# WHO consultation on the translation of tuberculosis research into global policy guidelines

## 2-4 March 2021

## Meeting Report

World Health Organization

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## Abbreviations and acronyms

| | |
|---|---|
| DST | Drug susceptibility testing |
| DS-TB | Drug-susceptible tuberculosis |
| DR-TB | drug-resistant tuberculosis |
| DR-TB IPD | Global individual patient data platform for DR-TB treatment |
| IPC | Infection prevention control |
| NTP | National Tuberculosis Programme |
| PLHIV | People living with HIV |
| PMTPT | Programmatic management of TB preventive therapy |
| R&D | Research and development |
| TB | Tuberculosis |
| TPT | TB preventive therapy |

# Background

The Global Tuberculosis Programme of the World Health Organization (WHO/GTB) has the mandate to develop and disseminate evidence-based policy for tuberculosis (TB) prevention, diagnosis, treatment and care. Regular review of evidence, and assessment of country needs for policy across the cascade of care is part of its core function. In this regard, GTB organized a consultation assembling scientists, public health experts, partners, civil society and countries to exchange views on emerging areas of need for global TB policy guidance to achieve the goals and targets of the WHO End TB Strategy.

The specific objectives of this consultation were:

I. to exchange views on emerging needs of Member States for policy guidance in TB prevention, diagnosis, treatment and care;
II. to discuss critical evidence gaps related to emerging global TB policy development needs; and,
III. to identify topical strategies best positioned to enhance the implementation and evaluation of global TB policy guidance.

The expected outcome of this meeting is a report (herewith) summarizing current thinking and suggested actions aligned to these objectives.

# Introduction

After a welcome by Tereza Kasaeva and Matteo Zingol, Gerry Davies, Chair of the first day of the consultation, opened the meeting at 13:10 on March 2, 2021. The Chair presented the programme of the meeting and the participants (Annexes 1 and 2).

# Session 1: WHO TB policy guidance: current status, update plans and evidence gaps

## 1.1 WHO TB policy guidance: current status, update plans and evidence gaps: *Prevention*

*Avinash Kanchar, Global TB Programme, WHO*

Avinash Kanchar presented the evolution of WHO policy guidance in the programmatic management of TB preventive therapy (PMTPT) over the past decade, as well as the scope of the current guideline and operational handbook. Global progress in the provision of TB Preventive Therapy (TPT) in 2018 and 2019 compared with cumulative target set for 2018-2022 in the UNHLM Political Declaration on TB was presented, and current challenges in meeting these targets were elaborated. Emerging policy needs for testing and treating TB infection, and in implementation of current approaches were discussed in the context of available evidence. Lastly, planned updates (2021/2022) to infection prevention control (IPC) handbook, TPT guidelines and other supportive tools such as the *Prevent TB* mobile application (version 3 with TB screening) were shared.

The Chair opened the floor for discussion framed around (but not limited to) the following two questions:

1. What is the opinion of the group on the way forward in the short and medium term in regards planned policy review/development for PMTPT and TB IPC?
2. What adjustments may be needed or new areas covered, in global policy development considering any other evidence and/or specific country needs to scaleup PMTPT and TB IPC?

*Discussion:*

- For people living with HIV (PLHIV), updating TB policy recommendations on co-administration of antiretroviral therapy and short course TPT remains important for 2021 and 2022. Considering that drug to drug interaction between antiretrovirals and TPT remains a barrier in accelerating implementation of new treatment options, early engagement and dialogue with antiretroviral developers is needed to reduce the lag time between ARV approval and availability of safety and pharmacokinetics data, for example, by incorporating TB considerations into initial studies on new antiretrovirals . An update to WHO TB guidance that considers drug to drug interaction with dolutegravir, doravirine, tenofovir alafenamide, cobicistat boosted darunavir should be explored once results are available (2021-22). Better guidance on the pharmacokinetics, effectiveness and safety of rifamycin-containing regimens for people who use illicit drugs or for people on opioid substitution therapy is also needed.
- For pediatric population, updating recommendations on the use of short course TPT regimens among very young children remains a priority in the context of available and upcoming evidence both among HIV infected and uninfected: This includes three months of rifapentine plus isoniazid weekly regimen (3HP) and one month of daily rifapentine plus isoniazid (1HP) regimen. Data from current study sometime in 2023 and availability of water dispersible, functionally scored rifapentine is likely to completely change TPT landscape in children.
- For contacts of people with different forms of drug-resistant TB (DR-TB), results from clinical trials VQUIN (adults and adolescents) and TB CHAMP (children) should be considered in informing TPT provision policy in this population as soon as results are available (2022). In the interim, demand creation among national TB programmes is needed to improve the implementation of current recommendations, as well as to drive generation of new evidence for better treatment options.
- On implementation of guidance, improving TPT uptake among eligible groups other than PLHIV remains a

challenge. In the short term, bolstering availability of up-to-date policy in countries; training healthcare workers to improve their confidence in PMTPT; addressing concerns in confidently ruling out TB disease; and programmatic guidance for developing/strengthening existing mechanisms for pharmacovigilance for TPTs are a priority: Guidance on managing nitrosamine impurities will also support national TB programmes in scaling up shorter TPT. Guidance and practical tools to allay fears with regards to ruling out TB disease among asymptomatic patients (as seen in prevalence surveys) and risks of DR-TB are important considerations. Role of secondary TPT in areas with high force of infection needs clear guidance. Information on anticipated impact of TPT expansion on local TB epidemic will be helpful for decision makers. Specific recommendations regarding TPT use among other high-risk populations/other co morbidities should be explored.

