# Thematic Evaluation of Tuberculosis Prevention Secretariat-led with TERG oversight

Global Fund Secretariat Management Response, Technical Evaluation Reference Group (TERG) Commentary and Final Report.

September 2022

# Secretariat-Led Evaluation with oversight from the Technical Evaluation Reference Group: Tuberculosis Prevention

**Global Fund Secretariat Management Response, Technical Evaluation Reference Group (TERG) Commentary and Final Report.**

September 2022

# Secretariat Management Response -
Thematic evaluation on TB prevention

## Introduction

The Technical Evaluation Reference Group (TERG) is a critical component of the Global Partnership, providing independent evaluations or oversight to independent evaluations of the Global Fund's business model, investments, and impact to the Global Fund Board through its Strategy Committee. The Global Fund values transparency and publishes TERG reports according to the TERG Documents Procedure approved by the Strategy Committee.

In the preparation period for the 2023-2025 allocation cycle and the 2023-2028 Global Fund Strategy and following the TERG HIV prevention evaluation, the Board and Strategy Committee requested a similar evaluation for TB prevention to inform the 2023-2025 allocation period (NFM4). The evaluation was managed by the Secretariat with strong oversight and engagement by the TERG. As agreed under this evaluation operational modality, the TERG did not prepare a Position Paper, but rather a commentary on the quality of the evaluation The objectives of the evaluation were to review Global Fund policies, processes, and investments on TB prevention, especially in TB preventive treatment (TPT) and infection prevention and control (IPC), to help guide Global Fund's future role and investments in TB prevention.

## Observations on key findings and conclusions

The Secretariat broadly endorses the key findings, high-level conclusions, and recommendations of the evaluation. The Secretariat appreciates the acknowledgement that the Global Fund was responsive to evolving needs to address TB prevention better and increased its investments on highly relevant areas – TB preventive treatment (TPT) for household contacts <5 years and people living with HIV (PLHIV). TB prevention activities represented 6% of the TB grants in NFM2 and 8% in NFM3.

The Secretariat notes the limitation of this evaluation with regards to data availability and quality. As explained in the report, data on TPT and infection prevention and control (IPC) at the country level was incomplete. There was a discrepancy in TPT data submitted to WHO and Global Fund and what is available within National Tuberculosis Programs (NTP), as well as challenges in compiling data from Global Fund grants as TPT and IPC costs are spread across different grants, modules, interventions, and activities which does not facilitate easy tracking.

Due the limited time for the review, the evaluation team was unable to carry out in-country data validation activities through health facilities visits. The Secretariat was also unable to triangulate the findings on Global Fund investments with other source of information.

The Secretariat takes note that "while Global level policies and guidance including by the Global Fund appear appropriate, implementation of TB prevention has been sluggish' and that progress in implementation will need action beyond the allocation of more funding for TB prevention by the Global Fund. This will require work with NTPs and in-country partners to create demand for TB prevention and address the barriers to TPT and TB-IPC, which other partners may be better-placed to lead.

The evaluation confirms an increase in Global Fund investments for TB prevention representing 6% of the TB grant in NFM2 to 8% in NFM3 period. The Secretariat acknowledges that this increase remains relatively small as a proportion of the overall Global Fund TB grants. Having this information contextualized within the overall amount available for TB prevention globally (not just the Global Fund's share) would be helpful and could be considered in future evaluations on TB prevention.

Given the chronic underfunding of TB programs, the perception by some that increasing TB prevention budget will divert priority from identification and treatment of people with active TB needs to be addressed. The Global Fund will continue to promote the importance of TB prevention being addressed as an integral part of the continuum of TB care. For example, contact tracing investigations for finding people with active TB can integrate identifying people eligible for TPT, and active TB case finding interventions can be expanded to also find people with TB infection who will benefit from TPT.

The Secretariat's feedback on draft reports were considered in finalization of the report and due to the close collaboration, several provisional recommendations from draft reports were able to be reflected in updated funding request development guidance, for example the TB Information Note for the 2023-2025 allocation period.

## Areas of agreement

Table 1 presents the 13 recommendations from the evaluation report which have been classified as either 'high' or 'moderate' priority by the evaluators and for which a timeframe for addressing or implementing the recommendations has been specified. The Secretariat's level of agreement and level of control against each recommendation is also shown in the same table. The set of recommendations listed below are those that the Secretariat fully agrees with, has high level of control, and have already been actioned upon.

***Recommendation 1**. Consider including TB prevention, with a focus on TPT, in the list of priority interventions to benefit from catalytic investments for specific high-risk groups beyond PLHIV*

The Secretariat fully agrees, and this recommendation has been already actioned. The approved TB catalytic investments for the 2023-2025 allocation period (NFM4) includes TB prevention as one of the three priority areas for Matching Funds and for Strategic Initiative (SI) funding.

***Recommendation 4**. Define and elaborate key indicators for TB-IPC and TPT to enable target setting and assessment of cost efficiency and cost effectiveness of these interventions.*

In line with the recommendation, the updated modular framework for NFM4 now has a separate module on TB prevention, and new indicators on TPT have been added. Defining indicators and setting country-level targets for TB-IPC and TPT, and subsequent monitoring progress against these is important but one which the Global Fund has a limited level of control. This is particularly true for TB-IPC which needs to be prioritized by Ministries of Health, made part of overall infection and prevention control for the health systems, monitored through country health surveillance systems and be part of routine reporting to WHO and other agencies as applicable.

***Recommendation 6**. Define and publish program essentials for TB prevention that recipient countries should strive to achieve.*

This recommendation has been already actioned upon. Program essentials for TB, which includes TB preventive treatment, has been included in the updated TB Information Note for the 2023-2025 allocation period in July 2022.

***Recommendation 7.** Encourage and support countries to adopt and scale up more sensitive and specific TB screening approaches.*

***Recommendation 8.** Encourage and support countries to adopt and deploy more sensitive, specific and probably easier to deploy tests for TB infection.*

***Recommendation 9**. Reinforce messaging for TB-IPC, through the TB information, to countries to emphasize that the development and implementation of TB-IPC programs should be part of the wider health system effort to prevent transmission of infections at the health facility level and the community level.*

***Recommendation 10**. Encourage and support countries to engage communities in the delivery of TB prevention services through BCC and other measures, including community led monitoring.*

The Secretariat fully agrees with recommendations 7, 8, 9 and 10 and they are included as priority activities in the recently published TB Information Note. The evaluation report will also be shared with the TRP so the findings and recommendations may inform their review of funding requests. In addition, TB advisors will work with country teams to encourage and reinforce these messages during the funding request development process and with implementing partners.

## Observations on other recommendations

***Recommendation 2**. Collaborate and partner with others to develop and support countries to use budget templates and tools for TB prevention, both IPC and TPT.*

The Secretariat agrees that costing for TB prevention should be part of the overall budget templates and tools for TB programs. However, developers of existing costing tools, like WHO, are better placed to lead this work with the Secretariat contributing to efforts towards this.

***Recommendation 3**. Collaborate and partner with other stakeholders such as UNITAID and the Global Drug Facility as they undertake market shaping activities to address the challenge of cost, affordability and availability of newer shorter rifapentine based TPT regimens.*

The Secretariat will continue to support partner efforts to address the challenges associated with the high cost and availability of the shorter TPT regimens, by including these products in pharma tenders and by leveraging the Global Fund's cross-disease buying power with a common supplier base. We will continue to work with partners, through but not limited to, the multi-partner coordinated procurement working group.

***Recommendation 5.** Provide technical support to countries to set high but realistic targets for TB prevention and have a monitoring and evaluation framework in place that allows the Global Fund, partners and the countries to monitor and track TPT and IPC uptake, coverage, & outcomes.*

The Global Fund can and will continue to offer technical support through the existing TB SI and future SI upon country request. In addition, TB prevention is included as one of the three priority areas for 2023-2025 TB catalytic investments. Strengthening monitoring & evaluation for TPT has been identified as a priority intervention for NFM4 and TPT is included in the TB Program Essentials.

While the Secretariat continues to advance TB prevention through its mechanisms, the challenge is the low prioritization for TB prevention in most of the high TB burden countries where limited resources are prioritized to get back on track to meet active TB notification targets which were impacted by the COVID-19 pandemic. Implementing this recommendation will require coordinated support from all partners and for which the Global Fund can and will contribute to.

***Recommendation 11**. Work with partners to define and elaborate implementation level TB prevention knowledge gaps questions that can need to be addressed through well designed operations, implementation, or health system research.*

***Recommendation 12**. Consider setting up a mechanism to fund regional or multi-country level implementation or health system research and the use of "request for proposal" approach to undertake high quality research to provide evidence of approaches that will address global, regional, and multi-country obstacles to implementation of TB prevention interventions.*

The Secretariat agrees with the need to define operational/implementation research questions and generate evidence on the best implementation approaches for TB prevention interventions. However, research is not a core mandate of the Global Fund, so this is best led by technical partners with the requisite expertise.

In addition, Global Fund financial support for such an initiative would need to come from catalytic investments and the decisions around focus and prioritization have already been made by the Board for the 2023-2025 allocation period. The ability to action this

recommendation cannot be actioned upon in the 2023-2025 allocation period and requires further deliberation on the policy implications.

***Recommendation 13**. In the resource limited setting where programmatic implementation of TPT is undertaken, we suggest that the Global Fund and partners encourage countries to prioritize their target groups for TPT based on their epidemiological and funding context.*

The Secretariat agrees with the need for prioritization particularly in of the context of limited funding while noting that the examples of target groups provided as a part of this recommendation is not fully aligned with WHO guidance. The key findings and recommendations of the evaluation report were discussed with TB partners, TRP members including the focal points for TB and HIV, and based on these consultations, this recommendation has been reflected in the TB Information Note as follows:

*"In situations of limited funding, target groups for TPT may be prioritized based on the strength and certainty in the estimates of effect of the WHO recommendation for the specific population group, and the country context." – page 18*

## Conclusions

The Secretariat appreciates the strong oversight and engagement of the TERG in this evaluation. The timing of the evaluation and the strong collaboration with the evaluation team facilitated inclusion of several high priority recommendations into guidance materials for the next Global Fund allocation cycle. The Secretariat broadly agrees with all the recommendations and will work with relevant partners to contribute to those recommendations that others are better placed to implement.

Accelerating actions on TB prevention along with early diagnosis and successful treatment of people with TB is critical to end TB. Acknowledging the funding limitations faced by TB programs, the Secretariat encourages that TB prevention, particularly activities to promote TPT, be designed and implemented as a part of routine activities across the TB care cascade. Integrated approaches to case finding and TPT provision through contact investigation for both TB infection and disease, identifying people eligible for TPT as a part of active case finding by linking algorithms for screening and TPT will maximize impact and efficiency.

**Table 1: Summary of recommendations from the evaluation report**

| Recommendations | Timeframe | Level of agreement | Level of control |
|---|---|---|---|
| 1. Consider including TB prevention, with a focus on TPT, in the list of priority interventions to benefit from catalytic investments for specific high -risk groups beyond PLHIV.* | During NFM preparation | Fully agree | Full |

| | | | |
|---|---|---|---|
| 2. Collaborate and partner with others to develop and support countries to use budget templates and tools for TB prevention, both IPC and TPT.* | During NFM preparation | Mostly agree | Low |
| 3. Collaborate and partner with other stakeholders as they undertake market shaping activities to address the challenge of cost, affordability and availability of newer shorter rifapentine based TPT regimens.** | During NFM preparation and implementation | Mostly agree | Partial |
| 4. Define and elaborate key indicators for TB-IPC and TPT to enable target setting and assessment of cost efficiency and cost effectiveness of these interventions.* | During NFM preparation and implementation | TPT: Fully agree<br>IPC: partially agree | TPT: Full<br>IPC: Low |
| 5. Provide technical support to countries to set high but realistic targets for TB prevention and have a monitoring and evaluation framework in place that allows the Global Fund, partners and the countries to monitor and track TPT and IPC uptake, coverage, & outcomes.* | During NFM preparation and implementation | Mostly agree | Low |
| 6. Define and publish program essentials for TB prevention that recipient countries should strive to achieve.* | During NFM preparation | Fully agree | Full |
| 7. Encourage and support countries to adopt and scale up more sensitive and specific TB screening approaches.* | During NFM preparation and implementation | Fully agree | Full |
| 8. Encourage and support countries to adopt and deploy more sensitive, specific and probably easier to deploy tests for TB infection.* | During NFM preparation and implementation | Fully agree | Low |
| 9. Reinforce messaging for TB-IPC, through the TB information, to countries to emphasize that the development and implementation of TB-IPC programs should be part of the wider health system effort to prevent transmission of infections at the health facility level and the community level.* | During NFM preparation and implementation | Fully agree | Full |
| 10. Encourage and support countries to engage communities in the delivery of TB prevention services through BCC and other measures, including community led monitoring.* | During NFM preparation and implementation | Fully agree | Full |
| 11. Work with partners to define and elaborate implementation level TB prevention knowledge gaps questions that can need to be addressed through well designed operations, implementation, or health system research ** | During NFM preparation and implementation | Mostly agree | Low |
| 12. Consider setting up a mechanism to fund regional or multi-country level implementation or health system research and the use of “request for proposal” approach to undertake high quality research to provide evidence of approaches that will address global, regional, and multi- | During NFM preparation and implementation | Mostly agree | Low |

| | | | |
|---|---|---|---|
| country obstacles to implementation of TB prevention interventions.** | | | |
| 13. In the resource limited setting where programmatic implementation of TPT is undertaken, we suggest that the Global Fund and partners encourage countries to prioritize their target groups for TPT based on their epidemiological and funding context. For example:<br>• Group 1: Household contacts of bacteriologically positive people who are below 5 years old and PLHIV - highest priority.<br>• Group 2: Household contacts of bacteriologically positive people > 5 years with additional risk factors for progression to active TB such as those who are malnourished, diabetics, older than 65 and alcohol use disorders – high priority.<br>• Group 3: Non household contacts with high rates of TB such as persons older than age 65, health care workers, prisoners, etc. - medium priority | During NFM preparation and implementation | Mostly agree | Low |

* High priority recommendation; ** Moderate priority recommendation

# The Technical Evaluation Reference Group (TERG) Report

## Quality assessment and utility of the evaluation

**Name of Evaluation: Evaluation on Tuberculosis Prevention**

**Year of report: 2022**

### a). The Technical Evaluation Reference Group (TERG) rated this report as:

| | |
|---|---|
| ☐ | Fully met or exceeded TERG's standards |
| ☒ | Met TERG's standards with only minor shortcomings |
| ☐ | Partially met TERG's standards with some shortcomings |
| ☐ | Did not meet TERG's standards with major shortcomings |

### b). General comments

***Context – Purpose of the evaluation, how it was conducted and how it was managed as a hybrid evaluation, relevance of the issue to the broader global health context***

Tuberculosis (TB) prevention is a broad term covering infection prevention and control (IPC), TB preventive treatment (TPT), and BCG vaccination. It is also understood as measures that decrease a person's susceptibility to TB infection and TB disease due to social, behavioral and clinical risk factors. Following the publication of WHO's guidelines on programmatic management of latent TB in 2018, the Global Fund updated its TB Information Note promoting TPT as a high-impact intervention during the New Funding Model 3 (NFM3) implementation period. Additionally, one of the five TB sub-objectives for the next Global Fund strategy (2023-2028) is to scale-up TB prevention with an emphasis on TPT and IPC.

It is expected that prevention of TB disease combined with the rapid identification and treatment of people with active TB would accelerate the rate of decline in the burden of TB especially in settings where the burden is high.

In this context, the Global Fund Secretariat and the Global Fund's Technical Evaluation Reference Group (TERG) conducted an evaluation to assess the Global Fund's role and support to TB prevention efforts. It is hoped that the results of the evaluation will better inform future Global Fund policies, processes and programming to support TB prevention.

The evaluation was conducted by a consortium of Technical Assistance for Management (TeAM) and Itad Ltd. The selection of the service provider was done by a team that included a TERG member and staff of the Global Fund Secretariat.

The inception report for the evaluation was reviewed by TERG members, and staff of the Global Fund Secretariat. STOP TB Partnership provided inputs during the development of the Terms of Reference (TOR), following which comments and feedback were consolidated and provided to the consultants. Meetings were held between the TERG Focal Points and consultants to discuss and further clarify the feedback provided.

The evaluation was conducted using mixed methods, including document reviews; analysis of existing quantitative and qualitative data; key informant interviews, nine country case studies; and a portfolio analysis. The Secretariat provided the service provider with relevant grant data. Assessments, analysis, and synthesis were conducted at both global and country levels.

The draft report was presented at a TERG meeting during which initial feedback on the draft report was provided. A joint validation meeting was held between the consultants, the TERG Focal Points and staff of the Global Fund Secretariat to provide feedback to the consultants on the draft report. The meeting was chaired by one of the TERG Focal Points with breakout group meetings to allow the secretariat to consolidate their feedback on the draft report. The consolidated feedback was provided to the consultants during the final plenary of the validation meeting. A presentation was made at the recently concluded 47$^{th}$ TERG Meeting during which final feedback was provided to enable the consultants finalize their work.

**c). Strengths and Shortcomings of the Report**

**Strengths of the Report** - The evaluation is timely, coming just before the next funding cycle and at a time when guidance for countries and decisions on processes are being made by the Global Fund Secretariat. In fact, several of the provisional findings and recommendations from the report have already been taken up by the Global Fund Secretariat, influencing the content of the Information Note to countries and the revision of the modular framework and indicators among others. The findings are insightful and relevant. The overall utility of the report is therefore high.

The evaluation combined both primary and secondary data. It identifies major shortcomings with TB prevention, which has been identified as a high-impact intervention globally. It also identifies major data capture issues within and between global health institutions that make it challenging to assess progress towards stated global targets.

Overall, the scope of work has been met and evaluation questions satisfactorily addressed. However, the consultants were unable to assess the cost-effectiveness of TB prevention interventions as planned due to data limitations. An attempt to estimate cost efficiency of TPT was only possible in two countries.

**Shortcomings of the Report** The overall structure and formatting of the report could be further improved for easier reading. Triangulation of the data needs to be improved as there remain a few areas where results from key informant interviews are presented separately from those from other sources.

**d). Observations on Conclusions and Recommendations**

The key findings and the strength of the evidence has been provided. Conclusions are based on the evidence presented in the report. Recommendations are clearly stated and prioritized. The type of recommendation (policy or operational), the responsibility, as well as timeline for implementing the recommendation has been clearly stated.

The conclusions and recommendations of this report suggest that more substantive attention and resources are needed by the Global Fund and partners to reduce TB incidence through concerted prevention efforts. The recommendations lay out a number of ways that this could be done if taken up across the partnership. It is helpful to see that some of these recommendations are already being put into action by the Global Fund and hope to see this translated into action in countries through grant implementation.

Technical Assistance for Management

itad

**Final report TGF-21-119**

Report for the Global Fund's Technical Evaluation Reference Group (TERG) and Secretariat - Evaluation on Tuberculosis Prevention

13rd June 2022

# Table of contents

# Abbreviations and Acronyms

| | |
|---|---|
| ACF | Active Case finding |
| CCM | Country Coordinating Mechanism |
| CTE | Core Team of Experts |
| CXR | Chest X-ray |
| FGDs | Focused Group Discussions |
| Global Fund | The Global Fund to Fight AIDS, Tuberculosis and Malaria |
| HAI | Health care Associated Infection |
| HIV/AIDS | Human Immunodeficiency Virus/ Acquired Immune Deficiency Syndrome |
| IPC | Infection prevention and Control |
| IPT | Isoniazid Preventive Treatment |
| M&E | Monitoring & Evaluation |
| NGOs | Non-governmental organization |
| NSPs | National Strategic Plans |
| PF | Performance Framework |
| PLHIV | People Living with HIV |
| RSSH | Resilient & Sustainable Systems for Health |
| STP | Stop TB Partnership |
| TA | Technical Assistance |
| TAP | Technical Assistance and Partnership |
| TB | Tuberculosis |
| ToC | Theory of Change |
| TERG | Technical Evaluation Reference Group |
| TL | Team Leader |
| TPT | Tuberculosis Preventive Treatment |
| UNAIDS | The Joint United Nations Program on HIV/AIDS |
| UNDP | United Nations Development Program |
| UNFPA | United Nations Populations Fund |
| UNHLM | The United Nations General-Assembly High-Level Meeting on the Fight Against Tuberculosis – 26 September 2018 |
| UNICEF | The United Nations Children's Fund |
| WHO | World Health Organization |

# List of Tables

# List of Figures

# Report for the Global Fund's TERG and Secretariat - Evaluation on Tuberculosis Prevention

## High level summary

**The evaluation had five objectives:**

| | |
|---|---|
| 1 | To review the Global Fund policies, processes, and guidance to shape and enhance the inclusion of TB prevention programs in the next funding allocation (NFM 4) and the 2023-2028 strategy period. |
| 2 | To outline the Global Fund's role to date (alone or with partners) in supporting TB prevention. |
| 3 | To assess the scope, scale, and results of previous Global Fund investments in TB prevention. |
| 4 | To identify obstacles or enhancements on TB prevention during the ongoing COVID-19 pandemic. |
| 5 | To identify recommendations to inform the Global Fund's future role and investment in TB prevention. |

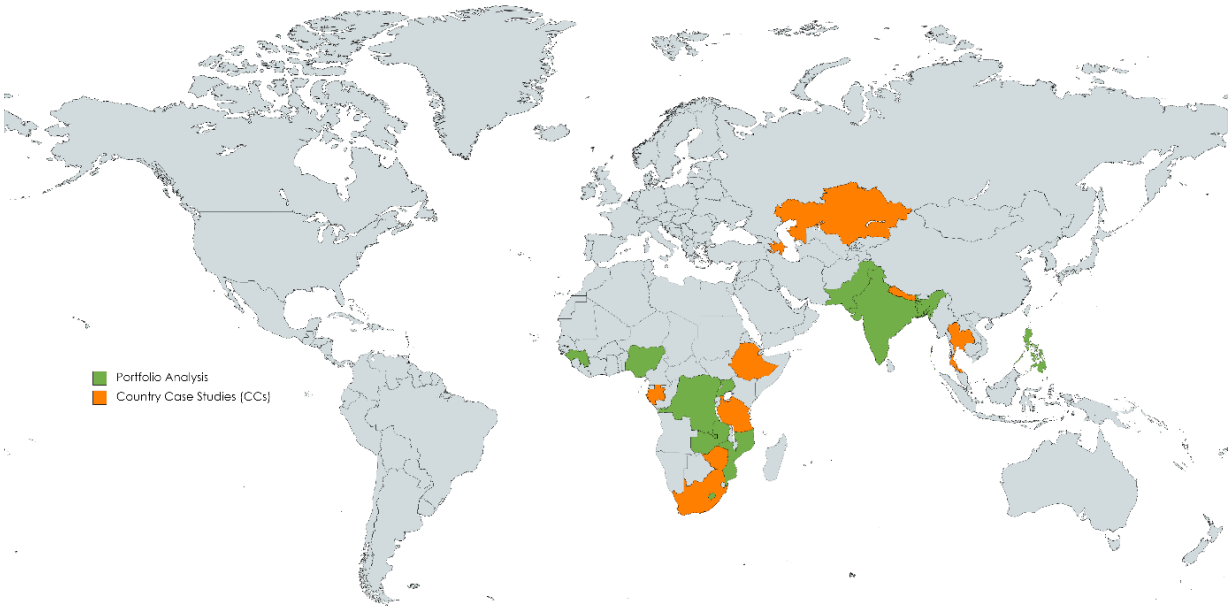
To address the relevance, outcome, efficiency, and effectiveness of Global Fund's investments in TB prevention, this evaluation focused on Infection Prevention Control (IPC) and TB Preventive Treatment (TPT) as TB prevention activities and analysed related gaps.

**Background:** TERG and the Global Fund Secretariat commissioned this evaluation on TPT and IPC investments due to the priority given by the Global Fund to TB prevention among the sub-objectives of the next 2023-2028 Global Fund Strategy. Attention to TB prevention is also warranted due to the fact that both; (i) the End TB Strategy target to reduce TB incidence by 90% by 2035; and (ii) the United Nations General Assembly High Level Meeting on TB target of providing TPT to 30 million people by 2022, appear off track – the latter reaching only 29% TPT coverage by 2020, with only 1.6% among household contact aged 5 years or more and 28% in household contacts aged less than 5 years.

**Scope of the work:** The evaluation was undertaken by TeAM and Itad. It reviewed global TB related policies and guidance as well as work undertaken on TB prevention in Global Fund supported countries within the last two funding allocations (NFM2 and NFM3) to identify potential gaps on IPC and/or TPT, as well as the barriers, opportunities, enablers, coordination, and partnerships for implementation of IPC and TPT. Lastly, the evaluation also examined the role the Global Fund could play in TB prevention beyond TPT & IPC.

