Latent tuberculosis infection: Updated and consolidated guidelines for programmatic management

Background document on the 2019 revision

WHO Global TB Programme

28 June 2019
Contents

Acronyms and abbreviations ............................................................................................. 3

1 Scope of the proposed guideline update ....................................................................... 4
  1.1. Background and rationale for the proposed update .............................................. 4
  1.2. Goal and objectives of the guideline update ....................................................... 5
  1.3. Target audience ................................................................................................... 5
  1.4. Persons affected by the recommendations .......................................................... 5
  1.5. Related WHO guidelines .................................................................................... 5
  1.6. Proposed updates to the existing guidelines ...................................................... 6

2 Contribution of expert groups to the update .............................................................. 7
  2.1 WHO Guideline Steering Group ........................................................................... 7
  2.2 Guideline Development Group (GDG) ................................................................. 7
  2.3 External Review Group (ERG) ............................................................................. 7

3 Management of the Guideline Development Group ....................................................... 8
  3.1 GDG leadership and oversight ............................................................................. 8
  3.2 Declarations of interest ....................................................................................... 8
  3.3 Decision making .................................................................................................. 8

4 Methods for the update of guidance .......................................................................... 9
  4.1 PICO questions ................................................................................................... 9
  4.2 Evidence retrieval ................................................................................................ 11

5 Planning Timeline ....................................................................................................... 12

6 Presentation and dissemination of the guidelines ....................................................... 12

7 Quality assessment of the guideline .......................................................................... 13

8 Updating the guidelines ............................................................................................ 13

9 References .................................................................................................................. 13

Annex 1. Guideline Development Group members ......................................................... 16
Annex 2. External Review Group members .................................................................. 17
Annex 3. Observers ...................................................................................................... 17
Annex 4. Brief biographies of GDG members ................................................................. 18
Acronyms and abbreviations

1HP One month of rifapentine plus isoniazid daily
3HP Three months of rifapentine plus isoniazid weekly
4R Four months of rifampicin daily
ART antiretroviral treatment
CoI conflict of interest
ERG External Review Group
EtD GRADE Evidence to Decision framework
GDG Guideline Development Group
GRADE Grading of Recommendations Assessment, Development and Evaluation
GRC WHO Guideline Review Committee
GTB Global TB Programme
H isoniazid
HIV human immunodeficiency virus
IGRA Interferon-Gamma Release Assays
INSTI integrase strand transfer inhibitor class of ART
IPT isoniazid preventive therapy
LTBI latent tuberculosis infection
M. tuberculosis Mycobacterium tuberculosis
MDR/RR-TB multidrug- or rifampicin-resistant tuberculosis
NNRTI non-nucleoside reverse-transcriptase inhibitor class of ART
P rifapentine
PI protease inhibitor class of ART
PICO Population, Intervention, Comparator, Outcomes
PLHIV people living with HIV
R rifampicin
RCT randomized controlled trial
TB tuberculosis
TNF tumour necrosis factor
1 Scope of the proposed guideline update

1.1. Background and rationale for the proposed update

Globally, there were an estimated 10.0 million incident tuberculosis (TB) cases and 1.6 million TB deaths in 2017(1). About one fourth of the world’s population is estimated to be infected with *M. tuberculosis*(2). In order to end the global TB epidemic, the WHO End TB Strategy considers the treatment of latent tuberculosis infection (LTBI) as critical(3). Effective treatment of LTBI has been shown to reduce the risk of progression and its scale-up can thus contribute to bringing down global TB incidence to the levels envisaged by the End TB Strategy. In September 2018, at the first ever UN High Level Meeting on Tuberculosis, Member States committed to ambitious global targets which included provision of TB preventive treatment to 30 million individuals by 2022 (up from a current global coverage of about 1 million per year)(4). Countries therefore anticipate a rapid scale-up of TB preventive treatment among people living with HIV (PLHIV) and all other target populations. LTBI involves a persistent immune response to stimulation by *M tuberculosis* antigens without evidence of clinically manifested active TB(5). The vast majority of infected persons have no signs or symptoms of TB disease and are not infectious, but they are at risk for developing active TB disease and becoming infectious. Several studies have shown that, on average, 5-10% of those infected will develop active TB over the course of their lives, with the majority developing TB disease within the first 2-5 years after the initial infection(6). The individual risk of progression to active TB disease, however, is strongly affected by number of risk factors. People belonging to high risk populations will be targeted for LTBI management.

WHO published the updated and consolidated guidelines for programmatic management of LTBI in 2018(7). These guidelines superseded the previous WHO policy documents on management of LTBI among PLHIV, household contacts of people with active TB and other target groups at risk of developing TB. For the first time the 2018 guidelines provided recommendations for high burden countries on target populations beyond PLHIV and child household contacts of TB patients, on use of shorter rifamycin based TB preventive treatment and on use of tuberculin skin test (TST) or Interferon Gamma Release Assay (IGRA) test for LTBI.

However, since the release of 2018 WHO guidance, two landmark trials looking at the shortening of preventive treatment using rifamycins involving high TB burden countries were published(8),(9),(10). Shorter treatment can enhance the scalability of preventive treatment by improving adherence and completion as well as the safety profile. In addition to these two studies, adverse pregnancy outcomes and other safety concerns were reported from one trial among female PLHIV exposed to isoniazid, the most widely used LTBI treatment option recommended by WHO(11). Finally, WHO received feedback since the 2018 guidelines were released pointing to areas that could benefit from further clarifications and additional operational advice to facilitate implementation.

In the light of these new developments and continued demand by Member States for guidance on how to enhance the coverage and performance of TB preventive treatment services, an update of the consolidated LTBI guidelines 2018 is proposed to ensure that it continues to be driven by the latest available evidence.
1.2. Goal and objectives of the guideline update

The overall goal of this guideline revision is to support a more effective global scale up of TB preventive treatment and contribute to ending the TB epidemic.

The specific objectives are to

(i) provide a broader menu of shorter TB preventive treatment options aligned with the best available evidence on effectiveness and safety; and
(ii) enhance operational guidance by clarifying existing recommendations and accompanying remarks, updating additional background knowledge on the safety of current regimens and simplifying dosing schedules

This guideline update will allow policy makers in ministries of health and medical staff to choose the best suited LTBI management approach for all target groups depending on the context. It will also provide a sound basis for the development or the update of national guidelines for LTBI management based on the epidemiology of TB and the health care delivery system in the country. Furthermore, the guideline will address the request from Member States asking for one comprehensive policy document for the programmatic management of LTBI.

1.3. Target audience

The proposed guideline update is intended to benefit health care workers implementing TB preventive services in all WHO Member States, regardless of TB epidemiology. The guidelines specifically target staff in the national TB programmes, national AIDS programmes or their equivalents in the Ministries of Health; other health policy makers, clinicians and public health practitioners working on TB and HIV and infectious diseases in public and private sectors, in the Ministry of Justice or Correctional Services, and other line ministries working on prison health services.

1.4. Persons affected by the recommendations

Individuals with the highest risk of progression to active disease such as PLHIV (including pregnant and postpartum women), adult and child contacts of pulmonary TB cases, patients initiating anti-tumour necrosis factor (TNF) treatment, patients receiving dialysis, patients preparing for organ or haematologic transplantation, and people with silicosis.