- In the medium term, a guidance on how to choose TPT regimen among various recommended options would be useful. Studies to compare 3HP and 3RH for children should be encouraged. To improve TPT scale up, future operational guidance should provide further evidence of protection offered by different TPTs (including in high transmission setting) and effective models of care (differential service delivery models among PLHIV, household contact investigations and from lessons learnt from the pandemic). Information on cost effectiveness and acceptability would also allow NTPs, implementing partners, communities and procurement agencies to comparatively evaluate different treatment options for scaleup. Better evidence-based guidance on short course TPT regimen use during pregnancy and lactation is also needed. In the meantime, countries will need technical, operational and financial support to translate available policies into action.

- On research and development, over longer-term horizon, it is important to proactively push and/or align the attributes of regimens that prospective users wish to see (e.g., 5-6 years from now) to shape the clinical development pipeline already moving (e.g., long-acting formulations). This may help shape future TB policy development based on preferences of end users rather than simply, availability of evidence.

- On non-treatment related infection prevention principles, update of earlier recommendations based on weak evidence is needed as well as a handbook to promote and support implementation. Assessing the impact of COVID-19 *i*nfection control measures on TB e.g., universal masking, expanded use of personal protective equipment, etc. may help inform future environmental control principles.

## 1.2 WHO TB policy guidance: current status, update plans and evidence gaps: ***Screening***

*Cecily Miller, Global TB Programme, WHO*

Cecily Miller presented the major updates that will make part of the new WHO TB screening guideline and implementation guidance, both of which will be launched this year. The current evidence landscape summarizing trials and implementation science studies for large scale screening or approaches targeted to vulnerable groups was presented. Evidence gaps in the context of pending policy needs was briefly presented. Lastly, planned release date of the consolidated policy guidance and operational handbook (World TB day 2021) as well as further plans for dissemination workshop and technical assistance to promote rapid implementation of these interventions were presented.
The Chair opened the floor for discussion framed around (but not limited to) the following two questions:

1. Are you aware of other upcoming research or implementation experiences that could change the landscape for global guidance for TB screening?
2. Do you agree with our proposed way forward? Are there other needs that countries have that we need to address? What else do you suggest?

*Discussion:*

- All participants agreed intensified screening is key to help find and treat more people with TB, without which we cannot meet the End TB Strategy targets. Evidence is emerging on the utility of various technologies and strategies for TB screening. However, more studies are needed to co-evaluate the effectiveness and cost effectiveness of these approaches to support decision-making. To make this practical, better guidance is also needed to help countries identify and prioritize specific populations to target for screening, for example, by age, gender and/or vulnerability. Additional information on the frequency of screening needs under different

settings, as well as feasibility and acceptability of various algorithms needs further elaboration through implementation science.

- TB patient pathway analysis or diagnostic delay assessment can help prioritize target populations and strategies for screening, while helping build a local investment case for policy makers. An investment case is needed to increase political commitment and for resource mobilization of screening interventions.
- Applied health research remains key in determining and addressing downstream barriers in implementation of screening strategies in the context of local health systems and target populations, as well as in integrating TB screening as part of broader health screening programmes. Training healthcare workers on screening strategies is an important element for scale up. Participants also encouraged better coordination between TB screening and TB prevention work, as is already evident through the data collection and integration platform Prevent TB mobile application (version 3 with TB screening), presented earlier.

## 1.3 WHO TB policy guidance: current status, update plans and evidence gaps: Diagnostics

*Nazir Ismail, Global TB Programme, WHO*

Nazir Ismail presented the evolution of WHO policy guidance in TB diagnostics over the past decade, in the context of changing TB research landscape. Recommendations have moved from phenotypic methods, to faster and simpler nucleic acid amplification tests and more recently biomarkers. Since December 2020, WHO/GTB has shifted to making class-based recommendations for diagnostics, to allow for better competition in the market and provide Member States with potentially more options suited to their context. Although current policy work is mainly focused on TB disease with Nucleic Acid Amplification Tests, and to some degree biomarker tests as the primary tools, there is emerging recognition that TB is a continuum from infection to disease. Additional disease manifestations of incipient TB and subclinical TB are now important areas for research and both biomarker and host- based diagnostics are emerging and need to be shaped for impact. Planned policy guidance updates (2021/2022), evidence landscape, as well as pending policy and implementation gaps were presented. This includes tests for TB infection, improved urine LAM tests for TB detection as well as next generation sequencing for comprehensive drug susceptibility testing (DST). WHO/GTB plans to publish other norms and standards to shape the diagnostics field. These include a catalogue of mutations associated with TB drug resistance as well as update to target product profiles for new TB diagnostics.

The Chair opened the floor for discussion framed around (but not limited to) the following questions:

1. Are there any further critical evidence gaps or upcoming studies?
2. What further guidance/updates should we consider to enhance the implementation of global TB policy guidance in these areas?
3. Are there any initiatives we could consider to direct new areas for research?

