability (before, during, and after the intervention) across the sample attributes.

Results: PWTB across adherence histories showed a positive affective attitude towards using the monitor and receiving the DCA support. PWTB appreciated SMS reminders and phone calls as they felt that providers cared for their health allowing them to accept their TB diagnosis. Home visits were less acceptable to those who felt stigmatized by their neighbours. Some PWTB across gender and adherence history felt that the monitor was large, and the alarm drew attention to their TB status, potentially causing embarrassment and stigma. Due to perceptions of stigma, PWTB adapted the intervention by taking pills out of the monitor and leaving it at home so someone else could track usage for them while they used alternative reminders such as cell phones to take their medication.

Conclusions: Perceptions of stigma motivate PWTB to adapt use of medication monitors to their lifestyle. Achieving people-centered TB care, including the introduction of DATs, will require that TB programmes incorporate patient insights to maximize their adoption and effectiveness.

OA24-377-10 Developing a method to incorporate multidimensional wealth indices into analysis of TB patient cost surveys

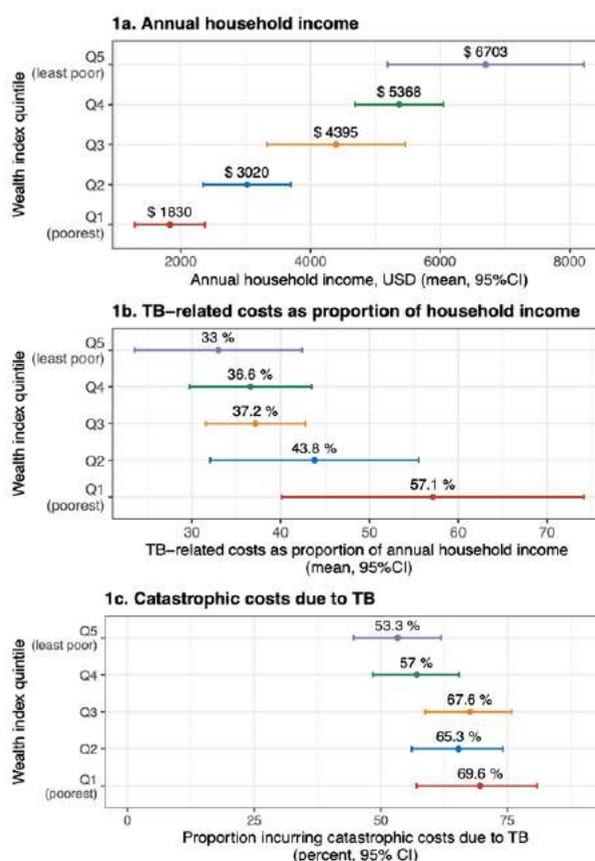
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Background: Half of TB-affected households face catastrophic costs related to illness, care-seeking and treatment globally. Anecdotally, the poorest TB-affected households are most likely to incur catastrophic costs. WHO National TB-Patient Cost Surveys (TB-PCS) have used household income/expenditure quintile to estimate

the distribution of catastrophic costs by socioeconomic strata. This is methodologically arbitrary because household income/expenditure is also used to calculate catastrophic costs (total TB-related costs >20% of a TB-affected household's annual income/expenditure). Using data from the Lao People's Democratic Republic (Lao PDR) TB-PCS, we developed a wealth index to support equity analyses of catastrophic costs distribution.

Design/Methods: We conducted secondary analyses of the 2019 Lao PDR national TB-PCS, which included 725 people with TB from 25 districts selected by cluster randomisation. Using principal component analysis of baseline data on ownership of 20 household assets and living standards (housing, water source, toilet facilities, cooking fuel), we derived a multidimensional wealth index for TB-affected households. We then evaluated the index's association with household income and catastrophic costs.

Results: The wealth index was associated with household income prior to TB diagnosis in multivariable linear regression adjusted for gender, primary income earner status, age, education, occupation and household size ($\beta=7.22$, $p<0.001$).



Household income increased across wealth quintiles (Figure 1a). Mean total TB-related costs as a percentage of annual household income was 57.1% (95%CI 40.1-71.2%) in the poorest quintile, compared to 33.0% (95%CI 23.6-42.4%) in the least poor quintile (Figure 1b). The proportion of households incurring cata-

strophic costs due to TB in the poorest and least poor quintiles were 69.6% (95%CI 57.0-80.8%) and 53.3% (95%CI 44.6-61.8%) respectively (Figure 1c).

Background and challenges to implementation: Half of TB-affected households face catastrophic costs related to illness, care-seeking and treatment globally. Anecdotally, the poorest TB-affected households are most likely to incur catastrophic costs. WHO National TB-Patient Cost Surveys (TB-PCS) have used household income/expenditure quintile to estimate the distribution of catastrophic costs by socioeconomic strata. This is methodologically arbitrary because household income/expenditure is also used in the calculation of catastrophic costs (total TB-related costs >20% of a TB-affected household's annual income/expenditure). Using data from the Lao People's Democratic Republic (Lao PDR) TB-PCS, we developed a wealth index to support equity analyses of catastrophic costs distribution.

Intervention or response: We conducted secondary analyses of the 2019 Lao PDR national TB-PCS, which included 725 people with TB from 25 districts selected by cluster randomisation. Using principal component analysis of baseline data on ownership of 20 household assets and living standards (housing, water source, toilet facilities, cooking fuel), we derived a multidimensional wealth index for TB-affected households. We then evaluated the index's association with household income and catastrophic costs.

Results/Impact: The wealth index was associated with household income prior to TB diagnosis in multivariable linear regression adjusted for gender, primary income earner status, age, education, occupation and household size ($\beta=7.22$, $p<0.001$). Annual household income increased across wealth quintiles (Figure 1a). Mean total TB-related costs as a percentage of annual household income was 57.1% (95%CI 40.1-71.2%) in the poorest quintile, compared to 33.0% (95%CI 23.6-42.4%) in the least poor quintile (Figure 1b). The proportion of households incurring catastrophic costs due to TB in the poorest and least poor quintiles were 69.6% (95%CI 57.0-80.8%) and 53.3% (95%CI 44.6-61.8%) respectively (Figure 1c).

Conclusions: A multidimensional wealth index based on asset ownership and living standards correlated with annual household income. Wealth index scores could be used in TB-PCS equity analyses to evaluate the distribution of catastrophic costs across socioeconomic strata.

OA24-378-10 Integrated management of childhood illness: a potential platform to identify the missing under-five children with tuberculosis in Bangladesh

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Background and challenges to implementation: Globally as well as in Bangladesh, a large number of estimated children with TB are still missed (4% vs 9%) and majority are assumed to be under-5. Integrated Management of Childhood Illness (IMCI) is an established platform for detecting under-5 childhood diseases, hence can be used to facilitate TB screening among children with TB-like symptoms leading to a reduction in misdiagnosis.

Intervention or response: Under-5 children visiting IMCI corners of 19 healthcare facilities in Bangladesh were screened through active case finding approach under activities of USAID's Alliance for Combating TB in Bangladesh (ACTB). Health workers of IMCI corners were oriented on child TB screening. Under-5 children visiting IMCI corners were screened using a standardized symptom-based checklist, and identified TB presumptives were referred to local physicians for further evaluation. Presumptives underwent necessary tests as advised by physicians. Diagnosis was made bacteriologically (B+ve) and clinically (CD) by physicians. All children with TB were treated according to national guideline.

Results/Impact: Between 01 March and 15 April 2022, among 46,025 under-5 children screened for TB [median age 1.5 (IQR:1,3) years], 836 (1.8%) were found as TB presumptives and 681 (81.5%) underwent TB testing. Among tested, 573 (87.4%) had cough ≥ 2 weeks, 595 (84.1%) had fever, 381 (56.0%) had weight loss, 205 (30.1%) breathing difficulty, 76 (11.2%) had family members with TB, 90 (13.2%) had fatigue and 59 (8.7%) had lump in body. Total 25 (3.7%) children were diagnosed with TB and 11 (44%) were <2 years old. Total 21 (84%) were pulmonary (B+ve: 3; CD: 18) and four were extra-pulmonary TB.

Conclusions: TB integration with IMCI can be helpful for under-5 child TB diagnosis and may add a new dimension in policy guideline. Training and sensitization of service providers on TB screening can help sustain this activity and thereby improve detection of under-5 child TB.

OA-25 Models and TB immunity

OA25-379-10 Blood transcriptional correlates of vaccine-induced protection against TB in macaques

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Background: Identifying correlates of vaccine-induced protection against tuberculosis (TB) is essential for improved vaccine development and evaluation. Prior efforts have focused on antigen-specific CD4 T cell responses measured weeks following vaccination, which have repeatedly failed to correlate with protection.

Design/Methods: Here, we analyzed the blood transcriptional response to vaccination in rhesus macaques vaccinated intravenously (IV) with high- (N=16) or low-dose (N=18) BCG that exhibited varying protection against *Mtb* challenge six months later. We identified correlates of protection in high-dose recipients and validated in low-dose recipients and in an independent cohort of BCG-vaccinated macaques. We also compared the blood transcriptional response to adaptive responses in the bronchoalveolar lavage (BAL).

Results: We identified and independently validated seven modules of 2,499 genes induced two days, two weeks, four weeks, and/or twelve weeks post-vaccination. Adaptive modules were associated with protection against challenge in low-dose recipients but not high-dose recipients. In contrast, an innate module (Module 1) on day 2 post-vaccination was associated with protection outcomes eight months later in both high- and low-dose recipients, as well as in an independent cohort of macaques. Module 1 scores at day 2 post-vaccination were also highly correlated with BAL adaptive responses, including *Mtb*-specific IgA and IgG titers at week 4, log T cell (CD4+, CD8+, MAIT, Vg9) counts at week 4, and antigen-specific CD4+ T cell responses (IFN γ , IL2, IL21, TNF) at week 8 ($r=0.7$, $p<0.0001$). None of these lung adaptive markers could reliably predict protection in both high- and low-dose recipients. However, module 1 scores at day 2 post-vaccination accurately predicted protection following *Mtb* challenge six months later (high-dose recipients, AUC=0.8; low-dose recipients, AUC=0.99).

Conclusions: These results suggest that adaptive responses are necessary but not sufficient for IV-BCG-induced protection. Instead, the early innate response in peripheral blood may be a more reliable and generalizable correlate of protection.

OA25-380-10 Harnessing machine learning to eliminate tuberculosis (HaMLET)

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Background: Every year, approximately 550,000 immigrants and refugees apply to enter the United States. As part of our mission to prevent the introduction of communicable diseases into the U.S., CDC's Immigrant Refugee and Migrant Health Branch requires applicants who are ≥ 15 years of age to receive a chest x-ray to screen for tuberculosis during their overseas medical examinations before arriving in the U.S. Since September 2018, digitized x-rays have been shared with CDC. The CDC HaMLET project is developing a machine-learning algorithm to identify normal/abnormal chest x-rays and assist with image quality assessments.

Design/Methods: The dataset collected was comprised of approximately 172,000 x-rays captured between 2013 and 2021. About 26,000 (15%) of the x-rays were abnormal, and about 1,600 (1%) were from patients with active TB disease. Our model architecture comprised an EfficientNet B7 convolutional neural network, pre-trained on ImageNet, along with custom layers for image augmentation and final classification. The dataset was split into 3 parts: a set of about 155,000 x-rays to train the model to identify x-rays with any abnormality; a validation set of 8,000 x-rays to tune hyperparameters and prevent overfitting; and a testing set of 8,000 x-rays to evaluate model performance.

Results: The model achieved an area under the receiver operating characteristic curve on the test data of 87%. Using the decision threshold that maximized Youden's J index, the model's sensitivity and specificity on the test data were 73% and 87%, respectively. Using the decision threshold that minimized the difference between sensitivity and specificity, the model estimated the number of abnormal x-rays to within 1%.

Conclusions: The model's performance on the test data appears to be sufficient to indicate usage for quality assessment of large batches of x-rays. This automated detection model can potentially provide additional quality assurance for radiographic interpretations of overseas medical examinations.

OA25-381-10 TIGIT marks potent effector CD8⁺ T cells in patients with active tuberculosis

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Background: Understanding T cell immune response against *Mycobacterium tuberculosis* (*M. tb*) is vital to developing novel treatment strategies. TIGIT is one of the most well-recognized immune checkpoint receptors, but how it regulates T cells in tuberculosis remains unclear.

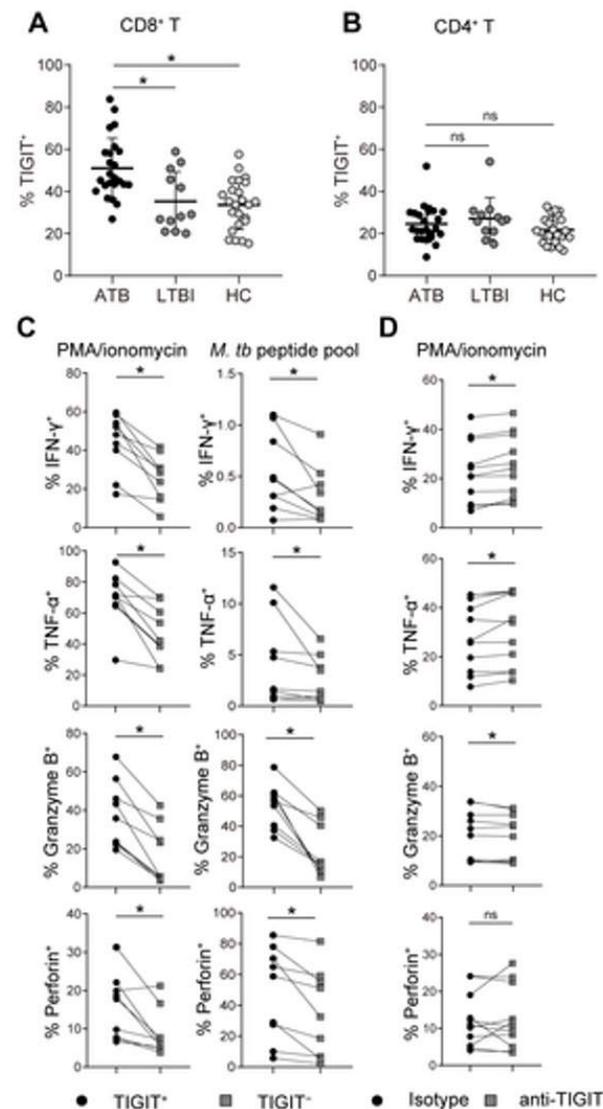


Figure 1. (A-B) TIGIT expression on T-cell subsets. Production of effector molecules (C) in TIGIT⁺ and TIGIT⁻ CD8⁺ T cells upon stimulation, and (D) in CD8⁺ T cells upon *in vitro* TIGIT blockade.

Design/Methods: This study enrolled 44 patients with active tuberculosis (ATB), 12 individuals with latent tuberculosis infection (LTBI) and 24 healthy volunteers (HC). Peripheral blood mononuclear cells were isolated and assessed by flow cytometry. A Kruskal-Wallis test followed by Dunn's test or paired Wilcoxon test was used to compare variables.

Results: TIGIT expression on CD8⁺ T cells was significantly higher in ATB patients (51.02 ± 14.36%) than in LTBI (35.28 ± 14.08%, *P* = 0.01) and healthy (33.63 ± 11.63%, *P* < 0.01) individuals (Figure 1A). Meanwhile, TIGIT expression on CD4⁺ T cells was comparable between three populations (Figure 1B). Upon *in vitro* with phorbol myristate acetate (PMA) and ionomycin or with *M. tb* peptide pool, significantly higher proportions of IFN-γ⁺, TNF-α⁺, granzyme B⁺ and perforin⁺ cells were observed in the TIGIT⁺ CD8⁺ T-cell subset than those in the TIGIT⁻ subset (all *P* < 0.05, Figure 1C).

Compared to those blocked with isotype IgG, *in vitro* blockade with anti-TIGIT antibody further enhanced the production of IFN-γ, TNF-α and granzyme B among CD8⁺ T cells (all *P* < 0.05), except for perforin (*P* = 0.90, Figure 1D).

Conclusions: In active tuberculosis, the upregulated immune checkpoint TIGIT marked potent effector CD8⁺ T cells, instead of exhausted ones. CD8⁺ T-cell functions were boosted by blocking TIGIT. These findings provide new insights into the regulation of anti-tuberculosis T cell immunity and may help develop novel immunotherapies for tuberculosis.

OA25-382-10 The presence of indoleamine 2,3-dioxygenase in an aerosol-mediated infant rhesus macaque tuberculosis model

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Background: Tuberculosis (TB) is a disease caused by the bacteria *Mycobacterium tuberculosis* (*Mtb*) and remains an important cause of morbidity and mortality worldwide. Although active and latent TB models have been well developed in adult macaques, little is known about the immune landscape of the lungs, disease progression or latency, and expression of IDO in infant rhesus macaques. We here established an aerosol-mediated infant NHP model to study immunopathogenesis of pediatric TB and expression of IDO in *Mtb*-exposed infant macaques.

Design/Methods: A total of eight 10-week-old infant rhesus macaques (*Macaca mulatta*) were infected with aerosolized *Mtb* CDC1551 with two different doses and then monitored for disease progression. All animals were euthanized for tissue collection at the end of the study to evaluate pathological and immunological changes re-

sulting from *Mtb* infection. Immunohistochemistry and microscopy were performed to examine the expression of IDO in the pulmonary tissues collected from necropsy.

Results: We found that TB symptoms in all 4 high-dose *Mtb*-exposed infants were more acute in onset and resulted in concurrent pulmonary and extra-pulmonary TB (EPTB), which is distinct from the 4 infants with reduced infectious dosing that had a more chronic disease course with pathology being limited to primary infectious sites. We also observed the acute infant TB models presented with high levels of IDO expression in pulmonary granulomas co-localizing within the band of epithelioid macrophages as previously reported in adult rhesus macaques with active TB, suggesting inhibition of tryptophan metabolism via IDO blockade may also enhance immune-mediated control of TB in the infants.

Conclusions: We have experimentally demonstrated increased susceptibility to TB disease by using *Mtb* aerosol inoculation in infant rhesus macaques, and this infant TB NHP mode can be used to understand immunopathogenesis of TB in young children and to evaluate promising pediatric treatments.

OA25-383-10 *Mycobacterium tuberculosis* infection among children and adolescent contacts of pulmonary tuberculosis cases in Brazil: a multi-center prospective cohort study

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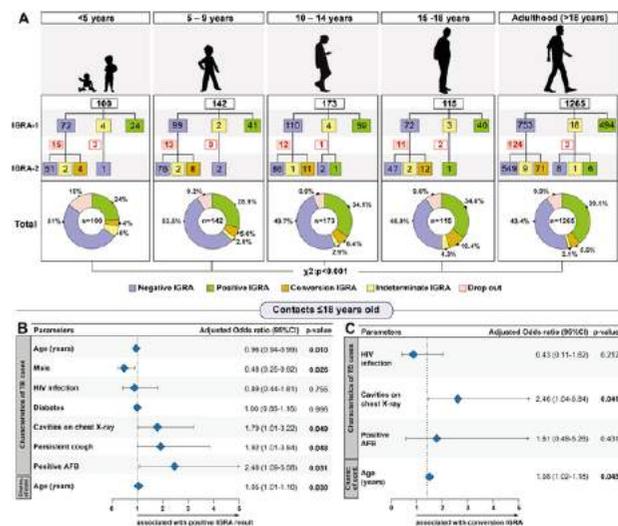
Background: Identification of children and adolescents with *Mycobacterium tuberculosis* infection (TBI) after TB exposure is essential to prevent TB in this high-risk population.

Design/Methods: Close contacts of pulmonary TB patients enrolled between 2015-2019 in a multi-center Brazilian cohort were followed for up to 24 months and classified according to age groups: <5 years, 5-9 years, 10-14 years and 15-18 and >18 years old (used as reference group). Clinical and radiographic evaluation,

interferon-gamma release assay (IGRA) testing at baseline and 6 months, among other data were collected. A multivariable mixed-effects logistic regression was performed to identify factors associated with TBI.

Results: Among 1,795 TB contacts identified, 530 (29.5%) were ≤18 years old. 28% of the <5 years group had a positive IGRA result (baseline + month 6), 34.5% in the 5-9 years group, 40.7% between the 10-14 years group and 44.7% among the 15-18 years group. However, at month 6, the highest frequency (10.4%) of IGRA conversion (negative at baseline and positive at month 6) was observed in persons 15-18 years old. Multivariable regression revealed that increased age, male sex, presence of cavitation on chest X-ray, persistent cough, and positive acid-fast bacilli of the TB index case as well as older age in contacts were independently associated with a positive IGRA result.

Furthermore, cavitation on chest X-ray of the TB index case and older age in contacts were also independently associated with IGRA conversion at month 6 in ≤18-year-old group.



Conclusions: Persons 15-18 years old were at high risk for IGRA conversion at month 6. The difficulty of obtaining a valid IGRA result among those under 5 years old, as well as the high conversion in persons 15-18 years old, highlight the need to develop better diagnostic tests and follow-up policies for those contacts of individuals with TB.

OA25-384-10 Pre-diagnosis and Pre-treatment loss to follow-up of presumptive tuberculosis patients presenting at selected health facilities in Uganda

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Background: Pre-diagnosis loss of presumptive tuberculosis (TB) patients and pre-treatment loss to follow-up (dropout of patients after diagnosis but before treatment initiation) are two major gaps in TB care globally and in Uganda. This study aimed to determine the proportion of presumptive TB patients that are lost to follow-up before diagnosis and before treatment initiation for confirmed TB cases; and associated factors in Uganda.

Design/Methods: This was a retrospective cohort analysis involving extraction of routinely collected data in TB registers of presumptive patients (all ages) who presented to four selected health facilities in Uganda (2019-2020). Variables captured included, age, sex, HIV status, dates of identification as presumptive, having a telephone number recorded, area of residence recorded, date of TB test result if done and date of TB treatment initiation. Frequencies and their corresponding proportions were used to summarise the data. Chi-square tests as well as Modified Poisson regression analysis using STATA version 15 was done to determine factors associated with pre-diagnosis and pre-treatment loss to follow up (LTFU).

Results: Of the 5,717 presumptive TB patients, 56.8% were females and 20.8% in the age range of 26 to 35 years. Pre-diagnosis LTFU was 24.1% and pre-treatment LTFU, 13.9%. Being HIV positive [Adjusted prevalence ratio (APR): 1.25; 95% CI 1.11-1.42], being female (APR: 1.12; 95% CI, 1.02-1.22) and having no telephone number recorded (APR: 1.14; 95% CI 1.04-1.25) were significantly associated with pre-diagnosis LTFU. Having no telephone number recorded (APR: 2.01; 95% CI 1.32-3.06) and no area of stay recorded (APR: 3.48; 95% CI 2.19-5.51) were significantly associated with pre-treatment LTFU.

Conclusions: The pre-diagnosis and pre-treatment LTFU reported in this study were high. Interventions need to be put in place to address this LTFU with a focus on people living with HIV.

OA25-385-10 Improving clients' satisfaction by reducing intra turnaround time in the Tuberculosis Reference Laboratory Douala from March to April, 2022

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Background and challenges to implementation: Turn-around time (TAT) is defined as time interval between specimen reception and results deliver. TAT is often regarded as one of the determinants of laboratory efficiency. The Xpert MTB/RIF ultra assay was introduced for timely and accurate detection of tuberculosis (TB). The entire laboratory testing process is divided into three phases: pre-analytical, analytical and post-analytical. To the best of our knowledge, data is not available on TAT and factors associated with failing TAT for TB testing in Cameroon.

This intervention aims at evaluating intra TAT in the diagnosis of TB by Xpert MTB/RIF ultra in the Tuberculosis Reference Laboratory Douala (TBRL-D'la) and to identify source of failed TAT.

Intervention or response: This laboratory-based intervention was conducted from 01st March to the 30th of April 2022. Brainstorming among the TBRL-D'la team using the 5-Whys problem investigation quality improvement and fish born methods was the root cause analysis tool used for identifying reasons for TAT failure. Acceptable TAT for Xpert testing was set at 24 hours.

Results/Impact: Overall, 526 clients were tested by Xpert MTB/RIF Ultra during the study period. The median TAT of samples in this study was 35 (2-120) hours. A total of 108 (20.5%) clients failed TAT. The pre-analytic, analytic, and post-analytics phases were associated with 42(38.9%), 54(50%), and 12(11.1%) TAT failure. Equipment-related causes represented 83.3% (45) of the analytic phase-related TAT failure amongst which modules associated problems accounted for over 88.9% (40).

Conclusions: Overall, this study revealed that delays in module replacement were most responsible for TAT failures. Training at least a super-user on module replacement in each gene Xpert testing laboratory rather than using one person for basic maintenance such as module replacement will greatly reduce intra turnaround time in the laboratory and consequently Improve clients' satisfaction.

E-POSTER SESSION (EP)

EP-21 Various lessons learnt from active case finding

EP-21-799 Pooled testing of sputum with Xpert MTB/RIF and Xpert MTB/RIF Ultra in tuberculosis active case finding intervention in Lima, Peru

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Background: Active case finding of tuberculosis suspected people is a key intervention to determine the real tuberculosis prevalence in the community. This requires testing many people with low positivity, generating a high cost when using molecular techniques endorsed by WHO. We assessed the diagnostic performance of Xpert-MTB/RIF and Xpert-MTB/RIF Ultra testing and their effectiveness in pooled samples in Lima, Peru.

Design/Methods: The active search strategy for people with respiratory signs and symptoms suspicious for tuberculosis was carried out in Lima; running Xpert MTB/RIF and Xpert MTB/RIF ULTRA. Pools of 5 and 10 sputum samples of TB suspects were analyzed and compared with individual testing results. Positivity, concordance and costs between the individual and pooled testing using Xpert-MTB/RIF and Xpert-MTB/RIF Ultra were assessed.

Results: From 290 specimens included, 2.8% (8/290) were culture positive.

In comparison to individual analysis, the sensitivity and specificity of 5-specimen pools utilizing Xpert-MTB/RIF were 77.8% (95% CI: 40%-97.2%) and 100% (95% CI: 98.7%-100%), respectively.

10-specimen pools shown 88.9% (95% CI: 51.8%-99.7%) and 100% (95% CI: 98.7 %-100%) of sensitivity and specificity, respectively.

Xpert-MTB/RIF ULTRA in 5- and 10-pools types shown a sensitivity of 100% (95% CI: 54.1%-100%) and specificity of 100% (95% CI: 98.7 %-100%).

Compared with individual analysis, 5-pools resulted in a 68% and 10-pools resulted in a 65% reduction in cartridge costs.

Background and challenges to implementation: La búsqueda activa de casos de personas sospechosas de tuberculosis es una intervención clave para determinar la prevalencia real de tuberculosis en la comunidad. Esto requiere testear a muchas personas con baja positividad, generando un alto costo al utilizar técnicas moleculares

avaladas por la OMS. Evaluamos el desempeño diagnóstico de las pruebas Xpert-MTB/RIF y Xpert-MTB/RIF Ultra y su efectividad en muestras agrupadas en Lima, Perú

Intervention or response: Se analizaron grupos de 5 y 10 muestras de esputo de sospechosos de TB y se compararon con los resultados de las pruebas individuales. Se evaluó la positividad, la concordancia y los costos entre las pruebas individuales y agrupadas utilizando Xpert-MTB/RIF y Xpert-MTB/RIF Ultra

Results/Impact: From 290 specimens included, 2.8% (8/290) were culture positive.

In comparison to individual analysis, the sensitivity and specificity of 5-specimen pools utilizing Xpert-MTB/RIF were 77.8% (95% CI: 40%-97.2%) and 100% (95% CI: 98.7%-100%), respectively.

10-specimen pools shown 88.9% (95% CI: 51.8%-99.7%) and 100% (95% CI: 98.7 %-100%) of sensitivity and specificity, respectively.

Xpert-MTB/RIF ULTRA in 5- and 10-pools types shown a sensitivity of 100% (95% CI: 54.1%-100%) and specificity of 100% (95% CI: 98.7 %-100%).

Compared with individual analysis, 5-pools resulted in a 68% reduction in cartridge costs

Conclusions: Good agreement between individual and pooled tests was found. The application of pool specimen analysis in community screening of tuberculosis may benefit resource-constrained countries.

EP-21-800 Intensified TB case finding using digital X-ray and CAD4TB among people living with HIV receiving care at health facilities in Uganda

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Background and challenges to implementation: Uganda is among the 30 high TB/HIV burden countries and among the 20 countries that contribute to 83% of the missing TB patients globally.

Systematic screening for TB using chest X-ray is recommended for people seeking care at health facilities to improve TB case identification.

We present findings from using digital X-ray and computer aided detection (CAD4TB) technology for TB screening among people living with HIV (PLHIV)

Intervention or response: Five health facilities with digital X-ray and CAD4TB were supported to conduct TB screening for patients seeking care using X-ray.

Health workers were mentored on X-ray screening and disseminated standard operating procedures on eligibility for X-ray examination, with emphasis on PLHIV and other high-risk groups including contacts, diabetic patients and prisoners.

Patients with CAD4TB score of 60% or more were presumed with TB and referred for GeneXpert MTB Rif testing. Those confirmed with TB were initiated on standard TB treatment.

X-ray screening data was reported using Off-line data kit and excel files downloaded centrally for analysis

Results/Impact: Cumulatively, 4,463 individuals were screened with X-ray at five health facilities from July 2020 to November 2021. Of these, 691 (15.5%) had abnormal chest X-ray and 368 (53.3%) individuals had sputum samples tested with GeneXpert MTB Rif of which 48 (13%) were bacteriologically confirmed.

Among those screened, 1,013 (22.7%) were PLHIV. Of these, 165 (16.3%) had suggestive X-ray and 93 (56.4%) patients had their sputum tested with GeneXpert of whom 20 (21.5%) PLHIV were bacteriologically confirmed with TB.

Category of patient		Total screened	Abnormal X-ray (%)	Tested by X-pert (%)	Confirmed with TB (%)
All	All	4463	691 (15.5)	368 (53.3)	48 (13.0)
Gender	Female	2454 (55.0)	315 (12.8)	152 (48.3)	12 (7.9)
	Male	2009 (45.0)	376 (18.7)	216 (57.4)	36 (16.7)
Age	0-14	182 (4.1)	34 (18.7)	7 (20.6)	1 (14.3)
	15+	428 (95.9)	657 (15.3)	361 (54.9)	47 (13.0)
Risk group	HIV positive	1013 (22.7)	165 (16.3)	93 (56.4)	20 (21.5)
	TB contact	778 (17.4)	139 (17.9)	85 (61.2)	17 (20.0)
	Health worker	153 (3.4)	16 (10.5)	8 (50.0)	0
	Prisoner	424 (9.5)	12 (2.8)	4 (33.3)	0

Conclusions: TB screening using CXR led to identification of substantial TB patients with TB yield almost twice among PLHIV and contacts compared to the yield among all individuals screened with X-ray.

Ministry of Health should prioritize digital X-ray and CAD4TB for routine screening of TB among PLHIV seeking health care for early TB detection, treatment initiation and improved outcomes.

EP-21-801 Finding “missing TB cases” using digital chest X-ray with computer-aided detection (CAD) during TB screening in South Africa

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Background and challenges to implementation: The national TB prevalence survey in South Africa showed that 57.7% of the TB cases had no symptoms but exhibited abnormalities on chest X-Rays. Chest radiography is a highly sensitive tool for detecting pulmonary tuberculosis. Today, digital chest X-Rays are cost-effective and standardised interpretation of CXRs is available instantly using AI CAD software to aid TB detection.

Intervention or response: THINK, in partnership with the KZN DoH is implementing an active case finding intervention in KwaZulu-Natal supported by USAID TB LON, wherein 3 mobile X-Ray vans have been deployed in 4 districts. As part of the TB screening, a CXR is taken, while the nurse does symptoms screening of all patients. CXR interpretations are instantly available using the AI CAD software, qXR, which are reviewed by the Radiographer. Those with CXR presumptive of TB or exhibiting TB symptoms or risk factors (irrespective of radiology results) are asked to provide sputum for GeneXpert.

Results/Impact: A total of 1584 patients (Female – 1088, Male 495, Unknown –1) with mean age 42 (25th percentile 31, 75 percentile 53, HIV +ve in 38.12%, Diabetes in 7.8%, Hypertension 20.1%) were tracked.

qXR achieved sensitivity of 0.867 and specificity 0.882 against GeneXpert ground truth.

Out of total 103 CXRs identified as Suggestive of TB by qXR, 32 cases were asymptomatic, of which 7 were initiated on TB treatment (3 cases were confirmed positive by GeneXpert, and 4 cases were clinically diagnosed). Overall, of the cases that were flagged as TB presumptive by AI, 19.7% were microbiologically confirmed with TB.

Conclusions: Early indications reveal the benefit of using mobile Digital CXR and CAD as one of the key strategies to identifying TB in asymptomatic patients and thereby contributing to finding the missing TB cases in South Africa. These are preliminary findings based on data available from the first 6 weeks of the program.

EP-21-803 Results from a contact investigation strategy piloting use of an ultraportable radiography system in Ho Chi Minh City, Viet Nam

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Background: Vietnam has made significant progress towards universal health coverage (UHC) through a government-provided Social Health Insurance (SHI) scheme, and over 90% of the general population is currently enrolled. However, 63% of TB-affected households face catastrophic costs. In late 2022, reimbursements for TB care will be expanded by the national SHI.

Design/Methods: This was a collective case study, with naturalistic design and theoretical sampling of persons without SHI using a mixed method, interpretivist approach. Using data from a pilot that enrolled people with TB in SHI, we employed descriptive statistics and framework analysis of in-depth individual interviews to identify the challenges faced by people with TB. Additionally, we conducted a national legislation review related the integration of TB care into SHI.

Results: From the quantitative analysis of the pilot data, we found that 78.8% of participants who began TB treatment without SHI were able to enrol. The median days it took between treatment enrolment and the issuance of the SHI card was 33. 18.3% of eligible households were never enrolled in SHI, mainly due to missing documentation (89.5%).

Quantitative results	Percentage of participants enrolled in SHI	78.8% (82 out of 104)
	Median days between TB treatment start and SHI issue	33
	Average household members included in SHI enrolment	2.4
	Average cost for SHI enrolment	1,551,492 VND/67.75 USD
	Proportion of participants never enrolled	18.2% (19 out of 104)
Qualitative results	Theme 1: People with TB perceive the cost of enrolment in SHI as high, especially for low-income families in Viet Nam.	
	Theme 2: People with TB perceive the SHI enrolment process as tedious and complicated.	
	Theme 3: Some people with TB face difficulties in meeting the administrative requirements to enrol in SHI.	
Legislation review	Law of Health Insurance, 2013: increases co-payment rate and transitions to household-based registration for health insurance, rather than individuals.	
	Circular 36/2021/TT-BYT, 2022: defines the beneficiaries, medical expenses related to TB diagnosis and treatment eligible for SHI reimbursement.	

From the qualitative framework analysis, three challenges were identified:

1. The cost of SHI enrolment was perceived as high;
2. SHI enrolment was viewed as tedious and complicated;
3. Some face difficulties meeting the administrative requirements to enrol in SHI.

From the legislation review, we identified nine legal documents guiding the integration of TB and SHI. However, no specific provisions have been made for the uninsured initiating TB treatment.

Background and challenges to implementation: An estimated 60% of people with TB in Viet Nam do not report TB symptoms, and the only way to detect these people is through chest X-ray (CXR) screening. However, people often face barriers in accessing facility-based radiography services, particularly contacts of TB patients who otherwise feel healthy.

As a result, the proportion of eligible people who are fully evaluated for TB is often low, reducing the effectiveness of screening programs.

Intervention or response: We addressed this access barrier by piloting dedicated screening events for household and community contacts at Commune Health Stations (CHSs) using an ultraportable radiography system (Fujifilm CALNEO X-air). CHSs are often much closer to the homes of contacts than District TB Units, and the CXR screening at the dedicated events was provided free-of-cost.

People with an abnormal CXR result provided a good-quality sputum specimen on the spot, which was transported to a laboratory for testing with the Xpert MTB/RIF Ultra (Xpert) assay.

Results/Impact: Between November 2021 and April 2022, we piloted 17 days of dedicated screening events for contacts across five districts of Ho Chi Minh City, Viet Nam. 630 contacts (1.8 per index patient) were mobilized and screened using CXR, resulting in the detection of 209 contacts (33.2%) with an abnormal radiograph.

Over 95% of eligible contacts provided a sputum specimen which was tested with the Xpert assay. Eight contacts were diagnosed with TB, resulting in a detection rate of 1,270 / 100,000 -- 7.2x the national TB incidence rate. Five (62.5%) contacts diagnosed with TB did not report TB symptoms and their detection would likely have been missed/delayed without CXR screening.

	Male	Female	Total
Number of days	-	-	17
VITIMES patients with contact investigation	235	121	356
Contacts enumerated	261	369	630
Contacts screened by CXR	261	369	630
Contacts with abnormal CXR	100	109	209
- with symptoms	21	27	48
- without symptoms	79	82	161
Contacts tested after abnormal CXR result	97	105	202
Contacts with Bac(+) sputum test after abnormal CXR	7	1	8
- with symptoms	2	1	3
- without symptoms	5	0	5

Table.

Conclusions: This pilot of dedicated screening events for contacts using an ultraportable radiography system successfully mitigated the access barriers associated with facility-based radiography screening, and achieved a high yield of TB among the target population.

EP-21-804 Programmatic approach to positively screened tuberculosis (TB) active case finding (ACF) participants with negative molecular confirmatory test

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Background and challenges to implementation: TB ACF aims to detect TB among population with high TB transmission, who have not sought treatment in health facilities. Symptom and chest-X-ray (CXR) screening followed by molecular testing are usually conducted during TB ACF. We review the operational challenge of diagnosing TB among ACF participants with negative molecular testing, and propose a programmatic approach to decide the TB diagnosis.

Intervention or response: We analyze the diagnostic cascade of ACF participants conducted by Zero TB Yogyakarta (ZTB) from 12 April 2021 – 8 April 2022. Participants with CXR read by computer aided detection (CAD), qXR® Qure.AI, Mumbai India, were included. qXR® classify those with score ≥ 0.5 to 1 as presumptive TB, to whom a sputum sample was requested and tested with Xpert MTB/Rif. The doctors in 39 primary health facilities, supported by two pulmonologists, one pediatrician, and one radiologist, decided the final TB diagnosis. Monthly case discussion was conducted to review the participants for whom TB diagnosis was challenging.

Results/Impact: There were 23,455 screened participants included with qXR® results. Based on symptoms and CXR/qXR screening, 3172 participants were classified as presumptive TB. There were 317 TB cases diagnosed: 96 bacteriologically confirmed and 221 clinically diagnosed TB. When reviewing the CAD score provided by the program, the higher the score, the higher the proportion of bacteriologically confirmed TB. Among those with negative Xpert MTB/Rif, clinical TB was diagnosed on 0.9% (7/819), 6.8% (116/1718), 17% (62/364) of participants with positive symptoms, suggestive CXR, and positive on both symptoms and CXR respectively.

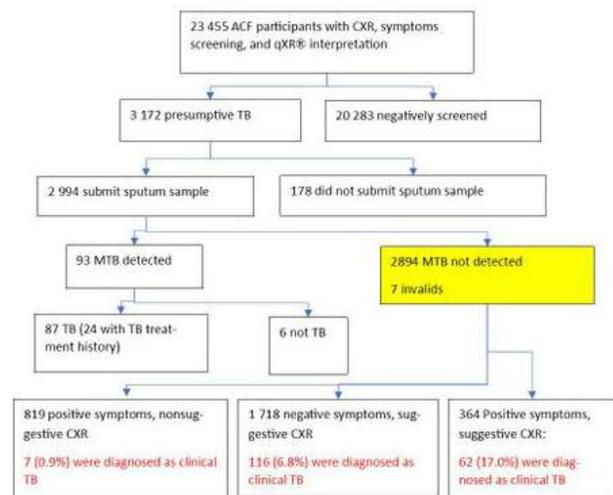


Figure 1. The cascade of TB ACF, ZTB Yogyakarta, April 2021-April 2022.

Conclusions: Presumptive TB participants from ACF, with negative bacteriological confirmation requires further clinical reviews increasing the workload of primary health facility doctors. The combination of symptoms, CXR lesions, and CAD score help establishing likelihood of TB diagnosis among negative bacteriological TB patients.

Providing technical support to primary health facility doctors to incorporate CXR results in TB diagnostic algorithm is necessary.

EP-21-805 Implementation of an electronic information channel for data exchange on TB cases in Uzbekistan

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Background and challenges to implementation: The national data collection system in Uzbekistan records data on a tuberculosis (TB) case as linked to the place where the person with TB (PWTB) begins treatment.

When a PWTB starts treatment outside his province/district of residence, the case may not be registered properly or will be recorded with delay, leading to late contact tracing, mistakes in drug forecasting and incom-

plete epidemiological data. Loss of follow-up is another risk, if the PWTB returns to their home province after initial treatment.

Intervention or response: In January 2021, the USAID Eliminating TB in Central Asia (Activity) launched a data exchange channel developed through a consultative process with the National TB Program (NTP) and country partners. The channel notifies provincial TB facilities when a PWTB begins treatment outside their home region. No personally identifying information is shared via the channel. During 2021, information on 326 PWTB (162 drug resistant (DR) TB) was transmitted from provincial TB hospitals all over the country to peripheral facilities. In 2022 using the same system, the data on 35 PWTB (5 DR-TB) have been transmitted between TB facilities within the province.

Results/Impact: Two indicators were chosen to evaluate the effectiveness of the data exchange channel: 1. Case registration based on transmitted data; 2. Contact tracing of registered cases.

In four provinces selected for evaluation, data on 50 cases (28 DR-TB) was exchanged and all 50 cases were registered at their home facilities.

For the second indicator, 131 close contacts of these 50 PWTB were screened, which reflects 92% of those eligible for screening.

Conclusions: The data exchange channel enables monitoring the timely registration of persons undergoing treatment outside their place of residence. According to the evaluation data, the registration rate of these cases is 100%. Most contact persons were screened in a timely manner.

EP-21-806 Improving targeting of active case finding in India through an index for individual vulnerability for TB

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Background and challenges to implementation: Active case finding (ACF) for TB has been part of India's programmatic response since 2017. However, yield of ACF campaigns have been low, between 23-30 persons diagnosed per 100,000 screened. To improve diagnostic sensitivity, the Greater Chennai Corporation introduced chest x-ray (CXR) screening in ACF through mobile di-

agnostic units (MDUs) for individuals with chest symptoms. This algorithm, however, can be expected to miss a significant number of asymptomatic individuals.

Intervention or response: The intervention sought to offer CXRs to asymptomatic individuals at risk of TB. 34,214 individuals > 5 years of age residing in nine high-burden urban slums in Chennai were interviewed about chest symptoms and clinical, social, and behavioral risks. Each risk factor was assigned a score based on their prevalence and relative risk for TB, and an additive vulnerability index (VI) was created, with a threshold of 13 and above for being assessed as 'vulnerable'.

Each vulnerable or symptomatic individual was referred to a MDU health camp which included CXR, and measurement of height, weight, and blood pressure. Sputum samples were collected from symptomatic individuals and / or with a CXR showing TB abnormality (current or old), and microbiologically tested.

Results/Impact: CXR TB abnormality rate was 3.96% compared to 4.00% in the historical control. Sensitivity and specificity of the index towards CXR TB abnormality was 64% and 44% respectively, and ratio of abnormality rates between vulnerable and non-vulnerable cohorts was 1.39. At a higher hypothetical threshold of 16, the sensitivity and specificity were 36% and 90% respectively, and ratio was 4.27, with abnormality rates within the vulnerable cohort rising to 12.8%. At thresholds of 13 and 16, the proportions of the population classified as vulnerable were 4.6% and 0.9% respectively.

Conclusions: Results suggest that a highly specific VI may be created, which may be used to conduct high-yield and potentially cost-effective ACF.

EP-21-807 Programmatic implementation of contact investigation in eight African countries

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Background and challenges to implementation: Although recommendations for contact investigation (CI) has been recommended for several years, it is rarely fully implemented and poorly documented in low and middle income settings. The objective was to implement CI in programmatic condition of national tuberculosis programme and to advocate for its scaling up.

Intervention or response: CI was implemented in 150 Basic Management Units identified across the eight countries of the project: Benin, Burkina Faso, Cameroon, Guinea, Niger, Central African Republic, Senegal and Togo. Four hundred and fifteen nurses and healthcare worker were trained. Children under 5 and person living with HIV (PLHIV) are the two contact's target population. They were evaluated during home and clinic visits using standardized questionnaire, clinical examination and according to each country additional tests. Contacts with active TB received TB treatment and other preventive therapy (TPT). Data were collected each quarter using standardised forms. Meetings were organized with partners to share the preliminary results and to advocate for the scaling up.

Results/Impact: From October 2020 to December 2021, 9044 home visits were performed. Ninety-three percent of children under 5 living at home [(13 356/14 297)*100]

received TPT (12980) or TB treatment (376). Ninety-eight percent of PLHIV living at home [(283/376)*100] received TPT (254) or TB Treatment (29). The ratio of children < 5 years and PLHIV per index case were respectively 1,6 and 0.013.

The advocacy permits the scale up of CI in 6 countries throughout the Global Fund funding. For two countries, Togo and CAR advocacy are still ongoing.

Conclusions: These results indicate that CI is feasible in programmatic condition within NTP of African countries. Lessons learned through this implementation are currently used for the scale-up phase.

The scaling up financed by the Global Fund reflects the good collaboration between NTPs and international partners.

EP-21-808 Finding the missing childhood TB cases: use of stool sample for Xpert MTB Rif ultra assay amongst malnourished children in Kano state

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Background and challenges to implementation: Nationally, childhood Tb case notification dropped from 8% in 2019 to 6% in 2020. Kano state notified 17,939 TB patients of which 937 (5%) were childhood TB patients, with an estimated 1,754 (11%) missed childhood TB cases. Nigerian demographic health survey in 2018 had malnutrition among the under 5 children in Kano at 35.5% The USAID funded KNCV Nigeria TB LON Project supports the use of stool samples to diagnosis TB in children using Xpert ultra assay in all Gene Xpert laboratories. UNICEF and MSF provide support to select Nutrition clinics where malnourished children are managed in Kano state.

Intervention or response: Sensitization drives and awareness creation on stool sample use to test for TB was done with staff and caregivers. Mass stool sample collection among the under 5 malnourished children regardless of their TB presumptive status was achieved in 17 Nutrition clinics during the first quarter of 2022. Collected samples were logged by a dedicated healthcare worker to the nearest laboratory for processing. All samples were processed using the Xpert ultra assay.

Results/Impact: 529 attendees were recorded within the review period, 338 (64%) had samples processed and 40 (7.5%) new Tb cases were diagnosed representing 12% Tb yield among the evaluated malnourished children.

Conclusions: Sputum sample collection through gastric lavage for bacteriologic diagnosis of TB amongst under 5 age group has for long been a challenge and invasive. This study demonstrates the ease and feasibility of use

of stool sample for TB diagnosis among this age group. The Study also found TB yield from malnourished children in Kano to be high.

EP-22 Imaging tuberculosis infection

EP-22-809 Artificial intelligence to support reading of chest X-ray to triage pulmonary tuberculosis at health facilities in Vietnam: initial results

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Background and challenges to implementation: Vietnam National Tuberculosis Program (VNTP) is piloting the application of artificial intelligence (AI, Qure.ai software) to support reading chest X-ray (CXR) for screening pulmonary tuberculosis (TB) among presumptive TB patients in Khanh Hoa Province, Vietnam, at the community level and in one provincial lung hospital and two health district centers.

Intervention or response: A study was conducted to review the implementation process for AI-enabled CXR at the sites to determine if AI reading of CXR could contribute to the national algorithm of X-ray and Xpert (Double X strategy). Results from AI-based CXR reading, as well as CXR reading by trained radiologists, were sent together to clinicians.

People with CXR abnormalities consistent with active pulmonary TB were tested with Xpert[®]MTB/RIF for diagnosis of TB and rifampicin resistance and started appropriate treatment based on VNTP's algorithm.

Results/Impact: From January 17–March 31, 2022, 2,416 people received CXR reading by Qure.ai software at the three health facilities. Exclusions included: <15 years (n=164); taking TB treatment (n=109); and people currently infected with COVID-19 (n=93).

The remaining 2,050 CXRs were included in the analysis. AI reading of CXR concordance with radiologist reading was 1,945/2,050 CXRs (94.9%; CI 95%: 93.9%~95.8%). 533 patients with abnormal CXR were identified by AI and referred for Xpert[®]MTB/RIF testing. While 572 patients were referred for testing after a radiologist read the CXR, 42 patients did not submit sputum for Xpert[®]MTB/RIF testing.

The number of confirmed TB diagnoses (133) among people tested by Xpert was higher than expected (51%), indicating possible delays in detection[1][CD2], especially at the provincial health facility.

Conclusions: AI-based CXR was feasible and the reading accuracy comparable to radiologists' reading of CXR. This indicates that AI-based CXR reading could improve the Double X strategy and TB case detection among patients with abnormal CXR.

EP-22-810 Computer-aided triaging of chest X-ray images to reduce radiologists workloads during TB screening: a three software comparative evaluation

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Background: The World Health Organization (WHO) recently updated its TB screening guidelines to recommend the use of computer-aided detection (CAD) software. However, the guidelines only reference a single CAD software use case: radiologist replacement.

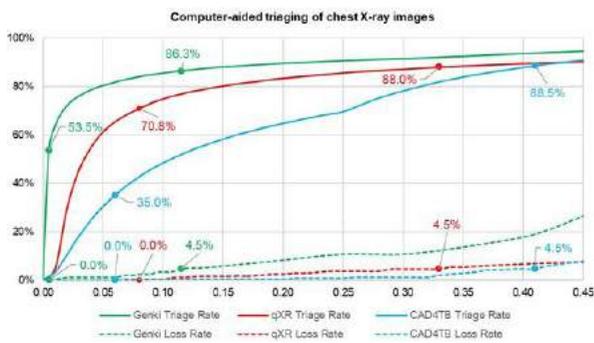
In settings where there is no shortage of quality and affordable radiology services, CAD software could be used in conjunction with human readers as a triage screen for chest X-ray (CXR) images containing no abnormalities.

Design/Methods: We collected 21,443 DICOM files from a community-based CXR screening initiative in Ho Chi Minh City and Can Tho, Viet Nam, and then processed the files using CAD4TB v7 (Delft Imaging), Genki v2 (DeepTek) and qXR v3 (Qure.ai) CAD software.

We analyzed the proportion of normal CXR images which would have been excluded/triaged away from human reading at 0.01 CAD score increments.

We then identified the highest possible CAD score threshold at two points for each software: one corresponding to a zero percent loss of Xpert-positive TB during follow-on testing and a second corresponding to a five percent loss. Five percent was deemed an acceptable loss of yield for this evaluation, based on the Target Product Profile for a TB triage test.

Results: qXR software achieved a maximum triage rate of 70.8% with zero loss of TB yields, compared to 53.5% for Genki and 35.0% for CAD4TB. Each CAD software performed similarly at the score thresholds achieving a less than five percent loss of TB yields (CAD4TB: 88.5%, qXR: 88.0%, and Genki: 86.3%).



Conclusions: These commercially available CAD software can significantly reduce radiologist workloads with high accuracy, allowing personnel to focus on value-added tasks.

This retrospective analysis highlights the potential of a novel use case for CAD software during TB screening whose acceptability and performance should be prospectively evaluated.

EP-22-813 Utility of a social media platform to aid the interpretation of chest X-ray (CXR) in Cambodia

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Background: Telegram (www.telegram.org) is an online instant messaging social media platform. Cambodia has been using the Telegram platform since 2018 wherein a group of expert radiologists supported remote interpretation of difficult-to-read CXR for improving tuberculosis screening. We assessed use of the platform and measures needed for improvements.

Design/Methods: The Telegram CXR group's operational structure and guiding documents were reviewed, and activities were assessed. A total of 245 CXR images, posted on the platform between 2018-2021, were analyzed. A short on-line survey among 34 CXR Telegram platform users was conducted to understand utility and improvements.

Results: 103 medical doctors from public referral hospitals in 13 operational districts of Cambodia were registered on the Telegram platform. 245 difficult-to-

interpret CXRs read by a group of four radiologists as moderators. Two thirds of CXRs were interpreted by more than one expert. The number of the CXRs posted on the platform decreased from 113 (71%) in 2018 to 17 (54%) by 2021 (Figure 1) due to delays in prompt CXR results, and lack of clear guidance on inconclusive CXR results leading to high inter-reader discordance (75% in 2021). Poor quality of CXR images (22%), inadequate clinical information of the patients, lack of performance assessment system contributed to its declining use.

On-line survey indicated a need for periodic orientations on the standardized interpretation of CXRs, an external quality assessment scheme, and elimination of CXR user-charges.

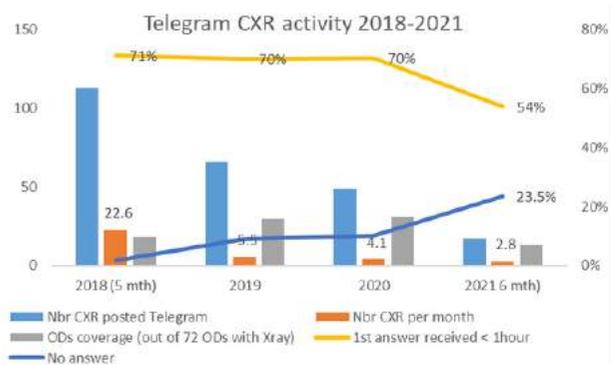


Figure 1.

Abbreviations: 1 Nbr = Number; CXR = Chest X-Ray;

OD = Operational District

X-axis-equals number- and Y-axis percent- of CXRs posted on Telegram platform for the interpretation

Conclusions: Ensuring clear guidance on inconclusive CXR images, introducing a quality assurance system addressing delays in response times, quality of CXRs, periodic performance assessment, and prompt corrective measures would improve the telegram CXR platform as an effective tool for tuberculosis in Cambodia.

EP-22-814 Domain agnostic tuberculosis screening using deep neural network for chest X-rays

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Background: Recently, many deep learning-based tuberculosis (TB) screening methods for chest X-rays (CXRs) have been proposed. However, network trained using CXRs from one domain provides reduced performances when applied to CXRs of different domains (e.g., vendors and institutions).

Here, we propose domain agnostic image processing (DAIP) pipeline based on knowledge of X-ray physics to minimize performance degradation.

Design/Methods: [Datasets] CXRs from Vietnam hospital (digital radiography (DR)); 4949 CXRs between May 2020 and February 2021), CXRs from four Indonesia hospitals (three computed radiography (CR) and one DR; 1961 CXRs between September 2020 and October 2020), and two publicly available CXRs (Shenzhen and Montgomery). All acquired CXRs were labelled as TB or normal by a radiologist with 20-years' experience.

[DAIP] First, exposure of CXRs were corrected by histogram normalization. To correct SID, lung regions of CXRs were cropped. For robustness of X-ray scattering (e.g., blurring), high or low frequency filters were applied to CXRs. Contrast of CXRs was changed using gamma correction for robustness of X-ray voltage variation. By applying above procedures, we obtained "generalized" dataset that covers diversity of CXRs.

[Experiments] Two networks (EfficientNet-B0), with and without applying DAIP pipeline, were trained using CXRs from Vietnam hospital. Classification performances were evaluated for all datasets.

Results: For dataset from Vietnam hospital, performances were almost same before and after applying pipeline (see Figure). For unseen datasets, performances consistently improved at similar level to Vietnam dataset (mean AUC gain: 0.06; $p < 0.0001$). In particular, one dataset (Indonesia 4) having substantially different image characteristics showed dramatic performance gain (AUC: 0.56 to 0.94). Our results indicate DAIP successfully generalized characteristics of CXRs.

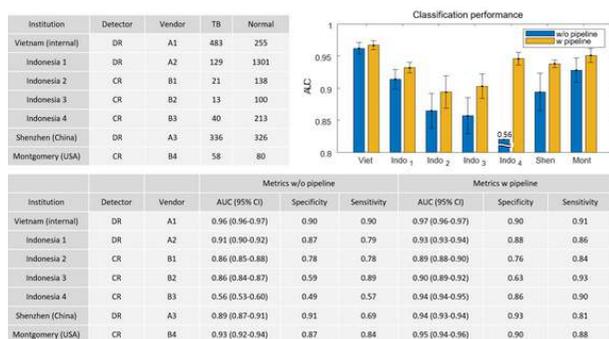


Figure. Detailed description of the multiple domain datasets and summary of the performances of the deep learning-based TB screening models before and after applying the DAIP pipeline. Moreover, sensitivities, specificities were measured on the cut-off value of 90% specificity of the trained dataset (i.e., CXRs from the Vietnam hospital).

Conclusions: Classification performances were significantly improved for datasets from different domains using DAIP. We expect our method to improve efficiency of screening TB in clinical environment where quality of CXRs is not ensured.

EP-22-815 Improving TB case detection in Cambodia through systematic screening using chest X-rays using artificial intelligence computer aided detection software for X-ray interpretation

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Background and challenges to implementation: Cambodia continues to be a TB endemic country, with one-third of TB cases in the country being "missing cases". Local non-TB health centres are the primary sites for care-seeking by most people in Cambodia, however most staff at these facilities are not trained to implement basic TB screening.

Intervention or response: Sihanouk Hospital Centre of Hope implemented a project aimed at finding TB patients missing from routine TB program channels in Phnom Penh, wherein healthcare staff at non-TB health facilities such as local health centres, private clinics, antenatal care facilities were trained to implement systematic TB screening and linkage to diagnosis and treatment. Patients visiting these facilities underwent TB symptoms screening and presumptive TB cases were referred for Chest X-Ray or bacteriological test. Chest X-Rays taken were processed using Artificial Intelligence Computer Aided Detection software, qXR. The chest X-Rays were also independently read by a field physician (FP) and those classified as abnormal were re-read by a senior radiologist (SR).

Results/Impact: 1836 presumptive were included in this analysis. The mean age of patients was 56.3 and 60.3% were females. Of this 1543 (84%) were classified as abnormal by FP and sent for second read. The overall agreement between qXR and FP was 84.2%.

SR reported 282 of the referred CXR as possible TB. The FP and qXR correctly identified 60.2% and 76.9% of these cases respectively.

569 participants underwent Xpert test. Youden's index (NND) was 0.557 (1.79), 0.470 (2.12), and 0.598 (1.67) for qXR, FP and SR respectively.

Modality	Sensitivity	Specificity	Binormal AUC	Youden's Index	Number needed to Diagnose (1/Youden's Index)
qXR	82.4	73.3	0.864	0.557	1.79
Field Physician	60.3	87.0	0.837	0.470	2.12
Senior Radiologist	76.9	82.8	0.883	0.598	1.67

Conclusions: Performance of qXR was comparable to SR and better than FP with default threshold setting. Higher specificity of FP might be due to clinical data.

An increase in threshold by 0.05 improved qXR specificity without loss of sensitivity. qXR can be used to aid systematic TB screening to facilitate immediate referral of presumptives for further testing.

EP-22-816 Interobserver agreement of household contacts chest X-ray: findings from a multicenter clinical trial

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Background: The reliability of chest x-ray (CXR) is controversial since it is a reader-dependent test and requires knowledge and observance of findings. We assessed the inter-observer agreement between primary-care physicians from Brazil and Benin and experienced respirologists from Canada.

Design/Methods: CXR from a clinical trial-conducted in Brazil and Benin- comparing different strategies for HHC investigation before tuberculosis preventive therapy (TPT) were used. CXR were first evaluated by the primary-care physicians and classified into 1) normal, 2) abnormal, possible active-tuberculosis (TB), 3) abnormal, but not TB. Then two blinded Canadian respirologists re-assessed the films and classified them as above. Proportions and kappa statistics were calculated to assess the agreement between the primary-care physicians and respirologists, and between two respirologists.

Results: Ninety-nine digital CXR were evaluated, among those, 87 were considered adequate for interpretation by both respirologists and were further analyzed. The overall agreement between the respirologists was 84%, kappa 0.63 [(95%CI 0.46 to 0.79), substantial agreement]. Both respirologists agreed that 58 (67%) CXR were normal, and nine (10%) had findings of possible active TB but disagreed on TB diagnosis in seven CXR (8%).

Respirologist 1/primary-care physicians	Normal	Abnormal not TB	Abnormal TB	Total
Normal	58 (67%)	4 (5%)	1 (1%)	63 (72%)
Abnormal not TB	5 (6%)	3 (3%)	2 (2%)	10 (11%)
Abnormal TB	8 (9%)	1 (1%)	5 (6%)	14 (16%)
Total	71 (82%)	8 (9%)	8 (9%)	87 (100%)
Respirologist 2 /primary-care physicians	Normal	Abnormal not TB	Abnormal TB	Total
Normal	58 (67%)	3 (3%)	3 (3%)	64 (74%)
Abnormal not TB	4 (5%)	6 (7%)	2 (2%)	12 (14%)
Abnormal TB	1 (1%)	1 (1%)	9 (10%)	11 (13%)
Total	63 (72%)	10 (11%)	14 (16%)	87 (100%)

Table 1.

Table 1 displays the agreement between the primary-care physicians and the respirologists. The overall agreement between primary-care physicians and respirologists 1 and 2 was 76% and 78%, respectively [kappa 0.42 (95%CI 0.22 to 0.62), 0.37 (95%CI 0.18 to 0.57, fair for both comparisons)].

Conclusions: Although disagreement was higher between primary-care physicians and respirologists, the latter group also disagreed in 10% on the diagnosis of active-TB. Disagreements on CXR reading are not new. Since the 70s, studies have shown that reproducibility is poor for active-TB.

Our study reinforces that this challenge remains - even using modern CXR equipment. Physician training and use of new tools such as computer-aided devices for CXR interpretation play an important role, especially in a context of scaling up TPT.

EP-22-817 Comparison of CAD-reported Chest X-ray findings of culture-confirmed pulmonary tuberculosis in persons with and without diabetes

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Background: We assessed if diabetes status was associated with the radiographic presentation of pulmonary tuberculosis (PTB) using computer-aided detection (CAD) software.

Design/Methods: From March 2017 to July 2018, we enrolled individuals aged 15 years or older, evaluated for tuberculosis due to symptoms or as a household contact at the Ghori TB Clinic in Karachi, Pakistan. Three sputa, digital chest X-ray (CXR), and a random glucose test were performed. Individuals were classified as PTB if ≥ 1 positive culture, and diabetic if self-reported or if random blood glucose >11.1 mMol/L.

CXR were analyzed using a commercially-available CAD software. We compared continuous tuberculosis scores, and the prevalence of the individual abnormalities between participants with PTB, with and without diabetes.

We used multivariable linear regression to estimate the difference in CAD score associated with diabetes, adjusting for potential confounders. We assessed for associations between diabetes and location of radiographic abnormalities.

Results: We included 272 PTB participants. Median age (IQR) was 29 (22–45), 48% (n=130) were female, and 23% (n=63) had diabetes. Those with diabetes were older (48 vs 25, $p<0.0001$), less likely to previously had TB (4.8% vs 15.8%, $p=0.02$), more likely to self-report fever (96.8% vs 87.4%, $p=0.03$), and had higher BMI (21.4 vs 17.3, $p<0.0001$). After adjustment, diabetes was associated with a higher tuberculosis abnormality score.

There were no statistically significant differences between people with and without diabetes for specific radiographic abnormalities, nor for location. However, with diabetes, cavitory disease was more frequent (74.6% vs 61.2% $p=0.07$), and more likely to be in lower/mid zones (17% vs 7.8%, $p=0.09$).

Conclusions: Diabetes was associated with more extensive radiographic abnormalities at tuberculosis presentation, and greater likelihood of cavities not in upper zones, although upper zone cavities were most common regardless of diabetes status.

EP-22-819 Early experience from the Portable Digital X-ray implementation in special populations in Kano and Katsina states, Nigeria; lessons learnt and recommendations for scale up

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Background and challenges to implementation: Equal access opportunities to TB diagnostic platforms remain key to achieving control of Tuberculosis in Nigeria. KNCV Nigeria with funding from USAID is implementing the new tools project. The project has procured Portable digital X-ray machines (PDX) with CAD4TB software to bring diagnostic innovations to the doorstep of hard-to-reach communities. The security centric design emphasis of Prison structures in Nigeria ensures prison cells are poorly cross ventilated. The average inmate design capacity for medium security custodial centers (MSCC) in Nigeria is 600. We present results from an intervention targeting prison inmates in 2 states within the country.

Intervention or response: Our intervention focus was persons at increased risk for exposure with limited access to quality TB services. Three 2 person teams, each equipped with the PDX and CAD4TB software were deployed to screen all inmates in 16 prisons across the states. Persons with a CAD4TB score >50 had sputum samples collected for Xpert MTB rif ultra-assay and further clinical evaluation.

The intervention was from December 2021–February 2022.

Results/Impact: 4920 inmates were screened across all prisons, 87% of them housed within the 5 MSCC, the MSCC's had a mean inmate population of 857. Presumptive TB yield from MSCC and Satellite custodial centers (SCC) was 9.4% and 6.9% respectively. A total of 72 TB cases was diagnosed, 67 cases (93%) from MSCC. TB yield amongst screened inmates in MSCC's was twice that of the SCC's.

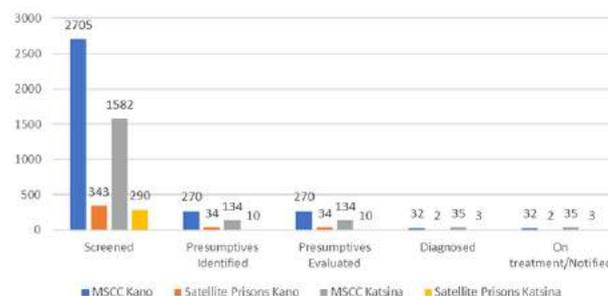


Figure. TB screening in medium security custodial centers and satellite prisons in Kano & Katsina states.

Conclusions: The medium security custodial centers located within the state metropolis were more congested, less ventilated and the inmates welfare including feeding generally poorer, this explains the higher yield of TB in the bigger prisons. The Nigerian correctional service and relevant health authorities should institute measures to decongest the bigger centers that are overcrowded to halt the spread of infectious diseases such as Tuberculosis within those congregate settings.

EP-23 Pathways to tuberculosis diagnosis and treatment

EP-23-820 Diagnosis of tuberculosis among COVID-19 suspected cases in Ghana

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Background: Tuberculosis (TB) and COVID-19 pandemics are both diseases of public health threat globally. Both diseases are caused by pathogens that infect mainly the respiratory system and are involved in airborne transmission; they also share some clinical signs and symptoms.

We, therefore, took advantage of collected sputum samples at the early stage of the COVID-19 outbreak in Ghana to conduct differential diagnoses of long-standing endemic respiratory illnesses, particularly tuberculosis.

Design/Methods: Sputum samples collected through the enhanced national surveys from suspected COVID-19 patients and contact tracing cases were analyzed for TB. The sputum samples were processed using Cepheid's GeneXpert MTB/RIF assay in pools of 4 samples to determine the presence of the *Mycobacterium tuberculosis* complex. Positive pools were then decoupled and analyzed individually. Details of positive TB samples were forwarded to the NTP for appropriate case management.

Results: Seven hundred and seventy-four sputum samples were analyzed for *Mycobacterium tuberculosis* in both suspected COVID-19 cases (679/774, 87.7%) and their contacts (95/774, 12.3%). A total of 111 (14.3%) were diagnosed with SARS CoV-2 infection and six (0.8%) out of the 774 individuals tested positive for pulmonary tuberculosis: five (83.3%) males and one female (16.7%). Drug susceptibility analysis identified 1 (16.7%) rifampicin-resistant tuberculosis case.

Out of the six TB positive cases, 2 (33.3%) tested positive for COVID-19 indicating a coinfection. Stratifying by demography, three out of the six (50%) were from the Ayawaso West District. All positive cases received appropriate treatment at the respective sub-district according to the national guidelines.

Conclusions: Our findings highlight the need for differential diagnosis among COVID-19 suspected cases and regular active TB surveillance in TB endemic settings.

Intervention or response: During August 3-16, 2021, healthcare workers were trained to perform screening among the miners using two approaches:

1. Field-based search for presumptive TB at mining shafts, and;
2. Enhanced triaging among outpatient department (OPD) attendants at three hospitals serving TB KAP community. TB diagnosis was made using GeneXpert RIF for TB.

Results/Impact: TB screening was done at 37 mining shafts and enhanced central triaging was done at three high client-load hospitals. A total of 15,248 goldminers and their families [14952 (98%) aged >15 years and 296 (2%) aged <15 years] were screened for TB. Of the screened, 723 (5%) screened positive for TB and 45 (6.22%) were diagnosed with active TB, of which 2 were rifampicin-resistance TB (RR-TB).

Among the 3,590 screened OPD attendants, 202 presumptive TB were identified and evaluated, of which 42 drug susceptible TB, and 1 RR-TB cases were detected. In all, from 925 presumptive TB cases identified, 88 (9.5%) active TB cases were detected and started on TB treatment.

Moreover, 4 active TB cases were detected from 46 close contacts of 26 bacteriologically confirmed index TB cases and initiated on treatment.

Conclusions: Active search for TB among goldminers in Guji zone of Oromia Region of Ethiopia has shown that goldminers are disproportionately affected by TB/MDR-TB. Targeted programming at mining sites is crucially important due to the higher rates of TB at these sites.

EP-23-821 Workable strategies for active TB case finding among goldminers in Ethiopia

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Background and challenges to implementation: Tuberculosis key affected populations (KAP) are those segments of the general population who experience a higher TB burden but have limited access to services for the disease. The End TB Strategy recommends screening KAP for active TB case finding. In Ethiopia, miners are top on the list of nationally identified TB KAP. We aimed to identify workable strategies for enhancing TB case finding among goldminers of Guji zone in the Oromia region of Ethiopia.

EP-23-822 Patient pathways and delays to diagnosis and treatment of tuberculosis in a peri-urban setting in Mozambique

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Background: People with TB often seek care in facilities without TB services or are treated for other diseases before they are correctly diagnosed with TB. Delays in initiating TB treatment can contribute to costs related to TB and care-seeking.

We describe the pathway to TB diagnosis including missed diagnostic opportunities and number of facilities visited between the onset of symptoms and the start of TB treatment in Maputo, Mozambique.

Design/Methods: From December 2017 to January 2020, adults with pulmonary TB (≥ 18 years) initiating treatment at health facilities in Mozambique were enrolled. We used an adapted version of the WHO's generic TB Patient Cost Survey to collect data on the presence and duration of TB symptoms, and the type and number of health facilities visited.

Time to diagnosis (TTD) was calculated as time (weeks) between the onset of the first TB symptom and the diagnosis.

We used a Cox regression model to predict hazard ratios of factors associated with delay of diagnosis.

Results: A total of 418 adults were included (64.6% male, median age was 34.0 IQR: 27.0-42.0 years, 41.5% were breadwinners).

Nearly two-thirds (60.7%, 254/418) visited two or more health facilities before diagnosis. Among all patients, 22.7% (95/418) sought initial care in a health facility without TB care provision.

Median TTD for those who visited one and two or more health facilities was 4.0 (IQR: 3.0-4.0) and 6.0 (IQR: 4.0-8.0) weeks respectively.

Compared to females, males had a higher risk of diagnostic delay (HR 1.3 95% CI 1.0-1.7).

Determinants	Delay to diagnosis			
	Univariable Cox Regression		Multivariable Cox Regression	
	cHR (95% CI)	p-value	aHR (95% CI)	p-value
Age	1.03 (0.99 - 1.01)	0.461	-	-
Sex				
Female	-	-	-	-
Male	1.30 (1.04 - 1.62)	0.020	1.28 (1.03 - 1.60)	0.028
Occupation				
Employed	-	-	-	-
Unemployed	0.91 (0.71 - 1.16)	0.434	-	-
Education				
No formal schooling	-	-	-	-
Primary school	1.03 (0.69 - 1.53)	0.891	-	-
Secondary school	1.02 (0.69 - 1.50)	0.897	-	-
University	0.60 (0.31 - 1.15)	0.128	-	-
Number of symptoms	0.89 (0.81 - 0.98)	0.010	0.89 (0.81 - 0.98)	0.014

Table 1: Cox regression analysis of sociodemographic factors on delay to diagnosis.

Conclusions: More than half of study participants visited two or more health facilities before diagnosis and care. Males had a higher risk of delay to diagnosis.

EP-23-823 Impact of the COVID-19 pandemic on patients' experiences obtaining a tuberculosis diagnosis in Lima, Peru

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Background: In 2020, TB diagnoses decreased by 18% globally and by 25% in Peru. We sought to understand the impact of the pandemic from the perspective of patients who dealt with various challenges in accessing a timely TB diagnosis.

Design/Methods: We implemented a mixed-methods study among patients diagnosed with TB at 12 health facilities in Carabayllo District (northern Lima, Peru) during two periods: October 2020-April 2021 and November 2021-February 2022. Structured interviews measured diagnostic delay, defined as the time between symptom onset and TB diagnosis.

We conducted in-depth interviews and analyzed transcripts using an inductive content analysis approach focusing on content related to the pandemic.

Results: We enrolled 100 patients for surveys and 26 for interviews. Patients diagnosed with TB during the first year of the pandemic (October 2020-April 2021) had a median diagnostic delay of 15 weeks (interquartile range

5-26), compared to 6 weeks (interquartile range 3-14) for patients diagnosed in the later period (Wilcoxon rank-sum test $p=0.027$). In qualitative analysis, we found that the pandemic affected the care-seeking behavior of patients because they feared getting sick, were busy caring for sick family members, and self-medicated when they attributed their symptoms to COVID-19.

In addition, the pandemic reduced access to TB diagnostic services because health facilities were only treating patients with COVID-19, and doctors and pulmonologists were deployed to hospitals.

Patients reported delays in diagnosis because doctors attributed their TB symptoms to COVID-19 or side effects of the COVID-19 vaccine. This initial misdiagnosis contributed to delayed TB treatment, unnecessary expenses, and deterioration of patients' health.

Conclusions: The pandemic affected access to timely TB diagnosis through different mechanisms at the patient, provider, and health system levels, contributing to prolonged illness.

EP-23-824 Can point-of-care ultrasound support tuberculosis diagnosis in children? The experience of MSF in Guinea-Bissau

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Background: Over half of childhood TB remains undiagnosed every year and majority of cases in low-resource settings are diagnosed on clinical grounds. We aimed to describe the findings of TB-focused point-of-care ultrasound (POCUS) for children with presumptive TB at a tertiary care hospital in Bissau.

Design/Methods: This observational study took place at Simão Mendes hospital from July 2019 to April 2020. Patients aged between 6 months and 15 years with presumptive TB underwent clinical, laboratory assessment and unblinded clinician-performed POCUS evaluation. POCUS assessed for subpleural nodules (SUNs), lung consolidation, pleural effusion, pericardial effusion,

ascites, liver and splenic focal lesions, and abdominal lymph nodes. Presence of any of these signs prompted a POCUS-positive result. Images and clips were evaluated by an expert reviewer and, if discordant, by a second expert reviewer.

Results: A total of 139 children were enrolled. HIV infection and severe acute malnutrition (SAM) were found in 59(42%) and 83(60%), respectively. Confirmation of TB was achieved in 27(19%); 62(45%) had unconfirmed TB, and 50(36%) had unlikely TB. TB patients were more likely to have a POCUS positive (93%) as compared to children with unlikely TB (34%).

The most common POCUS signs in TB patients were: lung consolidation (57%) and SUNs (55%). In children with confirmed TB, POCUS sensitivity was 85.2% (95% CI 67.5-94.1). In unlikely TB, specificity was 66% (95% CI 2.2-77.6). Unlike HIV infection, SAM was associated with higher risk of positive POCUS. Cohen's kappa coefficient for concordance ranged from 0.6 to 0.9, while overall POCUS concordance was 0.8.

Conclusions: We found high prevalence of any POCUS sign in children with TB, as compared to children with unlikely TB. POCUS positivity was dependent of nutritional status but not to HIV status or age. POCUS concordance with expert was moderate to high. TB-focused POCUS may play a supportive role in the diagnosis of TB in children.

EP-23-825 Benefits of strengthening TB/HIV collaboration: a case study of General Hospital Oron

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Background and challenges to implementation: In Nigeria, tuberculosis (TB) and human immunodeficiency virus (HIV) has proven to be deadly and reinforcing combinations. Persons living with HIV (PLHIV) have a greater risk of developing TB; as a result, increasing HIV prevalence has led to a rapid rise in the number of TB cases among HIV clients.

In turn, TB contributes to high mortality of the estimated deaths due to HIV infection. In Akwa Ibom State, Oron is a hub for HIV cases in a predominately high HIV incidence part of the State.

Intervention or response: Following an interagency visit of USAID/PEPFAR/CDC in September 2021, feedback on improving TB/HIV collaborations was highlighted. Both TB and HIV implementing partners met to institute the following collaborative mechanisms: assigning coverage of ART clinics for TB screening services to TB

partners, daily data harmonization exercise, and use of community ART service daily platforms for client tracking and TB treatment adherence.

Results/Impact: Between the baseline period of March–August 2021 and the intervention period of October 2021 – March 2022 the following results were achieved: ART client screened for TB 2051 (-5% decrease from baseline), Presumptive identified 290 (27% increase), Presumptive evaluated 288 (26% increase), Diagnosed cases 77 (54% increase) and Enrolled cases 76 (52% increase).

Despite the decrease in screening, all other cascade points experienced a significant increase. There was also an increase in case contribution from the ART clinic from 44% at baseline to 60% post-intervention.

Conclusions: TB screening is better conducted by TB implementing partners as all options are explored to identify presumptive clients, test for TB, and find more TB cases among HIV-positive clients. The need to actively screen for TB and reconcile TB cascade data will further strengthen collaboration if scaled up to all health facilities where both services co-exist.

EP-23-826 Evaluating the impact of a radio campaign on tuberculosis testing and case notifications in Zambezia, Mozambique

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Background: Mass media interventions can effectively raise knowledge about diseases and change peoples' healthcare seeking behaviours. Evaluations of mass media interventions for Tuberculosis (TB) are extremely limited.

We evaluated the impact of a radio campaign broadcast in Zambezia province in Mozambique to promote TB knowledge and testing.

Design/Methods: Development Media International developed and broadcast an intensive radio campaign following the *saturation+* methodology. Twelve one-minute radio messages, produced in three of the most-spoken languages in Zambezia, were broadcast on one provincial and twelve community radio stations, ten times a day during September 2020–June 2021.

Using routinely collected district-level TB data, absolute numbers of people tested for TB and case notifications (all forms and bacteriologically positive cases) were compared over the pre-intervention (January 2017 to August 2020) and intervention period in Zambezia and Tete (control province), and percentage changes were calculated. Data were adjusted for historical trends in TB case notifications.

Results: During the campaign period, the increase in TB testing was higher in Zambezia (57%) than in Tete province (48%). Compared to the pre-intervention period, during the campaign period, all forms TB case notifications increased in both, Zambezia (22%) and Tete (23%). However, the percentage change in bacteriologically positive notifications was higher in Zambezia (38%) than Tete (22%).

Conclusions: Health education for TB via radio can enhance TB testing and case detection. The roll-out of various community-based interventions during the radio campaign to increase TB case finding in both, Zambezia and Tete, potentially explains the observed increase in TB notifications in these provinces. The greater increase in TB testing and case notifications observed in Zambezia province provides evidence of the added value of a radio campaign in facilitating TB case detection.

EP-23-827 Electronic case-based surveillance system (Drug Resistant TB program): improving drug resistant TB reporting rates in Uganda

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Background and challenges to implementation: In 2012, Uganda Ministry of Health's National Tuberculosis and Leprosy Program (NTLP) rolled out a paper-based information system for TB inclusive programmatic management of drug resistant TB (PMDT). Microsoft Excel and Access databases were utilized, data was not easily accessible as reports were compiled manually. In 2017, NTLP with support from implementing partners, developed the first electronic drug-resistant TB electronic management information system (DR-TB MIS) in Uganda. USAID-funded Defeat TB project revamped this system in 2019. In 2020, NTLP created the electronic case-based surveillance system (eCBSS) piloted, rolled out nationally. DR TB MIS was migrated to eCBSS, it's closely monitored and sought to examine its impact on timely, quality Drug Resistant TB reporting and addressing information needs.

Intervention or response: USAID Defeat TB led the revision of HMIS DR TB treatment card and oriented health facility staff on its use. It is based on this that the DR-TB MIS was revamped and simplified ensuring better user-friendliness. The system was reviewed, and orientations conducted in collaboration with TB stakeholders hence ensuring greater partner ownership. The orientations addressed emerging challenges, expe-

riences, and suggestions for improvement. Due to the simplicity of the revised DR-TB MIS, users were able to utilize the system to address their day-to-day data management needs and this facilitated compilation of health facility quarterly reports.

Results/Impact: DHIS2 DR TB report timeliness improved from 53% in the quarter of April to June 2018 to 88% during the quarter of January to March 2022. The system allows sites to automatically generate quality information to feed into quarterly reports without necessarily performing manual counts.

Conclusions: Revamping the eCBSS DR TB program beginning with the treatment card enhanced use and greatly improved DR TB reporting in Uganda. Electronic patient level information system plays a vital role in ensuring timely data availability for quick decision making.

EP-23-828 Factors associated with the first consultation at private health providers at the onset of TB symptoms: a cross-sectional study in The Gambia

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Background: Public-Private Mix (PPM) programs, implemented in many low-income countries to cope with TB, have been shown to promote case detection, treatment outcomes and case management. Understanding the treatment seeking behavior of TB patients is vital to successful PPM programs.

Design/Methods: This cross-sectional study was part of the multi-country TB sequel study. Adults with pulmonary TB were identified at various treatment centers in the urban Greater Banjul Area of The Gambia. At enrollment, we documented treatment seeking behavior from the onset of symptoms until the start of TB treatment. We investigated where TB patients first presented for care, their travel time, and time spent, with their reasons for first presenting outside public facilities. Logistic regression used to identify factors associated with first consultation with private health provider.

Results: A total of 283 patients were included in the study (median age 30 years interquartile range 23- 40; 72% male). Majority of patients (59%) presented at private facilities when they first experienced TB symptoms; 31.5% drug stores/ pharmacy, 21.2% private clinics, and 6% traditional practitioner. Travel time and visit length

at the traditional practitioner or at either public or private hospital was significantly longer than drug stores/ pharmacy visits (Table 1).

Older age (>30 years; aOR 2.1 95% CI 1.1- 3.9) and being unmarried (aOR 1.9 95% CI 1.1- 3.7) were associated with presenting at private health provider. Mistrust in public facilities (30.7%) and perceived TB symptoms as insignificant (30.1%) were main reasons for attending private facilities (Table not shown).

Characteristics	n(%)	Median (IQR), minutes		Crude OR (95% CI)	
		Travel time	Time spent	Travel time	Time spent
Drug stores/ pharmacy	89 (31.5)	30 (10, 45)	10 (5, 30)	Reference	Reference
Traditional practitioner	17 (6.0)	60 (30, 120)	120 (60, 480)	3.3 (1.1- 9.5)	48.1 (9.7- 237.4)
Public primary care	41 (14.5)	45 (20, 60)	60 (30, 120)	2.7 (1.2- 5.7)	9.1 (3.8- 21.6)
Private clinic/ hospital	20 (7.1)	60 (25, 60)	60 (45, 120)	2.8 (1.0- 7.6)	14.9 (4.8- 46.5)
Public hospital	76 (26.9)	60 (30, 90)	100 (52.5, 195)	3.7 (1.9- 7.1)	19.2 (8.6- 42.8)
Private mission clinic/ hospital	40 (14.1)	85 (45, 135)	180 (60, 360)	7.9 (3.3- 18.8)	25.7 (9.6- 68.7)
Total	283 (100)				

Table 1: Median travel time and time spent at first health care provider by newly diagnosed pulmonary TB patients.

Conclusions: Older and unmarried pulmonary TB patients initiate care at private health provider, with a third at drug stores/ pharmacies, which requires significantly less travel and time spent per visit than other providers. The PPM programs should consider engaging these providers to reduce patient and health care system delay in the diagnosis of TB.

EP-23-829 Feasibility, acceptability, and yield of systematic TB screening in children at primary health centres and district hospitals - a multi-country mixed methods study

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Background: There is a gap between the number of estimated and notified childhood TB cases. Symptom-based TB screening of every sick child attending health facilities could increase presumptive TB and case detection, though not currently recommended.

We sought to assess feasibility, acceptability, and yield of systematic childhood TB screening in primary health centres (PHC) and district hospitals (DH) in Cambodia, Cameroon, Côte d'Ivoire, Mozambique, Sierra Leone and Uganda.

Design/Methods: As part of the TB-Speed Decentralization study (2020-2022), we extracted aggregated data from paediatric outpatients' department (OPD) registers of 8 PHCs and 2 DHs per country that implemented systematic TB symptom (cough or fever > 2 weeks or weight loss) and contact history screening.

We described implementation challenges documented within support supervision reports and monthly coordination meetings minutes. We conducted semi-structured interviews with Health Care Workers (HCWs) to describe their experience and perceptions of screening.

Results: TB screening was implemented by health care workers, lay workers or clinicians, at triage or within routine consultations. Patient flows sometimes were adapted to avoid missing children, especially at DH. Of 186,504 children attending OPD, 151,938 (81.5%) were screened for TB and 3,982 (2.6%) were identified with TB presumptive (see country and facility level details in table).

All HCWs shared positive feelings about systematic screening as an effective entry point for diagnosis, as a "wake-up" on the importance of childhood TB. HCWs reported being more engaged in systematic screening

when they were able to deliver other diagnostic approaches. HCWs perceived that screening questions on weight loss, contact history or days with fever were not always understood or accepted by parents.

	Overall			By Country					
	DH	PHC	All	Cambodia	Cameroon	Côte d'Ivoire	Mozambique	Sierra Leone	Uganda
OPD attendance	62918	123586	186504	18428	6830	36834	43957	34140	46315
Screened (% among OPD attendance)	47686 (75.8)	104252 (84.4)	151938 (81.5)	18391 (99.8)	6330 (92.7)	29860 (81.1)	28374 (64.5)	25762 (75.5)	43221 (93.3)
Presumptive TB (% among screened)	1805 (3.8)	2177 (2.1)	3982 (2.6)	314 (1.7)	694 (11)	434 (1.5)	910 (3.2)	592 (2.3)	1038 (2.4)

Conclusions: Systematic TB screening was perceived positively as a tool for improving diagnosis for childhood TB. Yield was higher at DH than PHC-level, suggesting possible differences in (quality of) implementation and/or health status among OPD attendances.

EP-24 Drugs, dosing and resistance

EP-24-830 Re-evaluation of the critical concentration of newer and repurposed anti-TB drugs for the phenotype based wild-type *M. tuberculosis* isolates in and around Chennai

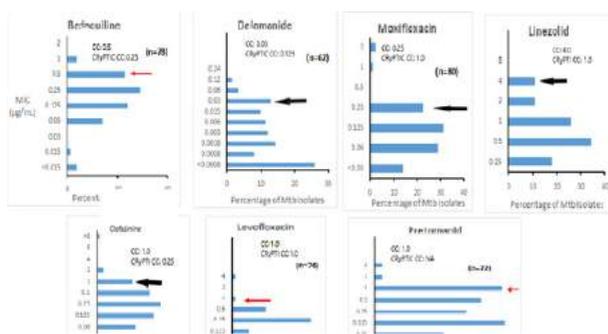
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Background: In this study we aimed to determine the critical concentration (CC) levels of the newer and repurposed drugs for the wildtype *Mycobacterium tuberculosis* isolates prevalent in Chennai region.

Design/Methods: Minimal inhibitory concentrations were determined for Bedaquiline⁽ⁿ⁼⁷⁸⁾, Delamanid⁽ⁿ⁼⁶²⁾, PA824⁽ⁿ⁼⁷²⁾, Moxifloxacin⁽ⁿ⁼⁸⁰⁾, Linezolid⁽ⁿ⁼⁷³⁾, Clofazimine⁽ⁿ⁼⁸⁰⁾ and levofloxacin⁽ⁿ⁼⁷⁶⁾ by broth micro dilution method using 1 McFarland inoculums diluted 20 times (1) using Middlebrook 7H9 with OADC in glycerol (BD) (1 to 0.5 x 10⁵CFU/ml) in duplicates (96 well plates).

They were read under inverted microscope after incubation at 37°C for 10 to 14 days kept in sealed plastic bags. It was ensured to have sufficient growth in the drug free inoculum controls (100% and 1% diluted).

Results: Critical concentrations were determined based on the definition stated by Gumbo (2) and were found to be dissimilar (Figure) for all the drugs tested except levofloxacin when compared with the ECOFF proposed by the CRYPTIC Consortium (3) which uses 0.5 McFarland inoculum diluted 111 times. For instance Janssen (4) used 1 McFarland inoculum diluted 98 times and arrived at a CC of 0.125 mg/L for bedaquiline as against 0.25 mg/L with more diluted inoculum (3, 4) of CRYPTIC, whereas it was 0.5 mg/L for BDQ in our study. But incubation period used by the CRYPTIC consortium and that of Janssen was 21 days with lesser inoculum, but the turnaround time ranged between 9 - 12 days by our method. CC for Pa824 was not available and our study reports it to be 1 mg/L.



Conclusions: WHO proposed the same level of the inoculum size reported by the CRYPTIC consortium (4) with CO₂ but our study with higher inoculum size resulted in the same range of CFU without CO₂ in lesser incubation period.

EP-24-831 Characterization of *embB406* mutations and variable ethambutol resistance among *Mycobacterium tuberculosis* isolates in Canada

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Background: Comprehensive knowledge of molecular predictors of *Mycobacterium tuberculosis* (MTB) drug resistance is essential to inform rapid drug susceptibility testing (DST) and improve treatment outcomes. Ethambutol (EMB) is a first line drug that targets arabinosyltransferases encoded by the *embCAB* operon. Phenotypic DST for EMB employs a critical concentration of 5 µg/mL while genotypic methods often detect mutations in *embB*, including *embB406*, for rapid sensitivity predictions. However, discordance between phenotypic and genotypic DST bring into question the clinical significance of *embB406*. We aim to decipher implications of *embB406* mutations on EMB resistance in MTB.

Design/Methods: MTB isolates screened for the *embB406* mutation (n=16) and pan-sensitive control MTB isolates (n=10) were selected from the National Reference Centre for Mycobacteriology culture collection. Phenotypic DST for EMB was performed on the BACTEC MGIT 960 system in duplicate by proportion method (2, 3, 4, 5 µg/mL) with H37Rv as a control. Genomic DNA was extracted and whole genome sequencing achieved on Illumina MiSeq. Phylogenetic analysis was performed using SNVPhyl. MyKrobe Predictor and Snippy were employed to detect single nucleotide polymorphisms within the *embCAB* operon and other genomic loci associated with EMB resistance. Mutations compiled into genotypic resistance profiles were compared with phenotypic resistance using multiple regression analysis to determine high vs. low confidence mutations.

Results: Sequencing revealed two subgroups of *embB406* mutations: *gly406asp* and *gly406ala*. Phenotypic DST showed no clear relationship between mutation subgroups and EMB resistance levels. The highest concentration of resistance for mutation-harboring strains ranged from 2-5 µg/mL.

We predict novel mutations outside *embB* exacerbate variability in EMB susceptibility within strains harboring identical *embB406* mutations.

Conclusions: Mutations in *embB406* may be low confidence associated with low-level EMB resistance undetectable by the current critical concentration for EMB DST (5 µg/mL). Amendment to genotypic and phenotypic DST is required to accurately inform EMB resistance predictions.

EP-24-832 Management of active drug safety monitoring implementation for new anti-tuberculosis drugs in Kazakhstan

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Background: Kazakhstan is a high burden DR-TB country. Since 2016, new TB regimens to treat DR-TB were introduced under operational research conditions. Mandatory active drug safety monitoring (aDSM) was introduced for bedaquiline (Bdq) and delamanid (Dlm). In 2020, the Kazakhstan NTP began roll-out of these new drugs in regular medical practice.

Successfully transitioning aDSM from operational research conditions to regular prescription of Bdq and Dlm required revisions to the regulatory and operational framework.

Design/Methods: To ensure a comprehensive approach to the management of new DR-TB medicines, the Kazakhstan NTP assessed the pharmacovigilance system at different levels of the healthcare system and defined phases for introduction of aDSM for the now routinely prescribed new TB drugs. The NTP, with support of the partners and USAID Eliminating TB in Central Asia Activity, advocated to establish a P pharmacovigilance working group and include aDSM activities as a special chapter in the 2022–2026 Comprehensive Plan for TB Services.

In February 2021, 20 pharmacovigilance specialists from across the country received aDSM training using a module developed by the USAID activity. The NTP, in collaboration with the National Drug Regulatory Authority, updated the information flow on adverse events (AEs).

Results: Standardization and integration of the reporting flow on AEs and clinical and laboratory monitoring tools strengthened reporting and improved the quality of data entered in national information systems. Official reports of AEs submitted by doctors countrywide increased by over 30% from 2020–2021.

Background and challenges to implementation: Since 2016, Kazakhstan as a high-burden DRTB country has introduced new TB regimens to treat DR-TB under operational research conditions. In 2020, the Kazakhstan

NTP began roll-out of bedaquiline (Bdq) and delamanid (Dlm) in regular medical practice, which required mandatory active drug safety monitoring (aDSM). Successfully transitioning aDSM from operational research conditions to regular prescription of Bdq and Dlm required revisions to the regulatory and operational framework.

Intervention or response: To ensure a comprehensive approach to the management of new DR-TB medicines, the Kazakhstan NTP assessed the pharmacovigilance system at different levels of the healthcare system and defined phases for introduction of aDSM for the now routinely prescribed new TB drugs. The NTP, with support of the partners and USAID Eliminating TB in Central Asia Activity, advocated to establish a pharmacovigilance working group and include aDSM activities as a special chapter in the 2022–2026 Comprehensive Plan for TB Services.

In February 2021, 20 pharmacovigilance specialists from across the country received aDSM training using a module developed by the USAID activity. The NTP, in collaboration with the National Drug Regulatory Authority, updated the information flow on adverse events (AEs).

Results/Impact: Standardization and integration of the reporting flow on AEs and clinical and laboratory monitoring tools strengthened reporting and improved the quality of data entered in national information systems. Official reports of AEs submitted by doctors countrywide increased by over 30% from 2020–2021.

Conclusions: Adaptation of regulations, operational framework and tools for aDSM facilitated its implementation in ordinary practice of new medicines and consequently improved reporting of AEs. Kazakhstan's NTP also institutionalized the USAID activity training module in its professional development process for TB doctors and adapted the module for an online learning platform on aDSM.

EP-24-833 Assessment of whole-genome sequencing for predicting the drug resistance and transmission of tuberculosis

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Background: Whole-genome sequencing (WGS) is recommended for predicting drug resistance and investigating the transmission of tuberculosis (TB). To evaluate the performance of WGS to improve laboratory services, we conducted a feasibility study.

Design/Methods: We collected 200 drug-resistant (DR) *Mycobacterium tuberculosis* isolates. Phenotypic drug susceptibility testing (DST) was performed for 12 anti-TB drugs. A cluster was defined as at least 2 isolates with identical spoligotypes and MIRU genotypes. WGS was performed using the Illumina platform. Drug resis-

tance profiles, lineages and genotypes were predicted *in-silico* using the Total Genotyping Solution for TB (TGS-TB) and the BioNumerics.