1.5. Related WHO guidelines

The new updated and consolidated guidelines for programmatic management of LTBI will also be relevant for the following guidelines:

3. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. Recommendations for a public health(14).
Updates to these documents will be done at the next available opportunity to reflect any changes to be made to the 2018 LTBI treatment policies following the proposed review.

1.6. Proposed updates to the existing guidelines

WHO is appointing external experts to a Guideline Development Group (GDG) and External Review Group (ERG) to review new findings and recommend changes to existing evidence-based recommendations, in line with WHO Guideline Review Committee (GRC) requirements (15)(GDG and ERG membership listed at Annexes 1 and 2). Revision of new evidence and formulation of recommendations that will be conducted using the GRADE (Grading of Recommendations Assessment, Development and Evaluation) approach(16). The GDG will convene two virtual meetings via Webex (see more details in Section 2 below). The initial scoping for the work envisaged has been prepared by the WHO Guideline Steering Group, based on a provisional review of the relevant studies.

Firstly, the GDG will assess the performance of a regimen with one month of rifapentine plus isoniazid daily (1HP) and its potential applicability to target groups other than those included in the trial(10), such as contacts of TB patients in high TB burden countries. Secondly, the GDG will review evidence on the use of 4-months rifampicin daily (4R) among both children and adult contacts of TB patients, PLHIV and other target groups in high TB burden settings(8),(9). If these regimens are approved they would increase the treatment options already recommended by WHO. Thirdly, current WHO guidelines recommend the use of isoniazid preventive treatment (IPT) among pregnant women subject to certain conditions and clinical judgement. Given a recent report of higher frequency of adverse pregnancy outcomes in women with HIV exposed to isoniazid in pregnancy the GDG will review available data and decide whether updates to the recommendations or conditions of use need to change.

The rest of the 2018 guidelines is expected to remain valid and will be reproduced in the update. Edits to the wording of existing guidelines may be needed to improve their clarity and implementation. These changes will be discussed and approved by the GDG members. It is envisaged that these new changes will involve the following:

1. Removing the distinction between high and low TB incidence countries for the LTBI treatment recommendations that actually apply to all settings (excepting 36 months of H in PLHIV). Any cautions on the proper application of these recommendations will be highlighted in the remarks accompanying the recommendation. The arbitrary threshold of TB incidence of 100 TB cases per 100,000 used to demarcate between low and high settings will also be reviewed by the GDG.
2. Aligning the algorithm requiring LTBI test confirmation with the text in existing guidelines.
3. Rewording of remarks on the safety of co-administration of 3HP with dolutegravir-based ART to reflect recent trial findings(17).
4. Simplifying the drug dosing schedule for 3HP in children and adults based on a review of pharmacokinetics data and in discussion with other experts from WHO’s Global task force on the pharmacokinetics and pharmacodynamics (PK/PD) of TB medicines (18),(19).
2 Contribution of expert groups to the update

2.1 WHO Guideline Steering Group
The WHO Global TB Programme has appointed a WHO Guideline Steering Group composed of WHO staff from the Global TB Programme; the Department of HIV/AIDS and Hepatitis; the Department of Information, Evidence and Research; and the Department of Essential Medicines and Health Products. This group undertook the initial scanning for fresh evidence that required a review with a view to revision of existing recommendations or formulation of new ones. This first scoping exercise resulted in the drafting of the PICO questions and proposed process for evidence retrieval and grading. In addition, the Group is responsible for the selection of the members of the GDG and ERG. The Steering Group will also organize webinars with the GDG and trial investigators, will oversee the writing of the guideline meeting report, its submission to the GRC and the finalization of the updated guidelines.

2.2 Guideline Development Group (GDG)
The GDG will be made up of external experts whose central task is to formulate evidence-based recommendations. In order to maintain continuity in both procedures and the content of the guidelines, the majority of GDG experts - 13 of the 18 members – had already served on the 2018 LTBI guidelines update (Annex 1; biographies in Annex 4). Some members have been replaced because of unavailability, emergent conflict of interest (Col), and to ensure a balance in representation of technical expertise, gender and geography of the group. Given the limited scope of the review being addressed no face-to-face meeting is being held and the group will communicate through email and webinar to complete its work. The GDG members will finalize the guideline questions, the scoring of outcomes, comment on the evidence to be reviewed, complete the GRADE tables, formulate any new or updated recommendations and approve the final document. The GDG members have submitted their CVs, declarations of interest and signed confidentiality undertaking. All declared interests of confirmed GDG members will be reported in the final guideline document. Representatives of funding agencies and other observers will also be invited to attend the webinars (Annex 3).

2.3 External Review Group (ERG)
The ERG will be composed of experts with a similar profile to the GDG members and with technical competence in the subject of the guidelines (Annex 2). Members will be asked to review the draft version of the guidelines as updated by the GDG and provide peer-review comments in line with the GRC requirements(15). The contribution of the ERG will be incorporated in the final version of the Guidelines. The ERG members have all served in a similar capacity in past WHO guideline processes. Declarations of interest and signed confidentiality undertakings will also be required of members of the ERG. The steering group will assess comments by ERG members for validity on a case-by-case basis and any significant concerns may need to be discussed with the GDG chairs and members.

A public call for volunteers to review the new guidance before its finalization will be made in July 2019. The public review will be conducted alongside the ERG examination of the guidance and will also be subject to a confidentiality agreement by contributors.
3 Management of the Guideline Development Group

3.1 GDG leadership and oversight

The work of the GDG members will be stewarded by a guideline methodologist and a content expert who will jointly chair the group.

Dr Nandi Siegfried, who was the methodologist for the 2018 LTBI guidelines update, will continue to serve in this capacity. This will include the scoping, the preparation of the evidence summaries and the proper application of evidence to decision (EtD) tables in accordance with GRADE. Dr Siegfried is an independent clinical epidemiologist and public health physician based in Cape Town, South Africa. She has worked for a decade at senior management level at the South African Medical Research Council, where she was co-director of the South African Cochrane Centre and Deputy Coordinating Editor of the Cochrane HIV/AIDS Review Group. As an independent consultant, she provides technical support to international, national, institutional and non-government agencies in the healthcare sector. She has served as Chair, Technical Advisor and/or Methodologist to several TB and HIV WHO Clinical Guideline Development Groups in recent years.

Dr. Lindiwe Mvusi will serve as the main content expert for the GDG. She is a public health physician and Director of the TB Control and Management Cluster, at the National Department of Health of South Africa, effectively fulfilling most of the responsibilities of a national TB programme manager. She has extensive experience in the development and implementation of clinical guidelines including TB/HIV and LTBI.

3.2 Declarations of interest

All members of the GDG and the ERG have been asked to provide a written declaration of interest using standard WHO forms. The WHO secretariat will perform additional background checks on GDG members via Internet. Any potential CoI – financial or otherwise - will be evaluated by the Steering Group - in consultation with the WHO Office of Compliance, Risk Management and Ethics whenever necessary - to assess whether the conflict warrants moderation of the member’s inputs, recusal from some sessions or outright exclusion from the GDG. In accordance with the WHO policy on CoI and to strengthen public trust and transparency, WHO/GTB will post on its website the names and brief biographies of all GDG members at least two weeks prior to the GDG meeting. At the GDG meeting the declaration of interests will be summarized and presented to the entire group so that the group is aware of any CoI that may exist among the members. Each member will be offered the opportunity to update and/or amend their declaration at the start of the guideline discussions. All declared interests will be reported in the final guideline document.