*Discussion:*

- On policy guidance, there is an increasing demand for the evaluation of sequencing as a diagnostic tool for TB. Considering that many countries have scaled up their sequencing capacity for COVID-19, some participants argued some NTPs have access to, and can leverage such platforms and for TB diagnosis. Further to this, next-generation sequencing is being applied in some high-income countries for clinical use, and as such, engagement and regulation in managing clinical interpretation is needed. For people with subclinical TB disease, more research to inform better guidance is needed on how available tools may be used for testing, albeit with different parameters of interpretation. For population groups where existing diagnostics may yield low sensitivity (e.g., for pleural effusion samples), guidance would be helpful on how existing tools can be better applied (e.g., through sequential testing). For difficult to treat cases, countries may need guidance on how and when to co-apply phenotypic and genotypic drug-susceptibility testing (DST).
- On implementation, participants reflected on the importance of incorporating decision tools for countries on how to select diagnostic technologies appropriate for their context, which may in turn facilitate the rapid adoption of appropriate tools, contextualization of algorithms and related logistical strategies (e.g., sample transport). Clarity is needed (in discussion with the manufacturer) on assay interpretation rules for various technologies, and this information should be integrated properly in successful models of training for end users.
- On research and development (R&D), participants acknowledged the significant achievements made in R&D of TB diagnostics during the past decade, and welcomed class-based recommendation linked with WHO's

prequalification approach to help ensure high quality tests enter the market, where manufacturers are primed to meet market demands for scale up. From lessons learnt in the past, having access to DST before new drugs are introduced is important. Existing platforms and consortia can be leveraged to advance this space. Engagement with manufacturers/developers to encourage microtiter plate development is a high priority in overcoming the impending bottleneck for multi-drug DST. Promotion of biomarker assay development to measure reponse to TB treatment is another missing tool critical for optimizing treatment duration. The research community also needs to work on optimizing existing tools so they can perform well in low resource settings, with limited user skills.

## 1.4 WHO TB policy guidance: current status, update plans and evidence gaps

### *Treatment*

*Fuad Mirzayev, Global TB Programme, WHO*

Fuad Mirzayev presented the evolution of WHO policy guidelines in TB treatment and supportive tools over the past 25 years, as well as the scope and structure of the current guideline. Planned updates (2021 and 2022) to WHO policy guidance for treatment of both drug-susceptible TB (DS-TB) and drug-resistant TB (DR-TB) and accompanying operational handbooks were presented, in the context of the current evidence landscape. Results from ongoing clinical and operations research anticipated for 2022/2023 may be delayed due to direct and indirect impacts of the COVID-19 pandemic. WHO/GTB plans to publish other norms and standards to shape the TB treatment field in 2021 and 2022. These includes an update to the definitions on reporting framework as well as an update to target TB treatment regimens (2022). Plans to develop a Global individual patient data platform for DR-TB treatment (DR-TB IPD) was also shared. The DR-TB IPD is a collaborative initiative to facilitate pooling of individual patient data issued from researchers, local or national databases to inform future guideline development, as well as public health research.

The Chair opened the floor for discussion framed around (but not limited to) the following questions:

1. Are there any critical evidence gaps that we should highlight, promote and stimulate research in that area?
2. Are there any emerging needs in the TB treatment policies, derivative operational guidance and other normative documents?

*Discussion:*

- On DR-TB, participants acknowledged the positive developments pertaining to the availability of short-course oral regimen. Considering that there are many other short course regimens in the clinical pipeline with different drug compositions, it may be useful to consider identifying the optimal number of drugs and which ones are the most important for safe and effective treatment, during future research informing guideline developments. While the target duration in most of those trials is six months, results may show uncertainty and preparations are needed on how to address duration uncertainty through non-trial data, indirect comparisons between trials or develop better methods of estimating optimal treatment duration. Going forward, trialists should coordinate to explore better ways of measuring duration. The field also needs reliable critical concentration for bedaquiline -DST. More attention is needed to the issue of isoniazid resistance, both to identify a better pathway for patients with mono-resistance and to identify the relative importance of isoniazid use in the DR-TB regimens. Having better information on isoniazid monoresistance at country level will also contribute to future DR-TB regimen development.
- On the DR-IPD platform, participants welcomed this initiative, and discussed how this vision will be operationalized through a partnership model between WHO and an academic institution (to be identified through an open call). WHO/GTB envisions establishing an oversight body to coordinate data access requests from the public.
- On DS-TB, participants welcomed results of the TBTC study 31 as it signals a possibility to develop shorter regimens, but also cautioned that this may be testing-the-limit of first-line drugs and fluoroquinolones. Considering the uncertainty on effectiveness of shortened regimens for treating severe forms of TB disease,

some participants suggested a stratification concept to subgroup people based on factors predictive of clinical outcomes. This may increase confidence in treatment decision making with shorter regimens, and for future research on treatment duration optimization. Lack of validated biomarker(s) for disease severity continues to be a challenge in operationalizing this vision.