**Methodology** The evaluation team conducted a desk review of published and grey literature and policy documents on IPC and TPT as well as country evaluation reports, TB NSPs for NFM2 and NFM3 in 20 countries. More than 150 key informant stakeholders were interviewed at country (90), global and regional level (66). Portfolio analysis was carried out in 11 countries[1] and in-depth Country Case Studies (CCs) conducted in another 9 countries[2] (see map below). Data from WHO, GF and NTP sources was also reviewed and analysed.

[1] India, Bangladesh, Pakistan, Nigeria, Uganda, Zambia, Mozambique, DR Congo, Lesotho, Guinea, Philippines
[2] Azerbaijan, Ethiopia, Gabon, Kazakhstan, Nepal, South Africa, Tanzania, Thailand, Zimbabwe




**Limitations:** Lack of reliable and complete data on TPT and IPC at country level was one of the main limitations, due to non-systematic inclusion of TPT/IPC-related data in countries' TB Health Information System (HIS) and TB patient forms. Data reported to WHO were found to be incomplete and discordant with data from national TB programmes as well as from the Global Fund because both TB and HIV programmes report information on TPT among PLHIV independently, and these data are not cross-checked. TB-IPC is difficult to measure because TB in health care workers (the key proxy indicator used) is associated with high levels of stigma and thus it is largely not monitored. TPT and IPC budgets are difficult to track in the Global Fund Modular Framework due to the absence of a TB prevention module or characterized interventions except TPT among PLHIV in the TB/HIV module. Unfortunately, the evaluation could not visit facilities in the 9-country case-studies due to the COVID-19 situation which hampered data validation. Of note, analysis of the role of social determinants of TB (such as under-nutrition, alcohol-tobacco-drug use and living conditions) was outside the scope of this evaluation, so were not considered in the discussions with partners working on these issues.

**Findings and conclusion**

- The inadequacy of accurate data to track TPT and IPC at country level is a key finding. Specifically, the evaluation team noted wide **variability in the capacity of county level Health Information Systems to record data on TPT, undermining the collection of reliable data for ongoing performance appraisal** and budget evaluation including the Global Fund data source.
- **There has been a flattening of TPT uptake and declining coverage in HH contacts under the age of 5** between 2018 and 2020. This decline in TPT coverage could be due to the impact of the COVID-19 pandemic**.** Lowest coverage of TPT in HH contacts was over the age 5, with no data on TPT coverage for other high-risk groups for whom TPT may be beneficial, such as prisoners, migrants, health care workers, and those with medical conditions
- **Finding missing people with TB remains the priority for most TB programmes** including NFM2 and NFM3 grants**, with a relative de-prioritization of TB prevention**. A change in mindset and approach is needed to progressively bring prevention to the fore as a full part of the TB care cascade.
- Although community engagement for TPT is critical, **we found no evidence of the engagement of communities in TB prevention in NFM2 and NFM3 as in other areas of TB care** (e.g., active case finding) or in HIV prevention.
- **TPT hesitancy from both providers and beneficiaries is limiting uptake of TPT** and there is no evidence-based strategy to combat this hesitancy.
- TB IPC is a standalone approach not coordinated with labour and patient protection; however, **the COVID-19 pandemic has brought IPC to the fore**, requiring more and expanded health care worker training, and greater integration of TB IPC to the general national and facility-based IPC programs.

**Recommendations** (high priority in **bold**, lower priority in *italics*)

<table>
<tr><td colspan="4">The Global Fund and partners are urged to continue mobilizing additional financial resources to support robust programming of TB prevention in TB endemic settings.</td></tr>
<tr><td colspan="2">Include TB prevention, particularly TPT, in the list of priority interventions to benefit from catalytic investments (SI and MF) for specific high-risk groups beyond PLHIV.</td><td>Collaborate and partner with stakeholders to support countries to use budget templates and develop tools for implementation of both IPC and TPT</td><td>Collaborate with other market shaping stakeholders such as UNITAID and GDF to address the challenge of cost, affordability, and availability of newer, shorter, rifapentine based TPT regimens.</td></tr>
<tr><td colspan="4">The Global Fund and partners are encouraged to support countries to develop (if not existing) and enhance TB prevention health information system that captures the entire cascade of processes, outputs, outcomes and impact.</td></tr>
<tr><td colspan="2">Develop improved key indicators for TB-IPC and TPT to enable target setting and assessment of cost efficiency and cost effectiveness of these interventions</td><td colspan="2">Provide technical support to countries to set-up high, but realistic, targets for TB prevention, and have a monitoring and evaluation framework in place that allows the Global Fund, partners, and the countries to monitor and track TPT and IPC uptake, coverage and outcomes.</td></tr>
<tr><td colspan="4">The Global Fund and partners are encouraged to develop mechanisms to support countries to provide high quality TB prevention services.</td></tr>
<tr><td>Define and publish programme essentials for TB prevention that recipient countries should strive to achieve</td><td>Encourage and support countries to adopt and scale up more sensitive and specific TB screening approaches such as digital chest x-ray with artificial intelligence (computer aided diagnostics)</td><td>Encourage and support countries to adopt and deploy more sensitive, specific and probably easier to deploy tests for TB infection like TST patches</td><td>Reinforce messaging for TB-IPC to emphasize that development and implementation of TB-IPC should be part of the wider health system effort to prevent transmission of infections at the health facility and the community level</td></tr>
<tr><td colspan="4">The Global Fund is urged to encourage and push countries to include and engage communities in development, implementation and monitoring of interventions for TB prevention</td></tr>
<tr><td colspan="4">Encourage and support countries to engage communities in the delivery of TB prevention services through Behaviour Change Communication and other measures, including community led monitoring</td></tr>
<tr><td colspan="4">The Global Fund and partners are encouraged to support appropriate research, including operations and implementation research to better define how TB-IPC and PMTPT should be implemented and or delivered.</td></tr>
<tr><td colspan="2">Work with partners to identify implementation level TB prevention knowledge gaps that can be addressed through well designed operations, implementation, or health system research</td><td colspan="2">Consider setting up a mechanism to fund regional or multi-country level implementation or health system research and the use of “request for proposal” approach to undertake high quality research to provide evidence of approaches that will address global, regional, and multi-country obstacles to implementation of TB prevention interventions.</td></tr>
<tr><td colspan="4">In resource limited settings where programmatic implementation of TPT is undertaken, we suggest that the Global Fund and partners encourage countries to prioritize their target groups for TPT based on their epidemiological and funding context. For example:<br>• Group 1: Household contacts of bacteriologically positive people who are below 5 years old and PLHIV - highest priority.<br>• Group 2: Household contacts of bacteriologically positive people > 5 years with additional risk factors for progression to active TB such as those who are malnourished, diabetics, older than 65 and alcohol use disorders – high priority.<br>Group 3: Non HH contacts with high rates of TB such as persons older than age 65, health care workers, prisoners, etc - medium priority</td></tr>
</table>

# 1. Executive summary

## 1.1. Background

Tuberculosis remains a major global public health threat. The disease has been the commonest cause of death from a single infectious pathogen for a long time until 2020 when it ceded this position to COVID-19.

In 2014 the World Health Assembly adopted the End TB Strategy with its ambitious targets to reduce TB incidence and mortality by 90% and 95% respectively by 2035 compared with the rates in 2015. Interim targets and milestones were set to be achieved by 2020, 2025 and 2030. As of now (2022), a decline in TB incidence and mortality of at least 20% and 35%, respectively, should have been achieved. To stimulate action and spur progress, world leaders at the first ever United Nations General Assembly High Level meeting on TB (UNHLM) held at the UN headquarters in New York in 2018 made commitments which included the treatment of 30 million people infected with Mycobacterium tuberculosis but not displaying symptoms and signs of this infection to prevent progression to active TB.

Up until recently, little attention had been paid to the prevention of TB disease in high TB endemic settings. Interventions that can be applied to prevent TB in vulnerable populations include the provision of TB preventive treatment (TPT) which targets persons infected with the causative agent of TB (Mycobacterium tuberculosis), but who are not displaying clinical symptoms and signs of the disease, and implementation of measures to prevent TB transmission at health care facilities. These interventions are known to have individual and population level benefits. Additionally, addressing the social determinants of the disease, through pursuit of poverty reduction measures and general improvement in the living conditions of people, combined with the rapid identification and treatment of people with active TB would be expected to accelerate the rate of decline in the burden of TB, as was observed in high income countries in the last century.

Tuberculosis preventive treatment is currently targeted at populations most at risk of progression to active disease following infection with Mycobacterium tuberculosis. These include household contacts of persons with TB, people living with HIV (PLHIV), persons initiating long term treatment with immune suppressing medicines (such as anti-Tumour Necrosis Factor (anti-TNF), people with chronic kidney disease on dialysis and people preparing to receive solid organ or haematological transplantation among others.

Tuberculosis Infection transmission Prevention and Control (TB-IPC), ideally should be an integral component of national and health facility associated infection transmission prevention programs, intended to limit the spread of health care-associated infections (HAI). HAI is a public health problem with a significant economic burden, preventable through effective IPC measures and awareness at national and health facility level.

Programs supported by the Global Fund have reported progress on the number of people receiving TB preventive treatment. Progress has, however, been slow and insufficient. In 2020, the WHO reported that only a small proportion (29%) of the 30 million people targeted globally to receive TPT between 2018 and 2022 were provided with this treatment. The performance was worse for persons over the age of 5 years who are household (HH) contacts of persons with active TB: only 1.6% of the targeted 20 million people had received TPT by 2020 (WHO Global TB Report 2021). For these reasons, the Global Fund has prioritized TB prevention and included it among the sub-objectives of the

next Global Fund Strategy covering the period 2023-2028 – therefore this evaluation is timely.

## 1.2. Review rationale and objectives

This evaluation was intended to provide essential information to help the Global Fund as it looks forward to investing in future policies, processes, and programming to support TB prevention. The evaluation also aimed to provide information to support the Global Fund to operationalize sub-objective 2 of the TB component of the 2023-2028 Global Fund Strategy.

The evaluation had five objectives:

1. Review the Global Fund policies, processes, and guidance to shape and enhance the inclusion of TB prevention programs in the next funding allocation cycle (NFM 4) and the 2023-2028 Strategy period.
2. Outline the Global Fund's role to date (alone or with partners) in supporting TB prevention.
3. Assess the scope, scale, and results of previous Global Fund investments in TB prevention.
4. Identify obstacles, or enhancements, to the implementation of TPT and IPC during the ongoing COVID-19 pandemic.
5. Identify recommendations to inform the Global Fund's future role and investment in TB prevention.

This evaluation focused on TB-IPC and TPT, based on the understanding that addressing social determinants of TB and TB vaccine development and deployment are outside the core mandate of the Global Fund.

## 1.3. Evaluation design, data collection and analysis

The evaluation was operationalized through five Evaluation Questions (EQs) and four complementary modules presented in the inception report and in Annex 1 of this document. The questionnaires used to guide data collection can be found in Annex 2.

To obtain relevant information and data on TB prevention, we reviewed documents and reports provided by the Global Fund and scanned published literature on TB prevention. We also interviewed many key informants at the global and country level including through an online Monkey survey. The data presented in this report was obtained from the Global Fund, through portfolio analysis in 20 selected countries and in-depth country case studies in 9 (**in Bold**) of the 20 countries, WHO and National TB Programmes. The selected countries include **Azerbaijan**, Bangladesh, Congo (Democratic Republic), **Ethiopia**, **Gabon**, Guinea, India, **Kazakhstan**, Lesotho, Mozambique, **Nepal**, Nigeria, Pakistan, Philippines, **South Africa**, **Tanzania (United Republic)**, **Thailand**, Uganda, Zambia and **Zimbabwe.** The evaluation covered the NFM2 and NFM3 funding period. Uptake (absolute numbers) and coverage (proportion of targets) of TPT were compared with the targets set at UNHLM for each country that were sourced from the Stop TB Partnership. Data on the surveillance of active TB among health care workers was used to assess TB infection control. The evaluation team used a mixed methods approach to triangulate the quantitative data and the qualitative information obtained from key informant interviews.

## 1.4. Key findings of the evaluation.

### 1.4.1. Relevance of Global Funds Investments in TB prevention -Evaluation Question 1

The Global Fund responded to the global need to increase uptake and coverage of TPT among various at-risk populations by increasing its investments in TB prevention. The amount of funding allocated to TB prevention by the Global Fund increased from USD 136.7 million to USD 176.1 million between the NFM2 and NFM3 periods. **TB prevention activities represented 6% of the TB grants in the NFM2 budget period and 8% under the NFM3** budget. While the Global Fund investments in TB prevention were highly relevant, the proportion of the financial resource envelope allocated to TB prevention remained low. The Global Fund is stepping into the NFM 4 period and the 2023 -2028 Global Fund Strategy period while facing a large funding gap for TB prevention that has been estimated to be close to USD 5 billion. The USD 176.1 million allocated to TB prevention by the Global Fund in NFM3 represents less than 10% of the estimated global need.

### 1.4.2. Outputs and outcomes of Global Fund investments in TB prevention (Evaluation Question 2).

**TPT uptake**

The evaluation team obtained data from WHO, the Global Fund and National TB programs on the number of people placed on TB preventive treatment. WHO and the Global Fund may be collecting different sets of data, with the WHO receiving national level data, while data submitted to the Global Fund may be from sub- national areas where Global Fund resources are applied. Consequently, the primary purpose of examining this data was to determine trends rather than make comparisons of the data from these two sources.

According to data from WHO, in the 20 evaluation countries, the number of children under 5 provided TPT increased from 218,694 in 2018 to 280,877 in 2019 and then declined to 258,071 in 2020. Using data from the Global Fund, the relevant figures are 70,059 in 2018, 87,205 in 2019 and 100,491 in 2020.

For PLHIV, data from WHO shows that in the 20 evaluation countries, 1,396,174 people were treated for TB infection in 2020 while the numbers from data sourced from the Global Fund were 682,138 in 2018, 1,452,101 in 2019 and 2,234,712 in 2020.

The Global Fund does not collect data on the number of HH contacts over 5 years who were provided with TPT between 2018 and 2020. TB preventive therapy in HH contacts over the age of 5 was not considered a global priority until after the UNHLM on TB in 2018, and so was not included in the Global Fund Performance Framework for NFM2 and NFM3 grants. Data from NTPs revealed that 34,365 people over the age of 5 who were HH contacts of people with TB were treated for TB infection in the 9 Country Case Study (CCs) countries during NFM2 timeline (4,742 in 2018, 11,306 in 2019 and 18,317 in 2020).

**TPT Coverage**

According to NTP sourced data, TPT coverage in HH contacts under the age of 5 using the UNHLM country target declined between 2018 and 2020 from 81% to 51% to 18%, in 2018, 2019 and 2020 respectively in 7 out of 9 CCs reporting data. Similarly, TPT coverage in PLHIV using the UNHLM country target declined from 99% in 2018 to 92% in 2020 in 6 out of 9 CCs reporting data. On the other hand, TPT coverage in HH contacts over the age of 5, against UNHLM country target was found to have slightly increased from 24% in 2018 to 28% in 2020 in 3 out of 9 CCs reporting data.

According to Global Fund sourced data, TPT coverage in HH contacts under the age of 5 using the UNHLM country target was found to have slightly increased from 13% in 2018 to 20% in 2020 in 3 out of 9 CCs reporting data. Similarly, TPT coverage in PLHIV against

UNHLM country target was found to have increased from 38% in 2018 to 277% in 2020 in 4 out of 9 CCs reporting data.

Data reported to the Global Fund on TPT coverage in HH contacts under the age of 5 likely covers a sub-set of national data and could be considered as a contribution of the Global Fund to the national coverage data provided by the NTP. Coverage of TPT in HH contacts under 5 in 3 countries (Nepal, SA, Zimbabwe) declined during NFM2 timeline and is not on track to reach the UNHLM target. The global estimated coverage was 29% in 2020 in the WHO Global TB report 2021.

The data on TPT coverage in PLHIV sourced from the Global Fund also likely covers a sub-set of national data and reveals higher coverage than data sourced from NTPs. This would happen if there were sub-optimal linkages in TPT data systems between NTPs and HIV control programs. However, the evaluation team was unable to verify this assumption, but speculate that data on TPT coverage submitted to the Global Fund by countries includes aggregated data from both HIV and TB control programmes. We observed an increase in coverage during the NFM2 timeline with this indicator on track to reach the UNHLM target. There is however a large variation of TPT coverage by country in the 4 countries implementing TPT among PLHIV with Global Fund grants (Nepal, SA, Thailand, Tanzania) from 38% in Nepal to 277% in Tanzania. The 2021 WHO Global TB report estimated a global TPT coverage in PLHIV of 120%.

In summary, Global Fund investments helped to increase uptake of TPT in children under 5 and PLHIV between 2018 and 2020. As a result of shifts in denominators, TPT coverage for children under 5 declined while in PLHIV it increased in some countries to beyond 100%.

**TB-IPC: surveillance of TB among health care workers**

The generally accepted proxy indicator for TB-IPC is the number of health care workers who develop active TB. Of the countries included in this evaluation, only Thailand and Zimbabwe reported data. In Thailand TB was notified among 325 health care workers out of a total of 507,013 health care workers (rate of 64/100,000), while in Zimbabwe 388 out of an estimated 50,144 health care workers[3] (rate 733/100,000) had TB in 2020.

### 1.4.3. Efficiency and effectiveness of Global Fund Financing for TB Prevention (Evaluation Questions 3 and 4).

The evaluation team was unable to calculate the cost-effectiveness of the TB prevention interventions (i.e., TPT and IPC) because of data limitations. Estimates of the cost efficiency of TPT, defined as the cost per person placed on treatment for TB infection was attempted, but this was only possible in South Africa and Tanzania. In NFM3 for Tanzania, it will cost an estimated $1.54 per PLHIV placed on TPT while in South Africa, the equivalent cost is estimated at $27.31 per PLHIV on TPT. Since most countries did not have data on the number of health care workers who developed TB, the cost efficiency of TB-IPC was not able to be estimated.

### 1.4.4. Gaps in TB care and prevention

There are no major policy gaps at both the global and national levels. All twenty countries included in this evaluation prioritize TPT in PLHIV and HH contacts of people with TB who are less than 5 years old, which conforms to the guidance provided by WHO and the 2019

[3] The state of the health workforce in the WHO African region, 2021. WHO, Regional Office for Africa. https://apps.who.int/iris/bitstream/handle/10665/348855/9789290234555-eng.pdf?sequence=1&isAllowed=y

TB information note from the Global Fund. Of the 9 CCs, 5 (Azerbaijan, Thailand, Ethiopia, Zimbabwe, and Kazakhstan) also target HH contacts over the age 5 for TPT. In all evaluated countries, screening for TB prior to provision of TPT is based on symptoms combined with CXR, with additional use of tuberculin skin test (TST) in 5 out of 9 countries using either the tuberculin skin, Interferon Gamma Release Assay (IGRA), or both.

Implementation of TB prevention is still lagging behind for many reasons including: (i)underfunding; (ii) inadequate access to sensitive screening tests (such as CXR) which are essential to exclude active TB before initiation of TPT; (iii) limited access to tests for TB infection to target TPT appropriately, especially in HH contacts over the age of 5; (iv) provider and targeted individuals/communities' hesitancy; and (v) continuing challenges in efforts to find people with TB and thereafter identify those in need of TPT. The challenges with finding people with active TB were worsened by the COVID-19 pandemic in 2020.

While TPT coverage in HH contacts under 5 declined in 2020, no similar drop in coverage in PLHIV was observed, probably due to rapid adoption of coping measures to ensure continuity of services in HIV programs. Important lessons that have come out of the COVID-19 pandemic include the strengthening of airborne infection prevention and control measures, the de-stigmatization of IPC measures such as isolation and mask wearing, and integration of responses to COVID-19, TB and other airborne infections.

Outlined below is the narrative analysis of information obtained from key informant interviews together with our interpretation of this data.

**Enablers and opportunities for IPC and TPT expansion**

Processes on TB-IPC are currently not recorded and reported. The COVID-19 pandemic resulted in increased awareness and recognition of the importance of prevention of airborne infections transmission which could benefit TB-IPC, but not necessarily improve recording and reporting of TB-IPC. The targets set at the UNHLM brought TPT to the fore, but there is no strong evidence that these targets contributed to the increase in funding for TB prevention by the Global Fund that occurred between NFM2 and NFM3. With TB prevention now included among the sub-objectives of the 2023-2028 Global Fund Strategy, a greater focus on TB prevention is to be expected, and there is real potential to use catalytic investments to accelerate TB prevention in the next funding cycle (NFM4).

**Partner coordination**

Despite a high level of alignment on TB prevention, there is no effective coordination among partners at the global level. There is a lack of engagement of partners outside TB and or the health sector that may support TB prevention through supporting actions to address social determinants of TB and vaccine development and preparedness. There may also be inadequate coordination of efforts at the country level too, including inadequate linkages between HIV and TB programs.

**Levers that the Global Fund could use to support TB prevention**

The Global Fund allocated funding for catalytic investments (Strategic Initiative (SI) and Matching Funds (MF)) for TPT in PLHIV in NFM3 to catalyse action at the country level which may be having a positive effect on uptake and coverage of TPT in this high-risk group. Improved guidance to countries through the TB, HIV and RSSH information notes probably also helped countries to prioritize TB prevention in funding requests to the Global Fund. The Global Fund's TRP has emphasized the role of TB prevention in its reports in both NFM2 and NFM3 which may have helped countries to include these interventions in their funding requests to the Global Fund.

**Information systems for TB prevention**

The monitoring, evaluation and learning (MEL) framework is inadequate for TB prevention with incomplete indicators for both IPC and TPT. In our view this is also a result of lack of prioritization of TB prevention.

**The Modular Framework**
The NFM2 and NFM3 Modular Framework buries TB prevention into a module that is overwhelmingly focused on finding people with TB and provide treatment. To address this constraint, there is on-going work to revise the modular framework, including the introduction of a new module on TB prevention, separate from the TB care and treatment module.

**Community Engagement in TB prevention**
This evaluation did not identify data on community engagement in TB prevention and on the contribution of the private sector. In a parallel TERG evaluation on community engagement and community led responses, quantifiable community TB case finding is cited as a good example of how communities can be engaged in the work supported by the Global Fund. The evaluation on Community Engagement (CE) and Community-led Response (CLR) evaluation does not mention specifically TPT intervention as one of the community interventions, since the aim of this evaluation was not to list and assess all CE interventions. The TB prevention evaluation found absence of global targets, technical guidance and global strategies on community engagement on TPT, highlighting that the mindset on CE was on finding missing people with TB without linkage of ACF to TPT.

**Global Fund's role in research for TB prevention**
In the 9 countries where country case studies were undertaken, the evaluation team did not observe or receive information about on-going or planned operations/implementation research on TB prevention, except in Thailand.

**The Global Fund's engagement with other areas of TB prevention**
The Global Fund is not best placed to address social determinants of TB, as that would be beyond its mandate. Equally the Global Fund is not well placed to address issues related to development and deployment of TB vaccines, which is best tackled by other global health partnerships, specifically GAVI. However, the Global Fund can engage with these entities and play a supportive role in promoting access to TB vaccines when these become available.

## 1.5. Conclusions

The Global Fund responded to evolving needs at the global level to better address TB prevention by increasing its investments in this area of work. Thus, the Global Fund has supported expansion of TPT in HH contacts under 5 and PLHIV and supported TB-IPC. These investments have been highly relevant but remain relatively small as a proportion of the overall Global Fund resource envelope and of TB grants.

The total available funding and the funding gap for TB prevention is difficult to estimate in Global Fund NFM2 and NFM3 country funding allocations, due largely to how TB prevention costs are integrated amongst Modules, Interventions, and Detailed Activities, and there is no clear way to consistently isolate and analyse expenditures and absorption rates across countries.

Proportionately TB prevention has a lower budget than HIV primary prevention. As reported in the TERG Thematic Review on HIV Primary Prevention, HIV Prevention accounted for 13% of the NFM3 HIV grant budget, compared with the 6.4% estimation for TB prevention in TB grant budget in NFM3.

A flattening of TPT uptake and declining coverage in HH contacts under the age of 5 between 2018 and 2020 was observed. This decline in TPT coverage in 2019 and 2020 could be due to the yearly increase of the UNHLM targets with decrease of TPT uptake due the impact of the COVID-19 pandemic**.** The evaluation team observed lowest coverage of TPT in HH contacts over the age 5, with no data on TPT coverage for other high-risk groups for whom TPT may be beneficial such as prisoners, immigrants, health care workers, and those with existing medical conditions

It is noted that the only indicator on IPC is the number of health staff with TB, which has not been included in the Global Fund grant Performance Frameworks for current grants and is not routinely reported to WHO. With the lack of measurement and tracking of performance, it is difficult to assess whether Global Fund investments in TB IPC represent value for money.