3.3 Decision making

During the GDG meeting, the Group will be responsible for formulating the language and strength of the recommendations based on the evidence compiled for these guidelines along with related background documents prepared by the WHO Guideline Steering Group. The certainty in the estimates of effect and the strength of recommendations will be rated using the GRADE approach. GRADE tables will summarize details about the included studies by outcomes and their limitations, possible inconsistencies,
indirectness, imprecision and other factors that could influence the quality of evidence. To finalize recommendations, various factors including values and preferences, the balance of expected benefits to harms and confidence in the evidence, health equity, resource use, acceptability and feasibility will be considered by the GDG by using the GRADE Evidence to Decision (EtD) framework to capture the main elements of the discussions on the different dimensions ahead of the formulation of recommendations. The GRADEpro platform(20) will be used to centralize the information.

As far as possible decisions will be made through a process of consensus coordinated by the GDG chairs. Whenever unanimity cannot be achieved, the members of the GDG will vote and a majority of 60% or more of voting members will be necessary to accept a recommendation. For a strong recommendation, if the vote reaches this threshold but is less than 66%, the recommendation will be conditional. The plan for decision-making will be discussed and finalised between GDG members before the first meeting. The process of decision making, any voting results and the other views expressed will be reflected in the remark section of each the GRADE EtD tables. A draft WHO guideline based on the recommendations of the GDG will then be prepared by the WHO Guideline Steering Group and reviewed by the GDG and the ERG members before finalisation and submission to the GRC.

4 Methods for the update of guidance

4.1 PICO questions

The evidence retrieval and reviews relevant to this update will be guided primarily by three key questions formulated in the PICO (Population, Intervention, Comparator, Outcomes) format. The method used conforms to the WHO requirements and the GRADE method (21),(15) (see also Section 2 about experts involved in formulation). The evidence retrieved to address these questions and any recommendations that may ensue are expected to be added to the existing policy in the 2018 LTBI guidelines.

<table>
<thead>
<tr>
<th>PICO question 1:</th>
<th>In people of all ages at risk of active TB, does 1-month daily rifapentine plus isoniazid regimen safely prevent TB disease compared to other recommended TB preventive treatment regimens?</th>
</tr>
</thead>
<tbody>
<tr>
<td>P</td>
<td>Adults, Adolescents and Children at risk of active TB (contacts of TB patients not know to have MDR-TB or RR-TB). Sub-populations: PLHIV</td>
</tr>
<tr>
<td>I</td>
<td>1-month daily rifapentine and isoniazid</td>
</tr>
<tr>
<td>C</td>
<td>Other recommended TB preventive treatment regimen: Isoniazid monotherapy (daily 6-month, 9-month or 36-month, 3 months weekly isoniazid plus rifapentine, 3 months daily isoniazid plus rifampicin, 4 months rifampicin)</td>
</tr>
<tr>
<td>O</td>
<td>Active TB incidence, mortality, adverse events (esp. differential effect of daily vs. weekly rifapentine), treatment completion, emergence of drug resistance</td>
</tr>
</tbody>
</table>

This question will review evidence on the use of the 1HP regimen, which is currently available from one trial conducted among PLHIV(10). As far as possible the analyses will be stratified by age group and setting. Indirect comparisons of the effectiveness / safety of 1HP against 3-months weekly rifapentine and isoniazid (3HP) and other LTBI treatments not studied in the trial will be attempted to inform GDG discussions on the potential role of the new regimen in different “use cases”, including HIV negative,
high TB risk populations such as household contacts of TB patients. The outcomes will include indices of effectiveness (incidence, survival) and toxicity (adverse events, mortality, acquisition of resistance).

**PICO question 2:**
In people of all ages at risk of active TB, does 4-month daily rifampicin regimen safely prevent TB disease compared to other recommended TB preventive treatment regimens?

| P | Adults, Adolescents and Children at risk of active TB (contacts of patients not know to have MDR-TB or RR-TB)  
Sub-population: PLHIV  
Sub-populations: LTBI test positive/unknown |
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>4-month daily rifampicin</td>
</tr>
<tr>
<td>C</td>
<td>Isoniazid monotherapy (6-month isoniazid, 9-month isoniazid, or 36-month isoniazid, etc.)</td>
</tr>
<tr>
<td>O</td>
<td>Active TB incidence, mortality, adverse events, treatment completion, emergence of drug resistance</td>
</tr>
</tbody>
</table>

This question will review the evidence on use of 4-months daily rifampicin (4R) regimen for TB prevention among target populations including PLHIV and household contacts of TB patients(8),(9),(22). As far as possible the analyses will be stratified by age group and setting. Sub-group analyses will be performed among PLHIV, people of all ages who are household contacts of TB patients and other individuals at high risk of progressing to active TB. The role of shorter rifampicin containing preventive treatment regimen of 4 month compared to other recommended preventive treatment regimen including 6-9 months isoniazid, 3HP and 1HP will be discussed with the GDG. The outcomes will include indices of effectiveness (incidence, survival) and toxicity (adverse events, mortality, acquisition of resistance).

**PICO question 3:**
In pregnant and postpartum women, is isoniazid preventive treatment for TB as safe as other preventive treatment regimens?

<table>
<thead>
<tr>
<th>P</th>
<th>Sub populations: Women at different stages of pregnancy, Post-partum women, HIV positive women on ARVs (disaggregate by NNRTI based, PI based and INSTI based if possible), HIV positive women not on ARVs, HIV negative women</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Daily isoniazid alone (of varying duration - &lt;6 months, &gt;=6 months)</td>
</tr>
<tr>
<td>C</td>
<td>Regimens other than isoniazid alone or no preventive treatment</td>
</tr>
</tbody>
</table>
| O* | Maternal outcomes: permanent drug discontinuation due to toxicity, maternal adverse drug reactions, maternal hepatotoxicity  
Pregnancy outcomes: In utero foetal death, neonatal death or stillbirth (all-cause), preterm delivery / prematurity, low birth weight, congenital anomalies |

*TB incidence - active TB in mother or infant-- is not included because this PICO is focused on the safety of IPT, given that there are no grounds to dispute its effectiveness, as shown from other studies and extrapolated from other populations

Pregnant women with HIV have a high risk of acquiring TB, which can have severe consequences for both mother and the foetus(23). Pregnancy should not disqualify PLHIV from receiving preventive treatment with isoniazid, which has a well-documented safety profile established from its long history of use in pregnant and breastfeeding mothers treated for both latent and active TB. The 2018 WHO LTBI guideline
however advises caution and clinical judgement when deciding the best time to start LTBI treatment. Although there is insufficient evidence to support testing of baseline liver function, WHO encourages clinical monitoring, where feasible, for individuals at increased risk of drug-induced liver toxicity, including pregnancy and 3 months postpartum. Preliminary results from a clinical trial presented at the Conference on Retroviruses and Opportunistic Infections (CROI) in 2018 reported higher adverse pregnancy outcomes among female PLHIV exposed to isoniazid during gestation(11). These findings motivated a review of safety outcomes in pregnant and postpartum women who received IPT, HIV positive or otherwise. PICO question 3 will aim to stratify the analysis by HIV and ART status, stage of pregnancy and setting. Given that there is no fresh evidence challenging the efficacy of IPT in pregnancy the outcomes will focus only on safety to the mother and infant. To review safety data especially among PLHIV for which the number of studies is expected to be limited we will include observational studies in addition to RCTs. The quality of evidence will be assessed, and recommendations will be developed using the GRADE methodology.