Results: Using the phenotypic DST results as a reference, WGS-based prediction demonstrated high concordance rates for isoniazid (93.5%), rifampicin (98.0%), pyrazinamide (98.5%) and fluoroquinolones (99.0%) and for second-line injectable drugs (96.0%-99.5%).

However, lower concordance rates for ethambutol (86.0%), streptomycin (87.0%) and ethionamide (83.5%). Furthermore, the *katG* S315T, *rpoB* S450L and *gyrA* D94G mutations conferred high resistance levels based on the obtained minimum inhibitory concentrations.

We found 8 novel mutations in the *katG* (D329Y, G370E, P375L), *gyrB* (G522S), and *thyA* (L38S, L218P, R235W, Y251*) genes. Among the 200DR-TB cases, 119 (59.5%) involved the predominant sublineage 2.2 genotype. Phylogenetic analysis revealed a Beijing genotype DR-TB cluster with 5 isolates showing between-patient fixation of two mutations, ethionamide *ethR* A95T and bedaquiline *Rv0678* c-11a, providing informatic markers for identifying a presumptive cluster.

Conclusions: WGS analysis is highly accurate for predicting drug resistance and might be useful for delineating transmission. It is a valuable tool to inform clinical and public health actions in the TB control program.

EP-24-834 Second line drug resistance to fluoroquinolone among the rifampicin resistant and multi-drug resistant TB patients in Nepal

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Background: Emergence of drug resistant tuberculosis is a major global public health problem and has affected Nepal as one of the high drug resistance TB burden countries. A cross sectional study of positive culture samples from rifampicin resistant/multi-drug resistant TB (RR/MDR-TB) was conducted at National Tuberculosis Control Center to determine the resistance pattern of second line anti-TB drugs, namely Moxifloxacin (MFX), Amikacin (AMK), Clofazimine (CFZ) and Linezolid (LZD). The resistance pattern of these drugs has not yet been fully studied in Nepal

Design/Methods: A total of 97 RR/MDR-TB initial culture positive isolates (88 liquid and 9 solid) from August 2021 to March 2022 were included in this study. Second line drug susceptibility test (DST) were performed using Bactec MGIT 960 with critical concentration of 0.25 and 1 µg/ml for MFX, 1 µg/ml for AMK, CFZ and LZD. Sigma drugs were used for DST, and drug solutions were prepared as described in WHO technical manual for drug susceptibility testing of medicines used in the treatment of tuberculosis.

Results: Of the 97 isolates, 46 were susceptible to all four drugs. Resistance to only MFX 0.25 µg/ml was 23, MFX 0.25 and 1 µg/ml was 20, MFX 0.25, 1 µg/ml and AMK was 1, MFX 0.25, 1 µg/ml and CFZ was 1, MFX 0.25, 1 µg/ml and LZD was 1, MFX 0.25, 1 µg/ml, CFZ and LZD was 2, AMK and LZD was 1, MFX 0.25, 1 µg/ml, AMK and LZD was 1 and MFX 0.25 µg/ml, AMK and LZD was 1 respectively. According to WHO new definition, 45 (46.4%) isolates were pre-XDR-TB and 6 (6.2%) were XDR-TB without Bedaquiline.

Conclusions: Resistance to MFX (quinolone) is very high among the RR/MDR-TB patients in Nepal. Early diagnosis and right treatment is very important to prevent further transmission of quinolone resistance TB in Nepal.

EP-24-835 MDR-TB data enhancement – role of data quality mentorship at MDR sites in Uganda

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Background and challenges to implementation: Uganda MoH rolled out HMIS reporting and streamlined it to DHIS2 electronic management information system back in July 2015. The National TB & Leprosy Programme (NTLP) still worked with independent data collection system. In 2018, USAID Defeat TB project closely worked with NTLP and streamlined TB reporting in DHIS2.

HMIS trainings were conducted, facility unit TB staff were oriented on TB report compilation and submission to DHIS2. Follow on data quality mentorship were implemented at MDR TB sites over the project life cycle. Initially in Oct-Dec'17, the median deviation was 50%

discrepancy between the figures reported in the MoH DHIS2 and data verified on site, this affected decision making processes. MDR TB sites median discrepancy was above the acceptable margin of $\pm 10\%$. Issue of concern then was understanding of data elements due to attrition of trained staff.

Intervention or response: Defeat TB constituted a team of DR-TB mentors at national level who were oriented in HMIS reporting forms and data elements. These were dispatched to all 17 DR-TB sites to provide mentorship to health workers in compilation of HMIS DR TB reports. Initial activities were performed in April - July 2018 and follow-on Data quality mentorship sessions were conducted in April-June 2021 after revision of HMIS tools. Teams were oriented on data elements in the DR-TB report and MoH DHIS2 submission. Action planning, improvement suggestions were discussed. Continuous mentorship sessions included TB unit and records staff who submitted reports into MoH DHIS2.

Results/Impact: DQA data collected in July 2018 showed a reduction in median deviation between the number of DR-TB patients reported in DHIS2 and those verified from 50% to 0% between quarter of October-December 2017 to quarter of April-June 2018. 0% median deviation DQA results showed similar performance in April-June 2021. Proportion of sites reporting within acceptable data quality margin ($\pm 10\%$) increased from 4 to 12 out of 17 treatment initiation sites.

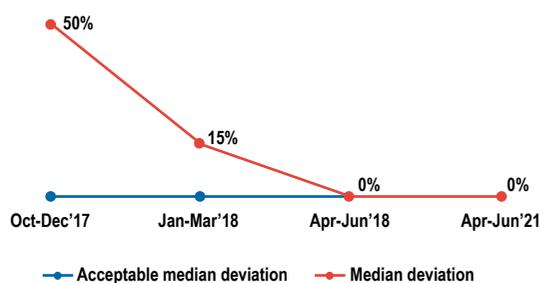


Figure 1. DQA results - median deviation.

Conclusions: Continuous periodic mentorships, engagement of unit TB and records staff in TB reporting, MOH DHIS2 system led to enhanced understanding of indicator compilation and report quality. MoH DHIS2 data greatly enhanced planning, program management, decision making at facility, district and national levels.

EP-24-836 Pathogen-targeted next-generation sequencing (ptNGS) for rapid and accurate diagnosis of tuberculosis in children

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Background and challenges to implementation: Pathogen-Targeted Next-Generation Sequencing (ptNGS) has been applied as a novel method of detection pathogens for infectious diseases, but its value in the rapid diagnosis of pediatric tuberculosis (TB) has not been clarified.

Intervention or response: A retrospective analysis was conducted on 82 children inpatients with suspected TB who underwent ptNGS and three other tests in BALF, sputum, pleural effusion, abdominal effusion, bone joint fluid, lymph node tissue and cerebrospinal fluid (CSF) samples.

Results/Impact: Among 82 included children patients, 40 cases were diagnosed as TB (24 pathogenic confirmed, 16 clinical diagnosed) and 42 cases as non-TB. Using final diagnosis as reference standard, the sensitivity, specificity, PPV (positive predictive value), and NPV (negative predictive value) of ptNGS in all samples for pediatric TB were 75.00% (30/40, 58.48%–86.75%), 100.00% (42/42, 89.56%–100.00%), 100.00% (30/30, 88.87%–100.00%) and 80.77% (42/52, 67.03%–89.91%).

The diagnostic sensitivity of ptNGS (75.00%) was significantly higher than that of MGIT 960 culture (20.00%, 8/40, $P = 0.000$), TB-LAMP (30.00%, 12/40, $P = 0.000$) and Xpert MTB/RIF (45.00%, 18/40, $P = 0.006$). 4 rifampicin resistance cases were detected by ptNGS, and the results were consistent with Xpert MTB/RIF. ptNGS also detected 8 other drug resistance cases, which were mutation of drug resistance mutation sites such as Mfx, Lfx, Cfz, and Ak, respectively.

Conclusions: ptNGS had high sensitivity, specificity and PPV in the diagnosis of pediatric TB. ptNGS using BALF, sputum, lymph node tissue samples provided faster results, enabling early and accurate pediatric TB diagnosis. ptNGS contributes to the identification of drug-resistant mutation sites, which may help children with drug-resistant tuberculosis to obtain early and accurate anti-tuberculosis treatment.

EP-24-837 Drug resistance profiles of *Mycobacterium tuberculosis* in Mimika, Papua, Indonesia 2014-2021

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Background: Drug-resistant tuberculosis (DR-TB) is considered as a major threat to public health. There is a substantial progress in the diagnosis technology and treatment of drug-resistant TB. However, access to drug-resistance testing, particularly in low-middle-income countries remains limited.

Design/Methods: We conducted a retrospective study to drug-resistant TB cases in Mimika district TB control program, in Papua, Indonesia. The TB information system was used to collect data on patient characteristics, drug resistance profiles, treatment regimen and treatment outcome between 2014-2021.

Results: Out of 89 drug-resistance TB cases in Mimika district, 69% showed phenotypic drug resistance to only Rifampicin, 10% to 2 TB drugs, and 21% to >2 TB drugs. The highest proportion of resistance was found among cases tested for resistance against Bedaquiline (8/13, 69%), followed by resistance to Streptomycin (9/22, 41%), Pyrazinamide (8/20, 40%), Isoniazid (15/39, 38%), High-dose of Isoniazid (9/31, 29%), Linezolid (2/7, 29%), Ethambutol (3/22, 14%), Levofloxacin (1/14, 7%), and Kanamycin (1/36, 3%).

The median delay from DR-TB diagnosis based on Xpert MTB/RIF to results of the drug-sensitivity test was 84 days (range 36-184 days), but the median delay from DR-TB diagnosis to the start of treatment was shorter at 19 days (range 4-87 days).

Treatment was provided to 76 patients (85.4%), 41 received a longer regimen (53.9%) and 35 (46.1%) received a shorter regimen. Treatment success between 2014 to 2020 was 40.9%, with 30.3% died, 12.1% lost to follow-up, 12.1% still on treatment, and 4.5% being transferred to other districts.

Conclusions: There was a high proportion of phenotypic drug resistance against Bedaquiline in Mimika district, Papua, Indonesia. The poor success rate, low coverage and long delay to the drug-sensitivity test result are concerning and require consideration before expanding the use of Bedaquiline for DR-TB treatment.

EP-24-838 Genotypic diversity and drug resistance of *Mycobacterium tuberculosis* strains in the Republic of Moldova

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Background: The incidence of multidrug resistant tuberculosis (MDR-TB) remains critically high in Eastern European countries. In the present study we aim to describe the genotypic diversity, spectrum of molecular drug resistance and associated clinical features of the MDR *Mycobacterium tuberculosis* (MTB) strains from the Republic of Moldova.

Design/Methods: We conducted analysis of the whole genome sequencing (WGS) data of the MDR MTB strains retrieved from the biobank of the National Reference Laboratory for Mycobacteriology in the Republic of Moldova isolated from adult pulmonary MDR-TB patients during 2013-2018. A similar number of MTB isolated were randomly retrieved for each year of the study period. Available clinical data were also collected and analyzed.

Results: After exclusion of mixed and non-MDR strains (according the WGS results) a total of 288 sequenced MTB isolates were included into the study. Phylogenetic reconstruction identified two large clades which comprised Lineage 2 (L2) - 43% and Lineage 4 (L4) - 57%, in a proportion stable over the study period.

A higher clustering rate was observed in L4 than L2 strains (63.4% vs 36.3% $p < 0.0001$) Significant differences in phenotypic and molecular resistances to fluoroquinolones, aminoglycosides, pyrazinamide, ethionamide, PAS, and ethambutol were observed among the lineages.

In the analyzed MTB strains 74 homoplastic polymorphisms were identified. Frequency of pulmonary cavity lesions (59% vs 46.2%, $p=0.04$) and treatment failure (12,9% vs 3,9%, $p=0.01$) were higher in patients with L2 than in those with L4 strains.

Conclusions: MDR-TB strains from the Republic of Moldova comprise two MTB lineages which differ in their resistance profile and some clinical features.

EP-24-839 Gender disparities in multi-drug resistant tuberculosis

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Background and challenges to implementation: Gender differences in multi-drug resistant tuberculosis (MDR) have been reported worldwide. The reason for this gender disparities is unclear.

The aim of our study was to assess gender differences in MDR incidence and treatment outcome.

Intervention or response: Retrospective and multicentric study including patients treated for MDR from 2000 to 2019 in pneumology departments of Abderrahmane Mami and Manzel Bourguiba hospitals, Tunisia. We compared clinical, bacteriological, radiological features and treatment outcome between genders.

Results/Impact: Among 140 MDR patients, 110 (79%) were men aged of 42±13 years. MDR cases was significantly higher in men compared to females after the third decade of life (67% vs 27%; p=0,04).

In men, the highest notification rate was 78 in the 40-49 age group and in women it was 27 in the 29-30 age group. Factors influencing the risk of MDR were more frequent in male patients(p=0,02).

Male patients were more likely to suffer from alcohol abuse (p=0,03), drug use (p=0,002), incarceration (p=0,001), previous TB treatment (p=0,03) and to be socioeconomically deprived (p=0,01).

Primary resistance was more frequent in female patients (25% vs 8%; p=0,04). Female patients had Higher rates of extrapulmonary TB (67%vs 22% ;p=0,04) and extensive TB (71% vs 23%; p=0,01). There was no difference in pre-treatment smear gradings.

However Women were faster to convert to culture negative than men (73 days vs 137 days; p=0,02).

After adjusting for subjects demographics and comorbidities, men showed poor adherence (OR=6,110 [2,740-12,450];p=0,021), higher treatment failure (OR=1,210 [1,187-32,657];p=0,045) and mortality (OR=1,71 [1,40-17,50];p=0,03). Women presented more adverse events (OR=3,644 [2,560- 27,268];p=0,041).

Conclusions: Gender differences in MDR may be explained by the higher prevalence of TB risk factors in men. Women reported more adverse effects without impacting treatment outcomes.

EP-25 Tuberculosis diagnostics quality and complexity

EP-25-840 A novel quantitative molecular assay for accurate diagnosis and monitoring response to antibiotic therapy of bacteria underlying COPD exacerbation

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Background: Aetiological agents underlying exacerbation of Chronic Obstructive Pulmonary Disease (COPD) and bronchiectasis are poorly diagnosed by the current culture-based methods. We evaluated RNA-based molecular method, COPD-Molecular Bacterial Load Assay (COPD-MBLA) for detection and quantification of the most common bacterial causes of exacerbation in patients.

Design/Methods: Exacerbating persons with COPD admitted at Victoria Hospital, Kirkcaldy, Scotland were enrolled for diagnosis and treatment response monitoring over 90 days of follow-up. Patient sputa were tested for six most common bacterial species underlying COPD exacerbation using COPD-MBLA, reverse transcriptase qPCR assay in comparison with culture.

Results: 29 patients (66% female, median age 72 years, median COPD Assessment Test (CAT) score 30, 58% COPD diagnosis, 41% bronchiectasis, median BMI 21.9kg/m², 26% on inhaled- and 42% oral- steroid respectively) were enrolled. Bacterial loads in patients reduced with antibiotic treatment over time, but in some cases relapsed after stopping antibiotic therapy. For instance, *P. aeruginosa* bacterial loads fell from 1.19E+09 CFU/mL at baseline to 1.48E+04 CFU/mL during the 2-week antibiotic course but rose to 5.52E+08 CFU/ml within three weeks of stopping medication.

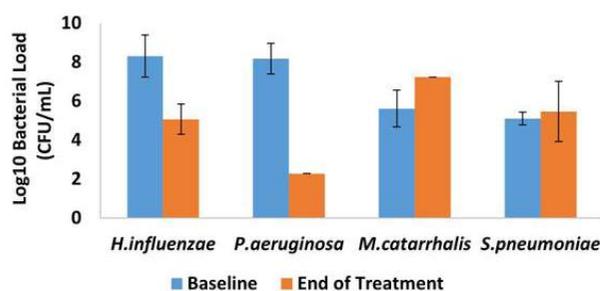


Figure 1. Baseline bacterial loads were highest for *P. aeruginosa* and *H. influenzae*, both reducing over treatment course.

At baseline, COPD-MBLA detected bacteria in 66% of patient culture negative samples. Within the first 3 days of treatment, culture positively detected 41% of

patients, compared to 89% by COPD-MBLA. Bacterial load of key species at baseline and end of therapy for *H. influenzae*, *P. aeruginosa*, *M. catarrhalis*, and *S. pneumoniae* was $2.03E+08 - 1.17E+05$ CFU/mL, $1.51E+08 - 1.92E+02$ CFU/mL, $4.17E+05 - 1.69E+07$ CFU/mL, and $1.27E+05 - 2.95E+05$ CFU/mL, respectively.

Conclusions: COPD-MBLA exhibited greater sensitivity and consistency than culture technique, which demonstrates utility for accurate diagnosis of bacteria underlying exacerbation, monitoring efficacy of antibiotic therapy, and informing antibiotic stewardship programmes in management of chronic bronchial sepsis.

EP-25-841 Humoral response to human cytomegalovirus and risk of pulmonary tuberculosis in adolescents: a case-control study

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Background: Emerging evidence suggests a link between infection with herpes viruses, particularly human cytomegalovirus (HCMV), and progression to tuberculosis (TB) disease. We aimed to determine whether there is an association between humoral responses to HCMV and Epstein-Barr Virus (EBV) and the risk of TB in adolescents.

Design/Methods: An unmatched case-control study was conducted amongst adolescents aged 10 - 19 years enrolled in an observational study (Teen TB), between November 2020 and November 2021, in Cape Town, South Africa. Fifty cases with pulmonary TB and 51 healthy controls were included. Demographics and clinical data were obtained, and serum samples at enrolment were tested for HCMV IgG and EBV Nuclear Antigen (EBNA) IgG using two automated enzyme immunoassays. Odds ratios (ORs) were estimated using unconditional logistic regression.

Results: The median age of 101 participants was 15 years (interquartile range [IQR] 13 to 17) and 55 (54%) were female. All participants were HCMV IgG seropositive and 95% were EBNA IgG seropositive. Individuals with TB had higher IgG levels than healthy controls ($p=0.04$; Figure). Individuals with HCMV IgG values in the upper tertile had a 3.7 times greater odds of pulmonary TB disease compared with IgG levels in the lower tertile (95% CI: 1.05–12.84; $p=0.04$). There was a trend for in-

creasing odds of pulmonary TB with increasing level of HCMV IgG ($p=0.04$). In contrast, there was no trend of increased odds of TB with higher EBNA IgG values.

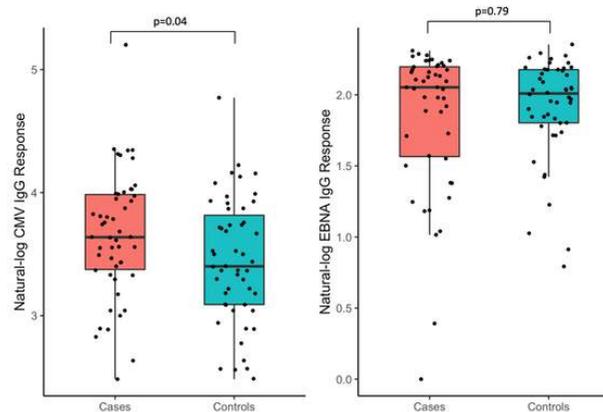


Figure. Log-transformed CMV IgG and EBNA IgG response values for Teen TB case and control groups with accompanying p-values from a Mann-Whitney U-test.

Conclusions: There is a high prevalence of HCMV and EBV amongst adolescents in this high-TB burden setting. The magnitude of HCMV IgG response may be associated with an increased risk of pulmonary TB in adolescents. Improved characterisation of the immunological interaction between HCMV and *M. tuberculosis* would permit targeted development of host-directed therapies and TB vaccines.

EP-25-842 External quality assurance of the tuberculosis sputum microscopy tests in Kampala, Uganda: a five-year (2014-2018) trends analysis

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Background: Tuberculosis (TB) is among the top 13 causes of death world over exacerbated by emergence of multi-drug resistant TB, Sub-Saharan Africa is the most affected region (WHO, 2022). Smear microscopy is the most widely used tool in resource limited countries, if well utilised can yield results of up to 95%. EQA aims at producing reliable and reproducible results. We aimed to access the performance of TB-EQA program and develop targeted interventions to address challenges.

Design/Methods: Retrospective longitudinal trend analysis study was adopted with a mixed method of data collection through using a questionnaire. The study adopted quantitative method to collect data on

trends in TB-EQA performance, we also adopted qualitative method (purposive sampling) through selected six key informant interviews on how institutional factors affect the program based on their vast knowledge and experience in the program.

Results: Proportion of facility enrolment was as follows; private for profit, private not for profit and public facilities (52%, 12% and 36%) respectively, facility level participation consisted of National Referral Hospital, General Hospital, Health Centre IV and Health Centre III contributing (7.2%, 7.2%, 16.6% and 69%) respectively, laboratory professionals consisted of certificate, diploma, degree and masters (21%, 40%, 30% and 9%) respectively.

A total of 46,670 smears were examined, smear sampling was done at 42% of the enrolled facilities, Program performance (Sensitivity, Specificity, Positive Predictive Value, Negative Predictive Value and Accuracy Levels) were at (95.2%, 98.8%, 95.2%, 98.99% and 98.2%) respectively due to prompt supervision, Concordance (True Positive & True Negative) improved from 97.4% to 98.24% and Discordance (False Positive & False Negative) reduced from 2.6% to 1.76% due to good facilitation, Turnaround Time improved from 84 days to 49 days due to good facilitation.

Conclusions: The overall performance of Microscopy Blinded-Smear Rechecking based External Quality Assurance program improved the diagnosis of tuberculosis but the impact was still low thus more effort is still needed.

EP-25-843 Usability and acceptability of TST and IGRA among healthcare workers and two groups at high-risk of TB infection in Mexicali

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Background: Tuberculin skin test (TST) remains the standard-of-care test for TB infection in many high TB-burden settings. Despite existing diagnostics overcoming challenges associated with TST implementation, there has been poor uptake programmatically.

We conducted formative research into patients' and providers' perceptions of acceptability and usability of a novel IGRA test, called QIAreach, compared to TST in a programmatic setting in Mexicali.

Design/Methods: Programmatic outreach to screen for TB disease and infection was conducted in Mexicali (December 2020-July 2021). A 5-point Likert scale sur-

vey was administered to two groups at high risk of TB infection—people who use drugs (PWUD) and household contacts (HHC) of TB patients—and who received testing via TST and QIAreach. This survey evaluated patients' comparative preferences for the two tests. Additionally, a modified system usability scale was administered to TB program staff who were involved in the administration and processing of TST and IGRA tests pre- and post-QIAreach implementation to measure their perceived usability of the tests.

Results: Of 201 patients, 103 (51.2%) were PWUD and 98 (48.8%) were HHCs. The acceptability survey found that the blood draw for QIAreach was preferred to, and considered more trustworthy, than the injection for TST. Also, only requiring one visit with providers for QIAreach was preferred among HHCs, but comparatively less preferable for PWUD. Both groups found in-person delivery of test results to be preferable and more trustworthy. The majority preferred QIAreach over TST; though this was higher among PWUD.

Nine staff completed the usability survey. Perceived usability of QIAreach increased for three participants, decreased for four participants, and remained the same for two participants.

Conclusions: IGRA was more acceptable to patients, and perceived usability was mixed among staff. Patient and provider preferences must be considered when integrating novel IGRA tests into settings where TST is routinely used.

EP-25-844 Comparison of positivity for tuberculosis infection and test concordance using two diagnostic tests among a prison population in Mexicali

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Background: Prison-based populations are at high risk of tuberculosis, but there is little research to understand the performance of tuberculosis infection tests in carceral settings. We compare the concordance of, and patient reactivity to, a novel IGRA—QIAreach—and TST among people deprived of liberty (PDL) and prison employees, by BCG vaccination status.

Design/Methods: In January 2022, PDL and prison employees underwent active case-finding for TB disease and infection. They were tested with TST and QIAreach after active disease was ruled out. We compared concordance of test results for PDL, employees, BCG- and non-

BCG vaccinated individuals using Wilcoxon Rank Test. We also assessed trends in reactivity, measured as time-to-results (TTR, in seconds) for QIAreach and induration size (in mm) for TST, using Spearman Correlation. **Results:** 300 IGRA and 218 TST administered to 289 PDL and 25 employees. A total of 177 (66.3%) were IGRA-positive (165, 68.2% PDL; 12, 48.0% employees) and 117 (53.7%) were TST-positive, per an induration ≥ 10 mm (110, 55.6% PDL; 7, 35.0% employees). A total of 289 individuals had documented BCG vaccination, of which 166 (66.7%) were IGRA-positive and 107 (54.6%) were TST positive. Both tests were positive for 92 (46.0%) people and negative for 53 (26.5%) people, with a 72.5% overall concordance. This increased to 84.5% when a TST-positive induration was ≥ 5 mm. Greater concordance with a lower induration cut-off was observed across most groups. Overall, median TTR for positive QIAreach results was 1080 seconds (IQR:680-1200). TTR among PDL was 1085 (IQR:680-1200) and among employees, 960 (IQR:638.75-1200; $p=0.596$). A trend was not observed between the reactivity of TST and IGRA ($p=0.169$). Results by BCG-status are also available.

Positive QIAreach time-to-results median, in seconds (IQR)					
	Total	PDL	Employees	BCG	No BCG
Median TTR for all Positive IGRA, in seconds	1080 (680-1200, n=177)	1085 (680-1200, n=165)	960 (683.75-1200, n=12)	1200 (877.5-1200, n=166)	1060 (660-1200, n=11)
		Wilcoxon p -value = 0.596		Wilcoxon p -value=0.253	
TST Induration:					
0-4mm	1155 (462.5-1200)	1155 (462.5-1200)	n/a	850 (421.25-1188.75)	1200 (1200-1200)
5-9mm	862.5 (652.5-1200)	862.5 (650-1200)	965 (850-1080)	845 (655-1200)	1200 (837.5-1200)
10-14mm	1180 (863.75-1200)	1180 (863.75-1200)	1055 (982.5-1127.5)	1200 (910-1200)	810 (810-810)
15-19mm	1097.5 (808.75-1200)	1097.5 (808.75-1200)	1105 (920-1200)	1097.5 (786.25-1200)	1125 (1023.5-1200)
20mm+	1200 (797.5-1200)	1200 (790-1200)	1200 (1200-1200)	1200 (790-1200)	1200 (1200-1200)
Spearman Correlation	n=133 $\rho = 0.120$, $p=0.169$	n=124 $\rho = -0.199$, $p=0.138$	n=9 $\rho = 0.264$, $p=0.492$	n=123 $\rho = 0.128$, $p=0.159$	n=10 $\rho = -0.075$, $p=0.837$

Concordance between QIAreach IGRA and TST results			
TST Results, All Participants (n=200)	IGRA Positive	IGRA Negative	Percent Total Agreement
TST positive ≥ 10 mm	92 (46.00%)	14 (7.00%)	72.5%
TST negative < 10 mm	41 (20.50%)	53 (26.50%)	
TST positive ≥ 5 mm	126 (63.00%)	24 (12.00%)	84.50%
TST negative < 5 mm	7 (3.50%)	43 (21.50%)	

Conclusions: All people, regardless of BCG-vaccination status, in prison settings should be considered a priority population for case-finding, care for TB infection, and recipients of preventive therapy.

EP-25-845 Introduction of external quality assessment (EQA) for Truenat™ MTB-RIF at peripheral level laboratories in Zimbabwe: lessons learned

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Background and challenges to implementation: The Truenat™ MTB and RIF Dx assays are being implemented for the first time at 20 peripheral-level laboratories in Zimbabwe supported by the Stop TB Partnership and USAID's Infectious Disease Detection and Surveillance (IDDS) project to decentralize and provide rapid molecular diagnostic testing near point of care.

Intervention or response: IDDS contracted with SmartSpot Quality, an accredited manufacturer of validated MTB-RIF EQA panels, to provide each site with three cycles of EQA. The EQA panels composed of inactivated Dry Culture Spots (DCS) that do not require refrigeration and are stable for up to 24 months. DCS panels were dispatched to each site in January 2022 using the national sample transport network. Virtual training was provided by SmartSpot to end users and other stakeholders for EQA sample processing and electronic reporting of results. Laboratories were expected to report results to SmartSpot within 30 days.

Results/Impact: The majority of Truenat™ sites (70%) successfully reported EQA results by the first cycle deadline. 42.9% achieved a perfect score (pass). The key challenges identified from end-user feedback was the lack of stable internet connection prohibiting attending virtual training sessions and uploading of results. Other challenges identified were testing of panels with a different instrument and non-delivery of panels to testing sites.

Conclusions: The introduction of EQA for Truenat™ MTB-RIF testing at the peripheral level demonstrated that EQA can be implemented effectively at sites with minimal expertise using new rapid molecular diagnostic tools. Lessons learned include:

1. Importance of introducing quality systems to end users;
2. Need for in-person training for EQA panel processing and reporting;
3. Need for more resources to support electronic reporting; and,
4. Need for EQA training to ministry of health staff, including district level, to support the laboratories in reporting EQA results.

EP-25-846 Concordance of tuberculosis infection diagnostic tests among two high-risk groups in Mexicali

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Background: In Mexico, tuberculin skin testing (TST) is the standard diagnostic test to detect tuberculosis infection. However, TST can be unreliable and has implementation-based challenges. Interferon gamma release assay (IGRA)—a newer infection test—may overcome these challenges. To inform guideline updates, we assess the concordance of, and patient reactivity to, these tests in high-risk populations in Mexicali, Baja California, Mexico.

Design/Methods: People who use drugs (PWUD) living in residential rehabilitation facilities and household contacts (HHC) of tuberculosis patients who underwent programmatic evaluation for tuberculosis disease and infection (December 2020-July 2021) were included. After ruling out active disease, patients were tested for TB infection using TST and QIAreach, a novel IGRA. We assessed concordance of results for TST and QIAreach, compare median time-to-results (TTR, in seconds) for PWUD and HHC using Wilcoxon Rank Test, and assess reactivity trends of TTR by TST-induration size with Spearman's Rank Correlation.

Results: Among 193 individuals, 95 were PWUD and 98 were HHC. In total, 92 (47.7%) were IGRA-positive (69, 72.6% PWUD and 23, 23.5% HHCs). Similarly, 92 (47.7%) were TST-positive, per an induration ≥ 10 mm (63, 66.3% PWUD and 29, 29.6% HHCs). Both tests were positive in 64 (34.4%) individuals and negative in 76 (40.9%), with an overall concordance of 75.3%; breakdowns for PWUD and HHC were similar. However, when defining TST-positive as an induration ≥ 5 mm, total concordance increased for PWUD and decreased for HHC.

Median TTR for positive IGRA tests was 925 seconds (IQR 555-1200) among PWUD and 1200 seconds (IQR 1020-1200) among HHC ($p=0.008$). We observed an inverse trend between TTR and TST; the larger the induration, the shorter the TTR ($p=0.034$).

Median Time-to-Results for Positive QIAreach Tests by TST and Patient Groups (in seconds, IQR)

TST Induration (mm)	Total (n=87)	PWUD (n=64)	HHC (n=23)	Wilcoxon Rank Test, p-value
0-4 (n=6)	1200 (1200-1200, n=6)	1170 (1155-1185, n=2)	1200 (1200-1200, n=4)	0.289
5-9 (n=17)	1200 (845-1200, n=17)	1200 (712.5-1200, n=11)	1040 (876.25-1200, n=6)	0.87
10-14 (n=23)	1110 (717.5-1200, n=23)	925 (640-1155, n=17)	1200 (1200-1200, n=6)	0.00842
15-19 (n=23)	835 (460-1200, n=23)	835 (460-1200, n=21)	790 (585-995, n=2)	0.955
20+ (n=18)	815 (545-1200, n=18)	825 (580-1200, n=13)	1200 (760-1200, n=5)	0.606
Total (n=87)	1097.5 (636.25-1200)	925 (555-1200)	1200 (1020-1200)	0.00773
Spearman's rank correlation (positive results only)	rho = -0.227 p-value = 0.0344	rho = -0.186 p-value = 0.142	rho = -0.138 p-value = 0.53	

Positive and Negative Agreement between QIAreach IGRA and TST Results

	TST Results	IGRA positive	IGRA negative	% Total agreement
PWUD (n=88)	TST positive (≥ 10 mm)	51 (57.95%)	7 (7.95%)	77.27%
	TST negative (< 10 mm)	13 (14.77%)	17 (19.32%)	
	TST positive (≥ 5 mm)	62 (70.45%)	9 (10.23%)	87.5%
	TST negative (< 5 mm)	2 (2.27%)	15 (17.05%)	
HHC (n=98)	TST positive (≥ 10 mm)	13 (13.27%)	16 (16.33%)	73.47%
	TST negative (< 10 mm)	10 (10.20%)	59 (60.20%)	
	TST positive (≥ 5 mm)	19 (19.39%)	32 (32.65%)	63.27%
TST negative (< 5 mm)	4 (4.08%)	43 (43.88%)		

Conclusions: Guidelines for management of tuberculosis infection, including initiation of tuberculosis preventive treatment, could be optimized by tailoring strategies for different and locally-defined, high-tuberculosis risk populations.

EP-25-847 Impact of decentralizing childhood TB diagnosis approaches at primary health center and district hospital level on case detection in high TB burden countries

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Background: In 2020, only 38% of 1 million estimated childhood tuberculosis (TB) cases were notified to World Health Organization (WHO). Low case detection is largely due to the lack of diagnostic capacity at peripheral level, challenges in specimen collection, and poor access to molecular testing and chest radiography. We sought to assess impact on TB case detection of decentralizing childhood TB diagnosis at district hospital (DH) and primary health center (PHC) level.

Design/Methods: We retrospectively collected data on TB diagnosis in children aged 0-14 years for 12 months (observation phase) in 2 districts (at PHC and DH level) in Cambodia, Cameroon, Ivory Coast, Mozambique, Sierra Leone and Uganda. We then implemented the innovative childhood TB diagnosis (the intervention: systematic TB screening for < 15 years; clinical evaluation and Xpert Ultra-testing on respiratory and stool samples and simplified reading of digitalized chest radiography performed at DH) in the same health facilities after site preparation and collected TB-diagnosis data (March 2020 - September 2021-intervention phase). Data was collected from the Outpatient and unit TB Registers on monthly basis. We compared the proportion of TB cases diagnosed during the observation phase and during the intervention phase.

Results: Overall, 256,114 and 186,504 children attended 59 study health facilities (including 47 PHC and 12 DH) during the observation and the intervention phase, respectively. Proportion of TB diagnosis was 0.22% (410/186504) in the intervention vs 0.08% (216/256114) in observation phases (OR = 3.17 [95% CI 1.79- 5.62], p<0.001).

After correcting for model overdispersion, OR =3.17 [95% CI 0.90- 11.2326], p=0.07. (see details per country in the table).

Country	TB case detection – ALL		TB case detection at DH		TB case detection at PHC	
	Observation n/N (%)	Intervention n/N (%)	Observation n/N (%)	Intervention n/N (%)	Observation n/N (%)	Intervention n/N (%)
Cambodia	14/32837 (0.04%)	12/18428 (0.07%)	1/3730 (0.03%)	10/627 (1.59%)	13/29107 (0.04%)	2/1780 (0.01%)
Cameroon	15/8114 (0.18%)	29/6830 (0.42%)	14/3458 (0.40%)	24/3128 (0.77%)	1/4656 (0.02%)	5/3702 (0.14%)
Côte d'Ivoire	5/54863 (0.01%)	87/36834 (0.24%)	5/23127 (0.02%)	73/16761 (0.44%)	0/31736 (0%)	14/20073 (0.07%)
Mozambique	114/67609 (0.17%)	94/43957 (0.21%)	74/23922 (0.31%)	56/13030 (0.43%)	40/43687 (0.09%)	38/30927 (0.12%)
Sierra Leone	43/39856 (0.11%)	147/34140 (0.43%)	39/20083 (0.19%)	117/18163 (0.64%)	4/19773 (0.02%)	30/15977 (0.19%)
Uganda	25/52835 (0.05%)	41/46315 (0.09%)	2/12402 (0.02%)	22/11209 (0.20%)	23/40433 (0.06%)	19/35106 (0.05%)
ALL	216/256114 (0.08%)	410/186504 (0.22%)	135/86722 (0.16%)	302/62918 (0.48%)	81/169392 (0.05%)	108/123586 (0.09%)

Conclusions: Our study shows that decentralizing childhood TB diagnosis led to an increase in TB-case detection globally, despite lower facility attendance during the intervention phase, concomitant with the Covid-19 outbreak.

EP-25-848 Clinical profiles of urine LAM positive children lacking microbiological confirmation in South Africa

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Background: Studies of AlereLAM to diagnose TB in children are limited, and clinical interpretation of a positive AlereLAM test without microbiological confirmation remains uncertain. Contaminated urine samples with *Corynebacterium spp* has been reported to cause false-positive AlereLAM results. We assessed the clinical profiles of children with positive AlereLAM testing but negative sputum or gastric aspirate Xpert and culture results.

Design/Methods: We prospectively enrolled children 1-12 years old with clinical symptoms suggestive of TB at Harry Gwala and Northdale Hospitals, between October 2020 – April 2022. Children received baseline clinical evaluations, as well as both Xpert MTB/Rif Ultra and MGIT liquid culture using sputum or na-

sogastric specimens. All children were tested for HIV. Urine specimens were tested using Determine TB LAM (AlereLAM). Urine samples were cultured up to 6 days to detect *Corynebacterium spp.* We compared descriptive statistics for clinical characteristics between LAM positive and microbiologically unconfirmed (LPMU) and LAM negative and microbiologically unconfirmed (LNMU) children (n=89).

Results: We evaluated 92 symptomatic children; 32 were classified as LPMU, 57 as LNMU and 3 were LAM negative with confirmed TB. LPMU children were younger (median age 1.9 years, IQR: 1.1) and had a lower HIV prevalence (9.4% vs 12.3%) compared to LNMU children. Symptom presentation was similar between LPMU and LNMU children, with a lower proportion with cervical lymphadenopathy (6.3% vs. 21.1%) in the LPMU group. Fewer children had a chest X-ray (CXR) suggestive of TB (5.6%, 0%) in the LPMU group, but had a higher history of exposure (18.8% vs 5.3%). *Corynebacterium spp.* was not detected in any children's samples.

Characteristics		AlereLAM+, Microbiologically Unconfirmed (LPMU) (n=32)	AlereLAM-, Microbiologically Unconfirmed (LNMU) (n=57)
Age	Age (years), Median (IQR)	1.9 (1.4 – 2.5)	3.7 (2.7 – 5.6)
History of TB Exposure	Lived with someone within the last 12 months, n (%)	6 (18.8)	3 (5.3)
Clinical Symptoms	Persistent Cough, n (%)	26 (81.3)	45 (78.9)
	Fever, n (%)	25 (78.1)	39 (68.4)
	Cervical LAN, n (%)	2(6.3)	12 (21.1)
	Unexplained Weight Loss, n (%)	16 (50.0)	31 (54.5)
CXR suggestive of TB	Yes, n (%)	1(5.6)	5 (8.8)
HIV Status	HIV positive, n (%)	3(9.4)	7 (12.3)
	Children with CD4 <200 cells/mm ³ , n (%)	0 (0.0)	2 (3.5)

Conclusions: LPMU children had similar clinical presentations, more frequent history of TB exposure, and fewer CXRs suggestive of TB. *Corynebacterium* contamination was not responsible for false positives AlereLAM in this cohort. Better diagnostics are urgently needed to improve clinical management of children with this clinical phenotype.

EP-25-849 Impact of monocytes differentiation pathways on Mycobacterium tuberculosis complex lineages infection

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Background: Macrophages are significant phagocytes of the *Mycobacterium tuberculosis* complex (MTBC), which also use them as their host. The macrophage's phenotypes determine the faith of phagocytosed MTBC. We investigated the influence of macrophages phenotype on clinical MTBC lineages infection outcomes using human monocyte-derived macrophages (HMDM) to informed host-directed therapeutics targeting macrophages polarization.

Design/Methods: Monocytes isolated from venous blood of healthy donors and were cultured in-vitro with medium alone, or in the presence of GM-CSF or M-CSF for 6 days, followed by an additional 2 days in medium alone, IFN-g, IL-4 or IL-13 to generate M0, M1, IL4-M2, and IL-13-M2 like-macrophages, respectively.

The polarized macrophages were infected with reporter-gene-tagged clinical isolates of *M. tuberculosis* lineage2 (*Mtb*-lineage2), lineage4 (*Mtb*-lineage4) and *M. africanum* lineage6 (*Maf*-lineage6) at MOI 1:1.

The intracellular bacteria growth was quantified over 7 days, and percentage of infected macrophage and functional surface markers expression at day3 of infection were evaluated by measuring bacteria fluorescence and flow cytometry analysis.

Results: Uninfected M1-like macrophage had more surface CD163⁺, CD206⁺, CD11b⁺ and CD86⁺ while M2-like macrophage had more HLA-DR⁺, CD16⁺, CD36⁺ and MERKT⁺. At day3 the percentage of MTBC-infected macrophages were significantly high in M0 and M2 following *Mtb*-lineage4 infection (p=0.022 and 0.011), and in M0, M1, and M2 in response to *Maf*-lineage6 infection (p=0.028; 0.034 and 0.0079) compared to the uninfected macrophage control.

Likewise, while *Maf*-lineage6 was significantly higher than *Mtb*-lineage4 in M1, *Mtb*-lineage4 was higher than *Maf*-lineage6 in M2 macrophages over 7 days infection (p=0.045; respectively). Following *Mtb*-lineage4 infection, CD86⁺ cells were significantly lower in M1 than M2 macrophages (p=0.034).

Conclusions: Macrophage polarization differentially affects MTBC lineages infection with M1-like macrophages controlling *Mtb*-lineage4 better than *Maf*-lineage6 infection. In contrast, M2-like macrophages were more permissive to *Mtb*-lineage4 than *Maf*-lineage6 infection.

The ongoing work will determine the mechanism of this response differences through measuring cytokines production.

EP-26 Improved methods for TB case finding

EP-26-850 Framework for implementation of Intensified TB case finding in health facilities: lessons from KNCV Nigeria TB LON Project

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Background and challenges to implementation: Nigeria ranks 6th among the high burden countries for TB with an estimated incidence of 219/100,000 and accounts for 12% of the gap of unidentified TB cases globally. This gap between notified and estimated cases is largely due to underreporting and under diagnosis. To address these two factors, KNCV Nigeria USAID-funded TB LON 1 and 2 project introduced intensified TB case finding in health facilities and developed a guiding framework.

Intervention or response: A stepwise guide for implementing intensified TB case finding in facilities (TB Surge) was developed. See Figure 1.

Using the guide, facilities were identified and engaged. Screening points were selected and 100% TB screening at various service delivery points (SDPs) by engaged ad hoc and facility staff using the WHO four TB Symptom Screening checklist was ensured. All identified presumptive TB were linked for diagnostic evaluation and diagnosed cases placed on appropriate treatment.

Data was reported in cascade using the CommCare application. Implementation was monitored weekly and Monthly Quality improvement and data review meetings were held.

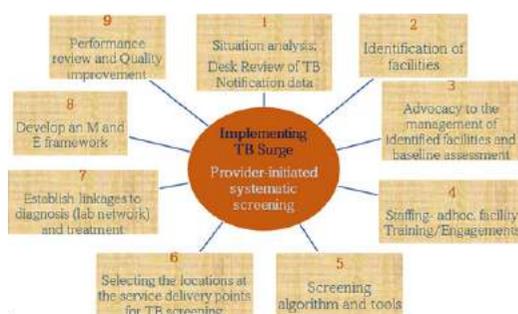


Figure 1. Framework for implementing TB Surge.

Results/Impact: Within 1 year of implementation October 2020 – September 2021, over 950 facilities comprising tertiary, secondary and primary health facilities were effectively engaged. There was increased TB awareness and screening among facility Health Care Workers. A total of 5,441,684 hospital attendees were screened for

TB, 341,628 identified presumptive TB had diagnostic evaluation out of which 28,481 TB cases were diagnosed giving a TB yield of 8.3%. 27,338 diagnosed TB cases were enrolled on treatment. The number needed to screen was 191 and Number needed to test was 12.

Conclusions: Having a guiding framework for intensified case finding in health facilities ensures quality across board and optimization of the intervention for maximum yield. We recommend use of this framework in similar settings.

EP-26-851 Multi-sector forum as an advocacy vessel to increase local funding for tuberculosis program in two cities in Indonesia

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Background and challenges to implementation: TB program funding still heavily depends on central government and foreign donors. There is an urgent need for increased local resources to sustain TB control activities at district level. Yayasan KNCV Indonesia supported the National Tuberculosis Program through Mandiri-TB, a USAID's LON project, which one of the key strategies aims to mobilize local networks to increase funding for TB activities through the establishment of Multi-sector Forum (MSF).

Intervention or response: Mandiri-TB's MSF model comprises five key elements of the society (pentahelix), namely government, private, academic/professionals, community, and media. The forum acts as a vessel for the members to advocate local key stakeholders to mobilize resources in increasing funding for TB program and activities.

Internally, the forum advocates their members to allocate resources for TB control activities, reflected in the annual workplan. Externally, the forum involves in the district budget planning process to increase funding commitment from the local governments.

Additionally, the forum mobilizes funds from the private sector through CSR programs and philanthropic donations. In 2021, Mandiri-TB facilitated the establishment of MSF in Medan and Makassar.

Results/Impact: Increase in government budget allocation for TB program were achieved in both cities, amounting to USD 71,034 in 2022. Furthermore, the Makassar government committed to add around USD 520,000 for TB patient support activities at sub-district level in 2023. In both cities between 2021 and 2022,

advocacy and lobbying to private companies and philanthropies resulted in a total of USD 7,527 additional funding for patient support activities and donation of 470 packages of nutritional support, which all together have benefitted 537 DR-TB patients.

Year	Funding Sources	Medan	Makassar	Total
2021	Government	USD -	USD -	USD -
	Private Sector	USD 2,002	USD -	USD 2,002
	Sub Total	USD 2,002	USD -	USD 2,002
2022	Government	USD 10,138	USD 60,897	USD 71,034
	Private Sector	USD 4,835	USD 690	USD 5,525
	Sub Total	USD 14,973	USD 61,586	USD 76,560
2023	Government	USD -	USD 527,586	USD 527,586
	Private Sector	USD -	USD -	USD -
	Sub Total	USD -	USD 527,586	USD 527,586
TOTAL				USD 606,147

Table. Additional funding for TB program budget in two Mandiri-TB supported cities.

Conclusions: MSF plays an important role to increase awareness and commitment of TB program's key stakeholders at district level. The MSFs' advocacy work has been found effective in increasing local funding and support for TB program from both public and private sectors.

EP-26-852 Developing a predictive tool to identify and prioritize people with TB at risk of incurring catastrophic costs for social protection in Vietnam

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Background: Approximately 63% of people with tuberculosis (TB) in Vietnam experience catastrophic costs (CC) during treatment. Social protection interventions, coupled with responsive health systems, have the potential to mitigate these costs. However, no tool exists to help identify those at risk of CC at the time of TB treatment initiation and to prioritize them for support.

Design/Methods: Data were used from a prospective cohort of 96 people initiated on drug-sensitive TB treatment in Ho Chi Minh City, Vietnam. Participants were surveyed throughout care by a modified WHO longitudinal patient cost survey. McGinn's Framework guided the development of the risk scoring tool. Multi-variable Poisson's regression analysis was conducted to

derive a predictive model for CC incurrence. A weighted score was assigned to the predictor variables based on coefficients and summed to give a composite predictive score.

For each value of the composite predictive score, the sensitivity, specificity, and proportion of correctly specified participants was calculated to determine a threshold at which households were most at risk of experiencing CC. The risk score was then used to construct the PROTECT tool.

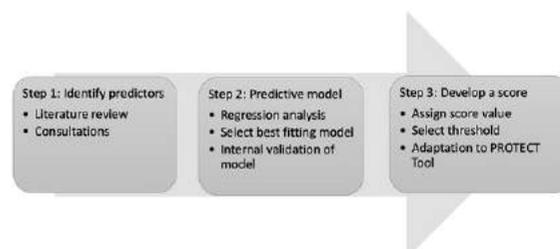


Figure. Overview of methods.

Results: Twenty two percent (22%) of study participants incurred catastrophic costs. The final risk score included four predictive factors of CC: positive HIV status, pre-treatment hospitalisation, ≥ 8 week interval between the onset of symptoms and initiation of treatment and low household income before TB. The area under the curve for the predictive ability of the model was 0.79 (95% CI 0.66-0.92). Internal cross-validation showed a similar predictive ability of 0.78.

Conclusions: The PROTECT tool identifies and stratifies people at risk of incurring CC so that TB programs can link at-risk people to differentiated social protection interventions. Targeting people with TB at highest risk of CC for mitigative interventions could guide the scale-up of social protection interventions.

EP-26-853 Exploring the role of the public-private-mix (PPM) in TB care in Afghanistan

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Background and challenges to implementation: Tuberculosis (TB) prevalence is higher in urban areas in Afghanistan. However, coordination is weak between public and private clinics, causing case detection to decline by 13% in 2020. In October 2021, the United States Agency for International Development (USAID)-funded project Urban Health Initiative (UHI) introduced the Public-Private Mix (PPM) and Urban Directly Observed Treatment, Short Course (DOTS) approaches in Kabul, Kandahar, Herat, Jalalabad and Mazar cities to cover the gap.

PPM strategies aimed to improve coordination and collaboration between the National TB Program (NTP), and public and private health sectors in selected health facilities (HFs).

Intervention or response: With UHI's support, the NTP provided TB training, anti-TB medications, laboratory consumables, and DOTS packages. These packages, sent to 45 clinics, included educational materials, sputum sample transferring materials and drug kit boxes containing complete TB treatment regimens. A technical team supervised and monitored clinics on a regular basis. In both public and private clinics, people received free TB diagnosis and treatment.

We assessed the impact of PPM and Urban DOTS on TB case notification and contact investigation outcomes and reviewed TB data from October 2021 to March 2022.

Results/Impact: In 2022, UHI covered 45 clinics. 13 were private HFs (28.8%); 552 (15.4%) out of 3,579 TB cases were notified by private HFs. Of 1,255 bacteriologically confirmed (BC) TB cases, 192 (15.2%) were notified by private clinics.

In those private clinics, a total of 3,240 household contacts were actively screened. 277 presumptive TB cases were tested, and 22 people with TB were identified. In total, 926 children under five years were prescribed Isoniazid Preventive Therapy (IPT).

Conclusions: Significant improvements in case notification were achieved using UHI's strategy and PPM. Private HFs make crucial contributions to case notification; both initiatives should be scaled up in other cities and similar contexts around the world.

EP-26-854 LTBR TB cascade of care in 4 provinces in Mozambique 2020-2021

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Background and challenges to implementation: Mozambique is a Drug Susceptible (DS) TB, TB/HIV and Drug Resistant (DR) TB high burden country. USAID Local TB Response (LTBR) project is implemented by ADPP and its partners in 4 provinces: Nampula, Zambezia, Sofala and Tete.

The project covers a total of 50/73 districts and serves a population of approximately 13 million. Limitations identified are: access to TB information, health facilities for TB services, limited laboratory services, long distances and poor roads, leading to miss opportunities on finding people with TB, contact screening and correct follow up of treatment.

Intervention or response: LTBR established partnership with mass media companies - h2n and DMI to develop and disseminate key TB messages and education through community radios and national television channel. 1000 LTBR community activists were trained and equipped to provide in person TB education, screening and referrals of people with signs and symptoms of TB to HFs; Sample transportation system through 50 motorbike riders to ensure rapid and early diagnosis and treatment; Screening for contacts of persons with TB and infection control measures at household in the communities and HFs.

Results/Impact: In 2020 and 2021, LTBR reach a total of 1,602,090 people with TB messages and 76% (1,224,679/1,602,090) were screened for TB. Project activists identified 14% (176,873/1,224,679) as persons presenting at least one TB sign or symptom, 79% (139,960/176,873) of persons with TB symptoms were referred to and reached HFs.

From this number of persons, 95% (132,740/139,960) were enrolled for a TB test (Smear Sputum and/or GeneXpert). In total 22% (28,818/132,740) of persons were diagnosed with TB AF and all of them initiating treatment.

Conclusions: In 2 years of implementation, LTBR efforts in 50 districts of 4 provinces contributed significantly to TB AF notification in Mozambique, with 21% (35,732/167,788) at national, 37% (35,732/95,743) at provincial and 56% (35,732/64,215) at district level respectively.

EP-26-855 Evaluation of the impact of public-private mix (PPM) intervention on private sector: retrospective study of Global Fund grant between 2019 - 2020 in Rivers

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Background and challenges to implementation: Control of tuberculosis was always supported in the public sector in Rivers State, Nigeria, prior to the formal engagement of the private sector with support from the Global Fund in 2019. The aim of this study is to evaluate the impact the Grant has made on TB management and outcome among patients notified across PPM facilities between 2019 – 2020.

Intervention or response: A Cohort study of patients notified from private facilities to State Tuberculosis Control Programme between January 2019 to December 2020 by 186 private DOTS sites trained with funds from the Grant was analyzed with epi-info, after filtering out private sector contribution from the treatment success rate (TSR) reporting template.

Results/Impact: Prior to the Grant, only 2 faith-based facilities and 13 private for profit facilities officially notified TB cases between 2017 and 2018: 45 patients in 2017 and 56 in 2018. The TSR was 86% and 90% respectively. Following the commencement of the Grant, TB services were scaled up to 186 private facilities. 812 patients were notified in 2019 and 950 in 2020, all these patients had records in the private DOTS sites with treatment outcome as an indicator, both in the TB treatment register and card. The TSR of patients notified in 2019 was 93% and 86% for 2020, although the research did not look at confounding determinants for successful treatment outcome in our bivariate analysis. However, it is probable the covid-19 pandemic affected the 2020 TSR.

Conclusions: Treatment outcome among patients notified in PPM sites with support from the Grant between 2019 – 2020 showed private sector effectiveness in managing TB patients after providing training and support. Increasing DOTS coverage using a targeted PPM intervention is a useful strategy towards attaining the WHO 2030 End TB target. TB services in the private sector in-country can enhance favorable treatment outcomes for TB patients.

EP-26-856 Closing TB notification gaps through registration of hospitalized clients

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Background and challenges to implementation: Eswatini's TB incidence and treatment coverage moved from 308/100,000 to 363/100,000 and 80% to 69% from 2017 to 2019 respectively (WHO), raising questions about known unregistered TB clients. In some EGPAF-supported sites, it was found that newly-diagnosed TB clients that did not go to the TB Unit on discharge or that died before registration, were not registered because health facilities did not want to be associated with mortality and were not keen to track outcomes of clients who opted to continue care elsewhere. Ensuring linkage of referrals was also not prioritized.

Intervention or response: From 2018, EGPAF utilized regional meetings and facility mentorship to advocate for routine registration of hospitalized TB clients. Benefits of registration were highlighted including adequate notification to inform allocation of resources and mortality reduction interventions, the strengthening of TB

education for hospitalized clients during registration and increased identification of contacts for treatment/TPT. Sites doing well were encouraged to share good practices.

In addition, 2 affected facilities implemented at least one of the following: identifying focal people to ensure registration of TB clients while admitted, immediate registration regardless of future plans for care elsewhere, ensuring linkage and registration of referrals and/or ensuring registration of the critically ill by their referring facility. Results were obtained from admission registers and TB registers as part of routine data collection.

Results/Impact: There was a decline from 44 (10% of 2018/19 quarterly PEPFAR target) to 0 unregistered TB clients, showing that poor registration contributed to poor notification and that sufficient advocacy and mentorship can improve notification of hospitalized TB clients.

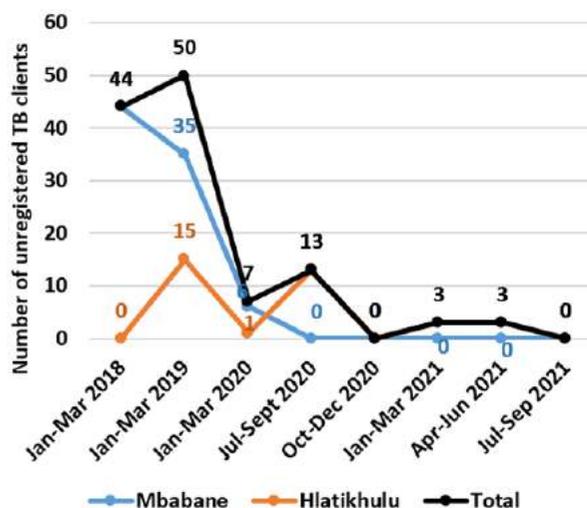


Figure. Trends of TB registration gaps for hospitalized clients in medical, paediatric, TB, COVID-19 and maternity wards of 2 hospitals.

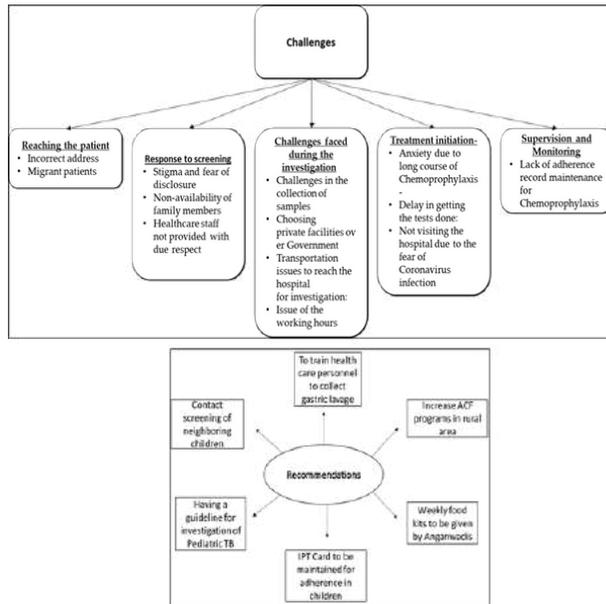
Conclusions: Routine registration of hospitalized TB clients should be a standard for all admitting facilities nationwide, to improve completeness of TB notification and related data used to guide TB/HIV service delivery. This could be enhanced by strengthening electronic triangulation of departmental and vital registration data.

EP-26-857 TB Contact screening and preventive therapy initiation in India: what do healthcare staff have to deal with?

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Background and challenges to implementation: Addressing the challenges in pediatric TB contact screening and Tuberculosis Preventive Therapy (TPT) initiation is one of the essential components of the TB elimination strategy in India. It is important to understand the challenges faced by the health workers on the field to improvise service delivery. We conducted a qualitative study during 2021-22 in the two districts (Population 9.67 million) of Karnataka, South India to explore the challenges and the possible solutions.

Intervention or response: In-depth interviews of key-informants were conducted by a trained researcher to explore the challenges and possible solutions. Thematic analysis was performed after analyzing the transcripts by generating themes and codes. The interviews were conducted till the saturation point was attained.



Results/Impact: A total of 64 interviews were conducted amongst different cadres of health staff, including NTEP health staff, Physicians, and General health staff. The key challenges identified were:

1. Stigma towards TB disease.
2. Migrant population.
3. Difficulty in sample collection.
4. Anxiety among parents due to the long duration of the prophylactic treatment.

5. Poorly documented adherence to TPT.
6. Inadequate transportation from rural areas.
7. The ongoing COVID-19 pandemic.

The solutions varied across the cadres; however, collectively it meant uplifting the awareness among the community and strengthening supervision and monitoring.

Conclusions: The challenges faced by health staff in the field are very pragmatic and have many social dimensions attached to them. The plausible solution is to educate the community, and parents and provide emphasis on the placement of IPT cards for the children for effective supervision and monitoring.

EP-26-858 Improved TB case detection rate during COVID-19: experience from National Tuberculosis Reference Laboratory (NTRL), Bangladesh

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Background: The number of presumptive TB patients referred for TB tests was low during the COVID-19 pandemic due to low patient visits at the health facilities and specimen referrals. National Tuberculosis Program (NTP) and partners oriented clinicians and health care staff on TB and COVID-19 bi-directional screening at the National Tuberculosis Reference Laboratory (NTRL), Dhaka based on symptoms. GeneXpert test was performed for TB and COVID-19 based on the symptoms. This bi-directional screening resulted in better screening and TB case detection rates in 2020 and 2021. This study compares the percentage of TB case detection pre and during the COVID-19 pandemic.

Design/Methods: We collected and analyzed GeneXpert test data from the laboratory registers at the NTRL from 2019 to 2021 to assess the impact of bidirectional screening on TB case detection during the pandemic.

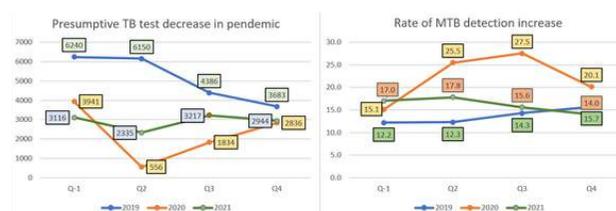


Figure.

Results: A total of 20,459 presumptive TB patients were tested by GeneXpert in 2019 compared to 20,779 in the following two years (9,167 tests in 2020 and 11,612 tests in 2021, during the COVID-19 pandemic).

Although the number of tests during the pandemic decreased, case detection increased from 13.3% in 2019 to 19.7% in 2020 and 16.0% in 2021.

Conclusions: Case detection rates for bacteriologically confirmed cases improved during the peak of COVID-19 despite a significant decrease in the number of GeneXpert tests performed. This could be due to selective referral. Further studies are required to ascertain the implementation modality of screening on improved TB case detection.

EP-26-859 Early implementation experience on the use of CAD enabled Ultra-Portable X-ray machine for active tuberculosis case finding in Oyo State Nigeria: results and lesson learnt

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Background and challenges to implementation: Tuberculosis (TB) remains one of the leading causes of mortality worldwide. There is an urgent need to effectively deploy evidence-based, innovative, and highly effective screening strategies for TB to reach the ambitious target of diagnosing and treating 40 million people from 2018 to 2022.

Recently, WHO recommended the use of CAD as an alternative to human readers to interpret CXR for screening and triage of Pulmonary Tuberculosis (PTB). Institute of Human Virology Nigeria on the USAID funded TB LON 3 project took a giant step, of procuring Fujifilm's portable X-ray FDR Xair system that is equipped with a new image processing Artificial intelligent box that runs on aqXRCAD software, which, analyze X-ray images to detect abnormal findings within seconds

Intervention or response: The machine was deployed to the field in Oyo State, Nigeria on 16th January 2022 for ACF in rural communities, special population (Such as Correctional Centre and Miners community) and school outreaches in mostly hard to reach areas. Outreach locations were selected based on prediction from EPCON, which is another artificial intelligent (AI) for Identification of high TB burden communities and target populations coupled with TB epidemiological data in collaboration with Oyo State TB control program.

Results/Impact: With the aid of CAD enabled Portable Digital X-ray for TB screening, we observe a significant increase across the TB cascade between January to March 2022, we are able to screen 67,944(25%↑) clients, identified 6,524(30%↑) presumptive, Evaluated 6,524(33%↑), Diagnosed 468(10%↑) TB cases and Placed 442 on treatment. Compared with 54,458 screened, 5023 presumptive, 4904 Evaluated, 424 diagnosed and 357 placed on treatment between October to December 2021.

Conclusions: The impact of CAD enable Portable Digital X-ray across all aspect of TB cascade is outstanding hence, there is an urgent need to scale up this intervention as soon as possible.

EP-27 How tailored care can make a difference.

EP-27-860 Person centred care for MDR-TB patients with alcohol use disorder

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Background: The risk of tuberculosis (TB) is higher among people with complex health and social issues, including alcohol use disorders (AUD). In 2016, a multidisciplinary, person-centred, psychosocial support programme for people with MDR/RR-TB and harmful use of alcohol was initiated in Belarus. We describe the programme evaluation which includes adherence, outcomes, patient and provider experiences.

Design/Methods: Mixed methods

1: In-depth individual interviews and focus group discussions with 12 and 20, purposively selected, patients and health-care workers (HCW). Results analysed thematically.

2: Cohort study of patients starting treatment between January 2019 and November 2021. Cohort closed for analysis February 2022. Counts, proportions, median adherence and interquartile ranges are described.

Results: The 89 people in the programme experience complex health and socioeconomic issues, such as past incarceration (n=58, 65.2%), unemployment (n=55, 61.9%), AUD (n=74, 83.1%), hepatitis C (n=32, 36%) dependence on other substances including cathinones and opioids (n=11, 12%) and personality disorders (n=3, 3.4%). Median overall adherence was high at 95.4% (IQR: 90.4- 99.6) but retention-in-care was average at 74.5% (95% CI: 65-85.3%) at 12 months. Lower adherence and attrition from care was associated with hepatitis C, and other substance dependence. HCW and patients describe that the programme's success hinges on building trust with patients. This opened the possibility to provide holistic support and guidance for patients' illnesses, personal and interpersonal problems to a population that had often previously felt marginalised or treated as 'incomprehensible flesh'. Practitioners described how trust was harder to build in some patients, especially in those who used other substances.

Conclusions: This person-centred, psycho-social support and harm reduction intervention led to good adherence to MDR/RR-TB treatment in patients who have harmful use of alcohol, a group usually at risk of poor adherence. People with hepatitis C, and those who use other substances remained at risk of poor adherence.

EP-27-861 Implementation of patient support strategies for drug-resistant tuberculosis (DR-TB) patients in palliative care, MSF independent clinic, Mumbai, India

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Background and challenges to implementation: The World Health Organization (WHO) defines palliative care as the prevention and relief of physical, psychological, social and spiritual suffering of patients with life-threatening illnesses and psycho-social (PS) support to patients and their families. In India, less than one percent of population has access to pain relief and palliative care.

As part of the vision for 'zero suffering' outlined in the WHO End TB strategy, Médecins Sans Frontières (MSF) clinic, Mumbai has been providing palliative care to drug-resistant tuberculosis (DRTB) patients on salvage regimen since 2019 with a team of doctors, nurses, psychologist, social workers and peer group.

Intervention or response: PS strategies in DRTB palliative care is an extensive activity with regular follow-up and counselling of the patients and care givers. Screening for depression symptoms is conducted with Patient Health Questionnaire-9 (PHQ9) at baseline then three monthly or as required.

Patients are referred for psychiatric consultation as per the need and followed up by counsellor's fortnightly. Monthly counselling sessions are designed on individual needs. Patient Support team along with doctors conducts sensitisation sessions of poor prognosis and failure disclosure is done with support of family.

Patients are encouraged to talk freely about their fears of death and their concerns are acknowledged. Specific relaxation techniques like breathing exercise and focusing on positive imagery are used to de-escalate their fears.

Patients are socially supported through need based direct benefit transfer and free oxygen concentrators. PS team also provides support to family members emotionally to prevent care-giver fatigue. At times of patient's unfortunate death, the team helps the family members to cope with the emotional crisis through counselling for grief.

Results/Impact: PS strategies face challenges in forming linkages for social support and hospice care due to lack of awareness and stigma among stakeholders.

Conclusions: Integration of patient support component in DRTB palliative care is essential.

EP-27-862 Orientation of clinicians at high-load health facilities improved TB case notification in Ethiopia

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Background and challenges to implementation: Although there has been a progressive decline in TB incidence from 192 per 100k in 2015 to 132 per 100k in 2021, the treatment coverage is stagnant at around 71% where a third of the people with TB are undetected. TB program-specific review in 2021 indicated that a considerable proportion of patients with TB are missed along the patient care pathway at health facilities.

Intervention or response: The USAID Eliminate TB Project started implementing a High-Load Health Facilities (HL HF) initiative at the project-supported HF during July-August 2021. A one-day orientation on active TB case finding modalities was conducted with clinicians from two hospitals to enable them to detect

missed TB cases. A comparison was made of TB cases before (July-December 2020) and one year after (July-December 2021) the approach was implemented. The number needed to screen (NNS) to get one TB case was computed.

Results/Impact: About 27,331 before and 40,028 patients after the training were visited in outpatient department (OPDs). The number of TB screened patients increased from 24,885 to 36,070, while the number of presumed TB cases increased from 105 to 503. The number of TB cases identified were 39 before and 136 after the approach was implemented. NNS for July-December 2020 was 638 while it was 265 for July-December 2021.

Service outlet	July-December 2020	July-December 2021	Comparison
# of HFs evaluated	2	2	
# of clients visited the HF	27,331	40,028	1.5X
# of clients screened	24,885	36,070	1.4X
# of presumptive TB identified	105	503	4.8X
# of presumptive TB tested	101	503	5.0X
# of TB cases identified	39	136	3.5X
NNS	638	265	

Comparison of OPD screening before and after intensified TB case finding at two HL HFs

Conclusions: After an intensive TB case search at HL HFs, there was five and four times increment in the number of presumptive TB cases and TB cases, respectively. NNS after intervention was lower by 2.5 as compared to the previous non-intervention period.

Hence, targeted orientation to clinicians on active TB case finding modalities can contribute to finding the potentially missed TB cases at health facilities and can further be enhanced using sensitive screening tools like chest x-ray.

EP-27-863 Provider attitudes towards ambulatory treatment and incentive payments: facilitating the transition towards patient-centered care in Kyrgyzstan

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Background: A national health facility survey using Quality of TB Services Assessment methodology was implemented from January to April 2021 in Kyrgyzstan.

An additional module was designed to explore provider attitudes in primary health care (PHC) and TB facilities towards fully ambulatory treatment.

Kyrgyzstan has been shifting from vertical hospital-based TB services towards a more patient-friendly ambulatory treatment model, but resistant attitudes towards this shift remain among providers. In 2017 an incentive payment system for successfully-treated TB cases was introduced to encourage PHC workers to provide ambulatory TB treatment.

Design/Methods: A total of 1,381 interviews were conducted in 258 facilities randomly selected using cluster sampling in all seven regions of Kyrgyzstan, including 350 interviews with providers assessing attitudes towards, concerns about, and experience with ambulatory treatment and receipt of incentive payments. Statistical analysis was conducted by facility type/level and location (region, rural/urban).

Results: Top concerns about ambulatory treatment included treatment adherence and drug resistance; TB providers were more concerned about PHC providers' competence (51%) than PHC providers (33%).

Overall, PHC workers held more positive attitudes towards ambulatory treatment than TB facility providers. The majority of PHC providers (80%) had experience starting patients on ambulatory treatment, and these providers had more positive attitudes and a higher level of confidence regarding ambulatory treatment (87%) compared to those without experience (55%).

One third of PHC providers received an incentive payment (34%) and these providers had the most positive attitudes overall.

Conclusions: These results suggest a positive influence of both incentive payments and direct experience with ambulatory treatment on providers' attitudes towards ambulatory care. Results suggest that providing incentive payments to PHC workers can encourage increased provision of ambulatory treatment. In addition, changing TB facility providers' attitudes towards ambulatory treatment is key to enabling the transition towards more outpatient care.

EP-27-864 Empowering TB patients with Information using TB Aarogya Sathi - a mobile application in the fight against TB in India!

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Background and challenges to implementation: Government of India is committed to providing patient-centered services and care with a keen focus on community engagement in the effort towards ending TB. As a step in this direction, TB Aarogya Sathi - an android mobile application to empower citizens, including patients under National TB Elimination Programme (NTEP) has been developed to serve as a direct interface with TB health-care services.

Intervention or response: The application has been launched pan-India on the occasion of World TB Day 2021. This android application provides information to general citizens and patients on basics of TB, nearest diagnostic and treatment facilities, screening tool to assess risk of TB, BMI Calculator and Nutritional Advice for nutritional support and counseling.

For those patients registered under NTEP, it serves as a portal to access digital health records on TB, including TB testing and treatment details, adherence details, details of benefit amount due/paid under various incentive schemes and access to health care provider and request for a teleconsultation or any information.

Results/Impact: Till April 2022, 0.16 million users have installed the application with ~500 daily active users spending close to 3 minutes each, majority of them having accessed sections on information on TB including symptoms and nearest health facility, BMI assessment and nutritional advice.

Among the users installing the application, ~65000 TB patients have accessed information on TB services under NTEP, majority from the public sector and majority accessing the amount paid under different incentive schemes and their treatment details.

Conclusions: In order to increase utility and hence adoption of the application, plans are underway for tracking treatment journeys, collecting qualitative feedback, teleconsultation and customized reminders.

EP-27-865 From a TB patient to a 'TB warrior'; a case study from Kampala, Uganda

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Background and challenges to implementation: About 30% of the estimated incident TB patients in Uganda are missed due to inadequate resources and structures to conduct active TB case finding initiatives in the community. Moreover, according to the 2016 national TB prevalence survey, about 39% of people with TB symptoms did not seek TB diagnostic and treatment services. TB patients and survivors can be resourceful but are seldom engaged in active TB case finding and treatment support.

We describe a casestudy of a TB patient who was transformed into a 'TB warrior' following his experience on the person-centered care and treatment programme.

Intervention or response: The USAID Defeat TB project provided technical assistance for active TB case finding in the urban districts of Kampala, Wakiso and Mukono in Uganda. Through a client-led contact tracing initiative, a 38-year-old male was diagnosed with TB alongside 3 other peers. The project facilitated a lay worker (community linkage facilitator) to support treatment adherence and education of the patients on TB symptoms, diagnostic and prevention processes.

Results/Impact: The 38-year-old male patient completed his treatment course and voluntarily started screening his community members for TB, physically referring persons with TB related symptoms to a nearby health facility for further evaluation and diagnosis. During one quarter, he referred 14 presumptive TB patients out of whom, 6 were diagnosed with bacteriologically confirmed TB and initiated on TB treatment.

Conclusions: Person-centered TB care programmes can empower and motivate beneficiaries to contribute towards ending TB through community education, screening, referral/linkage to diagnosis and treatment. We recommend replication of the model in Uganda and similar high burden settings.

EP-27-866 Gender disparities in drug-resistant TB (DRTB) treatment outcomes in KwaZulu-Natal, South Africa

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Background: Treatment Outcomes of Tuberculosis (TB) patients may be influenced by gender norms, affecting uptake of TB screening and treatment services. The purpose of this study was to investigate the influence of gender norms on barriers and enablers for achieving

successful treatment outcomes, among patients with Drug-Resistant TB (DR-TB), and the impact these have at different stages of care.

Design/Methods: A study utilising qualitative data from in-depth interviews (IDIs) with health care workers (N=4) and sex-stratified focus group discussions (FGDs) with current and previous DRTB patients (N=10) was analysed using thematic analysis to identify key themes impacting engagement with treatment outcomes.

	Common to both	Men only	Women only	Impact on care
Pre-treatment Barriers	Minimal DRTB knowledge	Traditional health-care seeking		Results in delays in seeking and beginning clinical care.
Pre-treatment Enablers			Positive health-seeking attitudes	Enhances chances for early treatment initiation
Intensive phase barriers	Limited HCW-derived education and support Pill burden and side effects Stigma and Discrimination	Substance abuse Treatment side effect: Impotence	Treatment side effects: Altered physical appearances	Reduced adherence and minimised social support at the start of treatment. Other participants reported developing symptoms of depression and anxiety as a negative outcome to beginning treatment.
Intensive phase enablers	Positive social capital with other patients			Social learning about DRTB among same-sex patients; disease and treatment education enhance early adherent behaviour.
Continuation phase barriers	Socioeconomic determinants (food insecurity & loss of income)			Low socioeconomic status presents and/or exacerbates challenges that make treatment continuation a challenge.
Continuation phase enablers	Family support	Peer derived psychosocial support during treatment Intimate partner support	Family responsibilities as a motivation to complete treatment Religion as a coping mechanism	Enhanced social support encourages positive mental well-being as well as consistent treatment compliance during treatment.

Table 1: Gender-specific barriers and enablers

*Pre-treatment: Health-seeking until diagnosis

*Intensive phase: From diagnosis till completion of the first 4 months of treatment

*Continuation phase: Month 5 until completion of treatment

Results: We identified six themes describing the barriers and enablers mediating treatment success for men and women at different treatment stages. The first theme, ‘pre-treatment barriers’, included limited DRTB knowledge among patients of both sexes and late diagnosis in male patients due to a preference for traditional models of care.

In contrast, the ‘pre-treatment enablers’ theme included positive health-seeking attitudes of women as key facilitators for favourable treatment outcomes. A third theme, intensive treatment phase barriers, included the following subthemes: stigma and discrimination, adverse treatment effects and pill burden; male-specific subthemes pertaining to substance use and treatment-induced impotence were also identified. The fourth theme, ‘intensive phase enablers’ focused on social capital as a facilitator of favourable outcomes for both

sexes. The final two themes related to ‘Continuation phase barriers’(influence of socioeconomic factors on unfavourable outcomes) and “Continuation phase enablers,” (social support from family members, partners, and peers, and religious institutions) which mediated treatment success.

Conclusions: Gender influences the treatment of DRTB patients at different stages of TB treatment. Gender-specific interventions that respond to the stage of TB treatment are imperative to designing more responsive DRTB treatment support interventions.

EP-27-867 The effect of medication event reminder monitoring upon adherence of patients taking treatment for tuberculosis in Vietnam

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Background: Tuberculosis (TB) control remains a serious public health problem, compounded by poor treatment adherence which increases the likelihood of onward transmission. Digital adherence technologies such as medication event reminder monitors (MERMs) have potential for improving treatment adherence, however evidence remains limited. We evaluated the effectiveness of MERMs upon treatment adherence in a high-burden TB setting.

Design/Methods: We conducted an open-label parallel group randomized controlled trial among newly-diagnosed patients with microbiologically-confirmed pulmonary TB, aged ≥15 years old, and had ≥4 months of oral treatment remaining at enrolment. Participants were individually randomized (1:1) to an intervention or control group. All participants were provided with a MERM device to store their medications until the end of their treatment. However, the MERM devices of the intervention participants provided daily medication intake reminders. Primary outcome was poor adherence, defined as the proportion of patient-months in which at least 6/30 doses were missed. Secondary outcomes included: 1) the proportion of patient-months in which at least 14/30 doses were missed, and (2) the proportion of doses missed over the remaining treatment period post-enrolment.

Results: Between October 2017 to March 2020, 2,142 patients were screened of whom 799 (37.3%) met the inclusion criteria and 250 participants were enrolled; 124 randomized to the intervention group and 126 to the

control group. The mean ratio (MR) for poor adherence between the intervention and control groups was 0.72, (95% confidence interval [CI] 0.55-0.86). The intervention was also associated with a reduction in the proportion of patients missing at least 14/30 doses (MR 0.61, 95% CI: 0.54-0.68) and the percentage of total doses missed (MR 0.75, 95% CI: 0.68-0.80).

Endpoint (Study group)	Number of patients	Geometric mean (95% CI)	Mean Ratio (95% CI)
Proportion of patient months with at least 6/30 doses missed[†]			
Control	126	35.8% (29.8-41.2%)	1
Intervention	124	25.8% (19.2-31.8%)	0.72 (0.67-0.77)
Proportion of patient months with at least 14/30 doses missed			
Control	126	20.2% (15.1-25.0%)	1
Intervention	124	12.4% (7.6-17.0%)	0.61 (0.54-0.68)
Proportion of total doses missed			
Control	126	21.2% (18.3-23.9%)	1
Intervention	124	15.8% (12.9-18.7%)	0.75 (0.68-0.80)

Table

[†]Primary endpoint. 95% CI = 95% confidence interval.

Conclusions: This study demonstrates the effectiveness of MERMs in improving TB treatment adherence in a high-burden, resource-limited environment.

EP-27-868 Intermediate results of implementation of video supported treatment in the USAID activity sites in Uzbekistan

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Background and challenges to implementation: Until recently, people with tuberculosis (TB) (PWTB) in Uzbekistan could only receive directly observed treatment (DOT) at a clinic, observed by a health care worker. This can often be time-consuming for PWTB, and transportation can be costly.

Intervention or response: In 2021, the USAID Eliminating TB in Central Asia (Activity) supported Uzbekistan's National TB Program (NTP) in introducing video supported treatment (VST). The country is using an asynchronous VST model, whereby PWTB use a smartphone and Telegram freeware to record and send videos of themselves taking their prescribed TB medication. Videos are then reviewed by a nurse and the results entered into the standard DOT forms. Activity has provided phones for PWTB who did not have them (39%) and tablets for nurses and covered mobile data costs. Activity also provided VST training.

Results/Impact: From May 1, 2021- April 1, 2022, 136 PWTB started VST, including 50.7% females; 62.5% living in urban settings; and 74% drug sensitive (DS) TB. Participants with DS-TB on average began VST 12.1 weeks into their treatment and those with drug resistant (DR) TB started VST 30 weeks into their treatment. As of April 1, 61 PWTB are receiving VST and 61 are no longer on treatment (including 59 with successful treatment outcome (97%); 1 who died; and 1 lost to follow-up).

The average duration of VST was 16 weeks for DS-TB and 22 weeks for DR-TB. Dropout rate was high, with fourteen PWTB (18.7%) left the VST cohort for the following reasons: difficulty using a smartphone or software (8 PWTB); fear of information leaks (3); continued treatment in a psychiatric hospital (1); moved to a place where VST is not available (1); use of equipment for other purposes (1).

Conclusions: VST pilot demonstrated high efficacy of VST (97%) with successful outcomes and identified barriers to be addressed in further implementation.

EP-27-869 People-centered care during the war in Ukraine: how TB patients' needs have changed

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Background and challenges to implementation: In 2022 Alliance provides medical and psycho-social support (MPSS) to 3,285 TB/DR-TB patients in eight regions of Ukraine. Since hostilities started we continue to provide MPSS adapting to new conditions.

Intervention or response: Project management system was not ready to the challengers caused by war. In first days 134 patients and 29 NGOs staff from Kyiv, Donetsk, Mykolaiv regions left their homes and became IDPs, now patients' and staff's needs are similar. TB patients' needs and the way of services provision depend on safety level in region. In regions with active hostilities (Donetsk, Kyiv-region, Mykolaiv) services' provision either put on hold or provided in minimum level: food parcels, water, PPE. In temporary occupied regions (Kherson) services are provided, but they experience lack of food, water and transport limitations. NGOs in relatively safe regions experience overload due to big number of IDPs.

Patients needs have changed dramatically - they mostly require:

- evacuation from the dangerous regions
- temporary housing,
- employment,
- hot food,
- hygienic kits,
- clothes and bed linen

The greatest challenge is to pick up all patients and enroll them in treatment and MPSS in regions where they arrive. Tight communication was established between NGOs and TB clinics in “dangerous” regions and in “safe” regions and with Public Health Center.

Results/Impact: As of beginning of May, there is no connection with 61 patients in Kyiv-region and with 222 patients in Mariupol. There is strong evidence about one patient killed in Bucha. Unprecedented efforts are being made to trace patients with whom contact has been lost. Needs of all patients are being revised to keep them on treatment.

Conclusions: Hostilities have become a great challenge to all: patients, NGOs staff and Alliance’ management. Situation in the regions changes very quickly that requires quick response system and services’ management flexibility to be in place.

EP-27-870 TB treatment adherence amongst drug-susceptible TB persons using medication monitor and differentiated care approach versus standard of care in South Africa

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Background: Digital adherence technologies like the evriMED device (monitor) have the potential to support persons taking TB treatment. We compare adherence to TB medication amongst persons with drug-susceptible TB (DS-TB) supported by medication monitor and differentiated care approach (intervention) versus standard care (SoC).

Design/Methods: We conducted a cluster-randomised trial in 18 primary health clinics in South Africa. Persons (aged ≥ 2 years) with DS-TB were enrolled. All participants were provided with monitors: intervention arm participants had visual/audio reminders for medication intake; SoC arm monitors had no reminders.

In the intervention arm weekly adherence reports were generated and participants received intensified support (text, phone call, home visit, motivational counselling) depending on number of missed doses. Percentage adherence was calculated as days monitor was opened (proxy for daily-dose taken)/total expected treatment

days; zero adherence imputed from lost to follow-up date to 168 days. The primary outcome was poor adherence ($<80\%$ versus $\geq 80\%$) and secondary outcome was overall adherence. Analysis took into account clustered design.

Results: We enrolled 2727 participants and report on 2584 participants: 983 (38%) were female, the median age was 36 years and 1353 (52%) were HIV positive. There were imbalances by arm for HIV/ART status, bacteriologically confirmed TB, and ethnic group. The primary outcome ($<80\%$ adherence) was lower in the intervention versus SoC arm (adjusted risk ratio 0.40 (0.30-0.54) and percentage adherence was higher in the intervention versus SoC arm (adjusted risk difference 17.2% (13.7%-20.38%).

Primary outcome (binary)	SoC (n=1278)	Intervention (n=1306)	Risk difference	P-value	Adjusted risk difference	P-value
% poor adherence	48.7%	18.8%	-30.0% (-36.9% to -23.0%)	<0.0001	-26.7 (-33.5% to -20.0%)	<0.0001
Primary outcome (binary)			Risk ratio	P-value	Adjusted Risk ratio*	P-value
% poor adherence	48.7%	18.8%	0.37 (0.28 to 0.49)	<0.0001	0.40 (0.30 to 0.54)	<0.0001
Secondary outcome (% adherence)			Mean difference		Adjusted Mean difference*	P-value
Arithmetic mean	69.7%	88.5%	18.8% (15.2% to 22.3%)	<0.0001	17.2% (13.7% to 20.8%)	<0.0001

* adjusted for sex, age group, bacteriologically-confirmed TB, HIV/ART status, ethnic group

Table 1. Summary of adherence outcomes. Over a period of 94 weeks, 1839 episodes amongst participants required a phone call and 1433 (78%) were successful.

Conclusions: Persons with DS-TB had improved treatment adherence in the intervention versus SoC arm. Whether this translates to better treatment outcomes/lower relapse is currently being assessed. Medication monitors with differentiated care approach could be used to support individuals with difficulties adhering to treatment.

EP-28 Key affected populations and person-centred care

EP-28-871 Increasing child TB patient-finding during the COVID-19 pandemic through a story-based social and behavior change campaign in Bataan, Philippines

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Background and challenges to implementation: The municipality of Dinalupihan in the province of Bataan has a population of 118,209, of whom, about 33,000 (31%) are children ages 0 to 14. From 2015 to 2019, the average annual number of child TB patients notified was 110, equivalent to 22% of all TB patients notified in the municipality. Interventions are needed to further improve child TB detection in the community, especially among the indigent populations, and increase the local community's awareness of the disease.

Intervention or response: The USAID's TB Platforms for Sustainable Detection, Care and Treatment Project, in collaboration with the Department of Interior and Local Government, the Department of Social Welfare and Development, and the local government unit of Dinalupihan, conducted the "*Tibay ng Dibdib*" ("Chest Resiliency"), a social and behavior change campaign for TB in children. The campaign promoted proactive care-seeking for childhood TB, by featuring the story of two young sisters who were diagnosed with DRTB and DSTB, and, through proactive health-seeking behaviors and early diagnosis and treatment, overcame the disease. The campaign was conducted in 49 daycare centers, followed by onsite TB screening and follow up testing.

Results/Impact: Through the initiative, 2,288 children were screened for TB. Forty-three (2%) were identified as presumptive and tested using GeneXpert. Among those tested, 27 (63%) were diagnosed with drug-susceptible TB and enrolled in treatment. Data analysis revealed that the activity led to a 37% increase in child TB detection in the municipality between 2020 and 2021.

Conclusions: The strategy served as an adaptive measure to facilitate and increase the detection and treatment of TB in children despite the limitations brought on by the COVID-19 pandemic. Multi-sectoral collaboration between the health and education sectors played a key role in addressing parent and caregiver hesitancy, bringing TB services closer to children during the pandemic.

EP-28-872 Context specific contact investigation approach: what community based organizations and healthcare workers bring to the fore in Kano state:

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Background and challenges to implementation: According to Global Tuberculosis report in 2020, Nigeria was one of the eight high burden countries with low treatment coverage for Tuberculosis. Contact investigation is the systematic evaluation for TB disease or TB infection in people who have close contact with TB patient. Such contacts have a high risk of concurrently having or subsequently developing TB disease and represent an accessible population from which new cases may be promptly diagnosed and treated, and to which TB preventive therapy may be targeted.

Intervention or response: A comparative study of the two implementation models for contact investigation in Kano state was conducted. Cascade data for contact investigation using healthcare worker model (HCW) and using community TB worker (CTW) model for first quarter 2022 was analysed using Microsoft windows excel 2020.

Results/Impact: A total of 549 bacteriologically confirmed index TB patients were traced to their houses (72% by HCWs and 28% by CTWs), 2,778 contacts were screened for TB, with 1,369 (49%) presumptive identified, 1,168 (85%) presumptive evaluated, 94 TB cases were diagnosed (CTW-35 and HCW 63) and all of them were placed on TB treatment. A total of 350 (37%-HCWs and 63%-CTW) contacts were started on TPT within the period under review.

Conclusions: The study shows that HCW model was a more efficient case finding strategy with a 2:1 presumptive to case ratio while the CTW model had more success enrolling contacts on TPT. We recommend further studies to ascertain reasons behind the low case yield from the CTW model and encourage the integration of both models (as mixed CI teams) for maximal case yield and TPT uptake.

EP-28-873 Enhanced TB case finding offset the anticipated reduction in TB case notification due to conflict in Ethiopia

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Background and challenges to implementation: The conflict in the northern part of Ethiopia had an overall impact on infrastructure including microscopes and GeneXpert machines used for TB diagnosis.

Intervention or response: The USAID Eliminate TB Project monitored the number of districts without a functional health information system. TB case notification during the peak quarter of the conflict (October-December 2021) was compared with the same quarter one year ago (October-December 2020).

Results/Impact: Prior to the conflict, about 8% of the districts (83/971) could not send TB case reports using the District Health Information System 2 (DHIS 2). After the conflict in October 2020, when the conflict expanded into Afar and Amhara (June 2021), the number of districts that could not report TB cases using DHIS 2 increased from 124 (13%) to 219 (23%) (68% in Afar and 31.3% in Amhara). A total of 31 GeneXpert and 793 AFB microscopes were either destroyed or looted.

From October to December 2021, 25,468 TB cases were notified, which was 5.8% less than the same quarter of the previous year (26,941), and 2.4% less than the immediate previous quarter of July-September 2021 (26,087). The conflict-affected regions faced a significant decline: 61% in Afar and 36% in Amhara.

However, there was an increment of TB case finding by 4% in Oromia, 36% in SNNP, and 13-19% in the city administrations of Addis Ababa, Dire Dawa, and Harari.

Conclusions: Districts without TB reports doubled while case notification reduced by only 6% during the peak conflict quarter. The higher anticipated effect of the conflict on national TB case notification was offset by the ongoing national enhanced missed TB case finding initiatives in the other conflict-free regions.

Designing and implementing context specific, shock-resilient TB case finding strategies is important to address needs of conflict-affected settings.

EP-28-874 A proudly South African youth experience: screening, finding the missing cases of TB in communities and linkage to care

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Background and challenges to implementation: There have been significant improvements in the care of children with drug-resistant tuberculosis (DR-TB) made in the last five years, and 2022/2023 stands to revolutionize treatment for this vulnerable population, with new guidelines from the World Health Organization in Quarter 3. The Health Ninja has identified the lack of community support as well as information available in communities, to help combat this deadly disease.

We aim to capitalize on these new recommendations, building on the robust and successful partnership between DOH and other NPOs.

Intervention or response: The Health Ninja, a truly South African Superhero concept, a superhero that is loved by children and adults. The Health Ninja concept aims to identify ambassadors in the community that “fight” for a healthier community, achieved through health education, advocacy and research. The Health Ninja aims to train unemployed youth to become leaders in healthcare and wellness in the community.

The cadre of trained youth, to be known as “Health Ninjas” are ambassadors in the community and use their training to create more “Health Ninjas”, fighting against communicable and non-communicable diseases. It is envisaged that the youth of today will become role-models for children and adults on how to become “active participants in healthcare rather than recipients of health”

Results/Impact:

- 2271 children participated in a health education day and learnt about communicable and non-communicable diseases.
- 100% received health educational packs.
- 5% children said yes to having possible TB symptoms and were contacted by the team and referred to the clinic for testing.
- 4% children were TB positive and started treatment.

School/ ECDs	Attended event n=2271	Screened n=1599	Said yes to symptoms n=79	Contacted to link to care/test n=79	Positive Started treatment n=3
Kilag Nibaka High School	421	0	0	0	0
Alphonsus Creche	12	11	1	1	1
Meehala Primary School	730	730	37	37	2
Green Light Pre-School	100	100	2	2	0
Shochere Creche	70	70	19	19	0
Egagetha Pre-Primary	120	120	5	5	0
Masibambane Creche	18	18	0	0	0
Ilombeni Creche	10	15	0	0	0
Thandabantu Day Care	30	20	0	0	0
Wubano Day Care and Disability Centre	21	21	0	0	0
Shiloh Creche	15	19	0	0	0
Senokulu Day Care Centre	84	58	0	0	0
Rhododendron Creche Unit B	86	55	2	2	1

Table 1. Number of children attended event, screened, possible TB symptoms, contacted to link to care and started treatment (October 2021-February 2022).

Conclusions: The Health Ninja Superhero is a concept to be adopted by all, to promote a healthier community for all and reduce stigma about communicable and non-communicable diseases. Child-friendly tools will be developed and distributed freely to find the missing cases and link them to care.

EP-28-875 Building capacity of healthcare workers to achieve excellence in TB care and services: experiences from India

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Background and challenges to implementation: REACH through the USAID supported LON-ALLIES project aims to create an enabling environment for TB elimination by enhancing the Quality of Care and Quality of services with the support of trained TB survivors working as TB Champions (TBC) and health care providers (HCP). HCP are the first point of contact for the community in need of any health issues.

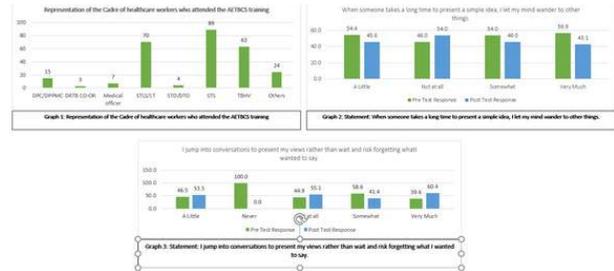
Training healthcare providers on Achieving Excellence in TB Care and Service (AETBCS) focuses on the skills to adopt people-centred services.

Intervention or response: This two-day training envisages HCP working in partnership with TBC and affected communities to address and find resolutions for quality of care and services in the TB programme, thus creating an enabling environment for people who access health facilities.

The training modules focus Listening, Respect, Ally, and Achieve. The objective is to set personal standards of ethical and professional excellence, Institute a rights-respectful and efficient work culture, educate and engage PWTB, their families, and communities and establish effective partnerships between self, facility and community.

Results/Impact: The project trained 275 HCP, including STS (32%), Lab technicians (25%), TB health visitors (23%), Medical officers (3%), District Programme Coordinators (5%) etc., who are the primary contacts of a TB affected person or their family. Among the participants, 33% were female HCP.

Providing some of the pre and post-test responses received through the Training across the 4 states- Chhattisgarh, Jharkhand, Odisha and Tamilnadu and the change in the health care worker's understanding and perception.



Conclusions: The project has witnessed positive responses after the training from the HCPs. To create an enabling environment and achieve the goals of NSP, equal participation of health care workers and communities is essential. The training aid in building compassion among the health care workers and focus on patient-centric care.