Currently, measurement gaps appear to be a major constraint for TB prevention. A lot of focus of TPT has been on uptake and coverage while equally important parameters such as completion rates and adverse event monitoring have been relatively ignored. The monitoring of TB-IPC is hinged on surveillance of active TB among health care workers which ignores evaluation of the coverage and quality of TB –IPC interventions at health care facilities.

This evaluation revealed a lack of strategy and data for the involvement of communities, yet TPT, especially for HH contacts and non-clinical at-risk population is likely to work best when the intervention is delivered at the community level. The optimal way to deliver both TB-IPC and TPT interventions to achieve effectiveness and efficiency is unclear. However, the Global Fund and recipient countries did not seem to have plans to carry out operations/implementation research to address this gap.

While global level policies and guidance including by the Global Fund appear appropriate, implementation of TB prevention has been sluggish. There are no major gaps in Global Fund processes for TB prevention except with the Modular Framework used in NFM2 and 3 which made identifying costs for TB prevention interventions and activities a difficult task. The Global Fund is contributing to the scale up of TPT uptake and coverage, but only in the traditional at-risk populations currently (children under 5 and PLHIV). While the Global Fund has been supporting TB infection prevention, measurement challenges for this intervention, preclude an assessment of the outcomes and impact of these interventions.

In line with sub-objective 2 of the new Global Fund Strategy, 2023-2028, it is recommended that the Global Fund undertake the following actions to support the expansion of TB prevention interventions (TPT and IPC) while ensuring a high quality of these interventions

## 1.6. Table of recommendations

The table below summarizes recommendations arising out of this evaluation: the recommendations in **bold** are prioritized high while those in *italics* are of moderate priority

| Area of focus | Overarching recommendation | Recommendations | Type | Responsibility | Timeline |
|---|---|---|---|---|---|
| **Financing for TB Prevention:** | The Global Fund and partners are urged to continue mobilizing additional financial resources to support robust programming of TB prevention in TB endemic settings. | **Consider including TB prevention, with a focus on TPT, in the list of priority interventions to benefit from catalytic investments (SI and MF) for specific high-risk groups beyond PLHIV.** | Policy | Global Fund Secretariat, Global Fund's Strategy Committee, Global Fund Board | During preparation for NFM4 |
| | | **Collaborate and partner with others to develop and support countries to use budget templates and tools for TB prevention, both IPC and TPT** | Operational | Global Fund Secretariat and partners | During preparation for NFM4 |
| | | *Collaborate and partner with other stakeholders such as UNITAID and the Global Drug Facility as they undertake market shaping activities to address the challenge of cost, affordability and availability of newer shorter rifapentine based TPT regimens.* | Operational | Global Fund Secretariat and partners | During preparation for and implementation of NFM4 |
| **TB prevention data availability and quality** | The Global Fund and partners are encouraged to support countries to develop (if not existing) and enhance TB prevention health information system that captures the entire cascade of processes, outputs, outcomes and impact. | **Define and elaborate key indicators for TB-IPC and TPT to enable target setting and assessment of cost efficiency and cost effectiveness of these interventions** | Operational | Global Fund Secretariat and partners | During preparation for and implementation of NFM4 |
| | | **Provide technical support to countries to set high, but realistic targets for TB prevention and have a monitoring and evaluation framework in place that allows the Global Fund, partners and the countries to monitor and track TPT and IPC uptake, coverage and outcomes.** | Operational | Global Fund Secretariat and partners | During preparation for and implementation of NFM4 |
| **Quality of TB prevention Services** | The Global Fund and partners are encouraged to develop mechanisms to support countries to provide high quality TB prevention services. | **Define and publish program essentials for TB prevention that recipient countries should strive to achieve** | Operational | Global Fund Secretariat and partners | During preparation for and implementation of NFM4 |
| | | **Encourage and support countries to adopt and scale up more sensitive and specific TB screening approaches such as digital chest x-ray with artificial intelligence (computer aided diagnostics)** | Operational | Global Fund Secretariat and partners | During preparation for and implementation of NFM4 |
| | | *Encourage and support countries to adopt and deploy more sensitive, specific and probably easier to deploy tests for TB infection* | Operational | Global Fund Secretariat and partners | During preparation for and implementation of NFM4 |

| | | | | | |
|---|---|---|---|---|---|
| | | *Reinforce messaging for TB-IPC, through the TB information provided to countries to emphasize that the development and implementation of TB-IPC programs should be part of the wider health system effort to prevent transmission of infections at the health facility level and the community level* | Operational | Global Fund Secretariat and partners | During preparation for and implementation of NFM4 |
| **Community engagement:** | The Global Fund is strongly urged to encourage and push countries to include and engage communities fully in the development, implementation and monitoring of interventions for TB prevention | **Encourage and support countries to engage communities in the delivery of TB prevention services through BCC and other measures, including community led monitoring** | Operational | Global Fund Secretariat and partners | During preparation for and implementation of NFM4 |
| **Operations and implementation research for TB prevention** | The Global Fund and partners are encouraged to support appropriate research, including operations and implementation research to better define how TB-IPC and PMTPT should be implemented and or delivered. | *Work with partners to define and elaborate implementation level TB prevention knowledge gaps and questions that need to be addressed through well designed operations, implementation, or health system research* | Operational | Global Fund Secretariat and partners | During preparation for and implementation of NFM4 |
| | | *Consider setting up a mechanism to fund regional or multi-country level implementation or health system research and the use of "request for proposal" approach to undertake high quality research to provide evidence of approaches that will address global, regional, and multi-country obstacles to implementation of TB prevention interventions.* | Policy | Global Fund Secretariat, Global Fund's Strategy Committee, Global Fund Board | During preparation and implementation of NFM4 |
| | The Global Fund and partners are encouraged to support countries to prioritize their target groups for TPT based on their epidemiological and funding context | **Group 1- Household contacts of bacteriologically positive people who are below 5 years old and PLHIV - highest priority.**<br>**Group 2: Household contacts of bacteriologically positive people > 5 years with additional risk factors for progression to active TB such as those who are malnourished, diabetics, older than 65 and alcohol use disorders – high priority.**<br>*Group 3: Non HH contacts with high rates of TB such as persons older than age 65, health care workers, prisoners, etc - medium priority* | Operational | Global Fund Secretariat and partners | During preparation for and implementation of NFM4 |

## 2. Introduction/Background

Tuberculosis remains a major global public health threat. In 2020 this disease was the second commonest cause of death from a single infectious pathogen, having ceded the first position, a place it had been for a long time, to COVID-19. The World Health Organization (WHO) estimated that more than 10 million people developed TB in 2020 and over 1.5 million people died of the disease. While the trend had been a small annual decline in the global incidence of the disease, in 2020, there was no observed change in the incidence of TB compared with the previous year and for the first time since 2012, estimated TB deaths increased[4]. These worrying epidemiological trends were attributed to the on-going COVID-19 pandemic which has reversed years of progress made in the fight against TB. As a consequence of measures to limit the transmission of SARS-COV2, including lockdowns and travel restrictions; diversion of health resources such as finances, human resources and equipment to the COVID-19 response; and societal perceptions of risk of acquiring SARS-COV 2 infection at health care settings, the number of people being screened, tested, diagnosed, and treated for TB decreased markedly in many TB endemic countries[5]. To confront this new challenge to TB care and prevention, the WHO and other global level players, including the Global Fund, urged TB endemic countries to first adopt measures to ensure continuity of TB services as the COVID-19 pandemic evolved, and later to enhance efforts to regain control and to accelerate progress towards ending TB as envisaged in the End TB Strategy.

In 2014 the World Health Assembly adopted the End TB Strategy with its ambitious targets to reduce TB incidence and mortality by 90% and 95% respectively by 2035 compared with the rates in 2015. Interim targets and milestones were set to be achieved by 2020, 2025 and 2030. As of now (2022), a decline in TB incidence and mortality of at least 20% and 35%, respectively, should have been achieved. To stimulate action and spur progress, world leaders at the first ever United Nations General Assembly High Level meeting on TB (UNHLM) held at the UN headquarters in New York in 2018 made commitments which included the identification and placement of 40 million people with active TB on TB treatment, and 30 million people on TB preventive treatment by 2022[6]. Unfortunately, all these targets are currently off track. The major constraints lie in insufficient global financing for TB, inadequate identification of people with TB and slow progress with TB prevention.

Since the declaration of TB as a global emergency by the WHO in 1993[7], the focus has been on finding people with TB and providing them with appropriate treatment. Until recently little attention has been paid to the prevention of TB disease in high TB endemic settings, even though there are good examples of the role that TB prevention played in the rapid reduction of the incidence of TB in high income settings. In these countries TB care and prevention programs included TB preventive treatment among

[4] WHO, Global TB Report, 2021
[5] The Global Fund 2021a
[6] Political Declaration of the UN General Assembly High Level Meeting, United Nations High Level Meeting on the fight against tuberculosis, 26 September 2018, UNHQ, New York. Resolution A/RES/73/3
[7] WHO Global Tuberculosis Programme. (1994). TB: a global emergency, WHO report on the TB epidemic. World Health Organization. https://apps.who.int/iris/handle/10665/58749

the key components[8] [9]. Comprehensive TB prevention currently requires a multi-pronged approach that includes addressing the social determinants of the disease, early identification and treatment of people with TB to limit transmission and the provision of TB preventive treatment (TPT) in persons latently infected with *Mycobacterium tuberculosis*. The emphasis of TB prevention has been on TPT in individuals at an elevated risk of progression to active TB disease and TB transmission prevention and control (IPC), not only at health facilities, but also at other congregate settings including at community level. In high TB endemic settings, targeting of TPT has, until recently, focused on children below the age of five who are HH contacts of persons with TB and in people living with HIV (PLHIV).

Over the past seven years since the World Health Assembly announced its End TB Strategy (2014) and after the UNHLM, there has been a shift and recognition of the importance of TB prevention to meet the goal of ending TB as a global public health threat by 2035. Modelling work has suggested that TB preventive treatment can contribute significantly to the decline in TB incidence. For example, in South-East Asia, it has been estimated that if full coverage of TB preventive treatment is achieved by 2030, the annual incidence of TB would be reduced by 8.30%, relative to 2015, if TB prevention intervention is implemented alone. Additionally, there would be an increase of 6.93 percentage points reduction in annual incidence of TB if TB prevention intervention is implemented in the backdrop of improved TB care cascade[10].

The Global Fund to Fight AIDS, Tuberculosis and Malaria (the Global Fund), established in 2002, is a partnership designed to accelerate the end of AIDS, tuberculosis and malaria as global epidemics**.** In the twenty years of its existence the Global Fund has become a major player in the financing of global health and is currently the largest external source of funds for TB care and prevention in low-and middle-income countries where the burden of TB is concentrated.

As a key global player in the fight against TB, and with the renewed global focus on TB prevention, the Global Fund has prioritized TB prevention, with an emphasis on TPT and airborne infection prevention and control (IPC). Tuberculosis prevention is now included as one of the TB sub-objectives of the next Global Fund Strategy covering the period 2023-2028. The other 4 sub-objectives are: finding and treating all people with TB (both drug susceptible and drug resistant TB); improving quality of TB services including management of co-morbidities; adaptation of TB programs to evolving situations including use of new tools and innovations; and promoting enabling environments in partnership with communities and affected populations to reduce stigma, discrimination and human rights and gender related barriers to care.

Programs supported by the Global Fund have reported progress with TPT coverage as the number of people receiving preventive treatment quadrupled from 1 million in 2015 to 4.7 million in 2020[11]. Despite this achievement, progress has been insufficient and slow with only a small proportion (29%) of the 30 million people targeted globally to receive TPT between 2018 and 2022 provided with this treatment by 2020. Performance was worse for older persons over the age of 5 years who are household

[8] Thomas HL, Harris RJ, Muzyamba MC et al Thorax 2018; 73:769-775
[9] George W Comstock, Robert N Philip Public health reports 1961; 76(1): 19-24
[10] Mandal S, Bhatia V, Sharma et al, BMC Med.2020 Jul 20; 18(1): 163
[11] Tuberculosis - The Global Fund

contacts of persons with active TB, for whom only 1.6% of the targeted 20 million people had received TPT by 2020[12].

Tuberculosis IPC ideally should be an integral component of national and health facility associated infection transmission prevention programs and is relevant to all health systems because it affects the health outcome of patients and health care workers. TB-IPC interventions are however, currently inadequately implemented. In an individual-based model of M.tb transmission in households and primary healthcare (PHC) clinics in South Africa, it was estimated that 7.6% [3.9%-13.9%] of TB and multidrug resistant TB in adults resulted directly from transmission in PHC clinics in 2019. The model estimates that between 2021–2030, IPC interventions could reduce incident TB in the community by 3.4%–8.0%, and TB deaths by 3.0%–7.2%[13]. WHO reported in its "guidelines on core component of infection prevention control at the national level and acute care health facility"[14] that on average at any given time, 10% of patients in developing countries will acquire at least one Health Care-Associated Infection (HAI). HAI is a public health problem with a significant economic burden, preventable through effective IPC measures and awareness at national and health facility level. Tuberculosis acquired at a health facility is an adverse event of care delivery not properly addressed, measured and prevented. Tuberculosis IPC is poorly reported and dramatically lacks an appropriate monitoring and evaluation framework including indicators and data on processes, outputs and outcomes. Therefore, the Global Fund's drive to make progress with TB prevention is timely.

[12] WHO Global TB Report, 2021
[13] Estimating the contribution of transmission in primary healthcare clinics to community-wide TB disease incidence, and the impact of infection prevention and control interventions, in KwaZulu-Natal, South Africa. McCreesh N, et al. BMJ Global Health 2022;7:e007136. doi:10.1136/bmjgh-2021-007136
[14] ISBN 973-92-4-154992-9 WHO 2016

# 3. Review rationale/Objectives

This TB prevention evaluation is a learning opportunity for the Global Fund as it seeks to assess its role in the support provided to TB prevention efforts. This evaluation is intended to provide essential information to help the Global Fund as it looks forward to investing in future policies, processes, and programming to support TB prevention. The evaluation also aimed to provide information to support the Global Fund to operationalize sub-objective 2 of the TB component of the 2023-2028 Global Fund Strategy.

## 3.1. This evaluation had five objectives:

1. Review the Global Fund policies, processes, and guidance to shape and enhance the inclusion of TB prevention programs in the next funding allocation cycle (NFM4) and the 2023-2028 Strategy period.
2. Outline the Global Fund's role to date (alone or with partners) in supporting TB prevention.
3. Assess the scope, scale, and results of previous Global Fund investments in TB prevention.
4. Identify obstacles, or enhancements, to the implementation of TPT and IPC during the ongoing COVID-19 pandemic.
5. Identify recommendations to inform the Global Fund's future role and investment in TB prevention.

The primary intended users of the evaluation are the Global Fund's Board and its Strategy Committee (SC), the TERG, and key Secretariat staff involved in TB prevention. Secondary intended users include Principal Recipients (PRs), National TB programs (NTP) and their partners, Country Coordinating Mechanisms (CCMs) and Global Fund Country Teams.

## 3.2. Scope of the evaluation

A comprehensive approach to TB prevention requires a multi-pronged approach to address social determinants of TB; i) identify all people with active TB early and initiation of appropriate treatment; ii) comprehensive implementation of IPC, especially at health facilities, congregate settings and community level; iii) TPT; and iv) the deployment of an effective vaccine when one becomes available. The rapid decline in TB incidence that was observed in high income countries in the last century is attributed to four factors: universal access to high quality TB diagnosis and treatment, implementation of social protection programs, general socio-economic development which included improved nutrition and living and working conditions. This evaluation could therefore have delved into all these areas of TB prevention, however, in discussion with the TERG and the Global Fund Secretariat, it was agreed that the focus of this evaluation will be on IPC and TPT. The evaluation team therefore paid attention to issues affecting the implementation of interventions related to TPT and IPC with a focus on:

- TPT among children under 5 years old who are HH contacts of people with TB.
- TPT among persons over 5 years old who are HH contacts of people with TB.

- TPT among People Living with HIV (PLHIV) on ART and who never received TPT before.
- TPT among high-risk or vulnerable groups such as prisoners, health care staff, poor urban populations, migrants, people undergoing dialysis among others as listed in the current WHO guidelines on treatment of TB infection.
- TB-IPC which consists of a combination of measures designed to minimize the risk of *Mycobacterium tuberculosis* (M.tb) transmission within populations. The evaluation team focused on airborne infection transmission prevention and control of *M.tb* at the health facility level. While airborne infection transmission prevention is recommended at the household and community level, there is no information, in general, on how often recommended actions are undertaken and the impact of these actions on TB infection and disease. At the health facility level, the three hierarchical areas of TB-IPC were examined, i.e., administrative control, environmental controls and respiratory protection.

Additionally, the evaluation examined if links were being made to link TB-IPC with efforts to combat anti-microbial resistance (AMR). It is also recognized that TB-IPC needs to be linked to occupational health and safety for all health care workers at health facility and community level. Related to this TB-IPC should be a component of national IPC programmes with TB surveillance in health care workers included among indicators for HAI. Tuberculosis transmission at health care settings is an adverse event for individuals who use these facilities, either as health care workers or those seeking health care services.

While the evaluation was focused on TPT and IPC, it is recognized that TPT cannot happen in isolation and is intricately linked with processes for identifying people with active TB, commonly referred to as Active (TB) Case Finding (ACF) Therefore, the evaluation team, as far as feasible, attempted to also include ACF interventions which are considered important initial steps for the provision of TPT. Assessment of ACF or early TB diagnosis focused on key populations who are eligible for TPT including HH contacts of index people with TB, persons receiving care for HIV/AIDS and other high-risk populations. Recognizing the close interrelation between ACF and TPT activities, this evaluation attempted to interrogate coverage of ACF for key populations eligible for TPT and the linkages between ACF and TPT.

An evaluation of TB responses and interventions taking place in the current time period would be incomplete if the impact of COVID-19 is not examined. In line with the evaluation's Terms of Reference (ToRs), this evaluation assessed the impact of COVID-19 on TB prevention with a focus on IPC, ACF and TPT activities. The evaluation team attempted to identify and document lessons learnt on the prevention of COVID-19 transmission at health facility and community level that may be applicable to the control of TB transmission in these settings, as well the reverse - the adoption of lessons from TB control that were adopted for the control of SARS-COV2 transmission. Knowledge of the interventions that worked well would place the world, and especially low- and middle-income countries, in a better position to tackle the next global pandemic, should that pandemic involve airborne transmission of a pathogen. Measures that potentially would simultaneously benefit control of TB and COVID-19 such as integrated and comprehensive approaches to IPC, contact management, and shared resources including human resources and equipment were also explored.

# 4. Review methodology

## 4.1. Approach and methodology

### 4.1.1. Overview

This evaluation was operationalized through five Evaluation Questions (EQs) and four complementary modules presented in the inception report and in Annex 1 of this document. The evaluation questions and the questionnaires used to guide data collection can be found in Annex 2.

The scope of investigation, summary of the topics, the type of information to be collected, the tools to be used, and the skills required were finalized after discussions between the evaluation team and the TERG and Global Fund Secretariat (TB advisors at the Technical Advice and Partnership Division (TAP) of the Global Fund) where expectations of the TERG and the Global Fund Secretariat were clarified.

### 4.1.2. Sampling approach for country case study selection

**Country Selection criteria**
The evaluation team proposed to the TERG the following criteria for the selection of countries to be included in this evaluation: a) being in the list of 30 high TB, TB/HIV, MDR-TB and TB incidence countries; b) geographic spread and c) income level. The team of consultants were selected based on knowledge and experience in this field of work and being resident within the country or in a country that is in close proximity to selected countries to allow physical meetings with country stakeholders and to mitigate the risk of travel bans due to COVID-19.

The final list of 20 countries that was provided by TERG after internal processes within the Global Fund had been carried out includes India, Pakistan, Bangladesh, Philippines, Mozambique, DR Congo, Uganda, Lesotho, Zambia, Guinea, Nigeria, South Africa, Nepal, Thailand, Azerbaijan, Gabon, Ethiopia, Kazakhstan, Tanzania and Zimbabwe.

Of these 20 countries, the evaluation team carried out portfolio analysis alone in 11 (India, Pakistan, Bangladesh, Philippines, Mozambique, DR Congo, Uganda, Lesotho, Zambia, Guinea, Nigeria) and both portfolio analysis and in-depth country case studies in 9 countries (South Africa, Nepal, Thailand, Azerbaijan, Gabon, Ethiopia, Kazakhstan, Tanzania and Zimbabwe) and visits to 8 countries (there was no country visit to Kazakhstan).

Of the 20 countries, 14 belong to the group of countries classified as high TB burden countries, 15 are high TB/HIV burden countries and 13 are on the list of high MDR TB burden countries. The countries span 5 of the six WHO regions: 12 countries from AFRO (both French and English-speaking countries), 4 from SEARO, 1 from WPRO, 1 from EMRO and 2 from EURO. Five countries are categorized as Low-Income Countries (LIC), 10 as Lower Middle-Income Countries (LMIC) and 5 as Upper Middle-Income Countries by the World Bank. Collectively the twenty countries are estimated to carry 61% of global burden of TB (6 out of 10 million people estimated to have had TB in 2020), 69% of global TB/ HIV burden (539,000 people with TB/HIV) and 51% of

notified MDR-TB. In terms of size of the Global Fund grants, the 9 countries for case study represent US$ 2.5 billion (15%) out of US$16.4 billion signed TB and TB/HIV grants to countries and with the addition of the 11 countries selected for portfolio analysis alone, the grant size in these countries rises to 45% of the total Global Fund funding for TB to countries.

**Collaboration between the evaluation team, the Global Fund and selected countries**

The approach to this evaluation included review of relevant key Global Fund and partner documents, analysis of a portfolio of grants and monitoring efforts of the Global Fund Secretariat, in addition to discussions with relevant stakeholders at the global and country level. This evaluation had a strong focus on assessment of the implementation of TB prevention activities in countries, and the effectiveness of TB prevention funding in 9 sampled countries for case studies out of the 20 countries sampled for portfolio analysis. In order to understand existing TB prevention gaps, the drivers of these gaps and potential solutions interviews were held with key informants at both the global and country level. We developed questionnaires to guide the dialogue between the evaluation team and key informants. The evaluation team sought to understand: a) if there were gaps in global policies and guidance on TB IPC and TPT; b) the major barriers to implementation of interventions for TB prevention; c) the enablers and opportunities for the expansion of TB prevention; d) the impact of COVID-19 on TB prevention including lessons learned from the COVID –19 response that could be adopted and scaled up for TB-IPC and on the other hand lessons from the TB response that were adopted for the COVID-19 response and which may be useful for the control of future pandemics; e) the existing partner coordination mechanisms and the gaps therein; f) the levers that the Global Fund could use to support and enhance TB prevention; g) the financing landscape for TB prevention including the type of choices that will need to be made in the future to adequately finance TB prevention efforts without compromising other areas of TB care; h) the information system that is currently used to provide data on TB prevention and the gaps that need to be addressed; and i) the Global Fund Modular Framework and how it is currently supporting TB prevention. While not within the remit of this evaluation, the evaluation team also sought to gauge the opinion of key informants on the role, if any, the Global Fund may play to address social determinants of TB and TB vaccine development and preparedness. The questionnaires used for these KIIs can be found in Annex 2

The evaluation team used a narrative analysis approach to summarize the information obtained from key informant interviews and linked the qualitative information to the quantitative data to gain insights on issues related to TB prevention and draw conclusions.

Throughout this evaluation an attempt was made to:

- Assess crosscutting health system oriented and practitioners'-centred approaches for TB prevention, including TB prevention program leadership and ownership, product procurement and management, health information system and role of community health care systems.
- Explore how "new" programmatic areas and needs such as TPT with shorter regimens and ACF with new screening tools are progressing, so as to begin to understand how the Global Fund should respond to these needs going forward.

- Explore the changes that will need to be made at the country level to implement enhanced programs for TB prevention: this was primarily intended to answer the question–what capacity is needed at the country level to manage a TB prevention program effectively and efficiently?
- Identify and characterize the temporal impact of the ongoing COVID-19 pandemic on TPT and IPC activities.