4.2 Evidence retrieval

For PICO questions 1 and 2, the principal investigators of the two trials will be invited to report numbers and rates from their respective published work for effects that are relevant to the main outcomes and subgroups using the GRADE evidence profile. The estimates of effect and associated footnotes will be cross-checked by the WHO technical leads from the Steering Group and then reviewed by the GRADE methodologist, who will also jointly undertake the quality assessment. The draft GRADE evidence profiles will be presented to the rest of the GDG for discussion and ahead of populating the GRADE EtD frameworks.

For PICO question 3 a systematic review for relevant, published evidence from trials and observational studies will be performed by an independent consultant. PubMed and other potential sources of published data will be included in the search. The search strategy will combine MeSH/EMTREE terms and other text and will be developed by the reviewer in consultation with the Steering Group and GDG members (discussion with WHO Library is also envisaged once the search text will be drafted by the reviewer). When the list of references found after the search has been drawn up and screened for relevant studies by the reviewer it will be shared with the GDG members so that they can propose any other studies they feel may also be useful. If any unpublished studies are to be included background information about the source will be provided as a summary. Full text reviews of all identified studies will be done. Where possible, the results of independent studies will be quantitatively synthesized by meta-analyses. If this is not feasible or appropriate due to heterogeneity, the results will be presented as tabulations with a narrative synthesis. Any estimates derived will be entered into a GRADE evidence summary table and quality of evidence will be assessed. The review report will also detail methods used with a PRISMA flow chart to present the results of the search, data extraction, and the inclusion and exclusion criteria applied. Edits to the existing guidance and extra operational details to be added to enhance clarity and implementation will be documented in the draft update being proposed with appropriate annotations that will be circulated to the GDG members and discussed ahead of the webinars.
5 Planning Timeline

<table>
<thead>
<tr>
<th>Event</th>
<th>Apr</th>
<th>May</th>
<th>June</th>
<th>July</th>
<th>Aug</th>
<th>Sept</th>
<th>Oct</th>
<th>Nov</th>
<th>Dec</th>
</tr>
</thead>
<tbody>
<tr>
<td>Convene WHO Guideline Steering Group</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Update proposal submission/approval by GRC</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Invite experts to Guideline Development Group</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Finalize PICOs and score outcomes</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Conduct systematic review and GRADE evidence summaries</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Background material of the guidelines including GDG member biographies published online; public call for reviewers</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Virtual meeting of the Guideline Development Group and drafting of recommendations</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Draft the guideline with comments from the Guideline Development Group</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Peer review of the guidelines by the External Review Group and others</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Submit the guidelines for GRC approval</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Finalization and translation into French, Russian and Spanish</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Release of updated guidelines</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

6 Presentation and dissemination of the guidelines

The guideline document will reproduce all recommendations from the 2018 guidelines as well as the updated recommendations from the current revision. We propose to work with the LTBI task force and other partners to incorporate the new recommendations into an operational guide in 2020. This will include “how to” details relevant for country implementation (e.g. “decision aids”, algorithms, dosing schedules, indicators).

The final draft will be formatted for print and a small-sized PDF file will be made available on the WHO/GTB website for free download to replace the 2018 document. The final guidelines will be printed in English and translated into French, Spanish, and Russian. Once finalized and posted on the web, notification emails will be sent out to all relevant email listservs (e.g. GTB listserv, the Global TB Laboratory Initiative and the Stop TB Partnership). Copies will also be sent to subscribers to WHO publications and to others on the WHO mailing lists (national chief health executives, ministers of health or directors-general of health, repository libraries for WHO publications, WHO representatives/liaison officers, WHO headquarters library, WHO Regional Offices and off-site offices libraries). Print copies will also be made available for sale at the WHO bookshop in Geneva.

The recommendations will be communicated widely by WHO and partner technical staff through audio-visual means, either in-person or remotely at different workshops organized at regional and country level.
Adaptations and integration of the new guidance into national TB and AIDS strategic plans are typically discussed during such meetings as well as country evaluation missions, taking into consideration local epidemiologic, cultural and socio-economic contexts. Resources will be solicited from external and domestic sources for this purpose. Upcoming international and regional HIV, TB and infectious diseases scientific conferences will be used to disseminate the guidelines updates too (e.g. IAS, CROI, UNION).

7 Quality assessment of the guideline
The impact of the guidelines will be assessed during meetings of the national TB programme managers held periodically by the WHO regional offices and during country missions.

Elements of the updated recommendations, such as the adoption of rifamycin-containing regimens and coverage of LTBI treatment, will be monitored during the annual cycles of country data collection organized by the WHO Global TB Programme ahead of the preparation for the Global TB Reports. Independent studies reviewing the impact of WHO LTBI policies (e.g. (24),(25)) or analyzing progress in management areas will also be monitored to assess the need for updates.

8 Updating the guidelines
The recommendations included in the proposed guidelines will be considered for update in 5 years’ time. Meanwhile the WHO Global TB Programme will continually monitor the availability of new evidence and assess the need to change the recommendations even earlier if necessary.