EP-28-876 The role of 99DOTS digital adherence technology to support tuberculosis treatment adherence among adolescents

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Background: Adolescents with tuberculosis (TB) have worse treatment adherence and outcomes compared to adults. Digital adherence technologies such as 99DOTS are increasingly being used as an alternative to directly observed therapy (DOT), but there are limited data on their use among adolescents. We evaluated the reach (*i.e.*, uptake) of 99DOTS and treatment outcomes (persistence through intensive phase and treatment completion) among adolescents treated for drug susceptible TB in Uganda.

Design/Methods: Adolescents (10-19 years) with drug-susceptible pulmonary TB were offered 99DOTS at 30 health facilities in Uganda from July 2020 to June 2021. We extracted demographic, clinical data, and treatment outcome from TB treatment registers. We determined the uptake (proportion enrolled on 99DOTS), and compared the proportions that persisted on treatment

through the intensive phase and completed treatment among adolescents enrolled on 99DOTS versus routine DOT. We used modified Poisson regression to adjust for differences between the two groups.

Results: Of the 441 adolescents initiated on TB treatment, 246 (56%) were female, median age;17 years (IQR 15-18), and 89 (20.1%) living with HIV. Overall, 309 (70%) adolescents were enrolled on 99DOTS. Adolescents who were older (15-19 years), had confirmed vs. clinically diagnosed TB, had a treatment supporter or were treated at lower-level health centers vs hospitals were more likely to enroll on 99DOTS.

In unadjusted analyses, treatment persistence through the intensive phase (92.2% vs. 67.4%, difference 25.3%, 95% CI 16.4%-33.5%, $p<0.001$) and completion (92% vs. 84%, difference 8%, 95% CI 0.1-16%, $p=0.02$) were higher among adolescents enrolled on 99DOTS. However, in adjusted analyses, enrollment on 99DOTS was not significantly associated with treatment persistence through the intensive phase PR 1.05, 95%CI 0.95-1.17, $p=0.33$) or completion (PR 1.65, 95% CI 0.5-5.5, $p=0.41$).

Outcome Variable	99DOTS n/N (%)	Routine DOT n/N (%)	Unadjusted PR (95% CI, p-value)	Adjusted PR (95% CI, p-value)
Reach/Uptake	309/441 (70%)	133/441 (30%)	-	-
Persistence on Treatment	285/309 (92.2%)	89/133 (66.9%)	1.06 (0.96-1.16, $P=0.19$)	1.05 (0.95-1.17, $P=0.33$)
Treatment completion	269/291 (92.4%)	80/95 (84.2%)	1.08 (0.96-1.2, $p=0.19$)	1.65 (0.5-5.5, $p=0.41$)

PR: Prevalence Ratio.

Adjusted for: Age category, disease classification, treatment supporter, level of care and HIV sero status.

Conclusions: 99DOTS had high uptake and is a viable alternative to DOT for many adolescents. Further studies are needed to optimize implementation particularly among younger adolescents.

EP-28-877 Feasibility and acceptability of smart pill box with differentiated response to support person-centred tuberculosis care: a multi-country study

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Background: Despite global recommendations to use digital adherence technologies (DATs), such as smart pillboxes to support tuberculosis (TB) treatment adherence, implementation continues to vary across countries and settings. We report on feasibility and acceptability of smart pillboxes with differentiated response to treatment adherence among adult participants in ongoing pragmatic cluster-randomized trials in the Adherence Support Coalition to End TB (ASCENT) project in Ethiopia, the Philippines, South Africa and Tanzania.

Design/Methods: Adult persons on drug-sensitive TB regimen for ≥ 2 months, using the smart pillbox and participating in the trial's sub-study were surveyed. The pillbox reminds persons to take treatment through audio-visual alerts; access to a mobile phone was not a requirement for the pillbox, though important for delivering aspects of differentiated care. Feasibility and acceptability were assessed through a questionnaire that evaluated participants' access to mobile phones and experience using the pillbox, based on level of agreement with 15 statements using a 5-point Likert scale (5 indicating strongly agree with statement), and described using summary statistics.

Results: Among 184 participants included (Tanzania, $n=62$; Ethiopia, $n=50$; South Africa, $n=43$; Philippines, $n=29$): percentage female was 43% and median age 40 years. Access to mobile phone ranged from 92% (Tanzania) to 96% (Ethiopia). Of participants who reported taking medication without using the box ($n=34$; 10% Tanzania, 19% South Africa, 22% Ethiopia, 31% Philippines), the most common reasons were not having the box with them (28% Philippines, 19% South Africa, 16% Ethiopia, 8% Tanzania), poor network (2% Ethiopia only) and charging problems (4% Philippines only). Participants found the intervention acceptable (Figure).

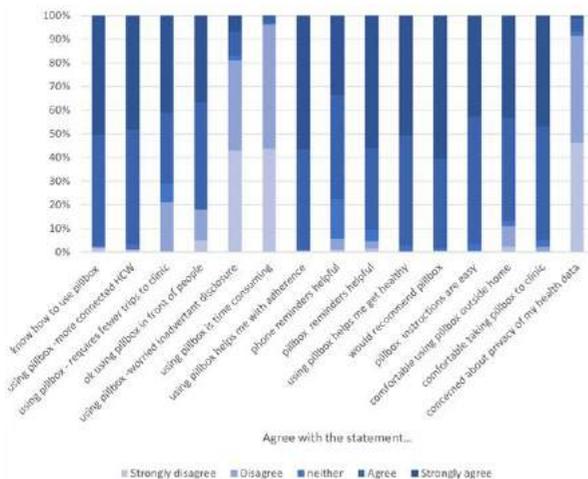


Figure. Acceptability of using the smart pillbox among ASCENT participants.

Conclusions: Smart pill boxes are acceptable, and good access to mobile phones highlights the feasibility of implementing differentiated response to treatment adherence of the intervention. Structural challenges such as power outages and network coverage should be addressed.

EP-28-878 Best practice and challenges in improving TB treatment enrollment and adherence support for private health facilities: an experience from Indonesia

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Background and challenges to implementation: Involvement of the private sector is one of the challenges for tuberculosis (TB) control in Indonesia. With 74% of patients preferring private health facilities either for initial diagnosis or treatment, efforts are needed to ensure private health facilities in Indonesia have sufficient programmatic supports.

Intervention or response: We developed a Microsoft Excel-based tool called TINJAU TB to monitor the treatment status of presumptive TB and TB patients in private health facilities. This was piloted in two subdistricts in North Jakarta: Cilincing and Tanjung Priok during March-September 2021. The tool is updated using data from National TB Information System (SITB) and reviewed during monthly TINJAU TB meetings with staff from District Health Office (DHOs) and Public Health Centers (Puskesmas).

Results/Impact: The data reviewed using the TINJAU TB tool during the pilot were from Q1 to Q3 2021. For analysis purposes, these data were compared with data from Q1 to Q3 2020. The results from this pilot are as follows:

1. Improved private health facilities compliance to timely record and notify TB cases through SITB,
2. Improved data quality including lab results which resulted in increased percentage of presumptive TB with available GeneXpert test results from 33% to 73%,
3. Decreased pre-treatment loss to follow up from 26% to 8%, and;
4. Identification of TB patients who missed scheduled appointment and improved coordination among stakeholders in following up these patients.

Conclusions: TINJAU TB helps building timely reporting habit of the private health facilities which improves data quality and allows facilities to identify patients who have not been enrolled on treatment and those who missed treatment appointments.

However, as this activity is conducted on a monthly basis, TINJAU TB needs to be complemented with a system that can identify patients who missed treatment appointment much earlier.

EP-28-879 Digging for case enrolment determinants for tuberculosis digital adherence technologies: a descriptive doer and non-doer analysis among healthcare workers in the Philippines

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Background: Digital adherence technologies, such as SMS-based medication sleeves (99DOTS) and smart pillboxes (EvriMed), help people with tuberculosis finish their treatment by allowing for digital pill-taking observation rather than paternalistic daily facility-based observation. Recently, DATs received more attention during the pandemic because they provided flexibility and access despite lockdown policies. The Philippines rolled out DATs in 32 intervention facilities as part of the ASCENT five-country pragmatic cluster-randomized trial; however, enrolment rates varied. To better understand this issue, we investigated the perspectives of healthcare workers who serve as DAT gatekeepers.

Design/Methods: Using a cross-sectional doer and non-doer descriptive survey, we interviewed 22 healthcare workers (26% female and 91% nurses) from facilities with the highest and lowest enrolled participants from the period June 2020 to April 2022.

Healthcare workers coming from the top five highest-ranking facilities, with a median enrolment of 310.5 participants, are known as “doers.” Healthcare workers classified as “non-doers” come from facilities with a median enrolment of 14.5 patients. Doers’ positive or “yes” responses were compared to those of non-doers.

Results: Descriptive analysis identified three questions with the most discrepancies between doers and non-doers. First, the greatest discrepancy was observed in the perceptions of adequate human resources to implement DATs, with doers (n=6) outpacing non-doers (n=1) by five responses (question v10 in Figure 1).

This was followed by the belief that “many TB patients are technophobes or technologically averse,” non-doers (n=8) edging doers (n=4) by four responses (question v14).

Finally, several non-doers (n=8) perceived that “many TB patients do not have access to a basic mobile phone” compared to doers (n=5) (question v13).

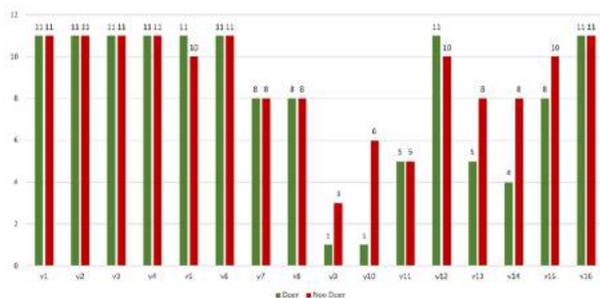


Figure 1. Comparison of survey responses from healthcare workers (n=22) in doer and „non-doer“ facilities.

Conclusions: Healthcare workers may have potentially differentiating determinants or perceptions that influence DAT enrolments. Understanding them may help in the implementation of a DAT program.

EP-29 TB prevention, diagnosis, treatment and costs

EP-29-880 Automation of data entry and processing in laboratories through barcoding and laboratory management information system (LMIS)

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Background and challenges to implementation: The COVID-19 pandemic exacerbated health system deficiencies in India. Government-identified gaps included limited testing capacity at facilities, diversion of human resources from other disease areas, and prolonged turn-around time (TAT) for test results (4–14 days), which created challenges for timely diagnosis of COVID-19 and other diseases, like tuberculosis (TB).

Intervention or response: PATH conducted laboratory assessments in Maharashtra and Punjab to understand the workflow in select collection centres and laboratories, which revealed inefficient sample tracking systems and data quality issues resulting from manual and multiple data entry points.

Accordingly, sample barcoding was implemented at the collection centres in two pilot districts. Cloud pathology (CP), a cloud-based Laboratory Information Management System integrated with the barcoding system, was introduced in laboratories.

The barcoded samples from collection centres were scanned at the laboratory. On CP, a line list was generated, which was used to batch samples for testing. CP allowed bulk uploading, allowing real-time results upload to the Indian Council of Medical Research website, and communication to patients.

Results/Impact: The parallel introduction of CP and barcoding created a single data entry point at collection centres, eliminating errors from multi-point manual data entry and sample rejection due to incomplete/illegible details. Barcoding reduced time taken to sort samples at the laboratory to 25% of baseline (3 hours/single batch).

By December 2021, over 1 million samples had been processed, and the results backlog reduced to zero. TAT for each 96-sample batch was shortened from 4 hours to 30 minutes, enhancing the testing capacity. Human resources required for data entry was downsized from 8 for 10,000 samples to 2 for all samples.

Conclusions: Introduction of barcoding and CP enhanced timely diagnosis through the optimization of human resources and programmatic tasks across the entire workflow at collection centers and laboratories. These innovations are platform solutions with applications beyond COVID-19, including for TB.

EP-29-881 Direct health care costs to achieve the targets for TB case detection and TB preventive treatment set by the 2018 UN High-Level Meeting on Tuberculosis

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Background and challenges to implementation: The 2018 UN High-Level Meeting on Tuberculosis (UNHLM) set targets for 2022 to advance towards the goals of WHO's End TB Strategy and proposed global investments of at least US\$ 13 billion/year for TB by 2022. Progress has been slow. Beginning 2022, an estimated 14 million TB patients still needed to be detected and treated, and 21 million household contacts given TB preventive treatment (TPT) globally. Ninety per cent of these individuals are in 33 high TB burden countries.

Intervention or response: We examined a scenario to achieve the UNHLM targets using WHO-recommended interventions for TB case detection and TPT. We used OneHealth-TIME Estimates model outputs combined with unit cost of interventions to derive total costs of health services. Above-facility costs and patient costs were excluded. Model inputs and parameters were obtained from published sources, the latest WHO guidance and data reported to WHO. Estimated costs are in US\$ 2022.

Results/Impact: Our model forecasts that >45 million people attending health facilities with symptoms (passive case finding) need to be evaluated for TB. An additional 23.1 million people with HIV, 19.4 million household contacts of TB patients and 303 million individuals belonging to high-risk groups require systematic screening for TB disease.

Estimated total costs amount to ~US\$ 6.6 billion, of which ~15% for passive case finding, ~10% to screen people with HIV, ~4% to screen household contacts, ~65% to screen other risk groups, and ~6% to provide TPT to household contacts.

Conclusions: Estimated direct health system costs for achieving UNHLM targets for TB case detection and TPT alone in 33 high TB burden countries exceeds the US\$ 5.3 billion available in 2022 for TB care in all 137 low- and middle-income countries reporting to WHO. Significant mobilization of additional domestic and international investments in TB healthcare services is needed in the short term.

EP-29-883 TB-affected households in Mali suffer unaffordable costs: results of first national TB patient cost survey, 2021

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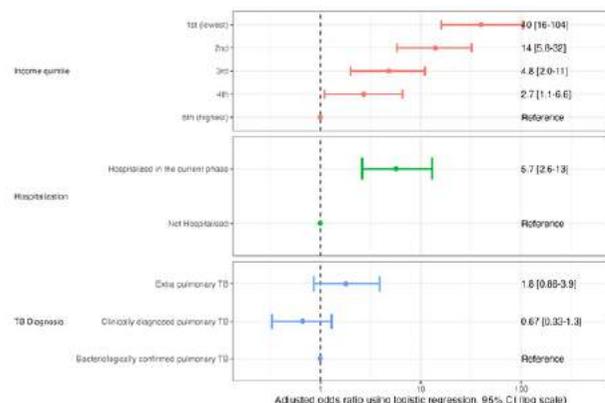
Background: Mali's TB strategy aims to reduce the morbidity and incidence of TB, as well as reduce the economic burden of TB on the population. While Mali has prioritized TB care and has committed to meet 39% of its TB budget through domestic funds, the country faced a significant funding gap of US\$ 0.7 million in 2021.

The first national TB patient cost survey aimed to estimate the costs faced by TB affected households while seeking care in health facilities within the NTP network, to assess the impact on the households, and examine associated risk factors in these households.

Design/Methods: A nationally representative, facility based cross-sectional survey was conducted with retrospective data collection, following WHO methods, reaching 453 persons with TB in 31 facilities including 1 TBMR.

Each respondent was interviewed on costs, time loss, coping measures, income and asset ownership. Total costs were calculated and presented as a percentage of annual household income.

Results: In 2021, 49.4% of TB affected households experienced costs above 20% of their annual household income. Mean costs amounted to US\$1039 (865-1213) and US\$2586 (1488-3683) per episode of first line and drug-resistant TB respectively.



The risk of incurring costs above the 20% threshold rose with hospitalization and among lower economic status households as shown in the adjacent figure. 60% of households caring for persons with TB resorted to coping strategies but only 8.6% reported receiving any social support.

Conclusions: TB-affected households are estimated to face costs averaging US\$ 1087 per episode of TB in Mali. Reducing costs faced may be achieved through adopting effective decentralisation policies, enhancing domestic financing, and implementing person centered care.

EP-29-884 Improving TB monitoring, evaluation, and surveillance with a virtual center of excellence model

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Background and challenges to implementation: The USAID-funded TB Data, Impact Assessment and Communications Hub (TB DIAH) project aims to ensure optimal demand for and analysis of TB data. One strategy to achieve this uses a center of excellence (COE) model.

The goal was to establish one virtual COE in three global regions to contribute to TB M&E research, dissemination, expertise, and teaching and serve as a model for best practices in TB M&E and surveillance to inform national TB policies, programs, and resource allocation. **Intervention or response:** TB DIAH developed standard qualitative and quantitative criteria to select the COE host countries. Using human-centered design, a COE website was created to establish and promote best practices with TB data collection, reporting, visualization, analysis, and use; engage national TB programs (NTPs) with necessary support, assistance, and resources; support trainings on TB M&E and surveillance; provide leadership, guiding the implementation of TB M&E and surveillance activities; and support capacity building and knowledge exchange.

Results/Impact: A pilot COE was established in Georgia for the EE region. The focus of the COE – and the two forthcoming COE virtual hubs – is two key pillars of success: standardization (promoting global best practices and standards in TB M&E) and leveraging assets (capitalizing on relationships, human capacity, and artifacts). The project is in the process of selecting the Africa and Asia COE countries. The Georgian COE has become a reliable platform for TB M&E resources and knowledge sharing in the EE region.

Conclusions: The virtual COE model has been an effective way to engage with NTPs and other key TB partners around the world to document successful practices in TB M&E, share experiences addressing identified areas for improvement, and access resources to inform TB programs and policies. The COE model has contributed to building regional TB M&E capacity through inter-country collaboration and a cross-fertilization of knowledge.

EP-29-885 Scaling up TB preventive therapy (TPT) for household contacts of all ages in Yogyakarta province, Indonesia

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Background and challenges to implementation: Post-pilot scale-up of tuberculosis (TB) program intervention is often challenging. In 2020, the National TB Program in Indonesia recommended TPT for household contacts of all ages but this is not yet widely implemented. We describe our experience scaling up TPT from a sub-district-level pilot project to district-wide implementation. **Intervention or response:** In 2020, we screened household contacts of bacteriologically TB cases registered at 3 health facilities and offered TPT to contacts with positive TST. In April 2021, we scaled up to cases registered at 39 health facilities in Yogyakarta Province. Eligible contacts were offered 3 months of isoniazid and rifampicin. In the pilot, we collaborated with district TB programmers, trained health facility TB teams, provide technical support to diagnose TB and LTBI, evaluate activities routinely, and enter data into the national TB information system (SITB). In scaling up, we used the results and lessons learnt from piloting to advocate government decision-makers, modify the model, and collaborate with the local community cadres.

Results/Impact: Thirty-nine health facility TB teams were trained, provided with drugs for TPT, and reported to SITB. As of December 2021, 1621 household contacts identified from 502 index cases have been screened. 654(44.4%) were eligible for TPT of 1471 evaluated eligibility, and 413(63.1%) were commenced on TPT. Of this, 365 (88.3%) contacts have completed TPT, 28(5.2%) were treatment incomplete, and 20(4.8%) have not been evaluated. TPT refusal because of feeling

healthy, refusal to participate in CXR screening, delay of TB diagnosis, and lack of human resources to monitor the treatment are the challenges to initiating and finishing the TPT on a large scale.

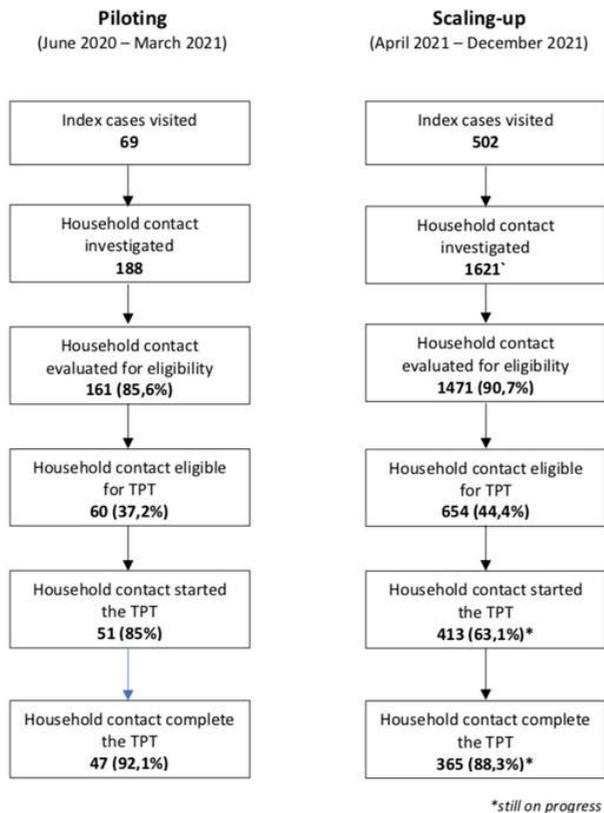


Figure. Cascade of TPT among household contact: comparing scaling-up to piloting.

Conclusions: Scale-up of TPT in household contacts of all ages resulted in good uptake and completion. Implementing TPT to all ages of household contacts requires investments, commitments, and collaboration from the governments and non-government partners.

EP-29-887 Incorporating sustainability in tuberculosis programming

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Background and challenges to implementation: Sustainability in tuberculosis (TB) program implementation needs to be incorporated from project inception. This ensures continuation of interventions beyond the lifespan of the project.

We outline the sustainability initiatives integrated into the United States Agency for International Development Infectious Disease Detection and Surveillance (IDDS) project in Zimbabwe.

Intervention or response: IDDS provides technical and financial support to the MoHCC to strengthen the TB diagnostic network. The project's interventions were designed to ensure sustainability in various ways. National strategic documents inform crafting of program interventions with input from other funding mechanisms to avoid duplication. Interventions build upon already existing health systems.

Experienced health care workers (HCWs) are capacitated to mentor other HCWs at provincial, district and facility levels. International consultants are engaged to collaborate with local consultants who continue providing technical support for sustained mentorship. Some activities are co-funded with local implementing partners. IDDS will procure electrical systems powered by renewable energy for use in TB laboratories.

Results/Impact: Working with other stakeholders in line with national strategies increases buy-in and reduces duplication of efforts. Collaboration with ministry structures improves existing systems and builds capacity at different levels. Skills gained are used to support other programs within the public health system. Capacitated local consultants can transfer skills to other consultants and local systems. The use of renewable resources reduces costs and promotes use of environmentally friendly resources. Extended mentorship promotes buy-in and strengthens adoption of recommendations and culture change towards quality-based service delivery.

Conclusions: Strengthening sustainability in TB programs should begin with engagement of national entities from the development of funding proposals. It requires sustainable concepts to be built into operational plans through program implementation.

Interventions that support national strategic plans and build on existing health systems have better chances of being sustainable in the long run.

EP-29-888 Effectiveness of IVRS as a health training delivery platform - a report from South India

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Background: Through a TB REACH Wave 7 grant supported project, we delivered a basic-health skilling over an IVRS (Interactive Voice Response System) based platform. The trainees could access dramatized content on different topics and listen to experts. Around 700 Community Health Mentors(CHMs) received training on TB, common illnesses including COVID and other aspects such as domestic violence and financial literacy. **Design/Methods:** The assessment of the intervention was done through a mixed-methods study by an independent agency. The quantitative assessment was done by trained interviewers and data collection was done on epicollect. FGDs were held for the qualitative assessment of acceptability and impact of the IVR-based training. Frequencies and percentages were calculated on excel. Qualitative data was transcribed, coded and thematic analysis was done.

Results: 80% CHMs expressed that the IVRS system was easy to navigate and use. 78% mentioned they were able to apply their learnings from IVRS for the betterment of their families and they were able to provide basic counselling for the illnesses to relatives or community members. 93% CHMs mentioned that they linked people in their community to health facilities. 78% of CHMs expressed that their ability to get involved in financial decision-making in the family had improved. One of the CHMs stated that "Earlier I used to say yes to everything that my family suggested. After listening to the audio modules, this has changed. These days, I think through pending decisions, I explain the pros and cons and we decide together".

Conclusions: IVRS is an effective interactive tool to deliver comprehensive health-related information to rural areas where the scope of implementing internet-based remote training solutions is limited. Provision of dramatized content on common health conditions could empower trainees to bring about lifestyle changes in families and also aid them to provide basic health counselling and make prompt referrals where required.

EP-29-889 Cost and time efficient approach for baseline TB awareness assessment in Indian youth. A digital targeted methodology

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Background and challenges to implementation: General awareness around TB in India is believed to be poor. Creating a targeted awareness campaign, requires identifying gaps in awareness to bring about a differential focus of efforts. As against an offline survey that is cumbersome & time consuming, an online survey is time efficient, scalable and can elicit targeted responses.

A baseline assessment of awareness around TB, its symptoms, diagnosis, and treatment would help to gauge the shift in awareness levels post campaign intervention period.

Intervention or response: A survey was conducted through digital mode using the DV360 platform amongst youth (18-34 years) across 8 Indian cities over 10 days. Using this platform's audience (primarily public job seekers, avid news readers, social media enthusiasts), high intent cohorts were targeted with a questionnaire comprising of eight single/multiple choice questions; four of them to gauge youth's knowledge of tuberculosis, two on symptoms & diagnostics for the disease and the remaining two to gauge treatment related awareness. The sample size was determined to achieve 1% confidence interval of the results.

Results/Impact: Through the DV360 platform, 6.95 million targeted youth cohort were reached in 10 days. 4898 youths responded to all eight questions. Only 177 youths provided correct responses to all eight questions. Overall awareness around TB, its symptoms, diagnosis, and treatment, was found to be low. Audience segmentation was done across four demographic markers; age, gender, household income and cities to enable precise messaging.

Cost per response was \$2.47 (INR 185.34) and the survey was completed within 10 days.

Conclusions: Differential levels of awareness on TB symptoms, diagnosis, and treatment were measured which served as a tool to form a framework for our awareness program. Digital technology was leveraged to reach out to youth audience at ease in a cost & time efficient manner.

EP-30 Knowledge is power!

EP-30-890 Overcoming stigma as a barrier to TB contact investigation: utility of the KNCV-Nigeria spot-to tent model

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Background and challenges to implementation: Stigma is a known barrier to uptake of Tuberculosis (TB) services and cuts across all steps in the TB patient pathway including contact investigation (CI). With the advent of COVID-19, its symptom similarity with TB introduced another dimension to existing TB stigma making it even more difficult to conduct household visits for CI. To overcome this compounded barrier, the USAID funded TB LON 1 and 2 project implemented by KNCV Nigeria introduced a 'spot to tent approach' to household CI.

Intervention or response: Spot to tent involved a house-to-house TB case search within a mapped 2 km radius of index patient location. Prior advocacy visit to community leaders was done. Trained Contact investigators line listed all bacteriologically diagnosed index TB patients visited their homes and screened household contacts. They also conducted house-to-house case search within a 2 km radius of index patient location using WHO four symptom screening. Identified presumptive TB had diagnostic evaluation. Diagnosed TB patients were linked to treatment. Weekly CI reporting and monthly quality improvement meetings were done.

Results/Impact: Within 6 months of implementation, there was increasing Community awareness on TB and Community leaders were actively involved in TB control. Index patient coverage (number of eligible index TB patients whose households were visited and contacts investigated) increased from 45% to 96%. Average Contacts- Index patient ratio increased from 4 to 10.

Overall, the number of TB cases diagnosed from CI increased by 129% from 916 to 2101 TB cases. TB yield among household presumptive TB tested was 12% while the yield from house-to-house case within 2km radius of index patient (spot to tent) was 5%.

Conclusions: The spot to tent approach broke the stigma barrier and increased acceptability of CI intervention. Furthermore, the TB cases diagnosed was an absolute additionality as these patients would have remained undiagnosed if only household CI was conducted.

EP-30-891 Health seeking behaviour, knowledge, and stigma around TB: findings from a baseline study of a behaviour change intervention with specific vulnerable population groups in India

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Background: India's goal to 'End TB' by 2025 is hindered by various social-barriers viz. lack of knowledge, stigma, and poor health-seeking behaviour, especially among key vulnerable populations who are at higher risk of TB-infection.

To explore their specific vulnerabilities, USAID funded Breaking the Barriers project of KHPT, undertook a baseline study covering migrant, tribal, tea-garden, and mining/industrial populations in the states of Assam, Bihar, Telangana, and Karnataka.

Design/Methods: Cross-sectional polling-booth surveys (PBS) with 480 participants in each vulnerable group were interviewed in separate sessions with 8-10 male and female participants in each, and 32 Focus Group Discussions (FGDs) along with 195 In-depth interviews (IDIs) were conducted for persons with TB, family-members/caregivers, community members/structures from vulnerable groups, and with National TB Elimination Programme staff during June-November, 2021. Ethical approval was obtained from Sigma Research and Consulting, New Delhi, India.

Results: PBS results showed a lack of awareness about TB symptoms, treatment and adherence across all groups; comprehensive knowledge was highest among migrants (57%) and lowest among mining/industrial population (16%). Males in mining and tea-garden population, had higher knowledge than females.

While over 50% of participants, who themselves or a family member have had TB, experienced stigma from communities and health facilities. A significant proportion possessed discriminatory attitudes towards TB. FGDs/IDIs revealed that primary preference for treatment was private facilities among vulnerable groups (50% among tea-garden group), however, in tribal, preference was for public hospitals.

FGDS/IDIs further highlighted superstitious beliefs and inclination toward traditional healers delaying treatment-seeking. Discontinuation of treatment was prominently due to pill burden, adverse drug reactions, and initial signs of recovery.

Conclusions: Vulnerable groups have different levels of TB knowledge, 'experienced stigma', and preferred health-sector access. Therefore, it is imperative to have awareness programs based on socio-cultural context, customized communication materials, and behaviour change solutions to improve knowledge and dissipate stigma.

EP-30-892 Tuberculosis stigma assessment in Mongolia

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Background: We aimed to assess the extent and dimensions of stigma related to tuberculosis (TB) in Mongolia, to understand stigma as a barrier to accessing care, and to develop recommendations with an action plan to address it.

Design/Methods: Mixed-methods study using a validated stigma scale and interviews from four key populations: people with TB (PWTB); family members of PWTB; community; and health care workers (HCW). All 21 provinces and nine districts of the capital city were included as were specific vulnerable populations such as mental health patients, prisoners and homeless people. 54 community-based HCWs were trained using the STOP TB Partnership's "TB Stigma data collection tools". Law and policy assessment was also undertaken, with thematic analysis of qualitative transcripts (NVivo, 2020).

Results: Between 21 February and 2 April 2022, 748 participants were interviewed. The response rate was 80.4%. Perceived stigma towards PWTB by HCW or community was 68% and 50% respectively, while self-stigma was reported by 44% of PWTB and family secondary stigma by 48% of respondents. Majority of the respondents reported experiencing most TB stigma in

healthcare facilities, followed by from family members and community. Up to 27% of the respondents reported that stigma inhibited them from seeking care. Moreover, perceived stigma is common among TB HCWs with 62% reporting experiencing stigma by other health care workers. Observed TB stigma was also common among these groups.

Conclusions: TB-related stigma is highly prevalent in Mongolia, and is a significant barrier to accessing health care services. Incorporation of stigma reduction strategies in the national TB response is required.

EP-30-893 Developing and testing training tools to engage informal healthcare providers in TB prevention, care and support services. Experiences from project implemented in India

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Background: Training needs of informal providers are very peculiar compared to other health care providers. TB Alert India (TBAI) implemented a project in Telangana state in India to engage informal providers in TB care to reduce the delayed diagnosis. A mixed method study was taken up as part to identify the training needs of the informal care providers, basis the findings develop training tools, and test the effectiveness of these tools in improving the performance of the informal providers.

Design/Methods: The first qualitative phase comprised of in-depth interviews with a sample of 24 informal providers to identify the training needs and to develop the training tools.

The second phase was a quantitative study, in which the effectiveness of the training tool was assessed in terms of numbers of informal providers engaged, number of TB symptomatic identified, number of persons with TB detected following the roll out of the training tool period.

Results: Informal provider practice, TB Care, Services coordination, Feedback/views, and practice in times of COVID emerged as key themes of qualitative study. A pictorial training tool was developed based on the findings and rolled out.

There was some disturbance in the training plan due to covid 19 pandemic. The median number of informal providers engaged per month during the post training tool development phase (374) was higher than the pre-tool development phase (306). Around 14% more (1128 pre training tool development and 1289 post training tool development (median value)) TB symptomatic identified by informal providers engaged. The median number of TB patients diagnosed per month during the post training tool development phase (244) was higher than the pre-tool development phase (229).

Background and challenges to implementation: Informal providers are the first contact for any health care services in rural/semi urban/slum settings in India. Proper training on key TB information, immediate referral mechanisms, and within limited time frame are key requirement for better results. TB Alert India (TBAI) implemented a project in Telangana, India engaging informal providers in TB care to reduce the delayed diagnosis, early treatment initiation, and prevent treatment shopping. There is a need to develop training tools that can be used to improve engagement.

Intervention or response: A needs assessment study was taken up to understand the needs of the informal providers. A training tool was developed based on the findings of the qualitative enquiry. Using the tool informal providers were trained.

However, training plan was affected due to COVID pandemic. A comparison was made with respect to engagement and performance of informal providers pre- tool developed period and post- tool development.

Results/Impact: Informal provider practice, TB Care, Services coordination, Feedback/views, and practice in times of COVID emerged as key themes of qualitative study. A pictorial training tool was developed based on the findings and rolled out.

There was some disturbance in the training plan due to covid 19 pandemic . The median number of informal providers engaged per month during the post training tool development phase (374) was higher than the pre-tool development phase (306). Around 14% more (1128 pre training tool development and 1289 post training tool development (median value)) TB symptomatic identified by informal providers engaged. The median number of TB patients diagnosed per month during the post training tool development phase (244) was higher than the pre-tool development phase (229).

Conclusions: Message, contact, and time frame of training program are the key components for active engagement of informal providers. When these aspects are addressed response from informal providers will be encouraging.

EP-30-894 The role of competency based training for HCWS in improving TB case notification in Nigeria

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Background and challenges to implementation: Health interventions in TB program rely on knowledgeable front line health care workers to screen, identify and ensure adequate treatment for TB. Despite the impacts of COVID 19 pandemic and Government restrictions of movements and social distancing, employers and professional non-government organizations still need to improve relevant competencies and skills of her personnel.

This paper showcases how focused workplace capacity building programs through virtual mobile competency-based trainings have contributed to increased TB case notifications

Intervention or response: The KNCV TB Foundation Nigeria through USAID funded TB-LON 1 & 2 project in 2020 implemented use of interactive online capacity building modules for 599 TB screening officers at service delivery points of tertiary and secondary health facilities across 14 states of Nigeria.

Module content include text, audio and video-based training materials focusing on knowledge basic knowledge of TB; TB symptomatic screening, identification of presumptive TB; treatment of TB cases and documentation of relevant national recording and reporting tools. Participants were granted login access to pre-recorded lectures for specific hours in a week, followed by multiple answer questions to ascertain their level of understanding with e-Certificate of completion issued to participants who passed the modules.

Results/Impact: There was a tremendous increase every quarter in number of presumptive and TB patients detected as shown in figure below.

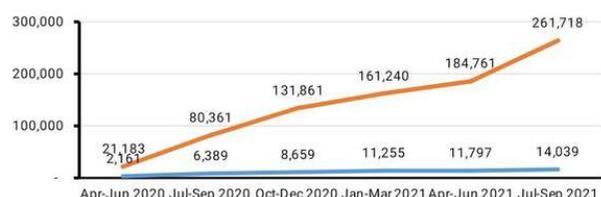


Figure. Trend of quarterly presumptive TB and TB patients detected across 14 states of TB LON 1 & 2 project.

Conclusions: A focus designed mobile virtual competency-based training module for front line health care workers contributed to improved TB service delivery competencies. Continuous capacity building and skills of program workforce can significantly increase TB program case notifications.

EP-30-895 TB Mukht Certificate (TB Treatment Completion Certificate), a powerful tool to address social and self-stigma

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Background and challenges to implementation: Tuberculosis (TB) is a major contributor to the global burden of disease. Despite various interventions aimed at reducing stigma and discrimination and improving treatment completion, still barriers and obstacles for the people adhering and completing the treatment. Substantial proportion of the persons with TB do not complete treatment due to stigma and discrimination, results different negative outcomes. Therefore, distribution of the TB Mukht Certificate helps reduce stigma and discrimination and complete treatment for TB.

Intervention or response: The intervention tried out is specifically for the urban vulnerable population with the USAID Supported Breaking the Barriers project of KHPT. Developed Care and Support Group platforms for supporting the treatment adherence. In collaboration with district NTEP team, list of patients going to complete the treatment is prepared. Persons with TB counselled and explained on TB Mukht Certificate. Organize a gathering at the DMC level and invite all listed completed TB treatment persons. Inform and highlight treatment completion milestone and appreciate for their achievement of completing journey of TB treatment, distributed the certificates.

Results/Impact: Over a period of 6 months, 415 TB Mukht certificates distributed to treatment completed persons. 84 used it for re-joining work, 13 re-joined colleges to continue studies, 15 re-joined families, 2 persons could use it for arranging their marriage, 59 are used for further health investigations, 35 members volunteered to support the TB infected community, 114 reported increased self-confidence and 93 reported resolved stigma issues faced in family and community.

Conclusions: The TB Mukht certificate acts as a dynamic tool to address stigma and discrimination faced by people with TB in health facilities, families, communities and the workplaces. This has increased confidence and self-esteem among people with TB, helping to fight self-perpetrated stigma not only among those who have completed TB treatment but among those receiving TB treatment too.

EP-30-896 Impact of community TB case finding through community sensitization, health education and community screening by patent medicine vendors (PMVs) in Kano State

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Background and challenges to implementation: Nigeria has a large and vibrant private health sector, the 30% total tuberculosis case contribution benchmark set in the countries in the 2020-2025 National strategic plan is still not met. Private Public Mix (PPM) interventions as implemented by KNCV TB LON Project in Kano state has 2 distinct arms, one targeting the client base of the (formal sector) private for profits (PFPs) and the other targeting the client base of the (informal sector) Proprietary Patent Medicine Vendors (PPMVs). As a strategy to boost case finding, PPMVs were supported to conduct outreaches within their immediate communities along with their routine patent medicine shop-based case finding activities.

Intervention or response: Select PMVs received training on infection prevention and control and also how to conduct outreaches. Markets, motor parks, Mosques, Churches and immediate vicinity of the community leader's house were targeted once a month for these outreaches. Advocacy to community gatekeepers prior to conduct of activity was mandatory. TB Beneficiaries are mostly used during TB screening to share their experiences and educate the attendees on the benefits of TB services. Cascade data from outreaches was segregated and compared with regular PPMV data over the period of 3 months.

Results/Impact: A total of 175,995 (PPM-95%, Outreach-5%) persons were screened for TB, across 20 communities within 11 LGAs. While 11,616 (PPM-73%, Outreach-27%) presumptive TB were identified, 11,610 (99%) were evaluated and 646 (PPM-63%, Outreach-37%) new confirmed TB cases were detected and placed on TB Treatment.

Conclusions: PPMV community outreaches is a useful strategy to find missing TB cases in the community. In this study, it accounted for over a third of cases from the PPM intervention and can be easily replicated in settings similar to that in Kano state.

EP-30-897 Empowering community health workers (CHWs) via health equity research training in tuberculosis prevention and control

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Background: Engaging community health workers (CHWs) via health equity research training contributes to strengthening their capacities to participate in the control of tuberculosis (TB) in their impacted communities.

We implemented an empowerment training program for CHWs within the framework of community-based participatory research (CBPR) in Perú.

Design/Methods: A case study on the implementation of health equity research training among CHWs in the district of Comas, a high burden area in Lima with a incidence rate of 103 cases per 100,000 inhabitants/year. We recruited and selected nine CHWs from a local TB survivor group in Comas.

Between January and July 2021, we completed a rigorous and culturally relevant training in research methods, research ethics, CBPR, social determinants of health (SDHs), and the photovoice technique.

We completed evaluations and offered refresher sessions when needed. A semi-structured interview was conducted to gather their experiences in the program.

Results: Nine CHWs participated in the empowerment training program. Overall, CHWs improved their level of knowledge about the basics of health equity research in TB (initial score 10 ± 3.84 vs final score 14 ± 2.95).

All CHWs mentioned that the program allowed them to enhance their leadership skills by improving their communication, responsibility, empathy, organizational and teamwork skills, and self-confidence.

CHWs concluded that the experience contributed to expanding and strengthening the role that their CBO has within the TB impacted community.

Conclusions: The culturally relevant training program for CHWs in health equity research contributed to their ability to serve as research facilitators.

Overall, the feedback received from the CHWs indicates that not only knowledge gain was achieved but also an overall sense of empowerment that would allow them

to become research facilitators not only in the proposed photovoice study, but in future health equity research engaging members of their impacted community.

EP-30-898 Tuberculosis knowledge among private providers not engaged with National Tuberculosis Program in urban Lagos, Nigeria

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Background and challenges to implementation: One strategy to achieve tuberculosis control is to engage private providers and equip them with needed skills and knowledge for TB management. Studies specifically evaluating tuberculosis knowledge of private doctors and nurses unengaged with the National TB Program are scarce in Nigeria. We aimed to determine private providers (PPs) knowledge regarding TB management and associated factors in Lagos, Nigeria.

Intervention or response: A descriptive cross-sectional study using self-administered questionnaire to assess different aspects of tuberculosis management among 152 PPs across 13 Local Government Areas (LGAs), Lagos, Nigeria. The survey contained 30 questions addressing different aspects of International Standards of TB Care (ISTC). Descriptive statistics to summarize the socio-demographic status and describe the knowledge (poor and good) of TB. Association between dependent variable (good knowledge) and independent variables (age, sex, qualifications, training, practice setting, and years of experience) was determined using bivariate and multivariate analyses.

Results/Impact: Majority were 20-34yr (36.8%), female (58.6%), have heard DOTS 116 (76.3%), not aware of DOTS facilities 93(61.2%), aware of NTBLCP 100 (65.8%), qualified nurse/midwives 92(60.5%), and never had TB specific training 106 (69.7%). Overall, median knowledge score was 12(52%, SD 3.8) achieved by 47% of the participants. Highest knowledge score was in TB/HIV (67%) and the lowest was in treatment standards (44%).

On multivariate analysis, being female (OR 0.3, CI: 0.1-0.6, $p < 0.0001$) and being a nurse private provider (OR 0.2, CI: 0.1-0.4, $p < 0.0001$) reduced odds of having good TB knowledge score while having previously managed >100 TB patients (OR 2.8, CI: 1.1-7.2, $p = 0.028$) increased odds of having good TB knowledge.

Conclusions: Knowledge gaps among unengaged PPs as identified in this study may result in substandard TB patient care. Specific deficiencies in understanding

standard TB regimen combination and Xpert MTB/RIF testing. The present study provides evidence for tailored mentorship and TB education among PPs using professional associations and training institutions platforms to disseminate TB updates.

EP-30-899 Building perspectives of field health practitioners and community leaders on core developmental concepts of vulnerability and gender to implement robust community engagement models for TB

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Background and challenges to implementation: India's National Strategic Plan (NSP) of National TB Elimination Program (NTEP) for 2020-25 emphasizes the need for the community's active participation in ending TB. But community-centricity in approaches for TB health service delivery have been shelved. Academicians, policy makers and civil society organizations agree that most aspects of TB programs are medicalized. The socio-economic determinants of TB and health need attention. For successful community engagement models to end TB, field health practitioners need deeper understanding of social systems and structures that make communities vulnerable to TB.

Intervention or response: We conducted perspective building exercises to help field health practitioners and community leaders strengthen their understanding of the complexities within individuals and socially vulnerable groups. In effect, enabling them to engage with and involve communities more effectively for TB.

We adopted a blended participatory learning approach over 4-5 days; using role playing, group activities, and demonstrations to encourage introspection and discussions within participants. Together with sessions on the basics of TB, these workshops covered concepts like deprivation, discrimination, vulnerability, gender, inequities, and disempowerment.

The participants included the field health practitioners and community leaders of USAID supported Breaking the Barriers project of KHPT, being implemented for TB amongst mining, migrants, industrial, tribal, and urban vulnerable communities across four Indian states: Assam, Bihar, Telangana and Karnataka.

Results/Impact: 180 workshops conducted with 6239 community leaders and 75 field health practitioners. Community leaders facilitated 1431890 screenings, of which 23878 referred, 20089 tested and 2291 diagnosed with TB. The project's contribution to total TU notification across all four states was 16%.

Conclusions: It is crucial for field health practitioners to gain deeper respect for local knowledge, views and practices, for developing shared goals of community responsiveness and ownership. This enables them to innovate solutions that respond to health crises keeping the community at the centre of the TB response.

**ABSTRACT PRESENTATIONS
FRIDAY
11 NOVEMBER 2021**

ORAL ABSTRACT SESSION (OA)

OA-26 Life after TB

OA26-386-11 Life events and tuberculosis

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Background: Stress is often assumed to predispose to tuberculosis disease. We aimed to assess the relationship between stressful life events and tuberculosis.

Design/Methods: A case-control study comparing life events recalled over the past 12 months recorded in the Holmes-Rahe stress inventory for participants aged ≥15 years in 16 Peruvian shantytown communities.

We surveyed the following groups: patients with tuberculosis at diagnosis (n=215); patients during tuberculosis treatment (n=141); household contacts living with patients with tuberculosis (n=294); people previously affected by tuberculosis (“post TB”, n=156); versus randomly selected community controls who had never been affected by tuberculosis (n=465).

Participants who were patients with successful treatment, household contacts, post TB or controls (n=1037) were followed up for median 8.6 years to assess whether life events recalled at the time of recruitment predicted subsequent incident tuberculosis disease. Regressions were adjusted for household clustering, and for analyses with repeated measures a multi-level model was used.

Results: The median life change unit (LCU) for controls was 220 (interquartile range=130-328) with 70% (325/465) reporting moderate-high stress (≥150 LCU). Compared to controls, patients at diagnosis, contacts and post TB participants had similar LCU (all p>0.05, see Figure).

However, patients interviewed during treatment reported 35 more LCU than controls, and more often reported moderate-high stress (81%, 114/141, odds ratio=1.8, 95% confidence interval=1.1-3.0, p=0.01). Compared to controls, patients interviewed during treatment had higher odds of divorce, redundancy, and changes in work (all p≤0.04). 62% (219/356) of recruited patients had confirmed successful treatment. In the participants who were followed up, 4.2% (44/1037) developed tuberculosis disease, which was not predicted by LCU at the time of the recruitment interview (p=0.8).

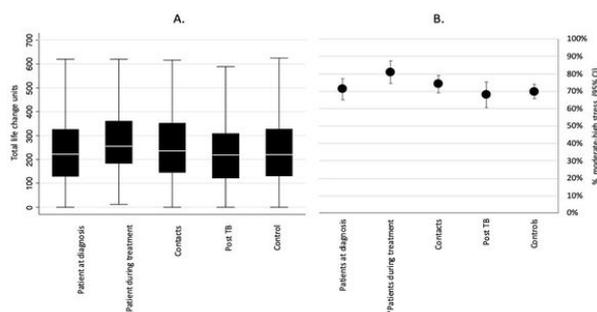


Figure. Bar graphs demonstrating the (A) box plots of the Rahe-Holmes score and (B) the proportion reporting moderate to high stress (defined as a Rahe-Holmes score of ≥150 life change units (LCU) and in: patients at diagnosis; patients during treatment; contacts; post TB and community controls. Note *=a statistically significant difference compare to controls (p<0.05).

Conclusions: Both retrospective and prospective analyses suggested that life event stress did not predispose individuals to TB disease. In contrast, tuberculosis treatment led to excess life events.

OA26-387-11 Economic burden of tuberculosis in India: during treatment and post treatment

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Background: Historically, economic research on tuberculosis have been mainly focused on costs of tuberculosis treatment and catastrophic health expenditure. Much less attention was paid on the economic burden of the disease in the post treatment period. We present the journey of the persons affected by tuberculosis in India since the onset of symptoms till one year post treatment.

Design/Methods: We interviewed a total of 705 persons with drug-susceptible tuberculosis from general population and from two high risk groups, urban slum dwellers and tea garden residents from two Indian states, at their

intensive and continuation phases of treatment and approximately one year post treatment using the adapted WHO tuberculosis patient cost survey instrument. Post treatment interviews covered identification of post treatment symptoms, cost of outpatient visits, hospitalization for post treatment sequelae, income and employment status, and other socioeconomic consequences. Tuberculosis treatment cost was the sum of direct and indirect cost. All costs were reported in 2020 US dollars (US\$).

Results: Before tuberculosis, 6%-10% study participants were unemployed, during intensive phase, unemployment rate ranged from 32%-64%, during continuation phase, 27%-47%, and in post treatment period, 21%-31%. Total cost of tuberculosis treatment ranged from US\$338 (standard deviation-SD 725) to US\$382 (SD 456).

Approximately 16%-18% patients visited health care facilities for post treatment sequelae and average outpatient visit cost ranged from US\$3 to US\$15. 29%-43% study participants reported having outstanding loan with average amount ranged from US\$103 to US\$261 during the post treatment period. 20%-28% participants borrowed during post treatment period and 7%-16% sold/mortgaged household items.

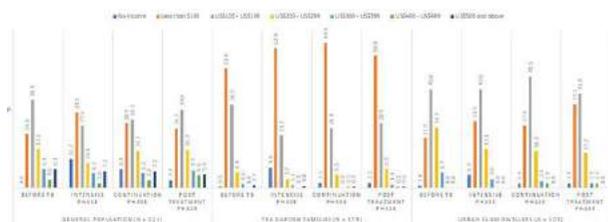


Figure. Income status of the households of study participants at different phases.

Conclusions: Major reason of continued financial hardship during the post treatment period was unemployment and reduced income. Tuberculosis care should be designed in such a way so that it does not disrupt the livelihood of the patients and therefore, job security for the tuberculosis patients should be considered.

OA26-388-11 Respiratory impairment and disability after successful treatment of pulmonary tuberculosis: a systematic review and meta-analysis

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Background: For many individuals, pulmonary tuberculosis (PTB) can result in a long-term health burden, even after successful treatment. We conducted a systematic review and meta-analysis (PROSPERO-CRD42021276327) to estimate the prevalence of respiratory impairment and functional disability following PTB treatment.

Design/Methods: We searched MEDLINE, Embase, Health Star, and Cochrane from 1960 through May 2021 to identify studies describing populations that successfully completed treatment for active PTB, in whom the development of long-term complications, disability and/or lung function abnormalities were described. Control populations were not required for inclusion. Study characteristics and outcome-related data were abstracted. Meta-analysis was performed using a random effects model.

Results: A total of 55 studies with 39,357 PTB participants were included (54% cross-sectional, 46% retrospective or prospective). In 36 studies reporting on post-TB spirometry, the pooled proportion of TB participants with abnormal spirometry was 58.4% compared to 5.4% of controls. Specifically, 18.3% had obstruction, 22.9% restriction, and 13.9% a mixed-pattern.

Among drug-sensitive TB (DS-TB) participants, 52.2% had abnormal spirometry compared to 85.9% of multi-drug resistant TB (MDR-TB) participants. Five studies reported data on incidence of lung cancer, with an incidence rate ratio of 4.0 (95%CI 2.1-7.6) and risk difference of 2.7% (95%CI 1.2-4.2) when compared to controls.

Among 11 studies with 3649 PTB participants, 74.6% of TB participants had an MRC (Medical Research Council) dyspnea score of 1-2 and 22.6% a score of 3-5. Mean six-minute walk distance (6MWD) in 14 studies was 491.7 metres in DS-TB participants (%predicted 86.2), 372.4 metres in MDR-TB participants (%predicted 70.7), and 427 metres in all TB participants (%predicted 76.5).

Conclusions: The prevalence of post-PTB respiratory and functional impairment as measured by spirometry, MRC scales and 6MWD is high. Our data also suggests

an increased risk of developing lung cancer after treatment for PTB. These findings reinforce the importance of TB prevention through tuberculosis preventive therapy.

OA26-389-11 Tracking of lung function during antituberculosis treatment in adolescents with pulmonary tuberculosis

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Background: Little is known about post tuberculosis (TB) lung disease (PTLD) in adolescents or how lung function changes during the early phase of treatment of disease. We aimed to track lung function in adolescents during the first 2 months of antituberculosis treatment.

Design/Methods: In a prospective cohort study, we enrolled 50 adolescents aged 10 to 19 years routinely diagnosed with bacteriologically confirmed pulmonary TB (PTB), between October 2020 and July 2021 in Cape Town, South Africa. Hand-held spirometry lung function measurements were completed at start of treatment, and 2 and 8 weeks later according to ERS/ ATS guidelines. Global lung initiative (GLI) reference ranges were used to calculate z-scores.

	Baseline	Week 2	Week 8	
	Mean (SD)	Mean (SD)	Mean (SD)	p-value
FEV1 pre, z score	-2.80 (1.61)	-2.83 (1.64)	-2.43 (1.66)	0.40
FEV1 post, z-score	-3.26 (1.42)	-2.98 (1.58)	-2.23 (1.67)	0.03
FVC pre, z score	-3.02 (1.74)	-2.92 (1.77)	-2.32 (1.59)	0.11
FVC post, z score	-3.44 (1.53)	-3.01 (1.65)	-2.40 (1.65)	0.04
FEV1/FVC pre, z-score	-0.25 (1.26)	-0.65 (1.25)	-0.91 (1.29)	0.13
FEV1/FVC post, z-score	-0.53 (1.45)	-0.76 (1.44)	-0.28 (1.10)	0.31

Table 1. Spirometry measurements in adolescents with confirmed PTB at diagnosis and during antituberculosis treatment.

Results: Of the 50 adolescents enrolled; 19 (38%) were male and the mean age was 16.4 years (standard deviation 2.0). Thirty-six of the 39 (92%) chest-radiographs with typical TB disease showed adult type TB disease with cavitation, which indicate severe disease. In total 18 (36%) were smokers, 5 (10%) were living with HIV and

9 (18%) reported a previous episode of TB. Forced expiratory volume in 1 second (FEV1) and Forced vital capacity (FVC) improved over time pre- and post-bronchodilation with salbutamol (Table 1), but remained below the -2 z-score. The FEV1/FVC ratio remained relatively normal over time.

Conclusions: Lung function in adolescents with PTB was well below normal reference ranges and indicate substantial restrictive impairment which improved during the early phase of TB treatment. Longer term follow-up of adolescents with PTB is important to assess the long-term impact of PTB on lung function and recovery and to correlate these findings with residual symptoms, quality of life, imaging and functional assessments.

OA26-390-11 One year on - the impact of COVID-19 and government restrictions on the health care seeking behavior, financial security and mental health of TB survivors

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Background: People with TB may face long-term physical and psycho-social-economic disability related to TB treatment. The COVID-19 pandemic and government restrictions had a negative impact on people accessing health care services and on services themselves.

We describe health-seeking behaviour, perceived financial impact and the mental health of TB survivors one year after the COVID-19 pandemic.

Design/Methods: Cross-sectional study nested in the ongoing observational TB Sequel cohort study. Adults (≥18yrs) who had completed treatment for drug-susceptible pulmonary TB through the national TB program in South Africa completed a COVID-19 questionnaire with the WHO tool for behavioural insights on COVID-19 tool and the Kessler Psychological Distress Scale (K10; score from 0-40). Questionnaires were administered during follow-up study visits between 04/2021-10/2021. We compared responses against the number of confirmed COVID-19 cases obtained from publicly-available data.

Results: 119 TB survivors (71% male, median 33 age in years IQR 33-42, median time since TB treatment completion 16 months IQR 13-27) completed the COVID-19 questionnaire. About a third of TB survivors reported

that their health-seeking behaviour for any health condition ($n=35$; 29%) or their financial status ($n=42$; 35%) had been seriously impacted by COVID-19 and the governments' response. The decline in health-seeking behavior between 06/202 and 10/2021 corresponded to the increase in confirmed COVID-19 cases during the same months (Figure 1). One in ten TB survivors reported any form of psychological distress (K10 score >20).

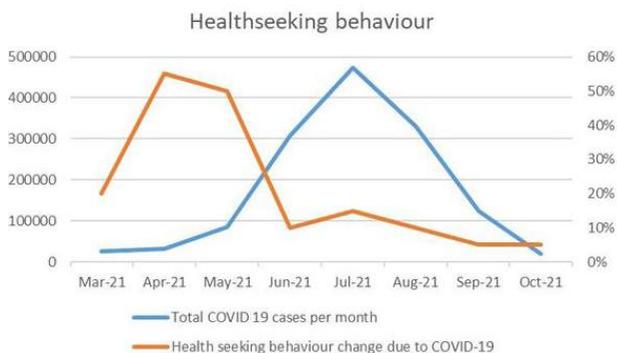


Figure 1. Health seeking behaviour of TB survivors and COVID-19 cases.

Conclusions: One year after the COVID-19 pandemic, TB survivors continued to feel the impact of COVID-19 and government restriction on their financial status. The long-term adverse effects on health-seeking behavior are important for TB survivors at increased risk for recurrent disease and long-term disability in the first two years after treatment completion and efforts will be needed to re-engage these individuals in care.

OA26-391-11 Risk of tuberculosis (TB) recurrence and mortality associated with smoking among people with TB: a systematic review and meta-analysis

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Background: The association between smoking and poor tuberculosis (TB) treatment outcomes is well documented. However, the evidence on important outcomes such as TB recurrence and mortality have not been sys-

tematically summarised. Our objective was to determine the effect of smoking on TB recurrence and mortality among people with TB.

Design/Methods: MEDLINE, EMBASE and CINAHL were searched on or before November 11, 2021, by combining terms for tobacco and TB outcomes. No geographical or language limits were applied and reference lists of included studies were scanned for additional records.

We applied random-effects models for all meta-analyses and assessed publication bias using funnel plots. Sources of heterogeneity were explored through subgroups, as documented in our PROSPERO protocol (CRD42017060821). The McMaster Quality Assessment tool for Quantitative Studies was used to assess study quality.

Results: Our searches identified 1130 records for screening. Of the 20 studies included under recurrence, 15 provided the necessary data for meta-analysis, showing significantly higher risk of TB recurrence associated with ever (RR=1.78, 95% CI=1.31-2.43, $I^2=85\%$), current (RR=1.95, 95% CI=1.59-2.40, $I^2=72\%$) and past smoking (RR=1.84, 95% CI=1.21-2.80, $I^2=4\%$). Subgroup analyses showed that heterogeneity likely arose from differences in study quality, study design and presence of comorbidities. Thirty-seven studies were included under the mortality outcome and 29 in the meta-analysis. Again, ever (RR=1.93, 95% CI=1.57-2.37, $I^2=95\%$), current (RR=1.30, 95% CI=1.12-1.51, $I^2=95\%$), and past (RR=2.22, 95% CI=1.59-3.11, $I^2=95\%$) smoking significantly increased the likelihood of mortality among people with TB. Differences in outcome definitions (all-cause/on-treatment/TB mortality) were a significant source of heterogeneity in the mortality analysis, while study quality and comorbidities were other likely sources. Funnel plots suggested that publication bias was unlikely.

Conclusions: Tobacco smoking significantly increases the risk of TB recurrence and mortality among people with TB, highlighting the need to address smoking in order to improve TB outcomes.

OA26-392-11 Tele-pulmonary rehabilitation experiences of post-COVID patients

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Background: COVID-19 may cause severe dyspnea, fatigue and reduced quality in the post-COVID phase. It is acknowledged that a multidimensional approach should evaluate the rehabilitation needs of COVID-19 survivors presenting with long-COVID symptoms. We aimed to present the results of a well structured hybrid tele-pulmonary rehabilitation programme for COVID-19 survivors.

Design/Methods: We evaluated PR programme results of COVID-19 survivors referred for a pulmonary rehabilitation programme. We applied a 8-week tele-pulmonary rehabilitation programme, with three supervised sessions per week. The programme comprised of endurance exercise (walking), strength training for upper and lower extremities, and educational sessions for breath retaining exercises and secretion management.

All of the participants underwent a 6-Minute Walking Testing (6MWT), Incremental Shuttle Walking Testing and Endurance Shuttle Walking Test. Quality of life was assessed by St. George's Respiratory Questionnaire. Hospital Anxiety and Depression Scale was obtained to assess anxiety and depression.

Results: A total of 30 COVID-19 survivors (M/F: 22/8) with a mean of 55.6 ± 12.9 years of age enrolled in a 8-week tele-pulmonary rehabilitation programme. 46.7% of the participants were on home-oxygen. 56.7% were ex-smokers, whereas 43.3% were never-smokers. Patients enrolled in the PR programme improved by 97 m on 6MWT ($p < 0.0001$), by 162 m on the Incremental Shuttle Walking Test ($p < 0.0001$) and 930 seconds on the Endurance Shuttle Walking Test ($p < 0.0001$).

There were no serious adverse events recorded, and there were no dropouts related to symptom worsening. Total SGRQ score improved from 47.8 ± 16.1 to 40.2 ± 14.0 at the end of the 8-week programme ($p = 0.007$). Similarly, Hospital Anxiety Depression scale depression scores significantly improved ($p = 0.010$).

Conclusions: Based on our results, tele-pulmonary rehabilitation for severe COVID-19 survivors significantly improves clinical outcomes. Of note, observed improvements were well beyond defined minimal important clinical difference limits for chronic respiratory diseases.

OA-27 Impact of Covid-19 on TB and other health services

OA27-393-11 Integrated SARS-CoV-2, TB, and HIV testing during 2 years of pandemic: a pragmatic care model in two rural districts in Lesotho

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Background and challenges to implementation: The COVID-19 epidemic has posed an exceptional test to the health system and the population of Lesotho. As emergency preparedness was scaled up and social measures were imposed, routine access to tuberculosis (TB) and HIV diagnosis was compromised.

We describe the impact of a response designed to sustain hospital-based, integrated SARS-CoV-2/TB/HIV testing in two remote districts in Lesotho, from August 2020 to May 2022.

Intervention or response: Integrated Screening Centers were built up at the entrance of the St Charles Mission Hospital Seboche and Mokhotlong Government Hospital. Adults and children presenting at the facilities were screened for SARS-CoV-2/TB symptoms, i.e. fever, cough, tiredness, dyspnea, sore throat, body pain, diarrhea, loss of taste/smell, recent weight loss, night sweats or close contact to a probable or confirmed COVID-19 case. Screen-positive individuals were sent for simultaneous diagnosis of SARS-CoV-2/TB/HIV. Clinical procedures included nasopharyngeal/nasal swabs for SARS-CoV-2 diagnosis, HIV testing according to national guidelines, and computer-aided radiological screening for TB, combined with Xpert MTB/RIF Ultra test in sputum.

Results/Impact: Of more than 222,000 people screened for COVID-19/TB, a total of 5,897 had a positive screening result and 3,610 followed the testing algorithm. A total of 2,551 individuals were tested using PCR and 3,573 using rapid tests for SARS-CoV-2. Xpert MTB/RIF Ultra and HIV diagnosis was done in 806 and 79 individuals. A total of 148, 42 and 21 individuals were newly diagnosed with COVID-19, TB, and HIV respectively.

Follow up after 28 days revealed that 101/148(66%) COVID-19 diagnosed individuals could be reached and 95/101(94%) were alive; further, 11/15 (73%) and 6/10

(60%) of individuals diagnosed with TB and HIV had started treatment.

Conclusions: Adapting to a fast-evolving context, this simultaneous, integrated COVID-19/TB and HIV diagnosis service provided sustained detection and referral for treatment for three critical conditions. The number of COVID-19 diagnosis in our setting was unexpectedly low.

OA27-394-11 Post-COVID, a risk group for targeted TB case finding: programmatic experience from Tamilnadu

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Background and challenges to implementation: COVID-19 pandemic and its containment measures had significantly disrupted the performance of the National Tuberculosis Elimination Programme (NTEP) in Tamil Nadu. In this context, to understand the risk of TB disease among COVID affected individuals, the following study to guide the programme managers in developing policies was commissioned.

Intervention or response: Under programmatic settings individuals with post-COVID (affected with COVID illness between March-May 2021) were contacted over telephone in 4 districts between June to August-2021. Individuals were telephonically interviewed, well being assessed, verbal consent obtained, and upon visit to a health facility administered a pre-tested study questionnaire and underwent chest X-ray (CXR), sputum (CBNAAT) and random blood sugar (RBS) testing.

Results/Impact: A total of 5378 individuals affected with COVID during the second wave were contacted over telephone. Of which 25% (1363) agreed to visit and

5.8% (n=310) visited the facility for screening. Approximately 82.3% (255) self-reported to have been hospitalized during the COVID illness and 39% (123) self-reported to have taken steroids during the illness. 38% of them had an RBS value in the pre-diabetic range of more than 140 mg/dl needing further investigations (9% higher than those with self-reported diabetic history).

Overall, 80% underwent a CXR and only 34% agreed to deposit a sputum sample for CBNAAT and of which 5(4.6%) were microbiologically confirmed to have TB cases.

Conclusions: The yield for TB among post-COVID was found to be higher than the risk groups for which ACF activities were routinely conducted under the programme. Also, higher number of post-COVID individuals were prediabetic which again increases the risk for diabetes thereby for active TB disease in future. This offers a great opportunity for awareness generation as well as management from the perspective of communicable and non-communicable disease programmes in implementing integrated screening for TB-diabetes-COVID.

OA27-395-11 Teamwork and combined effective response to minimize the impact of COVID-19 on TB elimination; an example of National TB Program of Nepal

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Background and challenges to implementation: Tuberculosis (TB) remains the leading cause of respiratory communicable diseases and a public health challenge in Nepal. The COVID-19 pandemic grossly affected all key TB elimination activities, after the first case was identified in Nepal in March 2020 and Nationwide lockdown. The TB program was also on high alert and put in place a number of measures to minimize the impact of COVID-19 on the National TB Program of Nepal as was seen in other countries.

Intervention or response: Rapid response team was established to effectively respond to program needs for both diseases, interim guidance of TB services during COVID 19 were endorsed and included 1 month's supply of anti-TB drugs to patients. Active TB case finding activities were initiated in the high-risk communities to find the missing TB patients. Bi-directional testing initiated using GeneXpert platform, and operational research on COVID-19 and TB conducted.

Results/Impact: Rapid response team has actively engaged on its role during pandemic. No stock out of ATT has been reported from any health facility during COVID-19 pandemic. 174 drug sensitive and 7 drug resistance cases diagnosed from the community screening after COVID pandemic. TB case notification is increased by 932 cases with respect the TB cases of 2020 (27745). The treatment outcome of TB treatment sustained on 90%.

Conclusions: Timely implementation of various strategic rapid response activities for TB elimination during COVID-19 pandemic enabled the National TB Program of Nepal to maintain adequate service delivery in the country and achieve high notification and treatment success rate in 2021.

OA27-396-11 Combined community screening and active case finding for COVID-19 and tuberculosis in Anambra state, south-east Nigeria

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Background and challenges to implementation: Anambra state had an estimated 11,184 Tuberculosis (TB) cases in 2020, but only 27% were detected. The emergence of the COVID-19 pandemic posed a further challenge in finding the missing cases in the state. This study aims to demonstrate the contribution of a community bi-directional screening for COVID-19 and TB in the state.

Intervention or response: The intervention took place from February to November 2021 with technical support from the WHO TB team in collaboration with the state TB and surveillance teams. An integrated screening algorithm for COVID-19 and TB was developed and shared with the Local Government TB Supervisors (LGTBLS) and the Disease Surveillance Notification Officers (DSNO) who were oriented at the onset.

Outreaches were carried out in marketplaces, motor parks, community centers, etc in the local government areas, during which people were sensitized and screened on the signs and symptoms of COVID-19 and TB.

Thereafter, a mobile sample collection center was set up and collected samples were shipped to a designated integrated laboratory for COVID-19 and TB testing. Persons confirmed to have COVID-19 or TB were tracked and started on appropriate treatment. National tools and specially designed reporting templates were utilized for data collection. Data was aggregated from the activity reports and analyzed statistically using Excel.



Figure. LGA Officer sensitizing people on COVID-19 and TB in a market place.

Results/Impact: A total of 1,807 persons were screened for COVID-19 and TB. Out of those screened, 69 COVID-19 suspects and 31 presumptive TB cases were identified and tested for COVID-19 and TB. Out of those tested, 19 (37% males, 63% females) COVID-19 cases were diagnosed and 30 (40% males, 60% females) persons were confirmed to have active TB and linked to treatment.

Conclusions: The bi-directional screening of COVID-19 and TB is a strategy that has shown to be effective in finding missing TB cases. This strategy should be incorporated into national TB program treatment and management guidelines.

OA27-397-11 Effectiveness of vaccination in preventing COVID-19 reinfection: a retrospective, population-based cohort study

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Background: The added benefit of vaccination for preventing reinfection among individuals who have been previously infected with COVID-19 is largely unknown. We sought to obtain population-based estimates of the probability of reinfection and the effectiveness of vaccination following recovery from COVID-19.

Design/Methods: We conducted a retrospective, population-based cohort study using statewide surveillance data on COVID-19 vaccinations, lab-confirmed cases, and hospitalizations collected by the Rhode Island Department of Health between March 1, 2020, and December 9, 2021, during periods when wild type, Alpha, and Delta strains were predominant. We included Rhode Island residents aged 12 years and older who were previously diagnosed as cases and unvaccinated at the time of first infection, stratified into three subpopulations: long-term congregate care (LTCC) residents, LTCC employees, and the general population. We conducted a survival analysis to characterize the risk of reinfection by subpopulation and to estimate the effectiveness of vaccination in preventing reinfections among people who have recovered from prior COVID-19.

Results: Overall, 3,124 LTCC residents, 2,877 LTCC employees, and 94,535 members of the general population met our eligibility criteria. The probability of reinfection at 9 months for those who remained unvaccinated after recovery from prior COVID-19 was 13.0% among LTCC residents (95% confidence interval [CI]=12.0-14.0%), 10.0% among LTCC employees (95% CI=8.8-11.5%), and 1.9% among the general population (95% CI=1.8-2.0%). Among LTCC residents, LTCC employees, and the general population recovered from prior COVID-19, subsequent completion of the primary vaccination series was 49% (95% CI=27-65%), 47% (95% CI=19-65%), and 62% (95% CI=56-68%) effective, respectively, in preventing reinfection, adjusting for potential sociodemographic and clinical confounders and temporal variation in infection rates.

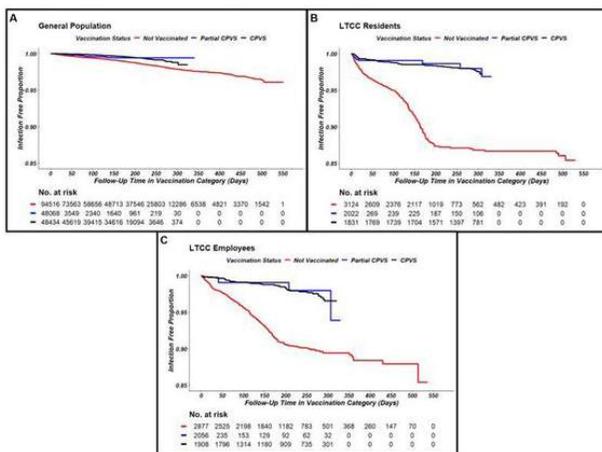


Figure. Kaplan Meier curves by vaccination status for the general population (A), long-term congregate care (LTCC) residents (B), and LTCC employees (C). CPVS indicates completion of the primary vaccination series.

Conclusions: Risk of reinfection after recovery from COVID-19 was relatively high among those who remained unvaccinated. Vaccination after recovery from COVID-19 provides substantial benefits, reducing risk of reinfection by about half.

OA27-399-11 Previous TB as a predictor of mortality among mine workers diagnosed with COVID-19

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Background: Previous tuberculosis (TB) disease has been found to lead to long-term lung sequelae. Mine-workers have increased rates of TB and silicosis and we postulated that lung infections among may lead to higher mortality than in other populations.

A difference in mortality among gold miners, as opposed to other mining groups, prompted a review of the mortality data among gold miners to determine predictors of mortality.

Design/Methods: We conducted a cross-sectional study from March 2020 to 31 October 2020 where we collected prior medical and lung function data from COVID-19 patients from two gold mining companies. Using directed acyclic graphs, we fitted a logistic regression model to analyse associations of mortality and previous TB, controlling for confounders.

Results: From a total of 1902 mine workers (454, 24.6% female) with lab-confirmed COVID-19 infection, 57 (3.0%) died. Of the 59 persons with previous TB, 9 (15.3%) died. There were 19 persons with silicosis, and 2 (10.5%) died.

Multivariable analysis, controlling for HIV status, age, diabetes, gender and workplace showed that previous TB was significantly associated with death from COVID-19 with odds ratio (OR) 4.7 [95% C. I (1.8-9.9)]. Age group [45-54 years, (OR 3.7, 95% CI 1.8-7.6); >54years (OR 5.0, 95% CI 2.3-10.7) compared to age <45 years] and diabetes [OR 4.6, 95% CI 2.5- 8.7] were significantly associated with increased mortality. HIV status was not shown to be significantly associated with mortality.

Variables	Odds Ratio	P-Value	[95% Conf. Interval]
History of TB			
No	(base)		
Yes	4.2	0,001	1.8 9.9
Age grp			
< 45	(base)		
45-54	3,677	0,000	1,785 7,578
>54	4,951	0,000	2,285 10,725
Gender			
Female	(base)		
Male	0,910	0,794	0,447 1,850
Diabetes			
No	(base)		
Yes	4,651	0,000	2,483 8,710
HIV Status			
Negative	(base)		
Positive	1,171	0,622	0,625 2,191
Work place			
Surface	(base)		
Underground	0,681	0,209	0,374 1,240

Table.

Conclusions: Death from COVID-19 was associated with Previous TB together with age and diabetes. In countries with a high TB burden, the previous TB may be an important predictor of mortality from COVID-19 in these patients and should be prioritized for more intensive management and antiviral treatment if available.

OA27-400-11 Effectiveness and durability of protection from infection-acquired immunity and vaccination against Omicron infection, hospitalization, and death: a population-based cohort study in Ontario, Canada

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Background: There remains limited data on the effectiveness of infection-acquired immunity against the Omicron variant and how vaccination might modify the effectiveness of infection-acquired immunity.

Our study aimed to assess the effectiveness of infection-acquired immunity and a “hybrid immunity” from infection and vaccination against Omicron infection, hospitalization, and death, using a population-based cohort of six million residents in Ontario, Canada.

Design/Methods: Protection from infection-acquired immunity was assessed by comparing risks of Omicron infection, hospitalization, and death between individuals with and without a previous infection, using Cox regression models with adjustment for demographic characteristics and vaccination status.

We further stratified the analysis on protection against Omicron infection by vaccination status to examine how vaccination modified infection-acquired protection.

Results: From November 22 to December 31 2021, we observed 181,937 Omicron infections, 2062 hospitalized and 272 deceased cases among 6,685,137 participants. A prior infection provided 80% (95% CI 79-81) protection against Omicron infection, 84% (95% CI 77-88) against hospitalization, and 95% (95% CI 67-99) against death. The protection was maximal at 3-5 months post-infection (87%; [95% CI 84-89]), and at 6-9 months post-infection for hospitalization (91% [95% CI 79-90]). The protection declined over time, but was maintained at 70% against Omicron infection (95% CI 67-73) and 74% (95% CI 41-88) against hospitalization over 15 months post-infection.

Among individuals vaccinated with two doses, a prior infection had an additional 87% (95% CI 85-90) protection against Omicron infection at 3-5 months post-infection.

This effect declined over time but was maintained at 72% (95% CI 69-75) over 15 months post-infection. We observed similar trends in other vaccinated groups, but the effect size was lower in the three-dose group.

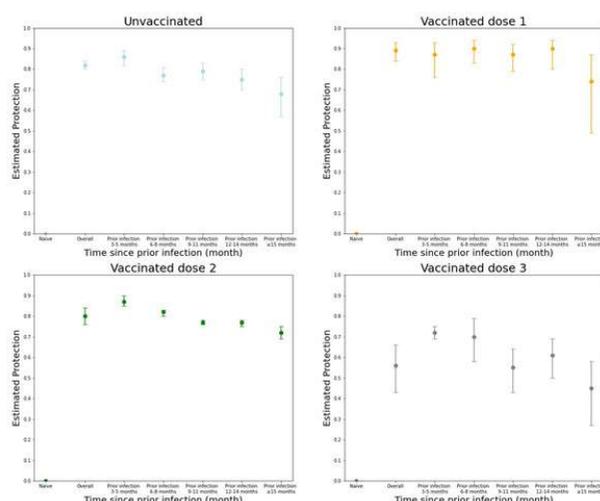


Figure 1. Protection from infection-acquired immunity against Omicron infection, stratified by vaccination status.

Conclusions: Infection-acquired immunity is effective in protecting against the Omicron variant and provides additional protection against Omicron infection and its severe outcomes among vaccinated individuals. This additional protection remains high one year after infection in fully vaccinated individuals.

OA-28 Find and treat; the hurdles and how to overcome

OA28-401-11 Changing the narrative in public-private mix (PPM) case finding: impact of intensified sensitization and demand creation by PPM providers - the Bauchi experience

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Background and challenges to implementation: Tuberculosis is one of the deadliest infectious diseases in the world even though it is preventable and curable. Yearly, 10 million people develop TB disease, with 3.6 million of these individuals not placed on treatment¹. To find these missing TB cases, engagement of private health providers is paramount as they can significantly contribute to TB case notification. To optimize the engagement of these private providers, there is a need to create demand for TB services in communities where they are located.

Intervention or response: KNCV TB foundation Nigeria supports private health facilities in 15 LGAs in Bauchi state to manage TB cases. Initially, most of these engaged facilities were passive in their case finding approach – waiting for clients to come to them, and this resulted in suboptimal performance. To change the narrative, providers were sensitized on active case finding and awareness creation within the community. A comparative review of the TB case finding from these facilities six months before (October 2020 - March 2021) and six months after (April – September 2021) the intervention was carried out and analyzed to ascertain the impact of the intervention.

Results/Impact: A total of 8,204 presumptive TB clients were identified, and 207 TB cases diagnosed in the 6 months prior to the implementation of the intervention. Following the intervention, there was a 95% increase in the TB case finding.

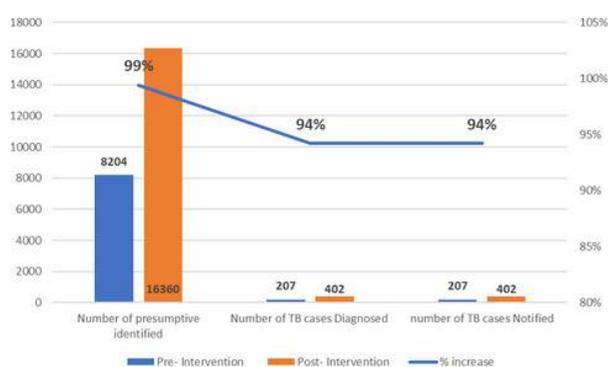


Figure. TB case finding data six months before and six months after sensitizing private health providers on demand creation for TB services.

Conclusions: This finding shows the surge of TB case detection through active TB case search and demand creation by PPM providers in Bauchi. It is recommended that during the engagement of private providers, they should be sensitized on the importance of demand creation and active TB case finding.

OA28-402-11 Screening for tuberculosis, COVID-19, and mental health conditions in juvenile detention centers in Lima, Peru

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Background and challenges to implementation: Youth deprived of liberty have an elevated risk of health problems due to overcrowding, violence, limited access to medical care, and other challenges. This situation has been exacerbated by the COVID-19 pandemic. Peru has the second highest TB burden in Latin America, as well as high COVID-19 mortality. An intervention for youth deprived of liberty was implemented with the goal of addressing the gaps in diagnosis for multiple conditions. **Intervention or response:** In May 2021, an intervention was implemented in two juvenile detention facilities in Lima. Chest radiography with an automated detection system (Qure.ai) was used to screen for TB and COVID-19, with molecular testing for TB (Xpert Ultra) and antigen testing for SARS-CoV-2 (SD Biosensor). Screening for depression via PHQ-9 and anxiety via GAD-7 were performed. Patients were referred to a health center for any necessary care.

Results/Impact: Among 585 evaluated youth 14-25 years of age, 18% (106/585) had an abnormal radiograph consistent with TB or TB symptoms, of whom 8% (8/106) had TB diagnosed; 3 (38%) of these individuals had rifampin-resistant TB. In addition, 31 (5%) had an abnormal radiograph suggestive of COVID-19, but all had negative antigen tests. Depression and anxiety screening was performed for 341 (58%) of the youth, of whom 291 (85%) screened positive for depression, 232 (68%) for anxiety, and 189 (55%) for both. In total, 114 youth (33%) were referred for mental health care, including those with severe depression, suicidal ideation or ideation of self-harm, and others who required specialized intervention.

Conclusions: Our intervention identified youth deprived of liberty who were affected by tuberculosis and mental health conditions during the COVID-19 pandemic. Fortunately, we did not detect any acute cases of COVID-19. It is necessary to improve activities for active case-finding and timely diagnosis of TB, depression and anxiety in this vulnerable population.

OA28-403-11 Are individuals with TB receiving person-centered care?: a multi-country comparison

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Background: Person-centered care offers a path to improved TB outcomes by providing care that is responsive to and respectful of individuals’ needs and desires and uses these preferences and priorities to guide clinical decisions. Countries have recently strived to identify and provide responsive treatment support services with a person-centered approach, though considerable gaps still exist.

Design/Methods: Quality of TB service assessments (QTSAs) were conducted in Afghanistan, Ethiopia, Philippines, and Uganda from 2018–2021. Across the four countries, 1,989 individuals on TB treatment were asked to specify TB treatment services they deemed beneficial, and of those services, which ones they received.

Results: When comparing services desired by people with TB against services received, significant gaps existed across all four countries. Free TB medicines had the smallest gap, as many individuals with TB reported that they received free TB medicines. In general, Uganda was found to have smaller gaps among the most desired services and those most often received. The largest gaps between desired and received services across all four countries were related to transportation assistance and nutritional support (e.g., food baskets).



Figure 1. Desired vs. received TB support services reported by individuals with TB in Afghanistan, Ethiopia, Philippines and Uganda.

Conclusions: Findings indicate that TB support services received do not meet the demand, demonstrating that health systems are not meeting the needs of people with

TB. Providing care that is responsive to the needs and desires of individuals with TB leads to improved experiences, confidence in the health system, and better treatment outcomes. As national TB programs incorporate principles of person-centered care into their strategic plans, closing the gaps between TB treatment support services desired and those provided by facilities is vital to reaching TB targets and reducing a country’s TB burden.

OA28-404-11 “You’re mistaken. I didn’t default, I’m just not well.” Insights from a qualitative study to understand community-based TB stigma in South Africa

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Background: There is increasing recognition that communities should be involved in the design of interventions to reduce tuberculosis (TB) stigma, which remains a major barrier to TB care. We conducted community-based stigma assessments in one urban (Khayelitsha, Western Cape Province) and one rural community (Hammanskraal, Gauteng Province) in South Africa. Surveys done in both communities demonstrated high levels of internal, anticipated, and enacted stigma, throughout the care cascade. We sought to triangulate these findings with qualitative data to understand how people affected by TB and their caregivers experienced TB-related stigma.

Design/Methods: We conducted 25 in-depth interviews with people affected by TB (22) and caregivers (3), of whom 8 had drug-resistant TB and 6 had HIV. Using an inductive approach to thematic analysis, we performed open coding to identify emergent themes, and selective coding to identify relevant text citations. We organised themes using the CARD (Constraints, Actions, Risks and Desires) framework.

Results: Eight emergent themes were analyzed according to CARD domains (Table). Within Constraints, the themes were intersectional stigma due to HIV, alcohol use, and gender, and socio-economic barriers that were often exacerbated by TB with long-term ramifications. Within Actions, participants reported variable approaches to disclosure impacted by anticipated stigma versus their own lack of stigma towards TB, and stigma resilience due to understanding TB can happen to

anyone and many people have TB. Within *Risks*, participants mentioned fears related to infectiousness and transmission as stigma drivers, and both anticipated and enacted stigma impacted care engagement. Within *Desires*, participants mentioned the need for counselling, with a specific role for peer counsellors, and education.

CARD DOMAINS and Themes	Quotations
CONSTRAINTS – Intersectional stigma: HIV, alcohol use, gender	"If you lose weight then they assume that you have HIV. They would say you might have HIV and you should go and get tested." "He was drinking alcohol and he died." "Us male people, we are worse. We are embarrassed to go to the clinic and take treatment"
CONSTRAINTS – Socio-economic barriers and exacerbation of these due to TB	"I struggled when it comes to food and I am still struggling now because I am not working." "I don't have money, I don't have anything to eat. If I take these pills, they make me sick".
ACTIONS – Disclosure decisions varied depending on anticipation and experiences of enacted stigma	"[I did not tell my friends I had TB]. I knew that they were going to gossip about me." "I never told her [participant's girlfriend] anything - even today. We even broke up because I was ashamed what I would say."
ACTIONS – Stigma resilience demonstrated by understanding TB can affect anyone	"I didn't fear anything when it came to that [decision to seek healthcare], I just thought everyone can be infected by TB." "I was telling her that she [child with TB] is not the only one that has TB. There are a lot of people that have TB."
RISKS – Fear of infectiousness and transmission	"People who were my friends, who I used to help, isolated themselves from me." "I think he [child with TB] was also scared to go play with them since people say that TB is infectious."
RISKS – Anticipated and enacted stigma negatively impact engagement in care	"What is so and so going to say when I'm on the side of people with TB, who are taking the TB treatment?" "Once a person has started treatment we go around talking about them, saying that "So and so has TB". This person is even afraid to leave the house, to go to the clinic."
DESIRES – Counselling, including specific role for peer counsellors	"I never received any counselling." "I would say that they [counsellors] are needed, but should be someone who has experience of what you are dealing with, who has felt the pain you would be feeling like the side effects."
DESIRES – Education for communities, patients and health workers	"I listen a lot to the things being taught at the clinics. We could have a venue where people will be invited to be taught about TB." I said to the doctor "You educated people have a name saying 'default'. You're mistaken. I didn't default, I'm just not well".

Table. Themes related to TB stigma reported by people with TB and caregivers of someone with TB, organized according to the CARD framework domains.

Conclusions: Participants' experiences highlighted the impact of internal, anticipated, and enacted stigma at different care cascade stages, and emphasized intersectional stigma and the lack of holistic support. Counselling was identified as an intervention to decrease stigma and promote person-centred care.

OA28-405-11 Pathways to impact of interventions to reduce tuberculosis-related stigma: a structured literature review, quality appraisal, and conceptual framework

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Background: Reducing tuberculosis (TB)-stigma is a key strategy to achieve the World Health Organisation's (WHO) End TB target of eliminating TB. However, process and impact evaluation of stigma-reduction interventions is limited. This structured literature review aimed to examine the quality, design, and implementation challenges and successes, and create a novel conceptual framework of mechanisms for impact of TB-stigma intervention studies.

Design/Methods: Using pre-defined criteria, we searched four scientific databases and grey literature repositories for studies published between 1999 and 2022. We assessed the quality of studies using the 'Crowe Critical Appraisal Tool'(CCAT), and extracted and tabulated study characteristics, data on stigma measurement tools used, interventions implemented, and mechanism of stigma reduction. A conceptual framework was designed to illustrate the mechanisms of stigma reduction identified.

Results: Of 14,259 articles identified, eleven met inclusion criteria. Three studies have high quality according to CCAT criteria. Eight studies used questionnaires to assess stigma levels, three of which had been previously validated. Stigma reduction intervention designs broadly consisted of educational or psychosocial support. Eight studies reported a reduction in stigma attributed to the intervention. Despite the benefits, most psychosocial interventions for people with TB-Stigma did not set stigma reduction as their primary or co-primary aim and were limited by a corresponding dearth of validated stigma measurement tools. Despite this, we were able to generate a conceptual framework that mapped the population targeted, interventions delivered, and their potential effects to reduce stigma towards and experienced by people with TB and TB-related healthcare workers.

Conclusions: The evidence base on TB stigma-reduction interventions is weakened by heterogeneity of measurement tools and intervention design. High quality stigma-reduction interventions that use standardized, validated stigma measurement tools are required. Advocacy to promote stigma-reducing interventions should be strengthened by the inclusion of TB-stigma as an indicator in WHO's global TB strategy.

OA28-406-11 Continuation of active TB case finding among at-risk population during the hostilities in Ukraine

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Background and challenges to implementation: Since 2014, active TB case finding among MARPs (homeless, ex-prisoners, Roma population, PWID, alcohol abusers, contacts etc.) intervention have been implemented in 19 regions of Ukraine by 24 NGOs. Since February 24th with the Russian aggression starts NGOs faced barriers with this intervention implementation. These barriers depends on the region status: active hostilities, temporary occupation or relatively safe regions that accept refugees.

Intervention or response: Both healthcare facilities and NGOs experience lack of staff (due to staff evacuation) or overloaded (due to the arrival of evacuees). In the regions where active hostilities continues all outreach work has stopped (Donetsk, Luhansk, part of Zaporizhzhya and Mykolaiv regions). In Kharkiv which is under heavy fire but without ground military operations active screening on TB symptoms is conducted in the subway and bomb shelters where many people spend the most time. In the occupied regions (Kherson) TB screening is conducted in NGOs' premises or via phone. Screening-positive people are referred to assigned TB doctors in assigned hours. NGOs in relatively free areas faced a big number of IDPs. NGOs staff is overloaded, they have to hire additional social workers to conduct screening among refugees. Healthcare facilities are not always able to provide clinical examination to all people with TB symptoms.

Results/Impact: TB diagnostics becomes less prioritized by vulnerable population and healthcare facilities during the war. As a result of 2-months hostilities, number of diagnosed TB has decreased by 50% in PWID and by 30% among other at-risk groups. In the same time, we observe the increased number of diagnosed TB in IDPs. The same phenomenon was observed in 2014-2015 in IDPs from Donbas during the restricted hostilities.

Conclusions: Current hostilities in Ukraine led to creation of additional barriers in active TB case finding services provision and cause the increase of missing TB cases in most at-risk populations.

OA28-407-11 Tuberculosis yield from targeted community based active TB case finding activities; implications for programming to end TB in Uganda

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Background and challenges to implementation: Prior to 2018, TB case finding efforts in Uganda were predominantly passive and health facility based with limited community based and engagement activities. Moreover, about 39% of people with TB symptoms did not seek health care according to the national TB prevalence survey. As a result, about 40% of estimated incident TB cases were missed in Uganda contributing to the missed global TB cases. Limited engagement of community structures and limited resources affected active TB case finding at community level. We evaluated the yield of TB and number needed to screen (NNS) from targeted active TB case finding activities.

Intervention or response: The USAID Defeat TB project engaged and trained community based civil society organizations (CSOs) to conduct systematic TB screening activities in Kampala, Wakiso and Mukono. Routine programme data was used to inform mapping and targeting of populations at increased risk of Tuberculosis. During 2018 -2021, the CSOs conducted the community screening activities and used tools to track completion of the diagnostic cascade and linkage to treatment.

Results/Impact: A total of 146,420 persons were sensitized and screened, 25,501(17.4%) were presumed and evaluated, 4,577 (3.13%) were diagnosed and linked to treatment. Overall, the TB yield was 3.13%, NNS was 32 with variation for the different population groups/ settings as illustrated in figure 1.

Categories of people sensitized and screened for TB during other community activities	Oct 2018 to Sep 2021				
	Number screened	Number of presumptives identified	Number diagnosed with TB	Number needed to screen (NNS)	Yield (%)
Prisons	6,687	1,755	233	29	3.48%
Slums	70,651	11,995	2,090	34	2.96%
Labor Camps	7,637	1,020	189	40	2.47%
Schools	7,997	1,464	104	77	1.30%
Fisher folks	5,458	770	119	46	2.18%
Male Congregate setting	2,830	666	89	32	3.14%
Youth Congregate setting	2,784	488	86	32	3.09%
Homesteads	26,868	5,274	1,223	22	4.55%
Refugee	447	66	12	37	2.68%
Other settings	15,061	2,003	432	35	2.87%
Total	146,420	25,501	4,577	32	3.13%

Figure 1: TB screening cascade and yield from the different key affected populations

Conclusions: The high presumption rates and yield from the community based active TB case finding initiatives provides evidence for undiagnosed TB and ongoing transmission. The yield and NNS can be used to prioritise population groups for screening. Community en-

agement to conduct data driven active TB case finding and prevention initiatives for populations at increased risk of TB will greatly reduce the burden of Tuberculosis in Uganda.

OA28-408-11 Discordance among TB knowledge, attitudes and practices among 381 pharmacy professionals in Vietnam

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Background and challenges to implementation: In Vietnam, pharmacies are often the first contact with the health system when respiratory symptoms arise, but there is no formal coordination between private pharmacies and the National Tuberculosis Program (NTP). The USAID Support to End TB project surveyed pharmacy professionals to explore the potential for early TB detection in the pharmacy sector.

Intervention or response: We conducted an online survey of pharmacy professionals registered on mClinica Pharmacy Solutions' SwipeRx platform in nine provinces (Urban: Hanoi, Ho Chi Minh city; Rural: Nghe An, Thai Binh, Dong Thap, An Giang, Can Tho, Tien Giang and Tay Ninh). The participants accessed a Qualtrics link on SwipeRx, provided through email or push notification, and answered 39 questions.

Results/Impact: From June-July 2021, 381 pharmacy professionals completed the survey. On average, respondents chose the correct responses in 5.2 out of 9 TB knowledge domains. Most were aware of the treatment regimen (76%) and how TB is diagnosed (78%) but were not as knowledgeable about TB symptoms (43%), transmission (21%), and prevention (8%). The vast majority (92%) agreed or strongly agreed that pharmacy professionals have a role in screening and referring clients for TB testing. More than two-thirds (70%) were willing to refer clients with TB symptoms to a health facility without any incentive, but only 38% of respondents reported having done so.

Conclusions: Despite incomplete knowledge about TB transmission and prevention, most pharmacy professionals reportedly provide TB counseling to clients who have a cough and/or other TB symptoms. There is also a gap between positive attitudes about making referrals and the practice of referring clients for TB testing among pharmacy professionals. These results suggest that interventions to improve TB knowledge and facilitate pharmacy referral for TB detection could improve

early TB diagnosis in Vietnam. Additional research is needed to understand when and how pharmacy professionals counsel clients about TB.

Demographic	n (%)	Correct TB knowledge (selected domains)	n (%)	Attitudes about TB care	n (%)	TB Practices	n (%)
Age (mean)	32	TB cause	81 (21%)	Can protect self while caring for clients with TB	269 (71%)	Frequency of TB counseling	
Urban / Rural		Symptoms	164 (43%)	Able to counsel clients with TB	257 (67%)	Never/ refused	68 (18%)
Hanoi, HCMC	126 (33%)	TB vs. COVID-19	139 (37%)	TB treatment should be required	351 (93%)	Sometimes	275 (72%)
7 rural provinces	255 (67%)	Prevention	29 (8%)	Pharmacy professionals should screen and refer clients who have TB symptoms	348 (92%)	Often or always	38 (10%)
Sex		Confirming TB	296 (78%)	Willing to refer clients to health facilities		Past TB referrals	148 (38%)
Female	252 (66%)	Treatment regimen	288 (76%)	Would refer without incentive	266 (70%)		
Male	114 (30%)	Consequences of improper treatment	324 (85%)	Would refer with incentive	37 (10%)		
Clients with cough per day, Median [IQR]	13 [6-21]	Selling unauthorized drugs	317 (83%)	No	78 (20%)		

TB Knowledge, attitudes, and practices of pharmacy professionals in 9 provinces of Vietnam

OA-29 Innovative responses to airborne pandemics

OA29-409-11 Using SMS reminders to promote care seeking behavior and improve active tuberculosis case findings in Chennai

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Background: The Greater Chennai Corporation (GCC) has deployed chest x-ray (CXR) machine-retrofitted mobile diagnostic units (MDU) for active TB case-finding (ACF). We sought to assess the impact of targeting individuals with digital reminders and behavior change communication on MDU-based ACF camp attendance. **Design/Methods:** The pilot was embedded within the ACF program of the GCC and was conducted between February to April 2021 in nine high-burden slums in Chennai with high TB presumptive rates. Using a vulnerability index, 34,214 individuals were surveyed to identify 1,574 TB-vulnerable individuals. Of this group, consenting individuals were randomly enrolled into one of three treatment arms:

- (1) door-to-door mobilization only,
- (2) door-to-door mobilization and SMS reminders for the date, time, and location of MDU camp, and
- (3) door-to-door mobilization and SMS messages which included reminders and additional behavioral prompts.