To achieve the aims detailed in the preceding paragraphs the following activities were carried out:

- A "Kick-off" meeting at the beginning of the evaluation process with TERG and the Global Fund Secretariat in which the evaluation methodology was reviewed, anticipated challenges highlighted, expectation of the TERG and the Global Fund Secretariat clarified, and consensus built on the Theory of Change (ToC) of TB prevention and the evaluation.
- More than 150 key informant interviews at the global and country level with persons listed in annex 6. The key informants include 31 persons from the Global Fund Secretariat, 18 from WHO HQ and its regional offices, 3 from the Stop TB Partnership, 3 from USAID, 2 from CHAI, 2 from Milan Supra National Reference Laboratory, 1 from CDC, 1 from KNCV, 2 from the Union and 3 from the Global Fund's TRP.
- Country case studies were conducted in 9 countries[15] through face-to-face meetings and interviews with NTPs, PR, CCM members, WHO, CSOs and partners.
- Data and budget analysis was performed for 20 countries including 11 countries[16] where only the portfolio analysis (PA) was done and 9 countries where both PA and in-depth case study was carried out.
- A Monkey survey was sent out to stakeholders in the 9 countries where an in-depth country case study was carried out. The online survey was sent out via email at the time of the country visit to gather data from a wide group of TB stakeholders.

### 4.1.3. Data collection and analysis

The evaluation team was provided access to essential data by the TERG Secretariat and signed confidentiality agreements with the Global Fund. The TERG Secretariat and the evaluation team used a confidential data management system to: (i) store and organise documents and data efficiently; (ii) allow only evaluation team members to securely access data irrespective of where they are located geographically, and (iii) guarantee the maintenance of the confidentiality and sensitivity of data.

**TPT and IPC Data collection**

In this evaluation, TPT Uptake is defined as the number of individuals started on TPT in a calendar year.

TPT coverage is defined for each risk group (HH<5, HH>5, PLHIV) as the:

$$\frac{\text{Number of individuals in a risk group or population group started on TPT in a year}}{}$$

[15] South Africa, Nepal, Thailand, Azerbaijan, Gabon, Ethiopia, Kazakhstan, Tanzania and Zimbabwe
[16] India, Pakistan, Bangladesh, Philippines, Mozambique, DR Congo, Uganda, Lesotho, Zambia, Guinea, Nigeria

UNLHM target an age group/risk group in a year

Coverage with WHO and Global Fund data on TPT uptake are presented to assess their trend and level rather than to compare their performance.
This evaluation extracted TPT and IPC data from mainly the 2021 WHO Global TB report, the Stop TB Partnership-UNHLM target by country, country level data provided by NTPs and the Global Fund for both TPT indicators for NFM2 and NFM3 in the selected countries.

TPT uptake indicators monitored by the Global Fund in grants with TPT activities were a) TB/HIV-7-Percentage of PLHIV on ART who initiated TB preventive therapy among those eligible during the reporting period. In some cases, this data was disaggregated by age (<5, 5-14, ≥15), sex and regimen (3HP, 1HP, R, RH, H); b) TCP-5.1-Number of people in contact with TB patients who began preventive therapy, sometimes disaggregated by age (<5, 5-14, ≥15).

*Table 1 Data sources*

| Data | Source |
|---|---|
| **WHO Global TB report 2021** | WHO |
| **UNHLM Targets on TPT /risk group in a year per each country, dated 1st November 2019** | Stop TB Partnership |
| **National TB programme** | Country Ministry of Health- National TB Programme (MOH/NTP) |
| **The Global Fund** | Country Global Fund grant |

The evaluation team performed descriptive analysis and the results are presented as graphs and tables. Trends of coverage indicators were plotted and used to compare performance, for each country and over time. All data cleaning and analyses were performed using Stata version 15.1 (Stata Corp; Texas, United States of America).

**TPT and IPC budgeting and expenditure**
The evaluation team extracted cost data from the Global Fund Data Service on grant disbursements and progress updates and a consolidated dataset on NFM2 and NFM3 budget data. The evaluation team also extracted data from detailed budgets and consolidated files from NFM2 and NFM3 for each sampled country with available data.

Step 1: To estimate the **TB Budget/Grant** we included both the standalone TB Component and the TB Interventions/Activities under the HIV/TB Component

Step 2: Our estimate of the **TB Care and Prevention Module** is a straightforward summation of this Module (only) from both the standalone and HIV/TB Components.

Step 3: To estimate the total **TB Prevention Intervention** budget, we included the budget allocated to interventions identified in the Modular Framework as TB prevention interventions under the TB, HIV, HIV/TB and RSSH Components.

*Step 3 differs from the estimate of TB Prevention funding that was calculated by summing the TPT and IPC budget estimates as described in step 4 below.*

Step 4: To estimate the **TB Prevention as the sum of TPT and IPC** firstly, the amount of the budget that was allocated to each TPT and IPC interventions respectively was estimated. To arrive at an estimate of TPT and IPC costs the correct budget period and Modules of interest (TB, HIV/TB, HIV, RSSH) were filtered. Then he Detailed Budget Activity fields were searched for a list of possible key search words (i.e., inclusion criteria) to estimate the TPT and IPC costs respectively (see Table 2 below).

*Table 2 Key words selected in activities*

| | |
|---|---|
| **TPT** | **preventive treatment** |
| | preventive therapy |
| | TPT |
| | 3HP |
| | IGRA |
| **IPC** | infection control |
| | TST |
| | PPE |
| | Personal Protective Equipment |
| | UVGI |
| | Ultraviolet GUV |

Step 5: The resulting estimates were used to explore various relationships between the TPT and IPC budget figures with TB Grants and TB Prevention budgets in both the NFM2 and NFM3 budget period. This was performed at both the global and country case study levels.

Where feasible, data as obtained from the grant finance managers (or equivalent) at the Global Fund and at the country level. The Global Fund data explorer[1] was an additional source of data.

Then the interventions and activities under the HIV/TB and TB components were analysed in depth, to build an understanding of the proportion of the Global Fund Budget that the TB grants comprise and the proportion of TB grants that TB prevention comprises.[17] The interventions and activities included in TB prevention estimates are spread out and embedded in various components, modules and interventions which makes the calculation of TB prevention budget approximative, however, it was possible to calculate the approximate budget in NFM2 and NFM3 from the following modules, interventions and activities:

- TB Care and Prevention module
- MDR-TB module
- TB/HIV module / TB prevention intervention
- HIV and HIV/TB-related legal services interventions
- Human rights and medical ethics related to HIV and HIV/TB for health care providers
- Improving laws, regulations and polices relating to HIV and HIV/TB

[17] We are only able to do this detailed analysis of TB activities under the TB and HIV/TB components due to data constraints.

- HIV component
- RSSH component

#### 4.1.4. Quality Assurance

Our approach on quality assurance for this evaluation was presented in the inception report and is in Annex 5 of this report.

**Risk and mitigation factors**

At the inception of the evaluation, the evaluation team identified a small number of potential challenges to this evaluation, which are presented below alongside the solutions or mitigation measures undertaken. There were no high risks that needed to be communicated and escalated as required to the Global Fund.

*Table 3 Risk mitigation table*

| Potential challenge | Risk | Proposed solution | Residual | Status |
|---|---|---|---|---|
| Disruption to in-person data collection due to Covid-19. | H | Given the ongoing Covid-19 pandemic, there are a few potential risks to the data collection, such as disruptions to timelines and in-person data collection. To minimise the risk from in-person data collection, we had planned to provide teams with appropriate training and equipment regarding Covid-19. Our team was made up of in-country experts to minimise international travel and the associated risks, and we were ready to rapidly adjust to remote data collection methods should this become necessary. | M | Did not materialize |
| Delays to data collection due to unavailability low response rate of respondents. | L | Qualitative data collection is always dependent on the availability of respondents, which may be compromised by unforeseen events, time limitations, etc. The data collection process was closely monitored in all countries, to identify any concerns early on. Further, the evaluation team worked closely with the Global Fund and key stakeholders in-country to identify options and alternatives. | L | Low uptake of the on online survey, mitigated by repeated reminders and extending timelines |
| Stakeholders contest the results found by the impact evaluation | M | The evaluation team strived to be as transparent and clear in the methodology used, to ensure high quality results. Further, the creation of open communication channels between all parties was planned. | L | Has not yet materialised |
| Timelines are tight | M | The foreseen timelines, for the evaluation especially for inception and preparations are tight and requires good time management for the evaluation team to ensure data is collected on time and of high quality. We actively managed time as per the outlined workplan and sought guidance from the Global Fund where needed to allow for smooth implementation. | L | Delays in confirmation of countries selected for the evaluation. The evaluation team rapidly adjusted to the new timelines |

# 6.Review findings

## 6.1 Relevance of the Global Fund Investments in TB prevention

### 6.1.1 The global need for TB prevention

The focus of TB control programs has long been on finding people with TB to improve treatment coverage (proportion of estimated new people with TB in a population/country that are identified and placed on treatment), and to achieve the best possible treatment outcomes. Up to 2008, successive global strategies and guidance by WHO (the DOTS strategy, the Stop TB Strategy[18]) considered TPT as an intervention directed at the individual and not for "public health" to impact the epidemiology of the disease. Thus, TPT was directed at young children under the age of 5 who were household contacts of persons with infectious TB, PLHIV and those with other clinical risk factors for progression from TB infection to active disease. These are the individuals that were expected to benefit most from TPT.

The need to enhance measures to prevent TB transmission in health care settings was brought to the fore by the unfolding epidemic of drug resistant TB that was observed in the 1990s including in some high-income settings[19]. Disturbing reports of a breakout of cases of extensive drug resistant TB (XDR-TB) among HIV infected persons in South Africa[20] and the documentation in Mumbai, India, of a group of individuals who were identified to have TB considered untreatable at that time (drug resistance beyond XDR)[21], energized the TB community to develop robust guidance on prevention of TB transmission in health care settings. For a while TB prevention was seen in the eyes of drug resistant TB.

While both the DOTs strategy and the Stop TB strategy contributed significantly to the fight against TB, they were found to be inadequate and unlikely to lead to the desired epidemiological changes. This led to the development of the End TB Strategy, the current global blueprint for TB care and prevention. The End TB Strategy encourages comprehensive approaches that include addressing the social determinants of the disease; early identification and treatment of people with TB to stop transmission; prevention of TB transmission in health care settings, other congregate settings and in the community; and the provision of TB preventive treatment (TPT) to persons latently infected with *Mycobacterium tuberculosis* to not only benefit the individual person, but also contribute to the global goal of reducing incidence, mortality and catastrophic costs of TB. At the UNHLM commitments were made by Heads of Governments to scale up treatment of TB infection and go beyond HH contacts below age 5 and PLHIV. The targets were set at 30 million people to be placed on TPT including 4 million children <5, 6 million PLHIV and 20 million HH contacts over the age 5, between 2018 and 2022.

It is now widely accepted that TPT is a proven and effective intervention that is able to avert the development of TB disease, reducing this risk by about 60–90% when

[18] DOTS Strategy and the Stop TB Strategy
[19] MMWR 1993; 42 (22): 427-434
[20] PLoS One. 2011;6(5):e17513.doi: 10.1371/journal.pone.0017513.
[21] Udwadia ZF et al. Clin Infect Dis 2012; 54:579-581

compared to people who do not get TPT[22]. The intervention is endorsed by many key international institutions (WHO, Global Fund, UNAIDS, UNICEF, etc.). Studies in Vietnam showed that systematic screening of household contacts for TB disease has a very high yield and is a cost-effective ACF strategy [23]. Active case finding further paves way to effective treatment for TB disease and TPT in HH contacts and thus optimizes the public health impact on transmission, as well as improves TB-related outcomes for contacts (WHO TB prevention guidelines 2020). It is a key strategy for infection control as well in all settings.

A modelling study in WHO Southeast Asia (SEA) region showed that, at the regional level, full uptake of preventive therapy amongst identified risk groups would reduce annual incidence rates in 2030 by 8.30% (95% CI 6.48–10.83) relative to 2015, in the absence of any additional interventions. If implemented against a backdrop of improved TB treatment cascades, preventive therapy would achieve an incremental 6.93 percentage point (95% CI 5.81–8.51) reduction in annual incidence rates, compared to 2015. There is also a wide body of literature on cost-effectiveness and the impact of systematic provision of TPT in PLHIV on TB incidence in this population[24] [25] which supports greater resource allocation in all settings to expand programmes to deliver TPT to PLHIV.

As a global TB financing organization, the pertinent question therefore is how much did the Global Fund invest in TB prevention over the NFM2 and NFM3 periods in support of the global commitments and needs for TB prevention? This evaluation attempts to provide the answer to this question in the proceeding section.

### Financing of TB prevention by the Global Fund

Between the NFM2 and NFM3 budget periods, the overall Global Fund budget increased from $12,135,548,141 to $16,293,626,134. Within this total budget, the TB budget increased from $2,222,610,867 to $2,750,493,149 including funds allocated to TB in the standalone TB component, and in the TB budget within the TB/HIV component reaching together, 18% of the overall Global Fund budget in NFM2 & NFM3 (Table 4, Figure 1).[26]

[22] Getahun et al NEJM 2015 ; 136

[23] Lung T, Lancet Glob Health, 2019

[24] Uppal et al, PLOS Med 2021

[25] Shin H et al. JAIDS 2020

[26] Under NFM3 there was additional catalytic investment for TB (specifically TPT for people living with HIV) in seven of the 20 countries included in this evaluation. However, there is lack of data available on the size of this catalytic investment to use for this analysis, therefore the evaluation team have not included this in Tables 7-9, but has attempted to consider this additional investment by including TPT and IPC costs from all Components (i.e., not just TB and HIV/TB).

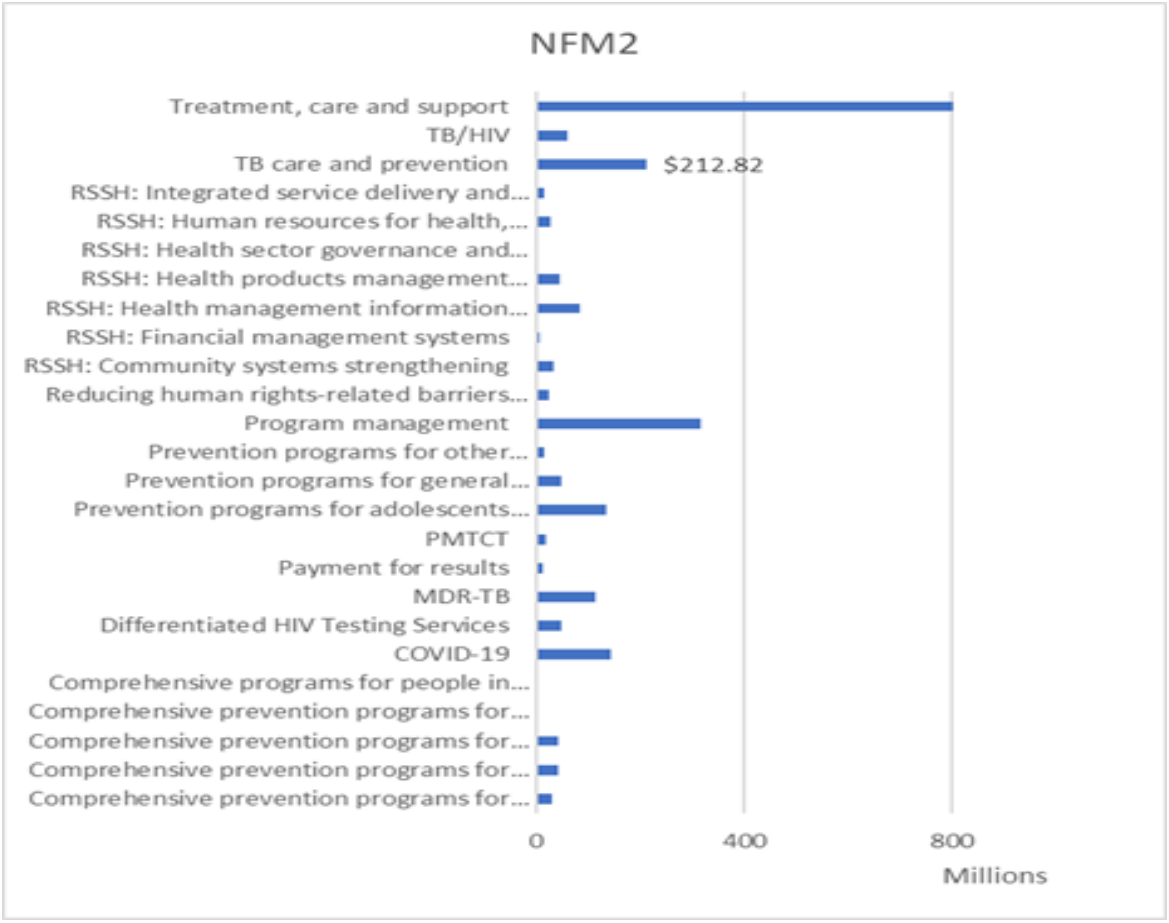
*Figure 1 Global Fund Budgets for TB and Other Components by Budget Periods*


*Table 4 TB Budget Across the GF Budget*

| | NFM2 | NFM3 |
|---|---|---|
| **Total Global Fund Budget** | $12,135,548,142 | $16,293,626,135 |
| **TB Standalone Component Budget** | $1,820,361,351 | $2,096,846,103 |
| **TB Budget (under the HIV/TB Component)** | $402,249,516 | $653,647,046 |
| **Sub-Total of TB Budget/Grant (across TB and HIV/TB Components)** | $2,222,610,867 | $2,750,493,149 |

The TB Care and Prevention Module accounted for 42% of the TB grants and 8% of the overall Global Fund Budget in the NFM2 budget period and about the same in NFM3, reaching 41% of the TB grants and 7% of the overall Global Fund Budget (Figure 1). The funding distribution by module and by Global Fund region is illustrated in Figure 2 and Figure 3 below.

*Figure 2 Distribution of Global Fund TB Budget by Modules within both TB and HIV/TB components*



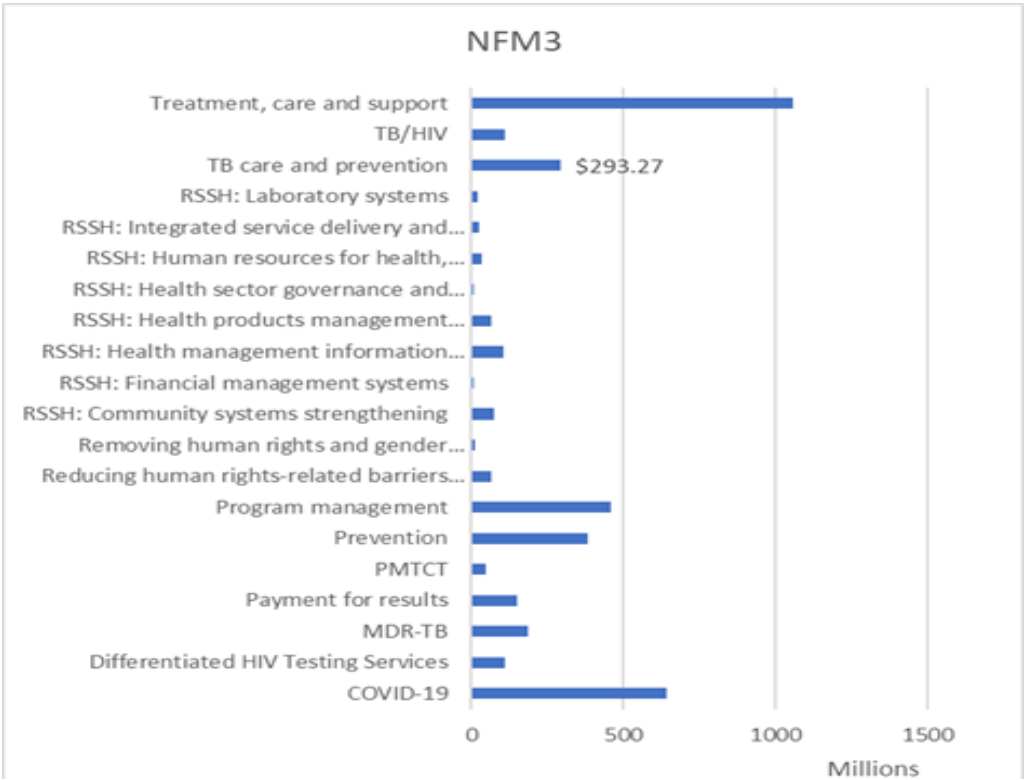



*Figure 3 TB Care and Prevention Budget by Region and Budget Periods (within both TB and HIV/TB Components)*

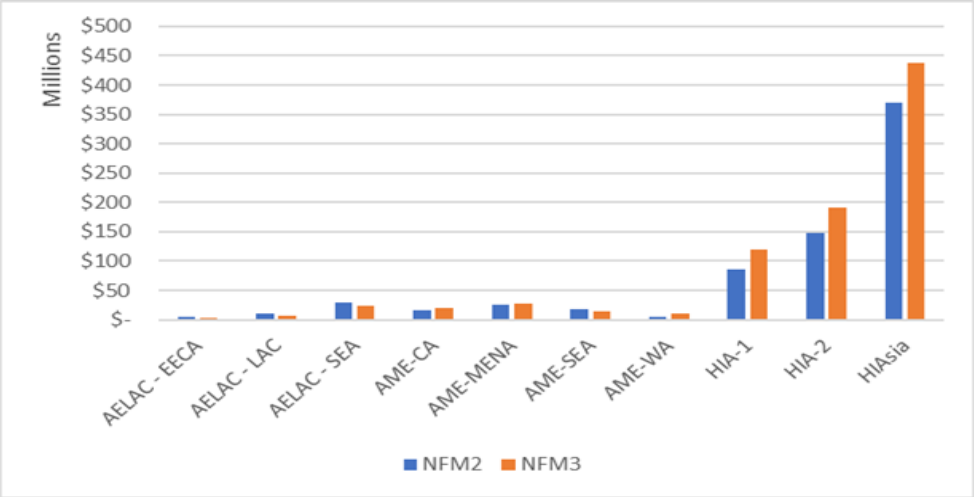



Figure 29 below shows the distribution of interventions within the TB Care and Prevention Module. There are 15 interventions that were budgeted for across the two Global Fund budget periods (11 in NFM2 and 11 in NFM3, but the list was slightly different). The TB Prevention interventions within the TB Care and Prevention Module represent mostly TPT.

*Figure 4 TB Care and Prevention Budget (Module) by Interventions and Global Fund Budget Periods (within both TB and HIV/TB Components)*

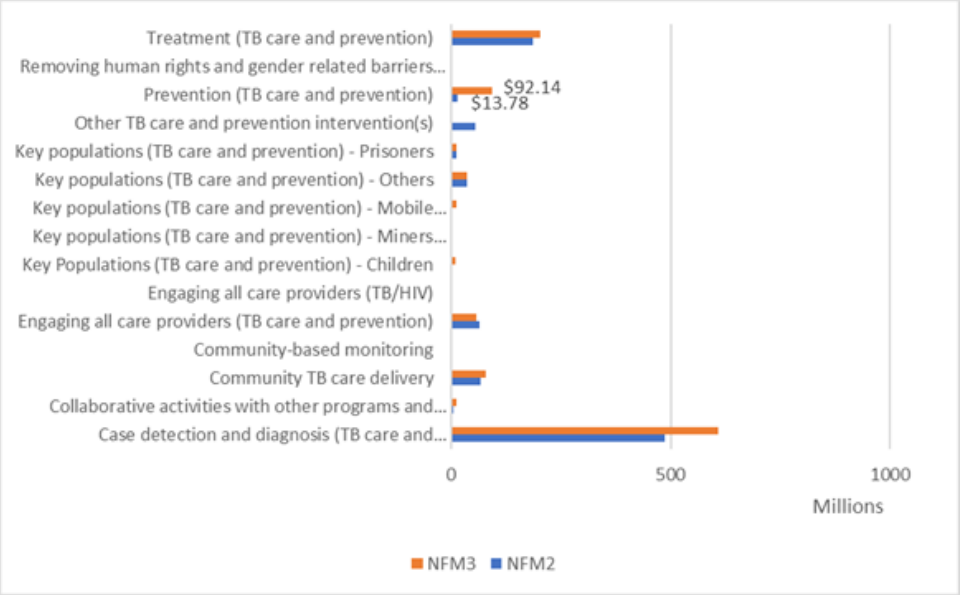



*Table 5 Summary of NFM2 and NFM3 Results*

| | | NFM2 | NFM3 |
|---|---|---|---|
| TB grant | (1) | $2,222,610,867 | $ 2,750,493,149 |
| TPT | (2) | $12,799,275 | $40 969 291.18 |
| TPT as % of TB grant | (2/1) | 0.6% | 1.7% |

| | | | |
|---|---|---|---|
| **IPC** | (3) | $123,587,386 | $129,091,380 |
| **IPC as % of TB grant** | (3/1*) | 5.6% | 4.7% |
| **TB prevention (TPT+IPC)** | (4=2+3) | $136,386,662 | $170,060,671 |
| **TB prevention as % TB grant** | (5=4/1) | 6.1% | 6.4% |
| **HIV prevention as % HIV grant** | (6) | 11% | 13% |
| **Prevention ratio HIV/TB** | (6/5) | 2 | 2 |

*Table 6 Distribution of TPT budget by component*

| | TPT | | |
|---|---|---|---|
| **Component name** | NFM2 dollars | NFM3 dollars | Total dollars |
| **HIV/TB** | 12 276 600.15 | 17 403 841.22 | 29 680 441.37 |
| **Tuberculosis** | 522 675.16 | 17 117 552.85 | 17 640 228.01 |
| **Multi-component** | - | 922 962.87 | 922 962.87 |
| **HIV/AIDS** | - | 5 524 934.24 | 5 524 934.24 |
| **RSSH** | - | - | - |
| **Total** | 12 799 275.31 | 40 969 291.18 | 53 768 566.49 |

*NB: While this calculation provides estimates of the IPC budget within the TB grant, it is important to note that some of the IPC costs are potentially found outside of the TB grant including in RSSH and HIV/TB interventions. This is due to limitations in the module budget framework as it is related to TB prevention (i.e., there is difficulty in separating out which costs within HIV/TB and RSSH modules are specifically allocated to the TB grant). Thus, this IPC budget estimate may possibly include some IPC costs that are related to another disease, not TB, leading to an overestimate.