9 References


Annex 1. Guideline Development Group members

<table>
<thead>
<tr>
<th>Name</th>
<th>Affiliation</th>
<th>Sex</th>
<th>WHO region</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Mohammed Al Lawati*</td>
<td>Department of Communicable Disease Surveillance &amp; Control DGHA Ministry of Health, Oman</td>
<td>M</td>
<td>EMR</td>
</tr>
<tr>
<td>2. Helen Ayles*</td>
<td>Infectious Diseases and International Health, LSHTM, Lusaka, Zambia</td>
<td>F</td>
<td>AFR</td>
</tr>
<tr>
<td>3. Rolando A. Cedillos*</td>
<td>Servicio de Infectología y Programade Atención Integral en ITS/VIH/SIDA, San Salvador, El Salvador</td>
<td>M</td>
<td>AMR</td>
</tr>
<tr>
<td>4. Padmapriyadarsini Chandrasekaran*</td>
<td>National Institute for Research in Tuberculosis, India</td>
<td>F</td>
<td>SEAR</td>
</tr>
<tr>
<td>5. Diana Gibb*</td>
<td>Professor of Epidemiology and Programme Leader, MRC Clinical Trials Unit, University College London, UK</td>
<td>F</td>
<td>EUR</td>
</tr>
<tr>
<td>6. Stephen Graham*</td>
<td>Center for International Child Health University of Melbourne, Australia</td>
<td>M</td>
<td>WPR</td>
</tr>
<tr>
<td>7. Yohhei Hamada</td>
<td>JICA, Philippines</td>
<td>M</td>
<td>WPR</td>
</tr>
<tr>
<td>8. Anthony D Harries</td>
<td>International Union Against Tuberculosis and Lung Disease, Paris, France; London School of Hygiene and Tropical Medicine, London, UK</td>
<td>M</td>
<td>EUR</td>
</tr>
<tr>
<td>9. Alexander Kay</td>
<td>Baylor College of Medicine, Global TB Program, Eswatini</td>
<td>M</td>
<td>AFR</td>
</tr>
<tr>
<td>10. Nasehi Mahshid*</td>
<td>Department of TB and Leprosy Control- Center for Control of Communicable Diseases- Ministry of Health and Medical Education, Iran</td>
<td>F</td>
<td>EMR</td>
</tr>
<tr>
<td>11. Alberto Matteelli*</td>
<td>Associate Professor, Clinic of Infectious and Tropical Diseases; University of Brescia and Brescia Ospedali, Italy</td>
<td>M</td>
<td>EUR</td>
</tr>
<tr>
<td>12. Lindiwe Mvusi*</td>
<td>TB Control and Management Cluster National Department of Health, Pretoria, South Africa</td>
<td>F</td>
<td>AFR</td>
</tr>
<tr>
<td>13. Kuldeep Singh Sachdeva</td>
<td>National TB programme, India</td>
<td>M</td>
<td>SEAR</td>
</tr>
<tr>
<td>14. Nandi Siegfried (Chair)*</td>
<td>Independent Consultant, South Africa</td>
<td>F</td>
<td>AFR</td>
</tr>
<tr>
<td>15. Ezio Távora dos Santos Filho</td>
<td>c/o CS Task Force (Brazil)</td>
<td>M</td>
<td>AMR</td>
</tr>
<tr>
<td>16. Marieke van der Werf*</td>
<td>European Centre for Disease Prevention and Control (ECDC), Stockholm, Sweden</td>
<td>F</td>
<td>EUR</td>
</tr>
<tr>
<td>17. Wim Vandevelde*</td>
<td>Chair TBCAB (Global TB Community Advisory Board) Cape Town, South Africa</td>
<td>M</td>
<td>AFR</td>
</tr>
<tr>
<td>18. Irina Vasilyeva*</td>
<td>Central TB Research Institute, Russian Academy of Medical Sciences, Russian Federation</td>
<td>F</td>
<td>EUR</td>
</tr>
</tbody>
</table>

* served as GDG members on the WHO LTBI guidelines of 2018
### Annex 2. External Review Group members

<table>
<thead>
<tr>
<th>Name</th>
<th>Affiliation</th>
<th>Sex</th>
<th>WHO Region</th>
</tr>
</thead>
<tbody>
<tr>
<td>2. Giovanni B. Migliori</td>
<td>Maugeri Research Centre, Tradate, Italy</td>
<td>M</td>
<td>EUR</td>
</tr>
<tr>
<td>3. Nguyen Viet Nhung</td>
<td>National TB Programme, Viet Nam</td>
<td>M</td>
<td>WPR</td>
</tr>
<tr>
<td>4. Rohit Sarin</td>
<td>National Institute of TB and Respiratory Diseases, Delhi, India</td>
<td>M</td>
<td>SEAR</td>
</tr>
<tr>
<td>5. James Seddon</td>
<td>Imperial College, London, UK</td>
<td>M</td>
<td>EUR</td>
</tr>
<tr>
<td>6. Alena Skrahina</td>
<td>Republican TB Centre, Minsk, Belarus</td>
<td>F</td>
<td>EUR</td>
</tr>
<tr>
<td>7. Carrie Tudor</td>
<td>International Council of Nurses, S Africa</td>
<td>F</td>
<td>AFR</td>
</tr>
</tbody>
</table>

### Annex 3. Observers

<table>
<thead>
<tr>
<th>Name</th>
<th>Affiliation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Sevim Ahmedov</td>
<td>USAID</td>
</tr>
<tr>
<td>2. Mohammed Yassin</td>
<td>GFATM</td>
</tr>
<tr>
<td>3. Draurio Barreira Cravo Neto</td>
<td>UNITAID</td>
</tr>
<tr>
<td>4. Anand Date</td>
<td>US CDC</td>
</tr>
<tr>
<td>5. Harry Hausler (CS Task Force)</td>
<td>TBHIV Care, S Africa</td>
</tr>
</tbody>
</table>
Annex 4. Brief biographies of GDG members
* served as GDG members on the WHO LTBI guidelines of 2018

Mohammed Redha Al Lawati*
Institutional affiliation(s): Consultant Physician, Former Head of National HIV/AIDS, TB & Leprosy Control Programs
Academic degrees: MBBS, MSc
City and country of primary residence: Muscat, Oman
Biography: Dr Mohammed Al Lawati was trained in Respiratory Medicine in Brompton Hospital London and in Respiratory & HIV Medicine in St. Vincent’s Hospital and St. George’s Hospital Sydney. After returning from his training, he played key role in developing Respiratory, HIV and Tuberculosis Services in Oman. He currently serves as Consultant Physician in Muscat Private Hospital in Oman and until recently, as Head of National AIDS, TB and Leprosy Control Programs in MOH, Oman. Dr Mohammed has participated in teaching of undergraduate students and in 1999 was awarded as one of the best clinical tutors by Sultan Qaboos University. He also actively participates in the training of doctors in management of Asthma, HIV and Tuberculosis and has played pivotal role in forming National Guidelines for the management of Tuberculosis, Asthma and HIV/AIDS. Dr Mohammed has published papers in national and international journals on tuberculosis and HIV/AIDS. He is the founding member of Oman Respiratory Society and previously has served as its Vice President. He served as member of Global Validation Advisory Committee of WHO, for Elimination of Mother to Child Transmission of HIV infection.

Helen Ayles*
Institutional affiliation(s): Professor of Infectious Diseases and International Health, LSHTM, Director of Research Zambart, Consultant Infectious Diseases Physician
Academic degrees: MBBS, MSc, PhD
City and country of primary residence: Lusaka, Zambia
Biography: Helen Ayles is a Professor of Infectious Diseases and International Health in the Clinical Research Department at the London School of Hygiene and Tropical Medicine and has lived in Zambia for 20 years working at Zambart in Lusaka. After training in clinical infectious and tropical diseases in the UK she trained in epidemiology at the London School of Hygiene and Tropical Medicine. Helen’s research interest is in the combined epidemics of TB and HIV and in the evaluation of large public health interventions. Helen has conducted research into the new diagnostics for TB, HIV and TB infection as well as the implementation of TB and HIV prevention strategies in resource limited settings. She is the Zambia principal investigator for the PopART trial (HPTN071), a large community-randomized trial of treatment as prevention for HIV and the overall PI of the TREATs consortium, and EDCTP funded study evaluating he effect of the PopART intervention on tuberculosis.
Rolando A. Cedillos*

_Institutional affiliation(s):_ Chief of Infectious Diseases at Hospital Nacional Rosales and Professor of Medicine at the University of El Salvador.