- Participants also reflected on prospects of universal regimens or Pan-TB regimens and the challenge this field faces in identifying second-line drugs that are both potent and safe enough in comparison to first-line drugs, as well as from threats of drug resistance. Further studies in this field need to be complemented with development of DST for monitoring resistance. Participants reflected on the divergent directions towards precision medicine features in TB treatment, requiring rapid DST for all key medicines before designing a treatment regimen and the one towards Pan-TB treatment approach. It was highlighted that Pan-TB pathway should not de-emphasize the importance of DST for medicines used since acquisition of drug-resistance may still occur in time.
- On implementation, participants agreed that improving treatment outcomes in people with DR-TB requires early diagnosis, use of DST and less empiric treatments and facilitating patient-centred approaches to care, including psychosocial and other treatment adherence support. UNITAID is building evidence on the best strategies to improve treatment adherence. Availability of safe and effective long acting injectables in the future may generate an important therapeutic opportunity to improve adherence and treatment outcomes. Lack of consistent and speedy access to DST continues to pose barrier for clinicians and patients. Lack of reliable DST for some of the second-line drugs constitutes a challenge to programmatic surveillance of antimicrobial resistance. Considering these challenges, a "personalized medicine" approach to DR-TB is not within reach for national TB programmes in low- and middle-income countries.

To improve scale up in implementation of existing guidelines, participants encouraged WHO to update the strength of the recommendations pertaining to some new TB treatment regimens, as new evidence becomes available.

## 1.5 WHO TB policy guidance: current status, update plans and evidence gaps

### *Child and Adolescent TB*

*Sabine Verkuijl, Global TB Programme, WHO*

Sabine Verkuijl opened her presentation by highlighting the significant challenge in case detection and access to TPT for children and adolescents, in the context of the targets set for 2018-2022 in the UNHLM Political Declaration. The scope of planned comprehensive update to WHO policy guidance on the management of TB in Children and Adolescents (2021) was presented in the context of the current evidence landscape. An operational handbook will be made available in parallel. Research gaps and unmet needs for policy were elaborated. WHO/GTB's efforts to foster coordination across stakeholders to specifically address unmet needs in the development of paediatric TB formulations (Paediatric Anti-TB Drug Optimization, PADO-TB) was also presented.

The Chair opened the floor for discussion framed around (but not limited to) the following two questions:

1. Are there any further critical evidence gaps or upcoming studies?
2. What strategies may WHO/GTB use to encourage investment in paediatric TB R&D and shorten paediatric TB R&D timelines to improve global policies on TB care in these age groups?
3. What strategies may WHO/GTB employ to enhance the implementation and evaluation of global TB policy guidance for these age groups?

*Discussion:*

- On treatment, lack of age-appropriate formulations and misalignment with preferred regimens has created a disproportionate challenge for treating TB infection and disease in children and adolescents. For infants and young children, there is a significant lack of accessible and palatable formulations as well as clear treatment strategies. The paediatric R&D space is underfunded, lengthy, slow, and insufficiently streamlined to focus on priority formulations. Participants acknowledged WHO/GTB led PADO-TB is working in this space to prioritize pragmatic needs for formulations (for both TB infection and disease). To advance this field, WHO should advocate for more flexible research platforms, based on common protocols that can be easily amended to incorporate new drugs/regimens as they become available for pediatric testing, with long-term funding in high-TB burden-, low- and middle-income settings. Such platforms support early access to new medicines, in addition to building evidence. WHO should explore on how to better engage families, patients (children and adolescents) and healthcare providers to understand end-user preference and demand for medicines and other tools (across the cascade of care, inclusive of TPT).
- Participants acknowledged that translation of results from the SHINE trial on shortening treatment duration for non-severe DS-TB from 6 to 4 month into practice is an immediate priority, but this also requires better access to diagnostics in countries (Chest X-ray platforms), and associated capacity building and training. Recent findings from SHINE and TBTC Study 31 trials, may open the door for investigating further optimization/shortening of TB treatment duration for children and adolescents. However, some of the challenges with translation of the TBTC 31 study is that insufficient numbers of children were included in the trial and that there is a lack of appropriate formulations to operationalize it on the ground: Children younger than 12 years of age were also excluded. In future research, purposeful inclusion of children in clinical trials, including people with paucibacillary forms of disease remains key to allow for generalizability of findings. Operationalizing this optimally requires for the TB research community to resolve confusions around definitions of various age categories, as applicable for clinical investigation (definitions based on clinical disease spectrum rather than for reporting purpose).
- On screening and diagnosis, the research community and WHO, should work on optimizing the yield from respiratory and non-respiratory samples in children to allow for more accurate diagnosis. Evaluation of Computer Aided Detection software (CAD) with paediatric disease patterns is also needed to optimize and assess the utility of this tool in young children. Participants supported ongoing work by WHO to evaluate clinical diagnosis and treatment decision algorithms for children <5 years old, during the upcoming guideline development. Considering many children develop paucibacillary disease, non-sputum based rapid diagnostic approaches that can be used at point of care are needed.
- On R&D, WHO has an important role in coordinating efforts, from identifying evidence gaps, to advocating for research funding, and facilitating the availability of products to address unmet needs across the cascade of care. This includes promoting better trial designs that are inclusive of children and adolescents in phase 2b studies, so that formulations developed dearly. Contribution and vision of various platforms working in this space, including PADO-TB, WHO Global Accelerator for Paediatric Formulations (GAP-f) and Treatment Action Group was acknowledged. Participants also made a call for the childhood and adolescent TB research community to engage with WHO early to streamline on how research findings can be translated into policy, and how implementers can be supported beyond guidelines through field guides, etc.
- On implementation and access, integrated models of care, including with nutrition programmes or other comorbidities remains critical to scale up efforts and improve treatment outcomes. Costing and impact assessment of different drugs, treatment regimens and strategies are also important to make the case for more investments and scale up. Clinical trials also create a pathway for access to new tools. Countries and affected communities (with support from partners) should be empowered to negotiate for full and affordable access to new tools, post-trial completion in their community. Further guidance and/or research on how to promote the wellbeing of children and adolescents post-treatment (cure) is also needed.