The efficacy of the SMS interventions was evaluated based on MDU camp attendance and Pearson's chi-squared test was used to determine significance.

Results: Among attendees enrolled in the study, 16% of those who received an SMS attended camp compared with 14.6% of those who did not, which was not a statistically significant relationship ($p = 0.49$). Further, the behavioral prompts included in Arm 3 did not increase likelihood of camp attendance compared with just receiving an SMS in Arm 2 ($p = 0.73$). However, among those classified as 'highly vulnerable' (defined as having a vulnerability score >15 on a scale of 0-64), receiving an SMS was significantly associated with greater rates of camp attendance. Among this cohort, 9.09% of those who did not receive an SMS attended camp, as compared to 20.3% who did receive an SMS (p -value = 0.001).

Conclusions: Digital reminders can improve care-seeking rates to ACF camps when combined with door-to-door mobilization among those most susceptible to TB.

OA29-410-11 Mitigating the impact of COVID-19 through telecounseling support by trained TB survivors: lessons learnt from India

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Background and challenges to implementation: That the COVID-19 pandemic impacted access to TB services & derailed service provision is now well-established. In India, the pandemic & subsequent lockdowns severely limited mobility and affected access to information.

The widespread fear and stigma associated with COVID-19 had an impact on health-seeking behaviour for TB. In this context, the role of trained TB survivors as peer supporters became critical.

Intervention or response: In Bihar, a facility-based peer counselling initiative was originally conceptualised by REACH and TB Mukta Vahini (TMV), the state survivor-led network and subsequently redesigned to meet the changing needs of people with TB (PwTB) affected by the pandemic. Potential peer counsellors were identified from among TMV members and virtual training sessions were held. 44 TB Champions were engaged to provide telecounseling support for 6 months, and began contacting PwTB on the phone, seeking to understand any specific needs they had. Coordination groups were formed with NTEP officials at state and district levels to ensure prompt follow-up action.

Results/Impact: Over 6 months, 44 TB Champions provided timely peer support through telecounseling to 9500 PwTB in Bihar. Over 90% of PwTB received information on COVID-19 appropriate behaviours & the need for vaccination. Through daily calls, TB Champions provided essential information about TB, motivated PwTB to complete their treatment and addressed issues of stigma and discrimination.

In many instances, they found gaps and challenges related to follow-up examination, restarting treatment after missing several doses, migrating to their native districts etc.

Conclusions: This intervention demonstrated a coordination mechanism between survivor-led networks & the TB programme for identification & resolution of issues in real time. TB Champions were quick to adapt to and recognise the changing needs of their communities during the COVID-19 pandemic.

This intervention reinforces the need for continued investment in TB-affected communities to strengthen their capacity to find innovative solutions during pandemic times.

OA29-411-11 Addressing COVID-19 vaccine hesitancy in Nigeria through an integrated TB/COVID-19 community social and behaviour change approach; a pilot case of Akwa-Ibom, Bauchi and Kano State

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Background and challenges to implementation: Tuberculosis (TB) case finding remains a huge challenge in Nigeria. Limited awareness on TB contributed to low health seeking behaviour for TB care. The emergence of the COVID-19 pandemic created a challenge for traditional TB community active case finding interventions because gathering in groups was discouraged and social distancing was advised.

Slow uptake for COVID-19 vaccine is also well documented in Nigeria. Access to the vaccine is affected by multiple factors including vaccine hesitancy fuelled by mistrust, safety concerns, and low risk perception for COVID-19 infection.

The motorised campaign strategy, a community SBC approach was designed by Breakthrough ACTION Nigeria (BA-N), a USAID flagship program for social and behaviour change (SBC) and risk communication under the prime implementation of Johns Hopkins Centre for Communication Programs (CCP), to create awareness and demand for TB testing and services without breaking COVID-19 protocol.

Intervention or response: To improve the uptake of COVID-19 services while ensuring TB active community case finding, BA-N piloted and afterwards commenced an integrated TB/COVID-19 motorised campaign in collaboration with other partners, stakeholders; and pre-activity advocacy to community gatekeepers. Using joint TB/COVID-19 jingles and spots, members of the community were mobilised, while trained volunteers facilitated discussions with community members and referred them to the service points where they were offered COVID-19 testing/vaccination and screened for TB.

Results/Impact: Pilot results for COVID vaccination showed a 35-600% increase in daily vaccination rate in the same communities, and the COVID testing for non-travellers recorded a 200-275% increase. For TB, 1,450 people were screened, with 437 presumptive and 35 confirmed TB cases respectively.



Conclusions: Multiple service points as a result of the integration may have improved ease of access and a feeling of vaccination being a community norm, and in turn encouraged uptake of the COVID-19 vaccine. Integrating service outreaches may address vaccine hesitancy in Nigeria and beyond.

OA29-412-11 Boosting TB awareness in Ukraine by synergizing TV and web-based TB interventions amid COVID-19 recovery

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Background and challenges to implementation: TB detection rates in Ukraine decreased by almost 40% with the COVID-19 pandemic, weakening a decade of progress towards TB elimination. With the pandemic occupying much of the information space and affecting health system capacity and health-seeking behavior, public awareness of TB and likelihood to seek TB care suffered. Strengthened TB education, using effective tools and channels for information delivery across age cohorts and geographic areas, is urgently needed.

Intervention or response: From June–December 2021, STBCEU and the Convictus-Ukraine Charitable Foundation collaborated to develop a series of five monthly 45-minute televised TB discussions, covering a variety of topics. Each discussion was broadcast during a health-dedicated national TV program, and then posted on Facebook and YouTube channels to expand the audience and impact. The monitoring tool for audience feedback and broadcasting media metrics was developed.

Results/Impact: Through the five consecutive broadcasts, STBCEU saw steady audience growth and brought TB-related topics into the national health discourse. Viewership increased on average by 0.61% from show to show., by the final broadcast, the share of TB talk shows in all television airtime reached 2.83% in large (>50 K) and 1.1% in small (<50 K) settlements. In Kyiv, during the final broadcast the largest audience segment (3.91%)

was among people ages 35+; while 1.92% among younger viewers (18–34). When shared in web-based platforms (Facebook/YouTube), the five broadcasts elicited 7,775 views, with a steady increase from 747 views of the first discussion to 2,612 views of the final one.

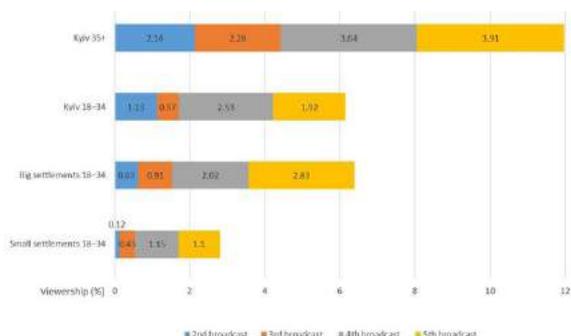


Figure. Steady viewership increase for consecutive TV broadcasts on TB awareness.

Conclusions: Pairing TV and web-based channels to share TB information enhances TB communication effectiveness. Maintaining viewer’s attention on TB over time is important and was achieved by providing information through a series of clear and intelligible discussions enabling renewed attention to TB amid the heightened media focus on COVID-19.

OA29-413-11 Pioneering a social enterprise model to notify people with TB through private pharmacies

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Background and challenges to implementation: Approximately 580,000 people in Pakistan develop TB each year, of whom 220,000 are missed. Private drug sales data revealed that 168,000 complete TB courses were sold in Pakistan’s private pharmacies during 2018, including 90,000 in Punjab province, indicating that a high proportion of people with TB were getting treatment, went unnotified. This implies that potentially 75% of people ‘missed’ could be traced simply by reaching those securing TB drugs from private pharmacies.

Intervention or response: We aimed to use an innovative digitalized model through a mobile application – ‘eTB’ specifically developed for notifying TB patients from engaged pharmacies. We used direct engagement

with pharmacies as well as strategic dialogue between the health leadership and pharmaceutical companies manufacturing TB drugs culminating in an agreement restricting over-the-counter sale of the medicines only to individuals on a registered practitioner’s prescription. The details of the prescription would be notified through eTB. Provincial health minister in a media briefing made it mandatory for all pharmacies to notify the details of people purchasing TB drugs through eTB.

Results/Impact: The project worked in four districts. Engaged 14 large pharmacy chains, and 2,943 actual drug dispensing sites between April 2021 and March 2022. Comprehensive dashboard designed to make data access readily available, we identified 15,669 people who had a prescription for TB and were able to notify them. The aggregated figures for Quarter 4 of 2022 are not available yet, case notifications went up from 28,637 from Quarter 2, 2020 till Quarter 4 of 2020 to 48,703 in the corresponding period of the next year, indicating that while case notifications rose by 20,070 cases in the four districts during these three quarters, Dopasi contributed to 57.5% (11,538) of the incremental cases from April-December 2021.

INTER-VENTION DISTRICTS	DOPASI CONTRIBUTION	DOPASI CONTRIBUTION	DOPASI CONTRIBUTION	DOPASI CONTRIBUTION	Total
	Q2 – 2021	Q3 – 2021	Q4 – 2021	Q1 – 2022	
Faisalabad	753	1,332	1,612	1,496	5,193
Lahore	427	1,285	1,350	869	3,931
Multan	583	815	983	920	3,301
Rawalpindi	305	819	1,274	846	3,244
Total	2,068	4,251	5,219	4,131	15,669

Conclusions: A huge number of the missing people with TB could be traced by reaching those securing TB drugs from pharmacies.

OA29-414-11 Channelizing the power of youth, creative communication, and digital technology in creating awareness towards TB

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Background and challenges to implementation: Youth (15-29 years) shoulders ~32% of the India's TB burden¹. With advancing technology and increasing social media usage, the youth are also highly connected to each other, and the world than ever before. It is critical to engage and empower youth as change catalysts. Involving and reaching to youth differentially and at scale is one of the critical challenges as well as an opportunity. Leveraging digital technology and creative communication is one of the novel approaches to reach youth in the fight against TB.

1. India TB Report 2021

Intervention or response: Johnson & Johnson India launched a youth-focused, digital-first initiative #BeTheChangeForTB as part of its commitment to the Corporate TB Pledge, on 24th March, 2022. Leveraging digital programmatic targeting across various digital & social media platforms, the initiative was launched, using music as a medium of message, with a rap anthem featuring youth icons. The creative messaging of the rap focused on changing the perception towards TB, advocating awareness of its symptom and testing early. The imagery of "warrior" used in the song aimed at bringing positivity to the suffering of disease. Additionally, various other creative, short, sticky, and engaging formats of social media content were released.

Results/Impact: Within a month of the launch, the campaign had an overall reach of 23 million and 100 million impressions in the targeted audience. The rap song had a reach of 567K, garnered 845K impressions and 261K video views across the social media platforms. Additionally, ~3000 TB changemakers signed up for the cause.

Conclusions: India has a young population. Its tech savvy, energetic youth can lead from the front bringing a change in tuberculosis care. Engaging the youth by leveraging digital technology & social media along with creative, simple, sticky messaging to bring scale and sustainability will be the way forward.

OA29-415-11 Asmara TBC: efforts to rebound the achievement of tuberculosis contact investigation during the COVID-19 pandemic in Tangerang City, Indonesia

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Background and challenges to implementation: The low of TB case finding is still one of the major issues in Tangerang City, Indonesia. In the first semester 2020, The main strategy of case finding through contact investigation has decreasing, only 5% index cases were contacted, due the Indonesian Government enforced large-scale social restrictions (PSBB) to facing out Covid-19 Pandemic and limited cadre engage in TB program.

Intervention or response: The DHO developed a strategy to increasing case finding through engaging the community cadres and utilizing digital health application in contact investigation without face-to-face meeting which is named *ASMARA-TBC*. The first step is trial the application in two Puskesmas with engaged 15 cadres to conduct contact investigation using the mobile app. The second step, DHO conducted monitoring and evaluation for *ASMARA TBC* trial. The third step based on MnE result, the *ASMARA TBC* was expanded to all of Puskesmas through trained and provide technical support all community cadre (not only TB's Cadre) to using the *ASMARA TBC* application on contact investigation activity.

Results/Impact: In 2021, 1089 cadres have been trained in using *ASMARA TBC* apps. The number of index cases conducted contact investigation has increased 8 times from 2020, from 268 to 2179 index cases, the number of contacts being screened has increased from 1055 to 16,309 contacts, and the case finding has increased significantly to 90 cases, while the previous year only 3 cases.

Conclusions: By using the *ASMARA TB* application, cadres have minimal contact during the TB screening for household contacts to prevent the Covid-19 transmitted and also very effective to increasing the case finding.

OA-30 Tobacco Industry Interference

OA30-417-11 How does tobacco industry bypass the menthol ban?

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Background: Menthol makes smokers inhale deeply due to its cooling effect on the airways. Use of mentol in tobacco products was banned in Turkey since 2020. This study aims to investigate the internet and point of sales marketing of a new product called „menthol ball“ which is made to inject mentol into regular cigarettes.

Design/Methods:

In order to disclose the methods of marketing of menthol balls:

- 696 websites identified through google search were further investigated. E-commerce websites, social media accounts were detected. Their promotinal activities, methods of trading were noted.
- Point of sales (POS) were visited in four commercially dense districts of Istanbul according to the shadow reporting methodology developed by Framework Convention Alliance to investigate the products sold.

The marketing methods and display of menthol balls were noted.

Results: 37 brands of menthol ball were detected on the internet. All brands promoted their products through videos describing the injection of the tiny menthol balls into the classical cigarettes. 25 used main e-commerce outlets to reach to the customers. Major e-commerce sites sold 1485 different menthol balls with various flavours under the category of air refresher or tobacco bags.

Out of 198 POS visited 31 marketed menthol balls. These tiny colorful balls of menthol mixed with various aromas were sold with an instrument that can inject into the cigarettes. The POS closest to schools were more likely to stock menthol balls. Majority of the POS placed the menthol balls close to candies, mints, chewing gums at the eye level of the children, just below the cigarette shelf.

Conclusions: Using menthol by injection into the cigarettes is a novel technique developed by the industry to appeal the youth, sustain addiction and bypass legislation. Public health community needs to be vigilant and take actions.

OA30-418-11 Pricing strategies and cigarette affordability in Taiwan - the opposite effect of increased taxation and economic growth

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Background: In Taiwan, after the 2009 amendment of the Tobacco Hazards Prevention Act, tobacco tax environment was basically stagnant for eight years, allowing tobacco companies to implement their pricing strategies with no interference. Only in June 2017, the Tobacco Excise Tax was finally raised, increasing taxation from 48% to 60% of the retail price of the most popular brand.

Our goal is to reveal changes in the tobacco industry’s pricing strategies after 2017 in Taiwan and evaluate the impact on cigarette affordability and real net revenue per pack.

Design/Methods: Using publicly available information from Taiwan Health Promotion Administration, Statistical Bureau, Ministry of Finance, and convenience stores, the following variables were estimated over the 2010-2021 period: real retail price, real net revenue, relative income price (which measures cigarette affordability), sales volume.

Brand	Company	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021
Relative income price (nominal retail price of 100 packs / nominal GDP per capita)													
Mevius	JT	1.23%	1.30%	1.35%	#N/A	#N/A	1.24%	1.27%	1.64%	1.60%	1.56%	1.49%	1.26%
Long Life	TTL	1.07%	1.06%	1.03%	#N/A	#N/A	0.89%	0.80%	1.18%	1.14%	1.12%	1.07%	0.98%
Davidoff	DB	1.32%	1.38%	1.35%	#N/A	#N/A	1.24%	1.27%	1.24%	1.60%	1.56%	1.49%	1.26%
Gentle	TTL	0.91%	0.89%	0.95%	#N/A	#N/A	0.96%	0.94%	1.31%	1.28%	1.25%	1.19%	1.09%
Mi-Ni	JT	1.56%	1.54%	1.59%	#N/A	#N/A	1.51%	1.61%	1.57%	1.92%	1.87%	1.79%	1.63%
Winston	JT	1.15%	1.14%	1.11%	#N/A	#N/A	0.90%	0.94%	1.29%	1.22%	1.23%	1.19%	1.09%
Dunhill	BAT	1.23%	1.22%	1.19%	#N/A	#N/A	1.24%	1.27%	1.24%	1.60%	1.56%	1.49%	1.26%
Pall Mall	BAT	0.91%	0.89%	0.87%	#N/A	#N/A	0.83%	0.80%	1.18%	1.14%	1.12%	1.07%	0.98%
Marlboro	PMI	1.23%	1.22%	1.27%	#N/A	#N/A	1.24%	1.27%	1.24%	1.61%	1.57%	1.51%	1.26%
Real net revenue (SNT)													
Mevius	JT	42.05	46.46	50.47	#N/A	#N/A	54.45	58.45	76.48	65.65	65.29	65.44	66.41
Long Life	TTL	31.93	31.47	30.88	#N/A	#N/A	30.37	25.2	43.44	33.05	32.86	32.94	32.42
Davidoff	DB	47.12	51.44	50.47	#N/A	#N/A	54.45	58.45	48.15	65.65	65.29	65.44	66.41
Gentle	TTL	21.8	21.49	25.98	#N/A	#N/A	35.18	34.7	52.87	42.37	42.12	42.22	41.56
Mi-Ni	JT	62.31	61.43	65.16	#N/A	#N/A	73.71	82.2	71.76	88.95	88.45	88.65	87.26
Winston	JT	36.99	36.47	35.77	#N/A	#N/A	35.18	34.7	48.15	37.71	42.12	42.22	41.56
Dunhill	BAT	42.05	41.46	40.67	#N/A	#N/A	54.45	58.45	48.15	65.65	65.29	65.44	66.41
Pall Mall	BAT	21.8	21.49	21.08	#N/A	#N/A	25.55	25.2	43.44	33.05	32.86	32.94	32.42
Marlboro	PMI	42.05	41.46	45.57	#N/A	#N/A	54.45	58.45	48.15	51.68	51.39	51.51	50.7

Table 1. Relative income price and real net revenue of the most popular cigarette brands in Taiwan 2010-2021.

Results: The real net revenue per pack increased by approximately NT\$7 for most of the brands between 2016 and 2018, while a sharp decrease in affordability was observed between 2017 and 2018. Nonetheless, the economic growth in Taiwan has accelerated since 2019 and cigarettes have become more affordable (Table 1). Sales volumes shrank right after the 2017 tax increase (-18% in 2018); however, in 2020 they increased again with a year-to-year variation of +6%.

Conclusions: The major tobacco companies operating in Taiwan reacted to the 2017 tax hike with a significant increase of the nominal retail price of their brands, prioritizing higher net revenues over customers lost. In addition, the effect of that increase seems to have already vanished - the number of packs sold has been quite sta-

ble from 2018 to 2020 - and the economic situation has further benefited tobacco companies, since the nominal GDP per capita has accelerated with negative effects on cigarette affordability and, for the future, on smoking prevalence.

Funding: MOST109-2314-B-038-144, Taiwan Ministry of Science and Technology

OA30-419-11 Framework development of the Tobacco Endgame Hub (TEDH): a roadmap to eradicate 'TOBACCO USE' in India

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Background and challenges to implementation: A “tobacco endgame” is a strategy for achieving the ultimate agenda of moving beyond controlling tobacco “toward a tobacco-free future wherein commercial and non-commercial tobacco products would be phased out or their use and availability will be significantly restricted. The Resource Center for Tobacco Control, Postgraduate Institute of Medical Education and Research, Chandigarh in collaboration with the Union has established a Tobacco Endgame Hub (TED^H) with an objective to accelerate the efforts to end the tobacco epidemic in India. This paper presents the process of framework development of the tobacco endgame hub in India.

Intervention or response: The preparation of the endgame framework underwent two stages, that is, item generation and item reduction. The former involved extensive literature search, consensus among tobacco control experts using the Delphi technique and its validation. A national consultation of a coalition of experts for framework development of tobacco endgame hub in India was organized for item reduction.

Results/Impact: The establishment of hub led to the formation of a pool of 24 honorary advisory members (tobacco control experts). Based upon the review and expert's consensus, we zeroed in on five themes of the hub— About the Hub; Hub Resources; Research; Endgame Reporter; Support Gateway. The National Consultation of Coalition of Experts for framework Development of tobacco endgame hub was attended by over 50 tobacco control experts for item reduction.

The item reduction led to the selection of themes and subthemes of the hub, placement of items in the selected themes and development of a final framework of the hub.

Conclusions: TED^H could be effectively used by the researchers, program managers, academicians, and policy makers for seeking evidence-based information about global good practices toward the tobacco endgame.

It also provides technical support to the governmental

and non-governmental organizations by hosting various webinars, meetings, and workshops on tobacco endgame.

OA30-420-11 How big is the smoked tobacco litters problem in India: a state-level analysis by using NSSO and GATS-2 data

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Background: Tobacco usage is associated with dual burden: health and environment. The environmental burden of tobacco consumption and production is a lesser studied arena due to several reasons including funding and partnerships of tobacco industry with environmental organizations.

This study investigates the total waste generated from cigarette and bidi consumption in the Indian states by using two nationally representative datasets and primary data.

Design/Methods: Wastes generated from various brands of cigarettes and bidis were calculated based on collected packets from West Bengal. Cigarette wastes constitute, empty packets, cellophane wrappers, foils and butts while bidi wastes constitute, empty packets and butts. Weights of these wastes were measured using an electronic balance. Data from Global Adult Tobacco Survey (GATS-2) and National Sample Survey Office (NSSO) were used for computing statewide consumption of cigarettes and bidis. These were weighted by weights of waste products generated after consumption to compute the total wastes generated.

Results: Total cigarette waste generated in India as per NSSO is estimated to be 13013.8 tonnes. Based on NSSO estimates', Andhra Pradesh (including Telangana) produces highest cigarette wastes. As per GATS-2 data, West Bengal produces the most cigarette waste. The total cigarette waste generation in India as per GATS-2 estimates amounts to 38819.6 tonnes. NSSO estimates show Uttar Pradesh generating maximum waste from bidi consumption. While, GATS-2 data shows that West Bengal generates maximum waste from bidi consumption. Total wastes generated from bidis at the all India level are 56105.9 and 60509.8 tonnes respectively based on NSSO and GATS-2 estimates.

Conclusions: There lies a difference in quantities of waste generated estimates based on the two data sources. However, the figures reflect that a significant amount of waste is generated from cigarettes and bidis, highlighting the importance of strengthening the tobacco smoking control and cessation measures considering its overall impact by incorporating environmental burden.

OA30-421-118-city study: advertisements, promotions and display of tobacco products at points-of-sale in Pakistan

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Background: In 2020, the Government of Pakistan issued regulations that banned tobacco advertising, promotions, sponsorships (TAPS), and tobacco product display at all points-of-sale (POS). This study examined the presence of TAPS and the required tobacco warning signage at the POS, between November and December 2021, across 8 cities in Pakistan: Gilgit, Islamabad, Karachi, Lahore, Multan, Muzaffarabad, Peshawar, and Quetta.

Design/Methods: Gallup, a local firm, identified 15 neighborhoods in Karachi and 9 in the other cities, based on socio-economic status. Next, two hubs, a major intersection and a school, were shortlisted within each neighborhood. Observations were conducted at the first seven tobacco vendors identified by following a systematic walking protocol from these pre-determined hubs. Data collectors noted the presence of tobacco advertisements, tobacco product display, and the presence of health warning signage.

Results: A sample of N=1094 tobacco vendors were observed across the 8 cities. Nearly 21% (n=233) of vendors had a tobacco advertisement on the outside of the POS, while 8% (n=90) had them inside. Overall, 87% (n=948) of vendors displayed tobacco products at the POS. 92% (n=874) of these vendors had the products displayed such that they were accessible to minors and 56% (n=528) had them displayed next to candies/sweets. Only 9% (n=97) of the vendors had warning signage displayed; among these, 10% did not comply with the required specifications.

Conclusions: Compliance with the new TAPS provisions banning tobacco advertising and promotion at the POS is low. Tobacco products are commonly displayed and accessible to minors. Efforts are required to strengthen enforcement and improve compliance with the tobacco control policies in the country. This could include training enforcement officers and educating retail venue owners on the national tobacco control law, and regularly monitoring tobacco vendors to ensure compliance.

OA30-422-11 Exploring the challenges faced by bidi workers and their readiness to shift to alternative livelihood

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Background: WHO's Framework Convention on Tobacco Control (FCTC) article-17 regards the provision of support for economically viable alternative activities and article-18 on the health of persons. Women constitute a very high percentage of labour force in the bidi industry. Numerous studies reveal that 90% of bidi workers suffer from occupational health hazards. These health concerns and exploitative work conditions compel bidi workers to look for alternative livelihood.

The present study attempted to explore the challenges faced by bidi workers and their readiness to shift to alternative livelihood.

Design/Methods: A descriptive household based cross-sectional survey was carried out in Tirunelveli and Vellore districts of Tamil Nadu- India, where the production of bidi is considerably high. A total of 1000 bidi rollers aged above 18 years were surveyed using a structured interview schedule. Descriptive statistics, chi-square test and binary logistic regression were performed to find association between the variables and the determinants of willingness to shift to alternative jobs.

Results: The study revealed that majority of the bidi rollers (92.5%) were women. While 69.1% reported to suffer from musculoskeletal issues, 12.6% reported respiratory, eye problems and 20% experienced other issues such as tiredness, body ache, skin and postural problems. Of all, 64% of the bidi rollers expressed their willingness to shift to alternative livelihood. Age ($p=0.006$), marital status ($p=0.043$), education ($p<0.000$) and health issues ($p<0.000$) were significantly associated with willingness to shift. Education (OR=0.116; $p=0.023$), benefits received (OR=0.536; $p=0.001$) Health problems (OR=2.043; $p=0.012$) emerged as predictors of willingness to shift.

Conclusions: Majority of the bidi rollers experience some health hazards due to rolling bidi and want to shift to alternate livelihood. Creating awareness on occupational hazards of bidi rolling and providing adequate skill-based training for those willing to shift will aid in successful shifting to healthy alternative.

OA30-423-11 Effective implementation of ban on smoking in public places and exposure to second-hand smoke – compliance assessment for COTPA section 4 in five districts of Karnataka

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Background and challenges to implementation: As per WHO-Global Adult Tobacco Survey (GATS) 2016-17, in Karnataka, 22.8% of adults are consuming tobacco in one or the other forms. 8.8% Smokers. 23.9% of people are exposed to second-hand smoke at any public place.

. This study presents a compliance assessment with COTPA section-4 from 2013 to 2020 in Karnataka.

Intervention or response: This comparative study was done in five out of 30 districts of Karnataka State in India. The study investigators made a direct observation of public places in the five districts to assess the compliance of smoke-free rules by using a structured, pre-tested checklist.

Results/Impact: In 2013, out of the total 2773 public places observed for section 4, 24.6% had displayed section 4 signages. In 2020 out of the total 1549 public places observed in the five districts for section 4, 49.4% of public places have displayed section 4 signages i.e.24.8% increase in compliance. Rate of active smoking had been reduced from 36.2% to 11.15% and evidence of cigarettes butts was reduced from 41.70% to 14.45%. Smell of smoking evidence was reduced from 54.10% to 11.58%. Overall smoke-free rules compliance in selected five districts of Karnataka has been observed a significant increase. This result showed the effective implementation of the National Tobacco Control Program and the effective implementation and monitoring of smoke-free rules.

Conclusions: This study shows that high compliance of smoke-free rules could be achieved through successful implementation of The Cigarettes and Other Tobacco products with effective inter and intra-department coordination.

OA-31 Community-centred, rights-based and gender responsive TB care

OA31-424-11 MHealth campaign to drive TB care-seeking among employed men in Chennai (Tamil Nadu, India)

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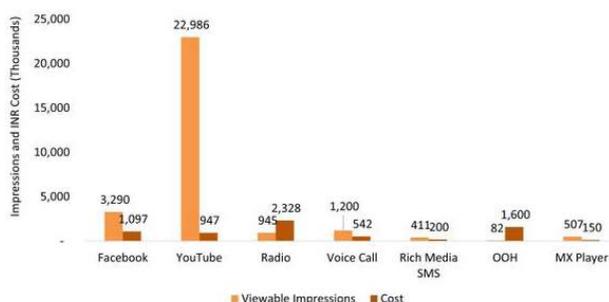
Background and challenges to implementation: Previous research identified that lower-income TB-symptomatic employed men of ages 36-60 in Chennai, India seek care at the lowest rates. We implemented an 8-month omni-channel digital-focused communication campaign aimed at this target group (TG) to cost-effectively trigger early care-seeking.

Intervention or response: The campaign employed behavioral messaging strategies to address six gaps in knowledge, attitudes, or behavior (KAB) identified in previous qualitative research. These included perceived invulnerability to early TB symptoms, preference for informal care, symptom normalization, expectation of monetary loss from care seeking, time constraints, and expectation of stigma.

Creatives in varied formats, including GIFs, images, text, audio and video, were disseminated on digital channels (Facebook, YouTube, rich media messages, outbound dialing, Gaana application, MX Player) and 'traditional' mass media channels (radio, bus shelters). Creatives were linked to interactive support tools including a WhatsApp chatbot, IVRS, website, and helpline. Key metrics like reach, link clicks, impressions, and views were collected from proprietary media reports such as Google Analytics and used to optimize the campaign.

Results/Impact: The campaign recorded 29.4 million viewable impressions ("reach") with an average engagement rate (ER) of 25.68%, with specific channels and messages driving performance. While collaterals on YouTube gathered 8 times the viewable impressions as Facebook (23 million), Facebook was almost twice as effective in triggering link clicks to support tools (380k). Video collaterals were effective on Facebook compared to static and GIF formats, with the lowest cost-per-click. The most successful overall collateral was the "TB Gaana song" music video, composed in a locally popular genre. Messaging around TB symptom recog-

nition saw the widest reach, while messaging aimed at preference for informal care garnered the largest number of clicks.



Conclusions: Cost by reach estimates suggest that digital campaigns may be effective in continuous TB communication, especially given limited healthcare resources and scope for low-cost experimentation and optimization.

OA31-425-11 Assessing the use of a Vietnamese stigma scale among people with drug-susceptible tuberculosis in Vietnam

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Background: Stigma is one of the significant barriers limiting accessibility and quality of tuberculosis (TB) services. To end TB stigma, we need to understand its prevalence and characteristics. This study aimed to assist stigma assessment in diverse groups of people with TB in Vietnam by evaluating the use of a drug-resistant (DR-) TB stigma scale on people with drug-susceptible (DS-) TB.

Design/Methods: A 14-item stigma scale and a visual analogue health-related quality of life (HRQoL) from the EQ-5D-5L scale were administered among 358 people with pulmonary DS-TB from both the public and private sectors between October 2020 to March 2022 in four cities of Vietnam. Surveys were conducted during the intensive phase. Data analysis included exploratory and confirmed factor analysis (EFA&CFA), internal consistency and construct validity assessments.

Results: EFA returned a four-factor model (guilt, social exclusion, physical isolation, blame). Internal consistency was moderate to good (Cronbach’s alpha 0.61-0.77). Within the “blame” factor, an item about the extent a

person feels they “deserve” to get TB was found to have low factor loading compared to the other items (0.4 vs. 0.9). Excluding this item increased Cronbach’s alpha of “blame” from 0.62 to 0.76. CFA showed satisfactory goodness-of-fit (Tucker&Lewis’ index=0.93, comparative fit index=0.95, root-mean-square error of approximation=0.05). Construct validity found a mild negative correlation with HRQoL ($r=-0.18$, $p=0.00$).

Factor (Cronbach's alpha)	Factor loading Item	Cronbach's alpha if item deleted
Physical isolation (0.61)	0.81 Even though I am not in the infectious period anymore, I still eat separately	0.46
	0.77 I don't sit close to my family members because I don't want to infect them	0.61
	0.64 My family ask me to sleep and eat separately for the duration of my treatment	0.56
Blame (0.62)	0.87 I got TB because I worked too hard	0.41
	0.88 People say that I got TB because of my job	0.75
	0.4 It was something that I did that caused me to get TB	0.76
Social exclusion (0.77)	0.65 Since being diagnosed, I feel unwanted when I attend social events	0.75
	0.79 I am expected to stay away from social activities	0.7
	0.81 People gossip about me and my disease	0.77
Guilt (0.77)	0.82 People stand or turn their head away from me when I am talking to them	0.69
	0.63 I have lost some of the joy in my life since being diagnosed	0.76
	0.81 I feel like I am a burden on my family	0.71
	0.86 I feel like I have let my community down	0.66
	0.14 I will be blamed if my acquaintance gets TB	0.75

Conclusions: This study identified a four-factor stigma scale and a negative correlation between stigma and HRQoL in people with DS-TB, which is similar to the original 14-item DR-TB stigma scale. However, an item measuring “blame” in TB stigma was suggested to be removed or wording adjusted to increase the validity of the scale when expanding the use of the scale to DS-TB groups. Further research with longitudinal design may ensure better psychometrics of the scale in measuring stigma over the course of TB treatment.

OA31-426-11 Developing a TB Champion Empowerment Index to measure power, agency and empowerment among TB-affected communities in India

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Background and challenges to implementation: Over the last five years, efforts to train & engage TB survivors from across India as TB Champions (TBCs) have been successful in establishing a cadre of community leaders who represent TB-affected communities. While trained TBCs supported people with TB and educated communities, an important outcome of this sustained engagement has been personal empowerment of the TBCs themselves.

Intervention or response: To quantify abstract experiences of individual and social power, a TB Champion Empowerment Index was developed by adopting a par-

ticipatory approach. A three-step process followed:

- i. Discussions with 30 TBCs around ideas of power and empowerment, with reflections of how their own power has evolved,
- ii. Translating, grouping & analysing statements to identify patterns, evolve themes and indicators, and develop a data collection tool with 10 thematic areas.
- iii. Piloting the tool to get self-reported responses from 55 TBCs & constructing an empowerment index.

Results/Impact: The TB Champion Empowerment Index is built with 10 statements and 3 'areas' of power: for individual or personal self, systemic self as a part of the TB ecosystem and social self as a part of family and community. Empowerment is measured at 3 levels with Level 1- Knowledge for self; Level 2: Knowledge for action and Level 3: Knowledge for sustainability and scores are assigned accordingly. The results of the pilot showed that 62% of TBCs were at Level 3 of empowerment, 36% at level 2 and only 1 TB Champion in Level 1 of empowerment.

Conclusions: For the very first time, an Index has been developed for measuring the empowerment of TB-affected communities. This initial attempt has quantified multi-faceted empowerment that measures key aspects including knowledge, strategic thinking, public speaking and problem-solving skills, income generation, inclusion in community, integration with networks and participation in the public health system.

OA31-427-11 The impact of civil society organizations in finding missed persons with TB disease among urban populations: experience from Central Uganda

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Background and challenges to implementation: In Uganda, about 16% of tuberculosis (TB) patients go undetected either because of missed opportunities at health facilities or failure to access information and diagnostic services by the community. Each undetected person with TB increases the risk of community spread. The WHO ENGAGE TB emphasizes integrating TB into the community work of Civil society Organizations (CSOs) and NGOs. The USAID Defeat TB project has since September 2018 been working with CSOs to provide TB services at the community level.

Intervention or response: In July 2018, the USAID Defeat TB project sub granted 10 CSOs to implement community-level TB interventions in 3 urban districts, with the objective of increasing TB case finding and improving TB treatment outcomes. Defeat TB and the district health teams built the capacity of CSOs through

didactic training, support supervision, and guidance on the use of standard operation procedures for community TB activities. By September 2018, the CSOs, in close collaboration with health facilities and community resources persons, started implementation community-level TB interventions to increase TB case finding such as TB sensitization and screening among close contacts of TB patients and high-risk populations. CSO led community-level TB activities, 162 community volunteers were established in the CSO operation locations to support TB activities.

Results/Impact: The number of TB patients notified from community CSO interventions increased from 3.4% (364) at 22 health facilities to 27.1% (2803) by end of PY4 (Oct 2020- Sep 2021). The number of identified TB patients increased during the intervention period compared to the preintervention period.

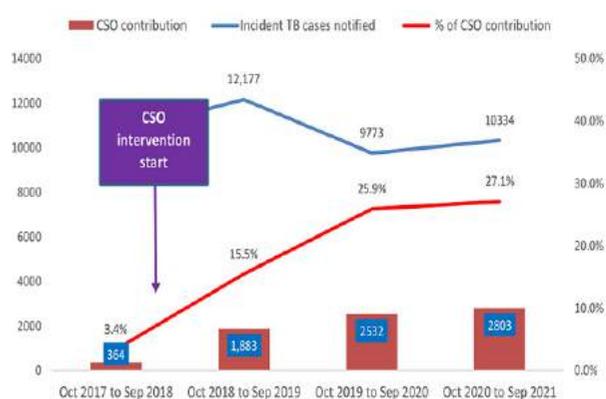


Figure. Urban TB case finding and CSO contribution.

Conclusions: Systematic engagement of CSOs in coordination of community TB services interventions presents a great opportunity for finding missed persons with TB disease. This establishes capacity of communities to end TB in urban and peri-urban settings in developing countries.

OA31-428-11 Success stories as an essential tool for TB awareness creation: a case study of KNCV TB Foundation Nigeria's social media page

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Background: KNCV Nigeria's communication team over the years has continued to expand and evolve its digital presence on numerous media platforms in a bid to put out content that is both authentic and message

driven. We present the results of the impact of communications using success stories during the 2022 world TB Day commemoration on the USAID funded TB LON 1 and 2 projects being implemented by KNCV Nigeria.

Design/Methods: A comparative assessment of the reach and response to success stories versus other organizational stories published in months leading up to the 2021 and 2022 World Tuberculosis Day (WTBD) commemorations by the communications team was conducted. Responses to these posts across KNCV Nigeria's social media handles were tracked and categorized under views, comments, and health-seeking questions requiring feedback. The period reviewed was February – March 2021 and 2022 respectively.

Results: In 2021 10 organizational stories published in the month leading to WTBD, 7817 persons were reached, and 249 people liked the posts with 14 comments and 4 inbox messages.

In 2022, 50 success stories were published on Facebook and Instagram in the month leading up to the WTBD, these posts reached 18,297 persons, 712 persons liked the stories with 68 comments and 15 inbox messages inquiring about TB test and treatment. This is 2.3 times more persons reached in 2021.

Conclusions: The results gathered from KNCV Nigeria's Social Media platforms, showed that there was significant increase in interaction and engagement to the success stories shared during the 2022 WTBD. For more impactful engagement, the use of success stories to communicate with the public on TB related information for awareness on TB is therefore recommended.

OA31-430-11 Engaging elected representatives (Panchyati Raj Member) on TB Free Village Initiative by TB Champions in Tamil Nadu India

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Background and challenges to implementation: Involving TB Survivors in TB elimination is one of the National TB strategies in India. The Accountability Leadership by Local communities for Inclusive, Enabling Services (ALLIES) Project is being implemented since Sep 2019 by REACH with the support of USAID in 4 states of India including 6 districts in Tamil Nadu. Trained TB Champions (TBC) act on sensitizing and engaging the elected members to improve the quality of care and support and to promote the stigma-free villages.

Intervention or response: Engaged through a systematic targeted approach of identification, sensitization, engagement, and availing the support for PwTB. Motivated TB Champions advocated the active PRI members through one-to-one intervention and accelerated their member's involvement in the TB-free initiative. Formal sensitization conducted to all the elected members with the support of District TB Officers. TB Champi-

ons shared their stories and highlighted their vital roles. TB-free village agenda is incorporated in all the Grama Shaba meetings. PRI members were involved in NTEP health camps and special events and promoted the inclusive and leveraging of community services.

Results/Impact: 75 TB Champions sensitized 479 PRI members in the last 6 months and 65 members of 63 panchayats engaged in awareness activities health camps and World TB Day. The TB Free village agenda was included in all the 63 panchayats and discussed during the Gram Sabha meetings and started functioning as local support groups for TB and health-related requirements. 24 PRI members directed support for Nutrition to 160 PwTBs and another 12 of them supported the nutrition from reference. PRI Members' involvement made a high impact in the community on ownership and close coordination with the TB program.

Conclusions: Effective engagement of PRI members by TBCs and involvement in every levels of TB elimination strategies is one of the accelerated pathways to achieve the elimination goal with community participation.

OA31-431-11 Quantifying stigma related to TB – results from a community based survey implemented by TB champions using the STOP TB Stigma Assessment Tool

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Background and challenges to implementation: Internalised or self-stigma among people with TB -the endorsement of negative beliefs and stereotypes along with secondary or anticipated stigma among family members is often a key determinant in the success of treatment, mental and emotional well-being of the person with TB. Anticipated stigma among community members and experienced stigma among those who meet and treat people with TB – health care providers, can lead to barriers in access to treatment. The STOP TB Stigma Assessment tool launched in March 2020 is designed to capture the multiple dimensions of stigma faced by a person with TB within her family, the community and the health providers she meets.

Intervention or response: The ALLIES (The Accountability Leadership by Local communities for Inclusive, Enabling Services) Project supported by USAID engaged TB Champions, trained TB Survivors to implement the tool in 12 districts across the 4 ALLIES states of Chhattisgarh, Jharkhand, Odisha and Tamilnadu. The assessment was rolled out in a span of 12 weeks including training of TB Champions, the data was entered and

analysed using STOP TB guidelines.

Results/Impact: The stigma scores for each category of respondent was calculated following the methodology outlined by STOP TB in Stigma Measurement Toolkit.

Type of Stigma	Stakeholder	Sample size	Range of Stigma Score	Mean Stigma Score	Equivalent prevalence
Internalized or Self Stigma	People with TB	281	0-48	16.3	34%
Anticipated or Perceived Stigma	Family Members	541	0-40	15	37.5%
Secondary Stigma	Community Members	577	0-44	19.5	44.3%
Enacted or Experienced Stigma	Healthcare workers	86	0-36	16.4	45.5%

Our Survey finds 2 out of 5 health care workers who treat people with TB or live in communities affected by TB experience or anticipate stigma related to TB. While every 1 out of 3 person with TB or their family member experience self or perceived stigma.

Conclusions: The TB Champions have emerged with skills to identify and interpret a measure of stigma through implementation of the assessment. They acted on the results to address the identified stigma through interpersonal counselling activities, community awareness events and targeted sensitisations for vulnerable community members.

OA-32 HIV and co-morbidities and interaction with TB

OA32-432-11 HIV remains responsible for most tuberculosis in Blantyre, Malawi, despite successful antiretroviral therapy scale-up: population attributable fractions from enhanced surveillance and a community prevalence survey

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Background: Successful antiretroviral therapy (ART) scale-up is driving reductions in HIV-associated tuberculosis (TB) in Africa. Here, we combine two city-wide data sources to estimate population attributable fractions (PAF) for key TB risk factors in Blantyre, Malawi. **Design/Methods:** "Cases" were all registering tuberculosis patients in Blantyre 2015-2021, who since 2015 have been interviewed and tested for HIV as part of an enhanced surveillance programme. Cross-sectional data on risk-factors amongst TB-negative "controls" were provided by a city-wide 2019-20 adult TB/HIV prevalence survey. We used multivariable logistic regression to estimate adjusted odds ratios for TB risk factors, and estimated PAFs using Miettinen's formula.

Results: Between 2015-2021, 11,250 adults registered for TB treatment in Blantyre. 7,443 (64.8%) had HIV, of whom 6,285 (84.4%) were already on ART at registration. In the separate community prevalence survey, 1,435/13,664 (10.5%) TB-negative community members were HIV-positive, with 1,370 (95.5%) on ART.

The aOR of TB was 17.2 (95% CI 14.8-20.1) for people living with HIV (PLHIV) taking ART; and 30.9 (19.8-51.5) for PLHIV not taking ART. Male sex (aOR 3.32, 95% CI 2.94-3.75), older age (aOR 1.16/5 years, 95% CI 1.10-1.22), ever-smoking (aOR 1.75, 95% CI 1.50-2.05) and TB household contact (aOR 7.91, 95% CI 5.12-12.8) were also associated with TB.

An estimated 62.6% of TB was attributable to HIV. This PAF was higher for women than men (68.4% vs 58.4%) and decreased with time (66.7% in 2015-2016 vs 56.9% in 2019-2021).

Overall, just 10.0% of population risk was attributable to untreated HIV, compared to 53.7% to HIV treated with ART.

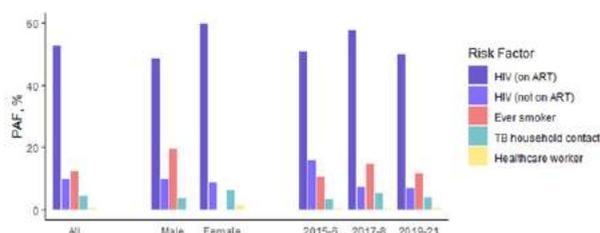


Figure. Population fraction of TB attributable to selected modifiable risk factors, by sex and time.

Conclusions: Despite successful ART scale-up, the majority of TB in this population remains attributable to HIV, predominantly amongst people who are taking ART. Ending TB requires targeted TB screening and preventive therapy for PLHIV, alongside adherence support and treatment monitoring to reach 95:95:95 targets.

OA32-433-11 Exploring the impact of participant-related factors on side effect profile and adherence to TB treatment

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Background: Alcohol use and HIV are risk factors for active TB and associated with poor treatment outcomes. We investigated the impact of alcohol use, HIV, and other participant demographics and comorbidities on the incidence of symptoms during TB treatment, and we assessed the impact of symptoms on treatment adherence.

Design/Methods: We analyzed data from 276 RIF-susceptible-TB participants from the TRUST cohort in Worcester, South Africa. We administered a monthly, interview-led symptoms questionnaire over the 6-month treatment period. Forty-three symptoms on treatment (SoT) were evaluated and grouped into 4 systems-based categories: dermatologic, gastrointestinal, musculoskeletal, and neurologic.

We used multivariable regression to identify associations between participant age, sex, HIV status, level of alcohol use (using phosphatidylethanol biomarker), and co-morbidities with SoT. To assess for immune reconstitution, participants with CD4<200 were stratified by whether they initiated antiretroviral therapy (ART) during or prior to the study.

A second multivariable regression model identified associations between SoT and directly observed treatment adherence, defined as a binomial variable (threshold of 80%).

Results: 53.6% reported at least one SoT; the most common were itching (14.9%), rash (13.8%), and headache (13.0%). HIV status was not significantly associated with SoT. Recent ART initiation was associated with dermatologic SoT, older age with musculoskeletal SoT, and female sex with neurologic SoT. The most common comorbidities were diabetes and hypertension, with the presence of at least one comorbidity associated with increased risk of any SoT (Table 1).

42.0% of participants had >80% adherence. Heavy alcohol use (PEth>200 ng/mL) was associated with <80% adherence (OR=0.45, p=0.019). Among those with low alcohol use (PEth<20 ng/mL), adherence was not associated with SoT.

	Odds Ratio	95% CI	P-value
CD4<200 with recent ART initiation*	2.98	1.06 – 8.38	0.039
Older age**	1.04	1.01 – 1.07	0.005
Female sex***	2.03	1.10 – 3.74	0.023
Presence of at least 1 comorbidity****	2.27	1.28 – 4.03	0.005

Legend: *Associated with dermatologic SoT, **Associated with musculoskeletal SoT, ***Associated with neurologic SoT, ****Associated with any SoT

Table 1: Variables significantly associated with SoT in multivariable regression.

Conclusions: SoT were frequently reported, and participants with comorbidities had higher odds of SoT. Heavy alcohol use, rather than SoT, was associated with lower adherence, suggesting the need for targeted interventions to improve treatment outcomes within this group.

OA32-434-11 Cardiac dysfunction in active pulmonary tuberculosis: double trouble! timely workup have positive outcome, multicentric study of 800 cases in tertiary care setting in India

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Background: Although cardiac involvement is extremely rare in tuberculosis, cardiac dysfunction is not uncommon.

Design/Methods: Prospective observational and interventional study conducted during July 2014 to December 2021, included 800 cases of active pulmonary tuberculosis confirmed microscopically or with Gene Xpert MTB/RIF in respiratory specimens like sputum/induced sputum and bronchoscopy guided bronchial wash or bronchoalveolar lavage whenever necessary.

Cases with known risk factor for cardiac disease and taking cardiac medicines, and cases with pericardial effusion were excluded from study. Disproportionate tachycardia and tachypnea with or without shock and

hypoxemia were key entry point criteria in this study. Chest radiograph, pulse oximetry, ECG, Sputum examination, cardiac enzymes, serum cortisol and Echocardiography is done in all study cases during enrollment, at 2 months and 6 months of treatment with Anti-tuberculosis medicines. Statistical analysis was carried out by chi-square test.

Results: In 800 cases with active pulmonary TB, cardiac dysfunction was documented in 26% cases, females were 44%; and 56% cases were having age>50 years. Echocardiography abnormality were documented as global hypokinesia in 62% cases, depressed left ventricular systolic and diastolic function in 44% & 28% cases respectively, dilated right atrium and right ventricle in 32% cases, and pulmonary hypertension in 6% cases. Serum cortisol level is significantly lower in cases with cardiac dysfunction (p<0.00001).

Hypoxemia has significant association with right and left heart dysfunction (p<0.00001). Cachexia, anemia and Hypoalbuminemia was documented to have significant association with cardiac dysfunction (p<0.00001). Treatment outcome shows significant improvement in cardiac function (p<0.00001). Coronary angiography is not showing significant coronary artery lesions and CT pulmonary angiography not showing pulmonary embolism.

Conclusions: Cardiac dysfunction in active pulmonary tuberculosis is underestimated and less evaluated routinely; disproportionate tachycardia and tachypnea with or without shock are the earliest clinical indicators. 'Global hypokinesia' as a predominant cardiac dysfunction, and right or left heart dysfunction depends on with or without hypoxemia respectively.

OA32-436-11 HIV viral suppression at RR-TB treatment initiation: factors driving the need for enhanced adherence support and viral load monitoring in South Africa

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Background: Co-infection with rifampicin-resistant tuberculosis (RR-TB) and HIV is common in South Africa (SA). A detectable viral load (VL) at RR-TB treatment initiation occurs frequently and may be a hallmark for poor RR-TB treatment adherence. Yet SA guidelines limit the frequency of VL monitoring and justification for drawing VL labs outside of these guidelines may be required. Understanding correlates of a detectable HIV viral load may help clinicians identify those at higher risk and facilitate VL screening at treatment initiation.

Design/Methods: We completed a nested cross-sectional analysis within a cluster randomized trial of RR-TB treatment. Individuals known to be living with HIV and

newly diagnosed with RR-TB were included if they either had a VL result available or were known to have a detectable VL due to not taking antiretroviral therapy (ART). Baseline demographic and medical characteristics were compared using descriptive statistics. Multivariable logistic regression with backward selection identified predictors of HIV viral suppression, defined as less than 400 copies per milliliter.

Results: Among 961 participants eligible based on the above criteria, 611 (63.6%) had an unsuppressed VL. The mean age was 37.3 years, 46.3% female, 52.9% taking ART. Results are shown in Table 1.

In multivariable analysis, older age (aOR 1.02, 95% CI: 1.00-1.04), higher baseline CD4 count (aOR 1.01, 95% CI: 1.00-1.01), and taking ART (aOR 16.90, 95% CI: 11.16-25.59) were associated with increased odds of HIV viral suppression. Among 508 individuals taking ART, patients presenting on second-line ART, specifically boosted lopinavir regimens, had 69% lower odds of viral suppression (aOR 0.31, 95% CI: 0.13-0.69) compared to those taking efavirenz-based regimens.

	HIV viral suppression a(OR)	95% CI
Age	1.02*	1.00 - 1.04
Baseline CD4	1.01***	1.00 - 1.01
Taking ART (ref. not taking ART)	16.90***	11.16 - 25.59
Among people actively taking ART at RR-TB baseline (N=508)		
Antiretroviral regimen nevirapine-based (ref. efavirenz-based)	1.75	0.77 - 3.97
Antiretroviral regimen ritonavir-boosted lopinavir-based	0.31**	0.13 - 0.69
Other or Unknown antiretroviral regimen	1.01	0.37 - 2.78

Legend: RR-TB, rifampicin-resistant tuberculosis; a(OR), adjusted odds ratio; CI, confidence interval; ref., reference; * p<0.05; ** p<0.01; *** p<0.001. Adjusted for housing location (rural, urban, or township).

Table 1. Predictors of HIV viral suppression at RR-TB baseline among people living with HIV (N=961)

Conclusions: Identifying those at risk for a detectable viral load is critically important for early intervention. Clinicians with limited VL and adherence information may use the ART regimen to identify those who require more frequent VL monitoring, adherence counseling and closer follow-up.

OA32-437-11 Mortality and associated factors in HIV infected children with tuberculosis assessed using the PAANTHER TB treatment decision score in high tuberculosis incidence settings

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Background: Tuberculosis (TB) is the leading cause of death in children living with HIV (CLWH). Treatment decision algorithms that allow prompt initiation of anti-tuberculosis treatment (ATT) could contribute to reduction in early mortality from TB.

We evaluated the incidence of mortality and its associated risk factors in CLWH with TB screened using the PAANTHER score.

Design/Methods: CLWH aged 1 month to 14 years with presumptive TB were enrolled from 7 hospitals across 4 African countries. At inclusion, children were subjected to the PAANTHER algorithm; a score ≥100 was diagnostic of TB and prompt ATT.

Clinical assessments included TB symptoms, contact history, Xpert Ultra testing on respiratory and stool samples, CXR and blood sampling. Children were followed up for 6 months.

We assessed mortality rate at 2 month and identified associated factors using Cox proportional hazard models.

Results: Of 277 children enrolled in the study, 210 (75.8%) had a PAANTHER score ≥100 and an additional 12 (4.3%) with a score <100 were diagnosed with TB and treated.

Of those 222 children with TB (107 (48.2%) males, median age 5 years (IQR: 1.9-9.7), haemoglobin 9.8 g/L (IQR: 8.4-11.8), ALT 25 U/L (IQR: 14-47), CD4% 21.0 (IQR: 10.2-29.9), 110 (47.3%) ART naïve, duration on ART 22.8 months (IQR: 6.68-53.6)), 22 tested positive on Ultra performed on respiratory samples or stools and 194 (87.4%) initiated ATT at a median of 1 day (IQR: 0-4). At 2 months there were 28 (12.6%) deaths. Factors associated with mortality are presented in the table.

	Reference	Hazard ratio (95% CI) univariate analysis	P-value	Hazard ratio (95% CI) multivariate analysis (n=168)	P-value
Age <5 years (n=218)	>5years	1.99 [0.92; 4.32]	0.08		
Sex Male (n=218)	Female	1.77 [0.83; 3.78]	0.14		
Not initiated on ATT (n=218)	Received ATT	0.43 [0.15; 1.21]	0.11 ^a		
Xpert positive (n=215)	Xpert negative	1.24 [0.37; 4.13]	0.72		
CXR military features (n=209)	Absence of military	0.97 [0.29; 3.24]	0.96		
Hb <9 g/dL (n=204)	>9 g/dL	5.02 [2.18; 11.57]	<0.01	5.86 [2.41; 14.27]	<0.01 ^a
ALT ≥60 U/L (n=193)	<60 U/L	1.36 [0.54; 3.41]	0.51		
Severe immunodepression (WHO staging) (n=170)	All others	1.82 [0.82; 4.07]	0.14		
ART naïve (n=218)	On ART	0.83 [0.40; 1.75]	0.63		

Table 1: Factors associated with mortality in CLWH diagnosed with tuberculosis

Conclusions: Despite prompt access to TB treatment in most children, mortality remained high at 2 months in this vulnerable group and may require other targeted interventions. A low Haemoglobin count (Hb < 9g/dL) was the only independent predictor of death in children diagnosed with TB.

OA32-438-11 HbA1c trajectories and their association with treatment outcomes among new pulmonary tuberculosis cases in Pune, India. A prospective cohort study

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Background: Transient hyperglycemia is commonly seen during tuberculosis (TB) treatment, yet its association with treatment outcomes is unclear. Our objective was to study the effect of transient hyperglycemia on TB treatment outcomes.

Design/Methods: A prospective cohort study was conducted among adults with new drug-sensitive pulmonary tuberculosis. Patients were recruited at TB treatment initiation from B.J. Govt. Medical College (BJGMC) and Sassoon Hospital and D.Y. Patil Hospital (DYPH) in Pune, India and prospectively evaluated for 18 months. HbA1c was measured at baseline and three months of treatment.

The primary exposure, HbA1c trajectory, was categorized as - No hyperglycemia: HbA1c < 6.5% at baseline and three-months; Persistent hyperglycemia: HbA1c ≥ 6.5% at baseline and three-months; Transient hyperglycemia: HbA1c ≥ 6.5% at baseline and <6.5% at three-months.

The primary outcome was a composite unfavourable treatment outcome of failure, recurrence, and all-cause mortality. Multivariable Poisson regression adjusting for age, sex, education, substance use, comorbidity, BMI, TB treatment regimen, and diabetes treatment was used to measure the association between HbA1c trajectories and unfavourable outcome.

Results: Of the 587 participants, 443 (76%) had no hyperglycemia, 118 (20%) had persistent hyperglycemia, and 26 (4%) had transient hyperglycemia. The incidence of unfavourable outcome was 4.95 /1000 person-weeks in patients with no hyperglycemia; 3.24/1000 person-weeks /1000 in those with persistent hyperglycemia and 9.21/1000 person-weeks in those with transient hyperglycemia. Participants with transient hyperglycemia were twice as likely to have an unfavourable outcome compared to those with no hyperglycemia. [aIRR=2.07,95% CI (1.04-4.15)].

Though there was a qualitative shift in the effect of persistent hyperglycemia on unfavourable outcome from an unadjusted IRR of 0.65 to an adjusted IRR of 1.64, this association was not statistically significant [aIRR=1.64,95% CI (0.71-3.79)].

Conclusions: TB patients with transient hyperglycemia have a high risk of unfavourable TB outcome and may benefit from early diabetes treatment initiation.

OA-33 Child and host and community

OA33-439-11 Acceptability of decentralizing childhood TB diagnosis at district level: experience and perceptions from health care workers in sub-Saharan Africa and South East Asia

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Background: Decentralization of childhood TB diagnosis may increase early detection and treatment in high TB-burden countries, but could be challenging for overburdened health care workers (HCW) in Primary Health Centres (PHC) and District Hospitals (DH).

Design/Methods: Within the TB-Speed Decentralization study (NCT04038632), two health districts of Cambodia, Cameroon, Cote d'Ivoire, Mozambique, Sierra Leone, and Uganda implemented innovative childhood TB diagnostic interventions including systematic screening, naso-pharyngeal aspiration (NPA), stool sampling, Xpert Ultra testing, and digital Chest-X-Ray (CXR) reports, either at PHC-level, or at DH-level with referral of children with presumptive TB from PHCs. We investigated the experience and perceptions of HCWs in delivering the interventions in 2020-21 using individual semi-structured interviews. Data was analysed using the Theoretical Framework of Acceptability, capturing attitudes, understanding, burden and perceived effectiveness of the interventions.

Results: According to HCWs (n=130, 54.6% female, median age 36 years, 52.3% nurses, 72.3% PHC-based), systematic screening improved childhood TB awareness. Although increasing workload, it was perceived as beneficial especially when presumptive TB children could be managed onsite. Referral to DH was experienced as burdensome: parents required referral counselling, faced time and cost barriers; communication between HCWs was suboptimal. Most HCWs, although initially

inexperienced, shared satisfaction and confidence in performing NPA, despite procedure duration, need to involve parents/colleagues and discomfort for children. HCWs shared positive attitudes towards stool sampling but were frustrated by parents delaying collection due to cultural practices, transport and distance challenges. Ultra testing, conducted by nurses or laboratory technicians, was perceived as providing quality results and services, contributing to diagnosis. HCWs valued CXR, however complained that technical and network problems limited access to digital reports.

Themes	Quotes
Xpert Ultra	"Some of the clinicians got the knowledge of how to identify those children who may be having TB. Others, at least instead of misdiagnosing them for other diseases, they have been able to diagnose using the Gene Xpert method." (Uganda, laboratory technician, DH, female)
Referral	"At the general hospital there are crowds of people, so always we have them (parents and presumptive TB children) accompanied by one of our collaborators, to be able to locate them. Otherwise, when you tell them to go there themselves, they will go and sit in the hospital until they last. (...) There are even difficulties, but I always take one of my collaborators, parents must be supported" (Côte d'Ivoire, nurse, PHC, male).

Conclusions: HCWs at DH and PHC-levels perceived and experienced decentralized childhood TB diagnosis as acceptable. Implementation however could be hampered by feasibility issues, and calls for innovative referral mechanisms for patients, samples and CXR.

OA33-440-11 Effects of integrating pediatric TB services into child health care on treatment outcomes: results of the INPUT stepped-wedge cluster-randomized study

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Background: Under-diagnosis of TB in children is a critical gap to address. The INPUT study is a stepped-wedge cluster-randomized study assessing the effect of integrating TB services into child health care services on TB case detection and treatment outcomes among under-five children.

Design/Methods: We compared the standard-of-care (SOC) in which pediatric TB care is provided in a vertical approach, with the Catalyzing Pediatric TB Innovations (CaP-TB) intervention in which pediatric TB care was integrated in all child health services. Twelve clusters in

Cameroon and Kenya started the study under the SOC and transitioned to the intervention at randomly assigned times from May 2019-March 2021. We obtained parental consent to enroll children with presumptive TB based on symptom screening and monitored them through diagnosis and treatment. We compared the proportion of favorable TB treatment outcome during SOC and intervention, accounting for secular trends and the clustering within facilities.

Results: We enrolled 736 children as TB presumptive with 153 (21%) diagnosed with TB, mean age was 1.5 years (SD 1.3). Respectively, 89% (136/153) and 11% (17/153) were diagnosed clinically/radiologically and bacteriologically-confirmed. All diagnosed children were initiated on treatment, a median of 9.7(IQR:2.7-26.8) weeks after the onset of symptoms during the SOC compared to 6.3(IQR:3.1-14.3) weeks during CaP-TB (table).

The proportion with a favorable WHO treatment outcome was 82% (65/79) and case fatality rate was 8% (6/79) during the SOC compared to 92% (68/74) and 3% (2/74) respectively during the intervention. After adjusting for country, clustering and secular trends and country, the risk ratio of a favorable treatment outcome associated with CaP-TB was 1.39 (0.01-216.70), $P=0.56$.

	Total (N=153)		Cameroon (N=35)		Kenya (N=118)	
	Standard-of-care N=79	Intervention N=74	Standard-of-care N=2	Intervention N=33	Standard-of-care N=77	Intervention N=41
	n or median (% or IQR)					
Time between symptom onset and treatment initiation (weeks)	9.7 (2.7-26.8)	6.3 (3.1-14.3)	28.1 (20.9-35.4)	5.6 (3.0-11.1)	9.3 (2.6-26.1)	7.7 (4.0-25.0)
Treatment outcome						
Cured	6 (7.6%)	4 (5.4%)	0	4 (12.1%)	6 (7.8%)	0
Treatment completed	59 (74.7%)	64 (86.5%)	2 (100%)	24 (72.7%)	57 (74.0%)	40 (97.6%)
Died	6 (7.6%)	2 (2.7%)	0	2 (6.1%)	6 (7.8%)	0
Lost to follow-up	4 (5.1%)	3 (4.1%)	0	2 (6.1%)	4 (5.2%)	1 (2.4%)
Not evaluated	4 (5.1%)	1 (1.3%)	0	1 (3.0%)	4 (5.2%)	0
WHO-defined favorable treatment outcome (cured or treatment completed)	65 (82.3%)	68 (91.9%)	2 (100%)	28 (84.8%)	63 (81.8%)	40 (97.6%)

Table. Treatment outcomes by study phase and country.

Conclusions: We observed a clinically important improvement in treatment outcomes during CaP-TB with almost two-third reduction in case fatality. These results may be a consequence of the more timely TB diagnosis and earlier treatment initiation allowed by the intensified pediatric TB case finding.

OA33-441-11 Tuberculosis prevalence and clinical characteristics in children under 5 years hospitalized with severe acute malnutrition in Zambia and Uganda

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Background: Children with severe acute malnutrition (SAM) are more likely to develop TB once exposed and those with TB have an increased risk of death. Diagnosis of TB remains difficult in this vulnerable population. We assessed the prevalence and diagnostic accuracy of TB tests and clinical features in young children hospitalized with SAM.

Design/Methods: We enrolled children aged <5 years hospitalized with SAM in Zambia and in Uganda (November 2019 - December 2021). Children underwent tuberculosis symptom screening and contact history assessment, clinical examination, C-reactive protein, full blood count for monocyte-lymphocyte ratio, chest X-ray, abdominal ultrasound, Xpert MTB/RIF Ultra (respiratory and stool samples) and culture (respiratory sample). They were followed-up for 6 months. An expert committee reviewed TB cases and causes of death.

TB was defined as confirmed and unconfirmed using the 2015 updated Clinical Case Definition for Intrathoracic Tuberculosis in Children. We assessed TB prevalence and diagnostic accuracy of tests and clinical features for TB diagnosis.

Results: Of 603 children enrolled (335 in Uganda, 268 in Zambia, 345 (57.2%) male, median age 15 (IQR: 10-20) months, median weight-for-height Z score -3.26 (IQR: -4.09; -2.27), 64 (10.6%) HIV-infected), 79 (13.1%) were diagnosed with TB at baseline (50 confirmed TB). Additionally, 40 (6.63%) TB were secondarily diagnosed either during follow-up or post-mortem (13 confirmed TB) for a prevalence of 19.7% (119/603). Overall, 101 (16.7%) children were initiated on TB treatment at a median of 6 (IQR: 3-11) days after inclusion. Sensitivity and specificity of TB tests and clinical features for TB diagnosis are shown in the Table.

	Sensitivity (n/N*; %; 95%CI)			Specificity (n/N**; %; 95%CI)		
	*Total children with TB among N			**Total children without TB among N		
Prolonged cough > 2 weeks (N=592)	35/119	29.4	0.22-0.38	409/473	86.5	0.83-0.89
Prolonged fever > 2 weeks (N=592)	23/119	19.3	0.13-0.27	427/473	90.3	0.87-0.93
Xpert Ultra positive (N=588)	41/119	34.4	0.27-0.43	468/469	99.8	0.99-1.00
CRP > 2.5 mg/L (N=482)	41/95	43.2	0.34-0.53	231/387	59.7	0.55-0.64
Monocyte-lymphocyte ratio > 0.378 (N=484)	15/100	15.0	0.09-0.23	347/384	90.4	0.87-0.93
Alveolar opacities on CXR (N=567)	54/118	45.8	0.37-0.55	356/449	79.3	0.75-0.83
Miliary features on CXR (N=567)	5/118	4.2	0.02-0.10	447/449	99.6	0.98-1.00
Lymphadenopathies on CXR (N=567)	51/118	43.2	0.35-0.52	347/449	77.3	0.73-0.81
Lymphadenopathies on abdominal ultrasound (N=556)	16/114	14.0	0.09-0.22	426/442	96.4	0.94-0.98

Conclusions: Overall, TB prevalence was high among children hospitalized with SAM. Tests and clinical features had poor sensitivity for TB diagnosis, but high specificity overall except for CRP, alveolar opacities and lymphadenopathies on CXR, and should be combined in a diagnostic score specifically designed for this population.

OA33-442-11 Effect of dysglycemia on urinary lipid mediator profiles in persons with pulmonary tuberculosis

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Background: Oxidized lipid mediators such as eicosanoids play a central role in the inflammatory response associated with tuberculosis (TB) pathogenesis. However, the associations between diabetes mellitus (DM)-related changes in lipid mediators and clearance of *M. tuberculosis* (Mtb) among persons on anti-TB treatment (ATT) are unknown. Quantification of urinary eicosanoid metabolites can provide insights into the circulating lipid mediators associated with TB treatment response.

Design/Methods: We conducted a multi-site prospective study among adults with drug-sensitive pulmonary TB and controls without active TB; both groups included persons with or without dysglycemia (DM or pre-DM) at baseline according to baseline HbA1c levels. Participants were enrolled from RePORT-Brazil (Salvador site) and RePORT-South Africa (Durban site) and stratified according to TB status and baseline glycated hemoglobin levels:

- TB-dysglycemia (n=69);
- TB-normoglycemia (n=64);
- Non-TB/dysglycemia (n=31);
- Non-TB/non-dysglycemia (n=29).

We evaluated the following urinary eicosanoid metabolites:

11 α -hydroxy-9,15-dioxo-2,3,4,5-tetranor-prostane-1,20-dioic acid (major urinary metabolite of prostaglandin E2, PGE-M), tetranor-PGE₁ (metabolite of PGE2, TN-E), 9 α -hydroxy-11,15-dioxo-2,3,4,5-tetranor-prostane-1,20-dioic acid (metabolite of PGD2, PGD-M), 11-dehydro-thromboxane B2 (11dTxB2), 2,3-dinor-6-keto-PGF₁ α (prostaglandin I metabolite, PGI-M), and leukotriene E4 (LTE₄).

Comparisons between the study groups were performed before ATT and 2 and 6 months after initiating therapy.

Results: PGE-M and LTE₄ values were consistently higher at all three time-points in the TB-dysglycemia group compared to the other groups ($p < 0.001$). Additionally, there was a significant decrease in PGI-M and LTE₄ levels from baseline to month 6 in the TB-dysglycemia and TB-normoglycemia groups.

Finally, TB-dysglycemia was independently associated with increased concentrations of PGD-M, PGI-M, and LTE₄ at baseline in a multivariable model adjusting for age, sex, BMI, and study site. These associations were not affected by HIV status.

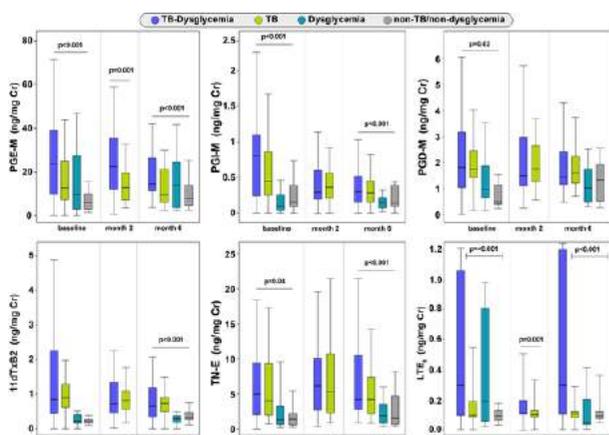


Figure 1. Comparison of the distribution of urinary eicosanoids between the study groups. Box plot depicting the distribution of eicosanoids (median and interquartile range) among TB-dysglycemia, TB, euglycemic patients and non-TB/normo-dysglycemia individuals at each timepoint. Groups were compared using Kruskal-Wallis (for four groups) and Mann-Whitney tests (for two groups). Individuals without TB (Dysglycemia and non-TB/normo-dysglycemia groups) had only two visits (baseline and month 6). Abbreviations: TB: tuberculosis, PGE-M: major urinary PGE2 metabolite, PGI-M: major urinary PGG2 metabolite, PGD-M: 2,3-dihydro-6-oxo-PGF1 α (PGI2 Metabolite), 11-LtdiB2: 11-dehydro-lipoic-acid-carboxylic acid B2 (TB2 urinary metabolite), TN-E: tetranor-PGE1 (urinary PGE2 metabolite), LTE4: Leukotriene E4.

Figure 1.

Conclusions: The urinary eicosanoid metabolites PGD-M, PGI-M, and LTE₄ are potential biomarkers of TB treatment outcomes, including among persons with dysglycemia, larger studies should evaluate possible associations between these eicosanoid urinary levels and TB treatment outcomes.

OA33-443-11 Assessing the variations of *M. tuberculosis*-induced IFN- γ responses in HIV-negative pregnant women

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Background: Pregnancy triggers an alteration of the immune functions and increases the risk of developing the active tuberculosis (TB) symptoms in exposed women. The effect of pregnancy on the *Mycobacterium tuberculosis*-specific immune responses used for most of the TB immunodiagnostic assays is not well documented. Here we investigated the changes in the *M. tuberculosis*-specific IFN- γ production in age-matched pregnant and non-pregnant women according to their TB exposition status.

Design/Methods: We conducted a prospective cohort study on HIV-seronegative pregnant and non-pregnant women with compatible pulmonary TB symptoms addressed to TB healthcare facilities in Antananarivo, Madagascar.

Active pulmonary TB was bacteriologically assessed with culture from sputum samples. Clinical data and blood samples were collected at inclusion and after 6 months of follow-up for each individual included.

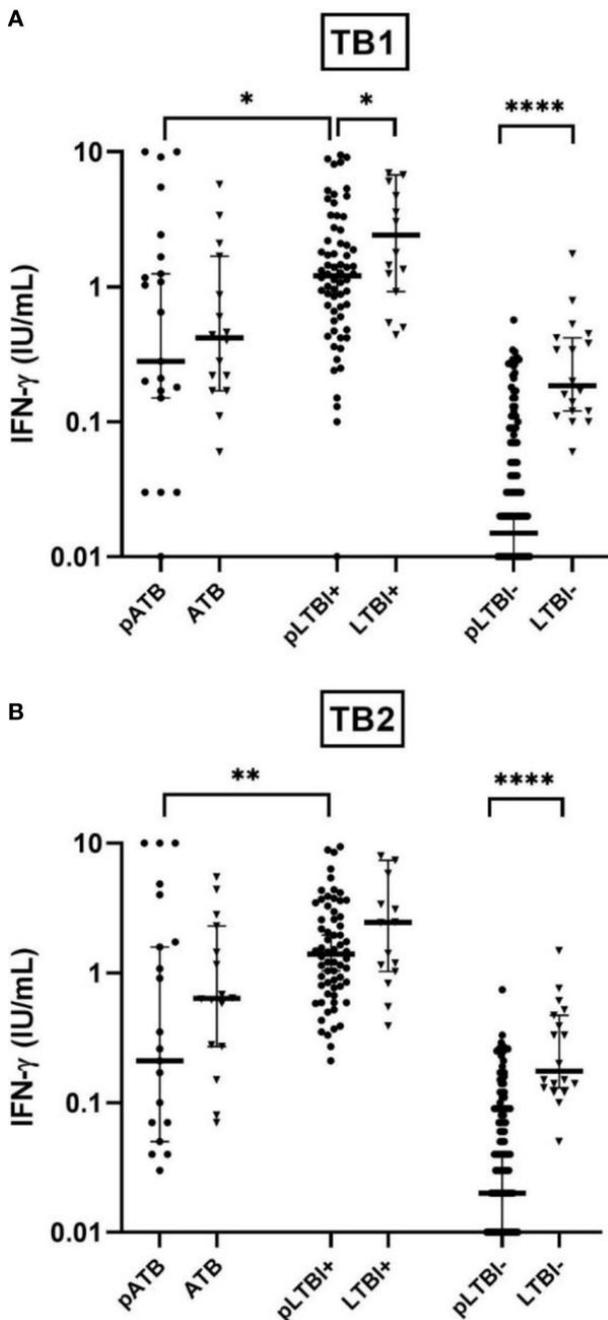
Whole blood samples were stimulated with QuantiFERON TB-Gold Plus (QFT-P) assay antigens. Plasma IFN- γ concentrations were then assessed by ELISA.

Results: A total of 284 women were investigated for the study including 209 pregnant women without confirmed TB (pNTB), 24 pregnant women with bacteriologically confirmed active TB (pATB), 16 non-pregnant women with active TB (ATB), and 35 non-pregnant healthy donors (HC).

At inclusion, IFN- γ responses are lower in the pregnant women compared to their age-matched non-pregnant counterparts and independently of their TB status.

After 6 months of follow-up, the *M. tuberculosis*-specific IFN- γ responses return to their baseline concentrations except for the pregnant women treated for TB for which none of the QFT-P positive reversed to negative (0%, 0/10) at the end of their TB treatment.

Conclusions: Our findings support the concept of specific immune priorities characterized by a concomitant reduction in inflammatory immunity during pregnancy and corroborate the important role of activating the *M. tuberculosis*-specific immune responses to control the infection when the pregnant women are exposed to the pathogen.



OA33-444-11 Estimating the prevalence of catastrophic costs before and during treatment of adults with tuberculosis in Mozambique

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Background: Mozambique is a major contributor to the global TB epidemic and is listed as one of the WHO's 30 high TB/HIV burden countries for 2021-2025, but the prevalence of catastrophic cost in Mozambique is still unknown. We estimate the percentage of TB patients and their households facing catastrophic costs (defined as a total cost related to TB management exceeding 20% of the annual pre-TB household income) or adopting coping strategies.

Design/Methods: Adults (≥ 18 years) initiating treatment for PTB between 12/2017-02/2020 at 12 health facilities in Maputo city and Province in Mozambique were enrolled. An adapted version of the WHO generic patient cost survey instrument was used to capture direct (medical and non-medical) and indirect costs (loss of income). We report costs from the patient perspective and the proportion facing catastrophic costs. Logistic regression was used to identify patient characteristics associated with experiencing catastrophic costs at treatment completion.

Results: 254 adults with PTB (64.1% male, median 33.5 years IQR 26-42, 41% breadwinners) were included. The total care seeking cost as a percentage of monthly income ranged from 4.6% in public clinics to 30.5% in private clinics. Nearly half (50/111, 45.0%) of participants incurred catastrophic costs. Use of savings (57%) was the most frequent coping strategy during care seeking and 11% of patients resorted to two or more strategies. The risk of incurring catastrophic cost increased 2.3 times (OR: 2.3, 95%CI: 1.05 – 5.17, $p=0.037$) if patients were unemployed compared to employed.

Incurring Cost	Care seeking cost Mean (SD)	Treatment cost Mean (SD)	Estimated catastrophic cost n(%)
Incurring Cost:			
Total direct medical costs	4.35 (18.01)	32.41 (114.56)	–
Total direct medical costs	0.32 (0.92)	20.62 (42.71)	–
Total direct cost (medical + non-medical)	4.67 (18.07)	49.98 (120.49)	–
Total indirect cost (Income Loss)	52.47 (96.22)	314.79 (577.34)	–
TOTAL Cost (Direct + Indirect cost)	57.79 (96.47)	363.30 (618.28)	–
Proportion of households incurring catastrophic costs (total cost exceeding 20% of annual household income)	–	–	50/111 (45.04%)
Coping strategies:			
Use of savings: 57%; Borrow money: 19.3%; Sell properties: 3%; Take children out of school: 1.6%			
Variables independently associated with catastrophic cost:			
Age, OR: 1.03 (95% CI: 1.0 - 1.01); Male sex, OR: 1.30 (95% CI: 1.04 - 1.62); Unemployment, OR: 2.3 (95% CI: 1.05 - 5.17)			

Conclusions: Nearly half of study participants incurred catastrophic costs during TB treatment and a sizeable number resorted to coping strategies such as using savings and borrowing money. Being unemployed was associated with the risk of incurring catastrophic cost. These results highlight the need for social protection and costs mitigation strategies to ensure zero TB-affected households incurring catastrophic costs in Mozambique.

OA33-445-11 Increasing tuberculosis diagnosis in the community: comparing EWORS and non EWORS guided community TB active case finding in Cross River State

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Background: An early warning system is an instrument for communicating information about impending risk to vulnerable people before a hazard event occurs, thereby enabling actions to be taken to mitigate potential harm, and sometimes, providing an opportunity to prevent the hazardous disease outbreak or event from occurring. The KNCV TB Foundation Nigeria deployed Early Warning Outbreak Recognition System (EWORS) to identify TB hotspots and inform community screening interventions under the USAID-funded TB LON regions 1&2 project. The strategy aims to improve TB yield and case detection.

Design/Methods: From January to March 2022, KNCV field officers conducted active TB screening in areas identified as TB hotspot and non-hotspot by EWORS within the Calabar South and Calabar Municipal local government areas of Cross-River State, Nigeria. TB

screening was done using portable digital x-ray system fitted with CAD4TB. Presumptive TB clients were further evaluated using GeneXpert and Radiologist as applicable. We analyzed and compared the TB yield between the TB hotspot and non-hotspot areas.

Results: A total of 1437 clients were screened (1098 from non_EWORS and 370 from EWORS hot-spot population), 173 presumptive (131 from non EWORS and 42 from EWORS hot-spot area) identified and 22 TB_cases (10 TB cases from non_EWORS and 12 TB cases from EWORS hot-spot area) were obtained. A 100% screening coverage was obtained from both EWORS and non_EWOR hot-spot, 42(11%) and 131(12%) presumptive TB yield was obtained from EWORS and non_EWORS hot-spot communities respectively. TB yield was 12(29%) and 10(9%) in EWORS hotspot and non_EWORS hot-spot communities respectively.

Conclusions: Active TB screening in hotspot areas resulted in a higher TB yield compared to the non-TB hotspot areas identified by EWORS. Our result shows that targeting community active TB case-finding in TB hotspot areas identified by EWORS is crucial to finding the missing TB cases and improving case-finding in Nigeria.

OA33-446-11 High rates of tuberculosis treatment success among children and adolescents in rural Eastern Cape, South Africa: a cohort study

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Background: It is vital to assess child and adolescent tuberculosis (TB) treatment outcomes to target interventions specific to their developmental stage and take family-centered approaches to TB care. Therefore, we aimed to assess TB treatment outcomes in children and adolescents, by age group, in a high TB prevalence setting.

Design/Methods: Data were retrospectively collected from a rural Eastern Cape, South Africa district hospital for individuals under 19 years, diagnosed with drug-sensitive TB who completed TB treatment between January 2017 and April 2020. Descriptive statistics were calculated for children in three age groups: 0-4, 5-9, and 10-19 years to compare TB treatment outcomes. Composite outcomes were created for success (cure, completed treatment), and unfavorable (died, treatment failure) while lost to follow-up and down referral remained separate categories.

Results: A total of 270 children were included. Fifty-four percent were male and 20% had HIV co-infection. Among those with HIV, 71% were on antiretroviral

therapy. Ninety percent of patients had successful treatment outcomes (4% cured, 85% completed treatment), another 7% were down referred to local clinics from the hospital during their course of treatment. Adolescents had 4.51 higher odds of being down referred compared to younger children (4.51 OR, 95% CI: 1.67-12.15). Additionally, 2% were lost to follow-up including six 0-4 year olds, one 5-9 year old, and one 10-19 year old and less than 1% had an unfavorable treatment outcome (n=2 adolescents died).

Conclusions: Children and adolescents had high rates of successful treatment outcomes, regardless of age with adolescents having the highest rate of down referral. Although very small numbers, more children in the youngest age group were lost to follow-up than school-aged and adolescents which warrants further exploration. There may be family-centered approaches to consider for decreasing loss to follow-up among all age groups.

OA-34 Important topics in child lung health

OA34-447-11 Facility-based TB mentors improve childhood TB diagnosis: experience from Eradicate TB Project, Zambia

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Background and challenges to implementation: In 2020, childhood tuberculosis (TB) cases from the six USAID Eradicate TB (ETB)-supported provinces in Zambia accounted for 6% of all TB notifications, less than the WHO-recommended estimate of 10%. This was mainly due to limited technical oversight supervision from experts to frontline health care workers (HCWs), low utilization of diagnostic tools, inadequate knowledge and skills to conduct pediatric-specific diagnostic procedures, and inadequate coordination of childhood TB activities.

Intervention or response: In May 2021, ETB identified 65 public-sector HCWs (medical doctors, clinical officers, and nurses) from patient entry points in 33 high-volume facilities and trained them in childhood TB case detection and management. Of these, ETB designated 33 high performers as childhood TB mentors. The mentors oriented and mentored frontline HCWs in their respective facilities to provide the diagnostic cascade of services and treatment including preventative therapy in eligible children. They also focused on consistent documentation, updating patient records and weekly/

monthly tracking of indicators. Additionally, the mentors provided technical support on childhood TB case detection using diagnostic tools and procedures, such as chest X-rays, urine LAM, stool for GeneXpert, and gastric lavage.

Results/Impact: The mentor strategy resulted in an increased number of presumptive TB and notified childhood TB cases. Comparing June through December 2020 to the same period in 2021, the proportion of children presumed to have TB increased by 74% (from 4,056 to 7,067), childhood TB notifications increased by 114% (from 387 to 830), and TB preventative treatment initiation went up by 238% (from 287 to 969).

Conclusions: By tracking childhood TB indicators and building capacity of staff from key entry points, the childhood TB mentor strategy helped to improve the proportion of childhood TB notifications from 6% to 17% of total notifications in the 33 health facilities. This strategy should be replicated across Zambia and considered in other countries.

OA34-448-11 The impact of COVID-19 on TB testing and diagnosis in children and adolescents in the Western Cape Province, South Africa

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Background: The COVID-19 pandemic has had devastating effects on tuberculosis (TB) care globally with repeated disruptions of routine services and reduced access to care. Little is known about the pandemic's impact on child and adolescent TB. We investigated trends in TB investigation and diagnosis in children and adolescents in routine healthcare services in the Western Cape Province, South Africa, before and after the onset of COVID-19 to assess the impact on and response of TB services.

Design/Methods: Aggregate, de-identified data on Xpert MTB/RIF investigations and all TB episodes diagnosed over a 5-year period (2017-2021) were extracted from the Provincial Health Data Centre. Age-disaggregated descriptive analyses were completed for 3 age groups: children (0-9 years), adolescents (10-19 years) and adults (20+ years), comparing pre-COVID TB detection during 2017-2019 with data from 2020-2021.

Results: There was a major decline in testing in children and adolescents in 2020 - approximately double the drop observed in adults (35% and 28%, compared to 15%).

In 2021, testing amongst adults almost returned to the pre-COVID average (2% remaining decrease). Testing amongst children and adolescents had to overcome a bigger gap, with remaining deficits of 14% and 16% respectively in 2021. The number of TB episodes also dropped in 2020, with 18% (children), 17% (adolescents) and 21% (adults) reductions and a concerningly slow return (remaining 11%, 16% and 14% deficits). The remaining deficit and slow return in adolescents are particularly alarming.

Conclusions: The substantial drop in TB testing and diagnosis during 2020 and 2021 in children and adolescents and services have not yet recovered across all age groups. Large pre-pandemic deficits are compounded by historically low testing and a lack of catch-up diagnosis. Adolescents appear particularly affected and may need special attention in COVID mitigation strategies. Improvements in TB case detection in children and adolescents is a priority.

OA34-449-11 Scaling up access to pediatric formulations for treating drug-resistant TB: a model for current and future child-friendly care

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Background and challenges to implementation: It is estimated that 30,000 children become sick with drug-resistant tuberculosis (DR-TB) each year, but care is highly centralized. Although there are many barriers to community-based treatment of children with DR-TB, lack of access to pediatric formulations of the second-line medications is one significant obstacle to decentralized pediatric services.

Here, we describe a global partnership approach used to facilitate the introduction of pediatric formulations of key second-line TB medications.

Intervention or response: In 2017, quality-assured, dispersible formulations of several key second-line drugs (levofloxacin, moxifloxacin, pyrazinamide, ethambutol, isoniazid, cycloserine and ethionamide) became available for use, and in 2019, a child-friendly formulation of clofazimine also became available. A coalition of partners formed whose goal was to support the global uptake of these medications.

Results/Impact: Key stakeholders from procurement agencies, technical support bodies, clinical providers, national TB programs, donors, non-governmental agencies, and affected communities carried out the following steps:

1. Purchasing a stock pile of the quality-assured pediatric formulations;
2. Securing funding so that countries could be supplied with a initial quantity of the medications and gain experience in their use;
3. Developing clinical support tools for the optimal use of these medications;
4. Assessing the acceptability of these formulations.

As of 2022, there were 64 countries using the pediatric formulations of the second-line medications, and most countries had procured these medications more than once. Acceptability was high for programs, providers, caregivers, and children. Challenges included a long turnaround time from ordering to receipt of the medications (6-8 months) and continued small market sizes for the products.

Conclusions: Pediatric formulations of second-line medications can be developed and successfully deployed for the care of children using a multi-stakeholder model. This model can be applied to new pediatric products not only for DR-TB but for other pandemics that affect children in the future.

OA34-450-11 A prediction score to improve tuberculosis treatment decision-making in children

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Background: Complications with tuberculosis (TB) diagnosis in children can lead to delays in diagnosis or misdiagnosis. However, in children who have TB disease, rapid initiation of TB treatment can be life-saving. It is suggested that when sufficient clinical evidence of TB in children is available, treatment should be initiated. To identify children who would benefit from rapid initiation of TB treatment, we developed a clinical prediction score.

Design/Methods: We conducted a prospective intensified TB patient-finding intervention in Pakistan (2014-2016). Children presumed to have TB based on a systematically implemented verbal symptom screen questionnaire were eligible. Using multivariable logistic regression, we identified demographic, medical history, or clinical characteristics that best predict a pulmonary TB diagnosis in children. We used bootstrap resampling for internal validation and selected the final model based on parsimony, model fit, discrimination, and calibration. Scores for each variable were calculated by divid-

ing the log odds by their standard error and rounding to the nearest integer. Cumulative prediction scores were calculated for each child. A receiver operating characteristics curve was used to select the score threshold that maximized the model's discriminatory properties. We then developed a treatment decision-making algorithm for operationalization.

Results: Of 5,162 children included, 1,417 (27.5%) were diagnosed with TB. The final model included age group (0-4, 5-9, 10-14), weight <5th percentile, cough, fever, weight loss, chest x-ray suggestive of TB disease, and family history of TB. The identified scores for covariates ranged from -3 to 17. The best cutoff score was 9, resulting in high discriminatory properties: area under the curve: 98.5%; sensitivity: 98.2%; specificity: 89.2%; positive predictive value: 76.9%; negative predictive value: 99.3%.

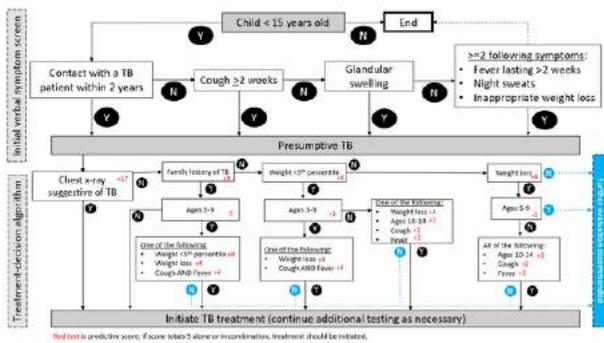


Figure 1. Tuberculosis treatment-decision algorithm for children.

Conclusions: Our score has high sensitivity compared to existing algorithms. This algorithm is beneficial for clinicians to inform rapid TB treatment initiation in children when bacteriologic confirmation is unavailable.

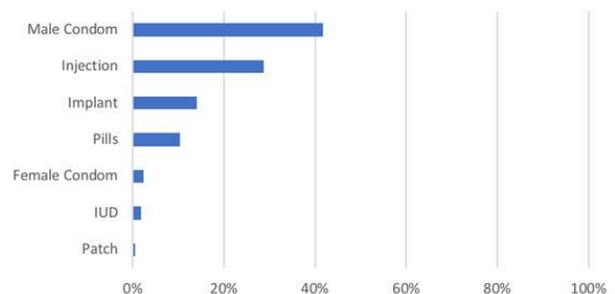
OA34-451-11 Tuberculosis and sexual and reproductive health of women in four African countries

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Background: Although men are more impacted by tuberculosis (TB) compared to women, the elevated percentage of women of reproductive age globally with TB is considered alarming. TB is a major reason of maternal mortality in low-income countries, and it increases the probability of adverse sexual and reproductive health (SRH) outcomes, including ectopic pregnancy and perinatal mortality.

Design/Methods: The data presented here is from the TB Sequel observational cohort conducted in four African countries since 2017: Mozambique, South Africa, Tanzania and The Gambia. For this study, we selected only female participants, who were diagnosed with drug susceptible TB and followed-up until the end of anti-TB treatment (month 6).

The data collection included questionnaires, clinical examination and laboratory tests at TB diagnosis, day 14, month 2, 4 and 6. We performed statistical analysis of socio-demographic, TB- and SRH-related variables.



Results: A total of 486 women, with 88.3% being 18-49 years old, were included in the analysis. Around 11.7% of women experienced past TB episode(s). Most of the participants (416/486; 88.7%) in our cohort were considered cured at month 6. Only 39.6% of non-pregnant women of reproductive age used contraception at TB diagnosis, predominantly male condom (41.7%, see figure below). Abstinence and fear of side effects were the main reasons for non-use.

A total of 31 out of 486 women experienced pregnancy during TB treatment, among whom 38.7% were HIV positive. Pregnancy outcomes varied between live birth (16/31; 51.6%), induced abortion (6/31; 19.4%), miscarriage (4/31; 12.9%) and stillbirth (3/31; 9.6%).

Conclusions: Our data demonstrates a low use of contraception and a relatively high percentage of adverse pregnancy outcomes (22.5%). Thus, integration and linking of SRH services with TB programmes in high-burden countries are vital to increase the contraception use and protect women from obstetric risks associated with pregnancy during TB treatment.

OA34-452-11 New World Health Organization guidelines on the management of tuberculosis in children and adolescents, 2022

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Background and challenges to implementation: Tuberculosis affects an estimated 1.1 million children and young adolescents annually, yet less than half are detected and treated. The World Health Organization's (WHO) Global Tuberculosis (TB) Programme develops policies and guidance to improve TB related outcomes, including for children, adolescents and their families.

Intervention or response: In 2021, WHO convened a Guideline Development Group to review the latest evidence on a number of questions on the management of TB in children and adolescents. These questions covered the topics of diagnostic approaches, shorter regimens for non-severe TB and TB meningitis, the treatment of drug-resistant TB, as well as models of TB care to improve the detection of children with TB infection and TB disease. Evidence from systematic reviews, a randomised controlled trial and complementary studies was assessed using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach.

Results/Impact: In 2022, WHO published 8 new recommendations which comprise: the use of Xpert Ultra on gastric aspirate and stool specimens to diagnose pulmonary TB, the use of integrated treatment decision algorithms to diagnose pulmonary TB, a shorter (4 month) regimen for non-severe (drug-susceptible) TB, a shorter (6 month) intensive regimen to treat drug-susceptible TB meningitis, the use of bedaquiline in children under the age of 6 and delamanid in children under the age of 3 to treat multidrug-resistant TB and the implementation of decentralised, family-centred and integrated models of TB care to improve diagnosis and provision of TB preventive treatment (Table 1).

Conclusions: New recommendations on the management of TB in children and adolescents have been issued by WHO. Widespread adoption and roll out of the

new recommendations have the potential to increase the number of children and adolescents who access treatment for TB infection and disease, as well as improving outcomes and reducing deaths.

OA34-453-11 The effect of household air pollution on pulmonary function among survivors of childhood pneumonia in Uganda

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Background: Household air pollution (HAP) is a well-described risk factor for respiratory disease in children and adults. Children who survive severe pneumonia may be at increased risk of the effects of HAP on lung development.