_Academic degrees:_ M.D. MSc. DTM&H

_City and country of primary residence:_ San Salvador, El Salvador

_Biography:_ graduated as a Medical Doctor in from the University of El Salvador and completed his residency in Internal Medicine at the Hospital Nacional Rosales in El Salvador in 1996. He holds an MSc in Infection & Health in the Tropics (Tropical Medicine & International Health) from the London School of Hygiene & Tropical Medicine and a Diploma in Tropical Medicine & Hygiene from the Royal College of Physicians, United Kingdom in 1997. Since 1998 he is Chief of Infectious Diseases at Hospital Nacional Rosales and Professor of Medicine at the University of El Salvador. In his country he has been a long-standing member of the TB and HIV committees of the Ministry of Health on national guidelines. He has collaborated with the World Health Organization (WHO) and the Pan American Health Organization (PAHO) in the development of clinical management of TB/HIV. Since 2017 he is a member of the PAHO TB Technical Advisory Group. He is the author and presenter of works on the natural history of HIV, TB/HIV, access to antiretroviral treatment in Central America and of the book _“La Epidemiá Invisible” Historias del SIDA en El Salvador._

Padmapriyadarsini Chandrasekaran*

_Institutional affiliation(s):_ Deputy Director (Medical); National Institute for Research in Tuberculosis, [Indian Council for Medical Research], Mayor Sathyamoorthy Road, Chetput, Chennai 600 031

_Academic degrees:_ M.B.B.S; D.N.B; M.S. (CR)

_City and country of primary residence:_ Chennai, India

_Biography:_ Dr. C. Padmapriyadarsini is a Clinician by training and is currently Deputy Director (medical) in the Department of Clinical Research at the National Institute for Research in Tuberculosis (NIRT) (formerly known as the Tuberculosis Research Centre), Chennai. She has a Short-term Fellowship in HIV epidemiology from University of California, Los Angeles and a master’s Degree in clinical and Translational Research from Tufts University Boston, USA. Over the last 15 years, she is involved in multiple clinical studies and trials involving HIV and TB coinfected adults and children at NIRT. She is the Principal investigator of multiple collaborative, multicentric projects, both at national and international level. She has more than 45 publications in peer reviewed national and International journals and 3 book chapters to her credit. She has been involved in framing National Guidelines for Management of Extrapulmonary TB (INDEX TB Guidelines) and Guidelines for the Introduction of Bedaquiline for drug resistant TB patients in the country. She is a member of the National Technical Group of RNTCP under Central TB Division as well as the National Technical Working group for HIV-TB under NACO, Ministry of Health and Family Welfare, Government of India
Diana Gibb*

Institutional affiliation(s): University College London

Academic degrees:
1977 MBChB Distinctions in Medicine, Paediatrics, Pathology (Subtle Gold medal for medicine) Bristol University
1979 Diploma Obstetrics and Gynaecology Auckland, New Zealand
1982 FRACP Paediatrics (Part 1) Royal Australian College Australia
1985 MRCP Paediatrics Royal College of Physicians, UK
1988 MD Markers of Renal Complications in Diabetic Children Bristol University
1990 MSc Epidemiology London School of Hygiene and Tropical Medicine

City and country of primary residence: Bristol, UK

Biography: Diana is professor of Epidemiology and Programme Leader of the Paediatric Programme of trials and cohorts at the MRC Clinical trials unit, London. Over the last 20 years she set up and coordinated a network of clinical trials and cohorts, across Europe, Thailand and South America mainly addressing questions in paediatric HIV infection. Since 1999 her focus has expanded to Africa and India where she runs large trials, addressing strategy questions in adult and paediatric HIV infection and doing phase III trials in malaria, tuberculosis and antimicrobials, collaborating widely with clinical and research centres in East and Southern Africa and India. Wide inter-disciplinary collaboration with health economists, pharmacologists, social and basic scientists and innovators of medicines for children are incorporated into trial programmes. Capacity development is an important feature of the overseas collaborations, including interactive courses in paediatric HIV, on-the-ground training in clinical trials and PhD mentorship. She serves on a number of WHO advisory and guideline committees and continues a clinical commitment at the HIV Family clinic at the Great Ormond Street Hospital for Children in London.

Stephen Graham*

Institutional affiliation(s): Centre for International Child Health, University of Melbourne, Australia, Consultant in child TB and lung health, The Union, France Senior Principal Research Fellow, The Burnet Institute, Australia, Group leader, International Child Health, Murdoch Children’s Research Institute, Melbourne

Academic degrees: MB BS, FRACP, DTCH, PhD

City and country of primary residence: Melbourne, Australia

Biography: Steve Graham is a paediatrician with over 20 years of clinical and research experience in resource-limited settings in a range of childhood diseases, including tuberculosis (TB), pneumonia and HIV. He has provided technical assistance on child TB to multiple National TB Programmes (NTPs) in the Asia-Pacific and African regions. Steve was Chair of the Stop TB Partnership and WHO’s Childhood TB subgroup from 2011 to 2016, is a member of WHO’s STAG TB, and Chair of WHO WPRO Taskforce on Child TB. He authored the international Childhood TB Roadmap (2013), WHO’s Guidance on child TB for NTPs (2006 and 2014), The Union’s Deskguide on child TB management, and in 2010 developed the recommendations for a new fixed-dose combinations for treatment of TB in young children. Steve’s research interest includes implementation of child TB contact screening and LTBI management in TB-endemic settings - including Malawi and in Indonesia, where
he supervised original prospective evaluation of WHO’s symptom-based child contact screening. He is currently collaborating on community-based child TB and contact screening projects in Viet Nam and Uganda. In 2015, he was awarded the Karel Styblo Public Health Prize for long-standing contributions to child TB and lung health.

**Yohhei Hamada**

*Institutional affiliation(s):* Medical Officer, Research Institute of Tuberculosis, Japan Anti-Tuberculosis Association, Japan  
*Academic degrees:* MD, MPH  
*City and country of primary residence:* Manila, The Philippines  
*Biography:* Dr. Hamada is a medical officer of the Research Institute of Tuberculosis, Japan. He is currently working with the Japan International Cooperation Agency (JICA) as an advisor for the national TB control program of the Department of Health, Philippines. From 2015 to 2017, he worked on policy and implementation of latent TB infection in the WHO Global TB Programme and coordinated the guidelines on the management of LTBI published in 2018. He obtained a doctorate in Medicine from Nagasaki University, Japan in 2008 and a Master of Public Health from Johns Hopkins Bloomberg School of Public Health in 2013.

**Anthony D Harries**

*Institutional Affiliations:* International Union Against Tuberculosis and Lung Disease, Paris, France; London School of Hygiene and Tropical Medicine, London, UK  
*Academic Degrees:* MA; MBBChir; MD; FRCP; FFPH; DTM&H  
*City and Country of Primary Residence:* Winchester, UK  
*Biography:* Anthony Harries is Senior Advisor at the International Union against Tuberculosis and Lung Disease in France and an honorary professor at the London School of Hygiene and Tropical Medicine in the UK. He is a physician and a registered specialist in the United Kingdom in infectious diseases and tropical medicine. He spent over 20 years living and working in sub-Saharan Africa, starting in North-east Nigeria in 1983. In 1986, he moved to Malawi where he was consecutively Consultant Physician, Foundation Professor of Medicine at the new medical school in Blantyre, National Advisor to the Malawi Tuberculosis Control Programme and National Advisor in HIV care and treatment in the Ministry of Health, responsible for scaling up antiretroviral therapy in the country. In 2008, he left Malawi and returned to the UK where he works for the International Union Against Tuberculosis and Lung Disease, Paris, France. His main interests are in the field of tuberculosis, HIV/AIDS, non-communicable diseases, tropical medicine and operational research.