## 1.6 WHO TB policy guidance: current status, update plans and evidence gaps
## *TB comorbidities and vulnerable populations*

*Annabel Baddeley, Global TB Programme, WHO*

Annabel Baddeley opened her presentation by defining priority drivers for TB and risk factors for poor treatment outcomes among persons with TB including alcohol use disorder, diabetes, HIV infection, malnutrition and smoking, as well as mental health. Member states have already committed to strengthen integrated care for TB, HIV, diabetes, smoking cessation, substance use, malnutrition and mental health disorders through the respective UN High-Level Meeting political declarations on HIV, TB and NCDs. However, despite the existence of guidelines on TB and these comorbidities and risk factors, countries have been slow to scale-up action to address TB comorbidities, with the exception of HIV-associated TB. To translate these commitments into action, WHO/GTB is developing a framework for collaborative action on TB and comorbidities which builds on the experience of the WHO TB/HIV Policy for Collaborative Activities and aims to enhance collaboration between programmes and ministry of health departments to assure integrated people-centred care. Updates to clinical guidelines for the different comorbidities will constitute part of this framework and will be updated accordingly, and in the context of the evidence landscape. To promote better implementation of existing guidance, WHO/GTB is in parallel conducting a review of policy uptake in the 30 high TB burden countries, as well as a consultation with countries to assess the barriers and enablers for scaling up joint action. A roadmap for action for TB and comorbidities is planned for 2022, to help catalyse scale-up. Updates on vulnerable populations was also presented, including planned guidance on vulnerability mapping.

The Chair opened the floor for discussion framed around (but not limited to) the following questions:

1. Are there any further critical evidence gaps or upcoming studies?
2. What further guidance/updates should we consider to enhance the implementation of global TB policy guidance in these areas?
3. How often should guidance on vulnerable populations be updated?

*Discussion:*

- Participants welcomed WHO/GTB's plans to bring together and update the various guidelines on TB comorbidities, and initiatives for integrating these into existing guidance on TB prevention, diagnosis and treatment, as applicable. It was stressed that research on TB comorbidities beyond HIV and on multi-morbidity needs to be stimulated, with particular focus on the "how" and what works on the ground to facilitate people-centred care for TB and comorbidities in high TB burden countries. Mechanisms for collaboration, dialogue and promotion of research in this area need to be strengthened. Building on the TB/HIV experience WHO has a role in coordinating the TB and comorbidity and multi-morbidity research prioritization in order to shape the research agenda and advocate and mobilize the necessary resources. Key stakeholders and collaborators for shaping and promoting the research agenda should include programmes, clinicians, researchers, civil society, people with TB and comorbidities, and affected communities. The need for a shift in focus from co-morbidities to multi-morbidity and syndemics was reiterated, given the real prevalence of multiple burden and the challenges faced, with inadequate patient follow-up, poor treatment outcomes and catastrophic costs incurred as a result of accessing related services from different healthcare providers in different facilities and locations.
- Participants supported the proposal of developing guidance for countries on vulnerability mapping, stressing the need for operational guidelines that help identify the most vulnerable populations and their specific needs including comorbidities, and that demonstrate successful approaches to addressing their needs and optimizing their care, using case studies and lessons from other areas.
- Participants acknowledged that political commitment remains integral to expanding access to the prevention and care of TB (and comorbidities) in all vulnerable groups, as well as to mobilize funding and to support capacity building. Considering the structural, political and commercial determinants of health linked to TB comorbidities and TB in vulnerable populations, the importance the multisectoral lens and linkage with the Multisectoral Accountability Framework was emphasized.

## 1.7 WHO TB policy guidance: current status, update plans and evidence gaps
## *Special needs of TB populations*

*Kerri Viney, Global TB Programme, WHO*

The health and quality of life of people with TB are affected by disease, treatment and social determinants of health. Kerri Viney presented WHO GTB's guidelines to provide social protection to prevent and reduce poverty and vulnerabilities of people affected by TB, which exacerbate poor TB treatment outcomes. Also presented was on how these guidelines can be further strengthened in the context of the End TB Strategy, the SDGs and commitments made by countries in the 2018 UN HLM Political Declaration on TB. Selected research on various aspects of TB and social protection was presented in the context of emerging needs for policy update and development. WHO/GTB's plans for the development of an operational handbook on social protection was also presented , which will cover psychological support , patient education and counselling, the use of digital tools to support treatment completion, and food security, among other topics.