This study seeks to measure the effect of HAP on pulmonary function among survivors of childhood pneumonia in Uganda.

Design/Methods: We followed up a cohort of children in Uganda hospitalized with pneumonia approximately 5 years prior to the present study (cases), along with siblings without a history of pneumonia (controls).

We administered a questionnaire regarding HAP exposures, measured personal carbon monoxide (CO) exposure over a two-week period as a marker of HAP, and performed spirometry.

Results: A total of 292 children (214 cases, 78 sibling controls) age 4 - 15 years completed CO monitoring and spirometry. Nearly all (99.4%) were from households who cooked or lit their homes with high-polluting fuels. Median CO concentration was (1.21 ppm [IQR 0.38, 3.48]), with a significant difference among families who cooked with charcoal only (2.13 ppm [IQR 0.92, 5.44]) vs. wood only (0.87 ppm [IQR 0.32, 2.31], $p=0.0007$).

Always cooking indoors, burning rubbish, and urban location were significantly associated with increased mean logCO exposure. The total number of kitchen and house windows was associated with a significant increase in FEV1 Z-score. Mean logCO was associated

with a significant reduction in FEV1 and FVC Z-score among those who cooked with charcoal but not among those who cooked with wood, with a greater effect among cases than among controls. (p-interaction=0.03).

Conclusions: We found a high prevalence of HAP exposure in a cohort of children who survived hospitalization for pneumonia. HAP exposure through charcoal cooking in poorly ventilated areas is associated with reduced pulmonary function, especially among children with a history of pneumonia who are particularly vulnerable to its harmful effects on the developing lung.

OA34-454-11 Integrating tuberculosis screening into the national immunization program to improve childhood tuberculosis: result from a study in Anambra state, south-east Nigeria

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Background and challenges to implementation: Childhood tuberculosis (TB) case finding remains a huge challenge. The National Programme on Immunization (NPI) is mainly focused on children but there is minimal integration with the National Tuberculosis Program (NTP) resulting in missed opportunities.

In Anambra State, 62.5% (875) of registered health facilities offer immunization services, but only 30% are TB treatment centers with 10% offering TB clinical screening for children attending immunization services.

Intervention or response: The intervention took place in quarter three 2021. At the beginning of the quarter, immunization staff at the 875 primary health centers in the State were oriented on pediatric TB clinical screening and provided with standard operating procedures. Sputum samples of presumptive TB cases were collected by the local government TB Supervisors and shipped to GeneXpert laboratories for diagnosis while those that could not produce sputum were tested using stool for GeneXpert and/or clinical diagnosis through chest radiograph. The NTP recording tools were used for data collection and analysis was done using Excel.

Results/Impact: A total of 136 childhood TB cases which was 41% of the total childhood TB cases notified in the state in quarter three of 2021 were confirmed and linked to treatment.

Childhood TB notification increased by 82% in quarter three of 2021 compared to quarter three in 2020. While the proportion of childhood TB among total TB notification in the state increased from 21% in quarter three

2020 to 24% in quarter three 2021. Integrating TB services in children-related programs is one way of addressing gaps in childhood TB.

Conclusions: This study demonstrates the feasibility of integrating TB screening for children into routine immunization. This approach has the potential to improve childhood TB case notification and reduce the number of missed TB cases. Future research should focus on the acceptability of the integration by healthcare workers and the cost analysis of the intervention.

E-POSTER SESSION (EP)

EP-31 Not one size fits all!

EP-31-910 Assessment of tuberculosis awareness and perceptions among four socio-economically disadvantaged communities in the Philippines

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Background and challenges to implementation: The 2017 Tuberculosis Prevalence Survey in the Philippines highlighted the poor TB health-seeking behavior of the population: less than 50% of people seek care for TB in a timely manner. TB symptomatology and disease, including early diagnosis, treatment and preventive measures against it, remain poorly understood.

Intervention or response: The USAID's TB Platforms for Sustainable Detection, Care and Treatment Project surveyed 621 individuals aged 18 and above in 4 socio-economically disadvantaged communities. Using a self-administered questionnaire, we assessed their knowledge of the causes and transmission of TB, including symptoms, and care costs.

We assessed perceptions on the timing for care-seeking, gaining more TB knowledge, duration of TB treatment and its impact on having a job, and whether the community supports or discriminates against persons with TB.

Results/Impact: The survey revealed significant gaps in TB knowledge and perceptions. More than a third believe TB is caused by smoking or air pollution and bacteria; 20% believe sharing utensils with TB patients can cause TB.

While 60% of respondents believed that keeping the surroundings clean, practicing cough etiquette and opening windows can prevent TB, 33% believed that consulting a physician can still prevent TB even when with signs and symptoms. Thirteen percent were unaware that TB screening and/or treatment were free at public health facilities.

About 75% believed TB treatment takes too long and 59% thought that it would affect one's ability to get a job. Sixty-five percent believe people with TB experience discrimination.

Conclusions: Local evidence on TB knowledge and perceptions is crucial to adapting social behavior change communication materials for target populations. Effective communication is important to support TB patient identification, ideally conveyed to families versus individuals, especially where families are the key support structure.

Additionally, TB services must be available, affordable, and acceptable, to offer the greatest benefit to the population.

EP-31-912 Stigma, mental health and quality of life of people with tuberculosis in Nepal: a longitudinal, prospective cohort study

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Background: Stigma and mental illness faced by people with tuberculosis (PTB) cause difficulties with TB treatment adherence, reduced rates of cure, and impeded progress towards achieving End TB Strategy goals. We assessed stigma, depression and quality of life (QoL) among PTB in Nepal.

Design/Methods: From August 2018 to April 2019, we prospectively recruited PTB in four districts of Nepal. We descriptively evaluated stigma, depression and quality of life longitudinally during the intensive (baseline) and continuation phases (follow-up).

Stigma was assessed using a locally-adapted Van Rie Stigma scale, which was scored from 0 (no stigma) to 30 (highest levels of stigma).

Depression was measured using a locally-adapted and validated Patient Health Questionnaire (PHQ-9). We assessed QoL using EQ-5D-5L and self-reported health-rating (0, worst possible health, to 100, best possible health).

Results: Participants included 221 adults with drug-sensitive pulmonary TB. The majority (147/221, 66%) were male, mean age was 48 years, and 119/221 (54%) had no formal education. Stigma scores were 11.7 (7.2) and 11.6 (6.5) at baseline and follow-up respectively (see table, following page).

Variable	Severity	Participants at baseline interview, N=221	Participants at follow-up interview, N=221
	Mean score (SD)	11.6 (6.5)	11.5 (6.5)
Stigma (adapted Van Rie Scale)	Low stigma score, n(%)	103 (47%)	101 (46%)
	Moderate stigma score, n(%)	94 (42%)	99 (45%)
	High stigma score, n(%)	24 (11%)	21 (9%)
	Mean score (SD)	10.5 (1.7)	9.8 (1.)
	No depression, n(%)	151 (68%)	157 (71%)
	Mild depression, n(%)	23 (34%)	26 (43%)
	Moderate depression, n(%)	43 (63%)	33 (55%)
Quality of life (EQ-5D-5L)	EQ-5D-5L score, mean (95%CI)	0.83 (0.82-0.86)	0.87 (0.86-0.88)

“People with TB fear telling people outside of their household about their diagnosis” was the Van Rie scale statement with which most participants agreed at baseline (114/221, 52%) and follow-up (100/221, 45%). Nearly one-third (66/221, 30%) of participants were found to have mild to moderate depression at baseline and still at follow-up (59/221, 27%).

Participants' self-reported health-rating appeared to improve from 69.0 (95% confidence interval, 67.3-71.3) at baseline to 80.3 (95% CI=79.5-82).0 at follow-up.

Conclusions: Amongst this cohort of PTB in Nepal, stigma and depression were found to be common and persistent throughout TB treatment. Self-reported quality of life was low at baseline but improved during TB treatment.

The findings highlight the need for locally-appropriate psychosocial interventions to decrease stigma and improve mental health and QoL of PTB in Nepal.

EP-31-913 A qualitative exploration of the psychosocial impact of tuberculosis in adolescents and young people

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Background and challenges to implementation: Adolescents and young adults (AYA) have not been prioritized in tuberculosis (TB) care, control, and research. AYA's who are distinct from children and adults, undergo developmental changes that affect their psychosocial needs.

This study used a qualitative and participatory approach to explore the psychosocial impact of TB on AYA's in Zimbabwe.

Intervention or response: Fifteen in-depth interviews and two participatory workshops were carried out with AYA's (aged 16 to 24 years) diagnosed with TB and living in Harare, Zimbabwe.

Key themes explored being diagnosed with TB, experiences with treatment, psychosocial challenges associated with disease and support needs. Data were organized, coded, and analyzed using grounded theory approach to thematic analysis.

This analysis uses data on participants' experiences with TB diagnosis and treatment and their interactions with healthcare providers, the health system, and family/friends.

Results/Impact: Findings from the study show that AYA's psychosocial wellbeing is negatively affected by TB. AYA's experienced psychosocial challenges including reliance on family support for care, inability to attend school or work, and strains on familial and other relationships. Health system barriers for optimal AYA TB care as perceived by AYAs included lack of intensive education and counseling, inadequate privacy and confidentiality during visits, and perceived stigma due to frequent clinic attendance.

AYAs supported the implementation of youth-friendly services, such as AYA-specific clinic days and spaces, specific health care workers training in AYA care, and peer support interventions.

Conclusions: This study shows that AYA's experience adverse impacts on their psychosocial wellbeing during their illness; current models of care do not meet their needs.

Programs should focus on working with AYA's, their parents/guardians, and healthcare providers to develop supportive environments and health services geared towards serving adolescents.

EP-31-914 Understanding disease disclosure patterns of people with tuberculosis and its outcomes: findings from a longitudinal follow up study in Chennai, South India

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Background: Disclosure of disease status by people with TB is an important step in their treatment journey. There is a lack of systematic understanding on the disclosure preferences of people with TB including when they disclose, whom they disclose to and post-disclosure outcomes.

Design/Methods: Between 2019 to 2021, adult newly diagnosed people with TB were screened for this prospective observational study in the public TB treatment facilities of Greater Chennai Corporation, Chennai, India. Proportions of people with TB who self-disclosed their TB status to their specific family and social network contacts was inquired during treatment initiation, end of intensive and continuous phase and was assessed for significant difference ($p < 0.05$) using Z test.

Different type of supports received by people with TB, post their disclosure from different types of contacts were measured and assessed for its significant association ($p < 0.05$) using Chi square test.

Results: Eligible people with TB ($n=446$) were followed-up, who listed a total of 4039 family, extra familial and social network contacts of them. At treatment initia-

tion, people with TB made maximum disclosures (93%) to their family contacts and less with non-family contacts (24-58%). Incremental disclosures made between treatment initiation and completion was statistically higher among close neighbors, followed by workplace and friends ($p < 0.05$).

Post-disclosure, tangible emotional support was predominantly received by people with TB from all of their family, and other contacts ($>70\%$). Level of practical and resources support provided for people with TB was statistically associated with the contact types ($p < 0.05$) (Table 1).

Conclusions: Self-disclosure of TB status with family members was predominant. Disclosures with extra familial and social network contacts significantly increased during the latter part of treatment. Post-disclosure, psychological emotional support was predominantly received by people with TB from their contacts. Findings highlight the need to facilitate self-disclosure of disease in a way beneficial for people with TB.

EP-31-915 Community-based care delivery improves retention in care and treatment completion among patients on TB treatment in a nomadic community in Uganda

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Background and challenges to implementation: The Karamoja sub-region, North Eastern Uganda has the lowest TB treatment completion rates in Uganda. Long distances and lack of transport to health facilities were identified as the commonest barriers to treatment completion. We sought to assess the impact of community-based drug delivery on retention in care among patients on TB treatment and subsequently, treatment completion for these patients.

Contact Type of people with TB	Disclosure status at treatment initiation	Disclosure status at end of intensive phase	Disclosure status at end of continuation phase	Total disclosures from treatment initiation to treatment end	Tangible resource support provided by disclosed contacts	Psychological Support provided by disclosed contacts	Practical Support provided by disclosed contacts
	No (%)	No (%)	No (%)	No (%)	No (%)	No (%)	No (%)
Family (N=998)	927 (93)	3(1%)	3(1%)	933(94%)*	419(44.9)*	685(73.4)§	330(35.3)*
Extended Family/ Relatives (N=2381)	1376(58)	63(3%)	79(3%)	1518(64%)*	216 (14.23)	1127(74.2)	137(9.0)
Friends (N=423)	185(44)	52(12%)	30(7%)	267(63%)*	50(18.7)	192(71.9)	37(13.8)
Neighbors (N=114)	27(24)	9(8%)	14(12%)	50(44%)	5(10)	37(74)	1(2)
Workplace (N=123)	68(55)	5(%)	14(11%)	87(71%)*	12(13.7)	66(75.8)	10(11.4)
Total (N=4039)	2583(64)	132(3%)	140(4%)	2855(71%)*	702(24.8)	2107(73.8)	515(18.0)

[^] p value < 0.05 for Z test ; ^{*} p value > 0.05 for Z test

[§]p value < 0.05 for Chi Square test ;[¶]p value < 0.05 for Chi Square test

EP-31-914 Table 1.

Intervention or response: The Program for Accelerated Control of TB in Karamoja (PACT-Karamoja) funded by the United States Agency for International Development (USAID) started implementing community-based drug delivery of TB medicines using integrated community TB treatment points (CTTPs). Using facility-based data, villages with at least 15 to 20 TB patients were mapped for the intervention. Key land marks e.g., schools, churches, community halls were priorities as CTTPs and integrated services offered included; TB screening, sputum sample collection and TB treatment refills.

Patient level data from unit TB register of facilities implementing CTTPs was abstracted between August 2020 to December 2021. Retention in care and treatment success for patients enrolled in CTTPs and those not in CTTPs were compared using the Chi-square test. Significance was determined at 0.05.

Results/Impact: Of the 846 patients included in the analysis, 390 (46.1%) had received their TB care through CTTPs and 333 (39.4%) were PBCs. Receiving treatment through CTTPs was associated with higher retention throughout care at (97.7% vs 93.4% at 2 months ($p=0.01$); 91.3% vs 82.4% at 5 months ($p<0.01$) and 89.1% vs 80.2% at 6 months ($p<0.01$).

Receiving care from CTTPs was also associated with an increase in TB treatment completion 93.3% vs 82.5% ($p<0.01$). (Table 1).

	CTTP N=390	Not on CTTP N=456	p-value
Retention in Care			
2 months	381 (97.7%)	426 (93.4%)	0.01*
5 months	355 (91.3%)	376 (82.4%)	<0.01*
6 months	344 (89.1%)	365 (80.2%)	<0.01*
Treatment Monitoring			
Cure rates (PBCs)	91 (44.3%)	51 (40.2%)	0.45
Treatment Success Rate	364 (93.3%)	377(82.5%)	< 0.01*

Table 1.

Conclusions: Moving TB care services closer to communities improved patient retention and hence the treatment completion. There is need to scale up this intervention.

EP-31-916 Rapid assessment of burden of depression and anxiety amongst TB patients through telephone

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Background and challenges to implementation: Tuberculosis remains a significant cause of the disease burden in India, killing over 1200 Indians daily. There is also increasing evidence that points towards the coexistence of depression and tuberculosis in epidemic proportions. As per the World Health Organization, between 40% and 70% of persons with TB have comorbid mental health disorders. Present study aimed to identify the level of depression and anxiety amongst persons with TB and to understand the feasibility of person-centred action for depression and anxiety among persons with TB through telephonic services.

Intervention or response: As part of an ongoing telephonic support being provided to persons taking treatment in private sector, trained counsellors undertook assessment for depression and anxiety using PHQ-9 and GAD-7 scales for 2 months. 586 participants, under telephonic follow-up, were administered with the tools after obtaining consent. Bivariate and multivariate analysis were used to explore possible association of depression and anxiety with various background and treatment related characteristics - age, sex, type of TB, length of treatment and presence of other stressors.

Results/Impact: We found around 20% of the participants having moderate to severe depression (20.9%) and anxiety (19.2%). Gender and treatment duration were significantly associated ($p<0.05$) with depression. Multivariate analysis showed that females were twice more likely ($p<0.05$) to have depression than males. Participants in the 2nd and 3rd month of treatment were around three times more likely ($p<0.05$) to have depression those in first month of treatment. No significant association was found between anxiety level and participant characteristics or duration of treatment.

Conclusions: Telephonic assessment for depression and anxiety amongst persons on TB treatment is possible through trained counsellors. A rapid assessment showed that depression is significantly higher in females and in the third month of treatment, indicating the need for a holistic approach to developing psychosocial support and referral to specialist treatment services.

EP-31-917 Understanding differentiated preferences for non adherence follow-up among TB patients across rural and urban India

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Background: Digital adherence technologies capture TB patients' dosing history to provide differentiated support to patients, however, impact is limited by low patient adoption.

The study aimed to identify acceptable non-adherence follow-up strategies and understand how these differ by patient to provide personalized adherence support.

Design/Methods: A purposively sampled study was conducted with 203 current TB patients in a rural district in northern India (Darbhanga, Bihar) and a metropolitan city in southern India (Chennai, Tamil Nadu) not currently using a digital adherence technology. Preferences for novel digital adherence technology products and follow up strategies were captured through a standardized patient walkthrough survey.

Latent cluster analysis (LCA) was used to derive patient clusters. A logistic regression model was used to profile clusters by identifying significant psychosocial differences across patient segments.

Results: Cluster analysis yielded 3 segments with varied preferences. The first segment (30%) of "urban independents" comprised educated urban smartphone owners without caregivers. The majority of this cluster did not want a doctor (72%) or a health worker (89%) viewing their adherence data, while 46% wanted to view data themselves.

The second segment (42%) of "digital contact seekers", was interested in receiving non-adherence follow-ups via call and wanted services such as dosage progression tracking, alarms, and medication refill reminders via phone.

The third segment (28%) of "doctor dependent, low digital access" patients only wanted their doctors to view adherence data (93%) and was keen to receive supportive services via an offline functionality rather than digitally. This segment was 91% rural and majority shared a phone.

Conclusions: TB patients segments have different preferences for the follow-up strategies adjacent to digital adherence technologies. This analysis could inform the

design of tailored supportive strategies based on content, delivery channel, privacy and provider involvement preferences to more effectively motivate patient digital adoption, engagement and adherence.

EP-31-918 We are TB-free: branding local health workers as TB navigators in the Philippines

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Background and challenges to implementation: Cebu City, a highly urbanized city in the Philippines, launched a systematic TB case finding initiative in two villages amid the COVID-19 pandemic.

Mobile chest X-ray vans were deployed and chest X-ray vouchers were distributed in Mambaling and Pasil villages, respectively. COVID-19 quarantine measures, a community fire, and a typhoon disaster significantly affected the initiative.

Intervention or response: A "We Are TB-free" communication strategy complemented the case finding initiative. It equipped health workers with skills and tools to act as TB navigators and guide residents across the cascade of TB care. It promoted the behavior of getting a chest X-ray for TB detection.

Based on a WHO tool, a baseline knowledge, attitude, and practice (KAP) survey was completed in May 2021. A cohort of 356 household heads in the two villages was randomly selected as respondents for the KAP survey series. The tool was translated into local dialect and pre-tested for internal consistency.

Survey items scored high for reliability (Cronbach's alpha 0.8621). A similar midline survey was completed in January 2022, with a post-intervention survey slated for October 2022.

Results/Impact: At the campaign's midline, survey respondents cited health workers as the preferred source of TB information above television and radio modalities. Mean scores on intention to seek early care, obtain a chest X-ray, and have sputum tested for TB improved at midline.

Further, those who talked to a health worker would more likely undergo sputum testing than those who did not talk to a health worker. The fear of COVID-19 remained a top barrier to health-seeking behaviors.

Conclusions: Community health workers should be engaged as TB navigators as part of a screen-all case finding strategy.

Exposure to TB navigators may influence intention to practice ideal TB behaviors like undergoing TB testing. Addressing the fear of COVID-19 should also be integrated in TB health promotion.

Indicator	Baseline	Midline	p Value
Age	Mean = 44.0, SD=+15.3		
Sex	Female = 82.6%/Male=17.4%		
Current employment status	Not working = 67.1%		
Monthly household income	US\$90-200 = 36.5%		
Highest educational attainment	High school = 50%		
Mean knowledge score (HPS=10)	8.03	8.06	0.7913
Mean attitude score (HPS=4)	2.92	2.73	0.0000
Mean practice score (HPS=5)	3.81	3.91	0.0001
Mean scores of respondents who will likely:			
- Seek immediate care at onset of symptoms	4.44	4.64	0.0000
- Obtain chest X-ray	4.56	4.66	0.0004
- Undergo sputum testing	4.50	4.65	0.0000
% of respondents exposed to TB messages via:			
- Health workers	62%	69%	0.0247
- Television	69%	60%	0.0064
- Family/Friends	27%	56%	0.0000
- Radio	45%	38%	0.0592
% of respondents who cannot seek health care because of:			
- Fear of COVID19	26%	42%	0.0000
- Community lockdown	56%	81%	0.0000
Comparison of mean scores of selected ideal behaviors by exposure to health workers at midline			
Respondents who intend to...	Talked to a health worker	Did not talk to a health worker	p Value
- Seek immediate care	4.65	4.63	0.7328
- Obtain chest X-ray	4.69	4.61	0.1391
- Undergo sputum testing	4.69	4.58	0.0454

Table. Profile of respondents and comparison of baseline and midline data, n=356, p<0.0500.

EP-31-919 Residents of missionary centers, mine workers, and prisoners are key populations affected by TB in Ethiopia

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Background and challenges to implementation: Stop TB Partnership Global Plan to End TB outlines the three 90's to be achieved by 2020, or 2025 at the latest. The second 90 is to reach at least 90% of the most vulnerable, underserved, and at-risk populations. The nationally representative proportion of at-risk popula-

tions for TB with TB service has not yet been determined in Ethiopia, yet it is essential to focus on the populations most at risk for TB for a tailored and cost-effective investment

Intervention or response: The USAID Eliminate TB Project mapped key populations in five regions supported by the project from July 2020 to September 2021. The project also provided orientation to healthcare providers on performing clinical TB screening among key affected populations to determine the second 90 target. GeneXpert was used as a diagnostic tool. The number need to screen (NNS) in order to diagnose TB among people at-risk was also estimated.

Key population	Estimated # of key population	# Key population registered	Screened	% Screened of registered	TB cases (% of screened)	NNS
Prison inmates	53,025	42,712	33,945	79.5	146 (0.4)	233
University/college/school students	119,773	90,671	8,107	8.9	8 (0.1)	1,013
Urban slum and homeless	44,073	26,046	3,032	11.6	7 (0.2)	433
Holy water attendants	175,600	173,585	110,755	63.8	8 (0.01)	13,844
Female sex workers	20,345	17,348	44	0.3	0 (0)	0
Mega project area (construction and factories)	41,318	14,993	8,148	54.3	5 (0.06)	1,630
Missionary center resident	60,277	34,573	33,905	98.1	594 (1.8)	57
Mining workers	610,399	605,476	215,115	35.5	928 (0.4)	232
Refugee/IDP	73,075	14,656	8,678	59.2	4 (0.05)	2,170
Total	1,197,885	1,020,060	421,729	41.3	1,700 (0.4)	248

Table 1: Mapped key populations, proportion screened and yield, July 2020-September 2021

Results/Impact: About 41.3% (421,729/1,020,060) of people in the identified key populations received TB screening service, with the highest being among the residents of missionary centers (98%) and prison inmates (80%). Nine groupings of key population were identified where NNS was lower among residents of missionary centers (58), prisoners (293), and mining workers (652).

Conclusions: Only two-fifths of the key populations were screened for TB. The country has more work to do in universal screening of TB to achieve the second 90 of the global targets. The residents of missionary centers, prisoners, and miners are the priority groups for targeted and tailored TB activities.

EP-32 Programmatic issues in the cascade of care

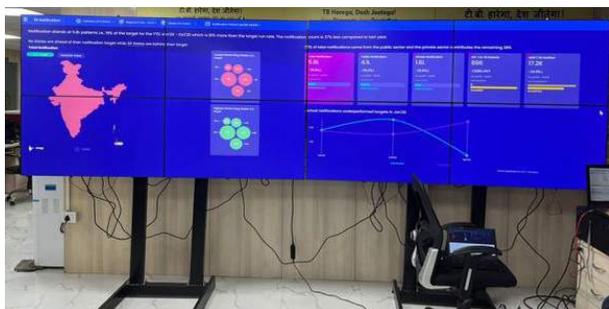
EP-32-920 Improving programme monitoring through TB Command Centre in NTEP India

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Background and challenges to implementation: As the NTEP accelerates towards its goal of TB Elimination by 2025, a consolidated data visualization platform has been deployed at the Central TB Division. 'The Strategic Operations Center for TB' has been established with the aim of fostering a data-driven culture at the CTD, by equipping officers and consultants with custom dashboards and a comfortable environment for brainstorming. The TB Command Center is a step forward towards evidence-based action for the program, and a tool to enable users to match pace of programmatic decision making with programmatic goals.

Intervention or response: While the idea of a Strategic Operations Center for TB is enticing, the journey has been eventful. From procuring the appropriate hardware, designing impactful storyboards and setting up the discussion area layout, it is a major collaborative effort from CTD and Partner organizations.

Results/Impact: There have been various design principles that have been taken into account at the time of ideation. Easy to understand indicators have been used to enable actionable insights leading to targeted decision making. Absolute values for metrics are augmented with relative values to highlight the Delta or Change. The indicators are replicable across geographies and timeframes. By design it allows for regular monitoring of program indicators and early identification of issues at the state level. It also makes tracking the impact of key policies and initiatives easier for given geographies.



Conclusions: Apart from the descriptive statistics that are reflected from Nikshay, going forward, the Operations Center would also boast information from ACSM sources, key parameters from other Programs and systems, and also an interactive simulation model for quantifying the impact of programmatic interventions on outcomes. It not only makes the data closer to everyone at the CTD office but also nudges the users to look for deeper reasoning.

EP-32-921 Rapid efficiencies in policy adoption through policy influence plan and consultative engagements revolutionize the TB preventive therapy (TPT) landscape in Zimbabwe

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Background and challenges to implementation: In 2019, tuberculosis (TB) claimed the lives of 30% of people living with HIV (PLHIV) worldwide.¹ A 54% TB/HIV co-infection rate contributes to Zimbabwe's considerable TB burden with an incidence of 193 per 100,000.¹ Since 2012, TPT uptake has been suboptimal at 39.1% (2020). Similarly, in 20 select IMPAACT4TB sites, only 38% of PLHIV initiating TPT with only 26% of those completing. Exclusion of shorter TPT regimens, health worker skepticism, fragmented TPT guidelines, and inadequate communication of guideline modifications are all associated with sub-optimal TPT initiation.

Intervention or response: The Clinton Health Access Initiative and Ministry of Health harmonized catalytic interventions to necessitate a smooth TPT policy update through:

LTBI stakeholder and resource mapping, integrated TB/HIV implementation, data-driven and consultative TPT engagements, dissemination of evidence-based TPT data guided by a robust policy influence plan, technical assistance on the development of the LTBI addendum, training materials and reporting tools.

Results/Impact: TPT guidelines and Essential Drugs List for Zimbabwe (EDLIZ) were updated. Additionally, an LTBI communication strategy, job aides, treatment algorithms, training manuals, and reporting tools were disseminated with the aim to improve TPT awareness among 820 healthcare workers and 85 community workers by December 2021.

Resultantly, this improved TPT documentation with – 15, 092 initiations, 93% completions and 0.5% of adverse events recorded complemented by a 100% TPT guidelines dissemination across all public health fa-

cilities. The inclusion of 3HP in the EDLIZ ring-fenced Global Fund and PEPFAR commitments to 3HP procurement.

Conclusions: Efficiencies in evidence-based policy adaptation based on global trends remains the cornerstone for TPT programming and the adoption of novel TPT regimens. A robust policy influence plan provides the detailed roadmap for stakeholder mapping and consultative engagements that foster ownership, sustainability, and scalability. This rapid policy adoption culminated in over 15 000 - 3HP initiations, sustained 3HP procurements and TPT surge plan to scale-up TPT.

EP-32-922 Early lessons of rolling out TB preventive therapy among household contacts of patients with pulmonary TB in India

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Background and challenges to implementation: FIND implemented a TB infection (TBI) initiative under the Joint Effort for Elimination of Tuberculosis project from September-2021. The objective of this initiative is to provide TB preventive therapy (TPT) to household contacts of pulmonary TB (PTB) patients at scale. The project is being implemented in 22 districts across four states of India covering a population of more than 70 million. We document the process and early findings of this initiative.

Intervention or response: The TBI initiative involved:

1. Contacting the PTB patients and requesting their consent for home visit,
2. Doorstep screening of their HHCs,
3. Linking them for medical evaluation to rule out active TB,
4. Initiation of TPT for eligible HHCs,
5. Linking to care in case of adverse-events and
6. Regular follow-up during treatment.

A national training was organised in August-2021 for field teams, sharing the knowledge and programmatic algorithms about TBI and TPT. This was followed by multiple state and district level trainings. The project was rolled out in September-2021.

Results/Impact: From Sept 2021 to March 2022, a total of 51,576 PTB patients were contacted, of whom 36,717 (71%) consented for home visit. Of these, 30,164 (82%) were visited. Of 99,125 HHCs identified, 88,851 (90%) were screened. Upon screening, 87,545 were identified as asymptomatic HHCs, eligible for TPT initiation.

A total of 36,398 were put on TPT and are currently being followed up. There were a few ground-level chal-

lenges faced during implementation which include availability of trained medical officers for evaluation, low acceptance for TPT by private sector providers and un-interrupted supply of TPT drugs.

Conclusions: This is one of the largest initiatives to address TBI in India and has the potential to substantially contribute towards TB elimination goal. Early findings of this context specific project are promising yet challenges need to be addressed to ensure successful implementation.

EP-32-923 Mycobacterium tuberculosis-specific multiplecytokineresponsein different tuberculosis infection status: anexploratory study

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Background: To explore the differences of multiple cytokines secretion stimulated by specific antigens of Mycobacterium tuberculosis (MTB), and to screen antigens and cytokines with potential to discriminate MTB infection status.

Design/Methods: Twenty patients diagnosed microbiologically with active tuberculosis (ATB) in Peking Union Medical College Hospital and Beijing Chest Hospital from February to April 2022 were enrolled. Fifteen healthcare workers (HCWs) with latent TB infection (LTBI), 10 HCWs with previous TB and 10 HCWs as healthy control (HC) were recruited during the same period. Whole blood was stimulated with early secreting antigen target-6 (ESAT-6), culture filtrate protein-10 (CFP-10), Rv2028c and synthetic long peptides derived from Rv1733c (Rv1733c SLP). The secretion of interferon gamma (IFN- γ), tumor necrosis factor- α (TNF- α), interleukin (IL)-2 (IL-2), IL-6, IL-5, IL-10, interferon-inducible protein-10 (IP-10), IL-1 receptor antagonist (IL-1Ra), chemokine (C-X-C) Ligand-1 (CXCL-1) and macrophage chemoattractant protein 1 (MCP-1) in Plasma were measured by Luminex Assays.

Results: After stimulation with ESAT-6 antigen, the secretion levels of IL-6, IP-10, IL-1Ra and CXCL-1 in ATB group were significantly higher than those in LTBI, previous TB and HC groups ($p < 0.05$). After stimulation with CFP-10 antigen, the secretion levels of IL-6, IP-10, IL-1Ra, CXCL-1 and MCP-1 in ATB group were significantly higher than those in previous TB and HC groups ($p < 0.05$). After stimulation with Rv1733c SLP antigen, the secretion levels of IFN- γ and IL-2 in ATB group were significantly lower than those in LTBI group, while the levels of IL-6 and CXCL-1 were significantly higher than those in LTBI group ($p < 0.01$).

After stimulation with Rv2028c antigen, the secretion levels of IFN- γ and IL-2 in ATB group were significantly lower than those in LTBI and previous TB groups, while the level of CXCL-1 was significantly higher than that in LTBI group ($p < 0.05$).

Conclusions: When combining MTB virulence factors with latency-associated antigens, detection of multiple cytokines including IFN- γ , IL-2, IL-6, IP-10, IL-1Ra and CXCL-1 may have the potential to identify different status of MTB infection.

EP-32-924 Why does the local matter when implementing mHealth interventions into routine MDR-TB care?

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Background: Optimising treatment outcomes is integral to combating the spread of multidrug resistant tuberculosis (MDR-TB) in Vietnam. Digital technologies are central to WHO's End TB Strategy, with their potential to provide more effective treatment and person-centred care. However, no different from any other clinical or public health intervention, their effectiveness and acceptability are bound to their responsiveness to the everyday illness experiences of patients, and for healthcare workers, working within resource stretched health systems. We use lessons learned from the implementation of a smartphone app aimed at improving adverse event management and treatment outcomes for patients, to emphasise the importance of understanding local needs and conditions prior to the design and implementation of mHealth interventions.

Design/Methods: We conducted 50 in-depth interviews with (n=30) patients receiving treatment for MDR-TB and their treating healthcare workers (n=20), all of whom were participating in the VSMART randomised controlled trial, in four provinces in Vietnam. We iteratively analysed the data using deductive and inductive thematic analysis.

Results: Patients and healthcare workers adapted use of the app to suit their individual purposes and social preferences. Implemented in addition to usual care, in some settings the app was competing with several alternative modes of AE management.

However, healthcare workers identified the immense potential of mHealth to improve delivery of MDR-TB care.

Conclusions: Social science can play a key role in ensuring that we understand patients' and health workers' local context. Effectiveness of mHealth interventions could be increased, and timelines and costs decreased if valuable qualitative work informs the design of mHealth interventions. Funding models should facilitate the inclusion of meaningful qualitative assessment and iterative learning in intervention and trial design. This will support the development of flexible, attuned mHealth for MDR-TB that is necessary to achieve person-centred care.

EP-32-925 Efficacy, adherence, and safety of latent tuberculosis infection treatments. Systematic review and network meta-analysis of randomized controlled trials

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Background: Treatment of latent tuberculosis infection (LTBI) is effective in preventing progression to TB disease. This study aimed to synthesize available evidence on the efficacy, adherence, and safety of LTBI treatment.

Design/Methods: The PRISMA-NMA was used to review and report this research. Randomized controlled trials which compared the efficacy and safety of LTBI treatments were included. A systematic literature search was done to identify relevant articles from online databases PubMed/ MEDLINE, Embase, and Cochrane Center for Clinical Trial database (CENTRAL). The analysis was done using frequentist approach and R-studio Version 1.4.1103 was used.

Results: The incidence of TB among people living with HIV (PLWHIV) who have taken 3RHZ (RR 0.40 95% CI 0.23,0.69) as TPT was lower followed by 3RH (RR 0.56 95% CI 0.36,0.89). However, 3HP (RR 0.38 95% CI 0.15,0.99) shows a significant reduction on the incidence of TB among HIV negative patients who had TB contact history. Patients' adherence to TPT was higher among patients who have taken 4R (RR 1.38 95% CI 1.0,1.89) followed by 3RH (RR 1.34 95% CI 1.03,1.74).

A permanent discontinuation of a study drug because of adverse event were higher in 3RZ (RR 9.31 95% CI 2.99,28.97). The risk of nausea and vomiting was higher

among patients who have taken 3HP (RR 5.91 95% CI 2.30,15.20). Furthermore, the risk of grade 3 and 4 liver toxicity was significantly higher among patients who have taken 12H (RR 26.04 95% CI 5.88, 115.38).

Conclusions: From this review, it can be concluded that 3RHZ, 3RH, 6H has a significant impact on the reduction of TB incidence among PLWHIV and 3HP among HIV negative people who had TB contact history. However, rifampicin and pyrazinamide combinations were significantly associated with adverse events which resulted in permanent discontinuation. This may support the current recommended TPT regimen of 3HP, 3RH, and 6H.

EP-32-926 Predicting factors of latent tuberculosis infection in long-term care facilities in Taiwan, 2018 - 2021

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Background: Tuberculosis (TB) specific incidence of age ≥ 65 years was 127.7 per 100,000 population in 2020, which has been the highest in Taiwan with moderate TB burden. The incidence in the long-term care facilities (LTCFs) was estimated to be 3 to 5 times higher than that of the elderly in communities.

An integrated program of case finding, and treatment of latent TB infection (LTBI) has been conducted since 2018. The aim of study is to analyze the prevalence and predicting factors of LTBI in LTCFs.

Design/Methods: We retrospectively analyzed the enrolled participants including health care workers (HCW) and residents in LTCFs from 2018 to 2021. The annual chest X-ray, symptoms screen, health education and IGRA testing were conducted through the collaboration of county health bureaus and participating facilities. Tuberculosis preventive therapy (TPT) of 9H or 3HP regimen were provided for free to those with positive IGRA results.

The demographics of gender, age, BMI, receiving hemodialysis or not, and smoking history were collected. Logistic regression model was applied to estimate the odds of positive IGRA results and 95% confidence interval among covariates.

Results: A total of 26,096 participants (84.5%) were enrolled from 285 LTCFs including 9198 (29.8%) health workers and 21,676 (70.2%) residents. Reasons for not testing IGRA included previous active TB (2.3%), previous positive IGRA or receiving TPT (0.7%), rejecting testing or transferring out of the facilities (8.0%) and unknown (89%). The median age of HCWs and residents was 41.6 and 79.1, respectively.

The overall LTBI rate was 16.1% with indeterminate result of 2.3%. The prevalence of LTBI among residents was significantly higher than HCWs (18.9% vs 9.8%,

$p < 0.001$). Age, male, mild obesity, non-nursing home facilities, and smoking were significantly associated with LTBI in multivariate analysis (Table 1).

	IGRA positive		Univariate		Multivariate (stepwise)	
	n	%	OR	95% CI	aOR	95% CI
Male	10302	1936	18.8	1.38	(1.29-1.48)	1.12 (1.04-1.21)
Age						
(per 10 years)				1.19	(1.17-1.21)	1.01 (1.01-1.01)
BMI						
BMI < 18.5	3211	507	15.8	0.97	(0.88-1.08)	0.84 (0.75-0.94)
18.5 \leq BMI < 24	12056	1947	16.2	1		1
24 \leq BMI < 30	6504	1123	17.3	1.08	(1.00-1.17)	1.14 (1.05-1.23)
BMI \geq 30	1208	168	13.9	0.84	(0.71-0.99)	1.03 (0.87-1.23)
Unknown	3117	458	14.7	0.89	(0.80-1.00)	1.01 (0.90-1.13)
Non-nursing home facilities	14118	2428	17.2	1.19	(1.12-1.28)	1.12 (1.05-1.20)
Participants						
residents	18124	3421	18.9	2.14	(1.97-2.32)	1.42 (1.25-1.60)
HCWs	7972	782	9.8	1		1
Smoking	3066	668	21.8	1.54	(1.40-1.69)	1.35 (1.22-1.50)
Dialysis	452	78	17.3	1.09	(0.85-1.39)	

Table 1. Predicting factors of latent tuberculosis infection in long-term Care Facilities (n=26096)

OR, odds ratio; aOR, adjusted odds ratio; BMI, body mass index; LTCF, long-term care facilities; HCWs, health care workers.

Conclusions: Latent tuberculosis infection was prevalent in LTCFs. Intensified case finding with TPT might help to reduce risk of developing TB and subsequent transmission.

EP-32-927 Beyond patient delay, navigating structural health system barriers to timely care and treatment in a TB-endemic setting in Papua New Guinea

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Background: Tuberculosis (TB) is a major public health issue in Papua New Guinea, with incidence rates particularly high in the South Fly District of Western Province. We present findings from interviews and focus groups

of people living in rural areas of the remote South Fly District depicting their challenges accessing timely TB diagnosis and care; most services within the district are only offered offshore on Daru Island.

We concern ourselves with understanding the structural cause of delays to timely TB diagnostics and treatment; delays related to the policy and health system environment.

Design/Methods: The findings presented are drawn from a large qualitative study that was designed to examine the socio-cultural dimensions of TB control in Papua New Guinea. The data set included 128 interviews with caregivers of children on TB preventive treatment and key informants, and 10 focus group discussions with community members, community and religious leaders, people on treatment for TB and healthcare workers.

Results: The findings detail that rather than “patient delay” attributed to poor health seeking behaviours and inadequate knowledge of TB symptoms, many people were actively trying to navigate the structural barriers associated with limited local TB services.

The findings highlight a fragile and fragmented health system, a lack of attention given to primary health services, and undue financial burdens placed on people living in rural and remote areas associated with costly transportation to access functioning health services.

Conclusions: We conclude that a renewed focus on ensuring the delivery of functioning primary health care services in rural and remote areas of Papua New Guinea is paramount.

To achieve this, all partners must work together to implement the policy of decentralised TB health services, which will require highly contextualised solutions to be sustainable.

EP-32-928 Community-based contact screening to enhance TPT uptake of household contacts in Sidama and SNNP regions

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Background and challenges to implementation: Tuberculosis preventive treatment (TPT) for high-risk populations is one of the key elements of the End TB strategy. The Ethiopian National TB and Leprosy Program recommends use of a shorter rifamycin containing regimen (3HP/3HR) for <15 years of age that are contacts of bacteriologically confirmed pulmonary tuberculosis PTB (BC-PTB) cases.

However, the annual uptake of TPT remains sub-optimal (34%) in 2020/21. We aimed to examine the uptake of TPT among <15 contacts of BC-PTB cases in Sidama and SNNP regions through an enhanced community-based approach.

Intervention or response: Using across-sectional study, data were collected during September-December 2021 from the TB contact screening and latent tuberculosis infection (LTBI) treatment follow-up registers. Community-based contact screening was implemented in twelve TB high-load health facilities from selected districts of Sidama and SNNP. The package of activities included training healthcare workers and health extension workers on screening and referral of <15 household (HH) contacts, provision of standard operating procedures and job aids, and regular performance tracking.

Among those eligible, screening was done with contacts of BC-PTB cases registered in 2020-2021. A Chi-square test was computed to compare the TPT uptake before and after the activities.

Results/Impact: A total of 864 <15 HH eligible contacts were identified and screened for TB. Six-hundred and eighty-eight (688) (84.7%) of the 812 eligible were initiated on 3RH. Compared to the previous 12 months' performance, TPT uptake among <15 HH contacts was twice as high with an enhanced community-based approach (94/125=75% vs. 685/812=85%, OR 1.8, 95% CI [1.17, 2.86]).

Data elements	SNNP (N=6)		Sidama (N=6)		Total (N=12)	
	Pre-intervention	Post-intervention	Pre-intervention	Post-intervention	Pre-intervention	Post-intervention
# of BC-PTB cases enrolled	143	257	258	375	401	632
# <15 HH contacts identified	39	355	92	517	131	872
# <15 contacts screened for TB	39 (100%)	347 (97.7%)	92 (100%)	517 (100%)	131 (100%)	864 (99.6%)
# <15 contacts screened negative for TB	36 (92.3%)	343 (98.8%)	89 (96.7%)	469 (90.7%)	125 (95.4%)	812 (94.0%)
# <15 HH contacts initiated on TPT	28 (77.8%)	322 (93.9%)	66 (74.2%)	366 (78.0%)	94 (75.2%)	688 (84.7%)

Conclusions: Contact screening and TPT through a community-based approach is a strategic and feasible intervention to identify and initiate TPT among <15 HH contacts in high-case load districts. Thus, targeted community-based interventions should be scaled up to other districts with high TB incidence to reach more contacts in need of TPT.

EP-32-929 Assessing and refining image analysis software to automate reading of objective home-based TB adherence tests

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Background: Non-adherence to tuberculosis (TB) medication is associated with poor outcomes, yet determining medication adherence is challenging. As part of a digital adherence tool intervention (the TB treatment support tools (TB-TST)) we have developed an objective drug metabolite test to monitor adherence from home, allowing for timely and individualized support. The test has been iteratively refined for ease of use and to facilitate automated result detection. The purpose of this study was to evaluate the accuracy of our prototype test reading software.

Design/Methods: Images of tests are submitted by participants through the TB-TST app in an ongoing pragmatic randomized control trial assessing the effectiveness of the intervention. Test images were coded for presence of isoniazid metabolite by treatment supporters in the trial, research staff, and reader software. The software extracts the results area from the images and analyzes the level of color in the test and control strips (Figure 1). Inaccurately coded images were reviewed to understand issues impacting readability.

Results: 689 images of the tests were used to evaluate the accuracy of the reader software. Compared to the images coded by the treatment supporters in the trial, the software had a sensitivity of 81% and specificity 95%.

Compared to the images coded by research staff, the software had a sensitivity of 86% and specificity 91%. The main issue impacting accuracy was inconsistent colors across lighting conditions.

Image processing steps



Step 1 - Image Capture

User captures photo, barcode and Aruco marker detected



Step 2 - Segmentation

Result region extracted from image



Step 3 - Analysis

Test and control regions isolated, colors analyzed for final result

Conclusions: Results show that our automated reader is feasible, but requires refinement to improve sensitivity and specificity. Next we will combine the existing software process with machine learning to improve detection of anomalies and enhance accuracy as more submissions are gathered. A process for normalizing colors across lighting conditions will be pursued. Findings will support understanding how objective measures of adherence can be integrated into routine TB care.

EP-33 Lung health across the life course and after TB

EP-33-930 Psychosocial sequelae following treatment for pulmonary tuberculosis: qualitative results from an international multi-stakeholder participatory workshop

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Background: Psychosocial sequelae following treatment of pulmonary tuberculosis (PTB) are increasingly being recognised as important debilitating outcomes in persons who suffered from PTB.

We present data from a multi-stakeholder participatory workshop where we explored the perspectives of former PTB patients, PTB-affected communities, and policymakers from six West African countries, and identified the strategies for coping with persistent physical and psychosocial health challenges after PTB treatment.

Design/Methods: We organised a participatory workshop on post-TB disability at the Medical Research Council (MRC) Unit in The Gambia, West Africa.

We used an exploratory, descriptive, qualitative approach for the primary data collection through focus group discussions (FGD). Participants included former PTB patients including adolescents, advocates from PTB-survivors support groups, and representatives of key policy sectors. All interviews were audio-recorded and transcribed verbatim, and the data were analysed using an inductive thematic approach.

Results: A total of 38 participants (50% females) from six West African countries (Benin, Burkina Faso, Gambia, Ghana, Nigeria, and Sierra Leone) participated in the workshop. The participants comprised 33 (74%) former TB patients and advocates and ten (26%) representatives of key policy sectors [5 (13%) TB programme managers, 1 (2.6%) WHO representative, and 4 (10.4%) others].

Our findings identified three emerging themes:

- i. **Reduced quality of life** (with physical health, family life, work and economic life, and social participation adversely impacted);
- ii. **TB-associated stigma** (including self and social stigma);
- iii. **Psychosocial support** (with family members and support groups identified as the main source of post-PTB psychosocial support).

There was consensus from the policymakers that there is still a huge knowledge gap on adverse health and psychosocial consequences following treatment for PTB with inadequate data to support policy change.

Conclusions: These findings support the need for more studies and awareness campaigns on health-related quality of life and psychosocial care beyond TB treatment completion.

EP-33-931 Factors associated with poor retention in the TB Sequel study after successful completion of TB treatment

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Background: The TB Sequel study was designed to understand factors affecting the long-term sequelae of pulmonary TB (PTB). Patients were followed for a minimum of 24 months from the start of TB treatment, so we aimed to identify factors associated with poor retention in the study after treatment completion.

Design/Methods: Ongoing observational cohort study among patients receiving treatment for TB through national TB programs in The Gambia, Mozambique, South Africa, and Tanzania. Adults (≥ 18 yrs) with PTB were recruited at TB treatment initiation between 09/2017-02/2020.

We used Poisson regression to identify patient factors at TB treatment completion associated with poor retention (i.e., failure to return for a scheduled follow-up visit 6 months after completing treatment). Covariates included demographics and social determinants of health (e.g., job security, stigma, food security, etc.).

Results: 1429 adults were enrolled, and 966 (68%) completed treatment for drug-susceptible PTB. Of these, 576 (60%) completed TB treatment before 09/2019 and

were eligible for a follow-up visit 6 months after completing treatment but before the start of the COVID-19 pandemic, which is known to have impacted clinic attendance and health-seeking behavior.

Of the 576 participants (64% male; median age 34 IQR 28-43; 39% HIV positive; 56% without high school; 9% previous TB), 503 (87%) returned for their scheduled follow-up visit.

Factors associated with poor retention included being a TB survivor from Tanzania (vs. The Gambia RR 2.61), female (RR 1.52), having a primary school education or less (RR 2.32), and perceiving the financial impact of TB to be moderate, serious or very serious (RR 1.60).

Characteristic		Without outcome (retained) 503/576 (87.3%)	With outcome (not retained) 73/576 (12.7%)	Crude Relative Risk 95% CI
Country	South Africa	102/117 (87.2%)	15/117 (12.8%)	1.71 (0.83-3.51)
	Tanzania	156/194 (80.4%)	38/194 (19.6%)	2.61 (1.41-4.83)
	The Gambia	148/160 (92.5%)	12/160 (7.5%)	1.00 (reference)
	Mozambique	97/105 (92.4%)	8/105 (7.6%)	1.02 (0.43-2.40)
Gender	Male	327/366 (89.3%)	39/366 (10.7%)	1.00 (reference)
	Female	176/210 (83.8%)	34/210 (16.2%)	1.52 (1.00-2.33)
Education	Less than Grade 8	274/322 (85.1%)	48/322 (14.9%)	2.32 (1.08-4.98)
	Grade 8-12	127/145 (87.6%)	18/145 (12.4%)	1.93 (0.84-4.46)
	Grade 12 or more	102/109 (93.6%)	7/109 (6.4%)	1.00 (reference)
Perceived financial impact of TB	No or little	295/327 (90.2%)	32/327 (9.8%)	1.00 (reference)
	Moderate to very serious	208/248 (83.9%)	40/248 (16.1%)	1.60 (1.04-2.47)

Conclusions: Experts recommend providing care to TB survivors for up to 2 years after treatment, with follow-up evaluations every 6 months. Therefore, it is important to understand which individuals are less likely to return so that appropriate interventions or incentives can be used to improve cohort retention.

EP-33-932 Pulmonary function in survivors of severe pneumonia in early childhood: a cohort study in Uganda

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Background: About 120 million children under age 5 years develop pneumonia annually, and severe pneumonia disproportionately affects children in low and middle-income countries (LMIC). The prevalence of reduced pulmonary function is also increased among people living in LMIC, and severe childhood pneumonia may increase the risk of reduced pulmonary function later in life.

Design/Methods: We conducted a follow up study of a cohort of 360 children in southwest Uganda hospitalized with pneumonia approximately 5 years prior to the present study. Of the surviving subjects, 243 consented to participate in our study (cases) as well as an additional 95 siblings without a history of pneumonia (controls). We administered a respiratory symptom questionnaire and performed spirometry among all participants.

Results: A total of 323 children (233 cases and 90 sibling controls) ages 4 - 15 years old successfully completed spirometry and were included in our analysis. Using the GLI African-American reference equations, the mean FEV1 and FVC Z-score for cases was -0.32 [95% CI -0.23, 0.17] and 0.28 (95% CI 0.03, 0.53) respectively. Compared to controls, cases were more likely to have obstruction (OR 1.96 [95% CI 0.83, 4.60]), reduced FVC (OR 4.12 [95% CI 1.22, 13.89]) and a significant bronchodilator response (OR 2.07 [95% CI 1.21, 3.53]). Cases were also more likely than controls to report a history of chronic cough (OR 2.41 [95% CI 1.22, 4.72]), but only one case and two controls had a reported diagnosis of asthma or any chronic respiratory disease.

Conclusions: Children who survived early childhood pneumonia have greater prevalence of obstruction, reduced FVC, bronchodilator responsiveness, and chronic cough compared to controls without a history of pneumonia.

These findings suggest that at least some children with severe childhood pneumonia in sub-Saharan Africa may have undiagnosed asthma. Further research is needed to determine the long-term trajectories of children who survive severe pneumonia.

EP-33-933 Comparing alcohol consumption by sex during and after tuberculosis treatment: a longitudinal study of a South African cohort

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Background: Alcohol consumption has been associated with increased tuberculosis (TB) incidence and poor TB treatment response. Little is known about sex differences in drinking patterns for people with TB, especially after TB treatment completion.

Design/Methods: We analyzed data from 234 (143 male, 91 female) participants in a TB treatment cohort study in Worcester, South Africa. We used the Timeline Followback (TLFB) method to capture past two-week alcohol consumption monthly during treatment and every 3 months for one-year post-treatment. We categorized recent alcohol consumption as heavy alcohol use (3+/4+ standard drinks for females/males consumed in one day or 14+/28+ drinks for females/males consumed in two weeks), non-heavy alcohol use, or abstinence. At TB diagnosis, we calculated the proportion of participants with any self-reported alcohol use, stratified by sex. At each time point, we assessed the association between alcohol use and sex using Chi-square tests. Finally, we used a subset of 136 (84 male, 52 female) participants with complete data to visually examine alcohol use longitudinally using alluvial plots.

Results: At diagnosis, 69 (48%) males and 27 (30%) females reported any recent alcohol use (prior 2 weeks). Males more often reported any alcohol use at TB diagnosis ($p=0.018$), and six ($p=0.030$), nine ($p=0.017$), and twelve ($p=0.013$) months post-treatment. For both sexes, overall alcohol consumption decreased during TB treatment then increased in the year following treatment (Figure 1).

There were 43 unique alcohol consumption patterns for males and 21 patterns for females. Among males and females, those abstinent at diagnosis were not the same individuals abstinent after TB treatment.

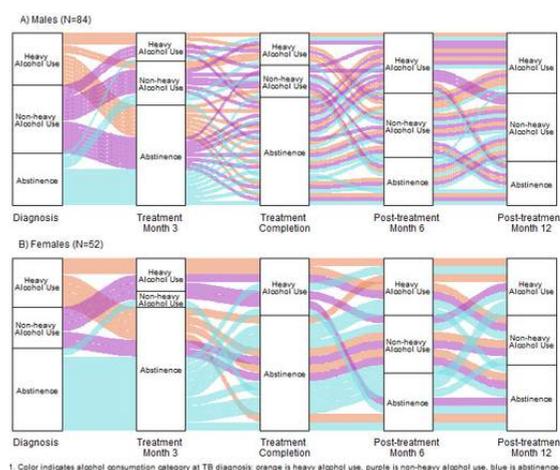


Figure 1. Alcohol use trajectories from TB diagnosis through one-year post-treatment completion, stratified by sex¹.

1. Color

Conclusions: Both female and especially male participants reported increased alcohol use after TB treatment. For both sexes, alcohol consumption at diagnosis was not representative of alcohol consumption after TB treatment. TB treatment may be an opportunity to address alcohol use and prevent future alcohol-related harms.

EP-33-934 Changes and differences in lung cancer death rates in Chinese population, 1991-2019

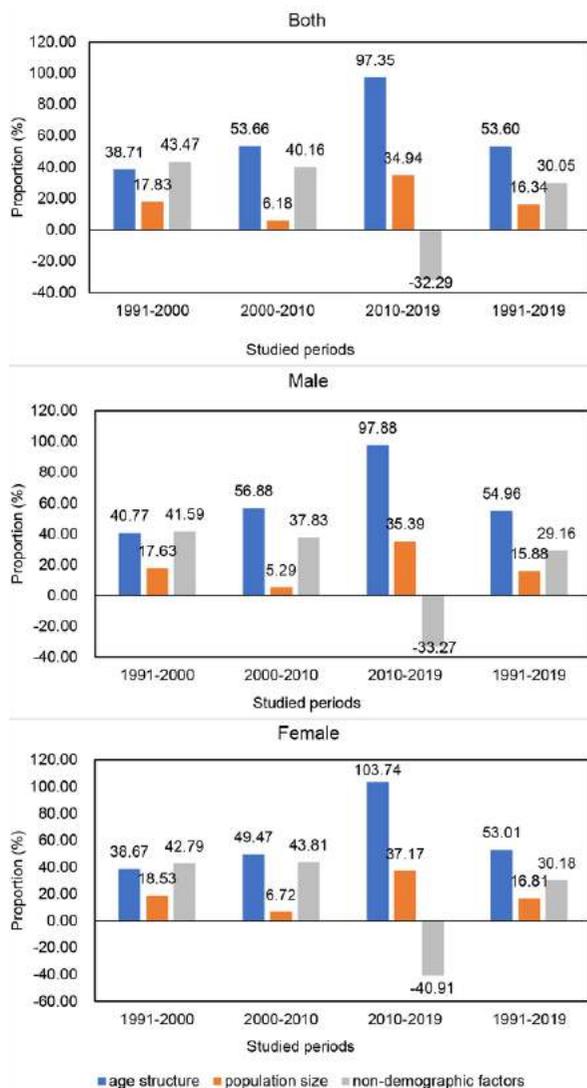
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Background: Lung Cancer deaths increased remarkably in China from 1991 to 2019, with their potential explainable components population size, age structure, and non-demographic factors also changing remarkably over time, however, each property remains undiscovered.

Design/Methods: In this retrospective cross-sectional surveillance study, original data in 1991 and 2000, and secondary data in 2010 and 2019 were collected from

Chinese Disease Surveillance Points systems across nationwide locations in China. Standardized death rates (SDRs) and crude death rates (CDRs) of the Chinese population in 1991, 2000, 2010, and 2019 were ascertained. The CDR difference (in %) in the studied periods (1991-2000, 2000-2010, 2010-2019, 1991-2019) was split into age structure, population size, and non-demographic factors using the three-factor factorial experimental method.

Results: From 1991 to 2019, the overall CDRs of lung cancer increased from 16.50/100,000 to 47.48/100,000, with the proportion continually increasing from 18.29% (ranked 3rd) to 29.22% (ranked 1st) in all cancers, whereas the SDRs increased from 1991 to 2010 and then slightly decreased from 2010 to 2019.



Males and females presented similar trends, with higher CDRs in males yearly. The increased overall CDRs of lung cancer were explained 53.60% by age structure, 16.34% by population size, and 30.05% by non-demographic factors from 1991 to 2019. In the three studied periods 1991-2000, 2000-2010, and 2010-2019, age

structure accounted most for CDRs in 2010-2019 period (97.35%), whereas non-demographic factors constantly decline with 43.47%, 40.16%, and -32.29% for the above three periods, respectively. Three factorial changes accounted slightly higher for CDRs increases in males than in females from 1991 to 2019.

Conclusions: Age structure contributed to an increasing positive share of lung cancer CDRs recently, whereas the non-demographic factors accounted constantly decreasing proportion for CDRs over time. Comprehensive measures to reduce lung cancer deaths are imperative in China.

EP-33-935 Diffusion impairment in asthma-COPD overlap: does it matter?

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Background: Unlike asthma and Chronic obstructive pulmonary disease (COPD), Asthma-COPD overlap (ACO) is a relatively new disease entity with distinct yet shared diagnostic and therapeutic approaches. In COPD, the diffusing capacity of the lungs for carbon monoxide (DLCO) is decreased, whereas, in asthma, it may be normal or increased. The present study was planned to evaluate the DLCO in ACO patients.

Design/Methods: The observational cross-sectional study was conducted in the Respiratory Medicine department at Indira Gandhi Government Medical College Hospital, Nagpur, India, from January 2020 to October 2021, wherein 43 consecutive ACO patients were enrolled. After detailed clinical evaluation, they underwent pulmonary function assessment, including DLCO assessment by single breath method. Data were analysed and presented using the proportion method. The quantitative data were presented as the means \pm SD (standard deviation) and median with 25th and 75th percentiles (interquartile range).

Results: There were 32 (74.42%) males and 11 (25.58%) female ACO patients with a mean age of 49.16 ± 16.3 years. The spirometric and DLCO parameters are shown in table 1. Normal to increased DLCO was observed in 22 (51.16%) ACO patients, whereas a decreased DLCO was observed in 21 (48.83%) ACO patients.

Pulmonary function test parameters	Mean \pm SD	Median (25th-75th percentile)	Range
FEV1(%)	44.45 \pm 18.56	40.79 (30.675-56.57)	13.58-94.78
FVC(%)	59.99 \pm 18.08	57.76 (47.66-71.735)	24.63-101.53
FEV1/FVC (%)	58.88 \pm 14.35	58.19 (50.015-66.425)	31.37-94.57
MEF 25-75 (%)	23.05 \pm 17.85	17.86 (11.555-26.055)	4.3-76.58
FEV1(%)	44.45 \pm 18.56	40.79 (30.675-56.57)	13.58-94.78
DLCO (%)	68.77 \pm 36.17	64.89 (52.94-81.655)	19.02-261.97

Table 1. Pulmonary Function Test Parameters.

Conclusions: Based on DLCO, we were able to identify at least two possibly distinct phenotypes of ACO, viz. asthma predominant ACO with a normal to increased DLCO and COPD predominant ACO with a decreased DLCO.

EP-33-936 Clinical characteristics and management of children below 5 years old admitted for very severe community-acquired pneumonia in Africa and South East Asia

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Background: Community-acquired pneumonia is the leading cause of death among children <5 yo. The WHO Standard of Care (SOC) for severe pneumonia is well standardized globally. Nevertheless, children's symptoms, co-morbidities, and management may differ according to countries, which may impact morbidity-mortality.

Design/Methods: Children aged 2-59 months with WHO-defined severe pneumonia were enrolled in 15 tertiary referral hospitals in Cambodia, Cameroon, Ivory Coast, Mozambique, Uganda, and Zambia from March 2019 to March 2021 in the TB-Speed Pneumonia study. Here, we describe country-level patients' characteristics and management in those with very severe pneumonia (SaO₂<90%, cyanosis, grunting, nasal flaring, or severe chest indrawing).

Results: Of 2570 children enrolled in the study, 2373 (92.3%) had criteria for very severe pneumonia: 381 (16.1%) from Cambodia, 376 (15.8%) Cameroon, 389 (16.4%) Ivory Coast, 269 (11.3%) Mozambique, 588 (24.8%) Uganda, and 370 (15.6%) from Zambia. 1352 (57.0%) were male and mean age was 10.7 [5.3-19.7] months. 121 (5.2%) patients were HIV positive,

including 31 (11.7%) in Mozambique. 40 (1.7%) patients had sickle cell disease and 237 (10.4%) had severe acute malnutrition (SAM). Overall, 2150 children (92.9%) received antibiotics at admission. 808 children (34.9%) received first-line antibiotics as per WHO guidelines, including 20 (7.4%) in Mozambique, 31 (9.9%) in Zambia and 98 (25.7%) in Cambodia. Among 899 (37.9%) patients with SpO₂<90% at inclusion, 721 (91.4%) received oxygen therapy. Among children with SAM, 108 (45.6%) received therapeutic feeding, but <18% in Cambodia, Mozambique and Zambia. Median length of stay in hospital was 5 days [4-8] and 124 (5.5%) of children died during hospitalization before 28 days, including 44 (14.0%) of Zambian children.

	All patients, n=2373	Cambodia, n=381	Cameroon, n= 376	Ivory Coast, n=389	Mozambique, n=269	Uganda, n=588	Zambia, n=370	p value
Age, months, median [IQR]	10.7 [5.3-19.7]	9.8 [5.2-18.7]	10.4 [5.8-19.2]	10.9 [4.8-22.5]	16.7 [7.6-28.9]	10.6 [5.8-16.6]	8.7 [4.3-16.3]	
Severe Acute Malnutrition (Weight for Height Z-score < -3 DS), n=2289	237 (10.4%)	23 (6.1%)	40 (11.0%)	56 (14.9%)	15 (5.7%)	67 (12.1%)	36 (10.2%)	<0.001
HIV positive before or at enrollment, n=2348	121 (5.2%)	2 (0.5%)	18 (4.9%)	8 (2.1%)	31 (11.7%)	33 (5.7%)	29 (8.0%)	<0.001
SpO ₂ < 90% (at admission)	899 (37.9%)	43 (11.3%)	110 (29.3%)	159 (40.9%)	51 (19.0%)	287 (48.8%)	249 (67.3%)	<0.001
Oxygen therapy if SpO ₂ < 90%, n=789	721 (91.4%)	42 (97.7%)	90 (84.1%)	134 (90.5%)	49 (96.1%)	245 (90.1%)	161 (95.8%)	0.01
Antibiotic (s) at admission or enrollment, IV or oral, n=2315	2150 (92.9%)	342 (89.8%)	356 (94.7%)	326 (83.8%)	249 (92.6%)	572 (97.3%)	305 (97.8%)	<0.001
Antibiotic (s) molecule (s) according to WHO guidelines (at admission or enrollment), n=2315	808 (34.9%)	98 (25.7%)	203 (54.0%)	144 (37.0%)	20 (7.4%)	312 (53.1%)	31 (9.9%)	<0.001
Therapeutic feeding if Severe Acute Malnutrition, n=237	108 (45.6%)	4 (17.4%)	32 (80.0%)	32 (57.1%)	0 (0.0%)	36 (53.7%)	4 (11.1%)	<0.001
Death during hospitalisation and ≤28 days, n=2274	124 (5.5%)	3 (0.8%)	20 (5.4%)	23 (6.1%)	6 (2.2%)	28 (4.9%)	44 (14.0%)	<0.001

Conclusions: Patients' characteristics and management of very severe pneumonia varied among countries. Antibiotics were not frequently prescribed according to the WHO SOC, possibly linked to the lack of specificity of severe pneumonia diagnosis.

EP-33-937 Perspectives of post-TB health care delivery amongst healthcare workers in urban Blantyre, Malawi

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Background: TB survivors face physical and mental health challenges after TB treatment completion. However, pathways for health care of TB survivors are poorly described. The study explored the beliefs and practices of HCWs in Malawi when managing TB survivors with post-TB morbidity.

Design/Methods: We completed two focus group discussions (FGDs) with TB officers (TBOs) and 16 in-depth interviews with HCWs from Blantyre, Malawi (January-April 2022). HCWs were identified using purposive and snowballing methods, and included TBOs, nurses, and clinicians. FGDs and interviews were completed in Chichewa and English. Data were translated, transcribed, and coded using a framework developed from the interview guide and primary data. Thematic analysis was used to interpret the data.

Results: HCWs frequently advise their patients on best practices following TB treatment, including diet, exercise, occupational exposures, alcohol use and smoking. However, they report little training around what this advice should include.

When TB survivors present with respiratory symptoms, HCWs often prescribe antibiotics as first line treatment, with investigations for recurrent TB or respiratory disease used if symptoms are not subsidizing.

HCWs place greater faith in the role of Xpert in diagnosing recurrent TB disease, compared to CXR. It is widely recognized that an abnormal CXR may reflect lesions from previous rather than active disease, but there is little awareness of false positive Xpert results amongst those who have been treated.

HCWs discuss complex cases of post-TB morbidity at facility level before referring to the central hospital or the National TB programme. There are no clear pathways for referral.

Conclusions: HCWs describe knowledge gaps around the provision of health advice to TB survivors. There are no clear guidelines on the use or interpretation of TB diagnostics in this patient group, and there is a need for formal pathways of referral for complex cases.

EP-33-938 Characterizing tuberculosis-related stigma and associated factors among patients in Uganda

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Background: Tuberculosis (TB) is one of the leading causes of death from a single infectious agent worldwide. TB-related stigma negatively affects various health outcomes including treatment adherence, but it has not been well characterized in Uganda.

The aim of this study was to characterize three types of TB-related stigma and the associated factors among patients on treatment.

Design/Methods: A cross-sectional study was conducted among patients with TB aged 18-65 in treatment at public clinics in Kampala, Uganda from July 2020 to March 2021. Data were collected on socio-demographics and 14-items were used to measure self-, anticipated-, and public-stigma as the outcome variables.

Self-stigma: the idea that individuals may endorse negative stereotypes and behave or think according to these fake portrayals and negative messages.

Anticipated stigma: worry that one will be devalued post disclosure of a TB diagnosis.

Public-stigma: negative attitudes, beliefs, and behaviors held by the wider community. The primary independent variable was sex and other factors were age, employment, HIV status.

We used logistic regression analysis to evaluate the association between sex and stigma outcomes controlling for other factors as potential confounders.

Results: Of 144 participants enrolled 50% were female, mean age was 35.8 (SD=12), 44% had a secondary education, 37.5% were unemployed, 32.6% were HIV co-infected. The prevalence of self-, anticipated-, and public-stigma was 77.1%, 75.7%, and 41.7% respectively. Female sex (Adj. OR: 2.35 95% CI 1.02-5.74) and unemployment (Adj. OR: 2.95 95% CI: 1.16-8.58) were significantly associated with self-stigma.

HIV-positive status was significantly associated with anticipated stigma (Adj. OR: 3.58 95% CI: 1.38-11.23). None of the variables evaluated were significantly associated with public stigma.

Conclusions: Female patients and those that were currently unemployed were more likely to experience self-stigma, while people with TB/HIV co-infection were at greater risk of anticipated stigma. These findings highlight potential targets for interventions for stigma reduction.

EP-33-939 Effectiveness of the post tuberculosis lung disease intervention in affected individuals in northern Tanzania

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Background: In resource constrained settings, interventions for curbing post-tuberculosis lung diseases (PTLD) are scarce and less prioritized. We designed an intervention model and assessed its effectiveness in pragmatic settings for individuals with PTLTLD.

Design/Methods: This longitudinal study design enrolled and followed individuals with PTLTLD for 12 weeks at Kibong'oto Infectious Diseases Hospital and Mire-rani health center in Tanzania. Individuals received pulmonary-rehabilitation (PR) services comprised of physical exercise and health education four times a week for 12 weeks. A daily Salmeterol 25mcg/fluticasone 250mcg inhaler and mucolytic agent were also prescribed if they had wheezes and breathlessness. Symptoms resolution, Six-minutes walked-distance (6MWD) and occurrence of PR-related adverse events determined the model's effectiveness.

Results: Among 85 individuals enrolled 75 (88%) were male and mean (SD) age of 40 ±10 years. Ten (12%) were living with HIV/AIDS, while 38(45%) and 54 (64%) had prior history working in mining and cigarette smoking, respectively. All 85 received PR services, 10 (12%) received both PR and salmeterol + fluticasone inhaler, and only 19 completed 12 weeks by march 2022. At week 12, individuals with cough reduced from 67/85 (79%) to 2/19 (11%, $p < 0.001$), breathlessness from 56/85 (66%) to 6/19 (32%, $p = 0.007$) and wheezes from 32/85 (38%) to 5/1 (26%, $p = 0.326$). Moreover, 6MWD significantly increased from 390±84 meters at baseline to 443±75 meters at 12 weeks of intervention ($p = 0.048$). Of 19 individuals, 16 (84%) experiences breathless compared to 5 (26%, $p < 0.001$). Easy fatigability and muscle cramps did not change with intervention ($p > 0.05$). Among 10 individuals on Salmeterol/fluticasone inhaler and mucolytic agent, 4 (40%) and 6 (60%) complained throat irritation and drowsiness respectively.

Conclusions: The short-term assessment of intervention shows clear benefits, however intermediate and long-term benefits are uncertain. Therefore, more evidences are needed to inform the practice.

EP-33-940 Burden of mental disorders in individuals with post TB lung diseases. A cross sectional survey in northern Tanzania

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Background: Mental health is an essential to overall health and well-being in patients with chronic lung diseases such as post tuberculosis lung diseases (PTLD). We described the burden of the mental health conditions experienced by individuals with PTLTLD in Tanzania.

Design/Methods: A cross sectional design that included adults affected with PTLTLD attending physical rehabilitation within Siha and Simanjoro catchment areas were assessed using Patient Health Questionnaire (PHQ-9) and Generalized Anxiety Disorder (GAD-7) tools for depression and anxiety respectively.

Patients with PHQ scores of 0-9 were categorized as having none to mild, 10-14 as moderate, 15-19 moderately severe, 20-27 severe form depression.

Patients with GAD-7 Scores of 0-5 were categorized as having mild, 6-10 moderate, 11-15 moderately severe, and 15-21 severe anxiety. During the patient review, clinical assessment for depression and anxiety as well as psychosocial explorations were done.

Results: In December 2021, 25 out of 85 individuals with PTLTLD were identified to have mental disorders. Among 25 patients with mental disorder, 23 (92%) and 2 (8%) had anxiety and depression with suicidal ideation, respectively. Furthermore, 9 (36%) of these 25 patients had symptoms of posttraumatic stress disorder comprised of pain ($n = 5$), exhaustion and insomnia ($n = 4$) and all had panic attacks. One of patients with suicidal ideation had multiple suicidal attempts partly related to key suicide risks such as alcohol use, depression, access to poisons and PTLTLD/HIV-co-morbidity.

In total, 5 (20%) of 25 PTLTLD patients reported to be stigmatized in the community whereas 8 (32%) were unable to perform their regular daily activities.

Conclusions: Mental disorders are common phenomena in patients with PTLD. Mental health interventions in clinical practice are key to alleviate patient's sufferers.

EP-34 Post TB lung health, case finding, DR-TB management

EP-34-941 Cavitory lesions are associated with increased levels of matrix metalloproteinases after successful tuberculosis treatment

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Background: Although post-tuberculosis (TB) lung disease (PTLD) is a major contributor to chronic respiratory disease globally, little is known about the nature of lung injury during and after TB treatment.

Among patients successfully treated for pulmonary TB, we explored the association between cavitory lesions on chest imaging and levels of matrix metalloproteinases (MMPs), enzymes that degrade extracellular matrix proteins.

Design/Methods: We performed a cross-sectional analysis of an ongoing prospective cohort study among HIV-negative adults who were successfully treated for pulmonary TB in the country of Georgia. Cavitory lesions were identified by chest computed tomography (CT); a subset of participants underwent fluorodeoxyglucose positron emission tomography-CT (FDG PET-CT). MMP8 and MMP9 levels were measured in plasma using a Luminex assay.

All study measures were obtained at the end of TB treatment. Wilcoxon rank-sum tests were used to estimate the association between cavitory lesions and FDG uptake on PET with MMP levels.

Results: Among 124 participants enrolled, 40 (32%) participants had MMP levels available for analysis, including 15 (38%) with ≥ 1 cavity on CT. The median MMP8 level was 505 pg/ml (interquartile range [IQR] 338 – 1,149) and median MMP9 level was 93,823 pg/ml (IQR 48,208 – 126,629). MMP8 and MMP9 levels were higher among those with cavities compared to those without (median difference 394 pg/ml for MMP8 [$p=0.07$] and 43,535 pg/ml for MMP9 [$p=0.05$]).

Among 21 participants with a PET-CT, median MMP8 and MMP9 levels were non-significantly higher among those with any pulmonary FDG uptake compared to those without (median difference 143 pg/ml for MMP8 [$p=0.34$] and 39,783 pg/ml for MMP9 [$p=0.28$]).

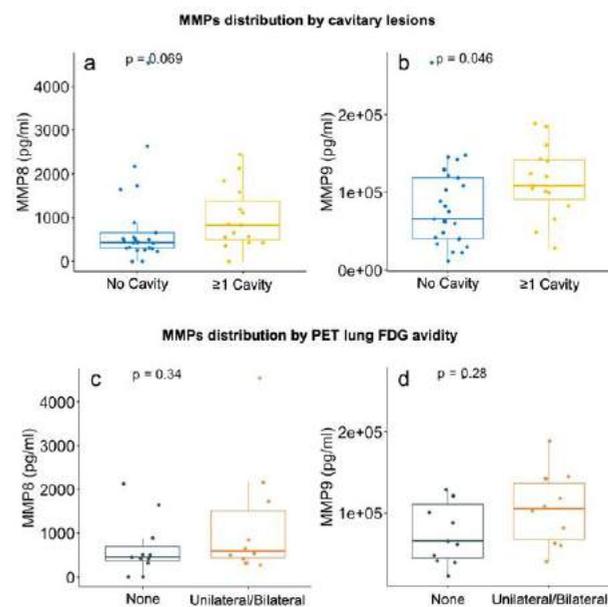


Figure 1. Distribution of MMP8 and MMP9 according to cavitory lesions at the end of tuberculosis treatment (a and b) and PET lung FDG avidity (c and d).

Conclusions: Persistent cavitation after successful TB treatment is associated with higher MMP8 and MMP9 levels, which may reflect ongoing pulmonary inflammation. Studies are needed to assess whether select patients with cavitory lesions despite successful TB treatment may benefit from further intervention such as host-directed therapy.

EP-34-942 TB recurrence among individuals recently treated for TB in India

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Background: Approximately seven percent of reported tuberculosis (TB) cases worldwide are recurrent. In India, TB recurrence is particularly common with approximately 10-13% of treatment-completed individuals developing TB again. To detect recurrent TB early and stop the chain of transmission, India has introduced active case finding (ACF) among individuals who have completed TB treatment. However, evidence around optimal timepoints for post-treatment ACF is scarce. We analyzed TB recurrences observed in the ongoing TB Aftermath trial.

Design/Methods: Adults (≥ 18 years) who completed TB treatment were enrolled between February 2021 and May 2022 from six public TB clinics in Pune district, India. At enrollment, sociodemographic and clinical data were collected and participants were counselled to seek care if they developed symptoms suggestive of TB. At six and twelve months post-treatment, participants received symptom-based ACF either telephonically or at home. We analyzed timing and characteristics of microbiologically-confirmed TB recurrence among individuals who contributed at least six months of follow-up since TB treatment completion.

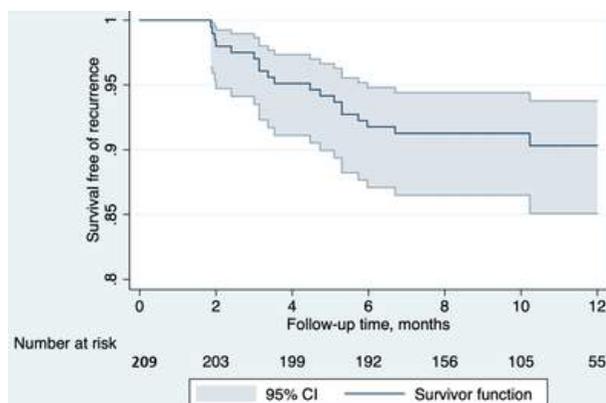


Figure. Kaplan-Meier survival curve for TB recurrence.

Results: Of 436 participants enrolled, 209 (48%) contributed at least six months of follow-up (median: 10 months; Interquartile range (IQR): 7.9-12.0). 124 (59%) were male, 24 (11%) were living with diabetes, and one with HIV. 196 (94%) had completed a regimen for drug-susceptible TB. The site of disease was pulmonary for

127 (61%), extrapulmonary for 72 (34%), and both for 10 (5%). Nineteen (9%) individuals were diagnosed with recurrent TB at a median of 3.5 months (IQR: 2.4-5.3) after treatment completion, including 17 with prior microbiological confirmation of cure. The recurrence rate was 11 per 100-person-years and the median diagnostic delay was 15 days (IQR: 8-15) from symptom onset.

Conclusions: We observed a high rate of TB recurrence occurring less than six months after treatment completion in the TB Aftermath trial. TB Aftermath is ongoing and is comparing two ACF strategies designed to detect recurrent TB.

EP-34-943 Prévalence et facteurs associés aux troubles respiratoires fonctionnels chez les travailleurs de l'égrenage de coton au Bénin en 2019

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Background: Au Bénin, les statistiques de santé respiratoire des travailleurs en milieu industriel est quasi inexistante. L'exposition à la poussière coton est susceptible d'entraîner des troubles respiratoires. L'objectif était d'étudier la prévalence et les facteurs associés à l'altération de la fonction pulmonaire (LFI) chez les travailleurs des usines d'égrenage du coton au Bénin en 2019.

Design/Methods: Il s'agissait d'une étude transversale, analytique et observationnelle menée du 31 janvier au 11 avril 2019. Nous avons inclus des travailleurs des usines d'égrenage de coton du Nord âgés de >15 ans après avis favorable du comité t. Les données ont été recueillies par entrevue en personne à l'aide d'un questionnaire suivi de tests de spirométrie. L'analyse des données a été effectuée par R 3.6.0 Software. Une régression logistique binaire par étapes a été effectuée; le seuil de signification était $p < 0,05$.

Results: Sur 1520 travailleurs, 91,25 % étaient des hommes. L'âge médian était de 38 ans (IQR: 28 - 49). La prévalence de l'IFL était de 17,04 % (IC à 95 % : [15,20-19,05]) avec une prédominance de troubles restrictifs (13,88 %, IC à 95 % : [12,20 -15,74]). Les symptômes respiratoires après le retour de la fin de semaine étaient répandus chez 27,89 % des travailleurs. Le symptôme respiratoire persistant était la toux (24,08 %). Les principaux facteurs associés à l'IFL étaient : l'âge (ORa = 2,62, IC à 95 % : [1,90-3,64]), le sexe (ORa = 2,58, IC à 95 % : [1,36-5, 36]), la non-utilisation de couverture nasale (ORa = 3,27; IC95 % : [2,28-4,70]); l'exposition à la poussière (ORa = 34,12, IC à 95 % : [17,71 à 76,49]).

Conclusions: Des mesures préventives contre l'inhalation de poussière de coton et d'autres facteurs de risque respiratoires.

EP-34-944 Improving childhood TB notification: lessons from a mix-method implementation in Katsina state

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Background and challenges to implementation: Childhood TB case detection and notification in Katsina state has proved to be challenging due to poor sample generation, inadequate number of clinicians to interpret CXR results outside metropolitan cities, and low resources for adequate contact investigation coverage. This paper aims to showcase improved Childhood TB case notification using a mix-method approach.

Intervention or response: The Mix-method implementation for childhood TB through USAID TB LON 1 & 2 project focused on improving the quality of TB screening, diagnosis, and notification. The steps taken were: Sensitization of clinicians and healthcare workers on adequate childhood screening to increase presumptive TB, establishing routine screening in childhood clinics, prioritizing stool sample collection in children (0-14) years of age, supporting access to CXR in rural and hard-to-reach communities, conducting reverse contact investigation for bacteriologically diagnosed children and ensuring DOTS services are provided at the nearest facility to patients.

Results/Impact: Quarterly case notification of childhood TB from January 2021 to December 2021 was reviewed against the total TB case notification for the same period. From the start of the mix-method implementation, the proportion of Childhood TB case detection has significantly improved from average quarterly notification of 165 childhood TB cases (11%) in 2020 to Q1 2021 – 212 (15%), Q2 2021 – 173 (15%), Q3 – 195 (13%), and Q4 – 163 (11%).

Conclusions: The mix-method approach in Katsina state improved childhood TB case notification to an average proportion of 14% which is comparable with WHO 12-15% and would be successful in improving childhood TB case notification in similar northwestern states across Nigeria.

EP-34-945 Reaching the unreached: TB diagnosis in children in Madhesh province of Nepal

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Background and challenges to implementation: Occurrence of Tuberculosis (TB) in children is associated with TB prevalence in adults. Risk of developing TB in children is high for regions with high TB prevalence and high population density. Madhesh province has both risk factors with a population density of 630 people Sq. Km and TB notification of 6586 cases. WHO estimates almost 15% of the notified TB cases to be children under 15 years while Madhesh province accounted for only 4% of the total notified cases (260/6586).

Despite major advances in TB diagnosis like expansion of GeneXpert sites, TB in children remains underdiagnosed and difficult as it rarely rests on bacteriological confirmation. To overcome the challenges, Bagmati Welfare Society Nepal (BWSN) a sub recipient of Save the children initiated referral of SAM and MAM children from community to trained pediatrician for diagnosis of TB in children.

Intervention or response: During August to December 2018, pediatricians were trained on the management of TB in children based on National guidelines. BWSN mobilized volunteers to identify SAM and MAM cases in community. The volunteers developed line list of SAM and MAM cases who were introduced with Mantoux test by trained laboratory person.

All the children were invited to a pre-identified venue for further examination with X-ray by a trained pediatrician. Children were provided with transport facility. During the period, we reached screened 4555 children and identified 724 SAM/MAM children at 13 venues in six districts.

Results/Impact: Pediatricians diagnosed 130 TB cases with yield of 18%. Total expenses occurred during the entire process was 20K USD. Recorded cost for detecting one childhood TB case was 158 USD which is almost half of the estimated cost to find one TB case through active case finding.

Conclusions: Mobilizing the trained pediatricians to rural community for TB screening helps to increase TB case notification among children.

EP-34-946 Treatment outcomes among drug resistant tuberculosis (DRTB) children below 10 years treated with newer drugs, in Médecins Sans Frontières Clinic (MSF), Mumbai, India

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Background: As per Global TB report, 1.1 million children and young adolescents aged <15 years fall ill with tuberculosis (TB) every year. Prevalence of drug resistant TB among paediatric population has increased to 9.6% in 2018 from 5.6% in 2010 in a Mumbai study dated 2016. MSF clinic since 2016 have been treating paediatric cases with new drugs.

Design/Methods: Descriptive retrospective study on children <10 years initiated from September 2016 to March 2022 in MSF clinic Mumbai, India. Drug Resistant tuberculosis (DRTB) confirmed on molecular test (Xpert and LPA) followed by culture and drug susceptibility testing (DST).

Patients were given individualized DST based regimens with newer TB drugs (BDQ & or DLM) under compassionate use. Monthly clinical/radiological monitoring and post treatment follow-up for a year.

Results: Cohort of 12 children constitutes, 59% (7/12) of female with median age of 5 years (14 month-10 years) and 75% (9/12) new TB cases. 100% microbiologically confirmed, 10/12 were fluoroquinolone resistance and 10/12 were household contacts of DRTB patients. (7/12) 58% had pulmonary TB (PTB), (3/12) 25% extrapulmonary TB (EPTB) and (2/12) 17% disseminated tuberculosis. 50% (6/12) were treated with DLM and rest 50% (6/12) with BDQ/DLM and optimised background regimen (OBR) including imipenem.

Out of 66.66% patients with treatment outcome, 7/12 had successful outcome 1/12 lost to follow-up. 83% (10/12) patients reported adverse drug reaction (ADR) which were vomiting (4/12), neuropsychiatric adverse events (5/12), anaemia (3/12), hepatitis (4/12) and optic neuritis (1/12).

All patients received BDQ or BDQ/DLM, and had gained average weight of 4 kg from baseline and growth by 9 cm. At one year follow-up 6 were asymptomatic and 1 child could not be traced. CS & LZD interruption not BDQ & DLM

Background and challenges to implementation: As per Global TB report, 1.1 million children and young adolescents aged <15 years fall ill with tuberculosis (TB) every year.

Prevalence of drug resistant TB (DRTB) among paediatric population has increased to 9.6% in 2018 from 5.6% in 2010 in a Mumbai study dated 2016.

Médecins Sans Frontières (MSF) clinic, Mumbai has been treating paediatric cases with new drugs since 2016.

Intervention or response: In MSF clinic, DRTB is confirmed on molecular test (Xpert and LPA) followed by culture and drug susceptibility testing (DST). Patients are given individualized DST based regimens with newer TB drugs (BDQ & or DLM) under compassionate use. Clinical/radiological monitoring and post treatment follow-up is done for a year.

Intervention for children <10 years initiated from September 2016 to March 2022 in MSF clinic Mumbai, India is analyzed.

Results/Impact: Out of 12 children, 59% (7/12) were female with median age of 5 years (14 month-10 years) and 75% (9/12) new TB cases. 100% microbiologically confirmed, 10/12 were fluoroquinolone (FQ) resistant and 10/12 were household contacts of DRTB patients. 58% (7/12) had pulmonary TB, 25% (3/12) extrapulmonary TB and 17% (2/12) disseminated TB. 50% (6/12) were treated with DLM, rest 50% (6/12) with BDQ/DLM and optimised background regimen including Imipenem. Out of 8 patients with treatment outcome, 88% (7/12) had successful outcome, 1/8 lost to follow-up. 83% (10/12) patients reported adverse drug reaction (ADR) which were vomiting (4/12), neuropsychiatric adverse events (5/12), anaemia (3/12), hepatitis (4/12) and optic neuritis (1/12). None of the ADR management necessitated treatment interruption. All patients received BDQ or BDQ/DLM and had gained average weight of 4 kg from baseline and growth by 9 cm. At one year follow-up 6 were asymptomatic and 1 child could not be traced.

Conclusions: Higher success rate in FQ resistant children less than 10 years require comprehensive monthly monitoring for stringent ADR management.

EP-34-948 Post-tuberculosis lung disease: community based lung rehabilitation. Experiences from Malawi

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Background and challenges to implementation: A recent study from Malawi showed that about 20 % of those that had completed treatment for pulmonary tuberculosis suffered from post-tuberculosis lung disease (PTLD) one year after cure. Other studies suggest PTLD in up to 50 %. There is no systematic follow-up of former TB patients in Malawi.

Intervention or response: As part of the project „Finally addressing Post TB disability in Malawi“, a low-cost community based Pulmonary Rehabilitation Program was designed by Paradiso, NONM, LHLI and physiotherapists. It was piloted in 3 areas and former TB patients suffering from PTLD were offered to participate. Thorough assessments (medical and quality of life) were done at baseline, after 6 weeks, and 12 weeks. The program had 2 sessions per week with health information and aerobic exercises. In each facility, volunteers and health workers were trained in order to equip them with the knowledge and tools to manage the program. Equipment needed for exercises were locally made.

Results/Impact: 38 people participated in the program. All showed considerable improvements in quality of life; in exercise capacity, in respiratory outcomes and also in mental health. Results after 12 weeks were much better than after 6 weeks. Based on the assessment of the pilot program, the lung rehabilitation program is scaled to six more districts.

Conclusions: Community based pulmonary rehabilitation is highly effective for people with PTLD. The intervention is low cost and contribute to securing care and support for former person(s) with TB experiencing aftereffects of TB. The initiative should be scaled up nationwide.

EP-35 TB and comorbidities

EP-35-949 Tuberculosis recurrence in cancer patients: the influence from prolongation of treatment course

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Background: Tuberculosis (TB) recurrence rate is higher in patients with cancer. Prolongation of the treatment course from 6 months to 9 months might be a solution to decrease TB recurrence but there is scarce study to investigate the effect.

Design/Methods: We recruited patients with TB during 2006~2018 in Taiwan National Health Insurance database. We excluded patients with extrapulmonary TB, using second line TB drug, treatment < 6 months or > 9 months. The wer classified as treatment of 6 months (180~225 days) and 9 months (225~270 days). We analyzed their TB two-year recurrence rate between the two groups.

Results: During study period, there was 9367 patients with TB and cancer, and 75 (0.8%) patients with TB recurrence. The age was similar between the two groups ($p=0.7447$) but there was more male proportion (77.9% vs 74.2%) in 9-month group than that in 6-month group ($p=0.0004$). Among the recurrence events, there were 57 (0.79%) and 18 (0.83%) TB recurrence within two-year follow-up in 6-month and 9-month treatment groups, respectively ($p=0.865$).

Conclusions: In the present study, TB recurrence rate within two years was around 0.80% among patients with cancer. TB treatment for 6 months and 9 months showed similar 2-year recurrence and unnecessary prolongation might not be needed.

EP-35-950 The role of continuous cough sound detection for tuberculosis treatment monitoring among people living with and without HIV

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Background: Cough frequency correlates with tuberculosis (TB) treatment response but to date has been subjectively assessed. We examined the potential of continuous cough sound detection to objectively monitor TB treatment response by HIV status.

Design/Methods: We prospectively enrolled patients initiating treatment for drug-susceptible pulmonary TB at two outpatient clinics in Uganda. Study participants continuously carried a smartphone installed with the Hye Research cough recording application for 14 days. Short 0.5 second bursts of sound were automatically detected by the application and classified as a cough based on a deep learning algorithm.

Clinical and demographic data were obtained from facility TB registers, and adherence was determined using the digital adherence technology 99DOTS and self-report. Cough frequency was defined as the median number of coughs per hour (mCPH) and compared between participants living with and without HIV at the time of TB diagnosis and after 14 days using Wilcoxon tests.

Results: Of the 86 patients included, 32 (41.6%) were living with HIV, 37 (43.0%) were female, and 49 (57.0%) had microbiologically confirmed TB. Adherence over the first 14 days of TB treatment was high and similar by HIV status (94.7% vs. 100% among people living with and without HIV, respectively; $p=0.16$). People living with HIV had a lower mCPH on day 1 (13.8 [IQR 9-19] vs. 22.8 [IQR 15-31], $p=0.06$) (Figure 1).

mCPH reduced to 7.2 (IQR 5-9) and 13.3 (IQR 8-19) by day 14 in people living with and without HIV, respectively. Overall, cough frequency reduced significantly by day 14 regardless of HIV status ($p<0.001$).

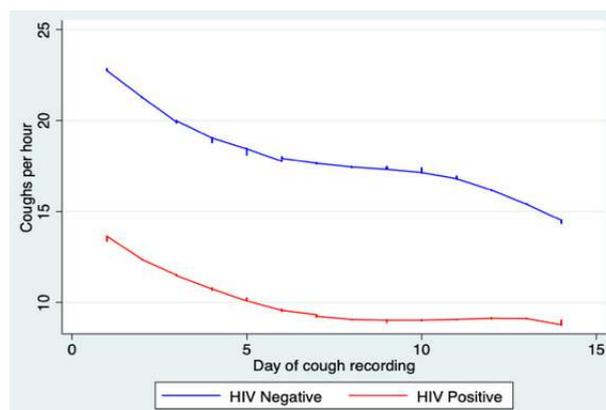


Figure 1. Changes in cough frequency by HIV status

Conclusions: Continuous cough monitoring was feasible and able to identify a unique lower-frequency cough pattern among people living with HIV. At the same time, cough frequency reduced regardless of HIV status, providing an objective marker for TB treatment monitoring.

EP-35-951 The impact of tuberculosis on lung cancer mortality

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Background: Pulmonary tuberculosis (TB) is a common infectious disease worldwide and previous studies show that preexisting TB increases the risk of lung cancer. Notably, lung cancer is one of the leading causes of cancer death but there is limited information on preexisting TB and lung cancer prognosis.

Therefore, our study aims to explore the survival impact of preexisting TB among the patients with lung cancer using the data from the Taiwan Cancer Registry database.

Design/Methods: We recruited patients with lung cancer from Taiwan Cancer Registry during 2011~2015. Patients were divided into two groups: one group with TB before lung cancer, and the remaining group without. We matched the two groups using propensity score matching in a ratio of 1:4 and compared the 3 year overall and cancer specific mortality between the two groups.

Results: During study period, there was 43472 patients with lung cancer and among them, 1211 (2.79%) patients with previous TB. After matching, there are 5,935 patients with lung cancer in this cohort including patients with TB before lung cancer (n=1,187) or those

without ($n=4,748$). The patients with previous TB had adjusted hazard ratio of 1.13 (95% CI: 1.04-1.23) and 1.11 (1.02-1.21) to have overall and cancer-specific three-year mortality after controlling for demographic factors and comorbidities.

Conclusions: Our study showed that previous TB existed in 2.79% in patients with lung cancer and might be associated with increasing mortality. Further care bundle should be targeted into this subgroup to improved their outcome.