Table 5 and Table 6 above shows that globally, the budget for TPT increased between the NFM2 to NFM3 budget periods, from $12.8 to $41 million. This is a significant increase in actual dollars budgeted and in the budget share of the TB budget (from 0.6% to 1.49%). Some possible reasons for this increase include additional budget for IGRA testing and rifapentine especially for TPT in PLHIV who benefited from dedicated catalytic investments (Matching Funds).

Table 6 above shows that globally, the budget for IPC increased between the NFM2 to NFM3 budget periods, from $123.6 to $129.1 million. While this is an increase in actual dollars budgeted, it accounts for a decrease in the budget share of the TB budget (from 5.6% to 4.7%). However, the IPC activities account for an amount that is greater than the TPT budget with some of these costs budgeted for outside of the TB Prevention and Care Module and outside TB grants in HIV/TB and RSSH grants.

The sum of TPT and IPC budget representing the TB Prevention budget increased from $136.4 to $176.1 million between the NFM2 and NFM3 periods essentially due to additional budget from dedicated catalytic investments for IGRA testing and Rifapentine for TPT in PLHIV from (Matching Funds). These activities (TPT and IPC) represent 6.1% of the TB grant under the NFM2 budget period and increased to 6.4% of the TB grant in the NFM3 budget period

A budget analysis of the 20 countries selected for this evaluation is presented in Figure 30, Figure 31, Figure 32, and Table 7 below. The amount and proportions of budget allocated to TPT, and IPC varied significantly by country. Of the sampled countries,

South Africa budgeted the most for TB Prevention (TPT and IPC) followed by India (whose TB grant was actually the highest). South Africa budgeted more for IPC than TPT in the NFM2 budget period and switched to budgeting more for TPT in the NFM3 budget period. India budgeted more for IPC in both the NFM2 and NFM3 budget periods.

*Figure 5 TPT and IPC Budgets Compared to the TB Budget/Grant at the Country Case Study-Level (NFM2 Budget Period)*

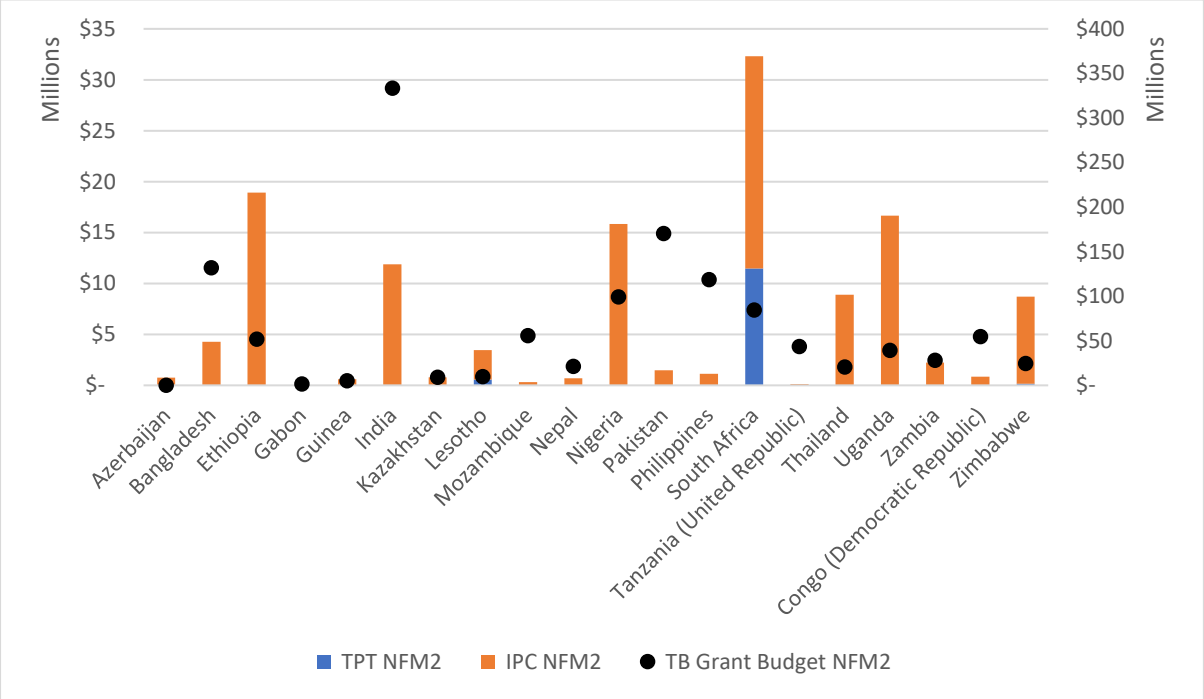



Figure 6 TPT and IPC Budgets Compared to the TB Budget/Grant at the Country Case Study-Level (NFM3 Budget Period)

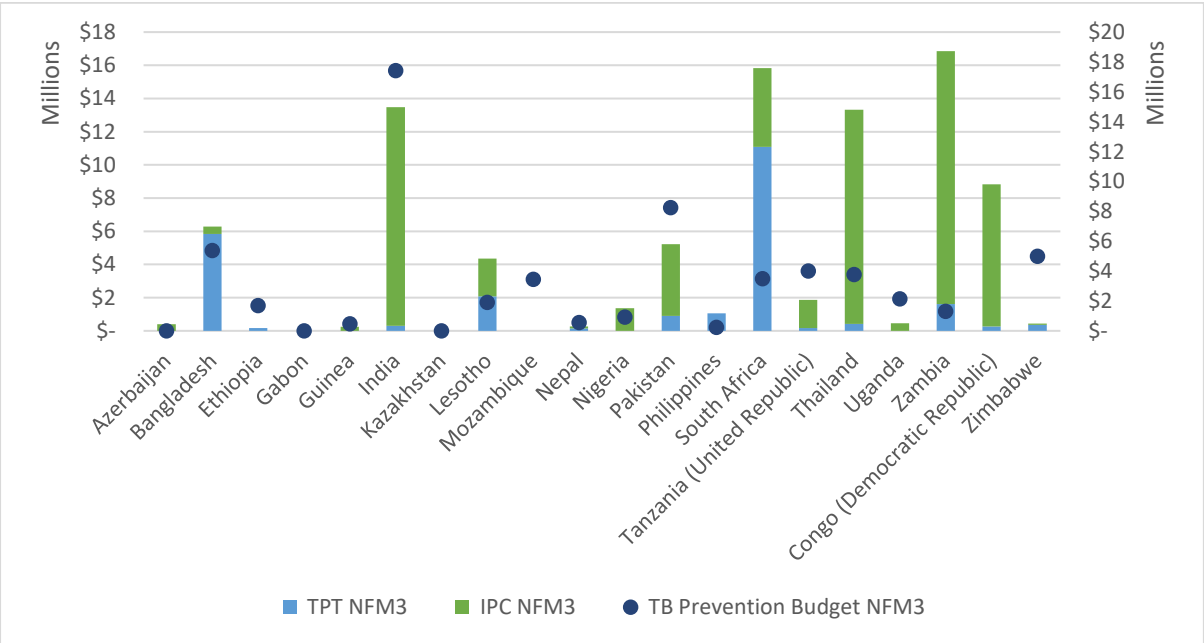


*Table 7 TPT and IPC percent share of TB Budget/Grant at the Country Case Study- Level*

| | NFM2 | | NFM3 | |
|---|---|---|---|---|
| **Country** | **TPT % of TB Grant** | **IPC % of TB Grant** | **TPT % of TB Grant** | **IPC % of TB Grant** |
| **Azerbaijan** | N/A | N/A | N/A | N/A |
| **Bangladesh** | 0 % | 2.56% | 4.11% | 0.31% |
| **Congo (Democratic Republic)** | 0 % | 1.59% | 0.40% | 12.63% |
| **Ethiopia** | 0 % | 0.44% | 0.31% | 0.00% |
| **Gabon** | 0 % | 0.31% | N/A | N/A |
| **Guinea** | 0 % | 0.01% | 0.00% | 3.66% |
| **India** | 0 % | 3.54% | 0.10% | 4.56% |
| **Kazakhstan** | 0 % | 8.76% | N/A | N/A |
| **Lesotho** | 5.80% | 29.50% | 17.91% | 19.58% |
| **Mozambique** | 0 % | 0.00% | 0.00% | 0.00% |
| **Nepal** | 0 % | 0.09% | 0.77% | 0.50% |
| **Nigeria** | 0 % | 0.36% | 0.00% | 0.87% |
| **Pakistan** | 0 % | 0.29% | 0.39% | 1.85% |
| **Philippines** | 0 % | 0.93% | 0.64% | 0.00% |
| **South Africa** | 13.62% | 24.69% | 6.62% | 2.84% |
| **Tanzania (United Republic)** | 0 % | 0.21% | 8.19% | 3.35% |
| **Thailand** | 0 % | 43.04% | 1.74% | 52.61% |
| **Uganda** | 0 % | 0.13% | 0.00% | 1.12% |
| **Zambia** | 0 % | 2.44% | 5.35% | 50.31% |
| **Zimbabwe** | 0.71% | 0.22% | 1.39% | 0.27% |

*Figure 7 Heat Map of the IPC Budget in the NFM2 and NFM3 Budget Periods*

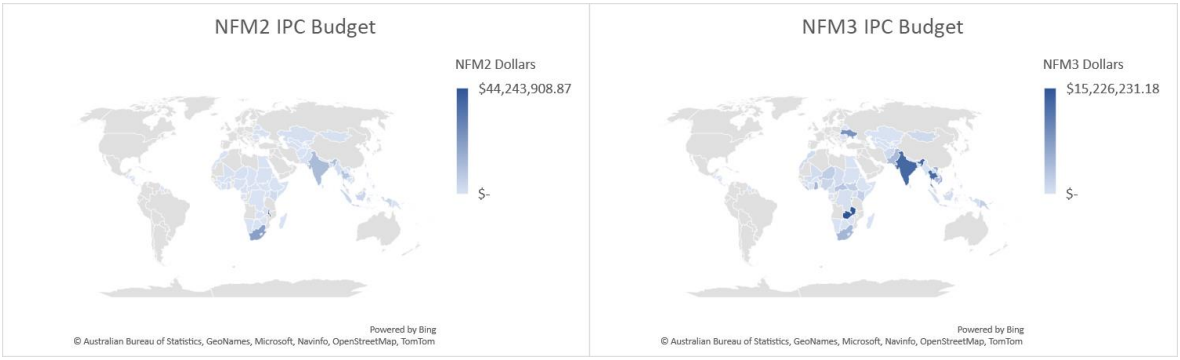
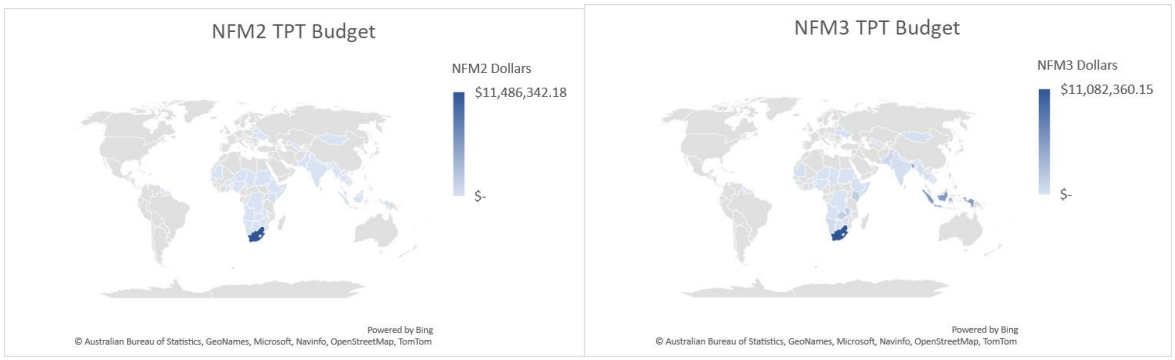


*Figure 8 Heat Map of the TPT Budget in the NFM2 and NFM3 Budget Periods*




Our analysis shows that an estimated 6.2% of the NFM3 TB budget was allocated to TB Prevention. The 2021 WHO Global TB Report estimated that TB Prevention accounts for 1.9% of global TB expenditures. Even the WHO estimate is vastly underestimated because the methodology used to arrive at this figure includes only TPT drugs and interventions specifically related to HIV-associated TB. This estimate does not include an adequate measure of support provided to household contacts to visit a health facility, community involvement to promote TPT among household contacts and among other adult risk groups (prisoners, health workers, immigrants, homeless people and people who use drugs), education of health staff and the population to address TPT hesitancy, operational research on TPT and IPC, HR for TB infection screening, and advocacy efforts to mobilize resources for TB prevention program management costs.

Similarly, and as stated above, some of the data limitations likely led to an overestimate of the IPC budget. As stated above, the IPC budget estimate may have included IPC costs that are related to another disease, not TB, leading to an overestimate of the TB-IPC budget. This is due to limitations in the module budget framework as it relates to TB prevention. It was difficult to separate out which IPC costs within HIV/TB and RSSH are specifically allocated to TB-IPC. Thus, the calculation of IPC as a percentage of the TB grant is also subject to this limitation.

There is no question that the funding gap for TB prevention is huge and currently underestimated. As reported in the TERG Thematic Review on HIV Primary Prevention, HIV Prevention accounted for 13% of the NFM3 HIV grant budget, compared to the 6.24% estimate we obtained for TB prevention in TB grant budget. This analysis and report make an important first step in improving estimates for the budget allocated to TB prevention. However, there are data limitations due largely to how TB prevention costs are integrated amongst Modules, Interventions, and Detailed Activities, posing challenges for these costs to be easily, clearly and consistently identified for analysis across countries. These challenges also limit the ability to analyse expenditures and absorption rates. Additionally, prevention costs have not been clearly and consistently budgeted using the Modules, Interventions, and Detailed Budget Activities.

The underfunding of TB prevention (IPC and TPT) is a result of de-prioritization of TB prevention relative to other TB interventions at the country level with applicants

consequently requesting relatively small amounts of money for this activity. Should reprioritization of TB prevention not occur, it is likely that applicants will continue to request for small sums of funds for this activity in NFM4, especially since the new rifapentine based shorter regimens are expensive, and may discourage countries to invest more resources in this area on the basis that the cost versus benefits may not be justified.

The WHO is currently assessing the cost of TPT to reach global UNHLM targets. The cost estimates will include funding required for screening and TB diagnostic tests, tests for TB infection and drugs for TPT. It is projected that the cost of PMTPT may exceed US$5 billion in 2022 alone.

It is important for all stakeholders, including the Global Fund and its partners, to understand that TB prevention will be expensive. We noted that there is ongoing work to try and cost the PMTPT package of interventions by WHO and the Stop TB Partnership. TB–IPC also needs to be appropriately costed with all elements of the IPC interventions appropriately prioritized and funded. Informants from the Global Fund highlighted the issue of applicants mostly requesting funds for facility refurbishment and nothing else. The evaluation team was unable to verify this information as a result of the spread of TB prevention activities in the Modular Framework as outlined above.

In NFM3 the Global Fund established catalytic investments for TPT in PLHIV covering 9 countries (Malawi, Tanzania, Zimbabwe, Lesotho, Eswatini, Ethiopia, Zambia, Nigeria, Mozambique), with 8 of these among those that were included in this evaluation. Of these 9 countries, 5 also have Matching Funds, including 3 (Tanzania, Zimbabwe and Lesotho) countries among the 20 evaluation countries. It was not possible in this evaluation to assess whether catalytic investments in NFM3, whose implementation in many countries is in the early phases, has had any impact on TPT uptake and coverage in the HIV infected population. While the Global Fund is able to establish catalytic investments for TB prevention, current policies that emphasize country ownership, would make it difficult for the Global Fund to set up a funding threshold for TB prevention. Other ways of encouraging countries to allocate an appropriate level of funding for TB prevention will need to be explored such as ensuring that applicants justify the absence of a request for TB prevention funding in NFM4 applications to the Global Fund without indicating the availability of funding for these interventions from other funding sources.

The evaluation team was unable to obtain estimates of the funding for TB prevention provided by partners or from domestic sources, and it is not clear how much alignment and synergism there is between Global Fund financing, other partner financing and domestic financing for of TB prevention. The major external source of funds for TB prevention beside the Global Fund is the United States Government through PEPFAR and USAID. While sub-optimal synergism between donors at the global level, is an issue, the bigger constraint is the relatively limited number of donors, and consequently a very small resource envelope for IPC and TPT.

In conclusion, the Global Fund has been actively supporting TB prevention, both IPC and TPT, in keeping with evolving priorities in the TB field and to meet global and country needs. The amount of funding for TB prevention increased between NFM2

and NFM3, which was in keeping with the increasing global importance and need for TB prevention. These investments have therefore been highly relevant, however, overall, the investments in this area have been proportionately small in relation to the overall available Global Fund financial resource envelope and to the resources allocated to TB. Within the Global Fund's overall resource envelope, funds allocated to TB prevention, comprised less than 1% of the total available Global Fund financial resources in both NFM2 and NFM3 and in the resources allocated to TB, TB prevention accounted for 6.1% and 6.24% in NFM2 and NFM3 respectively. A very large resource gap for TB prevention, estimated at close to USD 5 billion annually, persists.

## 5.1 Cost-Effectiveness and Cost-efficiency Analysis

Cost-effectiveness and cost-efficiency of Global Fund investments in TB prevention by first analysing budgets for TB prevention in NFM2 and NFM3 and then attempting to link the budgets to key TB prevention outputs and outcomes, including TPT uptake and coverage and TB rates in health care workers.

Based on the output and outcome indicator data that was available the evaluation team was able to make the following estimation related to cost-efficiency. We used the "PLHIV on TPT" indicator for South Africa and Tanzania because this data was available for both countries for the same years (one year each in NFM2 and NFM3).[27] As shown in Table 8 below, we estimated the per year cost for TB prevention in both NFM2 and NFM3 and used that figure to align with the 2019 (NMF2) and 2020 (NFM3) indicator data to calculate cost per PLHIV on TPT. As illustrated below, in Tanzania, it cost an estimated USD 0.05 per PLHIV on TPT in NFM2 (when there were no TPT costs, only IPC costs). Also in Tanzania, it cost an estimated USD 1.54 per PLHIV on TPT in NFM3 (29% of those costs were from TPT and 71% from IPC). In South Africa, it cost an estimated USD 83.86 per PLHIV on TPT in NFM2 (36% of those costs were from TPT and 64% from IPC). Also in South Africa, it cost an estimated USD 27.31 per PLHIV on TPT in NFM3 (70% of those costs were from TPT and 30% from IPC).

[27] None of the 20 CCS had data available for each year of the NFM2 and NFM3 budget periods, and data availability varied widely across countries (with major gaps in the data).

*Table 8 Cost-efficiency analysis of Global Fund TPT and IPC activities in South Africa and Tanzania*

| | | TB Prevention | | | |
|---|---|---|---|---|---|
| | | NFM2 | | NFM3 | |
| | | TPT | IPC | TPT | IPC |
| Tanzania | Full Cost | $ - | $ 93,169.39 | $ 4,159,620.61 | $ 1,703,846.52 |
| | Cost per year | $ - | $ 31,056.46 | $ 1,386,540.20 | $ 567,948.84 |
| | TB Prevention | $ 31,056.46 | | $ 1,954,489.04 | |
| | PLHIV on TPT | 578,401 | | 1,265,268 | |
| | Cost per PLHIV on TPT | $ - | $ 0.05 | $ 1.10 | $ 0.45 |
| | TB Prevention Cost per PLHIV on TPT | $ 0.05 | | $ 1.54 | |
| | | | | | |
| South Africa | South Africa | $ 11,486,342.18 | $ 20,821,546.38 | $ 11,082,360.15 | $ 4,751,321.00 |
| | Cost per year | $ 3,828,780.73 | $ 6,940,515.46 | $ 3,694,120.05 | $ 1,583,773.67 |
| | TB Prevention | $ 10,769,296.19 | | $ 5,277,893.72 | |
| | PLHIV on TPT | 128,419 | | 193,279 | |
| | Cost per PLHIV on TPT | $ 29.81 | $ 54.05 | $ 19.11 | $ 8.19 |
| | TB Prevention Cost per PLHIV on TPT | $ 83.86 | | $ 27.31 | |

Table 8 shows the cost-efficiency of TPT, the cost-efficiency of IPC, and the cost-efficiency of TB prevention (TPT + IPC) in both Tanzania and South Africa. We have displayed them together in the table to illustrate how the allocation of catalytic funding (which was provided in NFM3 in South Africa and not in Tanzania) may have had an impact on the cost-efficiency of activities. As with any such economic evaluation, it is very difficult to make comparisons across countries due to contextual differences, many of which are unable to be seen in the cost-efficiency results. As illustrated in the results, it became less cost-efficient in Tanzania to implement TB prevention activities between NFM2 and NFM3 (increasing from $0.05 to $1.54 per PLHIV on TPT). Conversely, it became more cost-efficient in South Africa to implement the same activities between NFM2 and NFM3 (decreasing from $83.86 to $27.31 per PLHIV on TPT)**.** There are many possible reasons for the higher costs in South Africa which were not able to be assessed through this analysis (including, for example, contextual differences, implementation models, health system ecosystem differences, etc.).

The evaluation team attempted to but was unable to calculate the cost-effectiveness of the TB prevention interventions (i.e., TPT and IPC) because of budget data limitations and further limitations with performance indicators (particularly for IPC where the indicator results are grossly underestimated and not comparable). Without being able to tie expenditures clearly and accurately to outcome indicators (for both TPT and IPC), a cost-effectiveness analysis is not possible. To do so would require availability of information on the impact of TB prevention on specific outcomes such

as new TB infections and cases averted. This information, as well as information to assess the relative contribution of Global Fund investment versus the contribution of other funders (i.e., USAID, national governments), is currently unavailable. Modelling work, however, suggests that TB prevention may contribute significantly to reductions in TB incidence, mortality, and costs.

Also, because there is a clear systems approach/framework to estimating the costs of service delivery (Figure 9), feeding into cost-effectiveness analyses, there needs to be more clarity and consistency in how TB prevention costs are budgeted within the Modular Framework so these can then be tracked consistently and analysed. This Framework illustrates the process in which costs (inputs) are linked to intermediary processes or actions that ultimately result in outputs and, eventually, long-term changes in TB outcomes.

*Figure 9 Example of Systems Framework for Understanding Costs*


[1] Ibin.
[2] Ibin.
[1] TB and HIV/TB Components which each contain TB Grants.
[2] Ibin.