The Chair then opened the floor for discussion framed (but not limited to) the following two questions:

1. What policy areas in TB social protection are missing in this agenda?
2. What is the most effective/efficient approach suggested to address the challenges to improve current policy approach to patient support and social protection?

*Discussion:*

- The relationship between social determinants and TB is complex and multi-directional. While social determinants contribute to vulnerability to TB infection, disease, and death, TB illness itself can amplify the effect of such determinants on quality of life by causing impoverishment. More efforts should be made to gather lessons learnt from both the HIV and COVID-19 pandemics in this space.
- In this regard, it was suggested for WHO/GTB to package social protection measures as a TB prevention approach for reducing vulnerability (including BCG vaccination and tuberculosis preventive therapy), and in reverse, to consider for example, packaging provision of TB preventive measures or active case finding as a social protection measure. Participants applauded WHO's current approach of including evidence from qualitative studies and cost effectiveness studies during TB guideline development to address the special needs of people affected by TB. The importance of qualitative studies as part of ongoing trials on the effectiveness of treatment was emphasised.
- To increase the uptake of social protection measures by NTPs, participants encouraged WHO/GTB to compile case studies of best practices to promote programmatic learning across countries. Impact assessment of social protection measures is also critical to help build evidence for action and decision making (e.g., identifying various risk groups for support, costing and effectiveness studies, etc). If feasible, WHO/GTB was encouraged to develop and use an indicator for measuring progress and for promoting accountability of social protection coverage, in addition to catastrophic cost surveys.
- It was acknowledged that there are some important learnings from the response to COVID-19 regarding social protection as a public health policy and that there are positive examples about the role of social protection from HIV services and published research on the provision of HIV care in the context of social protection.
- Participants suggested the promotion of integrated TB care (clinical and social) by promoting policy and service delivery linkages and working with partners in other sectors, inclusive of approaches for care post TB treatment completion, palliative care, decentralised care, as well as multisectoral accountability. Several suggestions on ways to promote adoption and effective use of guidelines were made in the session, such as for example the training of health providers on stigma and discrimination . Countries, depending on their context and challenges, may also implement legal measures to counter discrimination in areas such as retention in employment or access to medicines. Such approaches are primed for success when complemented with community engagement. Considering that the challenges in this space are broad, situational assessment and prioritization of research needs for global TB policy making were suggested.

# Session 2: Enhancing the implementation of global TB guidance

Dennis Falzon summarized WHO/GTB's wide ranging efforts to support the implementation of TB policy guidance in countries. This includes the development of a digital one-stop TB Knowledge Sharing Platform (web and mobile) where end-users can easily access consolidated TB guidelines, eLearning modules, and implementation tools (e.g. operational handbooks, dosage calculators, etc.) across the cascade of care. The platform will also provide access to all of the currently valid TB recommendations organized in a recommendations map (RecMap), an interactive, user-friendly, and searchable tool where each recommendation can be easily accessed with its respective evidence summary. The TB Knowledge Sharing Platform is projected for launch in April 2021. Additional details on WHO/GTB efforts to boost evidence-based scale-up of interventions such as collaborative implementation research projects and an implementation research toolkit for digital health developed jointly with TDR were discussed. WHO/GTB's efforts in supporting NTPs to address questions and challenges related to the adverse impact of the COVID-19 pandemic were also presented.

The Chair then opened the floor for discussion around this session, and facilitated a follow up roundtable discussion framed around (but not limited to) the following two questions:

1. What more can WHO do to enhance the implementation and scale-up of proven interventions?
2. How can WHO engage with partners to enhance country-led and -owned implementation and scale-up of interventions?

*Discussion:*

- To improve uptake of new TB guidelines, participants suggested WHO to consider launching new TB guidelines together with pathfinding countries that are committed to rapidly implement these changes. This can be followed by experience-exchange meetings among countries to promote learning. Participants also encouraged WHO to explore ways of developing accountability measures to assess timebound adoption/adaptation of new TB guidelines as well as to make available cost-effectiveness data which countries need for decision-making. Complementing cost-effectiveness assessment together with information on what is driving cost (rendering some interventions unaffordable) is also important to help address root causes.

- The success of TB programmes ultimately depends on country action. Provision of capacity building training and technical assistance (including on management and leadership) remains key to spur scale up of interventions, including through of collaborative activities with other relevant programmes such as HIV, Maternal and Child health programmes, as well as the private sector. Training or guidance on various ways strong programmes may be structured is one such way this can be materialized. WHO has a role in fostering partnership and peer-to-peer support among agencies and institutes that can support the NTP.

- Budget is an important element of scaling up interventions, including buydown negotiations with manufacturers and sponsors of new technologies.

- WHO rapid communications have played an important role in quickly informing funding partners and countries of changes to policy recommendations, so funding strategies are adapted in a timely manner. The "living guideline" approach is also anticipated to reduce the lag in reflecting new evidence in new TB recommendations and their adaptation/adoption into national policy.

- Civil society led demand for scale up of evidence-based interventions is another area WHO can promote by continuing to engage affected communities and advocacy groups in guideline development and dissemination processes. This also requires countries and partners to recognize, fund and meaningfully engage community organizations as legitimate stakeholders in their national TB response.