EP-35-952 Healthcare-seeking behavior among people living with HIV undergoing tuberculosis screening during the COVID-19 pandemic in Kampala, Uganda

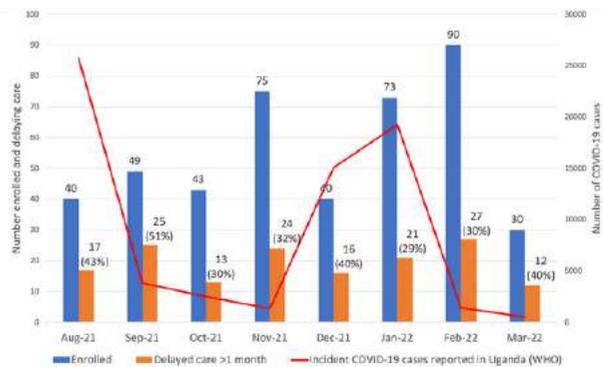
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Background: Disruptions related to the COVID-19 pandemic have contributed to major declines in tuberculosis (TB) case notifications and increased estimated TB mortality globally, reversing years of progress. We assessed the pandemic's impact on healthcare-seeking behavior among people living with HIV (PLWH) undergoing TB screening in a high TB/HIV burden setting.

Design/Methods: TB SCRIPT is an ongoing trial evaluating the impact of C-reactive protein-based TB screening on case-detection and TB preventive therapy (TPT) uptake in Kampala, Uganda (ClinicalTrials.gov NCT04557176). At study enrollment, adults new to HIV care are screened for TB, followed by confirmatory testing for participants who screen positive, and TPT eligibility assessment for participants who screen negative for TB. We used a standardized questionnaire to identify trends in healthcare-seeking behavior, barriers to seeking care, and access to COVID-19 testing and vaccination for participants enrolled from August 2021 through March 2022.

Results: Of 440 participants (257 [58.4%] female, median age 31.5 years [IQR 26-38], median CD4 count 192 cells/ μ L [IQR 83.0-302.5]), 424 (96.4%) reported some form of employment, and the median monthly household income was 20USD (IQR 11- 42[YC1][CL2][i3]). Sixty-seven participants (15%) were diagnosed with prevalent TB. Overall, 155 (35.2%) participants reported delaying care for >1 month. Common reasons for delaying care included work obligations ($n=59$, 38.1%) and transportation costs ($n=30$, 19.4%). COVID-relat-

ed travel restrictions ($n=21$, 13.5%), fear of COVID-19 infection ($n=12$, 7.7%), and coming-to-terms with a recent HIV diagnosis ($n=6$, 3.9%) were less frequently cited as reasons for delaying care. Fifty-nine (13.5%) reported prior COVID-19 testing, of whom 6 (10.2%) tested positive; 100 participants (22.7%) reported receiving ≥ 1 COVID-19 vaccine.



Conclusions: The COVID-19 pandemic has exacerbated barriers to care that were common prior to the pandemic. However, 15 months into the pandemic, 'traditional' barriers remain the most frequently cited reasons for delaying care despite high COVID-19 test positivity among those tested.

EP-35-953 Early experience of integrated diabetes model of care in drug resistant tuberculosis (DR-TB) treatment at the Nodal DRTB Center, Mumbai, India

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Background and challenges to implementation: Integrated care for people with tuberculosis (TB) and diabetes mellitus (DM) is embedded in Pillar-1 of the End-TB Strategy. The National Tuberculosis Elimination Program (NTEP) recommends screening DM during treatment initiation with referral to higher health centres. But there is gap in monitoring mechanism at Nodal DRTB.

Intervention or response: At Médecins Sans Frontières (MSF) supported DRTB outpatient department, M-East Ward Mumbai, the DM patients identified at the treatment initiation are further followed in DRTB -DM in-

tegrated model of care. All DRTB patients are screened for DM with random blood sugar (RBS), those having the RBS >140mg/dl are subjected to glycosylated haemoglobin (HBA1c). Based on HBA1c they are classified as controlled DM (<8) and uncontrolled DM (>8) as per WHO guideline. Patients with controlled and uncontrolled DM are routinely followed at 6-monthly and 3-monthly respectively. The DM patients are given oral anti-diabetic treatment at TB OPD. Routine follow up done by multi-disciplinary team.

Results/Impact: Among 1691 DRTB patients initiated on treatment between the year 2020 to 2021, 13% (224/1691) had DRTB-DM, 22% (50) were newly diagnosed. Patient with baseline HBA1c tested, 24% (50/209) had controlled and 76% (159/209) had uncontrolled DM. Out of the baseline-uncontrolled DRTB-DM 50% (40/81) were controlled at 6th month, showing half of the cohort continued to have uncontrolled DM. Out of the baseline-controlled DRTB-DM 61% (14/23) continued to have controlled status till 6th month. Findings shows that about 50% of the patients were difficult to monitor under the model of care since they followed up the DM treatment in other centre or refused treatment. Our early experience shows that DRTB-DM model of care needs a systematic follow-up monitoring mechanism.

Treatment outcome of DM patients at baseline and after 6 months of systematic monitoring and treatment as per the model of care

TB outcome	At Baseline (N=209)		At 6 months(N=103)	
	Controlled (n=50)	Uncontrolled (n=159)	Controlled (n=58)	Uncontrolled (n=45)
Favourable Outcome	22/28 (79%)	21/52 (40%)	16/21 (76%)	13/17 (76%)
Unfavourable Outcome	6/28 (21%)	31/52 (60%)	5/21 (24%)	4/17 (24%)

Conclusions: Early screening for DM in DRTB cohort should be implemented for early detection of DM and systematic monitoring (including HbA1c) with a multidisciplinary team ensures proper follow-up of DRTB-DM.

EP-35-954 Identifying patient driven factors limiting tuberculosis preventative therapy uptake amongst adults with advanced HIV disease

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Background: Tuberculosis (TB) remains the commonest cause of AIDS-related deaths worldwide and patients with advanced HIV disease (AHD) are at greatest risk. Despite robust data that TB preventive therapy (TPT) prevents TB disease and deaths amongst people living with HIV, TPT provision remains sub-optimal globally. Innovative delivery strategies to increase TPT reach are needed. If acceptable, inpatient initiation of ultra-short course TPT (one month of isoniazid-rifapentine (1HP)) may collapse the latent TB care cascade.

Design/Methods: A structured questionnaire to investigate TPT knowledge and acceptability was administered to Ugandan adults with AHD (i.e. CD4<200) and cryptococcal meningitis. Preference around TPT regimen and initiation setting were evaluated, alongside other potential barriers to TPT uptake.

Results: Between December 2021-ongoing, we interviewed 43 Ugandan adults with AHD and cryptococcal meningitis. Overall, 67% (29/43) were male. The mean age was 36 years (range 21-56 years), and median CD4+ cell count was 50 cells/ μ L (IQR 13-126 cells/ μ L). 17% (6/35) reported a history of TB, and 6% (2/35) had ever received TPT. Nearly all (39/43, 91%) were aware that HIV increased risk of TB disease, but only 60% (26/43) were aware of TPT. 1HP was the preferred regimen in 53%. Potential TPT barriers included: side effects (39%), pill burden (19%), and drug-drug interactions (16%). The majority reported preference to start TPT in the outpatient setting (77%) as compared to inpatient initiation (23%). Only 12% reported TPT adherence concerns.

Knowledge and acceptability statements	N (%) of participants in agreement
Have you heard of tuberculosis?	43 (100)
Cough is a symptom of TB disease?	42 (98)
Fever is a symptom of TB disease?	34 (79)
Night sweats are a symptom of TB disease?	33 (77)
Weight loss is a symptom of TB disease?	41 (95)
TB preventative therapy regimen preference:	
1HP – one month of daily isoniazid (INH) and rifapentine (RPT)	23 (53.5)
3HP – three months of weekly INH and RPT	10 (23.3)
6H – six months of daily INH	10 (23.3)
Are you concerned about any of the following related to TPT?	
Side effects (e.g liver problems)	17 (39.5)
Drug-drug interactions (e.g with ART)	7 (16.3)
Number of pills	8 (18.6)
Adherence	5 (11.6)

Table 1. Knowledge of tuberculosis disease, and tuberculosis preventative therapy preferences and concerns amongst 43 Ugandan adults with advanced HIV disease and cryptococcal meningitis.

Conclusions: TPT awareness and use was sub-optimal within our high-risk cohort with AHD. Participant-driven reported barriers to TPT uptake however were few, and knowledge about TB risk and disease was good. TPT promotion by healthcare workers including information about new ultra-short course, less-toxic regimens may therefore increase TPT reach, and reduce TB-associated deaths within this key population. Further qualitative research to understand concerns about TPT inpatient initiation is needed.

EP-35-955 Risk factors and complications in 947 tuberculosis patients hospitalized in the Pulmonology Department of Fann CHNU from 2017 to 2019

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Background and challenges to implementation: Despite current progress, tuberculosis remains a major public health problem, given its still high incidence, prevalence, and mortality, particularly in sub-Saharan African countries, including Senegal. This risk is higher for immunocompromised people.

Complications and comorbidities can also affect the course of the disease, affecting the prognosis. It is in this context that this study was undertaken with the objective of determining the risk factors and complications in patients hospitalized for tuberculosis.

Intervention or response: This was a retrospective and descriptive study carried out in 2021, from records of patients hospitalized for tuberculosis from January 1, 2017, to December 31, 2019, at the Pulmonology Department of Fann of Fann. Were included all patients placed on antituberculosis treatment after the diagnosis of tuberculosis has been bacteriologically confirmed or clinically made as defined by WHO. Multidrug-resistant TB was excluded.

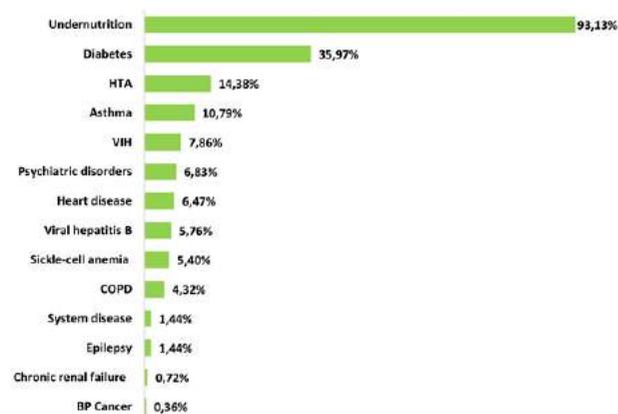


Figure.

Results/Impact: Out of 4516 hospitalized patients, 20.96% of patients were tuberculosis patients. The sex ratio was 2.18. The 4/5 of the patients were between 18 and 39 years old. The main contributing factors of TB found were undernutrition (93.13%), active smoking (36.75%) and diabetes (35.97%). The time between hospitalization and onset of symptoms was greater than 2 months in 60.53% of cases. A complication was noted in 89.10% of patients, particularly bacterial/viral bronchopulmonary superinfection (31.15%). The trend was favorable in 88.49% of cases. It resulted in death in 10.98% of cases.

Conclusions: Most integrated-care nutritional support programs focus on HIV. Undernutrition appears to play a much more important role than HIV in the extent of TB in poor countries. It creates a vicious circle with tuberculosis, one of the components of which is immunosuppression and the increased frequency of complications such as bacterial/viral community/nosocomial Sur infection, the actual incidence of which is poorly known and deserves special attention given the importance of added morbidity and mortality.

EP-35-956 Risk factors and treatment outcome of active tuberculosis in patients diagnosed with diabetes mellitus: a retrospective matched case-control study

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Background: Diabetes mellitus (DM) increases the risk of mortality and morbidities related to active tuberculosis (TB). Both diseases are common interlinked, particularly in high TB prevalence countries. Identifying the specific characteristics of patients with DM who later develop tuberculosis disease is crucial in promptly screening and early diagnosis of active TB. We therefore aimed to assess the predictor of active TB and TB treatment outcome among DM participants in Thailand.

Design/Methods: We conducted a retrospective cohort of 764 diabetic patients from January 2015 to December 2019 at King Chulalongkorn Memorial Hospital. Patients were categorized into “TB” and “no TB” group. To determine factors associated with incident TB were analyzed using Cox proportional hazard regression with 95% CI and p value < 0.05 considered significant.

Results: 57 participants had DM at time of TB diagnosis. Median year of follow-up was 3916.2 person-years follow-up, the TB incident rate among diabetic patients was 45.96 (95% CI 39.72-53.19) per 100 person-years follow-up. The median HbA1c at the TB diagnosis was 8 (IQR 6.6-10.3). In multivariate analysis BMI<18.5 (aHR 3.78; 95% CI 2.47-5.78; p<0.001), smoking (aHR 1.95; 95% CI 1.23-3.10; p=0.004), HIV infection (aHR 3.31; 95% CI 1.59-6.86; p=0.001) were associated with active TB.

Additionally, type of DM treatment was also related to active TB; insulin injection (aHR 1.60; 95% CI 1.02-2.51; $p=0.04$), combination treatment (aHR 1.66; 95% CI 1.02-2.70; $p=0.04$) and diet control (aHR 2.50; 95% CI 1.24-5.04; $p=0.01$) when compared with oral hypoglycemic drugs. Among TB cases, TB cure or treatment completion was 71.8%; 6.7% had TB relapse and 13.7% had drug resistance. Mortality rate of TB cases was 12.9%. **Conclusions:** The incidence of TB among DM cases observed in this study was high and it was associated with low BMI <18.5, smoking and HIV infection, pointing to the need to pay attention to these factors when managing these co-morbidities.

EP-35-957 Intersectionality of malnutrition, diabetes and TB – experiences from private sector setting in Chennai, India

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Background: Malnutrition has been shown to be associated with increased susceptibility to infections and non-communicable diseases. In particular, obesity is known to increase the risk of non-communicable diseases like Diabetes and being underweight predisposes people to the development of TB. However, there is limited data highlighting the intersectionality of TB, malnutrition and diabetes.

Design/Methods: Under TB free Chennai initiative, people seeking care in the private sector are provided access to free diagnosis and treatment at Nakshatra centres in the private hospital in Chennai, India. Through the Linkage to care project, people with TB (30 years & above) are screened for diabetes and linked to specialised care and support for both TB and diabetes. Sociodemographic details and clinical profile including height & weight were collected as part of routine program management. The cohort of people with malnutrition were provided diet related counselling and life style modifications.

Results: Among 2172 people with TB registered between Jan to Dec 2021 in the nakshatra centres, 2098 (97%) underwent diabetes screening. Around 1052 (50%) had diabetes with 86% having a previous history of diabetes and 14% were newly diagnosed. Proportion of underweight, overweight and obesity among people with TB was 32%, 18% & 9%, while among those with both TB & diabetes it was 18%, 19% and 6% respectively. Among people with both TB & DM 35% of females were overweight and obese as compared to 19% in males. On the other hand, among people with TB alone, 42% males were underweight as compared to 21% in females.

Intersectionality of malnutrition, diabetes and TB							
BMI levels	TBDM Female	TBDM Male	Total	TB Female	TB Male	Total TB	Grand Total
Underweight (<18.5)	56(16)	132(19)	188(18)	108(21)	228(42)	336(32)	524
Normal (18.6-24.9)	167(48)	443(63)	610(58)	219(43)	211(39)	430(41)	1040
Overweight (25-29.9)	84(24)	111(16)	195(19)	115(23)	72(13)	187(18)	382
Obese (>30)	39(11)	20(3)	59(6)	64(13)	29 (5)	93(9)	152
Total	346	706	1052	506	540	1046	2098

Conclusions: This abstract highlights the sex disaggregated difference in malnutrition levels among people with TB and people with TB and diabetes. Targeted counselling, differentiated nutrition strategies and life-style modification guidance should be provided for people with TB to improve TB outcomes and comorbidities management.

EP-35-958 The yield of chest X-ray based versus symptom-based TB screening among patients with diabetes mellitus in public health facilities in Addis Ababa, Ethiopia

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Background: Patients with diabetes mellitus (DM) are at increased risk of developing TB, but the best screening algorithm for early detection and treatment of TB remains unknown. Our objective was to determine if combining routine chest x-ray screening could have a better yield compared with symptom-based screening alone.

Design/Methods: We conducted cross-sectional study between September 2020 and September 2021 in 20 public health facilities in Addis Ababa, Ethiopia. All DM patients attending the clinics during the study period were offered symptom screening and chest X-ray and simultaneously followed by confirmatory Xpert testing. We analyzed the number and proportion of patients with TB by the diagnostic algorithm category and performed binary logistic regression analysis to identify predictors of TB diagnosis.

Results: Of 7394 patients screened, 54.6% were female with median (IQR) age was 53(45-61) years. Type-2 diabetes accounted for 89.6% of all participants. Symptom-based screening identified 172 symptomatic of whom chest x-ray suggested TB in 19, and 11 of the 19 were subsequently confirmed to have TB (8 bacteriologically confirmed and 3 clinically diagnosed). Only 2 of the 152 symptomatic patients without X-ray findings had TB (both bacteriologically confirmed). On the other hand, 28 of 7222 symptom-negative patients had X-ray findings suggestive of TB, and 7 of these were subsequently confirmed with TB (6 clinically diagnosed). The overall point prevalence of newly diagnosed active TB was thus 380 per 100,000. The direct cost associated with the x-ray-based screening was over 40 times higher.

Conclusions: Chest X-ray based screening led to detection of about a third of TB patients which otherwise would have been missed but the algorithm is more expensive. Its full cost implication needs further economic evaluation.

EP-35-1825 Older adults with diabetes mellitus (DM) have high odds of latent tuberculosis infection – findings from an outpatient DM clinic in Uganda

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Introduction: The dual epidemic of Diabetes Mellitus and tuberculosis is a growing public health challenge in Sub-Saharan Africa, Uganda inclusive. The odds of latent tuberculosis infection (LTBI); and progression to active TB are increased in DM, yet there is inadequate evidence to inform prioritization for TB preventive therapy in DM.

Objective: We aimed to determine the prevalence and predictors of LTBI, among adults with diabetes mellitus attending an outpatient DM clinic.

Methods: This was a cross-sectional study at Kiruddu National Referral Hospital, Uganda. Data on sociodemographic and clinical characteristics was collected using a pre-tested case report form. LTBI was defined as a positive QuantiFERON Test result (≥ 0.35 IU). Participants with and without LTBI were compared using Chi-square test for categorical data and Mann Whitney-U test for continuous data. Multivariable logistic regression analysis was performed to identify predictors of LTBI.

Results: Among 185 participants, 78.4% (145) were female, 30.8% (57) were aged 41 – 50 years, 33.5% (62) had been diagnosed with DM in less than six months, 87.6% (162) were on metformin therapy; 77.3% (143) had HbA1c $\geq 7.0\%$, 5.4% (10) had HIV and 34.1% (63) had kidney dysfunction. Prevalence of LTBI was 57.8% (107/185). LTBI prevalence was higher among males than among females (65% vs 55.9%) without statistical significance.

Compared to individuals aged less than 30 years old, individuals aged 51 – 60 years had higher odds of LTBI (OR = 8.10, $p = 0.01$, 95% CI = 1.59 – 41.21). Individuals with LTBI had lower CD8 counts ($p = 0.02$), lower white blood cell and platelet counts ($p = 0.02$ and $p = 0.01$ respectively).

Conclusions and recommendations: LTBI is prevalent among adults with DM. Older individuals aged 51 – 60 years have higher odds of LTBI and may be prioritized for TB preventive therapy, in high burden settings like Uganda.

EP-36 Global Examples of Tobacco Industry Interference

EP-36-959 Effective implementation of WHO Framework Convention on Tobacco Control article 17 in Mysuru district of Karnataka, India

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Background and challenges to implementation: Karnataka, particularly the Mysore region is the highest tobacco growing area in the country after Andhra Pradesh. The WHO FCTC Article 17 relates to the 'Provision of support for economically viable alternative activities' and Article 18 relates to the 'Protection of the environment and the health of persons'. As per Karnataka Tobacco Board data, 2018-19 number of registered tobacco growers are 42453 and 2021-22 is 42067. There is a slight decrease in the number of growers.

Intervention or response: Government of Karnataka has formed high level committee to encourage tobacco farmers to shift to alternative cropping and livelihood in. The Department of Horticulture during 2021-22 FY under Kisan Krishi Vikas Yojana scheme, Under CHD Scheme sensitized and conducted workshop for tobacco farmers to focus on alternative cropping and given awareness on drip irrigation technology. Government spent 53.97 lakh on them by giving incentives. Government supported farmers by providing financial support to adopt alternative cropping.

Results/Impact: In Periyapatna(140), Hunsur (125), HD Kote (30), K R Nagar (48) and Nanjangud (3) talukas 346 farmers switched off from tobacco to alternative cropping like growing banana, and other vegetables. Area of tobacco plantation is also reduced from

83696.00 hectares (2018-19) to 71877.09 hectares (2021-22). Quantity produced and sold during year 2018-19 was 85.08 kg and 2021-22 till March 3rd 2022 it was 58.35 kg. It shows that decrease of plantation area and quantity produced and sold.

Conclusions: There is positive response from Karnataka tobacco growers to adopt alternative cropping. Government of Karnataka is successful to convince the tobacco farmers to motivate them instead of tobacco industry interference and influence. Tobacco Farmers of Mysuru district has shown that WHO FCTC article 17 and 18 implementation is quite possible even after strong Tobacco Industry Interference. Tobacco farmers are ready for alternative cropping when department sensitized them and give some intensives.

EP-36-960 How household nutrition has been impacted by tobacco consumption in India: a state-level analysis

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Background: Tobacco consumption in low-income countries has been shown to aggravate poverty and malnutrition by contending for the already limited resources. Moreover, in the case of India, the problem is a pronounced one as according to Food and Agricultural Organisation (FAO) estimates of 2020, 189.2 million people (14%) are undernourished in India while according to Global Hunger Index 2021, India ranks 101st out of the 116 countries. This study quantifies the opportunity costs of tobacco expenditure in terms of nutrition foregone and the potential improvements in the household level food-energy status if the money is diverted from tobacco towards food consumption across all Indian states. A comparative analysis is done between the household's food expenditure of the tobacco consuming and non-consuming households.

Design/Methods: The study is based on unit-level secondary data sources wherein data on per capita household expenditure on food and tobacco use was obtained from 68th Round NSSO data corresponding to 2011-12. The price of tobacco products and essential cereals and proteins are computed to analyze the household level nutrition foregone across the states. Statistical analysis was carried out in SPSS v.20.

Results: The highest proportion of tobacco users was reported from Northeast (NE) states of Tripura, Mizoram and Manipur. The yearly expenditure on tobacco consumption for India is INR 582.08 billion which could well be translated to meeting the nutritional requirements of the undernourished population. This expenditure is equivalent to 80% of the Government of In-

dia's total food subsidy for the same period. The yearly tobacco expenditure is also equivalent to 4% of yearly vegetarian food expenditure and 3% of non-vegetarian food expenditure. Difference is found in the nutritional status of tobacco consuming and non-consuming households.

Conclusions: The existing difference in the nutritional status of tobacco consuming and non-consuming households validates the need for complete tobacco control in India.

EP-36-961 Understanding the reasons behind Bidi workers' protests in Bangladesh: a qualitative investigation

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Background and challenges to implementation: In Bangladesh, bidi industry offers "extremely low" wages and "extremely hazardous" work conditions for its workers. However, despite such major workers' rights issues, bidi workers all over Bangladesh take to the streets in highly coordinated manner each year before national budget, demanding tax reduction in the sector. As these demands are unrelated to workers' interests, this study aims at exploring the factors at work behind such protests, the level of participants' spontaneity and sources of funds and other support.

Intervention or response: The qualitative study, conducted between December 2020 and March 2021, utilized relevant media analysis, 11 focus group discussions, 4 Key Informant Interviews in four districts chosen based on the concentration of factories, frequency and intensity of protests. Participants (92 in number) include bidi workers, labor leaders, local civil society leaders.

Results/Impact: The study unveiled that the bidi workers' protests are orchestrated and funded by factory owners. Akiz Bidi, the largest player in the industry, is the primary organizer of the protests. Workers are often coerced into participating with threats of mass lay-offs, dismissal, and factory closure. Workers are often taken to the capital to draw national attention, with factory owners bearing all expenses. However, it is not the workers, but representatives from factory management who speak in protests.

The study also revealed that in 2019, after protests reversed a budgetary tax increase, profits for factory owners increased by BDT 28 per 1000 sticks whereas the increase for workers, was only BDT 8 per 1000 sticks.

Conclusions: The study concludes with recommendations that authorities impose higher taxes on bidi to discourage use and utilize additional revenues to support and incentivize switching to alternative livelihoods and

businesses for both bidi workers and factory owners. It also suggests rigorous monitoring on the industry to ensure full compliance with tax and labor laws.

EP-36-962 Effective mitigation of educational institution targeted tobacco industry interference – success, challenges, and learnings of Karnataka, India

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Background and challenges to implementation: The government of Karnataka has notified WHO FCTC article 5.3 state notification with protocols in 2019 to mitigate the tobacco industry interference. The state has established an effective surveillance system to monitor tobacco industry interference through district tobacco control cells and coalition members. The tobacco industry strategically and constantly targeted educational institutions to sustain their market, which is a great challenge to address and mitigate.

Intervention or response: State Tobacco Control Cell, Karnataka has sensitized key stakeholders after notifying FCTC article 5.3 notification. It also established systems and mechanisms to report FCTC article 5.3 violations. As per the State database, in the last three years, there were 56 cases had been reported. Out of it, 26(46%) cases were reported in relation to Educational Institutions and enforcement of COTPA in and around educational institutions. State tobacco control cell and district tobacco control cells along with coalition members addressed the issue and issued notice and sensitized officials of the Department of Secondary and Higher Education on FCTC Article 5.3.

Results/Impact: This indicates that tobacco industries are strategically targeting educational institutions and an encouraging point of sellers to sell tobacco within 100 yards of educational institutions. However, effective surveillance of tobacco industry interference and swift action from tobacco control agencies can reduce such interference to amplify the effectiveness of tobacco control programs.

Conclusions: There is a great need for sensitization of government officials on FCTC Article 5.3 protocol. More visibility has to be given to provisions of FCTC article 5.3. Tobacco industries are trying to reach young minds to expose them to tobacco products and motivate them to initiate tobacco products at an early age.

EP-36-963 Ill tactics of the tobacco industry in Bangladesh

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Background: Bangladesh agreed and ratified the WHO Framework Convention on Tobacco Control (FCTC) in 2004 and established a national law in 2005 that was amended later in 2013 but there has no guidance on how to implement FCTC Article 5.3. As a result, tobacco control, public health and other government programs are unprotected from tobacco industry interference (TII). The tobacco industry's violations over the tobacco control rules are common in Bangladesh.

To find out the Tobacco Industries Interference that hinders national and local level policy-making as well as decision making. Besides, making a tobacco-free Bangladesh by 2040 as per the government commitment.

Design/Methods: WBB Trust responded quickly wherever the interference of TI's became public and interrupted government policy. WBB trust collected TII information published in newspapers, magazines and social media in the year 2021, made those reports into significant TII news from the information obtained.

Results: From the analysis, WBB trust found that a total of 604 industry interference were reported between January-December 2021. Among these some notable interference such as planting trees on several areas in the name of Bonayan, implementing a project of safe drinking water named as 'Probaho', the MD of BATB presented a keynote speech on a NBR hosted event, and organized a workshop on a sustainable model of sugarcane cultivation practices, etc.

Conclusions: Tobacco businesses use cash to meddle tobacco control drives and common social orders working with moral fortitude. To stop TII, need to establish FCTC 5.3, strengthen the existing tobacco control laws by amendment, enforced the code of conduct for government employees and raise the anti-tobacco movement.

EP-36-964 How was the tobacco consumption in West Bengal, India: a district level comparative analysis by using DHS data

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Background: As per previous studies every third person in West Bengal is found to be addicted to tobacco and its usage has been found to be associated with a huge health burden. The usage of tobacco in the state has been linked to increased incidence and expenditure on Non-Communicable Diseases (NCDs) like cardiovas-

cular diseases, chronic obstructive pulmonary disorders (COPD), other respiratory diseases, tuberculosis and cancer. This study examines the change in tobacco consumption usage across the districts of West Bengal from the National Family Health Surveys (NFHS-3, NFHS-4 to NFHS-5) among men and women in the 15-49 age groups.

Design/Methods: This study uses NFHS-3, NFHS-4 and NFHS-5 unit-level data to assess the change in consumption patterns across the districts. A difference-in-differences two-part model was used to compare changes in tobacco consumption between National Tobacco Control Programme (NTCP) intervention and control districts, adjusting for social, demographic and economic characteristics and time-related heterogeneity.

Results: This study finds that there has been a 7% reduction in the consumption of tobacco from NFHS-3 to NFHS-5 in West Bengal. Decline in consumption is observed across all the districts. The results however do not show any significant difference between the NTCP districts and the other districts in terms of reduction in tobacco consumption.

Conclusions: The findings of this study bring to the forefront the importance of strengthening the existing tobacco control policies in West Bengal.

EP-36-966 Tobacco industry's insidious tactic to reach children in India: the case of Conrad Challenge 2021

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Background and challenges to implementation: Since 2017, The Conrad Spirit of Innovation Challenge (in collaboration with the Conrad Foundation) has been a grantee of the PMI funded Foundation for a Smoke-Free World (FSFW). Through small grants through Conrad Challenge, FSFW gains access to youth and youth influencers in educational institutions. Conrad Challenge 2021 Virtual Innovation Summit saw the participation from schools from at least two states (Maharashtra and Delhi), which violated several aforementioned orders that prohibit tobacco companies and their agents from inviting Indian children as participants to their programmes and competitions.

In an attempt to demonstrate evidence-based best practices, this study is primarily a reporting experience in monitoring and mitigating tobacco industry interference in India.

Intervention or response: The event was to take place virtually on 28-30 April 2021. Based on this discovery of FSFW/Conrad Challenge reaching out to schools, the respective State Tobacco Control Cells (STCCs) were alerted in the third week of April 2021 via direct and indirect channels.

Results/Impact: Given the swift response from the various government agencies (principally the respective state health and education departments) and the support of tobacco control advocates, the schools withdrew their participation from the event.

Conclusions: The Conrad Challenge not only repeatedly violates India's tobacco control legislation on tobacco and other products (2003) and electronic cigarettes (2019), and pre-existing rules by the educational bodies and other orders by the Ministry of Health & Family Welfare, Government of India and state specific regulations which prevent their engagement with youth.

Tobacco control advocates in India will need to stay vigilant against agents and front groups of tobacco companies as they will continue to find insidious ways to approach school children and lure them with prizes and sponsored educational trips.

EP-36-967 Assessing compliance with health warnings on tobacco packs marketed around 100 yards of educational institutions in an Eastern state of India

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Background and challenges to implementation: Graphic health warning labels (HWLs) on product packaging have been identified by the World Health Organization (WHO) as a cost-effective policy intervention to notify consumers about the health dangers of tobacco.

The Government of India introduced legislation in September 2014 requiring all tobacco packaging to display a health warning covering 85 percent (60 percent pictorial, 25 percent text) of the pack's principal display area, with legible text in white font on a black background and in English and/or the same Indian language as the language used on the pack. We assessed compliance with this legislation in the Bhubaneswar city of Odisha, India.

Intervention or response: A cross-sectional study was conducted between February 2022 to March 2022 in Bhubaneswar, Odisha, to determine the extent of compliance with the COTPA-mandated HWLs standards for packages of tobacco products sold within 100 yards of educational institutions.

Results/Impact: From 345 packets of tobacco bought from 68 vendors, 48 distinct brands were sampled. Of these, 25 were for smoking (cigarettes, beedis) and 23 were for smokeless tobacco (khaini, gutkha, betel quid with tobacco).

On the majority of product packages, especially those containing smokeless tobacco, the health warnings did not comply with COTPA requirements. The required health warnings did not occupy the required 85 percent

of the principal display area in the majority of tobacco products. Only six packets (35.3%) were in full compliance.

Conclusions: The tobacco products marketed were not in compliance with the health warning label law. Policy implementation and its monitoring should be given due importance in the national tobacco control programme.

EP-36-968 Do non-smokers live longer?: A comparison of life expectancy of male smokers and non-smokers in India

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Background: Tobacco smoking increases the risk of lung and other cancers, cardiovascular diseases, chronic obstructive pulmonary diseases (COPD) and other respiratory diseases. Smoking is found to be associated with 4,80,000 deaths annually and approximately 60% of the deaths are observed in males. This study compares the difference between the life expectancy of male smokers and non-smokers in India in 2019. Only the male population has been considered because in India only 2% of females are tobacco smokers.

Design/Methods: Life tables are used to compute the life expectancies of male smokers and non-smokers. Life tables have been constructed for two scenarios. One, by assuming deaths related risk factors occur uniformly within a given age interval while in another in increasing numbers within an age interval. Data on smokers' population is taken from Global Adult Tobacco Survey (GATS-2) while deaths associated with tobacco smoking are taken from Global Burden of Disease (GBD) database. Smoking associated deaths are reported from 30 years of age. Therefore, life expectancy is computed from 30 years in five years age intervals. Sensitivity analysis is done by considering upper and lower limits of deaths.

Results: The difference in life expectancy between average smokers and non-smokers is found to gradually increase with age. Substantial variation is observed by taking upper and lower bounds. The average difference in life expectancy of an average smoker and non-smoker is found to be approximately 2 years. Considering upper bound of the smokers, the average difference increases to 5.5 years. However, much difference is not observed in life expectancies in the two scenarios where death related risk factors are considered to occur uniformly or increase exponentially.

Conclusions: The difference in the life expectancies observed among male smokers and non-smokers especially after considering upper bound values provides substantial justification for strengthening tobacco smoking control and cessation measures in India.

EP-37 Tobacco, nicotine, cannabis products and health effects

EP-37-969 The fraction of Chinese lung cancer deaths attributable to smoking by using three methods, from 2000 to 2019

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Background: Lagged smoking prevalence, smoking impact ratio (SIR), and RRs based on dose-response relationship were three methods to estimate population attributable fractions (PAFs) in the different periods of Global Burden of Disease (GBD) study. Due to the lack of original data, most parameters were estimated from models globally for China.

Design/Methods: The PAFs of lung cancer in 2000-2019 were calculated by the three methods using six national surveys and causes of death surveillance data in China. The relative risks (RRs) were derived from the meta-analysis of the Chinese population. Linear and non-linear dose-response models between pack-years and RRs in current smokers, together with quit-years and RRs in former smokers were built to represent the dose-response relationship. Then the RRs were weighted by the probability density function of pack-years and quit-years fitted from national representative tobacco surveys. Last, the PAFs were calculated by using the three methods, respectively.

Results: The total PAFs calculated by the lagged smoking prevalence (45.04-47.97%) and SIR (45.85-47.19%) were similar, whereas the PAFs derived from dose-response relationship with pack-years and quit-years weighted RRs were higher (64.81-71.88%). Male PAFs estimated by prevalence, SIR, and dose-response were 56.59-61.49%, 59.02-60.42%, and 68.63-82.85%, respectively, whereas they were 12.51-21.78%, 12.51-18.22%, and 40.81-54.59% in females, accordingly. The prevalence- and SIR-derived age-specific PAFs stabilized in each age group.

Differently, the age-specific PAFs derived from the dose-response method increased from 46.01-51.25% in individuals aged 30-34 years to around 68.67%-87.87% in populations aged 70 years and above in males, whereas fluctuated irregularly in females.

Conclusions: The PAFs estimated from dose-response methods were higher than the other two methods. We infer that the dose-response method is a more reasonable way to estimate PAFs as it involves cumulative effects using pack-years and quit-years to weight RRs instead of using fixed RRs.

EP-37-970 Beyond hashtags and likes: an exploratory study of electronic cigarettes related social media posts in India

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Background: In India, the Prohibition of Electronic Cigarette Act (PECA) 2019 came into force on 5th December 2019 prohibiting sale, advertising and promotion of e-cigarettes. This study analyzed the status quo and characteristics of the e-cigarette related posts on the social media sites such as Instagram (IG) and Facebook (FB) after PECA 2019.

Design/Methods: During April-May 2021, content analysis was conducted using select keywords to collect information on e-cigarette related posts from IG and FB. Content Appealing to Youth (CAY) index was modified and used, which was categorized into 6 themes and 41 codes. Frequencies and percentages were calculated for each code. The compliance assessment for PECA was carried out for ENDS related IG posts and FB posts contents from 18th September 2019 to 15th April 2021.

Results: Keyword queries captured a total of 3,118 e-cigarette related posts and a sample of 273 posts were analyzed. 99.26% of the posts were colorful and three-fourth displayed e-cigarette device as the centerpiece. 60.43% posts featured a brand name. Half of the device images were matte (53.47%) with contrast colors (38.09%). 61.9% of the posts were uploaded by the e-cigarette vendors with maximum social media engagement.

Conclusions: The prevalent use of the social media platforms for promoting e-cigarettes using the visually appealing posts is a rising concern. Since there are a large number of social media users in India, more emphasis should be placed on developing media literacy skills to aware the general population about the harmful effects of the e-cigarette and provision of e-cigarette ban in the country.

EP-37-971 The association between exposure to second-hand smoke and diseases in the Chinese population: a systematic review

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Background: Relative Risk (RR) or Odds Ratio (OR) of diseases associated with second-hand smoke (SHS) exposure is an essential parameter for estimating the burden of disease due to tobacco use. In regard to active smoking, the risk is much lower among Chinese than among Westerners. However, there is a lack of compelling evidence supporting the effects of SHS exposure. Thus, we aimed to estimate the Chinese association between SHS exposure and diseases.

Design/Methods: After a thorough search for the relevant studies published before June 30th, 2021, the eligible studies were identified according to the PECOS format: Participants and Competitors (the Chinese population), Exposure (SHS), Outcomes (disease or death) and Study design (case-control or cohort).

Table 1. The Pooled Odds Ratios or Odds Ratios Caused by Second-hand Smoke Exposure

Diseases	Subgroup	Number of Observations	P	P-value	Model	POR/OR	LL	UL	I ²	Egger's test
Cancers	Lung Cancer*	46	74.4%	0.000	Random	1.79	1.29	2.56	2.74	0.000
		17	63.2%	0.000	Random	1.92	1.42	2.59	3.87	0.009
		4	0.3%	0.390	Fixed	1.64	1.33	2.03	-3.17	0.125
		9	64.7%	0.004	Random	1.34	1.03	1.74	3.02	0.072
		4	22.7%	0.275	Fixed	7.85	5.11	12.07	-1.14	0.687
		12	71.1%	0.000	Random	1.65	1.22	2.24	2.41	0.076
		2	0.0%	0.943	Fixed	1.12	0.77	1.63	0.38	
		5	92.5%	0.000	Random	2.76	1.29	5.96	8.51	0.062
		6	65.6%	0.012	Random	1.59	1.09	2.35	0.03	0.991
		2	72.1%	0.003	Random	1.38	0.94	2.04	4.54	0.023
	9	67.4%	0.000	Random	2.20	1.33	3.62	4.60	0.061	
	Breast Cancer*	8	38.8%	0.121	Fixed	1.57	1.40	1.76	2.11	0.044
		2	0.0%	0.763	Fixed	2.60	1.94	3.68	0.02	
		6	0.0%	0.853	Fixed	1.47	1.30	1.66	1.35	0.021
		2	0.0%	0.338	Fixed	1.38	1.15	1.65	3.42	
	Bladder Cancer*	4	40.9%	0.165	Fixed	1.52	1.12	2.05	0.76	0.591
		3	47.6%	0.148	Fixed	1.37	1.08	1.73	0.02	0.997
	Cervical Cancer	2				1.84	1.04	3.28		
		1				3.91	2.21	6.52		
	Acute Lymphoblastic Leukemia	1				3.32	1.94	5.68		
		2				1.78	1.10	2.86		
	Intracranial Tumors	1				1.91	1.10	3.33		
		1				4.87	1.48	16.02		
Colon Cancer	1				1.26	0.83	1.89			
	1				0.97	0.28	2.42			
Colorectal Cancer	1				1.79	1.09	2.96			
	1				2.04	1.14	3.70			
Endometrial cancer	1				2.38	1.47	3.85			
	1				3.86	1.47	10.15			
Stomach Cancer	1				2.69	1.67	4.32			
	1				1.14	0.73	1.79			
Esophageal Squamous Cell Carcinoma	1				2.04	1.14	3.70			
	1				2.38	1.47	3.85			
Oral Cancer	1				3.86	1.47	10.15			
	1				2.69	1.67	4.32			
Papillary Thyroid Cancer	1				1.14	0.73	1.79			
	1				1.14	0.73	1.79			
Diseases of the Circulatory System*	4	52.9%	0.095	Random	1.92	1.29	2.85	2.72	0.236	
	3	61.6%	0.074	Random	2.29	1.26	4.16	2.59	0.410	
Diseases of the Respiratory System*	1				1.44	0.94	2.21			
	7	67.7%	0.000	Random	1.76	1.13	2.74	6.70	0.053	
Asthma in Children*	6	89.7%	0.000	Random	1.82	1.07	3.11	6.71	0.085	
	1				1.54	1.06	2.22			
Small Airway Obstruction	6				1.62	0.92	2.85			
	2				1.70	1.04	2.80			
Other Diseases	1				2.10	1.22	3.63			
	1				2.24	1.52	3.16			
Legionnaires' Diseases (Children)	1				1.17	1.00	1.37			
	1				1.08	1.00	1.17			
Orbis Media (Children)	1				1.17	1.00	1.37			
	1				1.08	1.00	1.17			
Type 2 Diabetes Mellitus	1				1.17	1.00	1.37			
	1				1.08	1.00	1.17			
All Cause Mortality	1				1.17	1.00	1.37			
	1				1.08	1.00	1.17			

Note: For subgroups of the gender and the exposure sites, some studies contained more than one result, so the number of results included in the subgroup analysis could be more than that of the disease-specific results, respectively. *are the results of meta-analyses

Table 1. The pooled odds ratios or odds ratios caused by second-hand smoke exposure.

Results: A total of 53 studies were identified for 23 diseases. The OR of overall cancers was 1.79 (1.56-2.05). More specifically, it was 1.92 (1.42-2.59) for lung cancer, 1.57 (1.40-1.76) for breast cancer, 1.52 (1.12-2.05) for bladder cancer, and 1.37 (1.08-1.73) for liver cancer, respectively. The OR of Diseases of the Circulatory System was 1.92 (1.29-2.85) with 2.29 (1.26-4.159) for stroke. The OR of Diseases of the Respiratory System was 1.76 (1.13-2.74) with 1.82 (1.07-3.11) for asthma in children. In terms of 17 diseases without a meta-analy-

sis, the ORs for colorectal cancer, endometrial cancer, cardiovascular disease, and tuberculosis were not statistically significant, the ORs of the other diseases, such as cervical cancer and oral cancer, covered from 1.17 to 4.87. As for subgroup analysis, the OR of lung cancer reached highest in 2010-2019, and was significant during exposure in household and in female, respectively. The OR of breast cancer decreased from 2.60 in 1983-1995 to 1.47 in 1996-2009.

Conclusions: The effect of SHS exposure in China was similar to that in Western countries. Studies for stomach cancer with high incidence rates were insufficient.

EP-37-972 Tobacco smoking in the early months of the COVID-19 pandemic among online social media users in Russia

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Background: The COVID-19 pandemic has forced countries to take various restrictive measures, including “lockdowns”, that may have affected tobacco smoking. The study explored associations between an increase in smoking, sociodemographic, and related to pandemic factors in the early months of the pandemic among online social media users in Russia.

Design/Methods: Between June–September 2020, 1518 users of online social media participated in an online survey investigating changes in alcohol, tobacco, and substance use during the pandemic. Binary logistic regression was used to identify factors associated with an increase in tobacco smoking.

The analysis was adjusted for sex, level of education, perception of the severity of public life limitations, negative work/financial consequences of the pandemic, stress, changes in the frequency of drinking, heavy episodic drinking (6 or more drinks at a time), and volume of alcohol consumed on a typical occasion.

Results: 46.8% of the surveyed population were current smokers. 17.0% of them reduced, 37.9% increased, and 45.1% didn't change their smoking during the pandemic. Relative to those whose smoking reduced or didn't change, those who increased their smoking were more likely to be: 18–29 years old (OR=1.906; 95% CI=1.109–3.277), residents of medium to big cities (up to 1 mln inhabitants) (1.519; 1.017–2.270), had their income reduced (1.508; 1.024–2.222), faced severe restrictions in everyday life as a result of measures taken to contain SARS-CoV-2 (2.398; 1.440–3.758).

After introducing alcohol consumption variables to the model, only two factors were associated with an increase in smoking: severe restrictions in everyday life

(2.147; 1.227–3.993) and increased frequency of heavy episodic drinking during pandemic (2.338; 1.167–4.685).

Conclusions: To be more effective, tobacco control policy during the pandemic in Russia should consider the strength of COVID-19-related restrictions, and specific socio-demographic and behavioral characteristics (e.g. alcohol consumption) of individuals at risk to increase their tobacco use during the pandemic.

EP-37-975 Smoking cessation intervention for tuberculosis patients in routine health service in Benin and Burkina-Faso: preliminary results from CestA_TB pilot study

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Background and challenges to implementation: Although evidence has strongly highlighted the significant association between tobacco use and TB, smoking cessation intervention (SCI) is not a meaningful component of National TB Program (NTP) in African countries. We have therefore implemented a project of integration of SCI into routine TB service in Benin and Burkina Faso supported by French Government.

Intervention or response: Newly diagnosed pulmonary TB patients were recruited from 20 basic TB clinics in Benin and Burkina Faso. Demographic information, nature of TB disease and smoking behavior were collected. Patients were classified as never smokers, Ex-smokers and current smokers by self-report and verified via carbon monoxide test.

The patients were provided with knowledge of harmful effect of smoking and TB and asked if they are willing to quit. They received the same message at every patient

visit during treatment and their smoking status were updated. In the meantime, capacity building and smoke-free environment were implemented.

Results/Impact: From December 2021 to March 2022, 524 patients were included. 76% were male. Mean age of the patients was 38 ± 13.6 years. Of them, 304 (58.0%) were non-smokers, 68 (13.0%) Ex-smokers and 152 (29.0%) Smokers at baseline. Cigarette was the main type of tobacco product (40%). Of the current smokers, 55.0% were willing to quit and received ongoing cessation support. 100% of the implementing sites have become smoke-free. Healthcare workers stated that conducting SCI was feasible, useful and no special challenge encountered.

Conclusions: Preliminary results show that smoking rate of TB patients is much higher than the general population and a great need of SCI. Over half of smokers are willing to quit. The established healthcare workers carried out the additional work within the routine TB services without any extra resources needing to be brought in, demonstrating that SCI is feasible and can be conducted in resource limited settings.

EP-37-976 Designated smoking areas or dining cars? An observation assessment of trains in Bangladesh

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Background: Bangladesh's 2013 amendment to its tobacco control law introduced rules that allow multi-compartment public vehicles such as trains to install a marked DSA at the end or open space that is not crossed or used by non-smokers to access services. This cross-sectional observational study aimed to determine the prevalence and location of DSAs within trains traveling through Dhaka station.

Design/Methods: An initial list of 56 trains passing through Dhaka station was obtained from the Bangladesh Railway Agency. Three trains were eliminated from the final sample due to permanent closure. Following at least 20 minutes of observation of the entire train, trained data-collectors completed a survey to assess characteristics of the DSA. If observers could not locate the DSA, they were instructed to ask train staff.

Results: A total of 34 intercity trains, 14 mail/express trains, and five commuter trains were observed. 21 DSAs were observed across all train-types: 56% (n=19) of intercity trains, 14% (n=2) of mail/express trains, and none in commuter trains. Signage indicating DSAs were not present in any of the observed trains. For all identified DSAs, data-collectors were verbally directed by train staff to use the dining car as a DSA. Servers were present in nearly half (48%; n=10) of all identified DSAs. Three of 12 dining cars with patrons had smokers at the time of observation.

Conclusions: The results of this study suggest that dining cars of trains are being used as DSAs, indicating low compliance with the law which prohibits provision of any service inside the DSA. This violation creates a risk of secondhand smoke for servers and patrons in the dining car.

Recommendations to strengthen the Railway Minister's Initiative to make Bangladesh's railways 100% smoke-free include posting "No-Smoking" signage, targeting enforcement in dining cars, and providing training on updated smoke-free laws to railway employees.

EP-37-977 Determinants of cigarette smoking and smoking intensity among women of reproductive age in Nigeria

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Background: Given that the prevalence of current smokers is higher among men as compared to women, determinants of smoking practices among women are understudied.

This study assessed the determinants of smoking and smoking intensity among women of reproductive age (WRA) in Nigeria.

Design/Methods: Data from the 2018 Nigeria Demographic and Health Survey (NDHS) were used in this study (n = 41,821). The data were adjusted for sampling weight, stratification, and cluster sampling design.

The dependent variables were smoking status and smoking intensity. The independent variables included women's socio-demographic and household characteristics. Pearson's chi-squared test was used to evaluate the association between dependent and independent variables.

All variables found significant in bivariate analyses were further analysed using complex sample logistics regression.

Statistical significance was set at a p-value < 0.05.

Results: The prevalence of smoking among WRA is 0.3% while smoking intensity is 0.1% (every day) and 0.2% (some days).

Women aged 15-24 years (AOR:0.56, 95% CI:0.19-1.64) were less likely, whereas women aged 25-34 years (AOR:2.13, 95% CI:1.06-4.29) were more likely to smoke.

Smoking was more likely among women residing in the North-Central (AOR:16.41,95% CI:3.75-71.85), North-East (AOR:17.64, 95% CI:3.77-82.41), North-West (AOR:11.40,95% CI:2.09-62.12), South-South (AOR:9.45,95% CI:2.04-43.7), and South-West (AOR:22.86,95% CI:5.03-103.85) regions.

Formerly married women (AOR:3.75,95% CI:1.52-9.21), never been in union (AOR:3.53,95% CI:1.38-9.03), female-headed households (AOR:2.56,95% CI:1.29-5.08), and ownership of mobile telephone (AOR:2.10,95% CI:1.13-3.90) increased the likelihood of smoking.

Regarding smoking intensity, women aged 15-24 years (AOR:0.11, 95% CI:0.02-0.72) were less likely to smoke daily, whereas women aged 25-34 years (AOR:2.89, 95% CI:0.88-9.49) were more likely to smoke daily.

Formerly married women (AOR:6.54, 95% CI:1.71-25.03), never been in union (AOR:6.50, 95% CI:1.67-25.35), female-headed households (AOR:4.29, 95% CI:1.35-13.66), and ownership of mobile telephone (AOR:1.51, 95% CI:0.59-3.86) increased the likelihood of smoking daily.

Conclusions: Evidence-based cigarette cessation campaigns and programmes to mitigate the effects of smoking must be region-specific and target women aged 25-34 years, unmarried women, female-headed households, and women who own mobile telephones.

EP-37-978 Smokeless tobacco as a risk factor for type 2 diabetes mellitus in South East Asia Region - systematic review and meta-analysis

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Background: Type 2 Diabetes Mellitus (T2DM) is a chronic metabolic disorder with increasing world - wide prevalence.

Though the effect of tobacco on T2DM outcomes is understood, little is known about Smokeless Tobacco products (Chew tobacco-betel quid, sadapata, zarda, gul) on T2DM.

Focused Question -Is Smokeless Tobacco (SLT) a determinant for T2DM among patients/ survey participants in South East Asia Region (SEAR)?

Design/Methods: PubMed, Google Scholar, EBSCO and Scopus were reviewed to identify observational studies using MeSH words having odds ratio on SLT use among T2DM survey participants as defined by any diagnostic test.

Studies from June 2021- Dec 2021 with data on smoking was eliminated and 2 reviewers examined. Meta-analysis was carried out to find the odds of SLT use in T2DM with 95% CI using MedCalc statistical software by the Der Simonian and Laird method under random effect model.

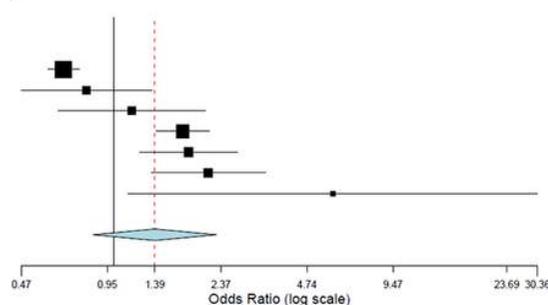
Results: After screening 27 abstracts, and 16 full texts, a total of 8 manuscripts were involved in the systematic review and 7 in the meta-analysis (n=98,279 participants). Odds of using SLT among T2DM participants is 1.38, which was not significant with CI 95% (0.843- 2.288) P< 0.001 with high heterogeneity.

Critical appraisal involving Joanna Briggs Institute (JBI) systematic reviews indicated publication bias. The point estimate of smokeless tobacco use in SEAR among Type

2 DM is 24.08% (CI 15.67-33.64) in 8 studies (n=930) from India and Bangladesh indicating that 1 in 4 SLT user has T2DM.

6 studies from India and Bangladesh indicated that female(n=1080) Vs male(n=2270) prevalence of T2DM is 39.51% Vs 64.13%.

Studies	Estimate (95% C.I.)	Ev/Trt	Ev/Ctrl
Rooban T. et al 2010	0.666 (0.588, 0.755)	370/30010	791/43016
Depthi R et al 2013	0.802 (0.474, 1.358)	30/314	32/275
Shrivastava SR et al 2014	1.156 (0.639, 2.089)	14/115	113/1055
Wu Fen et al 2015	1.741 (1.406, 2.156)	165/6883	178/12797
Vibha SP et al 2018	1.824 (1.226, 2.713)	83/131	238/489
Afsana Afroz et al 2019	2.141 (1.354, 3.385)	201/225	618/776
Zuhara N.V.F et al 2019	5.833 (1.121, 30.356)	5/7	174/580
Overall (I²=93.33% , P< 0.001)	1.389 (0.843, 2.288)	868/37685	2144/58988



Conclusions: This pooled analysis shows smokeless tobacco use is not a risk factor for Type 2 Diabetes Mellitus. The number of studies included in the Systematic Review and Meta-Analysis from SEAR is limited having no representation from Myanmar, Bhutan, Timor Leste, and Sri Lanka.

Prospero- ID 279310.

EP-38 Tobacco legislation and compliance

EP-38-979 Compliance assessment of cigarette and other tobacco products act in educational institutions in Surguja districts of Chhattisgarh, India

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Background: India passed legislation the Cigarettes and Other Tobacco Products Act 2003 (prohibition of advertising and regulation, distribution, supply and disposal of trade and commerce, manufacture, supply, and disposal) (COTPA).

Design/Methods: A cross-sectional survey was conducted in the Surguja District of Chhattisgarh from 22nd- to 24th July 2021. Out of 7 blocks in the Surguja district, randomly, five blocks were chosen for the survey. The sample size was calculated based on assumptions that public places are 50% compliant with COTPA guidelines which came to be 400. 533 public places were taken for better precision. The blocks selected public places based on population proportion to the size. Types of public places were proportionately selected based on the pre-existing list of public places. The data was transferred into MS- Excel 2019 for analysis. An unobtrusive observation was made during the survey, and a structured checklist was filled. The checklist was based on section 6 of COTPA-2003.

Results: 163 educational institutions were surveyed, out of which 82.2% were run via government, and 17.8% were private institutions. The compliance of section 6(b) at educational institutes was 93.1%. 90.2% of educational institutes have appropriately displayed the signage of ,NO SMOKING‘ along with the nodal officer’s name, designation, and telephone number. 96.6% of signage displays, it was as per the specification mandated by law in all educational institutes of the district. Very few places have sales of tobacco products within 100 yards of distance from the educational institutes. There was no sale of tobacco products inside the campus of any educational institute in the district.

COTPA Compliance of Educational Institutions	n=163 (%)
Features	Frequency (%)
Display of Signage as Mandated in The Law-Section 6 (B) Of COTPA	147 (90.2%)
Signage Per the Specification Mandated by Law (n=147)	142 (96.6%)
Sale of Tobacco Products Inside the Campus	0 (0%)
Sale of Tobacco Products within 100 Yards of Radial Distance from the Institute’s Main Gate or Boundary	156 (95.7%)

Conclusions: The compliance of section 6(b) at educational institutes was 93.1%. Very few places have sales of tobacco products within 100 yards of distance from the educational institutes. There was no sale of tobacco products inside the campus of any educational institute in the district.

EP-38-980 Intention to continue using tobacco among adolescents: a secondary analysis of the 2015 Global Youth Tobacco Survey in the Philippines

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Background: Smoking produces significant health problems affecting millions of people globally. It is the largest single cause of preventable deaths. To date, no study has explored factors that may contribute to the youth’s intention to use tobacco. Specifically, no study has determined which type of anti-tobacco message delivery method is associated with the youth’s susceptibility to tobacco use.

Design/Methods: This study did a secondary analysis of the 2015 Global Youth Tobacco Survey in the Philippines to determine the association of the following factors with intention to use tobacco in the next 12 months among current smokers:

- Exposure to anti-tobacco media messages,
- Exposure to health warnings on cigarette packages, and;
- Being taught about the dangers of tobacco in any class.

Results: The adjusted odds of continuing to use of any form of tobacco in the next 12 months was higher (AOR=1.24; 95% CI: 0.62–2.49) among those who have not seen health warnings on cigarette packages and higher (AOR=1.32; 95% CI: 0.71–2.45) when not taught about tobacco in any of their classes.

Finally, those who have not seen or heard anti-tobacco messages on television, radio, internet, billboards, posters, newspapers, magazines, or movies, were more likely (AOR=2.19; 95% CI: 1.14–4.21) to report their intention to continue to use tobacco.

Conclusions: Understanding the relationship of different tobacco control strategies to adolescents’ intention to use tobacco can contribute to the improvement of tobacco policies and programs and achieve effective tobacco control among the youth. A targeted anti-tobacco campaign in both traditional and new media should be considered an essential part of a comprehensive tobacco control program. A policy banning the sale of single stick cigarettes should support the implementation of graphic health warnings on cigarette and tobacco packages.

EP-38-981 Impact of a two-phase tobacco control regulation/legislation on incidence from ischemic stroke and hemorrhagic stroke: Shenzhen, China, 2007-2016

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Background: Shenzhen, China, enacted two consecutive tobacco control regulation/legislation in 2010 and 2014, respectively. This study aimed to evaluate the impact on the ischemic and hemorrhagic stroke incidences in Shenzhen by the two-phase smoke-free regulation/legislation implementation.

Design/Methods: The comprehensive smoke-free regulation among five types of important public places in 2010 was considered the phase I between March 9, 2010 to February 28, 2014. And the enforcement of a comprehensive legislation was considered the phase II between March 1, 2014 to December 31, 2016. The incidence data for subtypes of stroke between 2007 and 2016 were obtained from Shenzhen Stroke Registry System. An interrupted time series (ITS) study was used to capture immediate and annual changes of both ischemic and hemorrhagic stroke during two-phase tobacco control regulation/legislation.

Results: Between 2007 and 2016, 141237 cases of incident stroke (ischemic stroke: 110830, hemorrhagic stroke: 30407) were observed among the resident population aged 35 years and older in Shenzhen.

The regulation implementation in phase I was associated with a strong immediate decline in incidence rate for both ischemic stroke (-14%, 95% CI: -17% to -11%) and hemorrhagic stroke (-10%, 95% CI: -15% to -4%), but without showing the gradual effects before the law implementation in phase II ($P > 0.05$).

Disease	Sub-groups	Phase I		Phase II	
		Immediate effect (95%CI)	Gradual effect per annum (95%CI)	Immediate effect (95%CI)	Gradual effect per annum (95%CI)
Ischemic stroke	All	0.86 (0.83 to 0.89)	1.00 (0.98 to 1.02)	1.03 (1.00 to 1.05)	0.94 (0.92 to 0.95)
	35-49	0.94 (0.87 to 1.02)	0.96 (0.92 to 1.00)	1.03 (0.96 to 1.10)	0.94 (0.91 to 0.97)
	50-64	0.91 (0.86 to 0.97)	1.02 (0.99 to 1.05)	1.05 (0.98 to 1.12)	0.96 (0.94 to 0.98)
	≥65	0.80 (0.76 to 0.84)	1.00 (0.97 to 1.02)	1.01 (0.98 to 1.05)	0.92 (0.90 to 0.94)
Hemorrhagic stroke	All	0.90 (0.85 to 0.96)	1.05 (1.02 to 1.09)	0.93 (0.88 to 0.98)	0.95 (0.93 to 0.98)
	35-49	0.98 (0.89 to 1.08)	1.00 (0.95 to 1.05)	0.95 (0.87 to 1.04)	0.94 (0.90 to 0.99)
	50-64	0.92 (0.84 to 1.02)	1.12 (1.06 to 1.17)	0.94 (0.86 to 1.03)	0.96 (0.92 to 1.01)
	≥65	0.78 (0.70 to 0.87)	1.05 (0.99 to 1.11)	0.88 (0.80 to 0.98)	0.94 (0.89 to 0.99)

Following the implementation of the comprehensive law, the immediate effect only showed a significant reduction on hemorrhagic stroke, with 7% (RR: 0.93; 95% CI:

0.88 to 0.98) reduction. In terms of gradual effects, both ischemic and hemorrhagic stroke incidence showed the effects, with 6% (RR: 0.94; 95% CI: 5% to 8%) and 5% (95% CI: 2% to 7%) decrease per year, respectively.

Conclusions: The two-phase tobacco control regulation/legislation was implemented well in Shenzhen. The comprehensive smoke-free legislation brought more health effect with the immediate effect on hemorrhagic stroke reduction again.

EP-38-982 Compliance with smoke-free policies in public venues from 2018 to 2021 in Qingdao, China

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Background: The city of Qingdao passed their smoke-free law in 2013 banning smoking in indoor public places and requiring the no-smoking signage be posted in specific locations in these venues. This study examines compliance with this law in the same public places in Qingdao in 2018 and 2021.

Design/Methods: A mix of urban and suburban districts in Qingdao were selected as the study area. Trained data collectors observed 748 public settings in October-November 2018 and revisited these venues in September-October 2021 for “evidence of smoking” and the presence and location of no-smoking signage. Wilcoxon signed-rank test was used to test the pre-post change.

Results: The overall compliance rate of the composite indicator assessing “evidence of smoking” significantly increased from 61.4% to 72.9% from 2018 to 2021. The significant increase was also found in government buildings (59.3% vs 88.1%) and business office buildings (35.7% vs 66.1%). Although significantly higher compliance was found in internet bars (5.6% vs 33.3%), the smoke-free compliance rate was the lowest across venue types in both years. The posting of no-smoking signage at the main entrance of venues was poor, notwithstanding it significantly increased from 2018 to 2021 (16.8% vs 35.2%). No-smoking signage was found posted inside 80.3% venues in 2021, significantly greater than 2018 (67.1%). Compliance with posting no-smoking signage is a particular issue for public transit stops (3.3% in 2018; 10.0% in 2021).

Conclusions: Findings from this study provide evidence of the overall improvement in compliance with the composite indicator assessing “evidence of smoking” and

display of no-smoking signage inside venues; and highlight the opportunity for Qingdao to further enhance enforcement in internet bars and public transportation stations. More support from the city leadership is needed to ensure sustained enforcement efforts to achieve 100% compliance with the smoke-free law in Qingdao.

EP-38-984 Prevalence and compliance of designated smoking areas in hospitality venues and transportation in Dhaka, Bangladesh

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Background: The Bangladesh tobacco control law restricts location of designated smoking areas (DSAs) in public buildings including hospitality venues and public transportation, establishes internal safety standards and signage requirements, and bans smoking and smoking aids (such as ashtrays) in non-smoking areas. This study assessed prevalence and compliance of DSAs in hospitality venues and trains in Dhaka city, Bangladesh.

Design/Methods: Using government sources, an official list of restaurants and hotels was obtained. The hotels were stratified based on star-ratings and proportionally sampled to include 120 hotels in the sample, along with 387 restaurants. A list of 56 trains passing through Dhaka station was also obtained from the Bangladesh Railway Agency; all were included in the initial sample. However, 6.8% of venues were eliminated due to permanent business closures. The data collectors successfully contacted and completed a standard checklist on a smartphone to record observational findings for 526 venues.

Results: The study surveyed 355 restaurants, 118 hotels, and 53 trains; 8% (n=41) of venues had a DSA. Trains had the highest percentage of DSAs (40%; n=21), followed by hotels (5%; n=18). Of the 41 DSAs that could be assessed for compliance with the current tobacco law, none were compliant across all measures. Only 14.6% (n=6) of all venues with DSAs met the design standards, i.e the DSAs were physically separated from non-smoking area. None of the venues complied with the internal requirements of carrying a fire extinguisher, disposal container for tobacco products, and signage adhering to design specifications. Similarly, none of the venues banned smoking and smoking aids in the non-smoking areas.

Conclusions: DSAs are not very common in hospitality venues and transportation. Among the venues that had a DSA, the overall compliance with law specifications that were measured was low. Restricting smoking to DSAs does not provide adequate protection from dangerous tobacco smoke.

EP-38-985 Tobacco industry interference through corporate social responsibility using Education Department in Bengaluru rural, Karnataka, India

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Background and challenges to implementation: Article 5.3 of the WHO FCTC aims to protect strong tobacco control policies from the harmful influence of the tobacco industry. To attract the young minds to tobacco products, tobacco industries are trying to fund and support schools and colleges under its CSR program. Tobacco industries are trying create good image in the society, they are trying to support educational institutions. So that the sustainability of the tobacco industry in the future may relies on new users such as youth. To improve quality of education and government school infrastructure tobacco company started to donate fund in Bengaluru Rural district, Hosakote Taluk.

Intervention or response: In July 2021 State Tobacco Control Cell noticed this issue and shared with District Tobacco Control Cell (DTCC), Department of Health and Family Welfare, Government of Karnataka. In the year 2017, Bengaluru Rural District administration issued notification on WHO FCTC article 5.3 much earlier than The State Government, which was effective from January 2019. Though contentious follow up by district team and interference from tobacco industry it took time to clear the violation. October 2021 DTCC issued noticed to concerned school headmaster and Block Education officer to remove all the logos and stop taking fund from Tobacco Industry. Sensitized the Government Education department Officials on importance of implementation of article 5.3 in the State.

Results/Impact: District administration and Department of Health and Family Welfare Government of Karnataka took quick action. After follow up with concerned Deputy Director of Public Instruction and school headmaster removed all the logos and slogans from the wall of school building.

Conclusions: Use of other available laws not only COTPA but also effective implementation of Article 5.3 protects against the tobacco industry's attempts towards youth. Article 5.3 provides tobacco control advocates and governments an important tool to ensure that public health is prioritized over increasing tobacco industry.

EP-38-986 Perceptions and reasons for transitions between tobacco products: findings from four waves of the ITC Bangladesh Surveys

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Background: Transitions between different tobacco products are frequent among tobacco users in Bangladesh; however, the reasons leading to such transitions are not well researched.

The aim of the study is to examine the reasons reported by tobacco product users in Bangladesh to transition to other products or quit, and understand perceptions related to the change.

Design/Methods: Data from four waves (2009-2015) of the International Tobacco Control (ITC) Bangladesh Survey were used. Repeated data on perceptions and reasons for exclusive cigarette (n=538), bidis (n=160), and SLT users (n=143) to either start using other products or quit were analysed using cross-sectional ITC sampling weights, respective to the waves analysed. The percentages of responses across waves were used to calculate the pooled proportion data using a meta-analysis approach.

Results: The two most common causes for respondents switching to other tobacco products were: friends and family (73%-86%), and curiosity (44%-72%). For exclusive SLT users, the calming effect of smoking cigarettes and bidis (43%-57%), and the impression that bidis were less harmful (14%-52%), and taste better (27%-71%) were also major reasons to transition to other smoking products.

Health concerns (16%-63%) and disapproval from friends and family (30%-56%) were generally the main reasons for quitting.

For cigarette smokers, doctor's advice (42%) and packaging warning labels (32%) were also effective in encouraging cessation. As for bidi users, price (32%) seemed to be a driving factor for users to quit.

Conclusions: Results highlight that smoking behaviours in Bangladesh are heavily impacted by friends and family and those close to the respondents' social contacts. Receptivity to Tobacco Advertisement Promotion & Sponsorship (TAPS) may explain the high proportions of respondents susceptible to smoking due to curiosity. Cessation support, increased taxation of all products, and bans on TAPS of tobacco products should be deemed as key policies to reduce overall tobacco use in Bangladesh.

EP-38-987 Bibliometric analysis of scientific publications on tobacco endgame during the period 2011-2021

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Background: The concept of 'tobacco endgame' emerged in 2010 with an aim to eliminate tobacco use to achieve 'Tobacco Free World' for the future generations. However, the evaluation of scientific output in the field of tobacco endgame has not been studied yet. The study aims to analyze worldwide research output in the tobacco endgame, and the citations retrieved from the Pubmed Central database between 2011-2021.

Design/Methods: Data from January 1, 2011 through December 31, 2021 were searched for articles with "keywords" ("tobacco" [All Fields] OR ("tobacco" [All Fields] AND "products" [All Fields]) AND endgame [All Fields] in the title.

Scientific output was evaluated based on:

- Total and trends of contributions in tobacco endgame research between 2011 and 2021;
- Country contributions;
- Collaboration patterns;
- The citations received by the publications; and,
- Areas of interest of the published papers.

Results: Out of 549 articles screened, 41 publications were included. The largest number of publications on tobacco endgame were from the United States of America (USA) (41.5%), followed 9.8% each in UK, Canada and New Zealand and only 4.9% in India.

The total number of citations at the time of data analysis (May 11, 2022) was 825, with an average of 20.1 citations per document. Nearly half (46.3%) of the retrieved documents were commentary, editorial, perspective and letter to editors.

Maximum number of publications came in 2013 (34.1%) followed by 2019 (14.6%) and 2018 (12.2%). During the covid time in 2020, only 1 article on tobacco endgame was published.

Conclusions: The present data reveal a promising rise of research activity in the field of tobacco endgame in developed nations. However, evidence-based research on tobacco endgame in developing nations is very limited. More effort is needed to bridge the gap in tobacco endgame-based research and better evaluation of tobacco endgame policies and their implementation is recommended

EP-38-988 Implementer perceptions in non-FCTC smokeless tobacco ban's success; tobacco control program in Sri Lanka

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Background: Smokeless tobacco (ST) use is a global epidemic, with the main a massive burden on Southeast Asia, including Sri Lanka. Most of the affected countries are developing and implementing both FCTC and Non-FCTC policies to eliminate the epidemic.

Among those, four countries including Sri Lanka have completely banned ST since 2017 as one of the major tobacco policy decisions. The success of these bans has not been thoroughly evaluated yet.

Design/Methods: A qualitative study was conducted to explore the perspectives of regional implementers to understand the ban's success. An in-depth interview was conducted with 15 key stakeholders, including regional leaders in the different administrative districts in Sri Lanka.

Results: From the regional tobacco control stakeholder's perspective, the ST epidemic is a complex, diverse issue that needs different interventions rather than a comprehensive ban. A few said the ban has not been available to address the service needs of all kinds of main ST users. Moreover, the ban had been a drawback for the regional tobacco control campaign, mainly due to community denial and the increasing trend of oral cancers.

Furthermore, frontline implementers are reluctant to enforce the ban mainly due to community denial, empathy towards 'poor' sellers and lack of glamour when compared to smoking tobacco. A few said the strict rules such as bans would not be suitable for all layers of the community. Moreover, a few said the community considered the ban a cultural attack as chewing tobacco is a tradition.

Conclusions: The success of the ST ban as a tobacco control policy in different regions of Sri Lanka was found to be very much low according to the perceptions of implementers, mainly due to the complexity and diversity of the ST policy issue, failure to fulfil the different needs of a wide range of end-users and community denial.

EP-39 Community-based interventions to improve health for all

EP-39-989 Defeat childhood TB. Advocacy towards a positive national policy landscape and preparedness for childhood TB programming

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Background and challenges to implementation: For too long, childhood TB has been poorly addressed by the global public health agenda and children continues to face inequities in the TB response. Rapid adoption of innovative tools and policies based on WHO guidelines and recommendations is a critical step to ending childhood TB.

Intervention or response: As part of its Unitaid-supported CaP TB project, EGPAF carried on the following interventions to contribute to a better childhood TB policy landscape:

- Worked with governments (NTP) and WHO and other technical partners to jointly set up a consistent methodology to map and track national childhood TB policies.
- Developed a comparative analysis of national childhood TB policies in 2018 and 2021 in nine African countries and India.
- Developed national dashboards to identify national gaps and mobilize national stakeholders to act on them.
- Used the assessment as an advocacy tool for stakeholder mobilization.

Results/Impact: The assessment showed great improvements from 2018 in the 10 countries assessed. Nonetheless, important gaps remain. It provided an in-depth analysis of the policy landscape around: i) political leadership, ii) systematic screening and case finding, iii) diagnostics approaches, iv) treatment, v) preventive treatment, vi) integration in non-TB entry points, and vii) monitoring and evaluation.

The assessment has facilitated collaborations with stakeholders nationally and regionally. Collaboration with NTPs were critically important to validate information, address information gaps, and refine the national dashboards. Joint collaboration with the Global TB Caucus has allowed engagement of parliamentarians in addressing policy gaps both at regional and national levels.

This intervention has led to a consistent methodology that can be replicated in other countries to monitor and improve childhood TB policy national landscapes.

Conclusions: Monitoring childhood TB national policies is critical to ensure progress towards updated an enabling policy framework for childhood TB programming and provides a useful tool to sensitize partners to act on policy gaps.

EP-39-990 Civil society and government against COVID-19: a comprehensive and health equity promoting strategy by Partners In Health and the Ministry of Health

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Background and challenges to implementation: By January 2022, COVID-19 and its variants have infected 23,844 people and caused 2,299 deaths in the state of Chiapas, Mexico. Chiapas represents one of the regions most vulnerable to the pandemic, with a deficit of professionals, infrastructure and medical supplies. In response to this situation, Partners In Health, in collaboration with the Ministry of Health, developed the Infection Prevention and Control (PCI) program which aims to:

- Contain the spread of COVID-19,
- Guarantee equitable access to quality clinical care,
- Provide social support to facilitate isolation of cases and contacts, and;
- Generate community partnerships.

Intervention or response: The PCI program comprises two branches. The clinical branch is based on support with medical supplies, PPE, antigen testing and trained personnel to ten first level clinics, and the creation of a Center for Respiratory Diseases (CER) for outpatient and inpatient management of severe COVID-19 cases. It also includes telephone and home follow-up of cases and contacts, as well as the delivery of food supplies to complete isolations. The community branch is based on strengthening prevention -including the administration of vaccines- and health promotion through the implementation of risk communication campaigns and demystification of the virus and the anti-COVID-19 vaccine.

Results/Impact: Attention was provided to 2,613 suspected cases, 3.3% received hospital care; 4,000 antigen tests were performed, detecting 600 positive cases. Re-

mote or home follow-up was provided to 1,861 contacts; food pantries were delivered to 75% of positive cases for isolation; in addition, 495 vaccines were administered in communities reaching a 65% of coverage.

Conclusions: To strengthen the civil society-public sector alliance it is essential to face the medical and social challenges posed by the pandemic. Maintaining the functioning of services, social support, contact follow-up and the activation of community participation favor the lasting impact of public health interventions.

EP-39-991 Convergence approach to engage and empower Gram Panchayats to improve public health status and building TB free Gram Panchayats

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Background and challenges to implementation: The Gram panchayat (GP), as the local -government at the village level, has a crucial role in representing the voice of the people in decisions regarding health. At the same time, it needs to work in collaboration with other functionaries including health to ensure access to quality health care for the people in the GP area. Though there are important platforms available there the issues of health can be discussed, in reality there are gaps in convergence and coordination between GP and health functionaries in health service delivery including Tb health services.

Intervention or response: The Gram Panchayath Arogya Amrutha Abhiyaana (GPAAA), supported by USAID, is being implemented in 2816 GP in 14 districts of Karnataka, reaching to 4.5 million population. The aim was to take services to the doorstep of every poor household in rural Karnataka through the close collaboration of Panchayat and health services staff from health and wellness centers. GP task force members were trained to screen for TB, NCD and also address child marriage issues in their areas. Health management kits were distributed to GPs to aid the GPs in health promotion and prevention.

Results/Impact: GPs started using the health Management kits and conducted health camps in coordination with department of health. In 6 months, project period 9,925 vaccination camps organized, 5,02,860 vaccination doses were given. 4,514 NCD camps organized, 1,69,871 persons were screened for NCD, 3,86,394 persons were screened for TB, 5,831 referred for TB testing in which 1,597 tested and 108 found positive

Conclusions: GPs are the *centers of village administration, development*, with immense potential to provide decentralized services that can improve the health and

well-being of villagers and leveraging community networks to meet the needs of the most vulnerable and unreached populations. By involving GP it is possible to ensure viable, accessible, and community-centered program for TB free Gram panchayats.

EP-39-992 Strengthening TB survivor-led networks through structured leadership training: experiential learning from India

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Background and challenges to implementation: TB survivor-led networks were formed in India in 2017-18 and have continued to evolve over the last five years. With TB survivors primarily as members, these networks have expanded their presence and membership in their states, built relationships with the TB programme and become reliable support systems for people with TB. They have established governance structures, electing committee and core group members and in some cases, becoming formally registered as independent structures.

Networks with strong leadership, governance & accountability can play a critical role in sustaining engagement of affected-communities in the TB programme.

Intervention or response: REACH partnered with a global social sector leadership institute to develop a unique leadership training curriculum for survivor-led networks.

This was piloted in Bihar, with the governing body and executive committee members of TB Mukh Vahini (TMV), the state network. A needs assessment with TMV revealed two requirements: personal leadership and capacity building needs of individuals, and support structures to build the TMV group into a larger, organised movement.

Results/Impact: A structured training curriculum, focusing on specific leadership skills such as goal setting, conflict resolution, building self-confidence & impactful public speaking was developed. The curriculum was delivered virtually to 20 TMV network members in 2021, over six half-day sessions. Training methods included use of interactive presentations, role play, storytelling, case maps etc.

The participants expressed that they had a clearer understanding of the nature of the leadership required from them, were able to better understand the viewpoints of stakeholders they work with and felt more confident in managing conflicts.

Conclusions: The leadership training gave network members a renewed outlook on their roles within the networks, strategies to mobilise stakeholders and manage conflicts.

Leadership training is critical in enhancing the capacity of networks to advocate for affected communities and sustain their meaningful participation in the TB response.

EP-39-994 Community contribution in TB active case finding

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Background and challenges to implementation: KN-TB is a \$USD15 million, 5-year grant from USAID, under the TB local organization network (TB LON) funding mechanism being implemented by 4 partners UZT, Jointed Hands Welfare Organization (JHWO), BOHS and HOSPAZ.

JHWO is implementing community based TB prevention, active case finding and demand creation TB services in 4 districts (Gweru, Gwanda, Insiza and Zvishavane) in 2020 and were upscaled to 8 (additional districts are Mwenezi, Shurugwi, Chirumhanzu and Kwekwe) in 2021.

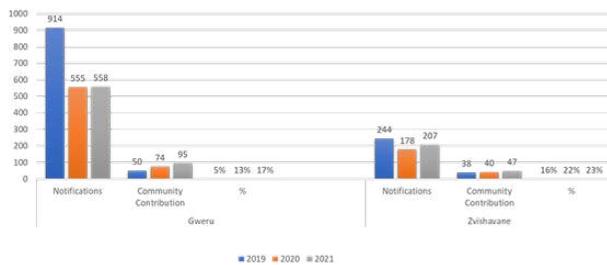
Intervention or response: Community leaders such as chiefs, councilors, headmen, Kraal heads and religious leaders, the local government structures, Rural District Councils and town councils were sensitised. High risk groups, including PLHIV, ASMs, the elderly, the diabetics, health care workers, peer educators and advocates were sensitised and screened for TB.

Community based volunteers (CBVs) were trained to offer TB prevention, care and treatment services. The training content covered the role of the community in project oversight.

The trained cadres then empowered their catchment areas and reached them through cascade trainings. To enhance their effectiveness and visibility, branded materials, IEC materials were provided and distributed to the communities.

Results/Impact: Sensitised 240 District stakeholders to get their buy in and support in demand generation, Community dialogue sessions with 3745 influential community leaders to create demand for TB services. Empowered 587 HCC Chairpersons who cascaded the trainings to 1818 HCC members. Health facility nurses trained 967 CBVs on TB active case finding.

These efforts resulted in increased number of clients screened, presumed and notified by community as shown by the graphs on the following page:



Conclusions: Community contribution has improved access to high-quality, person-centered TB, DR-TB, & TB/HIV services and has resulted in early screening as well as provision of DOT and palliative care services. Together we can end TB, there is need to invest in Community Cadres and save lives. Community systems strengthening is a sustainable.

EP-39-995 The journey continues... south to south collective learnings and challenges of communities working on TB stigma, discrimination and human rights

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Background: The Global Coalition of TB Advocates (GCTA) is a coalition of TB affected individuals bringing the lived experience of TB to the global platforms towards a people-centered rights-based TB response.

In the past few years addressing stigma and discrimination and focus on upholding the rights of people affected by TB has gained momentum. Communities, civil society organizations have begun to receive funding that has allowed them to implement activities to address stigma and discrimination.

The GCTA has successfully brought the issue of stigma and discrimination to the top levels advocating to address stigma and build a human rights-based TB response across the world. This session will be the presentation of the study findings.

The objective of the study was

- To collect and share best-practices around stigma reduction and anti-discrimination advocacy as experienced by TB communities across the regions,
- To document the challenges, barriers, and needs alongside progress towards a human rights-based and people-centered TB response.

Design/Methods:

- 1.Desk Research
- 2.Qualitative Data – KII, FGDs (LAC, EECA, AP, Africa, India)
- 3.Thematic Data Analysis
- 4.Dissemination at regional and global level.

Results:

- 1.Main Human Rights Issues (Stigma, Discrimination, Healthcare, treatment, diagnostics, COVID-19, Medicalized approach vs. community-centred, Government relations)

2.Progress on TB and Human Rights (Legal Approaches, Information and Human Rights Education, Government Relations, Coalition-building)

3.Main Challenges and Needs (Funding, Documentation and Advocacy, Meaningful Engagement, Government and Policymakers, Knowledge, Communications, and Materials).

Conclusions:

- TB organizations to demand that the social management of TB becomes a non-negotiable facet of TB care, with actionable principles and standards attached to any aspirational plans.
- Open dialogue between TB organizations and donor organizations on how TB community priorities and donor priorities can be further aligned.
- operationalizing and integrating the existing strategy into actionable and measurable advocacy, communication, and community engagement plans at the central, state and local levels.

EP-39-996 Identifying gender-related barriers in accessing TB diagnostic and treatment services in Kazakhstan, Tajikistan and Uzbekistan

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Background and challenges to implementation: A gender-based approach to tuberculosis (TB) care acknowledges and responds to social, legal, cultural and biological issues underpinning gender inequality and contributing to poor health outcomes.

To best tailor its TB interventions using a gender-based approach, the USAID Eliminating Tuberculosis in Central Asia Activity assessed gender, stigma and other social barriers to accessing TB services.

Intervention or response: We undertook country-level assessments relying primarily on quantitative cross-sectional household surveys and qualitative data collected through focus groups and in-depth interviews among people with TB, family members, high risk populations and service providers.

Results/Impact: Our research identified several themes related to gender barriers to accessing TB services:

Gender differences in decision-making for healthcare: Many respondents in Tajikistan (49% M; 40% W) need permission from their parent(s) or in-laws to seek

healthcare. Respondents reporting they do not need anyone's permission to seek healthcare include 6% W, 14% M in Tajikistan, 55% M and 39% W in Uzbekistan; and 68% M, 76% W in Kazakhstan.

Gender differences in access to treatment: Participants blamed financial difficulties as a reason for interrupting treatment by more women than men in Tajikistan (32% W, 22% M) and Uzbekistan (18%, 12% M), but by more men than women in Kazakhstan (22% M, 10% W).

Gender differences in access to social support: In Uzbekistan, significantly more men than women reported receiving government support during TB treatment (37% M, 27% W). Men were only slightly more likely than women to receive government support in Kazakhstan (66% M, 62% W) and Tajikistan (51% M, 49% W).

Gender stigmatization measured as belief that the family prioritizes men when for treatment was confirmed by respondents in Uzbekistan (53% W, 40% M). The results are reversed in Tajikistan (54% M, 40% W) and Kazakhstan (7% M, 5% W).



Conclusions: In Central Asian countries, gender-related barriers to accessing TB care vary significantly by country. The granular data from this assessment can inform future TB interventions.

EP-39-997 Assessing gender preferences among tuberculosis patients in three health-seeking settings of Vietnam

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Background: Despite an increasing focus, gender preferences for health-seeking in tuberculosis (TB) remains insufficiently documented. As part of the USAID-supported Erase TB project, this study aimed to elucidate gender preferences in health-seeking in urban settings of Vietnam.

Design/Methods: This cross-sectional study described the male-to-female ratios (MFR) in participation and TB yields from health seeking through routine TB program activities, community-based contact investigation (TBCI) and mobile X-ray screening, as well as referrals from private sector and private TB treatment.

Data were collected between April 2020 and September 2021 from 10 districts in Ho Chi Minh City and Hanoi, Vietnam.

Results: The cumulative MFR of people diagnosed with TB on Erase TB was 1.8, which was substantially lower than the MFR of 4.0 recorded during Vietnam's second TB prevalence survey. The routine TB program MFR was 2.3 (N=2,493) compared to MFRs of 4.5 (N=165) from community-based case finding and 1.8 in the private sector (N=4,595). Within community-based case finding, the MFR of TBCI was 4.2, while mobile X-ray screening reached an MFR of 4.6. The MFR among private sector referrals was 2.9, while in private TB treatment the MFR was 1.6.

	Total	Male	Female	MFR
Routine TB program activities	2,493	1,740	753	2.3
Erase TB case detection yields (all pathways)	4,760	3,051	1,709	1.8
Community-based activities	165	135	30	4.5
Facility-based TB contact investigations	26	21	5	4.2
Community-based mobile X-ray screening	139	114	25	4.6
Private sector care	4,595	2,916	1,679	1.7
Private sector referrals to the TB program	562	419	143	2.9
Private TB treatment	4,033	2,497	1,536	1.6

Table. TB patient gender breakdown by health-seeking setting. April 2020 to September 2021. Vietnam.

Conclusions: Our study showed that routine TB program activities continue to miss a substantial proportion of men with TB, for whom community-based TBCI and active case finding may be effective outreach and engagement strategies. Meanwhile, the privacy of private TB treatment may be an attractive value proposition for health-seeking among women with TB.

EP-39-998 COVID-19 lockdown related violence, at-risk populations, and TB-related health literacy in Uganda 2020-2022

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Background: Uganda's secularist stance is subverted by a lack of monopoly for human and social development services, most are run by religious or private entities which are claiming greater social and community relevance. For at-risk populations, this is connected to disproportionate access and fuels TB prevention and health literacy inequity, violence, abuse, discrimination, and stigma. This study links lack of optimal access to TB Prevention literacy to causes and outcomes of violence, abuse, discrimination, and stigma during the COVID-19 Lockdown period.

Design/Methods: 650 MSM (16 years to 64 years), 140 MSM (22%) cited shaming at the literacy workshops. 71 respondents (16 years to 52 years; 65 males and 06 females (18 years-25 years with a history of substance use cited lack of admittance and frequent arbitrary arrests. 05 (100%) were trans-gender (20 years and 45 years, all had faced child sexual abuse and later serious physical harm) and 11 (100%) were lesbians (18 years to 24 years) cited stigma and discrimination.

Results: 195 (100%) female sex-worker, 75 (38%) expressed a spike in abuses by clients and had bodily injuries to that effect); 25 (13%) had aggressive live-in partners who threatened them with black mail, confiscating property and abandonment if they failed to give them money from sex-work. From anecdotal responses, abuses, discrimination, and stigma towards HIV+ men and women, sexual minorities were conducted by the state, religious and other private entities. Respondents reported two aspects about violence: it was perpetrated by security agents and private citizens; and it was fueled by electoral, religious and media campaigns.

Conclusions: State structures enhance legitimacy, authority and capacity and if culturally sensitive, they can be leveraged to promote optimal TB Prevention during the COVID-19 lockdown. Studying the TB related health literacy by service providers in Uganda vis-à-vis at-risk populations informs health seeking programming.

EP-40 TB services coping with COVID-19

EP-40-1000 A COVID-19 screening strategy based on the use of rapid antigen tests in health care facilities in Niger

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Background: In Niger, as in other African countries, the diagnosis of Covid-19 remains very low, despite several seroprevalence studies suggesting a large spread of SARS-CoV2. Highly centralized testing capacities, based on PCR, hinder the access to Covid-19 diagnosis. The intervention aimed to assess feasibility, acceptability, impact and cost-effectiveness of a screening strategy based on rapid antigen testing (Ag-RDT) of symptomatic patients in clinical settings.

Design/Methods: From November 2021 to April 2022, all adults attending medical or emergency outpatient consultations of 5 primary health centers and 3 hospitals in Niamey and Dosso regions were screened for Covid-19 by trained nurses. WHO Covid-19 cases definition was used, facilitated by a digital decision-support tool. Suspected cases were tested with Covid-19 Ag-RDT (SD-Biosensor). Severity was defined by hospitalization decision.

Face-to-face interviews with health care workers (HCWs) and patients were conducted to evaluate intervention acceptability, and cost-effectiveness assessed accounting for expenses in human resources, equipment and tests.

Results: Among 12,014 patients triaged, 2,244 (19%) were classified as Covid-19 suspected cases, of whom 2,177 were tested with Ag-RDT (97%). 135 were positive (6%) (55% at hospital level, median age 42 years). 16/135 positive patients were hospitalized (12%), 7 died (5%). 15/16 severe cases were diagnosed in hospitals.

An estimated 78% of the targeted patients were triaged. The intervention was well accepted by HCWs and patients, despite a quite high level of stigma and denial. The average cost of diagnosing a Covid-19 case was estimated at 547 USD (severe case: 5,347 USD).

Conclusions: Screening based on RDT-Ag was feasible, well accepted and improved access to Covid-19 diagnosis at all levels of the health care system in Niger. The cost-effectiveness of the triage strategy is relative in Niger context, but focusing on hospital settings, or on

most-at-risk people, could increase its efficiency. Beyond diagnosis, improving the management of severe cases could reduce mortality.

EP-40-1002 Addressing COVID-19 and other communicable diseases among internally displaced persons in Poltava, Ukraine

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Background and challenges to implementation: Russian invasion into Ukraine in February 2022 triggered a massive refugee crisis in the country. According to IOM estimates, since March 21, 2022, there are more than 6.5 million internally displaced persons (IDP) within Ukraine. More than 56,000 IDPs are in the Poltava region, many of whom fled cities under bombardment which destroyed residential areas. The health system, including primary health care, screening, and immunization programs, is suffering due to the influx of large numbers of IDPs.

Intervention or response: The PATH-led, USAID-funded Support TB Control Efforts in Ukraine (STBCEU) project adjusted programmatic activities to respond to the new challenges caused by war and the increasing number of IDPs, which create a high-risk environment for the transmission of COVID-19, TB, and other infection diseases.

One of the interventions was to conduct monitoring visits to the shelters where IDPs were accommodated to ensure access to health services and COVID-19 vaccination. The monitoring multidisciplinary team consists of representatives of Poltava Regional Center of Diseases Control and Prevention, epidemiologists, primary health care providers, and infection diseases doctors.

This team works together to provide information on prevention of infectious disease spread in temporary shelters, COVID-19 prevention and vaccination, vaccine-preventable diseases, and routine vaccination during the war.

Results/Impact: From March 28 to April 19, 2022, 14 visits were conducted by the monitoring multidisciplinary team in Poltava region. As a result of the visits 1,380 people received health services, including: 288 COVID-19 vaccinations, 50 tetanus vaccinations, 53 diphtheria vaccinations, 75 inactivated polio vaccines; 423 COVID-19 tests; and 1,050 medical examinations.

Conclusions: The monitoring multidisciplinary team approach proved effective to increase IDPs' access to health care services in shelters, where large numbers of IDPs could be reached at once for preventive measures including vaccination. The STBCEU project will scale up this approach to other regions of Ukraine.

EP-40-1003 Multi-disease integrated outreaches to bridge the gap in TB & COVID-19 case detection in Bauchi state, Nigeria

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Background and challenges to implementation: Bauchi state is one of the high TB burden states in Nigeria and also one of the states affected by the COVID19 pandemic. The advent of COVID19 pandemic with the control measures introduced in Nigeria from March 2020 greatly impacted on the health service delivery including TB service provision with TB notification in Q2,2020 greatly affected. The similarity of TB and COVID-19 symptoms affected the patronage of the presumptive TB in the health facilities due to fear of being diagnosed with COVID19.

Intervention or response: Multi disease integrated outreaches of TB, COVID19, HIV & Malaria was therefore implemented in selected communities to reduce the effect of COVID19 associated stigma and enhance detection of both TB and COVID19 diseases in the state. This study highlights the results from this intervention

Results/Impact: 2,766 individuals were screened for TB, 34% (930) of the individual screened were identified as presumptive TB and tested for TB, 6% (53) of the presumptive TB were diagnosed with TB and 1 MDR/RR-TB was also diagnosed and placed on treatment. 70% (652) of the presumptive were tested for COVID19 using RTKs and 18% (120) of the presumptive were diagnosed with COVID19 and were managed accordingly. 1,558 of the individuals were also tested for HIV and 7 were HIV positive, 2,300 of the individuals were tested for Malaria and 583 Malaria cases were diagnosed, 92% (537) of the diagnosed Malaria cases were given Artemisinin-based combination therapy (ACT) during the outreaches.

Conclusions: Integrating TB and COVID19 outreaches in addition to other diseases has the potential of increasing TB and COVID19 notification, lessons from this outreaches should be used in scaling up integrated outreaches in other states and in country with high burden of TB and COVID19.

EP-40-1004 TB/COVID-19 integrated screening: preliminary lessons learned from the ACT-A project in Ethiopia

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Background and challenges to implementation: Through the Access to COVID-19 Tools Accelerator (ACT-A) MSH received funding from FIND to implement a TB/COVID Integration project in Ethiopia in collaboration with Ethiopian Public Health Institute (EPHI). Integrated testing for TB and COVID-19 has the potential to help recover a proportion of people who developed TB during the pandemic but are yet to be systematically evaluated and on whom data are lacking. This project piloted TB/COVID-19 integrated screening in 15 selected high burden tertiary hospitals across 4 regions (Amhara, Oromia, SNNP, and Sidama regions) of Ethiopia. **Intervention or response:** A baseline assessment (BLA) was conducted at the 15 project-supported tertiary hospitals. Key findings from the BLA included: siloed program interventions, gaps in trainings, challenges with the supply management of personal protective equipment (PPE) and SARS-CoV-2 Ag test kits, and limited patient access to chest x-ray (CXR) and GeneXpert testing. A TB/COVID-19 integration standard operating procedure was designed with a pre-triage screening approach, algorithm, and performance indicators, and piloted at the 15 high burden tertiary hospitals.

Number of trained staff in 15 hospitals selected for ACT-A

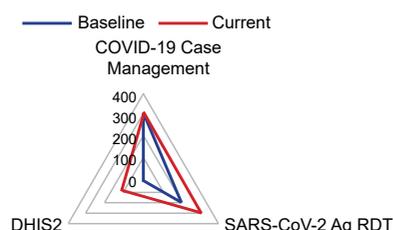


Figure 1. Training of health professionals (Clinicians, Lab professionals and nurses) at baseline and after ACT-A starting implementation in the 15 HF, February 2022.

Hospitals: 1-Debre Markos, 2-Gondar, 3-Debre Birhan, 4-Dessie, 5-Worabe, 6-Arba Minch, 7-Wolaita, 8-Adare, 9-Ambo, 10-Jimma, 11-Wolkite, 12-Dodola, 13-Shashemene, 14-Arsi and 15-Adama.