## 5.2. Outputs and outcomes of interventions to prevent TB

### 5.3.1. TB Preventive Therapy uptake at global level

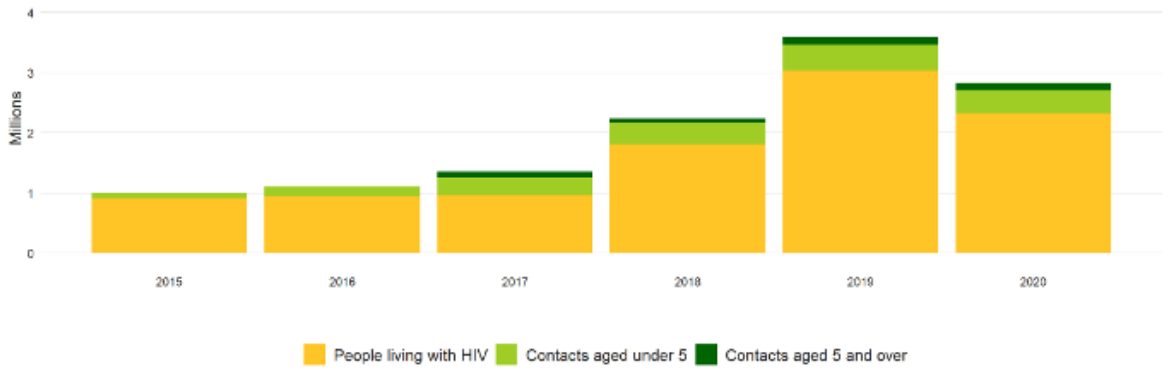
The global adaptation of the normative guidance by WHO to initiate TPT among at-risk groups has seen a steady increase in the number of people treated for TB infection since 2015, especially for PLHIV. Based on data from WHO, the total number of PLHIV who were placed on TPT rose from 2015 and peaked in 2019 but declined in 2020, most likely due to the negative effects of the COVID-19 pandemic.

There was a near flattening of the number of HH contacts of bacteriologically confirmed TB patients aged under-five years of age who received TPT between 2017 and 2020.

It is now recognized that a large proportion of active TB arises from people who were recently infected with Mycobacterium tuberculosis, the largest risk being in the first 2-5 years following infection[28]. This is the reason all HH contacts, including those over the age of 5 are included in the priority groups to be targeted for TPT. Despite the commitments made at the UNHLM in 2018, there has been minimal progress in the provision of TPT to HH contacts who are older than 5 years of age (see Figure 10).

[28] James M Trauer et al. Chest 2016; 149(2): 516-525

*Figure 10 The global number of people provided with TB preventive treatment, 2015–2020 (WHO source).*




### 5.3.1. TPT and IPC performance in the 20 evaluation countries

This section presents the data on TPT and IPC separately for the 9 case study countries and for all the 20 countries. Firstly, this analysis presents the number of people placed on TPT (uptake) and then the TPT coverage among HH contacts aged under 5 years, HH contacts aged over 5 years, and PLHIV. To reiterate, to standardise our estimate of coverage, in the absence of reliable denominators, or in situations where Global Fund support was limited to a limited geographic area of the country, we chose to use the UNHLM targets per country (as provided by the Stop TB Partnership) as a common reference. This analysis also includes available data on the number and incidence of TB among health staff, the indicator that is used to monitor TB-IPC.

#### 5.3.1.1. *Under-five TPT uptake- Data availability and uptake of TPT*

The evaluation team observed variations in TPT uptake in the 9 CCs and 11 Portfolio Analysis (PA) countries over the period 2018 to 2021. Seven of the 9 CCs reported to WHO the number of under-fives who are household contacts of bacteriologically confirmed (new and relapse) people with TB who were provided with TPT, whereas only three of the 9 countries (Nepal, South Africa and Zimbabwe) also reported data to the Global Fund (see Figure 11). The number of HH contacts placed on TPT reported to the Global Fund was lower than what was reported to WHO over the same period – most likely because data reported to the former originated from sub-national levels in the respective countries. This raises concerns about the alignment of data collection systems on TPT aimed at the Global Fund or WHO, when the source (NTP) is the same in the country.

#### 5.3.1.2. *Under-five TPT uptake - the data*

As indicated above 7 of 9 CCs countries reported data to the WHO on TPT uptake (absolute number) in this age group. Uptake of TPT in these 7 countries increased from 35,804 in 2018 to 42,904 in 2019, but decreased to 35,755 in 2020. A similar trend was observed for data reported by the 3 countries that submitted data to the Global Fund in 2018, 2019 and 2020: 8,961, 12,094 and 3,808 respectively. In

addition, data collected from the NTP during this evaluation had similar numbers to those reported to WHO and showed a similar trend. TPT uptake increased between 2018 to 2019 but declined in 2020 and in 2021. The TPT uptake in 2018, 2019, 2020 and 2021, was 31,807, 38,125, 22,292 and 19,199 respectively. Note, Ethiopia, Nepal, South Africa and Thailand had no data on TPT uptake in under-five for the years 2019 to 2021.

The observed decline in the uptake of TPT in under-fives in 2020 and 2021 is attributed to the COVID-19 pandemic which led to reductions in the number of people diagnosed with bacteriologically confirmed TB, and which also affected supply chains for commodities for TPT and GeneXpert cartridges.

*Figure 11 Under-five uptake of TPT in 9 CCS*

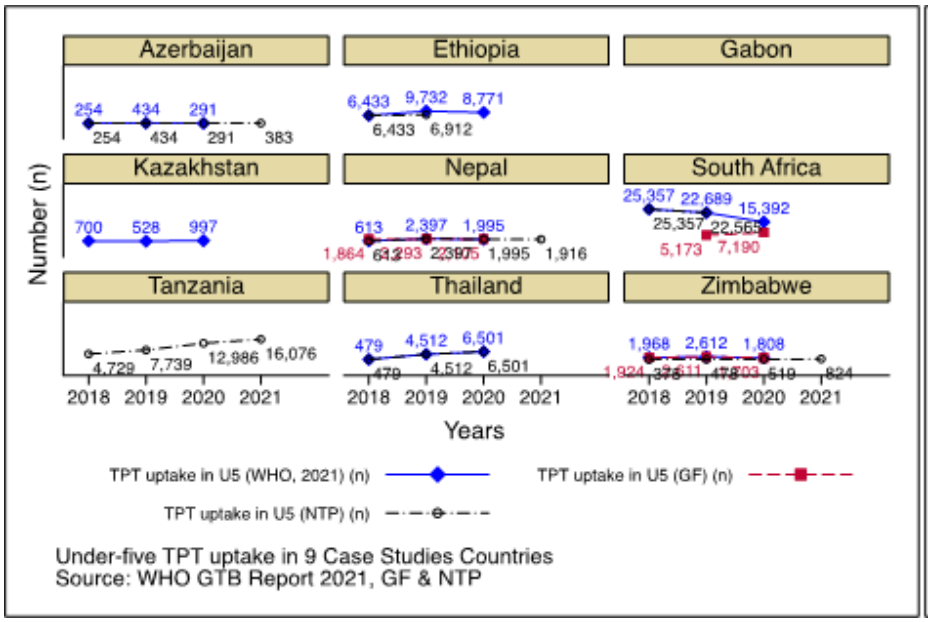
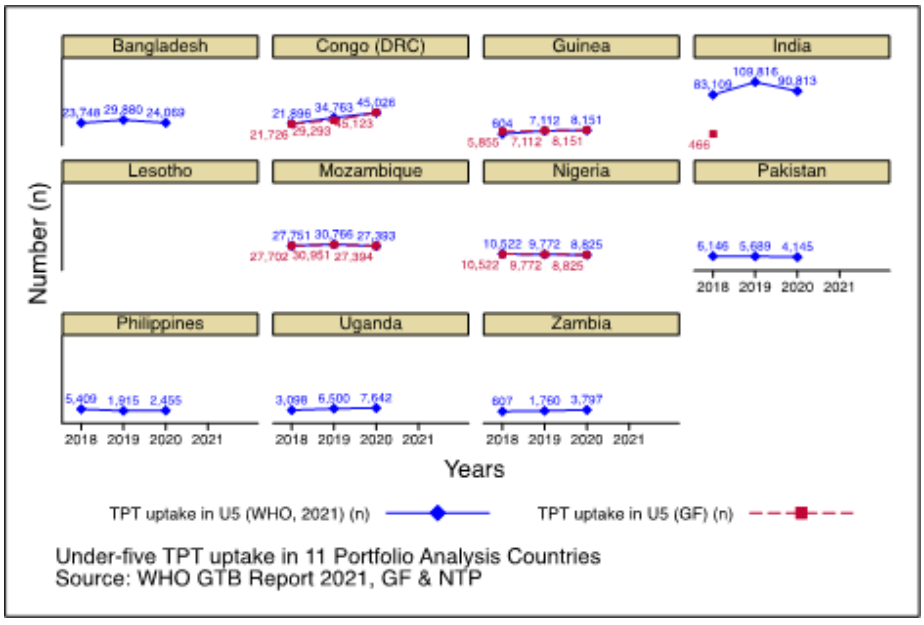
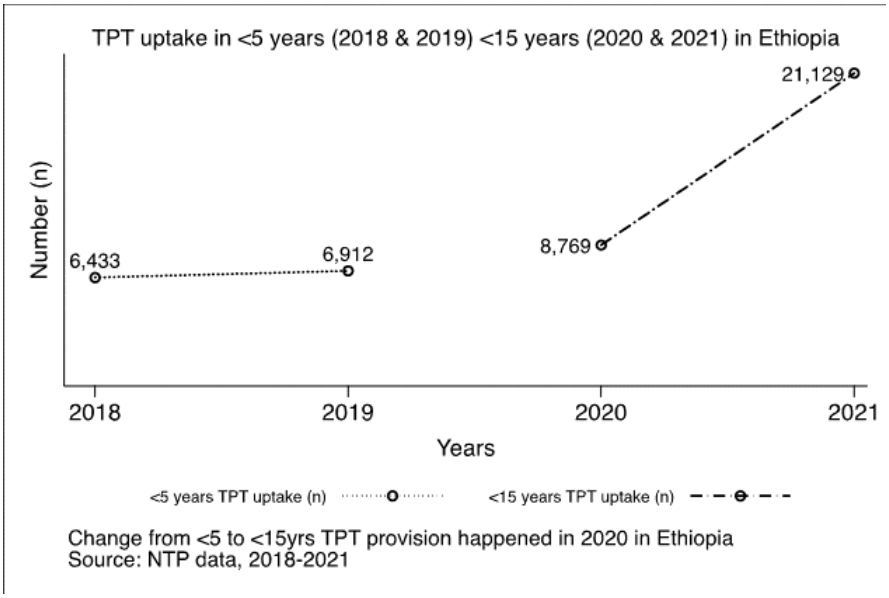



*Figure 12 Under-five uptake of TPT in 11 portfolio countries*



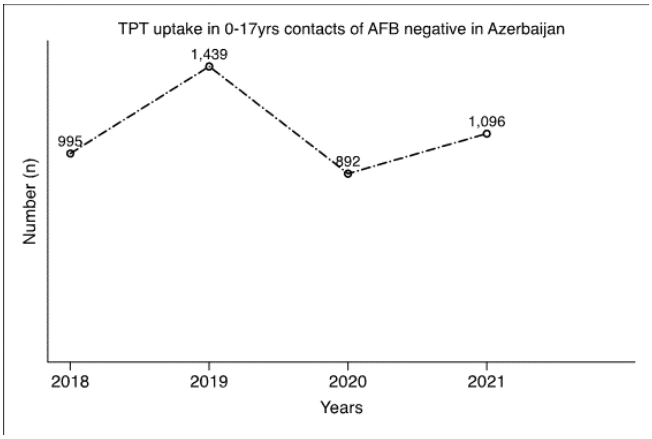
In 2020, Ethiopia increased the age limit of children eligible for TPT to below 15 years of age. The number of the <15 years receiving TPT saw a twofold increase in TPT uptake between 2020 to 2021 (see Figure 13) from 8,769 to 21,129.

*Figure 13 The uptake of TPT for children <15years in Ethiopia.*




In Azerbaijan, the country also provides TPT in young people between the ages of 0-17 years old who are household contacts of bacteriologically negative TB patients. TPT uptake in this population was observed to have increased sharply between 2018 and 2019, but dropped in 2020 with a slight increase in 2021.

*Figure 14 The uptake of TPT for children 0-17 years in Azerbaijan.*




### 5.3.1.3. TPT uptake in PLHIV- Data availability and uptake of TPT

Generally, about half of the countries reported TPT uptake in PLHIV to WHO. Of the 9 CCs 5 countries reported data to WHO and only in 2020. Similarly, in the countries where only a PA was carried out only 5 of the 11 countries reported data to the WHO

in 2020. Only Nepal, South Arica, Thailand, and Tanzania reported TPT uptake to the Global Fund. The NTPs from Ethiopia, South Africa, Thailand, Tanzania, and Zimbabwe provided additional data. Notably, for the case of Tanzania, the numbers reported to WHO were higher in 2020 compared to what was collected from the HIV program. The possible explanation for this discrepancy is that in 2020, what was reported to WHO was the cumulative number of PLHIV ever started on TPT as compared to the number of PLHIV started on TPT in 2020 that the NTP provided to the evaluation team.

#### 5.3.1.4. TPT Uptake in PLHIV – the data

Countries like Zimbabwe have demonstrated a steady increase in the number of PLHIV initiated on TPT (using NTP data). In Zimbabwe, in 2018 there were 72,812 PLHIV started on TPT as compared to 293, 574 PLHIV in 2021. For PA countries, 8 of the 11 countries reported to the Global Fund. The general trend is an increase in uptake of TPT. For instance, in Nigeria, TPT uptake in PLHIV was 111,402, 162,299 and 216,721 in 2018, 2019 and 2020, respectively.

*Figure 15 PLHIV uptake in 9 CS countries*

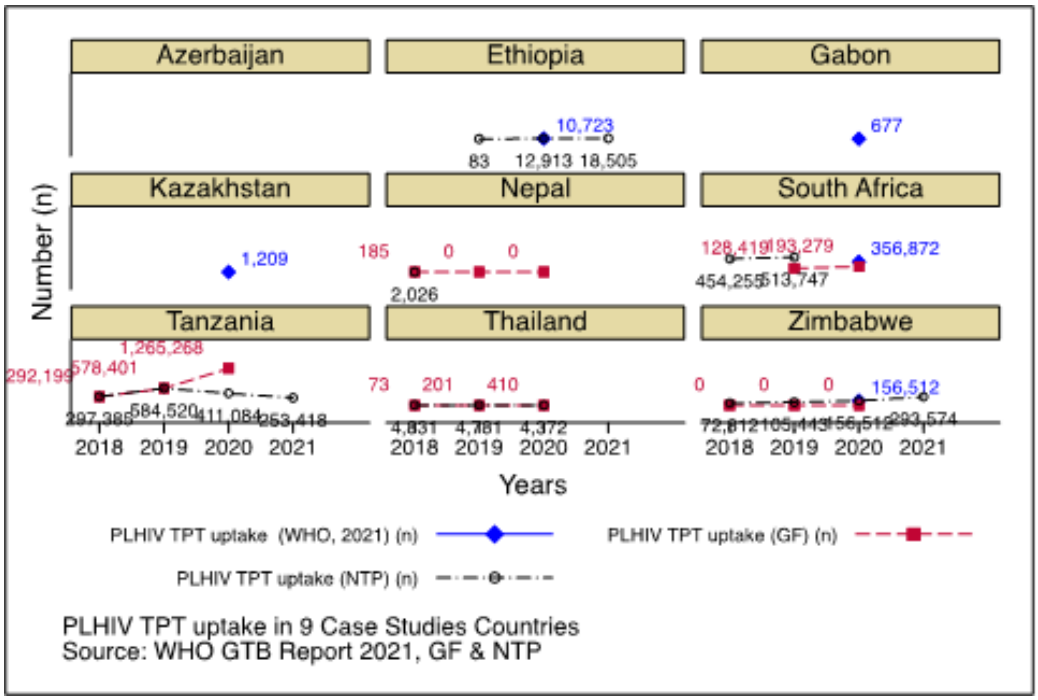
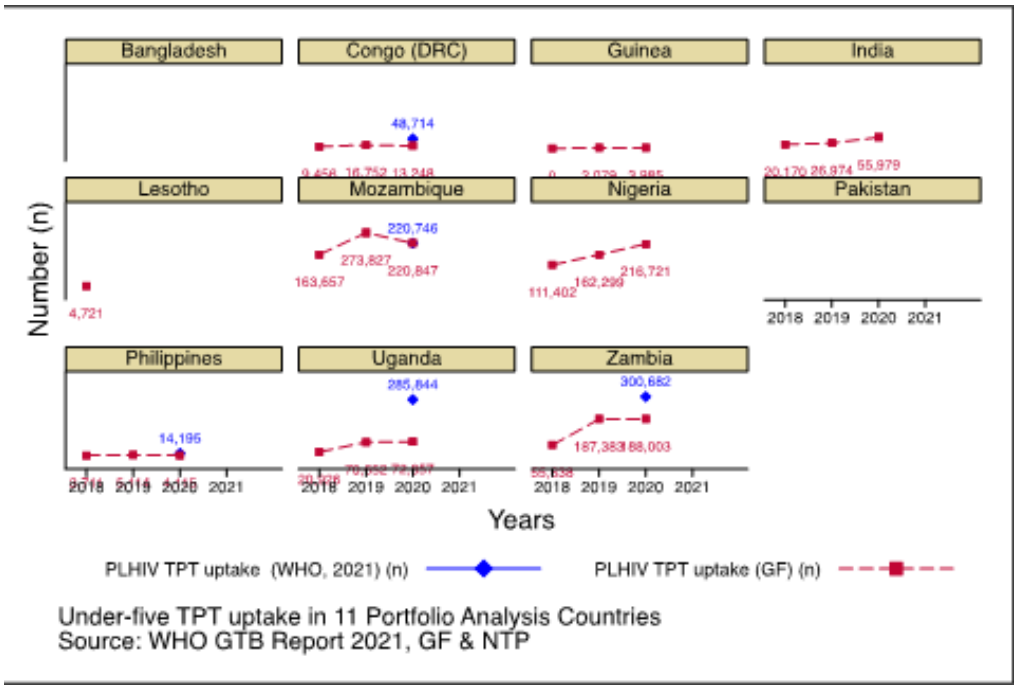


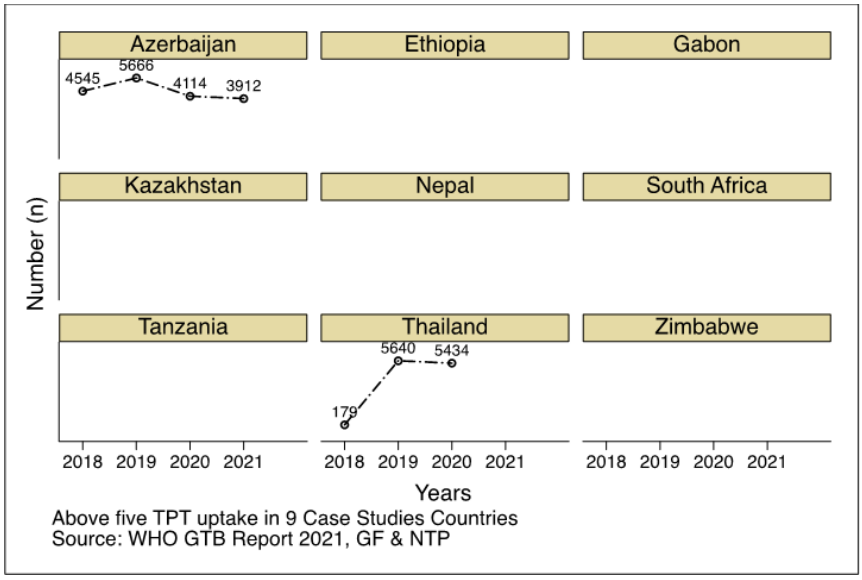
*Figure 16 PLHIV uptake in 11 portfolio analysis countries*




### 5.3.1.5. *TPT uptake in people above 5 years of age*

None of the countries included in this evaluation reported TPT uptake for people above 5 years of age to WHO or to the Global Fund. The data reported in this evaluation is the one provided by NTP in the 9 CCs countries. Only Azerbaijan and Thailand had NTP data on TPT initiation in people above 5 years who are HH contacts of persons with TB. In both countries there was a slight drop in TPT uptake between 2019 and 2020 (see Figure 17).

*Figure 17 TPT uptake in household contacts of 5 years and above*

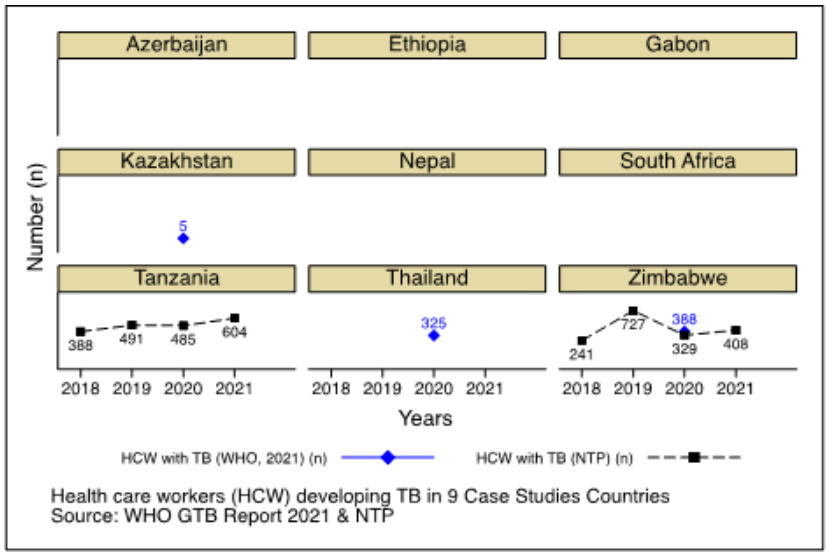


### 5.3.1.6. *HCW with TB*

TB-IPC is largely not measured. The number of health care workers diagnosed, treated and notified with active TB is used as a proxy measure of the adequacy of implementation of TB-IPC. It should be noted that this indicator is not collected by the Global Fund. It is likely that even in countries reporting this information to WHO, the number of health care workers treated for TB is much higher than what was reported. It is known that rates of TB disease in health care workers in TB endemic settings is significantly higher than in the general population[29], however, because of stigma and discrimination health care workers may not be willing to be identified to have TB in their places of work and may conceal their professional status when being registered for TB treatment in the health facility they choose to be treated[30].

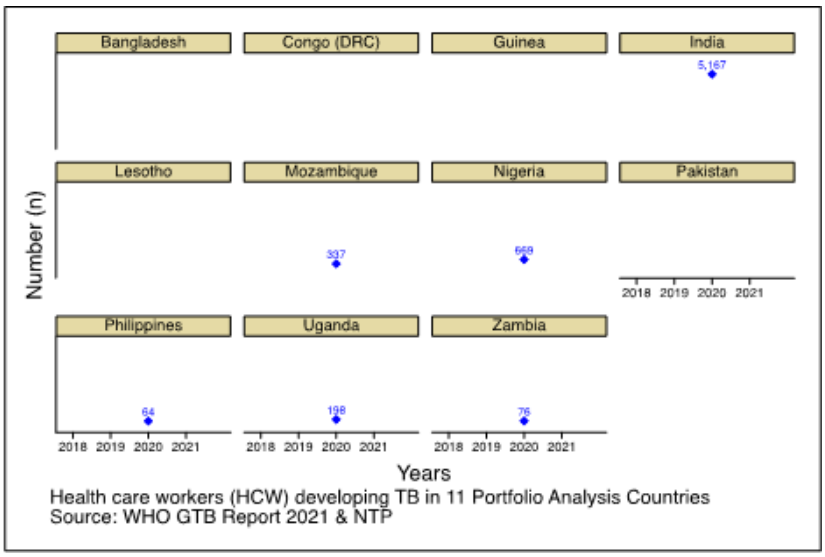
Of the 20 evaluation countries, those that had data on HCW with TB in 2020 in the WHO GTB report of 2021 include India (5,167), Kazakhstan (5), Mozambique (337), Nigeria (669), Philippines (64), Thailand (325), Uganda (198), Zambia (76) and Zimbabwe (388). Only Tanzania and Zimbabwe have consistently collected data of HCW developing TB since 2018, from the data collected from NTP. The overall trend is an increase in the number of HCW developing TB since 2018. For instance, in Tanzania in 2018 there were 388 HCW with TB which increased to 604 in 2021.

*Figure 18 HCW who developing TB in 9 CS countries*




[29] Joshi R et al. PLoS Med 2006; 3(12):e494
[30] Jacob Siegel et al. Glob Public Health 2015; 10(8): 995-1007

*Figure 19 HCW who developing TB in 11 portfolio analysis countries*




#### 5.3.1.7. *TPT Coverage*

The targets set at the UNHLM were selected to determine the coverage (proportion of the target offered the intervention) of TPT in all countries as a way of standardizing the target for all countries and because all countries committed to achieve these targets. It is noted that some countries have, after the UNHLM meeting and publication of the country specific targets by the Stop TB Partnership, revised these targets either downward or upward depending on the context and background epidemiology of TB. It is also appreciated that there are limitations to using UNHLM national targets for data from the Global Fund which may represent a sub-set of national data as opposed to the data from WHO which represent national data. However, presented in the following sub-sections is coverage of TPT in under-five and PLHIV, focusing mostly on trends in coverage for data reported to either WHO or Global Fund rather than making direct comparisons in coverage between these two data sources.