- Participants also advocated for the TB research community to systematically capture the values and preferences of patients at earlier stages of R&D, so policy making can be shaped by needs driven interventions.

- The digitalization of new TB guidelines (RecMap) was welcomed. Participants further encouraged WHO to consider translating the TB Knowledge Sharing Platform to other WHO languages, and enabling discussion

forums and video content to promote better user engagement and utilization. At the same time, efforts that enable access to TB guideline by countries where internet connection may be challenging should continue.

- On e-learning modules, WHO was encouraged to provide certificates of completion for the modules to motivate trainees and to proactively seek endorsement by professional associations (groups), to promote a wider utilization of the platform.
- On operations/implementation research, Participants suggested WHO to promote more research on TB screening, TB preventive treatment, comorbidity management, optimization of diagnostic algorithms and associated logistics (such as sample transportation); and approaches to multisectoral collaboration and accountability at country level. This will need to be in concert with approaches to improve *capacity building* for health research in countries with high TB burden and with engagement of civil society.
- On implementation of approaches to improve TB response during the COVID-19 pandemic, participants suggested increased focus on finding people with TB who are having challenges accessing TB services, rapidly scaling up provision of TB preventive treatment and capacity building for NTP staff.

## Conclusions and way forward

Tereza Kasaeva and Matteo Zignol thanked the participants and emphasized WHO's commitment to convening regular fora to share WHO/GTB policy development plans. The Chair closed the meeting at 5:15 PM. A meeting feedback survey was conducted via email post the consultation. Those who responded to the survey agreed the meeting was constructive in understanding better WHO/GTB's plans for policy development and encouraged regular (annual) meeting on this topic.

## Annex 1: Meeting programme

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| **2 March 2021**<br>**13:00 –16:00 Geneva time** | | **Chair: Gerry Davies** |
| 13:00 – 13:15 | Welcome and Introductions | Tereza Kasaeva<br>Matteo Zignol |
| **Session 1: WHO TB policy guidance: current status, update plans and evidence gaps [Part 1]** | | |
| 13:15 -15:50 | **TB prevention:** *Avinash Kanchar*<br>*Discussants: Mike Frick, Lindiwe Mvusi*<br><br>**TB screening:** *Cecily Miller*<br>*Discussants: Chakaya Muhwa, Nguyen Binh Hoa*<br><br>**TB diagnosis:** *Nazir Ismail*<br>*Discussants: Daniela Cirillo, Rumina Hasan, Zhao Yanlin* | *Presentations will cover planned updates to TB policy guidance (2021), and overview of the current evidence landscape*<br><br>*Discussant will reflect on emerging TB policy development needs, and imminent evidence gaps (2021-2023)* |
| 15:50-16:00 | Summary of Day 1 | Chair |
| **3 March 2021**<br>**13:00 –16:00 Geneva time** | | **Chair: Daniela Cirillo** |
| **Session 2: WHO TB policy guidance: current status, update plans and evidence gaps [Part 2]** | | |
| 13:00-13:10 | Agenda items | Chair |
| 13:10 -15:50 | **TB treatment:** *Fuad Mirzayev*<br>*Discussants: Gerry Davies, Rafael Laniado-Laborin*<br><br>**Child and adolescent TB:** *Sabine Verkuijl*<br>*Discussants: Anneke Hesseling, Imran Pambudi*<br><br>**Vulnerable populations and comorbidities:** *Annabel Baddeley*<br>*Discussants: Helen Ayles, Srinath Satyanarayana* | *Presentations will cover planned updates to TB policy guidance (2021), and overview of the evidence landscape 2021-2023*<br>*Discussant will reflect on emerging TB policy development needs, and evidence gaps (related to these policy needs 2021-2023)* |
| 15:50-16:00 | Summary of Day 2 | Chair |
| **4 March 2021**<br>**13:00 –16:00 Geneva time** | | **Chair: Lindiwe Mvusi** |
| **Session 3: WHO TB policy guidance: current status, update plans and evidence gaps [Part 3]** | | |
| 13:00-13:10 | Agenda items | Chair |
| 13:10- 14:00 | **Special needs in TB** *(Ernesto Jaramillo, Kerri Viney)*<br>*Discussants: Delia Boccia, Carrie Tudor* | *Presentations will cover planned updates to TB policy guidance (2021), and overview of the evidence landscape 2021-2023*<br>*Discussant will reflect on emerging TB policy development needs, and evidence gaps (related to these policy needs 2021-2023)* |
| **Session 4: Enhancing the implementation of global TB guidance** | | |
| 14:00-15:00 | WHO efforts to support the implementation of global TB policy *(Dennis Falzon)*<br>• *WHO Knowledge Sharing Platform* | *This session seeks to discuss WHO's efforts in assisting countries adapt evidence-based guidelines for decision* |

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| | • Surveys of global TB policy<br>• Operational and implementation research<br>• Adapting to the impact of COVID-19<br><br>*Discussants: Mike Frick; Imran Pambudi, Srinath Satyanarayana* | *making, and to exchange views on strategies that may be followed to improve country-owned scale-up of evidence-based interventions* |
| 15:00-15:45 | Roundtable discussion on further promoting and evaluating the implementation of TB policy guidance:<br><br>1. What more can WHO do to enhance the implementation and scale-up of proven interventions?<br>2. How can WHO engage with partners to enhance country-led and -owned implementation and scale-up of interventions? | |
| 15:45 – 16:00 | Summary and way forward | Tereza Kasaeva<br>Chair |