**Alexander Kay**

*Institutional affiliation:* Baylor Global TB Program, Eswatini  
*Academic degrees:* BA (Hist), MD, US Board certifications: internal medicine, paediatrics, paediatric infectious diseases  
*City and country of primary residence:* Mbabane, Eswatini  
*Biography:* Since 2016 Dr. Kay is Assistant Professor of Pediatrics at Baylor College of Medicine, USA and Associate Director of the Baylor Global TB Program in Eswatini. Apart from board certification in internal medicine, paediatrics and paediatric infectious diseases, he also has a certificate from the American Society of Tropical Medicine and Hygiene. Before his current
appointment with the Baylor Global TB Program he also worked as a medical officer in TB control at the California Department of Health, and as a paediatrician in the USA as well as with the Baylor International Paediatric AIDS Initiative in Lesotho. He is currently principal investigator on studies in the use of stool PCR for diagnosis of paediatric TB and of drug-resistant TB infection, supports clinical care at the Baylor TB/HIV clinic in Eswatini, works with colleagues across the Baylor Network to support TB programming, and has published several articles focused on tuberculosis epidemiology and diagnostics. Dr. Kay has also authored peer reviewed manuscripts on TB infection, focusing on the performance of interferon gamma release assays, the assessment of TB infection in organ donors, and reviews of TB prevention and case finding strategies. In 2018 he served as a member of the Guideline Development Group for the WHO treatment guidelines for rifampicin and multidrug-resistant tuberculosis.

**Mahshid Nasehi**

*Institutional affiliation(s):*
1. Department of TB and Leprosy Control- Center for Control of Communicable Diseases-Ministry of Health and Medical Education in I.R. Iran;
2. Department of Epidemiology and Biostatistics, School of Public Health- Iran University of Medical Sciences

*Academic degrees:* MD, MPH, PhD

*City and country of primary residence:* Tehran- Iran (Islamic Republic of)

*Biography:* Mahshid Nasehi is a medical doctor who has been working as National Director of TB and Leprosy Control Department in Iran since 2000 and simultaneously as an academic member and researcher in Department of Epidemiology and Biostatistics, in Iran University of Medical Sciences (since 2005). She started her work as a GP in a PHC center (Primary Health Care Center). Then, she has been working consecutively as District TB coordinator, TB Provincial TB coordinator, Director of Disease Control Office at Provincial level in Capital City, and finally she joined the national level in 2000 as National Director of TB and Leprosy Control Department. Some of her key contributions/achievements are as follow:

- National TB infection control guideline-2013;
- Member of Technical Development Group of WHO Treatment of Tuberculosis Guideline-4th edition;
- National M & E package on TB-2007;
- First national PPM protocol/guideline on TB -2013;
- TB component of Iran GFATM Project- R7 (2008-2014);
- Nominal Electronic Registration System for TB since 2005, which was switched to an online mechanism since 2013. Including data on contact tracing and preventive treatment.
- National Online CME system on TB for Physicians-2012
- DR-TB management infra-structures, including 4 MDR-TB wards, 8 qualified DST, 20 new culture and more than 100 DSM Laboratories -since 2010
- Nation-wide Drug Resistance Survey (DRS- 2014) as principal investigator.
29 published researches on TB. A Pilot study on comparing TST and IGRA test for all age close contacts in an integrated format in PHC to find the administrative and practical challenges.

Alberto Matteelli*

Institutional Affiliations: University of Brescia, Brescia, Italy, and Director of the World Health Organization (WHO) Collaborating Center on Tuberculosis/HIV and TB Elimination.
Academic degrees: MD, specialist in Infectious Diseases, Associate Professor in Infectious Diseases
City and country of primary residence: Brescia, Italy
Biography: His main fields of interest include tuberculosis, sexually transmitted diseases and migration health. Recently, he contributed to the development of global policies for the programmatic management latent tuberculosis infection (2015 WHO guideline on programmatic management of Latent TB infection). He was involved in the overall agenda for the scale-up of LTBI activities. He contributed to WHO guidelines development process in other areas, including the consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection – 2016 recommendations for a public health approach.

Lindiwe Mvusi*

Institutional affiliation(s): National Department of Health, South Africa
Academic degrees: B Sc, CDE, MBCHB
City and country of primary residence: Johannesburg, South Africa
Biography: Dr Mvusi is a medical practitioner with post graduate training in occupational and public health programmes. She has sixteen years’ experience in clinical work in the private and public sectors, before joining the National Department of Health as TB programme manager. Her current responsibilities include policy formulation, guideline development, strategic plan development, planning, coordination of training, surveillance, monitoring and evaluating the implementation of the national policies, overall coordination of the TB programme which includes the private sector, business/industry, correctional services and military health services. She has served as a technical advisor on the WHO DOTS Expansion Working Group, TB/HIV and MDR-TB Working Groups. Dr Mvusi was a reviewer for the Evidence to Inform South African Policies (EVISAT) project, which conducted a systematic review on the epidemiology of and programmatic response to TB and assessed existing systematic reviews on TB prevention, diagnosis, treatment and health systems strategies in South Africa. She currently serves in the National Essential Medicines List Committee. She has served as a member of the WHO GDGs for Latent TB Infection and TB Infection Prevention and Control Guidelines. She has been involved in the national guideline development for Tuberculosis, TB Preventive therapy, Multi drug resistant TB and Infection Prevention and Control. The specific skills and experience she brings into this process are clinical patient management, programmatic management and therefore provide end user perspectives; evidence reviews and formulation of the PICO questions
Kuldeep Singh Sachdeva

Institutional affiliation(s): Programme Manager, NTP India
Academic degrees: M.B.,B.S, D.T.C.D, M.B.A
City and country of primary residence: New Delhi, India

Biography: Dr Kuldeep Singh Sachdeva, currently serving as the Deputy Director General - Central TB Division and India Country Coordination Mechanism Global Fund, Ministry of Health & Family Welfare, Government of India. He is a public health physician and has worked as Deputy Director General at National AIDS Control Organisation, heading Data Analysis, Research & Evaluation, Basic Services and STI Divisions. He has also earlier served in the Central TB Division within the Ministry of Healthy and Family Welfare where he focused on drug resistant TB, Operations research, TB-HIV collaborative activities and Donor Coordination. Prior to this, he has worked as a medical officer in country’s premier hospital and headed the Essential Drugs Programme in the State of Delhi. He has a keen interest in operational research and has several publications in peer-reviewed international and national journals and has been a speaker on numerous forums on a wide range of topics relating to TB and HIV.