#### 5.3.1.8. Under-five TPT Coverage

The general trend of TPT coverage in the 9 CCs was decreasing for most countries based on the data reported to both WHO and the Global Fund. In 2018, coverage was highest at 100% in Azerbaijan and Kazakhstan and was at 99% in Ethiopia. There was a drop in coverage in 2019 which continued and was larger in 2020. The steep decline in TPT coverage in 2020 is attributed to the negative effects of COVID-19 pandemic which interrupted the supply of medicines for TPT, and access to TB diagnostic services. In the 11 PA countries, high TPT coverage was observed in 2018 and either remained unchanged or declined significantly in countries like Bangladesh, Congo and Mozambique (see Figure 20).

*Figure 20 Under-five TPT coverage for 9 CS countries*

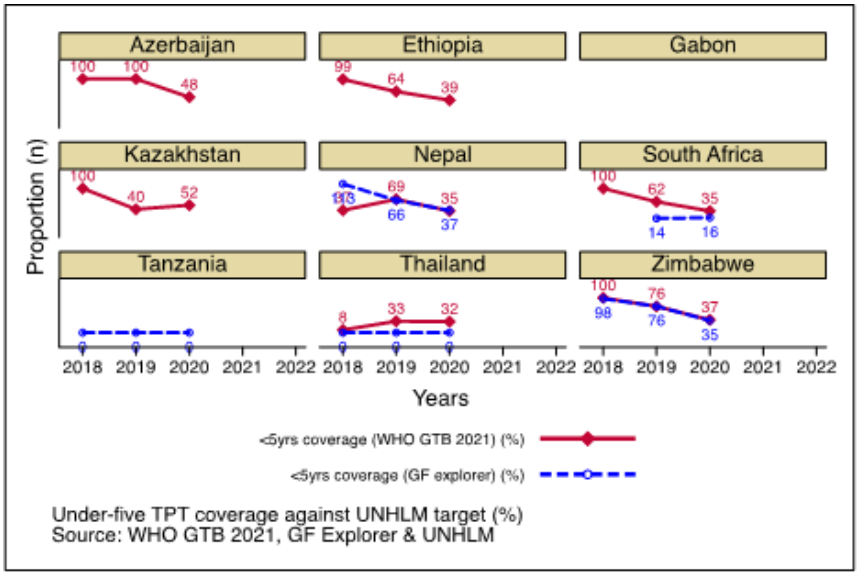
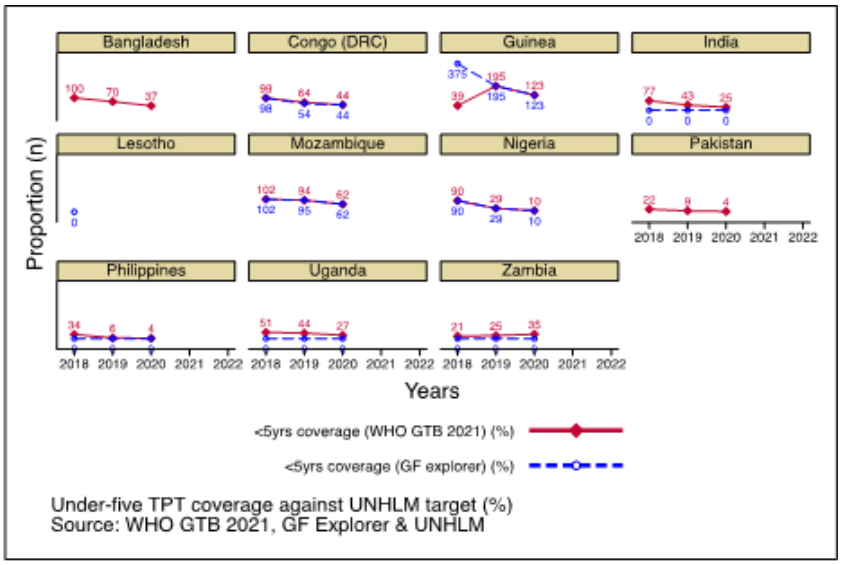
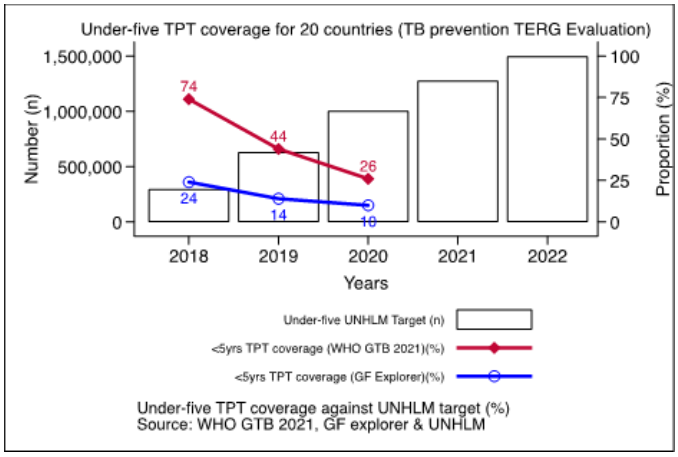



*Figure 21Under-five TPT coverage for 11 portfolio analysis countries*




For all the 20 evaluation countries, the trend of TPT coverage for under-five showed a steady decline from 74% in 2018 to 26% in 2020 (WHO data). This large drop in TPT coverage can easily be attributed to the COVID-19 pandemic, but it must be noted that the declining trend began in 2019 before COVID–19 set in. Therefore, other factors must have affected TPT coverage between 2019 and 2020. Data from the Global Fund explorer revealed much lower TPT coverage with also a declining trend which was much less steep than was observed from the data derived from the WHO. It is inferred that the lower coverage of TPT reported to the Global Fund represents the contribution of the Global Fund to national TPT coverage and consequently to the data reported to WHO. It is worth noting that these trends should be interpreted with caution, as not all countries reported data to WHO and Global Fund and the evaluation team was unable to verify that the data reported to the Global Fund was from sub-national level (as seen previously).

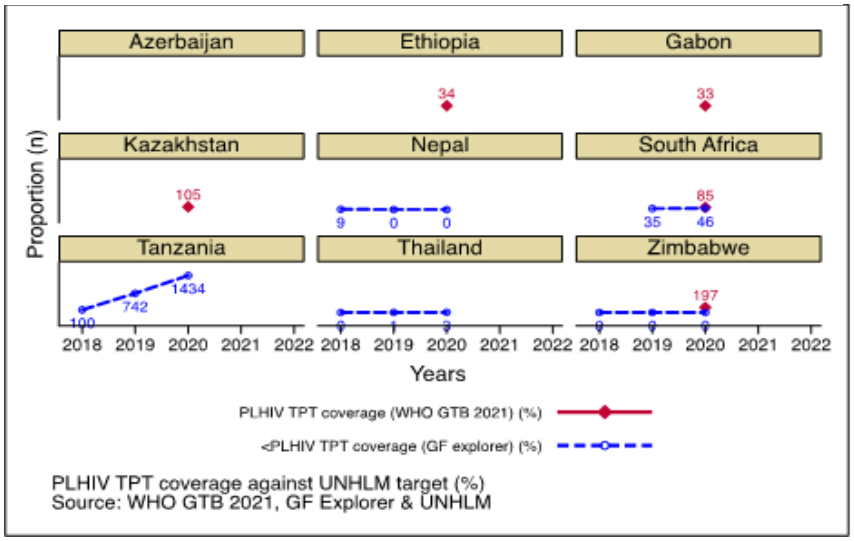
*Figure 22 Under-five TPT coverage for 20 selected countries for TB prevention evaluation.*

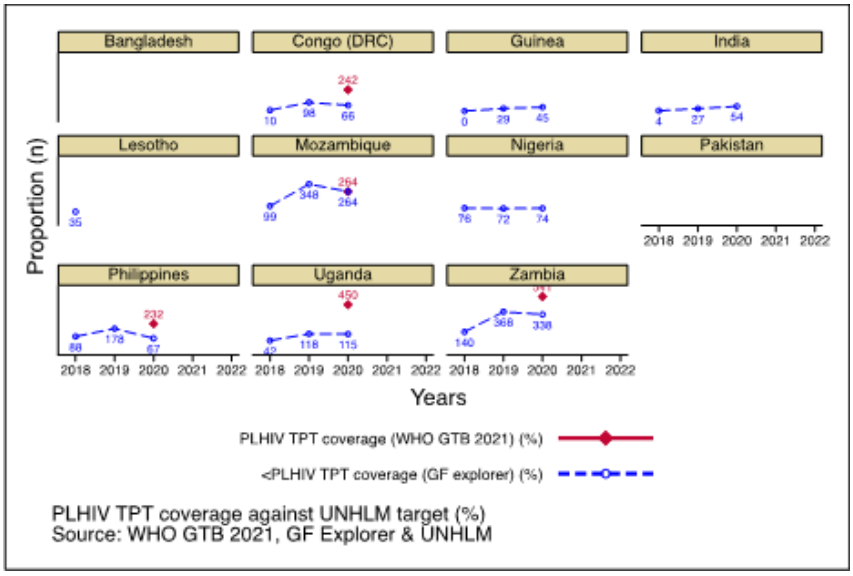



### 5.3.1.9. PLHIV TPT Coverage

The estimate of TPT coverage and trends among PLHIV has major limitations because of lack of data. However, the data reported to Global Fund shows modest performance for all countries except Tanzania and Zambia which achieved results far above the UNHLM targets. As explained in previous sections, both Tanzania and Zambia may have reported cumulative numbers of people ever placed on TPT and hence may not give a true reflection of the coverage (see Figure 23). The other explanation could be that the UNHLM targets were low and thus easily surpassed.

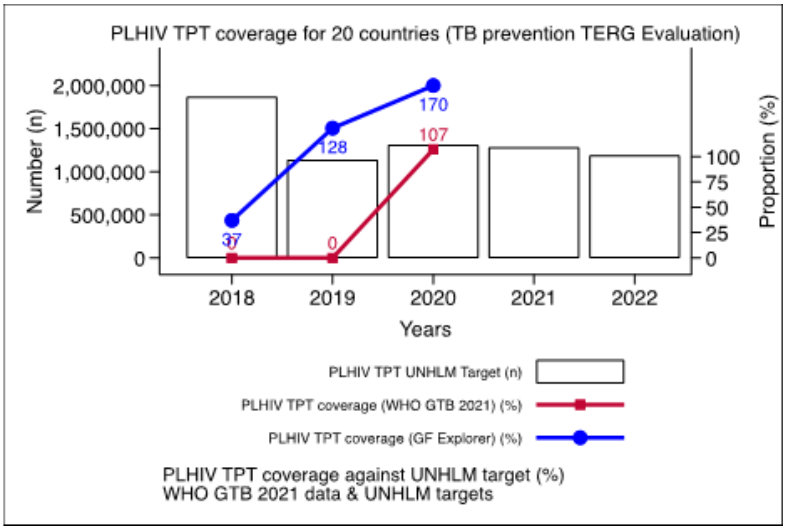
*Figure 23 PLHIV TPT coverage for 9 CCs countries (above) and 11 PA countries (below)*






The aggregated TPT coverage among PLHIV for all the 20 countries using both WHO and Global Fund data is found to increase sharply between 2020 and 2021 which may be due to additional efforts by other partners working on scaling up TPT among PLHIV. The Presidential Emergency Plan for AIDS Relief (PEPFAR) has been particularly active in this area and managed to support the initiation of a large and increasing number of PLHIV, from 546, 379 in the period April 1, 2017, to September 1, 2017, to 718, 521 in the period October 1, 2018 to March 31, 2019[31]. Among the 20 countries that were included in this evaluation, 9 (Lesotho, Congo DRC, Ethiopia, Mozambique, Nigeria, South Africa, Tanzania, Uganda and Zimbabwe) are included in the list of PEPFAR countries. The higher TPT coverage for PLHIV when using Global Fund data as compared to WHO data may be due to cumulative reporting of TPT among PLHIV from both the HIV and NTP programmes to the Global Fund when only TB programme data are reported to WHO (Figure 24).

*Figure 24 PLHIV TPT coverage for 20 selected countries for TERG evaluation.*




[31] Michael Melga et al. MMWR 2020; 69(12): 329-334

### 5.3.2. The TB-IPC and TPT Information System: availability and quality of TPT data.

For this evaluation, the quality of data was defined by completeness and concordance, in 2020, of TPT data for HH contacts under the age of 5, HH contacts over age of 5, PLHIV and TB among health staff derived from 3 sources: WHO, The Global Fund and the National TB Programme. These data are presented in Annex 8.

Completeness was defined as the number (%) of countries from the pool of 9 CCs that had TB prevention data in 2020 from WHO and NTP sources for the following indicators: TPT among HH contacts <5, HH contacts >5, PLHIV and TB among health staff and TB prevention data from the Global Fund source for the indicators TPT among HH contacts <5 and among PLHIV.

Completeness of the TB prevention data in the 9 CCs reach 42% for the 4 indicators examined using data derived from WHO and NTP sources. Only 33% of the 9 CCS provided TB prevention data on the 2 indicators derived from the Global Fund source of data (Table 9).

*Table 9 TB prevention data completeness from 3 data sources (WHO, Global Fund, National TB Programme) in 9 countries case study in 2020*

| 2020 data completeness in 9 CCs by data source | TPT among HH<5 | TPT among HH>5 | TPT among PLHIV | TB in Health staff | Completeness of 4 indicators in 9 CCs by data source | Completeness of 4 indicators in 9 CCs for 3 data sources |
|---|---|---|---|---|---|---|
| **WHO** | 78% (7/9 CCs) | 0% (0/9 CCs) | 56% (5/9 CCs) | 33% (3/9 CCs) | 42% (15/36) | 40% (36/90) |
| **GF** | 33% (3/9 CCs) | NA | 33% (3/9 CCs) | NA | 33% (6/18) | |
| **NTP** | 78% (7/9 CCs) | 33% (3/9 CCs) | 33% (3/9 CCs) | 22% (2/9 CCs) | 42% (15/36) | |

Concordance as a proxy of accuracy was defined as the number (%) of countries from the CCs that had similar TB prevention data in 2020 between WHO and NTP sources for 4 indicators of TB prevention (TPT among HH contacts<5, HH contacts >5, PLHIV and TB among health staff) in 7 countries where the WHO and NTP report these indicators (Azerbaijan, Ethiopia, Nepal, South Africa, Thailand, Tanzania, Zimbabwe). Concordance was also assessed in 2020 between Global Fund and NTP sources for 2 TB prevention indicators (TPT among HH contacts <5, TPT among PLHIV) in 3 countries (Nepal, SA, Tanzania) that reported data to the Global Fund on these indicators.

Concordance of the 4 TB prevention indicators in the CCs reached 33% for HH contacts under 5, 0% for HH contacts over 5, 20% for TPT among PLHIV and 0% for TB among health staff when comparing WHO and NTP data sources. In the 3 CCs in there was data from the Global Fund on the two indicators (TPT in HH contact <5 and

TPT in PLHIV) there was no concordance between data at the NTP and data held by the Global Fund (Table 10 and Annex 8).

*Table 10 TB prevention data concordance between WHO and NTP source and Global Fund and NTP source in 2020 in countries case study with countrywide Global Fund coverage*

| 2020 concordance between data source in CCS reporting data | TPT among HH<5 | TPT among HH>5 | TPT among PLH | TB among Health staff | Concordance of 4 indicators in WHO/NTP comparison and 2 indicators in Global Fund/NTP comparison, among CCs reporting data |
|---|---|---|---|---|---|
| **WHO-NTP** | 33% (2/6 CCs) | 0% (0/3 CCs) | 20% (1/5 CCs) | 0% (0/3 CCs) | 18% (3/17) |
| **GF-NTP** | 0% (0/3 CCs) | NA | 0% (0/3 CCs | NA | 0% (0/6) |

The low completeness and concordance of data are difficult to explain, but may be due to a sub-optimal recording and reporting system for TB prevention at the country level. In South Africa for example, TPT in HH contacts over the age of 5 has not yet been included in the TPT recording and reporting system. TPT for this age group is still only being conducted in pilot districts. In Azerbaijan and Thailand, there is an electronic data registry to record all people with active TB, however, data on TB contacts and TPT have not yet been included in the electronic database. In Azerbaijan and Thailand including data on TB contacts and on TPT uptake would help to better monitor TPT coverage It is understood that at the global level data is reviewed and revised before it is published, which may explain the lack of concordance between the data held at WHO and the Global Fund, from that held at the NTP. However, since the source documents for the data reported to WHO and the Global Fund is the National Health Information System, the data at the global level should be able to "speak to each other" irrespective of whether it is sourced from the Global Fund or WHO. It should also be possible to harmonize the data across the NTP, the Global Fund and WHO. The lack of data reported on TB prevention observed in a significant number of countries is a cause for concern.

The monitoring, evaluation, and learning (MEL) system for TB prevention therefore appears currently, to be grossly inadequate. Indicators for IPC and TPT are inadequate and incomplete, for example, the TPT completion rate is not included in the list of indicators. TPT for at risk populations such as prisoners, TB and MDR TB contacts is not measured in the Global Fund Performance Framework. WHO has developed a Prevent TB app to feed information into the DHIS2, but it is largely not available. There may be a need to focus on process indicators for IPC in addition to TB among health staff. A set of indicators that capture processes and if possible, outcomes of IPC will need to be developed together with those who have responsibility for IPC and AMR programs at the MOH.

TB among health staff could be one essential HAI (health care-associated infection) indicator in high TB incidence countries. TB among health staff requires hospital-based infection surveillance systems that measure HAI including central line-associated bloodstream infections, ventilator-associated pneumonia, urinary tract

infection and surgical site infection (SSI). While NTPs, should contribute to and be engaged in the development, implementation, and monitoring of national systems for IPC, they probably should not lead these initiatives. Measuring TB among health staff may be undertaken by NTPs with support from the Global Fund to contribute to one of the building blocks of national occupational health and safety programmes for health workers in line with recommendations of the WHO–ILO Global Framework. Ideally TB prevention in health care workers should be linked to an appropriate labour law indicator but this evaluation did not reveal such undertakings in the 9 CCs.

The indicators in the current Modular Framework prioritize PLHIV and HH contacts HH under 5. In the 9 CCs, monitoring of the TPT cascade to include parameters such as proportion of HH contacts investigated, proportion that initiated TPT and proportion of those who initiated treatment who completed it was not routinely carried out. In NFM2 and NFM3, the Modular Framework buried TB prevention into a module that is overwhelmingly focused on finding people with TB and their treatment. To address these shortcomings and to prepare for NFM4, there is on-going work to revise the Modular Framework, to have a TB prevention module separate from the TB care and treatment module. Interventions for TB prevention interventions and activities will be included in the new TB prevention module and in the TB/HIV and MDRTB modules. There is also ongoing work on the RSSH module that is expected to include IPC and to be complementary with TB/HIV module intervention on IPC.

In the ideal world, the TB prevention monitoring and evaluation framework should be comprehensive to include targets of people to be treated with TB preventive therapy linked to the number of people in whom active TB is to be prevented and ultimately to contribution of TPT to declines in TB incidence. Additionally, a comprehensive TPT monitoring, and evaluation system should include treatment initiation, adherence, adverse events, breakthrough TB and preventive therapy completion and should not just focus on coverage, but also on the quality of TB prevention services.

**In conclusion**, in 2020, the TPT coverage among household contacts below 5 years, (using UNHLM targets) reached 29% globally and in the 20 evaluation countries it was 26% and 10% using data from WHO and the Global Fund, respectively. While the two data sources may be providing different information such as sub-national data for the Global Fund versus national data for WHO, in ideal situations the information sent to the Global Fund and WHO should be linked because the data is sourced from the same national information system.

In the population of HH contacts below the age of 5, there was a significant drop in the coverage of TPT in 2020, attributed to the increase in the denominator following adoption of the UNHLM targets and the impact of the COVID-19 pandemic. The drop, of course, may underestimate the true coverage as not all countries report to WHO/Global Fund. In the population of HH contacts over the age of 5, TPT coverage was low and or there was no data. Similarly, there was no data on TPT coverage for other high-risk groups for whom TPT may be beneficial such as prisoners, immigrants, health care workers, and those with existing medical conditions such chronic kidney disease on dialysis, people initiating anti-TNF treatment and those preparing to receive solid organ or haematological transplantation.

The only indicator on IPC is the number of health staff with TB, which has not been included in the Global Fund grant Performance Frameworks and is not routinely reported to WHO.

Both TPT and IPC lack from a sufficient M&E framework but the deficiencies are worse with IPC**.** Both interventions lack appropriate indicators. With the absence of appropriate numbers and proportions in IPC there may be a reduced appetite by donors to fund IPC.

Sub-optimal collaboration between HIV and TB programs may still be contributing to TPT implementation challenges for PLHIV and may be responsible for the discrepancies in reported TPT uptake and coverage observed in this evaluation.

With the lack of measurement and tracking of performance, it is difficult to assess if Global Fund investments in TB prevention and in particular IPC represent value for money.

# 6. Current Gaps in Global Fund's investment in TB prevention

## 6.1. Key Informant Interviews (KIIs)

Stakeholders and key informants who participated in this evaluation were drawn from the Global Fund Secretariat, the Global Fund's Technical Review Panel, the Global Fund's TERG, WHO (HQ, SEARO, WPRO, AFRO, EMRO and Euro), Stop TB Partnership, KNCV, PATH, USAID, CDC, the Union, CHAI and the Emerging Bacterial Pathogens Centre/WHO Collaborating Centre and TB Supranational Reference Laboratory, in Milan, Italy. At the country level key informants included Country Coordinating Mechanisms (CCMs), Primary Recipients (PRs), Civil Society Organizations (CSOs), the National TB Control Program (NTP), the National HIV/AIDS Control Program and others (a complete list of key informants and their organizations is provided in Annex 6).

## 6.2 Global and national policies on TB prevention

The evaluation team began by examining how the most recent (2020) WHO recommendations on TB preventive therapy[32] and TB infection transmission prevention and control (2019), summarized in Annex 7 have been adopted by the 9 CCs. Based on the normative guidance by WHO, it was noted that the Global Fund's TB Information Note of July 2019 includes TPT and IPC in the list of high impact interventions and encourages applicants to include these interventions in their funding requests. The TB Information Note prioritizes HH contacts and PLHIV for TPT and advises countries to include TPT in these population groups within the continuum of interventions for early identification of people with TB.

The uptake of the global recommendations on TPT into national polices, national strategic plans, annual work plans in the 9 CCs is summarized in Table 11 below.

*Table 11 National policy on TPT from country TB NSP*

| Country | Evaluation approach before TPT | | | | Target groups | | | | | | Regimens |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | Symp | CXR | mWRD | TBI testing 1.TST; 2. IGRA 3. No | PLH | HH<5 | HH>5 | Prison | HCWs | Others | |
| SA[1] | Y | N | N | 1 if available, 3 | Y | Y | N | N | N | | 6H |
| Nepal | Y | N | N | 3 | Y | Y | N | N | N | | 6H,3HR |
| Thailand | Y | Y | | 2 | Y | Y | Y <18 | N | N | N | 6H |
| Azerbaijan | Y | Y | N | 2 | Y | Y | Y | Y | N | N | 6H, 3HR, 3HP (PLHIV &Prison) |
| Gabon | Y | N | N | 1 | Y | Y | N | N | N | N | 6H, 3HR[2] |
| Ethiopia | Y | Y | N | 3 | Y | Y | Y <15 | N | N | N | 6H, 3HR, 3HP |
| Tanzania | Y | Y | N | 3 | Y | Y | N | N | N | N | 6H |
| Zimbabwe | Y | N | N | 3 | Y | Y | Y | N | N | Silicosis pilot | 6H, 3HP |
| Kazakhstan | Y | Y | N | 1,2 | Y | Y | Y | | N | N | 6H,9H 3HR, 4R 6Lfx HP[3] |

[32] WHO consolidated guidelines on tuberculosis. Module 1: prevention – tuberculosis preventive treatment. Geneva: World Health Organization; 2020. Licence: CC BY-NC-SA 3.0 IGO.

[1]new TPT guidelines awaiting approval with TPT for all age groups as well as the use of rifamycin based short regimens.
[2] awaiting approval of the new TPT guidelines with short regimen 3HR
[3] awaiting Rifapentine (P) registration

As can be seen in Table 11 above, the population groups prioritized for TPT in these 9 countries are PLHIVs and HH contacts below the age of 5. Four countries have not prioritized HH contacts over the age of 5. Five countries (Thailand, Ethiopia, Azerbaijan, Kazakhstan, and Zimbabwe) have prioritized HH contacts aged 5 to 15 or 18 years. People are screened for TB before provision of TPT based on symptoms. Testing for TB infection before TPT is undertaken in 5 out of the 9 countries. The most commonly used TPT regimens are 6H and 3HR. The rifapentine based shorter regimen 3HP has been introduced in 3 countries. 1HP is not used in any country.