## Annex 2: Participant list

1. **Helen Ayles**
Research Director
Zambart Project
Lusaka, Zambia

2. **Draurio Barreira**
Technical Manager
UT/UTD UNITAID International
drug purchase facility
Geneva, Switzerland

3. **Delia Boccia**
Assistant Professor
Faculty of Public Health and Policy
The London School of Hygiene &
Tropical Medicine
London, United Kingdom

4. **Daniela Cirillo**
Head
Emerging Bacterial Pathogens Unit
San Raffaele Scientific Institute (HSR)
Milan, Italy

5. **Jeremiah Muhwa Chakaya**
Professor
Global Respiratory Health
The London School of Hygiene &
Tropical Medicine
Liverpool, United Kingdom

6. **Daniel Chin**
Deputy Director
Global Health
Bill and Melinda Gates Foundation
Seattle, WA, USA

7. **Gerry Davies**
Professor
Infection Pharmacology and
Honorary Consultant in
Infectious Diseases
University of Liverpool
Liverpool, United Kingdom

8. **Fernanda Dockhorn Costa**
Coordinator
Chronic and Airborne Disease
Surveillance Coordination
Health Surveillance Department
Ministry of Health
Brasilia, Brazil

9. **Mike Frick**
Senior Project Officer, TB/HIV
Treatment Action Group
New York, NY, USA

10. **Rumina Hasan**
Professor
Pathology and Microbiology
Aga Khan University
Karachi City, Pakistan

11. **Anneke Hesseling**
Professor and Director
Pediatric TB Research Programme
Desmond Tutu TB Centre
Stellenbosch University
Stellenbosch, South Africa

12. **Rafael Laniado**
Head
TB Clinic and Laboratory
Tijuana, Mexico

13. **YaDiul Mukadi**
Senior TB Technical Advisor
Infectious Disease Division
Global Health Bureau
USA Agency for International
Development (USAID)
Washington D.C., USA

14. **Lindiwe Mvusi**
Director
TB Control and Management
National Department of Health
Pretoria, South Africa

15. **Binh Hoa Nguyen**
Vice Manager and Secretary
National TB Control Programme
Secretary, NTP Vietnam
Coordinator, Vitenam Global Fund
TB Project
Hanoi, Viet Nam

16. **Imran Pambudi**
National TB Program Manager
Ministry of Health of the
Republic of Indonesia
Jakarta, Indonesia

**17. Anastasia Samoilova**
First Deputy Director
National Medical Research
Centre on Phthisiopulmonology
and Infectious diseases
Moscow, Russia

**18. Srinath Satyanara**
Deputy Director
Center for Operational Research
International Union Against
Tuberculosis and Lung Disease
The Union
Paris, France

**19. Ezio Tavora**
Civil Society Task Force Member (CSTF)
Rio de Janeiro, Brazil

**20. Carrie Tudor**
TB Project Director
International Council of Nurses
Durban, South Africa

**21. Zhao Yanlin**
Director
National Center for TB Control and
Prevention, Chinese Center for
Disease Control and Prevention
Director
National Tuberculosis Reference
Laboratory of China CDC
Beijing, China

**22. Mohammed Yassin**
Senior Disease Advisor
The Global Fund to Fight AIDS,
Tuberculosis and Malaria
Geneva, Switzerland

### WHO Regional Offices

**AFRO**

**23. Michel Gasana**
Medical Officer
DR-TB  and rGLC Focal Point

**24. Hugues Lago**
Coordinator HIV, Tuberculosis
and Hepatitis

**AMRO/PAHO**
**25. Ernesto Montoro**
Advisor
Laboratory Integration

**26. Freddy Perez**
Advisor
Communicable Diseases Research

**SEARO**

**27. Partha Pratim Mandal**
TB Medical Officer

**EURO**
**28. Askar Yedilbayev**
Unit Leader
Joint Tuberculosis. HIV/AIDS &
Hepatitis Programme (JTH)

**29. Andrei Dadu**
Medical Officer
Division of Country Health Programmes

**30. Oleksandr Korotych**
Consultant
Research Innovation

**EMRO**
**31. Kenza Bennai**
Regional Advisor for TB

**WPRO**
**32. Fukushi Morishita**
Technical Officer
End TB and Leprosy

### WHO/GTB

**33. Tereza Kasaeva, GTB Director**
**34. Matteo Zignol, Unit Lead, PCI**
**35. Farai Mavhunga, Unit Lead, VCC**
**36. Dennis Falzon, Team Lead, PCI**
**37. Nazir Ismail, Team Lead, PCI**
**38. Fuad Mirzayev, Team Lead, PCI**
**39. Annabel Baddeley, VCC**
**40. Annemieke Brands, VCC**
**41. Nebiat Gebreselassie, PCI**
**42. Ernesto Jaramillo, PCI**
**43. Avinash Kanchar, PCI**
**44. Tiziana Masini, VCC**
**45. Cecily Miller, PCI**
**46. Kerri Viney, PCI**
**47. Sabine Verkuijl, VCC**

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