Nandi L Siegfried*

Institutional affiliation(s): [current and in the prior four years] Independent (0.8fte), Chief Specialist Scientist, Medical Research Council of South Africa (0.2fte) Associate Professor, Faculty of Health Sciences, University of Cape Town
Academic degrees: MBChB, MPH (Hons), FCPHM (SA), DPhil (Oxon)
City and country of primary residence: Cape Town, South Africa

Biography: Dr Siegfried is a South African public health physician working as an independent consultant based in Cape Town. Following several years in clinical medicine, she transferred to a research career focused on clinical epidemiology and trials methods. Dr Siegfried has worked for a decade at senior management level at the South African Medical Research Council, where she was co-director of the South African Cochrane Centre and Deputy Co-ordinating Editor of the Cochrane HIV/AIDS Review Group. In 2011 she commenced working as an independent clinical epidemiology consultant. In this capacity she provides assistance and guidance, as well as technical support to international, national, institutional and non-government agencies in the healthcare sector. Most notable is her role as Chair, Technical Advisor and/or Methodologist to 13 World Health Organization Clinical Guidelines Development Groups and serving as the South African representative on the Organization for Cooperation and Economic Development Working Group on Multinational, Non-commercial Clinical Trials. Dr Siegfried has a thorough knowledge of the methods required for high quality clinical trial conduct, is highly experienced in systematic review methodology and knowledge translation, and her public health training affords her a broad perspective across the healthcare arena. As a South African who has worked in neighbouring African countries, she has experience and knowledge of the healthcare challenges facing low- and middle-income countries. Dr Siegfried has published widely and enjoys teaching and lecturing.
Ezio Távora dos Santos Filho

Institutional affiliation(s): Civil Society Task Force
Academic degrees: BA, MSc, PhD
City and country of primary residence: Rio de Janeiro, Brazil
Biography: Dr Távora is a community engagement researcher with a PhD on Health Policies from the Rio de Janeiro Federal University. He became an AIDS activist in the late 1980’s and pioneered in community engagement in tuberculosis both locally and globally in 2002. He has been developing community engagement in research in the Brazilian TB Research Network, currently coordinating the community engagement component of the STREAM Clinical Trial, SimpliciTB Trial CAB Coordinator in Rio de Janeiro (REDE-TB, TB Alliance, FIOCRUZ). Ezio has established several Community Advisory Boards at local and national level and at participated at the CRAG by the U.S. CDC's TBTC, and is a member of the Global TB Community Advisory Board. He has served at the coordinating boards of the Global Fund and the Stop TB Partnership and collaborated with WHO and PAHO in several documents and technical advisory groups, such as the AMRO rGLC. Ezio has been a long time advocate for LTBI with TB and AIDS programs, engaging in several policy discussion on the matter in the last 15 years and has participated in international discussion in this subject.

Marieke Van der Werf*

Institutional affiliation(s): European Centre for Disease Prevention and Control
Academic degrees: MD, PhD, MSc, MPH
City and country of primary residence: Stockholm, Sweden
Biography: Marieke J. van der Werf is the head of the Disease Programme Tuberculosis and the acting head of the Disease Programme Vaccine Preventable Diseases at the European Centre for Disease Prevention and Control in Stockholm. She is responsible for the scientific and technical work of the Centre on surveillance, diagnosis, guidance development, and country support for tuberculosis and vaccine preventable diseases. She was trained as a medical doctor, in biomedical sciences, and in public health and is a registered epidemiologist. She obtained her PhD in 2003 and published 140 articles in international peer-reviewed journals. She has worked in Europe, Africa and Asia and provided technical assistance and built capacity for epidemiological and operational research on topics relevant for tuberculosis prevention and control. She participated in international policy and guidelines development groups, such as the World Health Organization STAG-TB and the Task Force Impact Measurement.

Irina Vasilyeva*

Institutional affiliation: National Medical Research Center of Phthisiopulmonology and Infectious Diseases (NMRC PhPI), Ministry of Health of the Russian Federation (MoH)
Academic degrees: MD, Doctor of Medical Sciences, Professor
City and country of primary residence: Moscow, Russian Federation
Brief biography: Dr Vasilyeva is a professor and currently the Chief TB Expert of the Ministry of Health (MoH). She is the President of the Russian Society of Phthisiologists /Association of Phthisiologists and Director of the National Medical Research Center of Phthisiopulmonology and Infectious Diseases of the Ministry of Health of the Russian Federation. Dr Vasilyeva was a member of WHO Strategic and Technical Advisory Group (STAG) from 2014 till 2016. At present time she is a member of the Technical Advisory Group on Tuberculosis (TAG-TB) for the WHO
European Region. She has worked in different capacities in TB control since 1990. Dr. Vasilyeva’s research expertise includes various aspects of M/XDR-TB diagnosis and treatment, comorbidity (TB/HIV), development of TB chemotherapy regimens based on molecular genetic methods for DST, and the development of measures for the prevention of tuberculosis in patients with HIV and diabetes. As a Chief TB Expert of MoH, Dr. Vasilyeva contributes significantly to solving issues with TB care management in the Russian Federation. Under her leadership, the following documents have been developed: a strategy for the development of TB care in the Russian Federation until 2025, a national plan for the prevention of M/XDR-TB and TB/HIV spread, modern approaches to drug supply and TB treatment management, and an update of legal TB documents. She has been instrumental in guiding efforts to introduce modern medical and organizational technologies to TB practice.

Wim P. Vandevelde*
Institutional affiliation(s): Global TB Community Advisory Board  
Academic degrees: Bachelor of Laws studies  
City and country of primary residence: Cape Town, South Africa  
Biography: For more than a decade Wim has been committed to full time action on HIV, Hepatitis and TB advocacy and Community involvement in medical research in Europe and globally. Prior to his health advocacy work, Wim worked in the marketing communications sector. A native of Bruges, Belgium, Wim speaks fluently Dutch, English, French and Portuguese. He lives in Cape Town, South Africa, since 2012.

* served as GDG members on the WHO LTBI guidelines of 2018

In order to enhance its management of conflicts of interest as well as strengthen public trust and transparency in connection with WHO meetings and activities involving the provision of technical/normative advice, the names and brief biographies of individuals (“Published Information”) being considered for participation in a WHO-convened Guideline Development Group are disclosed for public notice and comment.

The Published Information is provided by the experts themselves and is the sole responsibility of the individuals concerned. WHO is not responsible for the accuracy, veracity and completeness of the Published Information provided. Furthermore, in no event will WHO be responsible or liable for damages in relation to the use of, and reliance upon, the Published Information.

The comments received by WHO through the public notice and comment process are treated confidentially and their receipt will be acknowledged through a generic email notification to the sender. Comments brought to the attention of WHO through this process are an integral component of WHO’s conflict of interest assessment process and are carefully reviewed. WHO reserves the right to discuss information received through this process with the relevant expert and disclose to this expert the name and affiliation of the provider of such information. Upon review and assessment of the information received through this process, WHO, in its sole discretion, may take appropriate management action in accordance with its policies.

Guideline Development Groups (GDG) provide technical and/or normative advice and recommendations to WHO. Participation in a GDG convened by WHO does not necessarily mean that the views expressed by the expert concerned are shared by WHO and/or represent the decisions or stated policy of WHO. In view of the relatively limited extent of this revision the GDG members for this update are mostly the same ones that participated in the GDG that produced the consolidated LTBI guidelines in 2018.

The list of participating experts, a summary of relevant interests disclosed by such experts, and any appropriate mitigation measures taken by WHO relating to the management of conflicts of interests, will be reported publicly in accordance with WHO policies.