Results/Impact: Dissemination of directives tools (fifteen SARS-CoV-2 Ag RDT and COVID-19 tools) coupled with orientations, and training of key end users were instrumental for changes in TB and COVID-19 service delivery in the project-supported facilities (figure 1). Data on the introduction of the TB/COVID-19 integrated algorithm will be presented with its impact on RDTs uptake, access to CXR, GeneXpert, and TB notification.

Conclusions: Key lessons learned include:

1. Disruption of TB, HIV can be addressed in an integrated approach with COVID-19 diagnosis and management, and;
2. An algorithm and a triage approach can make a difference in the selection of patients and impact the cost of interventions and reduce catastrophic expenditures for patients.

EP-40-1005 Community based integrated screening and testing for TB and COVID-19: a quantitative assessment In Nelson Mandela Bay District, South Africa

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Background and challenges to implementation: The COVID-19 pandemic affected the TB elimination efforts. Integration of COVID-19 with TB has been proposed as an important strategy to ensure that TB case detection is maintained during the pandemic. In collaboration with the District Department of Health and FIND, AQUITY INNOVATION implemented community-based COVID-19 and TB integration screening and testing services. We report here the effects of our intervention on detecting COVID-19 and TB as well as improving early referrals to hospitals.

Intervention or response: We provided integrated screening and testing for COVID-19 and TB at various community locations targeting COVID-19 hotspots. Clients seen are screened for both Covid 19 and TB symptoms using an integrated TB & covid screening tool, tested for COVID-19 using WHO-approved Ag-RDTs and GeneXpert for TB. We reviewed the routine programme data between 1 October 2021 and 31 March 2022 and presented the results descriptively.

Results/Impact: 19330 people were screened for COVID-19 and TB symptoms. The median age was 34 years (range - 0,5 - 95 years); 47% (9476) were male; 40% were unemployed and 59% self-reported to have not been vaccinated for COVID-19. 11713 (61%) Ag-RDTs were administered and 1094 (9%) tested COVID-19 positive translating to one COVID-19 positive case per 18 people screened. 723 (4%) presumptive TB were identified; 110 (15%) of TB diagnosed with GeneXpert translating to

one TB positive case diagnosed per 176 people screened. Among the 110 patients diagnosed with TB (104 DS-TB and 6 DR-TB), 86% (95) were confirmed to have started TB treatment at the nearest clinic following their linkages to care.

Conclusions: The results of this project show that employing decentralized testing with Ag-RDTs in a community-based setting can help detect positive COVID-19 and TB cases that would otherwise have gone undiagnosed.

Further rollout of the integrated TB/COVID-19 screening and testing services may also benefit areas with limited capacity.

EP-40-1006 Impact of COVID-19 on Directly Observed Treatment Short-Courses (DOTS) program for tuberculosis in Nepal

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Background: Tuberculosis remains a major public health program in Nepal and requires surveillance, clinical assessment, confirmation of diagnosis and supervised treatment regimens for effective management.

The COVID-19 pandemic has led to change in prioritization, which has affected many aspects including the functioning of tuberculosis control programs.

Design/Methods: The study aimed to assess the challenges due to COVID-19 pandemic on management of tuberculosis by assessing both patients and health care providers perspectives on facilitators and barriers to DOTS services.

We conducted qualitative interviews with the patients (n= 117) and the health providers (n=35) at the DOTS centers to understand the facilitators and barriers of the TB program during COVID-19 pandemic.

Similarly, we interviewed TB focal persons at all three government level including local level - health coordinators from corresponding municipalities (n=21) and TB focal persons and health office chiefs from corresponding district (n=37), provincial level-TB focal persons at corresponding provinces (n=6) and central level (n=2) to understand the perspectives to strengthen DOTS services during critical times like COVID-19. A thematic analysis approach was used for data analysis utilizing inductive and deductive coding.

Results: The unavailability of public transportation, strict social restriction in mobility were common problems encountered by the patients during lockdown.

Furthermore, both TB patients and health staff admitted to constant fear of transmission of COVID-19 particularly due to crowding in the health facilities. Although, majority of the DOTS centers reported to have

managed to provide timely TB medicine to the TB patients, occasionally, lab services were interrupted due to transfer of laboratory staff for the COVID duty.

Conclusions: Clinical care for diseases like tuberculosis, that require daily care are impacted hard by scenarios like COVID-19. The preparedness for such circumstances needs to be done considering the perspectives of the patients and the health providers.

EP-40-1007 The pandemic is not the great equalizer: Front line labor and the work of rationing in COVID-19 critical care

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Background: Many in healthcare and in the media framed the COVID-19 pandemic as “the great equalizer,” expressing a universal experience of healthcare systems under duress. However, COVID-19 has radically intensified the pressure to adapt critical care labor and has required rationing on the part of healthcare workers across the world. Pronounced disparities across lines of race, class, income, ability, and geography made the pandemic anything but equalizing. Our main objective is to critically investigate how hospital intensive care units (ICUs) are critical sites of care labor and see how and on what terms rationing highlights key features of healthcare labor and its inequalities.

Design/Methods: A practice-oriented ethnographic study was conducted in a United States academic ICU by a medical anthropologist and medical intensivists with global health expertise. The analysis drew on 25 months of participant observation and 57 in-depth interviews.

Results: We identify sites and practices of shortage or rationing and point to the ways embodied labor constitutes them. Rationing occurred along three domains: equipment and technology, labor, and emotions and energy. In depicting workers’ adaptation and resilience forged amidst profound moral distress, we point to a more robust global health labor politics based on assessing critical care rationing as work. This assessment takes into account both the materiality and practices of critical care.

Conclusions: Focused studies of pandemic rationing practices and critical care labor disrupt too-simple comparative narratives of Global North/South divides. Further studies and efforts must address the toll of healthcare labor.

EP-40-1008 Implementation of integrated service delivery strategies for effective TB and COVID-19 case finding in Nigeria

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Background and challenges to implementation: The COVID-19 pandemic has made it necessary for public health programs to adopt innovative approaches for Integrated Service Delivery (ISD). In Nigeria, existing GeneXpert networks for TB were leveraged for SARS-CoV-2 testing starting in April of 2020. We describe results of an ISD approach using this network to improve TB and COVID-19 case finding and mitigate negative impacts on TB case finding and treatment.

Intervention or response: We implemented the ISD approach across 30 antiretroviral therapy clinics in Benue and Plateau States from September 2021 to February 2022. The approach included integrated TB/COVID-19 screening among persons living with HIV (PLWH) using a standardized checklist and bi-directional TB/COVID-19 testing using GeneXpert. The checklist was based on the National COVID-19/TB Algorithm and included symptoms specific to TB and, separately, COVID-19. PLWH who screened positive for any symptom of TB and/or COVID-19 were offered testing for both diseases using sputum samples for TB and nasopharyngeal swabs for SARS-CoV-2. We collected demographic information and screening and testing outcomes using an mHealth application.

Results/Impact: Our findings showed 47,300 PLWH were screened for TB and COVID-19. Screening yielded 1,002 (2.1%) PLWH presumptive for only TB, 90 (0.2%) presumptive for only COVID-19, and 1,880 (4.0%) presumptive for both TB and COVID-19. Of the 2,972 PLWH with presumptive TB and/or COVID-19, 2,760 (92.9%) were tested for both diseases. Test acceptance was lowest among those presumptive for only COVID-19 with 66 (73.3%) accepting. The proportion of PLWH with *Mycobacterium tuberculosis* and/or SARS-CoV-2 detected was highest among those presumptive for COVID-19 only (MTB detected in 27.3%, SARS-CoV-2 detected in 36.4%).

Clients Screened for TB/COVID-19 (N=47,300)	Presumptive for TB Only	Presumptive for COVID-19 Only	Presumptive for both TB and COVID-19	Total Clients
Presumptive Cases	1,002 (2.1%)	90 (0.2%)	1,880 (4.0%)	2,972 (6.3%)
Tested for TB and COVID-19	947 (94.5%)	66 (73.3%)	1,747 (92.9%)	2,760 (92.9%)
Mycobacterium tuberculosis (MTB) Only Detected	44 (4.6%)	15 (22.7%)	115 (6.6%)	173 (6.3%)
SARS-CoV-2 Only Detected	18 (1.9%)	21 (31.8%)	84 (4.8%)	123 (4.5%)
Both MTB and SARS-CoV-2 Detected	0 (0.0%)	3 (4.5%)	6 (0.3%)	9 (0.3%)

Conclusions: Bi-directional TB/COVID-19 screening and testing have the potential to enhance diagnostic efficiency and case detection of both diseases. We recommend further exploration of this strategy to maintain accurate and efficient TB diagnosis while utilizing the functionality of GeneXpert diagnostic networks to diagnose multiple diseases.

EP-40-999 Challenges in TB treatment provision during the COVID-19 pandemic: perspectives from patients and health workers

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Background: Tuberculosis (TB) remains a major public health problem in Uganda. During the COVID-19 pandemic, TB notification rates and treatment completion rates fell. We describe challenges faced by patients and healthcare workers in TB clinics in Kampala.

Design/Methods: A qualitative study was conducted at four clinics: Infectious Diseases Institute; Mulago Hospital; and two city council facilities from June – September 2021, during Uganda's second surge of COVID-19 cases. Semi-structured in-depth interviews were undertaken to collect data from 20 TB patients (with presumptive TB or receiving treatment) and 10 healthcare workers. Audio data were transcribed and thematic analysis focused on challenges in care access and delivery.

Results: Interviewed patients (aged 20- 69 years, 50% male) reported high quality TB care during the pandemic, with shorter queues because clinics were quieter,

and described awareness of enhanced infection prevention procedures. However, lack of access to and increased cost of transport leading to lengthy walks, and strict legal enforcement of movement restrictions, made clinic attendance difficult. Unavailability and high costs of non-TB drugs and fear of contracting COVID-19 at healthcare facilities deterred clinic attendance.

Healthcare workers (aged 28-50 years, 60% male) reported increased transport costs when commuting to work, shortage of personal protective equipment, fear of contracting COVID-19, and reallocation of staff and equipment (e.g., Xpert machines) to COVID-19 duties as challenges experienced during the pandemic.

Healthcare workers also reported missed clinic visits by patients and drug stock outs as impediments to successful TB treatment completion.

Conclusions: Patients and healthcare workers in TB clinics described similar challenges to TB care access and delivery during the COVID-19 pandemic. Transportation difficulties, fear of contracting COVID-19 at clinic and resource allocation away from TB were common themes which should be proactively addressed to maintain TB control during concurrent respiratory infection outbreaks.

EP-41 COVID-19 a challenge for chest disease services

EP-41-1009 Lessons learned from the COVID-19 pandemic: Brazilian patients' perspective

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Background: The COVID-19 pandemic disrupted TB services, resulting in a decline in TB detection and an increase in TB deaths. However, lessons from the pandemic response can be learned to improve TB care and reverse this situation.

We conducted a survey among Brazilian patients and caregivers to understand their perspective on TB service disruptions and lessons learned from the pandemic. Despite having the 2nd highest toll of COVID-19 deaths, the Federal Government never imposed restrictive measures. A complete lockdown was never imposed by municipal or state governments.

Design/Methods: We applied an objective questionnaire, the interviews were face-to-face and the questions sought to compare services before and during the pandemic, as well as the access barriers faced during this period. Patients/caregivers who underwent treatment for conventional, multidrug-resistant or preventive treatment during the pandemic were eligible.

Results: 202 respondents from the 5 regions in the country were included. Most were women (53%), patients (79%) - undergoing conventional TB treatment (46%), MRTB treatment (29%), or TPT (19%). Participants suggested that the TB services have been the most affected by COVID-19. The diagnosis was delayed both because of the patients' fear of accessing services (46%) and the limitations of travel (45%). Participants also believe that there are lessons from the COVID-19 response that can be transferred to the TB program, particularly in better understanding the importance of contact tracing and the importance of wearing masks. They consider that there is a greater concern with the COVID-19 pandemic than with TB. Finally, they pointed to the need for greater social visibility of TB, especially with campaigns in traditional media.

Background and challenges to implementation: A pandemia de COVID-19 aumentou nos serviços de TB, resultando em um declínio na detecção de TB e um aumento nas mortes por TB. No entanto, as lições da resposta à pandemia podem ser aprendidas para melhorar os cuidados com a TB e reverter essa situação. Realizamos uma pesquisa entre pacientes e cuidados brasileiros para entender sua perspectiva e pesquisas sobre serviços de TB que aprendemos com a pandemia. Apesar de ter o 2º maior número de mortes por COVID-19, o Governo Federal nunca impôs medidas restritivas. Um bloqueio municipal completo nunca foi pelos imposto municipal ou estadual.

Intervention or response: Aplicamos um questionário objetivo, as entrevistas presenciais foram realizadas eletronicamente e as perguntas buscavam comparar os serviços antes e durante a pandemia, bem como as barreiras de acesso enfrentadas neste período. -resistentes ou tratamento preventivo durante a pandemia foram considerados elegíveis.

Conclusions: Patients/caregivers perceived a retraction in TB services and the prioritization of COVID-19 in services. However, they point to positive lessons that can be implemented and strengthen TB actions.

EP-41-1010 Gait speed is a promising functional performance measure in post-COVID patients

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Background: 4-meter gait (4MGS) is an easy functional performance test and predicts a greater risk of health outcomes. We aimed to evaluate the relationship between 4MGS with frailty, activities of daily living, and functional exercise tests in COVID-19 survivors.

Design/Methods: We included COVID-19 survivors. All of the participants underwent spirometry. Functional exercise performance was evaluated by 6-Minute Walking Testing (6MWT), Incremental Shuttle Walking Testing (ISWT), and Endurance Shuttle Walking Test (ESWT). Activities of daily living and frailty were assessed by the London Chest Daily Activity of Daily Living Scale (LCDADL) and FRAIL, respectively. Patients with 4-meter gait speed (4MGS) <1m/sec were grouped as patients with slow gait speed.

Results: A total of 30 COVID-19 survivors (55.6 ± 12.9 years old) were enrolled. 46.7% of the participants were on home oxygen. 4-meter gait speed was 1,03±0,20 m/sn; LCDADL 35,6±16,8 points; FRAIL scale 2,2±1.2 in the overall group. 4MGS showed high correlation with walking distance in 6MWT ($r=0,715, p<0,0001$) and ISWT ($r=0,707, p<0,0001$), respectively. 4MGS showed a moderate correlation with endurance time in ESWT ($r=0,487, p=0.007$). 4MGS has a moderate correlation with vital capacity, DLCO, and total LCDADL and FRAIL scores. Patients with slow gait speed had the significantly worse vital capacity and diffusion capacity. Similarly, activities of daily living were impaired more and more frailty was evident in the slow gait speed group.

Conclusions: 4MGS is correlated with pulmonary functions, exercise performance, frailty, activities of daily living and nutritional risk status in COVID-19 survivors in the post-COVID phase evaluation. Patients with slow gait speed have worse pulmonary functions and exercise capacity and their daily living activity and frailty scores are more impaired. 4MGS is a promising, easy, and cheap functional performance test in the evaluation of post-COVID patients physical and functional well-being.

EP-41-1011 The impact of the COVID-19 pandemic on essential health, tuberculosis and HIV services in the Free State Province, South Africa

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Background: COVID-19's impact on essential health, TB and HIV services (EHSs) could lead to loss of recent gains. It is necessary to balance efforts to combat the pandemic while sustaining EHSs. This research set out to establish the effects of COVID-19 on EHS services in the Free State province of South Africa during December 2019 to November 2021.

Design/Methods: The impact of COVID 19 on EHS delivery was assessed using a pre-post study design, comparing EHS performance between 2019 (pre-COVID-19) and 2020/2021 (post-COVID-19 commencement). Routinely-collected District Health Information System data were analysed using RStudio. Mean changes were compared using Student's t-tests. Tests were performed at the 0.1 significance level.

Results: Primary Health Care (PHC) utilisation declined by a statistically-significant 12.3% ($p < 0.01$). The mean number of DSTB patients starting treatment decreased statistically-significantly by 3.1% ($p < 0.01$). The number of ART-naïve patients starting treatment declined by 7.6% which was also statistically significant ($p < 0.01$). These findings are contrary to research elsewhere in Africa (Kenya) showing that during the COVID-19 period, there were small increases in TB treatment success and referral of HIV-positive persons to ART. A positive observation of the current study is that BCG coverage showed a statistically significant upward trend of 5.7% ($p < 0.05$).

Service	Mean before COVID	Mean during COVID	% change in mean	P-value
BCG coverage	88.9	94.0	↑ 5.7	0.02695
PHC utilisation (Number of visits per person per year)	1.87	1.64	↓ 12.3	0.0002219
DS-TB treatment commenced	95.5	92.5	↓ 3.1	0.06821
New cases commenced on ART	70.8	65.4	↓ 3.1	0.003486

Conclusions: Findings attest to the overall fragility of public health systems and delivery of EHS health services during pandemic conditions. Interesting, and attesting to a measure of resilience in EHS delivery, was that BCG coverage actually increased during the COVID-19 pandemic. However, the province should plan to strengthen the resilience of PHC and TB and HIV services during future pandemics.

EP-41-1012 Performance characteristics and operational feasibility assessment of a CRISPR based Tata MD™ CHECK diagnostic test for SARS-CoV-2 (COVID-19)

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Background: Tata MD CHECK SARS-CoV-2 test, a paper strip-based RT-PCR CRISPR (CRISPR) test was approved by Indian Council of Medical Research (ICMR) for COVID-19 diagnosis in India. To determine the potential for rapid roll-out of this test, FIND conducted performance characteristic and an operational feasibility assessment (OFA) of the Tata MD™ CHECK CRISPR test at a tertiary care setting.

Design/Methods: The study was conducted at the ICMR approved COVID-19 RT-PCR laboratory of KEM hospital, Mumbai, India. The CRISPR test was evaluated against the gold-standard RTPCR test using the same RNA sample extracted from clinical specimens collected from COVID-19 suspects for routine diagnosis. CRISPR results were determined manually as well as using the Tata MD CHECK application. An independent agency was appointed for interviewing relevant laboratory staff and supervisors (N=9).

Results: Overall, 2,332 (Fresh: 2,121, Frozen: 211) clinical specimens were analysed of which, 140 (6%) were detected positive for COVID-19 by CRISPR compared to 261 (11%) by RT-PCR. Discordance between CRISPR and RT-PCR results increased with increasing CT values & decreasing viral load (range: <20% to >85%). Overall sensitivity and specificity of CRISPR was 44% and 99% respectively when compared to RT-PCR. In OFA, all participants indicated no specific requirements of training for HR performing molecular work. However, additional post-PCR steps such as setting up the CRISPR reaction and handling of detection strips were time consuming and requiring special training. No significant difference was observed between manual and app-based readings, but issues such as erroneous results, difficulty in interpretation of faint bands, internet connectivity, data safety and security were highlighted as challenges and concerns with the app-based readings.

Conclusions: Results indicated that the CRISPR test cannot be a substitute for the RT-PCR test at the intended setting. However, there is a definite scope for improvement in next version of this assay.

EP-41-1013 Evaluation of a strategy combining medical triage and SARS-CoV-2 Ag-RDTs to improve the diagnosis of COVID-19 in health facilities in Mali

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Background: In Mali, COVID-19 diagnosis is based on PCR whose accessibility remains limited. In health facilities, screening is done at entry, but the search for clinical signs during consultation, whose duration is 5 min on average, is not systematic, leading to a sub-diagnosis. We evaluate a strategy combining systematic triage for COVID-19 for adults during consultation and Ag-RDTs for suspected cases.

Design/Methods: Prospective study from October 2021 to January 2022 in medical and emergency departments in 7 health facilities at different levels of the health care system in Mali. A median of 5 health care workers was recruited in each health facilities. PCR was requested for positive Ag-RDT (SD Biosensor). Operationality definition: proportion of patients who received triage and Ag-RDT for suspected cases (WHO criteria), among patients who consulted.

Results: Among 9744 eligible patients, the inclusion was proposed in 3067 (38%) due to the flow of patients. 2407 patients (25%) were included, median age: 36 years (IQR 25-51), women: 59%. Main reasons for patient refusal: lack of time (34%), denial of COVID-19 (28%). 1405/2407 patients (67%) were suspected for COVID-19, among whose 305/1405 (22%) had already been identified at entry screening. Median triage time: 4 minutes (IQR 2-6).

Naso-pharyngeal sampling and Ag-RDTs were performed in 1266/1405 patients (90%), median time: 20 minutes (IQR 15-20). Ag-RDTs were positive in 329 (26%). PCR results were available for 133/329 (40%), positive in 89.5% (figure). Severity was observed in 34 patients (1 died), and associated with age \geq 50 years ($p < 0.001$) and co-morbidities ($p = 0.03$). The operability was 34%, 15% and 12% at primary, secondary and tertiary levels respectively ($p < 0.001$).

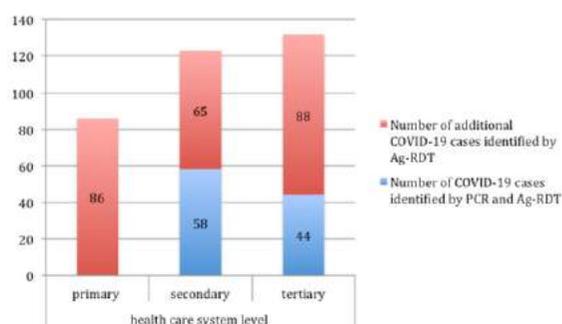


Figure. Number of COVID-19 cases identified by PCR and/or Ag-RDT in 7 health facilities in Mali (ECOVAM study).

Conclusions: Despite its effectiveness, the strategy is poorly operational. Given the frequency of suspected cases, the flow of patients and the time for triage and Ag-RDTs, prioritisation of patients at risk of severe disease could be more efficient.

EP-41-1014 Impact of the COVID-19 pandemic on mortality rates in Lima, Peru

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Background: Peru reported one of the highest excess death rates worldwide in 2020-2021. Excess mortality reflects COVID-19-specific and other causes of death affected during the pandemic. We document to what extent the mortality in Lima was attributed to COVID-19 and whether this varied across districts.

Design/Methods: This study has an ecological design with district clusters as the unit of analysis. We classified the 50 districts of Lima Metropolitana into six clusters based on population size, location, and socio-economic characteristics (crowding, human development index, monetary poverty), using hierarchical clustering (Euclidean distance, average linkage). We classified deaths from the national death registry (SINADEF) 2017-2021 as either COVID-19-related or non-COVID-19-related based on ICD-10 codes and COVID-19-specific search terms.

We compared direct age-standardised rates of all-cause, COVID-19-related, and non-COVID-19-related deaths across clusters (Cochran-Mantel-Haenszel test).

Results: All-cause age-standardised mortality rates/100,000 population for Lima were 275 in 2017, 315 in 2018, 258 in 2019, 617 in 2020, and 674 in 2021. All clusters experienced a substantial (1.4-to-2.6-fold) increase in all-cause mortality rates in 2020-2021 compared to 2019. During the pandemic, all-cause mortality rates varied across clusters: between 498 and 670 in 2020 ($p < 0.0001$) and between 690 and 747 in 2021 ($p < 0.0001$). In Lima during 2020-2021, 44% (83,123/187,232) of deaths were COVID-19-related. COVID-19 related-mortality rates/100,000 were 280 in 2020 and 307 in 2021. Non-COVID-19-related mortality rates were 336 in 2020 and 366 in 2021. Non-COVID-19-related mortality rates increased during the pandemic in all clusters except cluster 4 (high socio-economic profile). Both COVID-19- and non-COVID-19-related mortality rates varied across clusters ($p < 0.0001$).

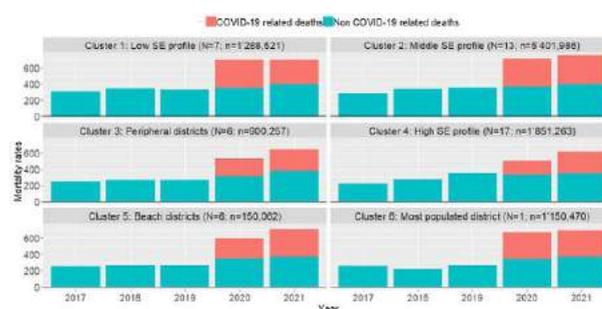


Figure. Age-standardised mortality rates per 100,000 population in district clusters of Lima Metropolitana (2017-2021).

N: Number of districts; n: number of inhabitants, SE profile: socioeconomic profile.

Conclusions: Small but sustained increases in non-COVID-19-related deaths contributed to the high mortality reported during the pandemic. Variations in non-COVID-19-related mortality across districts may reflect local health system capacity and access.

EP-41-1015 Lung function outcomes post-hospitalisation for symptomatic COVID-19 disease in patients from a tertiary facility, South Africa

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Background: Recent research suggests that Covid-19 and tuberculosis may cause post-infection lung impairment. This study provides a unique opportunity to assess lung outcomes in a post-hospitalisation Covid-19 cohort from a high TB-incidence population.

Design/Methods: Participants were enrolled on discharge, after treatment in hospital for Covid-19 disease. Patient data including demographics, hospital stay, management, hospital investigations (sputum microbiology), and clinical conditions including HIV status and TB history were collected. A follow up visit was scheduled within 20 days post-discharge. At the visit, St Georges respiratory questionnaire (SGRQ), blood tests (Interferon Gamma Release Assay [IGRA]), spirometry and 6-minute-walking-test (6MWT) were performed. Data was summarized using median and inter-quartile range for continuous and percentages for categorical variables. Regression analysis for potential risk factors is currently ongoing. GLI reference ranges were used to interpret spirometry results.

Results: Of 157 enrolled participants (female 61.9%, mean age 48 years), 34.2% were HIV positive (93.5% on antiretroviral therapy), 18.1% reported previous tuberculosis infection, 43.5% with latent tuberculosis, and 42.7% reported 2 or more comorbidities. The majority had moderate Covid-19 disease evidenced by WHO ordinal scores (stage 3 – 31%, stage 4 - 60%, stage 5-7 – 9.1%) with a mean hospital stay of 12.2 days. From the 157 participants, 109 completed the follow up visit. Spirometry results indicated a high proportion of restrictive lung disease (42.9%); much higher than obstruction (1%) and restriction and obstruction combined (3.8%); with 1.9% showing severe, 22.9% moderate and 21.9% mild impairment. Evidence in reduction of lung function extended to 6MWT (mean distance 306.9m) and elevated SGRQ scores (22.9 - 39.5).

Conclusions: COVID-19 is shown to largely cause a restrictive lung impairment in our patients post-hospitalisation, and this impact extends to functional limitations in 6MWT and respiratory symptoms. Analysis of the impact of tuberculosis and other risk factors on the development of post-infection lung impairment is currently ongoing.

EP-41-1016 High COVID-19 seroprevalence at Ugandan TB clinics underlines the need to protect vulnerable populations

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Background: Tuberculosis (TB) remains a major public health problem in Uganda and it is important that patients can safely seek care. However, healthcare facilities may be high-risk settings for COVID-19 transmission. Data on COVID-19 exposure amongst clinic attenders in high-burden TB settings are lacking but would be useful for planning of infection prevention strategies by TB control programmes.

Design/Methods: A cross-sectional study was conducted at four clinics in Kampala: Infectious Diseases Institute; Mulago Hospital; and two city council facilities from June – September 2021, during Uganda's second surge of COVID-19 cases. Sequential patients aged ≥18 years, attending the clinic for investigation of presumptive TB or as established TB patients on treatment were invited to undergo combined nose swabbing for SARS-CoV-2 PCR testing, and blood sampling for anti-N and anti-S SARS-CoV-2 antibody tests. Prevalence of current and previous COVID-19 were reported. Regression analyses were performed to identify risk factors for infection.

Results: 342 patients were recruited, 219 (64%) of whom were presumptive TB patients. 180 (53%) were female. Median age was 35 years (interquartile range [IQR]: 28-44). 177 (51%) were HIV-positive. 33 (9.7%) of clinic attenders were SARS-CoV-2 PCR positive on nose swabs, suggesting current Covid-19 disease.

Factors associated with positive PCR results were: residential location within Kampala, HIV-positive status, not being on ART, and presentation with loss of smell. 296 (87.6%) were positive for either anti-N or anti-S antibodies, and 226 (67.5%) were positive on both antibody tests. There was no access to COVID-19 vaccines at this time, suggesting that positive serology was related to prior infection.

Conclusions: TB clinics represent locations of concentrated higher risk during epidemics of concurrent respiratory infections. These locations should be high-priority for intensified infection prevention measures, vaccine roll-out (for staff and vulnerable populations), and access to rapid-turnaround testing.

EP-41-1017 Implementation of bi-directional screening of COVID-19 and tuberculosis in community posts in Mozambique

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Background and challenges to implementation: The COVID-19 pandemic has reduced the number of people diagnosed with TB in 2020 both in Mozambique and globally. This reflects a supply-side and demand-side disruption in TB diagnosis and treatment services: reduced capacity of the health system to provide services due to COVID-19; users' concern about the risk of COVID-19 in the health facilities (HF) and restrictions on door-to-door TB screening. We describe an innovative strategy to simultaneously screen for TB and COVID-19 in communities through the installation of Community Posts (CP) to improve the detection of both diseases.

Intervention or response: We implemented simultaneous COVID-19 & TB screening in all people with respiratory symptoms in seven sites in the urban and rural districts of Maputo and Gaza, with two community healthcare workers per site. Community-based organisations run mobilization workshops to build knowledge, provide person-centred counselling and promote screening for COVID-19&TB, thereby creating demand. People with respiratory symptoms and/or COVID-19 or TB contact receive AgRDT COVID-19 test and provide a sputum sample for GeneXpert testing according to national guidelines. Samples are transported to the reference HF daily, results are captured into routine data systems. People with confirmed TB and/or COVID-19 are linked to care.

Results/Impact: CPs screen about 1,500 people a day at peaks. From April 18th to date, 88 people were screened at two sites. Co-infection with TB is found in 66.6% of COVID-19 positive cases. The project is ongoing, the final results will be available in October 2022.

Conclusions: CPs allow TB and COVID testing to occur in communities and enable linkage to person-centred care. Screened people can receive preventive services such as TPT, and contacts of persons who tested positive can easily access these posts to receive diagnostic services. Furthermore, this early diagnosis strategy helps break the chain of transmission of the two diseases, avoiding the dissemination in the targeted populations.

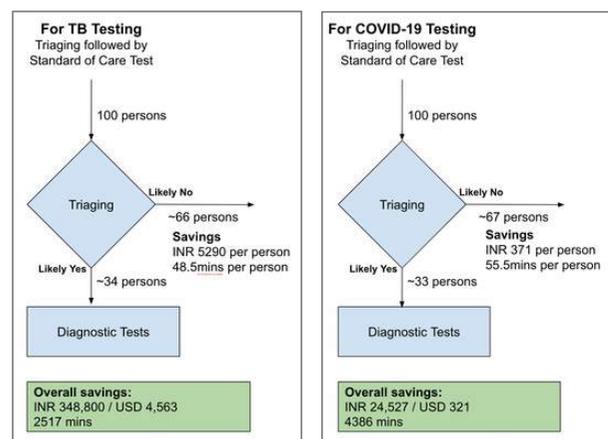
EP-41-1018 Reducing cost and time spent for screening, triaging and prioritizing patients for COVID-19 and TB using Swaasa AI platform

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Background and challenges to implementation: Every year, 7 million people die prematurely from respiratory diseases. The challenge is to screen and monitor lung health at scale in real-time. The available methods for respiratory health assessment cannot reach large and scattered populations due to the constraints of costs associated, equipment, and trained personnel.

Intervention or response: Our team, consisting of doctors, data scientists, and engineers, analyzed sounds produced during coughing. They extracted audiometric information which can be indicative of respiratory diseases. Swaasa AI Platform was developed and validated to analyze cough sounds in real-time, decipher anatomical and physiological information and predict the risk associated with COVID-19 and TB. The sensitivity of the tool is approx. 92% for COVID-19 and approx. 87% for TB, which is promising as compared to the rapid tests available worldwide. When deployed as a screening and triaging tool prior to molecular testing, Swaasa was statistically proven effective in prioritizing at-risk patients for testing.

Results/Impact: During the trials, along with the efficacy and accuracy, we established conclusive evidence of reduced cost and time associated with screening and testing. The screening helped reduce cases by approx. 65% for COVID-19 and TB, while the time was reduced by 36% for TB and 45% for COVID-19. Thus, from the findings, for each 100 people, this test reduced the burden on India's public health infrastructure by INR 348,800 (USD 4,563) for TB testing and INR 24527 (USD 321) for COVID-19.



Conclusions: In humanity's fight against tuberculosis and COVID-19, the results of Swaasa provide an opportunity to frequently screen for cases spread across the remote areas and reduce the burden of cost and time on the public health infrastructure. For India and other low-and-middle-income countries, this implementation opens doors to fight and eradicate TB and COVID-19 at scale

LATE BREAKER PRESENTATIONS WEDNESDAY 9 NOVEMBER 2022

LBCOV COVID late-breaker session

LBCOV-2002-09 Global opinions on SARS-CoV-2 Ag RDT self-testing policy and implementation: a cross-sectional survey

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Background: Introduction of the use of SARS-CoV-2 antigen-detection rapid diagnostic tests (Ag-RDTs) allowed decentralization of COVID-19 testing and opened the possibility of self-testing; the full scope of Ag-RDT utilization for self-testing is not well-described. To inform development of the recently released World Health Organization global guidelines on COVID-19 self-testing, a global survey was conducted.

Results: Between 01 and 11 February 2022, 844 individuals from 139 countries responded to the survey. 45% reported being affiliated with governments, and 47% were operating at national level. 504 respondents, from 101 countries reported existence of policy supporting C19ST for a range of use cases, including symptomatic and asymptomatic populations. More respondents from low-and-middle-income than high-income countries reported lack of C19ST policy (61 vs 11 countries), and low population-level reach of C19ST. Respondents with C19ST experience reported that the tests were mostly acceptable to the target populations, perceived programmatic benefits, and highlighted key challenges to be addressed for increased success.

Conclusions: Policies, implementation, and interest in C19ST are widespread globally, but access to C19ST remains higher in High Income Countries compared to Low-Middle Income Countries. Respondents who reported experience with C19ST highlight strong willingness and many perceived benefits. Costs reported varied widely, but some potentially affordable and free options were reported. The reported challenges should inform future policy and implementation.

LBCOV-2053-09 Evaluating the clinical impact of Nitazoxanide in patients with mild to moderate COVID-19: a randomised controlled trial (the C3-RCT)

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Background: There is an unmet need for pharmacological COVID-19 interventions in resource-poor settings. Nitazoxanide (NTZ), a low cost broad spectrum antiviral agent with activity against influenza, hepatitis A and hepatitis B, has been shown to reduce SARS-CoV-2 viral shedding but data about clinical outcomes are sparse.

Results: 322 participants were randomised (n=161 NTZ and n=161 placebo). Progression to severe disease was similar in the NTZ and placebo arm [4.3% (7/162) vs 5.0% (8/162); relative risk=0.88 (0.33-2.36); p=0.79]. The mean time to symptom resolution was shorter in the placebo arm [18.7; IQR=7-22 versus 14.7; IQR=6-15; p=0.04]. Adverse events occurred equally in the NTZ arm compared to the placebo arm [mild adverse events (162 vs 109; p=0.79); serious adverse events (11 vs 12; p=0.83)], however, gastro-intestinal events occurred more frequently in the NTZ arm [87/162 (53.7%) vs 45/109 (41.3%), p=0.045]. The trial was stopped prematurely due to futility.

Conclusions: In ambulatory patients with mild to moderate COVID-19 NTZ had no effect on symptom duration and, in at-risk persons, did not reduce progression to severe disease. These data inform management strategies for COVID-19 in resource-poor settings.

LBCOV-2067-09 Epidemiological analysis of mortality among COVID-affected TB patients in Ukraine

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Background: The COVID pandemic has affected the population of Ukraine, accounting for around 12% of mortality for 2021.

The virus is especially dangerous for patients who already have other health-related conditions; one of the vulnerable groups is TB patients. A mortality analysis was carried out amongst COVID-affected TB patients registered in 2021.

Results: Among the deaths of TB/COVID patients: 60 cases (69,8%) were new cases of TB infection, 20 cases (23,3%) were relapses, and 6 cases (6,9%) were under another category. Amongst concomitant diagnosis: 17 patients (19,7%) had Viral Hepatitis (C, B, C and B), 15 patients (17,4%) had HIV, 7 patients (8,1%) had anemia, 6 patients (6,9%) had Ischemic Heart Disease, 6 patients (6,9%) had diabetes, 4 patients (4,6%) had ulcer, and 3 patients had delirium (3,4%). The most common types were patients who had TB disseminated form (41,8%, 15 patients) and TB infiltrated form (15,1%, 13 patients).

Conclusions: Due to pre-existing diseases TB patients are vulnerable to having a severe COVID infection. Patients with comorbidities, such as TB and Hepatitis; TB and HIV are susceptible to being exposed to severe COVID. Mostly, TB patients have had several other comorbidities, such as HIV and Hepatitis; Hepatitis and Anemia. Also, the severity of TB forms, such as TB disseminated form and TB infiltrated form, affect the development of severe cases.

TB patients infected with COVID require additional attention for the treatment of comorbidities.

LBCOV-2080-09 Predictors of SARS-CoV-2 culture-conversion in a university-based cohort

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Background: Since March 2022, the United States Center for Disease Control and Prevention recommends isolation for 5 days after initial COVID-19 symptoms, assuming symptom improvement. However, little is known about predictors of individual culture-conversion by the end of isolation.

Results: Of 105 SARS-CoV-2 RT-PCR positive participants with sufficient culture and symptom information, 76% culture-converted by day 6. Seventy-five percent of participants remained symptomatic after day 5, of which 70% had culture-converted. Univariate analyses showed increased odds of culture-conversion when reporting no cough (OR=4.67, 95% CI: 1.83, 12.83), no stuffy nose (OR=3.87, 95% CI: 1.47, 11.56), or no runny nose (OR=3.30, 95% CI: 1.32, 8.73) after day 5. Participants reporting known exposures were less likely to convert (OR=0.35, 95% CI: 0.14, 0.88). Controlling for demographics, known exposure, previous infections, vaccinations, maximum symptom and viral load, and medical history, participants who were symptom-free after day 5 were more likely to culture-convert (OR=14.00, 95% CI: 1.95, 306.90).

Conclusions: Most participants culture-converted by the end of the recommended isolation period, though most also remained symptomatic beyond day 5. Current guidance of including symptoms in determining duration of isolation is supported, as we show those free of residual symptoms were significantly more likely to have culture-converted by day 6. Further, presence of cough, stuffy nose, or runny nose may prove helpful in determining increased likelihood of culture positivity beyond the isolation period.

LBCOV-2088-09 CM-101 Treatment in Patients with Lung Damage Derived from Covid-19 Reduced Inflammatory and Fibrotic Biomarkers

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Background: CCL24 is a soluble protein that was shown to play a significant role in advancing inflammation, fibrosis and vascular damage processes that are associated with the pathogenesis of lung diseases.

CM-101 is a CCL24 neutralizing monoclonal antibody that was found to attenuate inflammation and fibrosis in pre-clinical and early clinical studies. The aim of this study is to assess the effect of CM-101 in patients with lung injury derived from Covid-19.

Results: Serum levels of biomarkers associated with lung inflammation and vascular impairment were reduced as soon as 24 hours following treatment with CM-101. CXCL-10, was strongly inhibited by 65%, 24 hours post treatment. Procollagen 4 and C3M (represent formation and degradation of extra cellular matrix) were highly elevated in these patients, and significantly reduced by 25%, 72 hours post treatment.

Finally, CM-101 demonstrated a more rapid and robust reduction in CRP levels, as compared to retrospective Covid-19 control group. Importantly, treatment with CM-101 was safe and well tolerated.

Conclusions: CM-101 was safe and well tolerated and achieved reductions in markers associated with lung inflammation and fibrosis, consistent with previous clinical and pre clinical data that supports CM-101 anti-inflammatory and anti-fibrotic effect and are of high relevance in lung diseases.

LATE BREAKER PRESENTATIONS THURSDAY 10 NOVEMBER 2022

LBST RIT/JATA student late-breaker session on lung health

LB02-1700-10 Identifying best practices for offering telephonic adherence support to people on treatment for TB or HIV and/or TPT: A scoping review

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Background: While completing treatment is essential to cure tuberculosis (TB), treatment duration, side effects and structural barriers pose challenges to adherence. COVID-19 made out-of-clinic adherence support options more desirable. Little is known about telephonic adherence support (TAS) for TB. We conducted a scoping review of TAS outcomes among people on treatment for TB and/or HIV or TB Preventive Therapy (TPT).

Results: Eighteen articles were included in analysis: 15 on antiretrovirals, three on TB treatment, and zero on TPT. TAS differed by frequency: daily, weekly, intermittent, or monthly; duration: median=6, range=3-40 months; and comparison group: standard of care (n=16), directly observed therapy (DOT) (n=3), and/or SMS reminders (n=1).

TAS improved adherence from baseline in 6/9 studies (mean_{improve}=2.2%, range=-26.4-26.5%) and compared to controls in 10/15 studies (mean_{diff}=4.6%, range=-5.7-40.2%). In studies measuring clinical outcomes, TAS improved log₁₀ VL from baseline in 5/5 studies and outperformed comparators in 3/5 studies (mean VL_{improve}=1.8, range=0.6-3.2; mean VL_{diff}=0.6, range=-0.5-1.7). CD4 counts improved from baseline in 4/4 studies and against comparators in 3/4 studies (mean CD4_{improve}=65.2, range=9.1-146.0/_{mm3}; mean CD4_{diff}=19.6, range -32.0-75.4/_{mm3}).

One study showed a higher, but statistically insignificant, proportion of smear conversion for TAS compared to DOT (17.1% vs 13.1%, p=0.67).

Conclusions: There were few studies on TAS for TB; more for HIV. Overall TAS showed modest improvement, with wide variation between studies. Notably, TAS showed improvement from baseline for all clinical outcomes. Differences in TAS components and study design may explain the wide range in findings

LB02-1737-10 Age-associated tissue-specific amino acid and immune cell dysregulation in Mycobacterium tuberculosis-infected C57BL/6 mice

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Background: Tuberculosis (TB) disease is caused by the infection of *Mycobacterium tuberculosis* (Mtb), with an annual incidence of 10 million new cases and ~1.2 million deaths worldwide. Clinical presentation of TB (symptoms, disease progression, and treatment outcome) significantly varies between aged (>65 years) and adult patients.

The current anti-TB regimen and trials cater to the adult population (25-40 yrs), leaving behind the extreme age groups of the age pyramid (<18 and >65 yrs).

Results: Bacterial burden in the lungs, spleen, and liver increased exponentially till 4 weeks post-infection (w.p.i.) and plateaued till 6 w.p.i. in both the age groups. Treatment with rifampicin and isoniazid for 2 weeks resulted in a reduction of 2.5 log₁₀cfu in lungs of 2M animals while only ~0.5 log decrease in 17M animals. The aged animals always had higher circulatory PD-1⁺ T cells (at least 2 fold higher) compared to younger animals irrespective of their infection and treatment status. A similar proportion of lung CXCR5⁺T cells (~20% of activated T cells) was observed in both age groups.

Conclusions: Bacterial clearance in aged animals seems to be slower as compared to younger animals. An increased proportion of CXCR5⁺ cells was found in both the age groups, but an association of a delayed bacterial clearance suggests that the function of these cells could hold a clue as to how an aged system is managing the host.

LB02-1841-10 Development of a costing and cost-effectiveness framework for comparing use of TST and IGRA among high TB-burden populations

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Background: Identifying individuals with tuberculosis (TB) infection and initiating them on TB preventive treatment is a cornerstone of TB prevention. Tuberculin skin test (TST) is the standard of care to detect TB infection; however, it can be unreliable and has known implementation-based limitations. We estimate the practical costs incurred from, and programmatic impact related to, TB infection testing by comparing TST—a less sensitive test requiring two patient visits but no laboratory capacity—with interferon gamma release assay (IGRA)—a newer, more sensitive diagnostic that requires laboratory capacity.

Results: A health delivery program would save \$79.24 per test if IGRA was implemented over TST. This assumes a local functioning laboratory with the capacity to be upgraded to process the test. The one-time cost of equipping a laboratory with infrastructure capable of performing IGRA totaled \$37,784.43. When considering test performance, societal and health system costs, and programmatic requirements for implementation of both TST and IGRA, we found that once a laboratory processed 477 IGRA tests, it would be more cost-effective compared to TST, despite the larger upfront investment (Table 1).

Description of input	Assuming programmatically observed prevalence (27.28%)
Cost savings of administering IGRA (per test)	\$3.59
Cost savings to health system and society if IGRA is used over TST (per test)	\$75.65
Total cost savings to implement IGRA over TST (per test)	\$79.24
Total laboratory equipment cost for establishing IGRA capability (includes enzyme-linked immunosorbent assay [ELISA] reader and washer, refrigerator, incubator, micropipettes, centrifuge, and computer)	\$37,784.43
Number of tests needed to be conducted in lab to make IGRA more cost-effective	477

Table 1: Costs and cost effectiveness of implementing IGRA instead of TST

Conclusions: Given global shortages of TST and concerns about costs of IGRA testing and laboratory capacity building, this research provides a costing framework for public health officials and agencies to guide decision-making for future TB infection testing guidelines locally.

LB02-2050-10 How well the asthma knowledge among outpatient Bangladeshi asthmatics?

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Background: Even though effective treatment and regularly updated asthma management guidelines are available, asthma is still poorly controlled in significant number of patients. Psychosocial factors associated with asthma including knowledge level of asthma may contribute for better treatment outcomes and wellbeing of the asthmatics.

Results: The study instrument appeared to be linguistically valid and reliable by both modern response theory (MRT) and classical test theory (CTT). Overall the enrolled adult asthmatics possessed good AK. Binary logistic regression analyses showed significant predictors for AK were education-other (technical, madrasa/religious school), monthly family income: > US\$ 500, US\$ 251-500, years of asthma: < 5 years, 1-2 asthma triggering factors, asthma control: well-controlled and not well-controlled.

Conclusions: The psychometric validations of respective study instrument were acceptable. The evidences presented in this study supported the fact that numerous factors such as socio-demographic and medical factors are capable of influencing AK.

LATE BREAKER PRESENTATIONS FRIDAY 11 NOVEMBER 2022

LBTB The Union/CDC late-breaker session on TB

LBTB-1864-11 National expenditure on Tuberculosis and Tuberculosis incidence in low- and middle-income countries: an ecological study

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Background: Tuberculosis (TB) programmes in many low- and middle-income countries (LMICs) are underfunded. Understanding the relationship between TB expenditure and incidence could inform on how harmful the funding gap has been. The primary hypothesis was that increasing TB expenditure was associated with a lower subsequent TB incidence. The secondary hypothesis was that treatment success or coverage mediated the associations.

Results: Regression demonstrated that a 10% increase in expenditure per PWTB was associated with a 1.6% and 1.3% lower TB incidence with a two- and five-year lead, respectively. This was moderated by WHO region and World Bank group (Table 1).

WHO Region	African	Americas	Eastern Mediterranean	European	South-East Asia	Western Pacific
TB incidence with a Two-Year Lead^{a,b}						
Natural log expenditure per TB case (US\$)	-0.2 ^c	-0.02	-0.23 ^c	-0.17	-0.06	-0.28
TB incidence with a Five-Year Lead^{a,b}						
Natural log expenditure per TB case (US\$)	-0.18 ^c	-0.01	-0.19	-0.03	-0.05	-0.07
World Bank Income Group	Low		Lower Middle		Upper Middle	
TB incidence with a Two-Year Lead^{a,b}						
Natural log expenditure per TB case (US\$)	-0.18 ^c		-0.09		-0.24 ^c	
TB incidence with a Five Year Lead^{a,b}						
Natural log expenditure per TB case (US\$)	-0.16 ^c		-0.05		-0.12	

TB=tuberculosis, US\$= United States dollars
 a. Fixed effects model with robust standard errors adjusted for clustering. Model covariates were life expectancy (years), Human Development Index, natural log GDP per capita, natural log current health expenditure per capita, measles vaccination coverage, annual percentage change under-five mortality, mean governance, natural log estimated proportion of incident TB with HIV, natural log estimated proportion of incident TB with MDR/XDR.
 b. Coefficients can be interpreted as elasticities due to log-log specification of variables.
 c. P<.001

Table 1. Summary of beta coefficients from multivariable linear regression analyses of the natural log of tuberculosis incidence and the natural log expenditure per person with TB by WHO region and world bank income group.

In high TB-HIV coinfection burden countries, natural log expenditure per PWTB was associated with the natural log of TB incidence with a two-year lead (beta,-0.19,95% CI,-0.29 to -0.09,P<.001). Treatment success mediated the association In the African Region with a two-year lead (0.03% mediation effect) and in low-income countries with a two-year (0.02% mediation effect) and five-year lead (0.01% mediation effect).

Conclusions: Increasing TB expenditure was associated with a lower subsequent incidence in certain contexts, partially due to higher treatment success. This validates the importance placed on higher funding to address TB in LMICs, particularly given declining funding and insufficient progress towards ending TB.

LBTB-1937-11 Optimized delivery of isoniazid-rifapentine for tuberculosis prevention among people living with HIV: the 3HP Options Trial

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Background: Identifying delivery strategies that enhance acceptance and completion of once weekly isoniazid-rifapentine taken for three months (3HP) for tuberculosis (TB) prevention is critical for effective scale-up among people living with HIV (PLHIV).

Results: 1544 PLHIV were included in the preliminary intent-to-treat analysis (93% of 1656 enrolled from 2020-2022). The median age was 42 years, 68% were women, and median time on ART was 9.0 years. The proportion accepting and completing 3HP exceeded 0.80 (p<0.001) in all arms, and there was no evidence for differences between arms (p≥0.293 after Bonferroni adjustment).

There were no differences between arms in pre-specified subgroups including sex, age, previous TB and time on ART, however exploratory analyses found older participants in SAT (≥42 years) completed 3HP more compared to younger participants (RR=1.06, 97.5% CI: 1.00-1.12; p=0.03). 16 (1.0%) participants discontinued 3HP due

	Directly Observed Therapy (DOT) (n=514) Proportion (97.5% Confidence Interval (CI))	Self-Administered Therapy (SAT) (N=517) Proportion (97.5% CI)	Choice (N=513) Proportion (97.5% CI)	SAT vs. DOT Unadjusted Risk Ratio (RR) (97.5% CI) p-value	Choice vs. DOT Unadjusted RR (97.5% CI) p-value	Choice vs. SAT Unadjusted RR (97.5% CI) p-value
All participants	0.94 (0.91-0.96)	0.92 (0.89-0.94)	0.93 (0.90-0.95)	0.98 (0.94-1.02) p=0.293	1.00 (0.96-1.03) p=0.795	1.01 (0.97-1.06) p=0.427
Sex						
Male (n=490)	0.93 (0.87-0.97)	0.91 (0.84-0.95)	0.90 (0.84-0.94)	0.98 (0.91-1.05) p=0.462	0.97 (0.90-1.04) p=0.315	0.99 (0.91-1.07) p=0.791
Female (n=1054)	0.94 (0.90-0.96)	0.92 (0.89-0.95)	0.95 (0.91-0.97)	0.98 (0.94-1.03) p=0.447	1.01 (0.97-1.05) p=0.589	1.03 (0.98, 1.07) p=0.197
Age group (median split)						
18-41 years (n=743)	0.93 (0.88-0.96)	0.89 (0.84-0.93)	0.92 (0.87-0.95)	0.96 (0.90-1.02) p=0.153	0.99 (0.93-1.05) p=0.688	1.03 (0.97-1.10) p=0.304
≥42 years (n=801)	0.94 (0.90-0.97)	0.94 (0.90-0.97)	0.94 (0.90-0.97)	1.00 (0.95-1.05) p=0.958	1.00 (0.95-1.05) p=0.966	1.00 (0.95-1.05) p=0.992

LBCDC-1937-11 Table. Acceptance and Completion of 3HP in the 3HP Options Trial overall and by important pre-specified subgroups (n=1544).

to adverse events (8 were grade 3 (n=7) or grade 4 (n=1) events), which did not differ by study arm (DOT=5 (1.0%), SAT=6 (1.2%) and Choice=5 (1.0%); p=0.95).

Conclusions: 3HP was widely accepted by PLHIV in Uganda, and very high levels of treatment completion exceeding our pre-specified threshold of 0.80 were achieved in a programmatic setting across all facilitated delivery strategies.

3HP can enable effective scale-up of TB preventive therapy in high-burden countries, particularly when delivery strategies are tailored to target known barriers to treatment completion.

LBTB-2070-11 Effects of oral hygiene and food intake on oral swab qPCR results in South African tuberculosis patients

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Background: Oral (tongue dorsum) swabs have shown promise as novel TB diagnostic samples. Little is known about the effects of patient behaviours, such as diet and oral hygiene, on oral swab *Mycobacterium tuberculosis* (MTB) qPCR results. We evaluated the effects of oral hygiene and food intake on Oral Swab Analysis (OSA) sensitivity of tongue swab and Cq value among Xpert-confirmed TB patients

Results: We present results for 44 TB patients. AtCq38 cut-off, under Condition 1 (OH-, FD-), 32/44 TB patients were OSA-positive (sensitivity 73% [95 CI 66%, 81%]); under both Condition 2 (OH+, FD-) and 3 (OH-, FD+), 33/44 patients were OSA-positive (sensitivity 75% [95 CI 68%, 82%]). Mean (SD) Cq value was Condition 1 = 27.26 (4.73), Condition 2 = 27.79 (5.77), Condition 3 = 29.30(5.98), with no statistically significant difference between Condition 1 vs 2, p=0.6; Condition 1 vs 3, p=0.13; and Condition 2 vs 3, p=0.28

Conclusions: Oral hygiene and food/drink prior to sampling did not affect the sensitivity and quantitative PCR results of oral swab testing. This information will inform development of oral swab testing for TB.

LBTB-2074-11 High rate of successful outcomes treating RR-TB with a delamanid-bedaquiline regimen in BEAT Tuberculosis: an interim analysis

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Background: BEAT Tuberculosis is a pragmatic randomized controlled strategy trial to evaluate efficacy and safety of a 6-month all-oral regimen compared to the South African Standard of care for the treatment of rifampicin resistant tuberculosis (RR-TB) funded by USAID. An interim analysis was undertaken in May 2022 to inform South African RR-TB guidelines.

Primary Outcome	Study Strategy	Control Strategy	Total
Total randomized with a minimum of 52 weeks in the study (ITT population)	101	98	199
Successful outcome at end of treatment and follow-up	88 (87%)	84 (86%)	172 (86%)
Unsuccessful end of treatment outcome	7 (7%)	13 (13%)	20 (10%)
Treatment failed	4 (4%)	8 (8%)	12 (6%)
Died while on treatment	2 (2%)	4 (4%)	6 (3%)
Lost to follow-up on treatment or not evaluated	1 (1%)	1 (1%)	2 (2%)
Unsuccessful end of follow-up Total	6 (6%)	1 (1%)	7 (4%)
Recurrence after cure at end of treatment	4 (4%)	1 (1%)	5 (3%)
Died after cure at end of treatment	2 (2%)	0	2 (1%)

Results: Since August 2019, among 396 individuals with RR-TB screened, 374(94%) were randomized from two sites; 191 to study strategy and 183 to control strategy. There were 189(51%) persons with HIV were included, 216(58%) were male, 25(7%) were younger than 18. Grade 3-5 adverse events (AEs) were experienced by 49(25.7%) and 51(27.9%) of participants, and 33(17.3%) and 31(16.9%) participants experienced serious AEs in the study and control strategies respectively. The commonest severe AE was anaemia, among 19(9.9%) and 14(7.7%) participants in the study and control strategies respectively.

Death occurred in 7 participants in the study strategy and 6 in the control strategy. Only 138 (37%) participants had reached 76 weeks of follow up, we therefore used a revised primary outcome considering end of follow-up outcomes at 52 weeks or later. 87% and 86% of participants had successful outcomes in the study and control strategies respectively.

Conclusions: A 6-month bedaquiline-delamanid-linezolid based regimen had comparable efficacy and safety to the South African standard of care and could be an alternative to BPAL.

LBTB-2075-11 Pharmacokinetics and optimized dosing of novel dispersible and non-dispersible levofloxacin formulations in children

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Background: Levofloxacin is used routinely for the prevention and treatment of rifampicin-resistant tuberculosis (RR-TB) in children. Recent data showed higher exposures with novel dispersible levofloxacin tablets compared to non-dispersible tablet formulations. This difference has potential important implications for levofloxacin dosing in children globally, requiring better characterization and verification.

Results: Twenty-four children were included, median (interquartile range) weight, age 12.2(10.7-15.0)kg and 2.56(1.58-4.03) years, respectively. A two-compartment model with first-order elimination and transit compartment absorption best described levofloxacin pharmacokinetics. Allometric scaling adjusted for the effect of body size, and we characterized the maturation of clearance with age. The typical clearance in a 12-kg child was estimated at 4.17 L/h. Non-dispersible tablets had significantly reduced bioavailability of -21.5% compared to the dispersible formulation, with no significant differences detected for other absorption parameters.

Dosing simulations show that current World Health Organization 2022 dosing for both formulations results in median exposures below current routine adult targets, mainly in children >6months. To achieve adult-equivalent exposures at a 750-mg daily dose, higher levofloxacin doses of 16-30mg/kg for dispersible and 20-38mg/kg for crushed non-dispersible tablets may be required in children >6months. We suggest optimized age- and weight-banded dosing within the current international weight-banded framework for both these levofloxacin formulations with consideration of pharmacokinetic targets and safety.

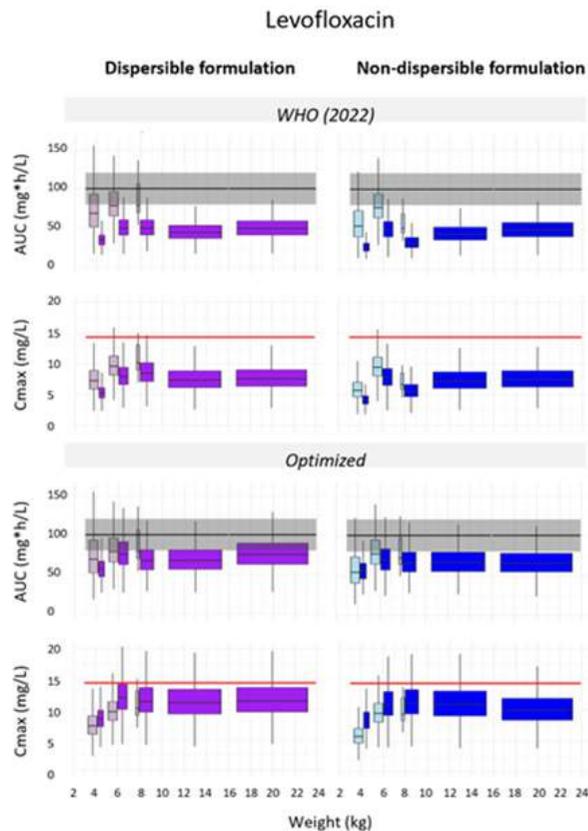


Figure 1. Simulated exposures ($AUC_{0-\infty}$) and maximum concentrations (C_{max}) of levofloxacin vs. body weight in children receiving dispersible (left/purple) and non-dispersible (right/blue) tablets, firstly at the current WHO (2022) recommended weight-band dosing (1st-section) and then at the new suggested optimized weight-band dosing (2nd-section). The blackline represents the median AUC_{0-24} of 101 mg·h/L, while the red band represents the median C_{max} (14.35 mg/L) observed with dosing at 750mg and 1,000mg daily, respectively, at the WHO recommended adult doses. For the AUC target, a $\pm 20\%$ tolerance was added (grey band). The lighter coloured boxplots represent children below 6 months of age.

Conclusions: The novel dispersible paediatric levofloxacin formulation results in improved bioavailability and exposure compared to the crushed non-dispersible formulation, but exposures remain below adult targets. New optimized dosing is suggested for prospective evaluation.

LBTB-2077-11 Changes in immune gene expression in rifampicin-susceptible tuberculosis following treatment with GSK3036656

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Background: Tuberculosis (TB) remains one of the leading global causes of death due to an infectious disease. In a Phase 2a open-label, randomized study (NCT03557281), the investigational antitubercular agent GSK3036656 demonstrated early bactericidal activity in participants with rifampicin-susceptible pulmonary TB at doses of 5–30 mg (but not 1 mg) once daily. Candidate immunological biomarker results obtained as an exploratory endpoint are presented here.

Results: RNA was analyzed in 33 participants (GSK3036656 1 mg, n=7; 30 mg, n=13; SOC, n=13). Drug treatment led to significant changes of gene expression in the different treatment arms. At Day 14 compared with baseline, 63 and 113 genes were up-regulated and 123 and 310 genes down-regulated in the GSK3036656 1 and 30 mg arms, respectively.

In the SOC arm, 231 genes were up-regulated and 292 genes down-regulated following 14 days' therapy. In all arms, the most pronounced treatment-induced changes in immune pathways were associated with humoral immune response, phagocytosis, complement activation, and neutrophil activation.

Conclusions: We demonstrated changes in gene expression and immune pathway involvement in GSK3036656 (1 and 30 mg) and SOC treatment arms within the first 14 days of treatment. Certain genes that were down-regulated following drug treatment may be useful as disease biomarkers and could be used in future studies to complement early bactericidal activity outcomes in antitubercular agent trials.

LBTB-2078-11 Phase 2a trial of GSK3036656 in rifampicin-susceptible, pulmonary tuberculosis: PET/CT scan results

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Background: Tuberculosis (TB) remains a global public health challenge. Results of a Phase 2a open-label study (NCT03557281) indicated that the investigational anti-tubercular agent GSK3036656 at 5–30 mg once daily has early bactericidal activity and is well tolerated in participants with bacteriologically confirmed, rifampicin-susceptible, pulmonary TB.

Here, we present positron emission tomography/computed tomography (PET/CT) scan results from the same study.

Results: PET/CT scans were obtained for 18 participants (GSK3036656 1 mg, n=6; 30 mg, n=12) presenting with varying disease severity. GSK3036656 at 30 mg led to a reduction in LV (by 10–60 ml) in all participants and to a reduction in lesion TGA in 11/12 participants.

Participants receiving 1 mg GSK3036656 showed unchanged or increasing LV and lesion TGA. GSK3036656 at 30 mg had the largest impact on dense lesions with high baseline FDG uptake (e.g. consolidations and infiltrates) and lesser impact on cavities.

Conclusions: GSK3036656 at 30 mg led to a potent reduction in LV and FDG uptake in most participants. These PET/CT features will aid in selecting the optimal GSK3036656 dose and appropriate partner agents to complement its lesion specificity.

LBTB-2079-11 Community-based directly observed therapy is effective and results in better treatment outcomes for patients with multi-drug resistant tuberculosis in Uganda

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Background: Health facility-based directly observed therapy (HF-DOT), the main strategy for the management of patients with multi-drug resistant tuberculosis (MDR-TB) in Uganda, has been documented to contribute to poor treatment outcomes. We set out to assess the effectiveness of community-based directly observed therapy (CB-DOT) compared to HF-DOT at five MDR-TB treatment centers in Uganda.

Results: We analyzed data from 264 DR-TB patients (HF-DOT=152, CB-DOT 112). Majority were males 67.8% with a median age of 36 years (IQR 29 to 44 years). Baseline characteristics were similar across the comparison groups, except for educational level. The treatment success rate in the CBDOT group was 12% higher compared to HF-DOT (adjusted prevalence ratio (aPR) 1.12 [95% CI 1.01, 1.24], P-value=0.03). Males were less likely to achieve treatment success (aPR=0.87 [95% CI 0.78, 0.98], P value=0.02). A total of 126 (47.7%) out of 264 patients reported at least one adverse event. HF-DOT group had a higher proportion of patients with at least one adverse event compared to the CB-DOT group (90/152 [59.2%] versus 36/112 [32.1], P-value<0.01), gastrointestinal disorders being the commonest (18.9%). The model was acceptable among patients (93.6%) and health workers (94.1%).

Conclusions: CB-DOT for MDR-TB care is effective and results in better treatment outcomes than HF-DOT. The cost-effectiveness of this model of care will be further evaluated.

TBSCIENCE2022 ORAL ABSTRACTS

TBS-02 TB risk and outcome - co-morbidities and environmental factors - Oral Abstracts

TBS02-05 Systemic influenza infection impairs whole blood mycobacterial control in a human challenge study

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Introduction: Following *Mycobacterium tuberculosis* (Mtb) infection, only a small proportion of people develop tuberculosis (TB) disease, with most immunologically containing or clearing Mtb. Factors influencing TB progression risk are incompletely understood. Co-infections, including influenza, have been proposed as a risk factor for TB progression via disruption of anti-Mtb immune responses. We employed a human influenza challenge study to investigate the effect of systemic influenza infection on host mycobacterial control.

Methods: A whole blood (WB) mycobacterial growth inhibition assay was utilised to compare mycobacterial growth and anti-mycobacterial immune responses before and after influenza infection. Thirty adults were per-nasally inoculated with H3N2 influenza virus (Day [D] 0). Influenza PCR assay of D4 nasal swab confirmed infection. WB, collected pre- (D0, "pre-influenza") and post-inoculation (D6, "post-influenza"), was infected with *Mycobacterium bovis* Bacille Calmette Guerin (BCG)-*lux*, incubated for 72 hours (h) and WB mycobacterial growth (expressed as growth ratio [GR]) measured. In parallel, BCG-*lux*-infected and uninfected blood aliquots were incubated for up to 72 h and measurements of cytokines (MesoScale) and gene expression (RNA-Sequencing) undertaken. Comparisons between pre-vs post-influenza infection blood samples were made.

Results: In 22 influenza PCR-positive (+) subjects, median GR was significantly higher in post- (1.69) vs pre-influenza samples (1.03, $p=0.0016$) with no significant difference in PCR-negative subjects (Figure 1). Significant differences in BCG-*lux*-stimulated cytokine production (including IL-10, TNF- α , IL-1 β) were observed between post- vs pre-influenza samples in PCR+ subjects. Transcriptomic analysis identified significantly

differentially expressed genes in the post- vs pre-influenza samples, including differences between the groups over time and differing responses to BCG-*lux*-stimulation, mapping to pathways related to TB susceptibility.

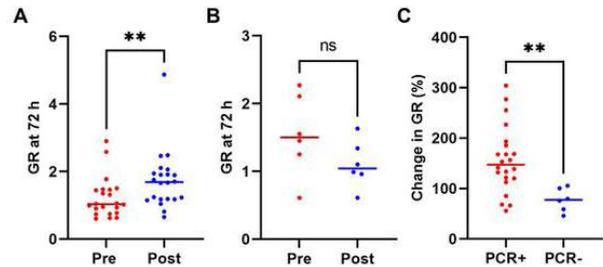


Figure 1. Whole blood BCG-*lux* growth (expressed as growth ratio [GR]) after 72h incubation before (pre-) and after (post-) H3N2 influenza infection. Comparisons of median GRs for (A) 22 influenza PCR-positive participants and (B) 6 PCR-negative participants pre- and post-influenza infection. (C) Change in GR from pre-influenza baseline was calculated for each individual (GR_{Post}/GR_{Pre} expressed as a percentage) and compared between the influenza PCR-positive and PCR-negative participants. Significance: ** $p \leq 0.01$; ns $p > 0.05$

Conclusions: Systemic influenza infection reduces WB containment of mycobacteria through modulation of anti-mycobacterial immune responses, suggesting influenza may be a risk factor for TB disease and influenza vaccine could have a non-specific effect on TB immunity.

TBS02-10 Influence of chronic hyperglycemia on macrophage innate immune responses in pulmonary tuberculosis

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Incidence of type 2 diabetes mellitus (T2DM) is recognized as a high-risk factor that may contribute to tuberculosis dissemination. The present study focuses on the understanding of alterations in innate immune responses in terms of macrophage dysfunction in TB-DM comorbidity. 50 individuals were recruited under four groups: uncontrolled DM patients with or without TB infection (PTB+DM and DM respectively) and non-diabetic individuals with TB infection (PTB) and non-diabetic-uninfected controls.

The majority of PTB+DM patients had 3+ sputum positivity (high bacterial burden) which suggests a plausible association of diabetes with increased disease severity in pulmonary tuberculosis patients. A systematic dysregulation in phagocytic capacity with concurrent alterations in the expression pattern of crucial patho-

gen recognition receptors (PRRs) was observed in the PTB+DM group. These altered PRR expressions were associated with the decreased phagocytic capacity of macrophages. Effector killing molecules namely ROS and NO were also measured. ROS was aberrantly higher while NO was found to be lower in PTB+DM.

These altered macrophage functions were positively correlated with increased disease severity in diabetic individuals. Since the patients had long standing DM condition, AGE-RAGE levels were also analyzed and found to be higher in chronic hyperglycemic condition.

Higher levels of AGEs may indicate the production of numerous irreversible glycated end products, which may impair macrophage function in the diabetic milieu. Increased RAGE in a diabetic environment could indicate overstimulation of the inflammatory cascade, which could result in tissue damage or dissemination of the infection in diabetic patients which was corroborated with higher ROS levels.

Our results highlight several key patterns of immune dysregulation against TB infection under hyperglycemic conditions. A significant reduction in macrophage effector functions in infected diabetic individuals which further correlated with an increase in disease severity reveals a negative impact of hyperglycemia with etiology and pathological progression of TB.

TBS02-15 Breath Volatile Organic Compounds for the Prediction of Childhood TB

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Background: Breath volatile organic compounds (VOCs) have the potential to be non-invasive biomarkers for diagnosing pulmonary tuberculosis (TB) in children. We examined the breath “volatilome” of children to determine the smallest set that could be translated into a diagnostic test for pediatric TB.

Methods: We enrolled children less than 15 years old being evaluated for pulmonary TB in Kampala, Uganda. Children completed a standard TB assessment including collection of respiratory specimens for Xpert MTB/RIF Ultra and mycobacterial culture. TB status was classified per NIH consensus definitions. Breath was collected in tedlar bags (10-20L) and VOCs were adsorbed onto a

Tenax tube for testing with gas chromatography-mass spectrometry. We calculated the abundance of each VOC as a percent area under the peak. We compared the log VOC abundance in children with Confirmed vs. Unlikely TB using pairwise t-testing. We then used logistic regression to develop a prediction model and assessed accuracy using five-fold cross validation.

Results: We included breath from 68 children (30 with Confirmed TB and 38 with Unlikely TB). Median age was 2 years (IQR 1-5) and 7 (10.3%) were living with HIV. We identified 215 unique VOCs, of which Phenyl acetate, p-tert-Butylphenol, Hexa-hydro-farnesol, 12,15-Octadecadiynoic acid methyl ester, Cyclohexanone, and Boronia butenal had significantly different abundance between children with Confirmed and Unlikely TB. When included in a logistic regression model, the six VOCs achieved an AUC of 0.91 (95% CI 0.75-1.0), with 90% sensitivity (95% CI 0.20-1.0) and 60% specificity (95% CI 0.56-1.0).

Conclusions: Breath VOCs differentiated children with and without pulmonary TB, and a breath-based biosignature approached the minimum target accuracy thresholds for a TB triage tool. Breath-based biosignatures should be further evaluated as a promising non-invasive tool for TB screening in children.

TBS02-20 Development of ultra-sensitive immunoassays for the detection of Mtb-proteins in the plasma and urine of adults with and without HIV

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Background: Non-sputum, biomarker-based tests for tuberculosis (TB) are urgently needed. However, there are limited candidate biomarkers that are specific to *M. tuberculosis* (Mtb). We used an ultrasensitive, multiplex, electrochemiluminescence (ECL) immunoassay to detect four Mtb-specific proteins (ESAT-6, CFP-10, Ag85B and MPT64) in the urine and plasma of adults, including people living with HIV (PLHIV).

Methods: We developed antibodies against the four proteins for inclusion in a prototype multiplexed immunoassay panel in the Meso Scale Diagnostics (MSD) S-PLEX® format.

We calculated the limit of detection (LOD) of each assay and measured the proteins in urine and plasma samples obtained from the FIND Specimen Bank from 60 adults

(30 smear-/culture-positive and 30 TB-negative controls; 50% living with HIV in each group) from Cambodia, Vietnam, Peru and South Africa.

Results: The LODs (in pg/mL) for ESAT-6, CFP-10, Ag85B and MPT64 were 0.95, 0.013, 8.3, and 1.7, respectively. In urine, the specificity was high for all proteins (97% for ESAT-6, CFP-10 and Ag85B, 93% for MPT64), and sensitivity ranged from 33% for MPT64 to 63% for Ag85B (Table).

Plasma Samples		ESAT-6	CFP-10	Ag85B	MPT64
Specificity		97% (81%, 100%)	97% (81%, 100%)	97% (81%, 100%)	97% (81%, 100%)
Sensitivity	All	47% (29%, 65%)	47% (29%, 65%)	27% (13%, 46%)	27% (13%, 46%)
	HIV-	27% (9%, 55%)	27% (9%, 55%)	7% (0%, 34%)	20% (5%, 49%)
	HIV+	67% (39%, 87%)	67% (39%, 87%)	47% (22%, 73%)	33% (13%, 61%)
Urine Samples		ESAT-6	CFP-10	Ag85B	MPT64
Specificity		97% (81%, 100%)	97% (81%, 100%)	97% (81%, 100%)	93% (76%, 99%)
Sensitivity	All	60% (41%, 77%)	53% (35%, 71%)	63% (44%, 79%)	33% (18%, 53%)
	HIV-	47% (22%, 73%)	47% (22%, 73%)	40% (17%, 67%)	33% (13%, 61%)
	HIV+	73% (45%, 91%)	60% (33%, 83%)	87% (58%, 98%)	33% (13%, 61%)

Specificity and Sensitivity are provided as point estimates with 95% confidence intervals

Sensitivity is provided for all TB positive samples, and for the HIV-negative and HIV-positive subgroups

Table. Sensitivity and specificity of 4-PLEX Mtb protein immunoassay panel.

In plasma, specificity remained high (97% for all proteins), while sensitivity was lower ranging from 27 to 47%. Higher sensitivity in both urine and plasma was observed for samples from people living with HIV (PLHIV). For PLHIV, Ag85B had the highest urine sensitivity at 87% and ESAT-6 and CFP-10 had the highest plasma sensitivity at 67%. Combining urine Ag85B with either urine ESAT-6 or CFP-10 was able to improve sensitivity to 77%, but at a loss of specificity to 93%.

Conclusions: We developed ultrasensitive immunoassays that could detect Mtb proteins in urine and plasma with high specificity and moderate sensitivity, with higher sensitivity among PLHIV.

Further improvement in the analytical sensitivity and use of protein combinations could increase accuracy and inform new non-sputum TB diagnostic tests.

TBS-05 Tackling TB disease across the spectrum - Oral Abstracts

TBS05-05 Isolation of viable aerosolized Mycobacterium tuberculosis during TB therapy and transient infection

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Rationale: Knowledge of the aerosol release of *Mycobacterium tuberculosis* (Mtb) during disease, treatment, recovery and asymptomatic infection is fundamental to better understanding tuberculosis (TB) transmission.

Objectives: To capture and quantify viable aerosolized-Mtb from TB clinic attendees.

Methods: 102 presumptive tuberculosis patients presented to the South African National TB Control Programme from two informal settlements in Cape Town. Patients were classified by laboratory, radiological, and clinical features into three mutually exclusive groups: A. Sputum GeneXpert-positive TB (n=52), B. Sputum GeneXpert-negative TB (n=20) and C. TB not diagnosed (n=30). A respiratory aerosol sampling chamber was used to sample exhaled Mtb organisms over a 15-minute period at baseline, and at 2-months and 6-months post initial presentation. Viable bacilli were visualised and enumerated based on incorporation of the fluorescent probe, DMN-trehalose.

Measures and main results: Mtb was isolated from 92%, 90% and 93% at baseline; 53%, 47% and 46% at 2 months; and 32%, 25%, 22% at 6-months for groups A, B and C, respectively. Mtb mean number (ranges) reduced from baseline to 6 months from 11 (1-38), 8 (1-31), 12 (1-38) to 2 (1-28), 2 (1-18) and 1 (1-14) for groups A, B and C, respectively. Numerical counts are shown in figure 1. TB symptoms resolved in all 3 groups.

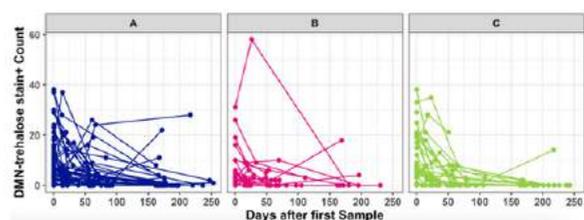


Figure 1. Mtb bacilli counts for the three groups with lines connecting samples from the same patient.

Conclusions: Aerosolized *Mtb* was isolated from the majority of TB patients at baseline and reduced during treatment. Small numbers of viable organisms remained in almost a third of patients despite completing 6-months treatment. Individual clearance of viable aerosolized *Mtb* may be a useful metric for informing TB treatment shortening strategies. Aerosolized *Mtb* in group C may reflect transient TB infection that did not reach a clinical threshold for TB diagnosis, consistent with recent models proposing cyclic subclinical disease states.

TBS05-10 Samples collected and quantified by qPCR show tongue swabs may approach sensitivity of sputum-based TB Dx

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Background: Tuberculosis (TB) diagnosis typically requires a quality sputum specimen, which is difficult to provide for people living with HIV, children, and others lacking productive cough. Alternate specimen types are needed to enhance TB diagnosis, including through community-based active case finding. In particular, tongue swabs may serve as an effective sampling alternative for TB diagnosis, but questions remain about the sensitivity ceiling.

Methods: We developed a triplex qPCR reference assay to quantify the number of *Mycobacterium tuberculosis* (MTB) bacilli present on the tongues of people presenting with TB symptoms to health centers in Kampala, Uganda. All participants underwent tongue swab collection (Copan FLOQswab) prior to sputum collection for Xpert MTB/RIF Ultra (Xpert) testing.

We evaluated multiple *Mycobacterium tuberculosis* lysis methods, ranging from simple to complex, by comparing MTB recovery. We also evaluated the accuracy of tongue swab qPCR in reference to sputum Xpert results.

Results: Of 184 participants enrolled to date, median age was 33 (IQR 25-41.5), 36.6% were female, 21.5% were living with HIV and 27.2% had positive sputum Xpert results. Preliminary data reinforce mechanical lysis as the most optimal procedure, but simple heating methods largely produced concordant diagnostic results, even with recorded 88-90% losses in recovery of MTB cells (Figure 1). Sensitivity of tongue swab qPCR was 93.0% (n=57) and specificity 99.2% (n=128). Sensitivity was 78% (n=9) among participants with low-positive Xpert results.

Conclusions: Our results emphasize the promise of tongue swabs as a viable alternative to sputum for the diagnosis of TB. However, there remain opportunities

to further increase the sensitivity of this approach by enhancing our understanding of preanalytical variables including maximizing sampling and storage efficiency.

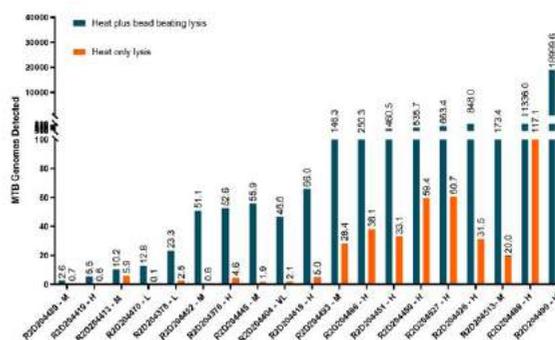


Figure. MTB genomes recovered from clinical tongue swab samples after two different lysis procedures

TBS05-15 Plasma proteomics for the discovery of novel biomarkers for childhood pulmonary tuberculosis

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Background: Biomarker discovery to facilitate the development of non-sputum based diagnostic tests for tuberculosis in children is a global priority. We examined the plasma proteome in children and determined the accuracy of a promising biosignature for predicting TB disease.

Methods: Children <15 years old with presumptive TB were enrolled from the Gambia, Peru, South Africa and Uganda, and completed a standard TB evaluation including respiratory-specimen testing with Xpert MTB/RIF and mycobacterial culture, and were classified per NIH consensus definitions as Confirmed, Unconfirmed or Unlikely TB. On stored plasma, we performed high-throughput data-independent acquisition mass-spectrometry for proteome discovery. Using a LASSO classifier on 80% of the data, we conducted variable importance analysis to identify the top five proteins that could best differentiate children with Confirmed vs. Unlikely TB. We then assessed the accuracy of these five proteins on the remaining test set

Results: We included 483 children, of whom 118 (24%) had Confirmed TB, 130 (27%) had Unconfirmed TB, and 235 (49%) had Unlikely TB. Median age was 4 years (IQR 2-7) and 55 (11.4%) were living with HIV. We found a mean 475 proteins per sample, and the top five

proteins that could distinguish children with Confirmed vs. Unlikely TB were SFTPB, IGHV3-30, IGKV1-16, APOM and KIT. The intensity of SFTPB, IGHV3-30 and IGKV1-16 were increased in children with Confirmed vs. Unlikely TB, while APOM and KIT were decreased. When these five proteins were assessed in the test set, the area under the receiver operating characteristic curve (AUC) was 0.86 (95% CI 0.69-0.91).

Conclusion: Proteomics is a valuable tool for discovering novel TB biomarkers for children, and we identified a five-protein host biosignature that had moderate accuracy to distinguish pediatric TB disease. Further work is needed to optimize the model and understand the role of these proteins in TB pathogenesis.

TBS05-20 Distinct lung and lymph node features on high resolution imaging of asymptomatic household contacts of TB attributed to immune cell-specific signatures in blood

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Transcriptomic analyses of tuberculosis (TB) progression have overlooked the cellular contribution to heterogeneity of immune responses across the spectrum of TB infection and disease states.

We defined a cohort of asymptomatic household contacts of drug-resistant TB cases in South Africa using [18F]-fluoro-2-deoxy-D-glucose (FDG) positron emission and computed tomography (PET/CT) to identify lung and lymph node (LN) abnormalities, and evaluated the sensitivity/specificity of the former for TB diagnosis over four years.

Whole blood samples drawn at each PET/CT visit were subjected to RNA-sequencing. To understand the relationship between modules of co-expressed genes and the underlying quantitative PET/CT lesion measurements and associated clinical and demographic features (e.g. age, sex, blood counts, CRP, ESR, microbiocidal outcomes), a weighted gene co-expression network analysis (WGCNA) was performed. Each module's cellular expression was then inferred using CIBERSORTx cell deconvolution.

Five modules related to interferon (IFN) responses, neutrophils, platelets, natural killer (NK) cells and immunoglobulins tested significant after applying Bonferroni correction ($p < 0.05$). A strong association was observed between expression of the IFN module and LN size and FDG-avidity. The neutrophil module was most positively associated with worsening of lung inflammation and GeneXpert positivity at PET/CT visit. The platelet and immunoglobulin modules had highest correlation with number of days from TB diagnosis, and worsening lung inflammation and CRP to different degrees.

Conversely, the NK module was negatively associated with inflammation characteristics and positively associated with lung lesion calcification.

These data indicate that IFN signalling is associated with LN inflammation, whilst neutrophil, platelet and immunoglobulin transcriptional signatures are better predictors of asymptomatic active inflammatory processes associated with TB progression.

Attribution of transcriptional programmes to immune cells and variables related to metabolic activity at the site of asymptomatic lung disease advances our understanding of the immune processes during early human disease which results in different infection outcomes.

TBS-08 TB data in a globalized world – Oral Abstracts

TBS08-05 Subclinical tuberculosis: assessment of burden and presentation using prevalence survey data from eight countries

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There is increasing recognition that sub-clinical pulmonary tuberculosis (scTB) is a potential barrier to control and elimination.

Additionally, the meaning of the term 'scTB' is ambiguous. Thus, there is a critical need for a robust assessment of the burden and clinical presentation of scTB and its risk factors, which are the primary aims of the current research.

We analyzed an aggregated database of multiple tuberculosis prevalence surveys (8 at the time of submission, 5 from Africa and 3 from Asia) containing records of 355,128 participants screened, 39,117 tested, and 1,553 culture positive on at least one sputum sample. Sub-clinical TB was defined as culture-positive pulmonary TB in the absence of persistent cough of two or more weeks.

Preliminary results show that up to 76% of all culture positive prevalent TB was sub-clinical, i.e., up to three quarters of all culture-positive prevalent tuberculosis was invisible to any case detection using the common screening rule of cough for 2 or more weeks. Up to 53% of culture-positive prevalent TB was not accompanied by cough of any duration.

Participants without cough frequently reported other TB related symptoms, particularly weight loss, supporting development of improved symptom-based screening rules.

From adjusted logistic regression, the odds of tuberculosis being subclinical in males was 20% lower than in females (95% CI: 14-26).

Infections amongst those in younger age groups were significantly more likely to be subclinical. Infections among those aged 65+ exhibited 46.5% lower odds (95% CI: 33-60) of being subclinical than those amongst ages 15-24.

TBS08-10 Deep learning allows for quantitative prediction of antibiotic resistance in *Mycobacterium tuberculosis*

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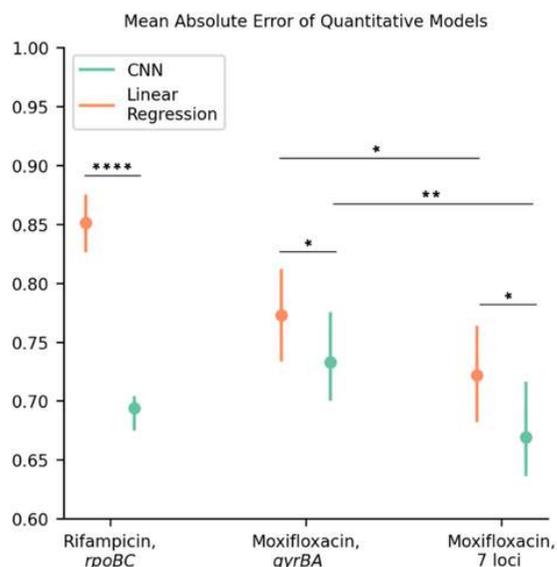
Background: To accelerate treatment of drug-resistant tuberculosis, rapid, accurate, and comprehensive diagnostic methods are needed. *In silico* resistance prediction models coupled with whole genome sequencing have significantly improved diagnostic sensitivity for binary resistance over commercial targeted assays.

However, these methods fail to consider novel mutations and interactions between genes. We constructed convolutional neural networks (CNNs) for quantitative resistance prediction, taking advantage of their abilities to learn complex functions of inputs and generalize to novel sequences.

Methods: We trained CNNs to predict minimum inhibitory concentrations (MICs) for the drugs rifampicin and moxifloxacin from sequence alignments of the *rpoBC* and *gyrBA* loci, respectively. Models were trained and tested on 9,682 *M. tuberculosis* (Mtb) isolates for rifampicin and 7,544 isolates for moxifloxacin. For model interpretability, we used the DeepLIFT algorithm to compute saliency scores for each input and determine their relative contributions to MIC predictions.

Results: Quantitative CNNs outperformed regularized linear regression with lower mean absolute error (MAE) for rifampicin (P=8e-7) and moxifloxacin (P=0.04).

Using DeepLIFT, we verified that CNNs learn from relevant sites in the Mtb genome, finding 88% of sites in *rpoBC* and 100% of sites in *gyrBA* associated with resistance according to the World Health Organization mutation catalogue. CNNs identified novel sites with high predictive value, many of which are found in fewer than 0.1% of isolates. Because the genetic determinants of fluoroquinolone MIC are not fully known, six additional loci were selected based on activity during DNA replication or homology with proteins that confer resistance in *E. coli*. MAEs were significantly lower for the 7-loci CNN than the *gyrBA*-only CNN (P=0.0083) and 7-loci regression (P=0.016).



Conclusion: Quantitative CNNs can predict MIC within one log-MIC on datasets that span 7-8 logs for rifampicin and moxifloxacin. They also identify novel genetic sites that are predictive of resistance and warrant further investigation.

TBS08-15 A multi-country assessment of digital lung sound analysis to predict pulmonary tuberculosis

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Background: Advances in automated lung sound analysis have improved detection of lower airway abnormalities. We evaluated the potential of artificial intelligence (AI)-based lung sound analysis as a triage tool for pulmonary tuberculosis (TB).

Methods: We screened adults presenting to health centers in India, the Philippines, Vietnam, South Africa and Uganda, and enrolled those with cough ≥ 2 weeks. Participants underwent sputum-based TB testing, and a digital stethoscope (Stetee Pro, M3DICINE, Australia) was used to record lung sounds from 20 anterior and posterior chest sites (each 20 seconds long). Features were extracted from 5-second segments of each 20-second recording and analyzed using a deep learning model to predict TB (defined using a microbiological reference standard [MRS]) in the training set (random 75% of participants). A recording was classified as TB-positive if a majority of segments had $>50\%$ probability of TB. The model was then applied to the remaining test set. Sensitivity and specificity were calculated in reference to the MRS at different thresholds (*i.e.*, percent of TB-positive lung recordings).

Results: We included 392 participants (median age of 42 years [IQR 27.5-55], 45% female, 15% living with HIV, 12% living with diabetes, and 117 [30%] with microbiologically-confirmed TB). At a 10% threshold (≥ 2 TB-positive recordings), AI-based lung sound analysis achieved 86.2% sensitivity (95% CI 85-88) and 55.5% specificity (95% CI 53-57). As the threshold increased to 50% (≥ 10 TB-positive recordings), sensitivity decreased to 72.4% (95% CI 70-76) while specificity increased to 77.8% (95% CI 75-79) (Table).

Percentage of TB-positive Recordings % (n/N)	Sensitivity % (95% CI)	Specificity % (95% CI)
5% (1/20)	80.8% (73-86)	53.3% (47-58)
10% (2/20)	86.2% (85-88)	55.5% (53-57)
20% (4/20)	75.9% (72-81)	69.8% (68-71)
30% (6/20)	75.9% (71-81)	69.8% (69-71)
40% (8/20)	75.9% (71-81)	69.8% (69-71)
50% (10/20)	72.4% (70-76)	77.8% (75-79)

Table. Diagnostic accuracy of automated lung sound analysis to predict pulmonary TB.

Conclusions: In preliminary assessment, AI-based lung sound analysis approached the minimum accuracy thresholds recommended for a TB triage test. Accuracy can be expected to further improve with a larger dataset for training and optimization of the analytic approach.

TBS08-20 Continuous cough monitoring with an AI-enabled mobile phone app for TB evaluation and treatment response

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Introduction: Although cough assessment is important for tuberculosis (TB) evaluation and monitoring, cough is typically assessed subjectively at single timepoints. Artificial-intelligence (AI) algorithms can automatically detect cough sounds and enable objective monitoring via mobile phones. We evaluated if changes in continuous cough patterns can distinguish patients with TB versus other respiratory conditions and reflect TB treatment response.

Methods: We prospectively enrolled people with presumptive TB at outpatient clinics in five countries (India, Philippines, South Africa, Uganda, and Vietnam) and classified TB status based on positive sputum Xpert Ultra or culture results (Confirmed TB) or empiric TB treatment initiation (Clinical TB). Participants continuously carried a smartphone for 14 days with the Hyfe cough recording application. Cough frequency was calculated as the median number of coughs per hour (mCPH), and the mCPH was compared between participants with Confirmed or Clinical TB and those with other respiratory diseases (ORD) using Wilcoxon testing.

Results: We included 519 participants (median age 39, 53.6% female, 12.7% living with HIV) who completed reference standard testing and cough recording. The mCPH for all participants on the first recording day was 5 (interquartile range [IQR] 3-9) and decreased to 3 mCPH (IQR 2-6) by day 14 (Figure 1).

On day 1, mCPH was higher in participants with Confirmed TB (8, IQR 3.5-20) vs. ORD (4, IQR 3-7.63) ($p < 0.001$), but similar between participants with Clini-

cal TB (4.75, IQR 2-9) vs. ORD ($p=0.89$). All three patient groups had significantly reduced cough frequency by day 14 ($p<0.01$; Figure 1) but the reductions were steepest among participants with Confirmed or Clinical TB initiated on treatment.

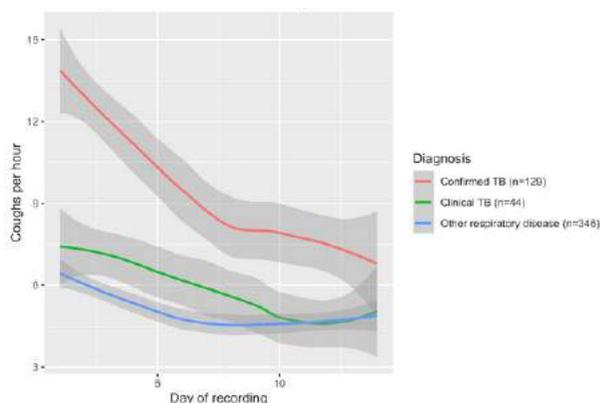


Figure 1. Locally weighted regression (LOESS) smoothing of median coughs per hour over days of longitudinal recording by diagnosis. Shaded regions indicate 95% confidence regions of LOESS models.

Conclusion: An AI-enabled smartphone was able to characterize distinct cough patterns and show treatment response in participants with Confirmed and Clinical TB. Objective cough monitoring should be further evaluated for TB evaluation and treatment response monitoring.

TBS-11 TB and respiratory microbiota – Oral Abstracts

TBS11-05 Sputum and gut microbiota perturbations persist one year after tuberculosis treatment

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Background: The microbiota has a critical role in health and is modified by antibiotics. However, little is known about the effect of tuberculosis treatment on the microbiota.

Methods: We collected induced sputa and stool from *Mycobacterium tuberculosis* culture-positive cases ($n=75$) from Cape Town, South Africa and profiled the microbiota before (month 0), during (months 2 and 6) and after treatment (months 12 and 18).

Culture-negative close contacts ($n=126$) of cases provided sputum and stool at months 0, 6, and 18. 16S rRNA gene sequences were analysed using QIIME2, *vegan*, *DESeq2*, and Dirichlet-Multinomial Mixture (DMM) modelling. Longitudinal clustering of patient timeseries was done using *LoClust*.

Results: The first two months of treatment reduced alpha diversity ($p<0.001$; Fig. A) and altered beta diversity (Bray-Curtis PERMANOVA, $p=0.001$; Fig. B) in sputum and stool, and these effects lasted until treatment end. In sputum, *Moraxella* was depleted, and *Campylobacter* enriched at months 2 and 6 (vs. month 0). In stool, *Akkermansia* was depleted and *Megasphaera* enriched at month 2, whereas *Actinobacillus* was depleted and *Collinsella* enriched at month 6 (vs. month 0). Sputum alpha diversity returned to baseline levels by month 12 ($p=0.149$). However, stool alpha diversity remained low at months 12 ($p=0.002$) and 18 ($p=0.014$). Sputum and stool beta diversity remained perturbed at one-year post-treatment. The extent of treatment-related microbiome perturbations was greater in stool than in sputum. DMM modelling identified *Atopobium* vs. *Neisseria*-enriched patient clusters in sputum and *Prevotella* vs. *Bacteroides*-enriched clusters in stool. Sputum and stool alpha diversity were stable throughout sampling in close contacts, though sputum beta diversity changes were noted at month 18 (vs. month 0).

Conclusions: Treatment induces microbial alterations in the airways and gut that persist at least one year later. Further investigations into linkages between perturbed microbial communities and important clinical outcomes like post-TB sequelae are needed.

TBS11-15 Volatile organic compounds in the headspace of sputum samples as biomarkers for culture-independent identification of Nontuberculous mycobacteria

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Nontuberculous mycobacteria (NTM) are a common pathogen in patients with cystic fibrosis (pwCF) with a 10% annual prevalence based on reports from the American Cystic Fibrosis (CF) Foundation (2020). The volatile organic compounds (VOCs) from sputum and exhaled breath are recognized as innovative and non-invasive biomarkers of specific respiratory pathogens. The hypothesis was tested that VOCs present in the headspace of sputum samples can distinguish between CF patients infected with *M. abscessus* (MAB) and *M. avium complex* (MAC).

Sputum samples were collected from CF patients enrolled in long-term clinical trials at multiple sites in the US. VOCs were collected from samples by headspace solid phase microextraction (HS-SPME). The SPME fibers were thermally desorbed to GCxGCtoFMS instrument for analysis. The data obtained were subjected to statistical analysis tools, including PCA, tSNE, PLS-DA, and Boruta feature selection. SPME extraction and chromatographic analysis were performed on 46 sputum samples from 29 CF patients infected with MAC and 17 patients with MAB.

the day of sputum collection (nMAC=15, nMAB=10). Two more models were built using samples linked to positive culture results within ± 30 days of sample collection (nMAC=19, nMAB=14) and ± 90 days of sample collection (nMAC=29, nMAB=17). All models showed meaningful separation between MAC and MAB samples and a list of overlapping molecules identified. Five sputum samples with negative culture but positive PCR results for MAB were used for validation of biomarkers. The models showed promising results for the prediction of PCR-positive samples as the MAB group (Figure 1). Results of this work pave the way for the development of a culture-independent diagnosis tool for differentiation between CF patients infected with MAC and MAB.

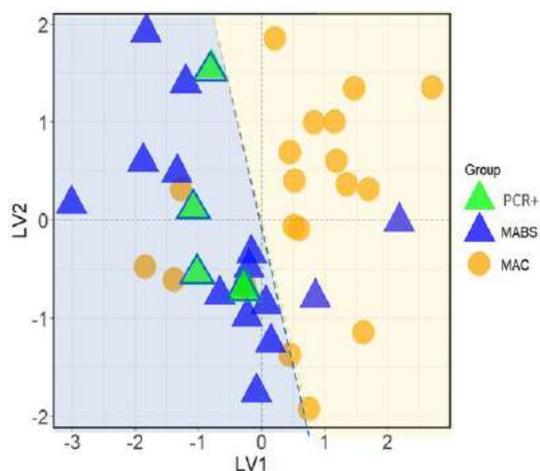


Figure 1. Projection of 33 sputum samples to the first two latent variables (LV) of the PLS-DA model built using the 7 features selected using the Boruta algorithm. The model could reasonably predict the PCR positive samples (for MABS) in the MABS group.

The potential power of the volatile features in distinguishing MAC and MABS was first tested by a model built using a set of samples linked to positive culture on

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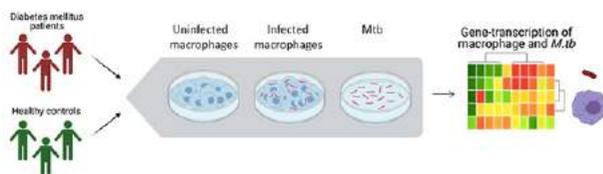
TBS-EP-01 Dual RNA-sequencing: unravelling host-pathogen interaction in the context of diabetes and tuberculosis

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Since diabetes and tuberculosis are co-emerging endemics, the control of tuberculosis is threatened by diabetes as a well-known risk factor. In diabetes functioning of immune cells, such as macrophages, is impaired creating a preferred niche for *Mycobacterium tuberculosis* (*M. tb*). Research indicates an altered crosstalk between host cells and *M.tb* in diabetes, but up until now, the exact biological mechanisms underlying this increased susceptibility to tuberculosis are unclear.

That's why in this project, the communication between *M. tb* and its main host cell, the macrophage, is studied in the setting of diabetes. Previous research only focused on one side of the story; either the response of the host or the pathogen. To get a grasp on the host-pathogen interaction, comprehensive knowledge of gene expression changes in both species is required.

By performing dual RNA-sequencing, gene transcriptional changes of macrophage and *M. tb* are identified simultaneously after infection. Macrophages derive from a cohort of people with diabetes and are infected with live *M.tb* ex-vivo, followed by RNA-sequencing. This approach is a unique way of getting deeper insights into what exactly the macrophages and mycobacteria are telling each other during infection in the context of diabetes.



TBS-EP-02 Metabolomic pathways of TB disease in children with and without HIV

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Background: Diagnostics for tuberculosis (TB) disease have poor sensitivity in children, particularly for those living with human immunodeficiency virus (HIV). We used high-resolution metabolomics (HRM) to investigate pathways and biomarkers that distinguish TB disease in children living with and without HIV.

Methods: We performed HRM on plasma samples from children being evaluated for pulmonary TB in South Africa. Children were classified per NIH consensus definitions (confirmed, unconfirmed, unlikely TB).

We used the mummichog pathway analysis program to determine differences in metabolic pathway activity in plasma and assessed the interaction between TB disease and HIV using a two-way ANOVA (Analysis of Variance).

Results: Of 52 participants included, 32 (62%) were male, the median age was 30 months (IQR 17, 47), 20 children (38%) were living with HIV, and 18 (35%) were underweight (weight-for-age Z-score less than -2). Thirty-one (60%) had TB disease; 21 (68%) with confirmed and 10 (32%) with unconfirmed disease.

Children with TB/HIV co-infection demonstrated marked metabolic dysregulation in prostaglandin formation from arachidonate ($p=0.002$), arachidonic acid metabolism ($p=0.01$), arginine and proline metabolism ($p=0.01$), and urea cycle metabolism ($p=0.03$).

Amongst children with TB disease, those with TB/HIV co-infection had significantly decreased plasma concentrations of metabolites matching prostaglandin E2 ($p<0.001$) and thromboxane A2 ($p=0.001$).

Arginine was significantly elevated in HIV-negative children with TB disease ($p=0.05$) but not in children living with HIV.

Conclusion: Significant dysregulation in prostaglandin, arachidonic acid, and arginine and proline metabolism occurred in young children with TB/HIV compared to HIV-uninfected children with TB disease. Further studies are needed to determine whether this metabolic dysregulation may contribute to the adverse outcomes associated with HIV co-infection and whether metabolites in these pathways can serve as biomarkers of TB disease.

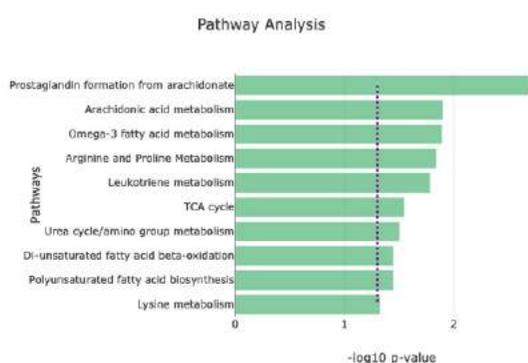


Figure 1: Metabolic pathways significantly regulated in TB/HIV co-infection

TBS-EP-03 Decentralized diagnosis and treatment of drug-resistant tuberculosis in Machakos County, Kenya

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Background: Access to drug susceptibility testing (DST) for drug-resistant tuberculosis (DR-TB) diagnosis is challenging. Between 2016-2019, in Machakos county, Kenya, Xpert MTB/RIF was available in 5 sites. Additional DST was done in the national lab. DR-TB treatment was available in 32 clinics.

Methods: Retrospective cohort study of DR-TB diagnosis, treatment outcomes, and their predictors in Machakos county, between 2016-2019. Rifampicin-resistant TB (RR-TB) was treated with a short treatment regimen (STR). A long regimen was used for patients not eligible for the STR.

Results: Of 85 DR-TB patients, 84 (99%) and 72 (73%) had Xpert MTB/RIF and phenotypic rifampicin DST results, respectively. Of 85, 36 (42%) had rifampicin-susceptible drug-resistant TB (RS/DR-TB); resistance to other first-line drugs than rifampicin) and 49 (58%) had RR-TB. Xpert MTB/RIF and phenotypic DST showed discordant results for rifampicin in 8 patients (7 with RR missed on Xpert MTB/RIF). Of 49 with RR-TB, 45 had second-line DST results.

One patient had TB resistant to fluoroquinolone and second-line injectables. Of 36 RS/DR-TB patients, 33 (92%) were treated successfully. Six RR-TB patients died before starting treatment.

One RR-TB patient was transferred out.

Among the remaining 42 RR-TB patients, treatment success was 50% (11/22) for the STR and 80% (16/20) for the long regimen ($p=0.04$), with more PLHIV among patients on the STR (70% (14/22) vs 30% (6/20), $p=0.03$). HIV co-infection (aOR 8.5, 95% CI:1.2-59.2) but not STR use (aOR 1.5, 95% CI:0.3-8.1) predicted having a clinically unfavorable outcome (mortality or

treatment failure). Seven patients (all RR-TB and HIV-positive) had severe or life-threatening adverse events, of whom 4 died.

Conclusion: RR-TB treatment success was lower than the 75% World Health Organization target. HIV co-infection and adverse events contributed to unsuccessful treatment outcomes. Decentralization of rapid DST, adverse event monitoring and management, and less toxic RR-TB regimens will be key towards improving outcomes.

TBS-EP-04 Drug-resistant tuberculosis before and in the COVID-19 period, Tajikistan

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Introduction: Tajikistan is among the top 30 high MDR TB countries where the estimated incidence of RR/MDR TB is 26 per 100 000 population. The national plans reflect the country's commitment to achieving the WHO Strategy to End TB by 2030, strengthening basic research with increased scientific capacity.

During the first period of the COVID-19 pandemic (14-46 weeks of 2020) there was a 37% decrease in TB registration compared to the same period in 2019.

Objectives: To identify changes in the structure and outcomes of DR-TB treatment associated with the COVID-19 pandemic through TB prevention implementation research (IR). IR was introduced in 2021 by strengthening the TB and DR TB surveillance system. IR received support from TDR, the Special Programme for Research and Training.

Methods: This was a cross-sectional study using both routine program and survey data of TB cases in Dushanbe for the 2017-2021 years.

Results: There were 356 DR-TB patients included in the study, among whom 48% were females, 277 (78%) had pulmonary TB, 79 (22%) - had extra-pulmonary TB, 265 (74%) were new and 91 (26%) previously treated cases. The mean age of the patients was 36 years (SD ± 16.88).

The TB notification rate increased to 2,7% in 2021 (49.1 per 100 thousand population) compared to 2020, and the DR TB notification rate increased to 11%.

The rate of MDR TB among DR TB patients increased from 2020 to 2021 (65.8% in 2019 and 80.5% in 2021). The successful outcomes in the cohort 2020 were higher than those in 2018 – 2019 (87% vs 84%).

Conclusion: This first research of DR-TB patients registered in Dushanbe, involving pre-COVID-19 and COVID-19 periods showed improvement in diagnostics and treatment of DR TB patients. Further research is needed to explore the financial burden.

Keywords: DR TB, implementation research, Tajikistan, TDR.

TBS-EP-05 Frequent Undiagnosed Cough, Alcohol, Substance Use and COVID-19 in Uganda: Who Promotes Cough and TB Literacy Among Adolescents and Young Persons?

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Background: Households and communities in Africa play a leading role for dwellers to engage in age-appropriate activities whose outcomes foster or subvert growth and development. Households and communities foster social cohesion, provide opportunities for growth and development in form of social capital. Social capital enhances decision-making, career-oriented efforts, ambition for higher qualifications, and reduces risks and vulnerabilities.

The objective of the study was to show the importance of households and communities in fostering decisions for engaging in quality life promoting practices for population groups 11-35 years old.

Methods: The findings are based on the household assessment conducted between July 2021 to May 2022. It involved 370 volunteers and 99 data collectors who visited 10,673 households and surveyed 18,033 respondents in 535 villages in 29 nationally represented districts.

Results: 80.7 percent of respondents knew a peer with a frequent cough, used alcohol and substances, used herbal medicines, and never visited a qualified health worker for chest screening or examination.

All respondents pointed out that the COVID-19 Pandemic affected decision support mechanisms enhancing motivation to seek care from qualified health workers in the form of lack of funds to pay for transport, medical care and attendant expenses. The use of alcohol and substances was an alternative many resorted to.

Conclusions: These findings suggest prevalence of undiagnosed cough, low screening rates, use of substances and other practices which may lead to chronic coughs and undiagnosed TB among 11–35-year-old in Uganda. Further research into initiatives to reach this population group can inform Cough Tracing techniques, early TB testing, care and COVID-19 Recovery and Response plans.

TBS-EP-06 Isoniazid mono-resistance tuberculosis: A mixed method study evaluating risk factors for poor outcome in South Indian population

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Over the past decade, given the alarming increase in isoniazid mono-resistance tuberculosis (Hr-Tb), an all-oral (levofloxacin) 6-month regimen was introduced in India in 2018. Following up on the India Tuberculosis report, one can appreciate the falling trend in cure rate (India Tb report, 2019:76% -India Tb report 2022: 55%).

A retrospective cohort study done in South India, in 2014, by Deepa D et al. showed that Hr-Tb, per se, was independently associated with poor treatment outcomes (Cure rate with the old regimen: 56%). Hence, to identify the key risk factors, we conducted a mixed method study from August 2018 to June 2022.

This study includes a review of the medical records and NIKSHAY database of 175 patients suffering from Hr-Tb and in-depth interviews of health care professionals and Hr-Tb patients from the Union Territory of Pondicherry, South India. The data on demographic and clinical characteristics, number of missed doses, delay in treatment initiation, resistance gene and early and late outcome status were extracted.

The descriptive data deduced that 74.3% of patients on this regimen had favourable outcomes (Favourable-Cured, treatment complete (WHO)). The various demographic characteristics were assessed for the association with risk for poor outcomes. Male gender, poor BMI (Body mass index), and poor sociodemographic characteristics and comorbidities showed a predilection for poor outcomes. Of the two genes implicated in resistance Kat G (MUT1) (65.7%) was associated with unfavourable outcomes.

Factors related to the regimen, viz. number of tablets, duration of treatment, and delay in initiation, were also collected. With this background information, interviews were conducted, substantiating the quantitative findings (Significant finding Table 1).

Hr-Tb is found to have a higher propensity to convert to MDR Tb. Thus, this mixed method on risk factors for regimen failure is crucial and grasps the field data as well.

Code with the highest density	Quantitative data	
	Mean (SD)	Range (Min, Max)
Increased number of tablets	8.14 (1.188)	7(4,11)

Table 1: Comparison of significant qualitative findings with quantitative data.

TBS-EP-07 Effect of smoking and malnutrition on early sputum culture conversion in multidrug-resistant tuberculosis patients with short-term drug regimen in South Sumatra, Indonesia

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Background and aims: Multidrug-resistance tuberculosis (MDR-TB) is an infection of *Mycobacterium tuberculosis* with resistance to at least two main first line medications, isoniazid and rifampicin. In Indonesia, the proportion of MDR TB patients who had successful treatment was only 47%. Several factors influence the treatment outcome. Early sputum culture conversion (at second month) associated with higher chance treatment success in compare to late sputum culture conversion and lead to poor outcomes.

This study aims to asses the effect of smoking history and malnutrition on early sputum culture conversion among MDR TB patients on a short term drug regimen in South Sumatra Indonesia.

Methods: This study design was observational study and was done at Mohammad Hoesin Hospital from April 2019 to January 2020. Participant who fulfill inclusion criteria was included. Smoking history, malnutrition status, and sputum culture conversion was collected and analyzed with statistic application tool.

Results: Total of 91 participants were included in this study. Analysis result shows MDR TB patients with smoking history had 1.1 risk ratio (RR), and 95% confidence interval 0.95 - 1.32. Malnourished MDR TB patient had 0.89 risk ratio (RR), and 95% confidence interval 0.62 - 1.28.

Conclusion: Malnourished MDR TB patients had a 0.89 time risk of not having early sputum culture conversion, compared to non-malnourished MDR TB patients. MDR TB patients with a history of smoking had a 1.1 times risk of not having early sputum culture conversion, compared to non-smoking MDR TB patient.

TBS-EP-08 Mycobacterium tuberculosis risk factors, drug resistance, strains of MTBC circulating and measures to accelerate TB elimination in NE region of India

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Tuberculosis (TB) is one of the major public health concerns in the North Eastern Region of India. Our studies reveal that important risk factors of pulmonary tuberculosis are illiteracy, alcohol consumption, history of TB patient within the family, irregular income and a lower BMI.

Our studies have also revealed remoteness, difficult terrains of many localities, and poor connectivity of roads to health centres leading to inadequate access to health services. Compounding the problem is the lack of awareness in remote communities about the early detection of TB. These factors pose an important threat to tuberculosis elimination programs.

Other challenges in the NE region for accelerated elimination of TB especially in remote communities having rugged terrains are increased risk of exposure to TB due to delay in TB case detection and proper treatment, more effective contact tracing at home and workplace resulting in high risk of spreading TB. Besides poverty and malnourishment increase the risk of developing active TB.

Thus, the development of a robust mechanism for early case detection and treatment of cases in remote and difficult areas is very important. Building a social support system in these remote communities towards TB, supply of antitubercular drugs at the doorsteps, and facilitating preventive and therapeutic nutrition will help to eliminate pulmonary TB in the NE region of India.

Moreover, the use of drones for sputum collection and sample transportation and providing drugs at the doorsteps in difficult-to-reach communities. Identification and training of local volunteers are critical so that TB cases can be identified and treated at the earliest.

Creation of awareness among community members so that the chances of spreading MTBC in the community can be reduced significantly.

TBS-EP-09 Molecular insights on the persistence of mycobacteria

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To control *M. tuberculosis* infection prolonged chemotherapy is recommended. A small population of cells escapes from the lethal effects of the drugs either by acquiring drug resistance or by switching to a quiescent state with low metabolic activity.

The latter population is antibiotic tolerant and remains dormant in the host. These are termed persisters and are responsible for the reactivation of the disease under conditions conducive to their growth.

New approaches are required to understand and kill the persisters for effective eradication of the bacilli from the host. *M. tuberculosis* has evolved to endure intracellular as well as extracellular hostile environments such as antibiotics, oxidative stress, pH stress, nutrient starvation, etc.

The underlying mechanisms of bacterial persistence are poorly understood and the key determinants are also not well defined. Therefore, we have undertaken this study to elucidate the molecular basis of persistence. Using transposon mutagenesis as a tool, we have identified mutants defective in parameters likely to be involved

in the epigenetic regulation of persistence. We present data using different antibiotic screens for the isolation of mutants of *M. smegmatis* as a model, in this study. In conclusion, we hypothesize that our approach will provide novel insights into the mechanisms of persister formation and survival of mycobacteria, revealing a new target for the development of persister-directed antibiotics.

TBS-EP-10 Novel Therapeutic DNA Vaccine targeting Mycobacterium Tuberculosis persisters enhances isoniazid activity

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Background: Lengthy tuberculosis (TB) treatment is required to overcome the ability of a subpopulation of persistent *Mycobacterium tuberculosis* (*Mtb*) to remain in a non-replicating, antibiotic-tolerant state characterized by metabolic remodeling, including induction of the *rel_{Mtb}* mediated stringent response. We previously showed that intramuscular delivery of a DNA vaccine expressing *rel_{Mtb}* enhanced the mycobactericidal activity of isoniazid.

Objective: We developed a novel therapeutic DNA vaccine containing a fusion of the *rel_{Mtb}* gene with the gene encoding the immature dendritic cell-targeting chemokine, *MIP-3 α /CCL20*. We sought to determine if this fusion strategy along with intranasal administration improves the synergistic therapeutic activity of the *rel_{Mtb}* DNA vaccine.

Design: We compared the adjunctive therapeutic activity of each DNA vaccine in a murine model of chronic TB. T-cell responses between the *rel_{Mtb}* vs. *MIP-3 α /rel_{Mtb}* DNA vaccination groups, as well as different administration routes, were evaluated in murine spleens and lungs.

Results: We found that intramuscular delivery of the *MIP-3 α /rel_{Mtb}* vaccine or intranasal delivery of the *rel_{Mtb}* vaccine potentiates isoniazid activity more than intramuscular delivery of the DNA vaccine expressing *rel_{Mtb}* ($P=0.0002$ and $P=0.0052$), inducing pronounced *Mtb*-protective immune signatures. The combined optimized approach involving intranasal delivery of the DNA *MIP-3 α /rel_{Mtb}* fusion vaccine demonstrated the greatest mycobactericidal activity when compared to each novel vaccination approach ($0.5 \log_{10}$, $P=0.0058$, and $0.61 \log_{10}$, $P<0.0001$) or isoniazid alone ($1.81 \log_{10}$, $P<0.0001$), as well as robust systemic and local Th1/Th17 responses.

Conclusions: We show that *MIP-3 α* fusion and intranasal delivery individually enhance the adjunctive therapeutic activity of a DNA vaccine targeting *Mtb* persisters in a chronic TB model. The combined, optimized approach, i.e., intranasal immunization with a DNA fusion vaccine expressing *MIP-3 α /rel_{Mtb}* is accompanied by additive Th1/Th17 responses, both systemically and at the infection site. This novel optimized vaccination strategy may be a promising adjunctive therapeutic approach combined with standard anti-TB therapy.

TBS-EP-11 Micro-variants associate with phenotypic resistance of Mycobacterium tuberculosis isolates

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Background: Whole-genome sequencing (WGS) of *Mtb* can detect genetic variants at low allele purity, also known as micro-variants. Micro-variation may arise when infecting subpopulations of *Mtb* acquire variants in-host or may be due to primary infection or reinfection with multiple *Mtb* strains.

Current research suggests that higher in-host diversity correlates positively with severity of disease, rate of TB recurrence, and likelihood of fixation of antibiotic resistance (AR).

Methods: We quantify the frequency of micro-variation with allele frequency (AF) 25-75% in 10,055 *Mtb* Illumina whole-genomes and associate micro-variation with AR.

After quality control of the WGS data using published criteria, we identified micro-variants using Pilon for read mapping to the H37Rv *Mtb* reference and a micro-variant detection pipeline that had a 99.6% agreement with the binoSNP variant caller. Homologous regions were excluded from analysis.

We characterize the link between micro-variation and AR using logistic regression on binary phenotypic drug susceptibility testing (pDST, $n=6,850$) and log-linear regression on minimum inhibitory concentrations (MICs, $n=1,241$). The regression approach allowed us to isolate the effect of micro-variation on phenotype controlling for other AR mutations in the same genome.

Results: The majority of variants in an isolate are micro-variants (median=61%); and 62% of AR positions had a micro-variant identified in at least one isolate. Specifically, *pncA* demonstrated the highest proportion of micro-variants of the AR genes (Figure 1A) while *embC* had the lowest (Figure 1B).

Micro-variants are more common in multi-drug resistant isolates than drug susceptible isolates ($p<0.001$), and there is a strong association between the allele frequency of AR micro-variants and increases in MIC for 5 of the 205 micro-variants tested. Results of the regression are forthcoming.

Discussion: The high frequency of micro-variation and the strong association between micro-variants and phenotypic resistance suggest the need to include micro-variants in models for AR diagnosis and prediction.

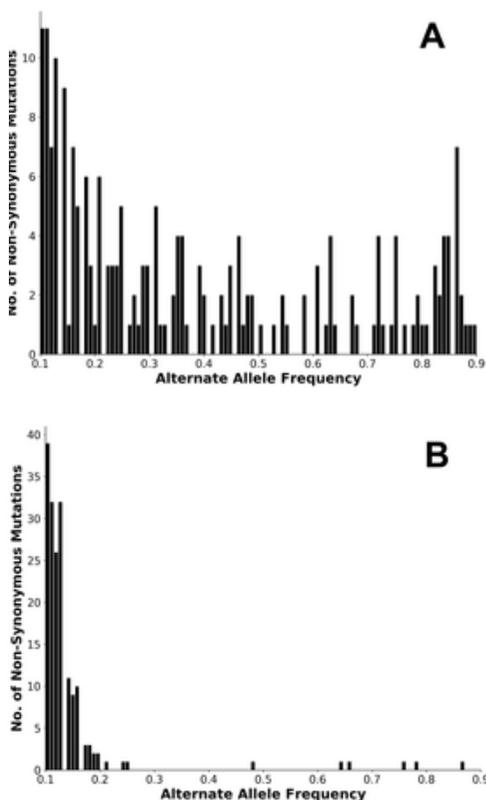


Figure 1. Micro-variation prevalence differs across DR genes. Alternate allele frequency distribution for non-synonymous micro-variants in *pncA* (A) and *embC* (B).

TBS-EP-12 Prospective Multicentre Accuracy Evaluation of the FUJIFILM SILVAMP TB LAM Test for the Diagnosis of Tuberculosis in People Living with HIV Demonstrates Lot-to-Lot Variability

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Background/ methods: The diagnostic accuracy of the point-of-care urine-based lipoarabinomannan assay, FUJIFILM SILVAMP TB LAM (FujiLAM), was evaluated in a prospective trial in seven high tuberculosis (TB) burden countries among inpatient and outpatient adult people living with HIV (PLHIV). Diagnostic performance was assessed against a reference standard (eMRS) comprising sputum culture, blood culture, and Xpert Ultra from urine and sputum at enrollment, and additional sputum culture ≤ 7 days later.

Findings: Of 1624 participants enrolled, 294 (18.0%) were classified as TB positive by eMRS. Median age was 40 years, median CD4 cell count was 372 cells/ul, 52% were female and 78% were taking antiretroviral therapy at enrollment.

Overall FujiLAM sensitivity was 54.8% (95% CI: 49.1–60.4), and overall specificity was 85.1% (83.1–86.9). Sensitivity and specificity estimates varied between sites, ranging from 26.5% (95% CI: 17.4%–38.0%) to 83.3% (43.6%–97.0%), and 75.0 (65.0%–82.9%) to 96.5 (92.1%–98.5%), respectively. Post-hoc regression analysis identified variability in the performance of the six different FujiLAM lots as the main driver of variation between sites (Figure 1).

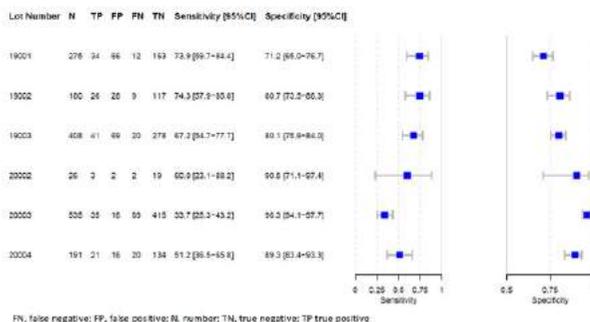


Figure 1.

The lot variability was confirmed when re-analysing 111 false positive samples from the study with all six FujiLAM lots.

Conclusion: Lot variability limited interpretation of FujiLAM test performance and the lot variability issue is a setback in the quest towards a POC non-sputum-based TB test. Although the results obtained using the current version of the FujiLAM test are too variable for clinical decision-making, a new version of the test could improve POC testing for TB diagnosis in PLHIV. Despite these challenges and unexpected observations, it is important to emphasize the promise that the LAM biomarker and LAM tests hold for TB testing.

TBS-EP-13 Linezolid exposure and Probability of Target Attainment in patients with MDR-TB treated in the TB-PRACTECAL clinical trial

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WHO recently recommended treatment of drug-resistant tuberculosis with linezolid (Lzd)-containing all-oral short regimens, but evidence is lacking on optimal dose and duration. A pharmacokinetic-pharmacodynamic (PK/PD) study was conducted in South Africa and Belarus in participants from TB-PRACTECAL Clinical Trial receiving bedaquiline, pretomanid and Lzd +/- moxifloxacin or clofazimine.

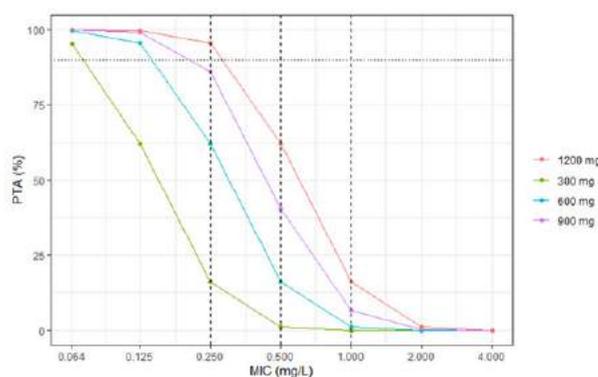
The study aimed to estimate the population exposure metrics for abovementioned compounds. We report preliminary results for daily Lzd 600 mg for 16 weeks decreased to 300 mg for 8 weeks.

Twelve samples at day 0 (0, 2, 23 hours post-dose), week 8 (0, 6.5, 23 hours post-dose) and up to 6 trough time-points (w12, 16, 20, 24, 32, 72) were collected. Lzd was measured using tandem mass spectrometry coupled with ultra-performance liquid chromatography. Serial pharmacokinetic data were analysed using nlmixr (2.0.4) R-package.

One- and two-compartment disposition models with linear elimination and linear or transit-absorption compartments were investigated ($p < 0.05$). Bodyweight allometry, HIV status, age, baseline creatinine clear-

ance, BMI and male gender were tested on clearance using stepwise covariate modelling ($p < 0.05$ forward step and $p < 0.01$ backward step). Probability of Target Attainment (PTA) of $fAUC/MIC > 119$ for 300mg, 600mg, 900mg and 1200mg doses were investigated using 2,000 stochastic simulations.

Fifty-nine participants (62.7% males) with median BMI 20.6 kg/m² (range 14.3-32.3) contributed 553 drug measurements for analyses. Median of the Lzd trough concentrations was 331.38 (range 80-9991.4) ng/mL. A one-compartment model with transit absorption (N=6) and bodyweight allometry best described the data. Estimated clearance was 11.2 L/h (95% CI: 9.11, 13.8), 4.36 % RSE, 59.2% BSV and <18.7% shrinkage. Observed median MIC was 0.5 mg/L (range 0.25-1). PTA was below 80% for all investigated doses (Figure 1).



Despite TB-PRACTECAL regimens showing high efficacy, Lzd PTA was low, aligned with previous reports. Further exploration of Lzd PK/PD targets used in combination with bedaquiline and pretomanid is merited.

TBS-EP-14 A Nanopore sequencing-based pharmacogenomic panel to personalize TB treatment dosing

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Background: Standardized dosing of anti-tubercular drugs contributes to a substantial incidence of toxicities, inadequate treatment response, and relapse, in part due to variable drug levels achieved. Polymorphisms in genes involved in drug metabolism explain interindividual pharmacokinetic variability and can be used to personalize dosing. We developed a Nanopore sequencing-based pharmacogenomic (PGx) panel to detect polymorphisms in genes that affect the metabolism of four anti-TB drugs.

Methods: We designed anchor-based primers to an 8-plex panel targeting 15 polymorphisms in genes (*NAT2*, *CYP2E1*, *SLCO1B1*, *AADAC*, *CYP3A5*) that affect the metabolism of isoniazid (INH), rifampin (RIF),

Higher coverage of the *Mtb* genome was obtained after treatment with the enzymes also indicating an increased amount of target DNA available for target capture and enrichment. We also compare the sequencing output to Direct sputum sequencing without target capture and enrichment.

Conclusion: Current results indicate that pre-processing to remove contaminating extracellular DNA prior to cell lysis and DNA extraction has a positive effect for the enrichment of *Mtb* DNA in decontaminated sediments.

TBS-EP-16 Effect of Everolimus as Adjunctive Host Directed Therapy with Isoniazid plus Rifampicin on Latency and Tuberculosis Reactivation in a Preclinical Model

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The standard therapeutic regimen for tuberculosis (TB) involves two months of Isoniazid (INH), Rifampicin (RIF), Pyrazinamide (PZA), and Ethambutol (ETH), followed by four months of INH plus RIF treatment.

Despite the availability and implementation of this regimen, *Mycobacterium tuberculosis* (*Mtb*) infection persists in the population; thus, these drugs are ineffective in killing slow-and/or non-replicating *Mtb*. It is also unclear whether INH+RIF treatment sterilizes *Mtb* and prevents reactivation of latent *Mtb* infection (LTBI).

We hypothesized that a robust host response drives a subpopulation of *Mtb* into a semi/non-replicating state, thereby rendering them to withstand the activities of anti-TB drugs.

We propose that alleviating the host inflammation through immunomodulation therapy would augment antibiotics-mediated *Mtb* killing. In a rabbit model of pulmonary LTBI/reactivation, we tested the efficacy of adjunctive Everolimus (Evr) therapy combined with INH+RIF in sterilizing *Mtb* (i.e., preventing reactivation).

Adult rabbits (n=6-10 per group/time point) were infected with *Mtb*CDC1551 through aerosol and treated with INH+RIF with/without Evr through daily gavage for two weeks starting at the onset of latency (12 weeks post-infection), followed by immune-suppression with intramuscular dexamethasone treatment (3 days per week) for four weeks, to reactivate LTBI.

Untreated but *Mtb*-infected animals were included as controls. The kinetics of lung bacterial load, histopathology, immune cell composition, and inflammatory cytokines were determined and analyzed at various time points during the latency and reactivation of all animals.

Results showed no *Mtb*-sterilizing effect after two weeks of INH+RIF with or without adjunct Evr therapy, although all the rabbits in the INH+RIF+Evr group

cleared the infection. Further, the INH+RIF+Evr therapy significantly reduced the proportion of LTBI reactivation, compared to INH+RIF treatment, upon immune suppression.

Thus, host-directed therapeutic (HDT) agents, such as Evr, can significantly reduce the development of the antibiotic-resistant *Mtb* population and improve the effectiveness of currently available anti-TB drugs.

TBS-EP-17 Bioevaluation of PLGA loaded with radio-labeled rifampicin: A prospective study.

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Introduction: The PLGA nanoparticles of the anti-tubercular drug were evaluated for sustained release profile over seven days previously in our lab. To the best of our knowledge, it is not known where these nanoparticles are deposited in the body and released. Therefore, we planned the study to explore the biodistribution and pharmacokinetics of PLGA rifampicin nanoparticles in healthy human volunteers.

Methodology: For biodistribution of nanoparticles, we labeled the 500 µg of rifampicin with Tc-99m, a radio-nuclide, and then encapsulated it into the nanoparticles.

Results: Nanoparticles were prepared by a single emulsion evaporation method. The average size of particles was 306 ± 170 , encapsulation efficiency $73\% \pm 2.8$, loading $59\% \pm 6.2$, Polydispersity Index (PDI) 0.2 ± 0.03 , and zeta potential -11.9 . *in-Vitro* release assay showed 33% burst release in the first 12 hours, followed by 100% release in SIF and 65% in SGF. In pharmacokinetic assessment, PK parameters (AUC, AUMC, MRT) of rifampicin nanoformulation after a single oral administration were significantly different compared to the conventional group. SPECT/CT images showed nanoparticle deposits in the distal parts of the gut, which is supported by our dosimetry evaluation. In the nanoformulation group, higher radioactivity counts were observed in large intestines, while fewer were observed in blood and urine at different scanning time points.

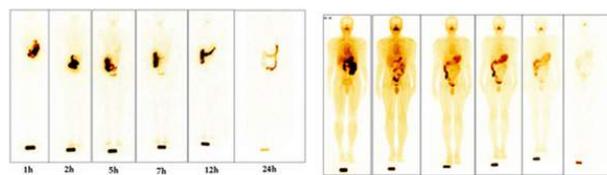


Fig. Representative SPECT/CT whole-body scans of nanoformulation of rifampicin

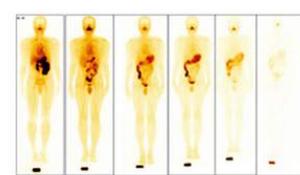


Fig. Representative SPECT/CT whole-body scans of conventional

Discussion and conclusion: We have successfully developed Tc-99m labeled rifampicin-loaded nanoparticles to evaluate their biodistribution in healthy human volunteers. Although we did not observe a sustained release

of nanoformulation for seven days, an increase in AUC, AUMC, and MRT was observed. This can potentially reduce the dose of nanoformulation of rifampicin for pulmonary TB. Noticeably the nanoformulation was distributed to the spleen and lymph nodes, with maximum deposition occurring in large intestine. This type of distribution pattern of nanoparticles could be beneficial for treating lymph nodes or intestinal TB.

TBS-EP-18 Evaluation of Xpert TB Host Response assay for triage of pulmonary tuberculosis

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Novel non-sputum-based triage tests for tuberculosis (TB) are needed. A blood-based PCR assay using a three-gene host *mRNA* signature has been developed to discriminate TB disease from other illnesses.

We screened adults presenting to health centers in Uganda, South Africa, Vietnam, the Philippines and India and enrolled those with at least 2 weeks of unexplained cough. Participants provided sputum samples for TB testing (Xpert Ultra x 1 and liquid culture x 2) and venous or capillary blood samples for the Xpert TB Host Response (HR) assay (Cepheid, USA). We calculated the gene expression score as per manufacturer recommendations and evaluated its accuracy in comparison to sputum Xpert Ultra plus culture (microbiological reference standard, MRS) and sputum Xpert Ultra alone (Xpert reference standard, XRS).

Of 1,365 adults enrolled, 638 (46.7%) were female, median age was 41 years (interquartile range 29-54), 209 (15.3%) were living with HIV, 189 (13.9%) were living with diabetes, and 295 (21.6%) had microbiologically-confirmed TB. The Xpert HR assay had high diagnostic accuracy using the MRS (area under the receiver operating characteristic curve 89.0%, 95%CI: 86.0-0.91). At a cut-off (1.25) that achieved sensitivity of at least 90%, specificity was 63.8% (95%CI 60.5-67.0; Table1). Results were similar when using the XRS (sensitivity: 91.0%, 95%CI: 88.0-93.0; specificity: 61.4%, 95%CI: 58.5-64.3). Across countries and certain key subgroups (women, people living with HIV, people living with diabetes), sensitivity remained largely consistent. Specific-

ity was similar across countries, and in women and people living with diabetes; however, it was lower in people living with HIV (42.2%, 95%CI: 33.8-51.0).

The Xpert TB HR assay nearly achieved the WHO-endorsed target product profile minimal accuracy thresholds for a TB triage test (90% sensitivity and 70% specificity) overall and across most sub-groups. Costs and cost-effectiveness of Xpert HR as a novel TB triage tool should be further explored.

	Total, N (%)	Sensitivity (% 95%CI)	Specificity (% 95%CI)
Overall	N=1,365	89.8 (85.5-93.0)	63.8 (60.5-67.0)
Country			
Uganda	334 (25.1%)	87.5 (79.9-93.0)	62.6 (55.5-69.2)
Philippines	352 (25.8%)	75.9 (56.6-89.7)	74.3 (68.6-79.4)
Vietnam	230 (16.8%)	94.3 (87.2-98.1)	55.7 (46.5-64.7)
India	224 (16.4%)	86.4 (65.1-97.1)	63.6 (54.6-71.9)
South Africa	225 (16.5%)	97.7 (88.0-99.0)	53.3 (45.0-61.4)
Female	638 (46.7%)	87.0 (78.8-92.9)	62.2 (57.5-66.7)
People living with HIV	209 (15.3%)	95.2 (83.8-99.4)	42.2 (33.8-51.0)
People living with diabetes	189 (13.9%)	86.0 (74.2-93.7)	69.2 (59.5-77.7)
Blood collection method			
Venous	1,143 (83.7%)	88.5 (83.9-92.2)	65.7 (62.1-69.1)
Capillary	206 (15.1%)	97.6 (87.1-99.9)	52.1 (43.5-60.7)

Table 1: Sensitivity and specificity by key subgroups

TBS-EP-19 A new approach in multidrug-resistant tuberculosis treatment

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The new drug FS-1 for multidrug-resistant tuberculosis (MDR TB) treatment was developed in JSC „Scientific Center for Anti-Infectious Drugs“ (SCAID), (Almaty, Kazakhstan). FS-1 is an iodine-containing nanomolecular complex. The oral solution form of FS-1 was used in the clinical trials.

SCAID team has performed preclinical and three phases of clinical trials within the period from 2004 to 2021. In the 1st phase of clinical trials 108 healthy volunteers have taken FS-1 in doses from 1.25 to 15.0 mg/kg. The safety and tolerability of the new drug were proven in doses up to 5.0 mg/kg. In the 2nd and 3rd phases of the clinical trials FS-1 was used for treating patients with

multidrug-resistant pulmonary tuberculosis (220 and 474 patients, accordingly). Patients took the study drug for 6 months and then were observed for 12 months of the follow-up period.

In the second phase were used doses 2.0 - 5.0 mg/kg; in the third phase – 2.5 mg/kg. There were interventional randomized two arms double-blinded placebo-controlled (add-on) multicenter parallel-group trials evaluating the therapeutic efficacy and safety of FS-1.

Results: Efficacy: FS-1 in complex therapy of MDR TB has decreased the time of sputum culture conversion (SCC) and the time to negative sputum microscopy. It has also increased the proportion of patients with SCC and cure rate of MDR TB; decreased the proportion of patients with relapse of tuberculosis; improved patients' body weight and clinical symptoms dynamics. Also it positively influenced patients' chest x-ray dynamics.

Safety: no serious adverse events associated with FS-1 were observed during the 2nd and 3rd phases of clinical trials; there were no differences between groups in frequency and severity of adverse events and drug-related adverse drug reactions.

Conclusion: The safety and efficacy of FS-1 were proven for MDR TB treatment in a dose of 2.5 mg/kg.

TBS-EP-20 Infectious and clinical tuberculosis trajectories: Bayesian modeling with case finding implications

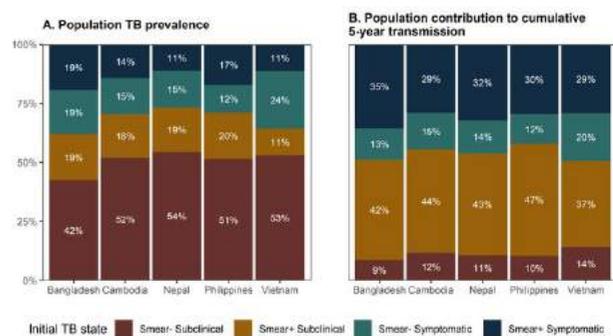
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Background: The importance of finding people with undiagnosed TB hinges on their future clinical and infectious trajectories. Ideally, assays for systematic screening would be optimized to find people with prevalent TB who will contribute most to future transmission or morbidity. Data from multiple sources (population-based prevalence surveys, notifications, and historical data on the clinical course of untreated TB) can be merged to provide insight into the temporal course of different forms of undiagnosed TB.

Methods: We constructed a mathematical model which tracks the trajectories of individuals with TB, classifying them dynamically by bacillary load (smear positive/negative) and symptom status (symptomatic/subclinical). We calibrated this model using Bayesian methods to historical survival data and to national notification, mortality, and prevalence survey data from five countries. We combined simulated individual disease trajectories with evidence on infectiousness to compare how much different subsets of people with prevalent TB contribute to future transmission events.

Results: Nearly all (89% [95% uncertainty range 83-93%]) smear-negative subclinical TB resolved before diagnosis or treatment, typically after a short disease course (4.3 [3.3-6.7] months). In contrast, people with smear-positive subclinical TB had a longer overall duration of undiagnosed disease (15.5 [11.0-21.3] months), and most eventually developed symptoms. Symptomatic TB was more likely to be detected and thus had a shorter disease course (10.9 [6.9-15.6] and 6.8 [5.4-8.9] months for smear-positive and -negative, respectively).

Despite accounting for only 11-20% of prevalent disease, smear-positive subclinical TB accounted for 37-47% of future transmission – a greater contribution than symptomatic TB or smear-negative TB (Figure).



Panel A. The distribution of smear and symptom status among individuals with prevalent TB.
Panel B. The cumulative transmission they will generate over the next five years.

Figure. Relative number of future transmission events from individuals with undiagnosed prevalent TB in different symptom and smear states.

Conclusions: Subclinical TB with a high bacillary burden accounts for a disproportionate share of future transmission. Priority should be given to developing inexpensive, easy-to-use assays (for example, lateral-flow antigen-detection tests) that could detect people with high-bacillary-burden TB at scale, even if these assays lack the sensitivity to detect paucibacillary disease.

TBS-EP-21 Multi-country assessment of metabolomic changes associated with pediatric tuberculosis

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Background: Diagnosing tuberculosis (TB) in children is challenging due to the low sensitivity of clinical diagnostics and difficulty obtaining sputum samples. High-resolution metabolomics (HRM) is an emerging platform with potential to identify new biomarkers for pediatric TB.

Methods: We examined the metabolic perturbations associated with TB disease in children <15 years old evaluated for TB in Lima, Peru and Kampala, Uganda. Children completed a standard TB assessment and were classified as Confirmed TB, Unconfirmed TB, or Unlikely TB. We performed HRM on stored plasma and identified metabolic pathways in children with Confirmed or Unconfirmed vs. Unlikely TB (Composite Reference Standard, CRS). We also compared metabolite intensities to determine candidate metabolic biomarkers of Confirmed or Unconfirmed TB. All analyses were adjusted for age, HIV status, and study site.

Results: We performed HRM on plasma from 214 children (median age 4 years [IQR 2,8]), of whom 102 (48%) had TB disease (41 [40%] Confirmed) and 7% were living with HIV. Compared to children with Unlikely TB, children with Confirmed or Unconfirmed TB were more likely to have perturbations in tryptophan ($p=0.003$) and linoleate metabolism ($p=0.006$). Within the tryptophan pathway, tryptophan and methoxyindoleacetate were decreased in children with TB (mean intensity $1.47E+08$ vs $1.59E+08$, $p=0.05$ and $1.80E+06$ vs $2.09E+06$, $p=0.02$ respectively), while quinolinate, a marker for tryptophan catabolism through the kynurenine pathway, was increased (mean intensity $4.10E+06$ vs $3.67E+06$, $p=0.004$). Changes associated with linoleate metabolism included increased levels of lysophosphatidylcholine and phosphatidylcholine in children with TB (mean intensity $1.94E+08$ vs $1.76E+08$, $p=0.03$ and $1.28E+07$ vs $9.17E+06$, $p=0.009$ respectively).

Conclusions: We found that TB disease in children was associated with significant changes in tryptophan and linoleate metabolism. Further study of these metabolic pathways will be important to improve understanding of the metabolic contributors to TB disease in children and identify metabolic biomarkers of disease.

TBS-EP-22 Experiences of Tuberculosis Patients and Ward-Based Outreach Teams (WBOTs) in Implementation of Interventions to Improve Tuberculosis Treatment Initiation

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Background: In South Africa, the target for Tuberculosis (TB) initial loss to follow up (LTFU) is yet to be achieved (14.9%/22.5% versus 5% national target). Some of the reasons are: the lack of proper communication between patient and staff on the next steps after testing, not being aware that results are ready; and other competing priorities such as family, school, work and business responsibilities. An interventional trial testing the use of reminder messages was conducted. We aimed to explore the experiences of study participants and of the implementers in the trial.

Methods: Using the health belief model pillar of patient perceptions of their illness and the socioecological model, we explored the integration of experiences from both the participants and the implementers in the trial. In-depth interviews were conducted with 10 WBOT members and 15 trial participants. The interviews were audio-recorded, transcribed, and exported to Nvivo 11 for coding and analysis using emerging themes.

Results: The WBOTs were involved in TB screening and in ensuring TB patients on treatment adhered to treatment. Their knowledge around TB improved after the training they received during preparation for the trial implementation. Their involvement in treatment initiation by delivering the reminder paper slips was new but possible to incorporate into their daily schedule. The challenges they faced during the trial were similar to what they encounter during their routine work. TB patients reported fear and worry when they received reminder messages and TB stigma was one of the reasons for this.

Conclusion: WBOTs have the potential to contribute more to the TB program through their holistic involvement in both preventative and curative medicine including treatment initiation. Policies to reduce TB stigma need to be in place in order for the reminder message system to work effectively as an intervention to reduce TB initial LTFU.

TBS-EP-23 Re-evaluating pathways through the spectrum of tuberculosis disease following *M. tuberculosis* infection

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Background: As technologies develop to prevent tuberculosis (TB) disease progression and to treat TB and post-TB morbidity, pathways following *Mycobacterium tuberculosis* (*Mtb*) infection must be re-evaluated to consider the spectrum of TB disease. We used a data-driven, mathematical modelling approach to quantify pathways through the spectrum of TB disease following *Mtb* infection.

Methods: We developed a deterministic modelling framework of *Mtb* infection and minimal (pathological damage but not infectious), subclinical (pathological damage and infectious) and clinical (infectious and symptomatic) TB disease (Figure).

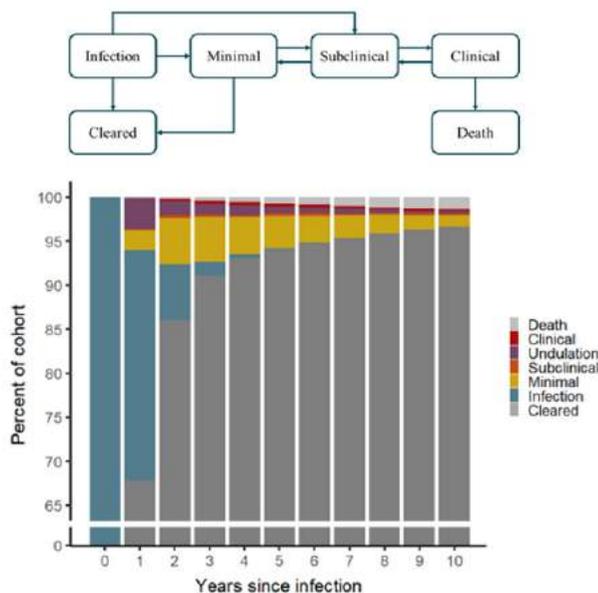


Figure.

We used a Bayesian approach to calibrate the model to data from historical cohorts that followed tuberculin-negative individuals to tuberculin conversion and subsequent disease, as well as historical cohort data on progression and regression between disease states, disease duration estimates, and disease state prevalence ratios. We assumed uninformed priors for all transition rates ($U(0,3)$) except mortality ($N(0.39,0.03)$).

We used posterior parameters to quantify pathways following infection for a simulated cohort of 100,000 infected individuals in the absence of treatment.

Results: We estimate 9.1% (95% credible interval, CrI, 8.3-9.9) of *Mtb*-infected individuals will progress to TB disease within two years of infection, with 6.7% (95% CrI 6.2-7.2), 4.0% (95% CrI 3.7-4.4), and 1.2% (95% CrI 1.0-1.4) developing incident minimal, subclinical, and clinical disease, respectively, in that period.

At two years post-infection, 84.9% of our simulated cohort had self-cleared, 7.8% remained infected without disease, and 0.2% had died after developing bacteriologically-positive disease. Of those with disease, 65.7%, 5.0%, and 4.7% had minimal, subclinical, and clinical disease, respectively, while 24.6% were undulating between states (Figure).

At ten years post-infection, a further 11.6% had self-cleared and a further 1.3% had died.

Conclusions: Our findings show heterogeneous pathways following *Mtb* infection, with important distinctions across disease states, building evidence for more effective prevention and treatment efforts across the spectrum of TB.

TBS-EP-24 Novel magnetic nanoparticle antibody-conjugate aptamer-based assay (Mag-nano-Ab-Ap assay) for the rapid diagnosis of pleural tuberculosis

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Pleural tuberculosis (pTB) is a diagnostic challenge owing to the paucibacillary nature of disease and non-specific clinical presentations. The present study aimed at the development of a magnetic nanoparticle antibody-conjugate aptamer-based assay (Mag-nano-Ab-Ap assay) using 4 different *M. tuberculosis* (*M. tb*) antigens (GlcB, MPT51, MPT64 and CFP10) for pTB diagnosis. The Mag-nano-Ab-Ap assay was developed by conjugation of polyclonal antibodies raised in rabbits (anti-GlcB, anti-MPT51, anti-MPT64 and anti-CFP10) on the surface of the magnetic nanoparticles.

These antibody-conjugated magnetic nanoparticles were used to capture the antigen present in pleural fluid (PF) sample and the resulting antigen-antibody complex

was detected using 5' biotinylated aptamers specific for *M. tb* antigens. The assay was standardized on PF samples included in the 'Development set' (n=17) and validated on n=114 PF samples in a blinded manner.

Patients were categorized as: 'Definite pTB' (n=10; Xpert MTB/RIF/*M. tb* culture/AFB smear positive), 'Probable pTB' (n=42; clinically diagnosed with anti-TB therapy response), 'Possible pTB' (n=28; clinical features suggestive of pTB with no ATT information) and 'Non-TB' (n=53) on the basis of composite reference standard (CRS) formulated for the study.

The assay results of 'Definite and Probable pTB' group (n=8) and 'non-TB' group (n=9) of 'Development set' (n=17) were used to establish cut-off values (Mean+3SD of OD values of 'Non-TB' group) for assay validation.

Of the 4 different antigens, MPT51-based Mag-nano-Ab-Ap assay performed the best with a sensitivity and specificity of 66.6% (95%CI:50.4-80.4) and 95.4% (95%CI:85.1-99.4) followed by MPT64, which had a sensitivity and specificity of 64.2% (95%CI:48-78.4) and 86.3% (95%CI:72.6-94.8) respectively in the 'Definite and Probable pTB' group.

The Mag-nano-Ab-Ap assay performed better than Xpert which demonstrated 14.2% (95%CI:5.4,28.5) sensitivity with 100% (95%CI:92.6,100) specificity. Mag-nano-Ab-Ap assay is a novel technology that has the potential to efficiently capture antigens from PF and can be used for rapid diagnosis of pleural TB.

TBS-EP-25 Comparison of screening strategies for active pulmonary tuberculosis among people in prison in in Malaysia

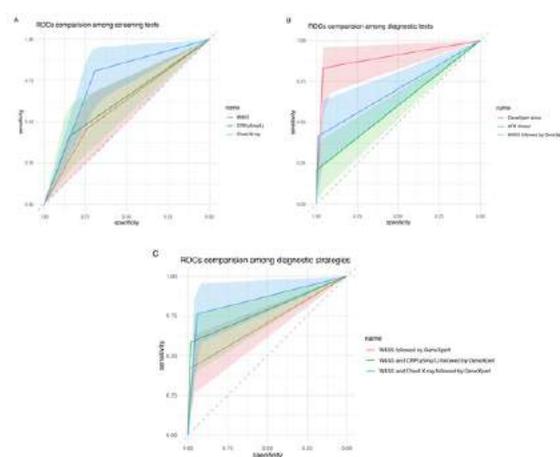
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Objectives: Although international guidelines recommend TB screening for people in prison, gaps regarding efficient and specific strategies exist. Symptom screen with c-reactive protein (CRP) has been recommended among people with HIV. We aimed to assess the accuracy of different screening and diagnostic strategies for active pulmonary tuberculosis (PTB) in people with history of opioid dependence in prison.

Methods: People entering Kajang men's prison, the largest prison in Malaysia, with history of opioid use disorder (OUD), were invited to participate. The W4SS (WHO-recommended four-symptom screen (cough, fever, night sweats, or weight loss), chest X-ray, and CRP, $\geq 5\text{mg/L}$) were used as PTB screening tests. The acid-fast bacilli (AFB) smear and Xpert MTB/RIF (Xpert) were

used as PTB diagnostic tests. The reference standard was culture. We defined three screening strategies and compared their receiver operator curves and area under the curve (AUC).

Results: We enrolled 439 participants with a history of opioid dependence, median age 43 (IQR 37-50), 9.6% living with HIV, 49.2% with Hepatitis C infection. Among participants, 24 (5.5%) were identified to have active TB disease. For screening tests, sensitivity of W4SS, CRP, and X-ray was 45.8% (25.6-67.2), 41.7% (22.1-63.4) and 81.0% (58.1-94.6). For diagnostic tests, Xpert had a sensitivity of 83.3% (95%CI 62.6-95.3) and a specificity of 95.9% (93.5-97.6). AFB smear had a much lower sensitivity (20.8% [7.1-42.2]) and a similar specificity (99.8% [98.7-100]). Screening strategy of "W4SS and/or abnormal X-ray" had highest AUC (66.5% [58.2-74.4]). Compared to "W4SS followed by Xpert" strategy, both "W4SS and/or CRP followed by Xpert" and "W4SS and/or abnormal X-ray followed by Xpert" strategies had a higher AUC (78.2% p=0.041 and 85.1% p=0.002, respectively).



Conclusions: Symptom screen and chest x-ray followed by Xpert had the highest screening value for active PTB among people in prison with OUD. CRP did not provide additional discrimination for screening.

TBS-EP-26 Active TB Case Finding in the COVID-19 Pandemic: Exploring the prospects of Patent Medicine Vendors in Ebonyi State Nigeria

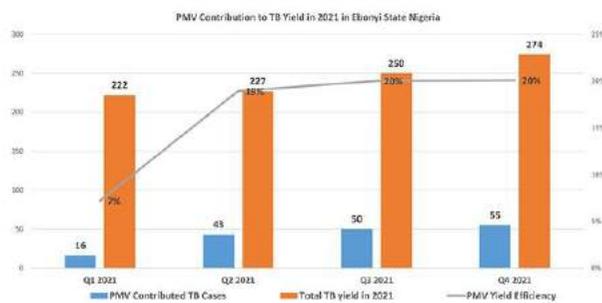
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Background: Covid-19 greatly disrupted the prevention and treatment services of communicable diseases such as TB, especially in low-income countries like Nigeria. Since the first case of COVID-19 was recorded in Nigeria in February 2020, there has been a progressive decline in clinic attendance, TB screening, and identification of

presumptive TB cases. COVID-19 Severely impacted Active TB Case finding, TB Case care, and treatment services in Nigeria.

Methods: A retrospective study was conducted using the TB program data generated from the Global Fund PPM TB project from January 2021 to December 2021 to assess the proportion of TB cases contributed by the Patent Medicine Vendors (PMVs) to the total TB cases generated from the program in Ebonyi State.

Results: The results of this intervention are reported at the country level. Over 12 months, 384 PMVs contributed a total of 1347 presumptive TB cases at an average of 4 Presumptive TB cases per PMV. 166 TB cases were diagnosed and 164 started TB treatment. The PMV contributed 25 % to the Total Presumptive TB cases identified in this period, 16% of diagnosed cases, and 17% of TB cases started treatment.



Conclusions: Despite the COVID-19 Interruptions and their effect on the health-seeking behaviors of TB patients in Low-income countries, the significant contributions of TB Cases from the PMVs were observed from the data reported during the intervention. This adds to reported evidence that decentralized health services increase access to patient care and increase patient involvement in their clinical management.

The engagement of PMVs increased access to TB screening and Active TB case finding through the hub-spoke referral system of the PMVs, despite the impacts of the Covid-19 pandemic.

TBS-EP-27 Non-depletion mass spectrometry identifies 118 differentially regulated proteins in the plasma of TB patients

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There is an urgent need for new diagnostic markers for tuberculosis (TB) disease, deployable in a simple low-cost point-of-care test. Existing diagnostic tests are limited by poor sensitivity, diagnostic delay, high costs and the need for adequate infrastructure and training. Prompt diagnosis of pulmonary TB will enable timely effective treatment and break the ongoing cycle of pathogen transmission.

We used a non-depletion shotgun proteomics methodology developed at the University of Southampton to profile the most comprehensive plasma proteome of patients with pulmonary TB to date. Plasma from 11 TB patients and 10 healthy controls of South African and Peruvian origin was characterised by a protocol comprising serial peptide fractionation using orthogonal chemistries, with no prior protein depletion steps.

We identified 118 significantly differentially expressed proteins over the entire dataset (figure, p value <0.05 after adjustment for false discovery rate), that were common to three complementary bioinformatic pipelines using linear modelling and weighted correlation network analysis. Gene ontology analysis demonstrated high fold enrichment for lipid catabolic processes, proteolysis, regulated exocytosis, inflammatory response and platelet degranulation.

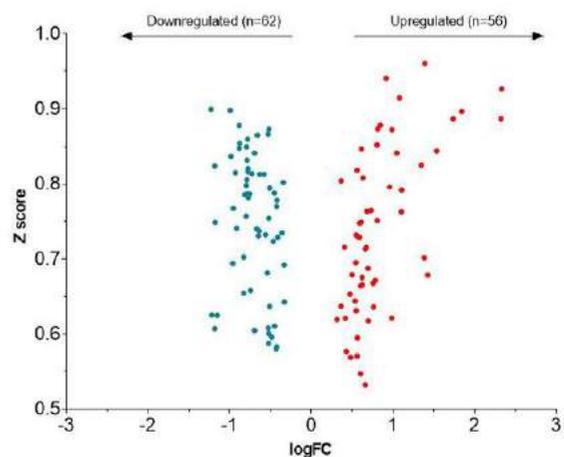


Figure. Volcano plot of significantly differentially expressed plasma proteins in pulmonary tuberculosis, plotted as logFC by limma and z score by weighted correlation network analysis.

To date, selected upregulated proteins have additionally been validated by antibody-based techniques in two large independent patient cohorts from the UK and South Africa, demonstrating the potential of this approach for the identification of clinically useful biomarkers for TB. Currently, further validation of potential TB-specific proteins is ongoing to characterise the best performing diagnostic panel. If developed into a multiplex lateral flow device, the optimised biomarker panel could then be prospectively evaluated as a point-of-care diagnostic in areas with high disease burden.

TBS-EP-28 Community leaders' engagement for increased Tuberculosis (TB) case finding-A case of USAID Afya Shirikishi Project in Geita region

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Background: Tanzania is still among high TB and TB/HIV burden countries with the incidence rate of 222/100,000 with 64% treatment coverage, making 48,000 TB missing patients continue causing transmission in the community. The COVID-19 pandemic has slowed progress against TB control around the world.

With funding from the USAID mission through Amref Tanzania in consortium with SHDEPHA+, the Afya Shirikishi program aims to address priority gaps in TB case findings and unmet family planning needs at the community level in nine regions of Tanzania by 2025.

Methods: The Afya Shirikishi program uses intensified case-finding approaches, including Active case Finding, Loss to follow-up tracking and Contacts Investigation (CI) at the community level to actively search for people with TB. Demand creation is done by CHWs collaboratively with the community local government leaders (WEO, VEO, Chairmen etc.) using microphones, hoe kicking or an invitation letter addressed to the street leaders to invite their people with signs and symptoms related to TB disease. At LGA offices, systematic active TB screening is done by CHWs, sputum samples are collected from all presumptive cases and tested with Microscope and GN Xpert.

Findings: Project data shows that, July 2021 to May 2022 period, 50,475 people received TB education, 40,821 (81%) were screened for TB, 14,473 (35%) were persons with presumed TB, 11,737 (81%) sputum samples were collected and transported for testing and 1,150 (11%) were confirmed with TB whereby 25 (2.2%) TB patients were notified under the influence of community leaders during community outreaches.

Conclusion: Improving access to early TB detection, treatment, and prevention using community-based approaches is an essential component of the End TB strategy. Having strong linkages and collaboration with Local government and CHWs promotes intervention success.

Local community involvement by both volunteers and communities needs to be strengthened through community health committees to promote more uptake of TB services.

TBS-EP-29 Diagnostic utility of M. tuberculosis-derived cell-free DNA for the rapid diagnosis of pleural tuberculosis

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Pleural tuberculosis (PTB) continues to pose a major diagnostic challenge due to its non-specific clinical presentation, paucibacillary nature of disease and lack of sensitive diagnostic tools.

The present study aimed at the development of a novel cell-free *M. tuberculosis* DNA (cfM.tb-DNA) probe-based qPCR assay for PTB diagnosis. A total of n=135 pleural fluid (PF) samples were included and processed for microbiological, cyto-biochemical and molecular assays. Total cell-free DNA (cfDNA) was extracted from PF (4-ml) and quantified by targeting *devR* (109 bp) gene of *M. tb* by qPCR probe-based assay.

The developed assay was standardized in the 'Development set' (n=17) and validated in n=118 samples in a blinded manner. Patients were categorized as 'Definite PTB' (n=10; Xpert MTB/RIF assay/*M. tb* culture positive), 'Probable PTB' (n=40; clinically diagnosed with anti-TB therapy response), 'Possible PTB' (n=28; clinical features suggestive of PTB with no information on anti-TB therapy) and 'non-TB' (n=57) using Composite Reference Standard formulated for the study.

ROC-curves were generated using assay results of 'Definite and Probable PTB' group (n=8) and 'non-TB' group (n=9) of 'Development set' (n=17) to establish cut-off values for evaluation of the developed assay. cfM.tb-DNA *devR* probe-based qPCR assay had a sensitivity of 62.5% (95% CI:24.4,91.4) in 'Definite PTB' group and 59.5% sensitivity (95% CI:43.2,74.3) in 'Definite and Probable' PTB group with 95.2% specificity.

The sensitivity decreased to 41.4% (95% CI:29.7,53.8) in the combined 'Definite,' 'Probable,' and 'Possible' PTB group with similar specificity. The cfM.tb-DNA qPCR assay performed better than Xpert which demonstrated 14.2% (95% CI:5.4,28.5) sensitivity with 100% (95% CI:92.6,100) specificity.

We conclude that *cfM.tb*-DNA *devR* probe-based qPCR assay is an accurate test that can provide direct evidence of *M. tuberculosis* and can pave the way for improving PTB diagnosis. To the best of our knowledge, this is the first report describing the utility of *cfM.tb*-DNA for PTB diagnosis in India.

TBS-EP-30 Can QFT-plus distinguish between recent and remote TB infection in adolescents and young people from 14 communities in Zambia and South Africa

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The difference of interferon gamma (IFN- γ) responses of the TB1 and TB2 antigen tubes (TB2-TB1) of the QuantiFERON-TB Gold Plus (QFT-Plus) assay may be related CD8+ T lymphocyte response, a possible marker of *Mycobacterium tuberculosis* (*M.tb*) infection. We investigated TB1 and TB2 IFN- γ responses in a cohort of adolescents and young people (AYP).

In 2018, a random sample of AYP (15-24 years) from 14 communities in Zambia and Western Cape, South Africa were enrolled into the TREATS Incidence of TB Infection Cohort Study. *M.tb* infection, measured by QFT-Plus was carried out in accordance with manufacturer's instructions at baseline, 12 and 24 months (M). Recent infection was defined as individuals with QFT-Plus conversion within a 12M period, remote infection as persistent QFT-Plus positivity $\geq 24M$.

We compared (TB2-TB1) in recent and remote infection, conservatively excluding participants with IFN- γ responses > 10.0 IU/ml from our analysis. Odds ratios were calculated to evaluate the association between TB2-TB1 and recency of infection for different cut-offs.

Of the QFT-Plus positives at baseline, 1029/1852 (55.4%) remained positive for 24M, whilst 152/2025 (7.5%) with negative baseline results converted within a 12M period. Both TB1 and TB2 IFN- γ responses were lower in recent compared to remote infection (TB1: median 1.5 vs 4.1 IU/ml, $p < 0.001$, TB2: median 1.9 vs 4.1 IU/ml, $p < 0.001$). The mean (TB2-TB1) in recent infection was 0.56 IU/ml, median 0.07 IU/ml whilst in remote infection -0.04 IU/ml, median 0.01 IU/ml, $p = 0.102$). Recent infection was not associated with a greater (TB2-TB1) irrespective of various cut-offs (Table 1).

We observed lower IFN- γ responses in recent as compared to remote infection. We found no evidence of a greater (TB2-TB1) magnitude in recent compared to

remote infection. Caution must be exercised when interpreting IFN- γ tube responses of QFT-Plus in terms of recency of infection.

Tube Differential Cut-off (IU/ml)	Infection Category	N	n	%	OR(95% CI)	p
TB2-TB1 ≥ 0.6	Recent	880	149	16.9%	1	0.634
	Remote	218	34	15.6%	0.91 (0.60-1.36)	
TB2-TB1 ≥ 0.9	Recent	880	88	10.0%	1	0.968
	Remote	218	22	10.0%	1.01 (0.62-1.65)	
TB2-TB1 ≥ 1.5	Recent	880	28	3.2%	1	0.488
	Remote	218	9	4.1	1.31 (0.61-2.82)	

Table 1.

TBS-EP-31 Development of antigen-based detection assay by using pleural fluid derived extracellular vesicles for the diagnosis of pleural tuberculosis

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Pleural TB (pTB) is one of the most frequent causes of pleural effusions and is a clinical diagnostic dilemma.

We, in our study evaluated the utility of pleural fluid derived-extracellular vesicles (PF-EVs) as a source of *Mycobacterium tuberculosis* (*M. tuberculosis*) antigens for pTB diagnosis. Characterization of PF-EVs (exosomes and microvesicles) was done by immunoblotting (by detecting EVs-specific CD63 protein) and scanning electron microscopy.

We targeted 2 *M. tuberculosis* proteins (MPT51 and MPT64) and standardized and developed antigen-based detection ELISAs. The presence of MPT51 and MPT64 was checked in PF as well as in PF-EVs first in a 'Development-set' (n=15).

Next, the developed ELISA was validated on PF-EVs and compared with levels of antigen(s) in paired PF samples (n=79) which included Definite pTB (Xpert/*M. tuberculosis* culture positive, n=7), Probable pTB (n=25), Possible pTB (n=21) and non-TB (n=26) group. Assay cut-off values were generated by using mean+3SD values of non-TB samples from 'Development-set' and further applied on 'Validation-set' (n=79).

The sensitivity of MPT51 ELISA was 57.1% (95%CI:18.4-90.1) in both PF-EVs and PF samples in Definite pTB group, while in 'Definite+Probable' pTB group, PF-EVs showed 59.3% (95%CI:40.6-76.3) sensitivity and PF-ELISA had 59.3% (95%CI:40.6-76.3) sensitivity.

The overall specificity for PF-EVs and PF-based ELISA was 88.5% (95%CI:69.8-97.5) and 57.7% (95%CI:36.9-76.6) respectively. The sensitivity of MPT64-based PF-

EVs ELISA was 57.1% (95%CI;18.4-90.1) in Definite pTB group, while PF-ELISA had only 14.3% (95% CI;0.36-57.8) sensitivity. In 'Definite+Probable' pTB group, PF-EVs showed 56.2% (95%CI;37.6-73.6) sensitivity for MPT64 antigen while PF-ELISA had 13.15% (95%CI;3.51-28.9) sensitivity. The overall specificity of MPT64 antigen-ELISA was 84.6% (95%CI;65.1-95.6) and 96.1% (95%CI;80.3-99.9) in PF-EVs and PF-ELISA respectively.

We conclude that *M. tuberculosis* specific antigens are concentrated in extracellular vesicle-fraction of pleural fluid. These results have important implications in assay development from PF samples for pTB diagnosis and need to be validated in large-scale studies.

TBS-EP-32 High hesitancy of household contact investigation in high TB transmission area

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Background: Indonesia has more than 800.000 yearly TB case, only 3.4% children under five got TB preventive treatment (TPT) and no report among household contacts. It's important to implement TPT as priority. This study aimed to investigate latent TB infection (LTBI) among household contacts and household contact investigation.

Methods: We investigated household contacts of TB patients who were treated in primary health care (PHC) East Jakarta between January to August 2019. Screening include TB signs and symptoms, followed by Xpert MTB/Rif test and chest X-ray (CXR). Contacts without symptoms were screened of LTBI using interferon gamma release assay (IGRA).

Results: We identified 137 index cases, 104 were excluded due to investigation refusal and 33 agreed to participate. Out of 168 contacts, 108 were investigated and 60 (35.7%) did not visit to PHC. At the end, 12 subjects refused to took IGRA test leading to 96 final subjects. The median of age of contacts was 29,66 years old, 66 (68.8%) were \geq 18 years old, and 51% were female. A total of 13 (13,5%) new TB cases were identified among contacts, 35 (36,5%) have LTBI and 48 (50%) were not infected.

Discussion: There were a large number of index cases that didn't want to be investigated due to refusal to be acknowledged as TB patients and household contact through testing and treating healthy person wasn't necessary. Most of contacts who were not in house at the visiting time didn't come to PHC for evaluation.

Regarding this, it is important to simplify active case finding (ACF) and CI algorithm. The use of IGRA was very useful since the staff only had to come once thus reducing time, budget, and simplifying ACF and CI procedures.

Conclusion: Household contact investigation remains as a big challenge in community with high transmission.

TBS-EP-33 Roll-out of Truenat Technology for the Diagnosis of TB and Rifampicin Resistance: Early Lessons from Zimbabwe

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Background: With the support of USAID's Infectious Disease Detection and Surveillance (IDDS) project, Zimbabwe adopted Truenat™ MTB Plus testing in 2021 to improve TB case finding in underserved/remote areas where GeneXpert cannot be used. The Truenat™ technology is a chip-based a chip-based real time PCR test and works on portable, light weight, battery powered equipment and can be used in remote areas with poor infrastructure¹, making it more suitable to be deployed in remote areas.

Interventions Implemented: Twenty (20) Truenat™ instruments were installed in remote underserved existing microscopy sites with high TB burdens. Truenat™ testing was integrated into the national diagnostic algorithm and reporting mechanisms.

In addition, staff from the national TB program, reference laboratory and field laboratory staff were trained with support from Molbio Diagnostics using adapted training materials. Field laboratory staff were trained on the operational aspects of the instruments on-site during instrument installations in December 2021.

Lessons Learnt & Challenges: Strategic placement of Truenat™ in remote and underserved but high burden microscopy increases TB case finding; with 200% increase in TB cases in March 2022 compared to December 2021 when rolled out (table below).

Key performance Indicator	Dec 2021	Jan 2022	Feb 2022	Mar 2022	Apr 2022	May 2022	Jun 2022*
Total MTB Plus tests done	49	177	218	301	251	295	220
Failed MTB Plus tests	6	19	5	28	17	21	9
Total MTB Detected	10	35	36	40	17	23	17

High failure rates were attributed to an inexperienced cadre of technicians and hence a pool of super-users is needed to provide facilitative support to end users.

Conclusions: Truenat technology can be easily introduced and integrated into the TB diagnostic network and sensitization of health care workers should be prioritized in all sites to increase awareness and utilization of the test.

TBS-EP-34 Impact of the COVID-19 pandemic on TB screening in children in Belarus

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Introduction: The COVID-19 pandemic has had an adverse impact on tuberculosis (TB) services.

The aim of the study was to research the impact of the COVID-19 pandemic on TB screening in children in Belarus.

Methods: We used data from the state statistical reporting on medical care for children of Belarus for 2018-2021. We studied two periods: the first period - before the COVID-19 pandemic, 2018-2019; the second period - during the COVID-19 pandemic, 2020-2021. The number of children screened for TB and the average annual growth rate (AAGR) of the number of children screened for TB were calculated.

Results: In the first period, on average per year, 97787,0 ± 4642,9 children aged 0-17 years old were examined for TB using fluorography. In the second period 98413,5 ± 2593,0 children were examined. AAGR of the number of children examined for TB using fluorography was +0,6%.

In the first period, on average per year, 107745,0 ± 18145,8 children aged 0-14 years old were examined for TB using skin tests (Mantoux test or Diaskintest). In the second period, 86435,0 ± 14903,0 children were screened for TB. AAGR of the number of children examined for TB using skin tests was -19,8%.

In the first period, on average per year, 56964,0 ± 5126,5 children aged 15-17 years old were examined for TB using skin tests. In the second period 47143,5 ± 440,5 children were screened for TB. AAGR of the number of children examined for TB using skin tests was -17,2%.

Conclusions: The COVID-19 pandemic has had a negative impact on TB screening of children using skin tests. AAGR of the number of children examined for TB using skin tests decreased by -19,8% in children aged 0-14 years old and by -17,2% in children aged 15-17 years old.

TBS-EP-35 Clinical and image findings among sputum smear negative pulmonary tuberculosis patients in Ethiopia: a comparative study

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Smear negative pulmonary tuberculosis (SNPTB) has been a diagnostic dilemma worldwide, potentially leading to diagnostic delays and difficulty in monitoring treatment outcomes.

This study aimed to determine the true magnitude of SNPTB and compare its clinical and chest x-ray findings with smear positive PTB (SPPTB).

A case-control study was conducted on 313 PTB patients, of whom 172 were SNPTB, recruited from health facilities in Addis Ababa, Ethiopia. Clinical data, including chest x-ray findings and sputum samples were collected from all enrolled participants.

An acid-fast microscopy, GeneXpert and culture analysis were performed on the collected sputum samples. Data was analyzed using SPSS (Version 25, IBM USA)) and a P-value <0.05 was considered statistically significant.

Of the 172 SNPTB patients 73(43.1%) were found to be positive on Lowenstein-Jensen culture media. Body mass index (BMI), previous TB history and shortness of breath classes were the only TB symptoms that had a statically significant association with SNPTB (P-value <0.05).

Among chest X-ray findings, pleural effusion was higher among SNPTB (41.8%) than SPPTB (24.3%) whereas cavitation was higher among the SPPTB (30.8%) than SNPTB (19.0%) (P -value < 0.05).SNPTB patients had a similar TB pertinent symptom with the SPPTB patients. However a higher BMI, severe shortness of breath and pleural effusion had an association with SNPTB that may help clinician decision making in TB clinical diagnosis in these patients however, careful assessment is also required to prevent false TB diagnosis since these clinical and image findings are also common for non-TB pulmonary diseases.

In the current study, significant number of patients were misclassified as SNPTB, which may need urgent measure to minimize delayed TB diagnosis and the potential disease transmission in the studied population.

TBS-EP-36 Identification of abnormalities on digital chest X-rays when utilizing computer-aided detection systems

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Background: Computer-aided detection (CAD) systems have been developed to aid in tuberculosis (TB) screening and triage but have not been evaluated in patients with chest X-ray (CXR) abnormalities which are not caused by TB.

The aim of this study is to evaluate the performance of CAD systems in capturing selected non-TB CXR abnormalities which require further clinical actions.

Methods: 20 highly-clinically relevant diagnoses other than TB, which are associated with abnormalities on CXRs and are seen in high TB incidence settings, were selected by a multi-disciplinary team. The databases of Heidelberg University Hospital were searched for these diagnoses using ICD-10 codes.

Selected abnormal CXRs resulting from these diagnoses, were annotated by an expert radiologist using a standardized annotation guide, which was considered as reference standard.

The CXRs were analyzed by two CAD solutions: qXR v2 (qure.ai, India) and Lunit INSIGHT CXR v3 (Lunit, South Korea).

For qXR, scores ranged from 0 to 1, with an abnormality threshold set as >0.5 . For Lunit, scores ranged from 0 to 100 with a high-sensitivity threshold for abnormality set as of $>15\%$.

Results: 521 patients were included. The median age was 65 years and 63% were male. qXR identified 485 (93.1%) CXR as being abnormal. Lunit considered 501 (96.2%) as being abnormal. Possible TB was identified on 126 (24.2%) CXRs from Lunit and 150 (28.8%) CXRs from qXR. The highest scores were in patients with lung abscess (0.80) and silicosis (0.79) for qXR (see Figure), while Lunit had the highest scores when a diagnosis of silicosis (47.9) and non-CF bronchiectasis (30.5) was present.

It is planned to compare the CAD solutions in terms of their performance for identification of specific non-TB CXR findings with each other as well as with the annotation from the radiologist. The final results will be presented at the conference.

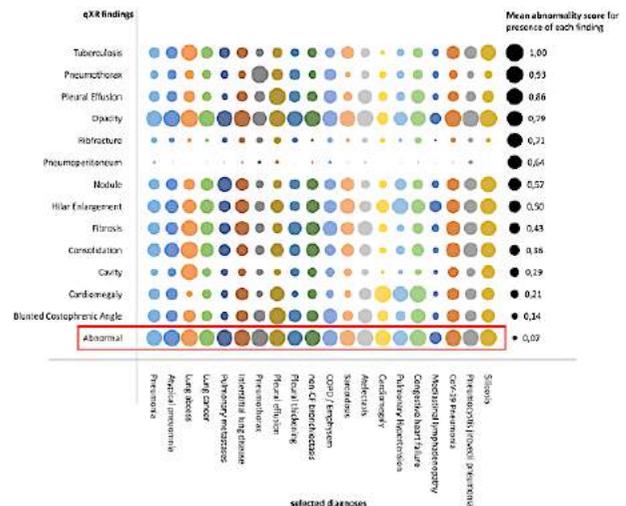


Figure. Mean abnormality scores for presence of qXR findings on each selected diagnosis (qXR findings on y-axis and selected diagnoses on x-axis).

TBS-EP-37 Genetic diagnosis of bedaquiline resistance - an individual isolate meta-analysis

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Introduction: Bedaquiline is an important treatment for drug-resistant tuberculosis. The main resistance mechanism is *Rv0678* mutations. Many individually rare mutations are reported, with many causing small minimum inhibitory concentration (MIC) increases to at/near the critical concentration (CC).

Sequencing approaches could diagnose resistance if genotypic-phenotypic correlations can be established, but resistance-associated variants (RAVs) are not established.

Here, we collate all genotypic and phenotypic resistance reported from clinical isolates to assess effectiveness of sequencing resistance-associated genes.

Methods: We screened public databases for articles published up until June 2022. Studies were included if they whole genome sequenced clinically-sourced bedaquiline-resistant isolates and measured MIC by MGIT, 7H11, or broth microdilution. Candidate resistance genes were: *Rv0678*, *atpE*, *pepQ*, *atpB*.

We categorised isolates with MICs $>CC$ as resistant, MICs = CC as intermediate, and MICs $<CC$ as susceptible. To calculate associations with resistance, we used

published methods on a combination of all extracted isolates from included studies and the Cryptic study 're-use' dataset.

Results: Twelve studies were included yielding 891 isolates containing ≥ 1 potential RAV, with 277 (30.9%) phenotypically intermediate/resistant. 261 intermediate/resistant isolates were identified with no candidate gene mutations. 943/1175 (80.3%) of isolates were from Cryptic. Sensitivities and positive predictive value of taking an 'any mutation' approach in candidate genes (assuming any mutation causes resistance) are shown (Table).

Twenty mutations had a significant association with an intermediate/resistant MIC ($p < 0.05$). All were strong associations ($OR > 10$), except 192_indel ($OR = 8.8$). When considering only resistant MICs, 11 mutations had a significant association, all strong except 192_indel ($OR = 4.6$).

Any mutation in <i>Rv0678 / atpE / atpB / pepQ</i>	Intermediate or resistant	Resistant only
Sensitivity	257/519 (49.6%)	146/229 (63.8%)
Positive predictive value	195/813 (24.0%)	81/732 (10.0%)
Specificity	11313/11932 (94.9%)	11491/12232 (93.9%)
Negative predictive value	11313/11574 (97.7%)	11491/11574 (99.3%)

Conclusions: The candidate gene 'any mutation' approach has limited sensitivity for identifying bedaquiline resistance (45-63%) but high specificity and negative predictive value ($> 97\%$) in highly drug resistant cohort (61% rifampicin-resistant).

We identify 20 mutations with a strong association with intermediate/resistant MICs (13 resistant). However, currently genetic methods alone are not sufficient to identify bedaquiline resistance.

TBS-EP-38 Forecasting the epidemiological trends of tuberculosis using mathematical simulation dynamic model in the region of the Russian Federation

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According to WHO, the spread of a new coronavirus infection and HIV infection preserves and even increases the potential for the spread of tuberculosis in the world. Sverdlovsk oblast (SO) of Russian Federation is a region with high levels of HIV and tuberculosis (TB) and co-infection. The search for new methods of analyzing the current and predicting the characteristics of the future epidemic situation for tuberculosis becomes particularly relevant.

The aim was to develop a system for predicting the epidemic situation of tuberculosis in the near future until 2030 in the whole region and for each of the districts using artificial intelligence technologies in the format of a dynamic simulation model (SDM). The SDM based on the modified K. Stiblo's model using artificial intelligence technologies. Statistical data was loaded from official forms of state statistical reporting on TB patients, the Federal Register of TB patients for 2007-2017.

Seven qualitative indicators connected by the system of inequalities were used which values forecast the change in the number of patients with active TB. The parameters were controlled through a system of inequalities and setting the rates of their increase.

The proposed SDM made it possible to identify, reliably calculate and graphically display trends of TB epidemiological indicators in each of the 63 municipalities and in the whole SO. Comparison of the predicted values made in 2018 with the actual values of 2018-2021 revealed a reliable coincidence of the trend of movement of TB epidemiological indicators in the region, the maximum deviation (SMAPE) was no more than 14.82%.

If the qualitative indicators remain at the level of 2021, then in the next 20 years the epidemiological situation in the region will develop in the same trend: decreasing number of: active TB cases, (including MBT+) more than minus 6.7%-7.7% annually.

TBS-EP-39 Longitudinal tracking of respiratory volatile organic compounds during phage therapy against *Mycobacterium abscessus* lung infection

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Background: Bacteriophages (phages) are viruses that attack bacteria selectively, and their therapeutic use has been evaluated for difficult-to-treat infections. The incidence of lung disease causing by *Nontuberculous mycobacteria* (NTM) infections, is increasing globally. NTM disease is challenging to diagnose, generally requiring > 1 positive cultures combined with an appropriate clinical presentation and radiographic findings.

Mycobacteria abscessus (*M. abscessus*), has high levels of intrinsic and acquired antibiotic resistance, often associated with poor treatment outcomes. Recently, successful phage treatment of *M. abscessus* was reported (Cell, 185, 1-15, 2022) in a patient with advanced lung disease and severe cystic fibrosis (CF) disease who was refractory to antibiotic treatment.

This report utilized several noninvasive, and culture-independent biomarkers to detect *M. abscessus* and assess phage treatment response. Breath and sputum are

promising noninvasive samples that can capture volatile organic compounds (VOCs) emitted by bacteria or host that can serve as biomarkers.

Methods: Two engineered phages were used for the treatment of *M. abscessus* infection in an individual with advanced CF lung disease. A variety of markers combined with extensive cultures indicated eradication of *M. abscessus* following a year of treatment, allowing for successful lung transplant. Breath and sputum samples were collected multiple times prior to the phage therapy till after the lung transplant operation.

Samples were analyzed using two-dimensional gas chromatography coupled with a time-of-flight mass spectrometry (GCxGC-TOFMS). Chemical compounds were identified by spectral library match and putative diagnostic figures were selected by statistical analysis using R programming.

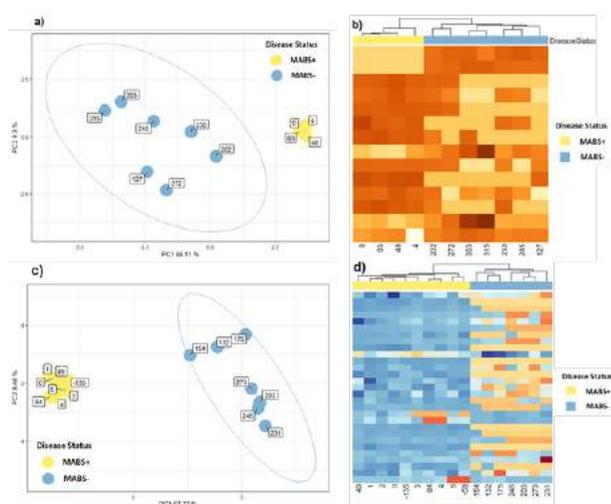


Figure 1: a) PCA plot of 11 breath samples with 95% confidence ellipses; b) Heatmap of 11 breath samples; c) PCA plot of 15 sputum samples with 95% confidence ellipses; d) Heatmap of 15 sputum samples. MABS+ refers to *M. abscessus* positive and MABS- refers to *M. abscessus* negative. The number labeling each sample represents the days since the phage therapy initiation.

Figure.

Results: 14 VOCs from breath can diagnose *M. abscessus* in lung, as do 29 VOCs from sputum headspace. The changes in the relative abundances of a subset of the 14 VOCs conform to the variation of other biomarkers, including microbial culture, antibody, urine LAM, and DNA.

TBS-EP-40 The respiratory microbiota composition in patients with different treatment effectiveness of pulmonary tuberculosis

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The efficacy of tuberculosis (TB) treatment is determined by many factors and respiratory microbiota composition can be one of them.

The aim: To analyze relationships of respiratory microbiota composition with tuberculosis treatment efficacy.

Methods: Bronchoalveolar washing (BAW) samples from 39 tuberculosis patients were studied. 26 patients had MDR TB, including 20 with fluoroquinolones resistance, 15 were new cases, 24 cases were retreatment. All patients received TB drugs according to drug susceptibility of the *M. tuberculosis*. Microbiota of the samples were analyzed by mass spectrometry for microbial markers method (MSMM), with quantitative identification of 57 microorganisms' taxa (Osipov GA. Beneficial Microbes 2011; 2:63-78). Effectiveness of tuberculosis treatment was assessed by the computer tomography results. STATISTICA 10 was used as statistical package.

Results: Respiratory microbiota composition differed between TB cases. In most cases *Clostridium ramosum* and *Eubacterium spp.* dominated (20% - 80%, mean 56.0% DI: 52.1%; 59.9%). Ratio of quantities of these two species differed in patients with different clinical responses to TB treatment: *C. ramosum* / *Eubacterium spp.* ratio was more than 9,2 in patients with positive dynamics of treatment (n=8), and less than 0,45 in failures (n=9). Ratio of 0.49-7.2 were detected both in patients with progression of the disease (n=13) and with positive dynamics (n=9) according to lung computer tomography scans.

Conclusion: In this study, we analyzed the characteristics of respiratory microbiota in patients receiving anti-TB drug therapy. Correlation between the *C. ramosum* and *Eubacterium spp.* ratio, detected by MSMM method in BAW and effectiveness of TB treatment were found. Further studies of more TB cases and detalization of microbiota composition are needed for revealing statistically reliable associations in this field.

TBS-EP-41 Phylogeography and transmission of *M. tuberculosis* spanning prisons and surrounding communities in Paraguay: a genomic epidemiology study.

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While genomic epidemiology approaches have increasingly been harnessed to characterize transmission and guide public health interventions elsewhere, they have not yet been applied in Paraguay. To characterize *M. tuberculosis* phylogenetic and geographic structure and recent transmission dynamics in Paraguay. We conducted prospective genomic surveillance inside and outside prisons in the districts of Central, and Alto Paraná, Paraguay, from 2016 to 2021. We investigated phylogenetic structure and inferred patterns of historic migration and population size changes with ancestral state reconstruction and coalescent-based Bayesian phylogeographic analysis. *M. tuberculosis* sampled from Paraguay fell within lineage 4, predominantly in the LAM (42.5%; 200/471), Haarlem (38.2%; 180/471), and S (12.3%; 58/471) clades. The majority (86%; 405/471) were pan-susceptible; 8.5% (10/471) had a genomic evidence of isoniazid resistance, and 0.4% (2/471) were multi-drug resistant. We reconstructed the emergence of a mutation in alkyl hydroperoxidase (*ahpC*), previously considered a compensatory mutation for isoniazid-resistant isolates, in a monophyletic clade of 56 otherwise susceptible isolates. Isolates from individuals diagnosed within prisons and the community were interspersed within a maximum likelihood phylogeny and isolates from individuals incarcerated at the time of TB diagnosis had a higher time-scaled haplotype density (median: 0.49, IQR: 0.22-0.70), a measure of epidemiological fitness, than did isolates from never incarcerated individuals (median: 0.25, IQR: -0.62-0.64; $p < 0.001$). We found a signal of frequent migration between Asunción and Ciudad del Este, the largest cities in Paraguay and a gradual increase in the effective population size of *M. tuberculosis* for the two largest genomic clusters. Together, our findings of transmission linkages spanning prisons and the community indicates TB control programs should prioritize reducing transmission risk within prisons, where incidence was 70 times that outside prisons. Drug resistance rates were relatively low, but research on the phenotypic consequences of *ahpC* mutations is needed to determine whether this mutation predicts acquisition of isoniazid resistance.

TBS-EP-42 Quality of Life of Multidrug Resistant Tuberculosis Patients Enrolled in Programmatic Management of Drug-Resistant Tuberculosis Satellite Treatment Center of Vicente Sotto Memorial Medical Center

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Tuberculosis is a communicable disease caused by *Mycobacterium tuberculosis*. The multi-drug resistant form of tuberculosis (MDRTB) has been called the worst of the worst diseases, and treating it is more difficult for the patient than dealing with the condition. Adverse effects could result from the varied clinical profiles and lengthy course of multiple medication therapy. The well-being and quality of life of patients have been impacted in a number of ways by MDRTB.

This is an analytical cross-sectional study of the quality of life (QoL) of MDRTB patients enrolled in the Programmatic Management of Drug-Resistant Tuberculosis Satellite Treatment Center (PMDT-STC) of Vicente Sotto Memorial Medical Center (VSMMC).

A total of 74 respondents gave their consent and answered the QoL Short Form (SF) 36 health survey and Smilkstein Family APGAR. Statistical analysis used included means, percentages, Chi Square and Fischer Exact tests to correlate the relationships between the QoL and socio-demographic profile.

Out of 74 MDRTB patients 54% were in the 30 to 50 years of age, mostly males (62.2%), finished secondary education (50%), married (55.4%), in the extended type of family (55.4%), earning a low monthly income (93.2%), in the intensive phase of treatment (67.6%) and a family who were highly functional (89.2%).

Most of the respondents had a defective physical QoL (58.1%) and maintained normal mental QoL (55.4%) but with a 44.6% who are at risk of depression.

There were no significant relationships between the QoL and socio-demographic profile of the patients.

TBS-EP-43 Peroxisome proliferator-activated receptor α and γ in patients with pulmonary tuberculosis

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Tuberculosis (TB) patients show an immune-endocrine-metabolic (IEM) unbalance with rise in proinflammatory mediators and cortisol plasma levels, among others. Peroxisome proliferator-activated receptors (PPAR- α , γ , and β/δ) are ligand-dependent transcription factors with modulatory actions on metabolism, cell differentiation, and inflammation.

We analyzed the role of PPAR- α and γ in the IEM response in pulmonary TB (TBP) patients (n=39) and healthy individuals (Co, n=24). The expression levels of mRNA-PPAR γ (RT-qPCR) were higher in peripheral blood mononuclear cells (PBMCs) in TBP than in Co (p<0.01) and were positively correlated with those of cortisol (p<0.01).

The expression of mRNA-PPAR α showed no difference in TBP respect to Co. One-hundred % of the monocytes and B lymphocytes (L) expressed both PPARs in TBP and Co (flow cytometry); however, the % of TLCD4+ and TLCD8+ that expressed both PPARs was higher in TBP than in Co. In the comorbidity TBP+Type 2 diabetes mellitus (TBP+DM; n=11) and in TBP, the mRNA-PPAR γ expression was higher compared to DM and Co (p<0.02).

THP1-derived macrophages (Mf) treated with glucose doses (normoglycaemia and hyperglycaemia -hgl-), in the presence or absence of 1 μ M cortisol (stress condition), and stimulated with gamma-irradiated Mycobacterium tuberculosis (Mtb) showed that: hgl did not affect the mRNA-PPAR γ expression after the Mtb stimulation but did cause an increase in mRNA-PPAR α expression (p<0.02) and in IL-1 β and IL-6 levels of the conditioned media. IL-10 levels increased by the bacteria stimulus, were reduced in the presence of hgl.

Cortisol inhibited the expression of mRNA-PPAR α respect to Mtb-stimulated cultures and raised mRNA-PPAR γ in the presence of glucose (dose-dependent, p<0.05), with a marked decline of IL-1 β (p<0.01).

The increase of the PPAR γ transcript levels associated with cortisol concentrations suggests the trigger of regulatory mechanisms to control an excessive inflammatory response. A hyperglycemic microenvironment together with cortisol-mediated stress might induce an Mtb permissive Mf phenotype.

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