Global policies and guiding documents on TB prevention, in general, appear to be adequate. This includes the WHO guidelines on IPC and TPT, the Global Fund's technical TB Information Note and guidance documents developed by partners such as USAID and CDC. Global recommendations for TB preventive therapy provide a clear pathway for individuals at very high risk of progression to active TB, and where there is a strong research evidence of clinical and individual benefit of TPT. These populations include household contacts under the age of 5 and people living with HIV where the recommendation is to provide TPT even when testing for TB infection is not available. As noted in Table 11 above, these are the populations that remain prioritized by national TB programs.

About half of the 9CCs have not prioritized HH contacts above the age of 5, which is not surprising, since policy setting in this population is not straightforward. Country level stakeholders need to debate and agree on several issues that impact programmatic provision of TPT for HH contacts over the age 5 and other at-risk populations. These include testing for TB infection before treatment and balancing between the public health goal of reducing TB morbidity and mortality against individual benefit and risk of TPT. In a situation where a country chooses not to test for TB infection before TPT in populations other than HH contacts under 5 and PLHIV, nearly half of these individuals may be subjected to an unnecessary risk of medicine adverse events because they are not infected with TB. One systematic review estimated that about 50% of household contacts of people with active TB have TB infection, implying that a treat all contacts without testing for TB infection national policy, will result in nearly one in two people being treated for a condition they do not have. Additionally, the fact that only a small proportion (5-10%) of people infected with TB, who are not infected with HIV or have other risk factors for development of active TB, will develop active TB in their lifetime, is problematic for TPT programming. It implies that a large proportion of people with TB infection may be treated with TPT when in fact they were not going to develop active disease. It is unclear in global policies and guidance, how countries should respond to all these complex situations.

While global recommendations on TPT emphasize the need to have this intervention linked with active case finding interventions, there seems to be insufficient synergism or linkages between ACF and TPT, more so in those situations where TB screening activities are carried out among vulnerable populations beyond HH contacts, such among slum dwellers and prisoners. This view is supported by the lack of data on TPT initiation rates among community members that were involved in active case finding

activities. Although the evaluation team intended to examine performance of ACF initiatives and how TPT and IPC was integrated into these initiatives, data to undertake this analysis was unable to be obtained. TB notification in most countries does not disaggregate by the approach used to identify people with TB.

From the foregoing, it is concluded that, while global guidance, including technical advice in the form of TB Information Note by the Global Fund, appears to be robust, adaptation at the country level may be challenging from an operational perspective. This may explain the finding in this evaluation of a very low uptake and coverage of TPT in older persons above the age of 5 who are household contacts of a person with active TB.

### 6.3 Major barriers for TB prevention IPC and TPT

This evaluation revealed a long list of barriers to the implementation of TB prevention which include the financing challenges outlined and discussed in section 5.1 and the inadequate information system highlighted in section 5.2.2.6. These barriers have been summarized and discussed by several authors in scientific publications. The evaluation team cites the paper by I. Pathmanathan and others, in which barriers to implementation of TPT in PLHIV, are highlighted and discussed[33]. These barriers include TPT hesitancy by individual providers and lack of buy-in by their professional societies and associations. There are persisting doubts, including within the Global Fund itself, about the effectiveness of TB prevention on TB morbidity and mortality.

As noted in Table 11 most countries still rely on symptom screening to exclude people who may have active TB from treatment for TB infection. Access to the CXR (or other sensitive screening tools recommended by WHO) as a screening tool for active TB remains a challenge in the low resource setting where TB is endemic. In the absence of this reliable tool for TB screening, clinical service providers may be unwilling to initiate TPT on account of absence of TB symptoms alone. This is not an unfounded fear, noting that in several studies of TB screening approaches across many high TB endemic settings, symptoms alone have performed poorly in the identification of people with active TB[34] .

A TBI test and treat strategy, while being efficient, may not be feasible in many settings. While recently approved antigen-based skin tests provide hope that TBI testing may be more readily available it is too soon to say if this will prove to be the case. As of now there is no test that is simple (and cheap) enough to be used at the household level to identify people who have TB infection. Additionally, currently available tests for TB infection are unable to predict or identify people who will develop TB in the future.

Tuberculosis preventive therapy may not be addressing the needs of both at risk individuals and communities[35,36] leading to major losses in the care cascade. People who are infected with TB may not perceive their future risk of TB to be high enough to require any treatment. There has been no elaboration of comprehensive approaches

[33] I.Pathmanathan et al. Int J Tuberc Lung Dis 2018; 22(6):596-605.
[34] Y Assefa, S Woldeyohannes, Y A Gelaw et al. IJTLD 2019; 23(6): 728-734
[35] Kalema N et al Int J Tuberc Lung Dis 2021; 25(5): 388-394
[36] Daria Szkwarko et al PLoS One 2017; 12(8):e0182185

to address hesitancy by at-risk persons and communities. Community hesitancy is compounded by TB stigma and discrimination.

The major challenge with TB – IPC, is the lack of data that made it impossible in this evaluation to assess whether TB-IPC was linked with national IPC programmes and programs to combat anti-microbial resistance (AMR). While it is currently recommended that TB among health staff be monitored and reported, most countries do not do so. The evaluation team was unable to document whether TB in health care workers is linked to programs to improve occupational health and safety of health workers.

Currently in the Global Fund Modular Framework, IPC appears in the TB/HIV, TB care and prevention, MDRTB, RSSH and more recently in the C19RM module/intervention. For a cross cutting intervention such as IPC, it is unclear who should take the lead and be accountable for IPC at the country level. This evaluation was not able to establish how well individuals responsible for the establishment and monitoring of national IPC programmes and the delivery of AMR national action plans within ministries of health are involved in the TB-IPC work supported by the Global Fund at the country level. The focus of funding requests for IPC by countries appears to be on facility refurbishment, however, we were not able to establish this beyond doubt because of the challenges of the complex way in which budget data is organized in the documents accessed as outlined in section 5.1.

At the country level, there may be a lack of recognition that robust implementation of PMTPT requires a health system approach spanning all the health system building blocks including Human Resource for Health (HRH), products supply and management system (PSM), and health information management system (HMIS). Supply of rifapentine may be a barrier and cost (or perceptions of high cost) may be a major bottleneck for the uptake of shorter TPT regimens. In South Africa, for example, there is on-going debate about the adoption of 3HP, a much more expensive regimen when the efficacy is considered similar to 6H, the cheaper option.

This evaluation did not reveal significant engagement of community health systems in the delivery of TB prevention, yet common sense suggests that the widescale implementation of PMTPT is likely to work best if the program is anchored in the primary health care (PHC) system and is community based. This is because TPT is targeted at people who are not sick and are going about their usual business in the community.

## 6.3 Enablers and opportunities for IPC and TPT expansion

Tuberculosis prevention is poised to benefit from the exploitation of several opportunities and enablers as highlighted in the following paragraphs below.

**Lessons from the COVID-19 response:** The COVID-19 pandemic increased awareness of airborne infection transmission prevention and control that can be used to ramp up IPC. These include social distancing, mask wearing and contact tracing and management. The use of chest x-rays, especially digital x-rays, for investigation of COVID-19 contacts may have contributed to strengthening ACF for TB and TPT. In countries such as Azerbaijan, the COVID-19 pandemic helped to move TB care

outside hospital, a positive development for TB, which can be utilized to support TPT. As the COVID-19 pandemic evolved, integration of responses for COVID-19 control and Tuberculosis care and control also began to emerge such as dual use of human resources for health and equipment to fight both diseases. Such integrated approaches support strengthening of health service delivery systems and will be useful for pandemic preparedness and control in the future.

**Use of Indicators in the Performance Framework**: These include TPT Indicators by risk groups, to also encourage countries to adopt these indicators in their NSPs and annual workplans.

**The UNHLM targets**: These targets continue to provide an opportunity to advocate for and promote TPT.

**The New Global Fund Strategy**: The fact that the new Global Fund Strategy includes TB prevention is a major opportunity for the Global Fund to advance TB prevention.

**Catalytic Investments:** The potential to set up Global Fund catalytic investments (Strategic Interventions (SI) and Matching Funds (MF)) for TPT among specific TB risk groups such as contacts, children, and prisoners. While catalytic investments (MF and SI) for TPT was established for PLHIV in 3 allowing for targeted TPT for this population group, it is still too early in the implementation phase of NFM3 to determine what outcomes will accrue. Other equally important vulnerable groups where TPT is expected to have both individual and public health benefits such as HH contacts under the age of 5 have not yet been covered by catalytic investments.

**Advances in Chest Radiography**: The continuing development of automated chest x-ray interpretation systems, and portable chest x-ray systems offer the opportunity to expand chest radiography and therefore to provide a greater degree of confidence that TB is absent before TPT is initiated. This may help to reduce health provider hesitancy.

**Antigen Based Skin Tests for TB infection**: Recently approved antigen-based skin tests for TB infection may be cheaper and more sensitive and specific than the TST. The roll out of these tests may help to reduce both provider and affected individual/community TPT hesitancy and also help to improve the cost efficiency of PMTPT.

**Shorter TPT regimens**: As these regimens are shorter, they may be more acceptable to people and be associated with higher adherence to treatment. In some countries like South Africa, there are ongoing pilots for the new shorter TPT regimen and these provide good learning for scale up once the new guidelines are launched. In addition, South Africa has developed an investment case for TPT which can be used as an advocacy tool to the provincial health administrators. In Azerbaijan the medical personnel at the HIV Center in Baku believed that the poor TPT adherence among PLHIV, could be addressed by providing shorter TPT for PLHIV, such as 3HR instead of 6H (note: 3HR is provided for PLHIV in the penitentiary system through support of the Global Fund, while 6H is provided for PLHIV in the civilian sector with resources from the government).

**Tuberculosis recovery plans post COVID-19:** The National Department of Health in South Africa through the TB program, TB think tank and partners, has developed a post COVID-19 TB recovery plan that in addition to improved screening and testing initiatives targets to scale up TB preventive treatment and improve protection of health care workers. This recovery plan is likely to increase TPT uptake.

## 6.4 Coordination of TB prevention

At the global level, there is a high degree of alignment by global level TB actors for the need for TB prevention but there are no effective coordination platforms. TB prevention could benefit from the engagement of other players with mandates, roles and functions beyond TB and even health, such as UNICEF, World Food Program, GAVI, ILO and others. This evaluation did not reveal strong multi agency partnerships for TB prevention at the global level. There may also be a disconnect among players at the country level, with for example, sub-optimal linkages between TB and HIV programs, national TB programs and the penitentiary system etc. While the TB Situation room currently has a limited number of members, it is a potential mechanism that can be used to enhance global coordination and partnerships among TB actors at the global level.

**Best practice in South Africa**
**A platform to bring together TB stakeholder- the TB think tank:** The National Department of Health (NDOH) TB Think Tank, established in 2014 with financial support from the Bill and Melinda Gates Foundation, brought together government leaders, policymakers, academics, researchers, Civil Society Organizations (CSOs), non-governmental organizations (NGO) and funders to identify gaps in the management of TB in South Africa. The TB Think Tank has played a major role in laying the foundation for recommending interventions for the NTP's strategic plan. The Think Tank reviews evidence to help inform TB policy. There is a TB prevention task team within the think tank with a major focus on TB prevention. Part of their mandate is to review available global and local evidence to shape South African policy on TPT. They have undertaken a review of barriers for IPT implementation, and this is an opportunity to work on the findings. In some provinces like Western Cape, they also have working groups like the TB tank that can be platforms to support TPT roll out.

## 6.5 Levers that the Global Fund could apply to support TB prevention

As the major external source of finance for the TB response in TB endemic countries, the Global Fund may use certain levers to promote scale up and quality of TB prevention. These include:

**Catalytic investments**: both Strategic Initiatives (SIs) and Matching Funds (MF) can be used effectively to spur and accelerate action to enhance TB prevention, especially TPT among specific risk groups such as HH contacts under the age of 5 in whom progress with TPT uptake and coverage has been sluggish, populations with very high rates of TB such as prisoners and recent contacts of people with TB over the age of 5. Both SI and MF have helped to advance TB care in areas such as finding missing people with TB and similar effects may result when these approaches are used for TPT.

Strategic use of Global Fund processes including guidance to countries through the TB information, TRP and GAC reviews have been used to nudge countries to include TB prevention in their funding requests to the Global Fund.

While the key player in anti-TB medicine market shaping activities has been the Global Drug Facility (GDF) of the Stop TB Partnership, the Global Fund has been collaborating with the GDF to support these activities. These activities are intended to improve availability of new TB preventive therapy regimens, especially 3HP and 1HP, through actions such as urging manufactures to develop fixed dose combination formulations of these medicines, increase the number of manufacturers and better forecasting of demand.

Indicators included in the Global Fund's Performance Framework provide a major incentive for countries to report on these indicators, which is a powerful tool for promoting the implementation of various interventions for TB control.

## 6.6 TB prevention beyond TPT and TB-IPC

While the Global Fund is not well placed to address social determinants of TB vaccines, these issues are critical for ending TB as a global public health threat. This evaluation was not focused on these areas of TB prevention, however, overall, there appeared to be no obvious appetite for the Global Fund to be more deeply engaged in these areas of TB prevention.

# 7. TB prevention Theory of Change

The goal of TB prevention is to address individual risk of acquiring TB infection and progression of this infection to active TB disease. When interventions for TB prevention reach high coverage, a public health benefit is expected. Thus, implementation of TB prevention interventions and activities should ultimately contribute to a reduction in TB incidence, mortality and TB associated costs for individuals and families affected by the disease. The inputs that are needed to be able to carry out essential interventions which then lead to the right outputs and outcomes for the epidemiological impact to occur are shown in Figure 25 below.

*Figure 25 Theory of Change*

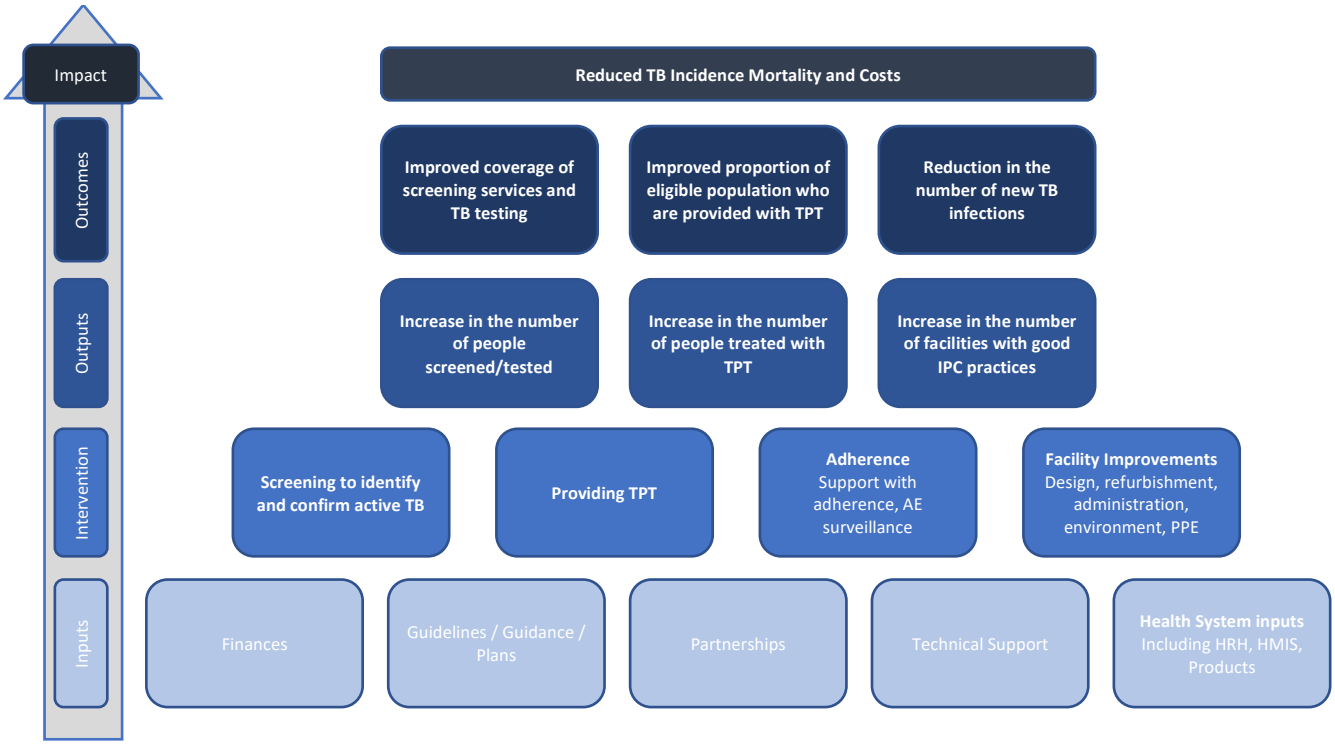



*Table 12 Summary of Key Findings of the Evaluation and Strength of the Evidence*

| Key finding | Strength of the evidence |
|---|---|
| **Relevance of Global Fund investments in TB prevention** | |
| Increase in Global Fund investments in TB prevention between NFM2 and NFM3 | Strong |
| Low proportion of overall Global Fund resources and funding for TB allocated to TB prevention | Strong |
| Greater proportion of TB prevention funding allocated to TB-IPC as compared to TPT | Strong |
| **Outputs and Outcomes of Global Fund Investments in TB prevention** | |
| Unchanging TPT uptake and coverage for HH contacts <5 between 2018 and 2020 | Strong |
| Increasing uptake and coverage of TPT for PLHIV between 2018 and 2020 | Strong |
| Lack of data for TPT uptake and coverage in HH contacts >5 and among other at risk populations | Strong |

| | |
|---|---|
| **Effectiveness and efficiency of Global Fund investments in TB prevention** | |
| Limited and variable data on cost-efficiency of Global Fund investments in TB prevention | Weak |
| No outcome and impact data to enable estimate estimates of cost effectiveness of Global Fund investments in TB prevention | Strong |
| **Gaps in Global Fund Investments in TB prevention** | |
| Deprioritized and consequently Inadequate financing for TB prevention | Strong |
| Inadequate TB prevention information system | Strong |
| Lack of engagement of communities | Weak |
| Lack of implementation/health systems research on TB prevention | Weak |

# 8. Evaluation limitations

The major limitation of this evaluation was the lack of data on TB prevention. It was for example not possible to link ACF to TPT provision, because TB notification data does not disaggregate how people with TB were identified. The lack of data was larger for TB-IPC than for TPT. For cost data it was difficult to find, aggregate and thus analyse data because information was spread out in many modules, interventions, and activities.

A lack of data does not mean that an intervention is not being carried out. To be conclusive about the state of implementation of TB-IPC, visits to a representative sample of health care facilities would have clarified whether the challenge with TB-IPC was related to reporting of implementation or actual lack of implementation or a combination of both. As a result of time and budgetary constraints, in addition to ongoing concerns about the health risk of COVID-19, facility visits in the 9 CCs were not carried out, even though they had been planned. Similarly, to better understand the data challenges affecting TPT, data verification and validation including perusal of registers at health facilities would have been very useful. Again, time constraints did not allow these activities to be carried out.

An assessment of the interventions that are being carried out at the global and country level to address social determinants of TB would have added value to this evaluation since TB is driven by these determinants, but were not included in the scope of this evaluation because both the TERG and the Global Fund Secretariat considered these areas beyond the core mandate of the Global Fund. Under nutrition, the consequence of social and economic deprivation in particular is a major driver of TB with a highest population attributable fraction. Preventing TB requires that such population level drivers of TB are comprehensively addressed, however, it is noted that these areas are not included in the list of interventions for TB prevention in the new Global Fund Strategy and therefore were not pursued in great depth in this evaluation. This is a missed opportunity. At the very least the TB community needs to be aware of the agencies at the global and country level that are addressing nutrition problems, including the opposite problem of easy access to inappropriate foods (so called junk foods) which increases the risk of obesity and diabetes which then ends up increasing the risk of active TB in those infected with Mycobacterium tuberculosis. The fact that the evaluation team did not engage with agencies that are working on development, testing and deployment of TB vaccines is also another limitation of this evaluation.

# 9. Conclusions

The need to end TB as a global public health threat is not in doubt. Tuberculosis prevention, in its many facets, is key to the achievement of the goal to end the global epidemic of TB. This age-old infectious disease is closely linked to poverty and social deprivation and therefore probably the most effective way of preventing TB is to end poverty. Being an infectious disease, the development and deployment of an efficacious and effective vaccine would also go a long way to support efforts to end TB. Addressing social determinants of TB and vaccine development and deployment are not direct mandates of the Global Fund, even though it may be argued that fighting TB (and the other two diseases – HIV and Malaria) contributes to the fight against poverty. In addition to fighting poverty and tackling the social determinants of TB other measures applied to contribute to the effort to end TB include early identification of people with active TB disease and placing them promptly on treatment, prevention of TB transmission in settings known to increase risk of exposure to Mycobacterium tuberculosis such as in health care service delivery sites and the treatment of TB infection. This evaluation focused on the latter two interventions – TB-IPC and TPT.

This evaluation was undertaken to better understand the relevance of the Global Fund investments in TB prevention, outputs, and outcomes of these investments, and how effective and efficient these investments have been used in the funding periods of NFM2 and NFM3. This evaluation also sought to understand gaps in current programming for TB prevention.

In terms of relevance of Global Fund investments in TB prevention, it is noted that the Global Fund has been actively supporting TB prevention, both IPC and TPT, in keeping with evolving priorities in the TB field, to meet global and country needs. The work of the Global Fund in supporting TB prevention is contributing to the development of country level policies and practices as evidenced by the adoption by countries of the recommendations on TB prevention in the TB technical Information Note. The evaluation team were not able to observe a link between Global Fund investments and global level policies and strategies. It is understood that global policies (implying normative guidance developed by WHO) are based primarily on review of research evidence. The evaluation team did not observe robust operational or implementation research programs of the kind that may feed into global level policy development for TB prevention in any of the 20 selected countries for this evaluation, except in Thailand.

Between NFM2 and NFM3 the Global Fund increased its investment in TPT from USD 13.8 to USD 92.1 million. In terms of budget share this increase in actual dollars translated to an increase from 0.6% of total funding in NFM2 to 3.4% in NFM3. The IPC budget increased from $123.5 million in NFM2 to $129 million in the NFM3 budget period. The sum of TPT and IPC budget representing TB Prevention budget increased from $137.4 to $176.1 million between the NFM2 and NFM3 periods essentially due to additional budget for IGRA test and Rifapentine in dedicated catalytic investments (Matching Funds) for TPT in PLHIV. While these trends are encouraging, they represent only a small proportion of the financial need for TB prevention. In the

concluding Global Plan to End TB, it was estimated that $ 77.8 billion was required to fully fund the TB response between 2018 and 2022. Of the $ 77.8 billion that was needed to fully fund the global TB response, $ 65 billion was needed for TB care and prevention and of this, it was estimated that 3% (or nearly $ 2 billion) would be required to fund TB preventive therapy alone.

The differential between allocated amounts and actual needs with regards to TB prevention is likely to increase significantly in future years. A new global plan to end TB covering the period 2023 to 2030 is under development and it will be interesting to see what the new estimated costs for TB prevention, including IPC, will be. The WHO, in its 2021 report provided data on the actual amounts of financial resources that had been mobilized for the TB response from 2010 to 2020. Funds mobilized for the global response to TB increased from $ 5.2 billion in 2010 to $ 6.1 billion in 2016 and then plateaued at about $ 5.8 billion a year between 2017 and 2019. In 2020, financing for the global response for TB declined to $ 5.3 billion which was less than 50% of the total estimated need, based on the 2018-2022 estimates of the global plan to end TB (WHO, Global TB Report, 2021). Based on these findings and the evaluation team's analysis of the data on Global Fund budgets, it is observed that TB prevention, both IPC and TPT, have been grossly under-funded over the years. TB-IPC is better funded than TPT, yet in terms of outputs and outcomes there is very little to show for it, and questions may be asked if investing in this intervention in its current form, represents value for money.

In this evaluation it was not possible to assess the impact of Global Fund investments in TB prevention on the overall burden of TB in terms of its incidence, mortality, and the associated catastrophic costs that those who suffer the disease incur. Only limited data was available to estimate cost-efficiency of Global Fund investments in TB prevention. To estimate cost-effectiveness of Global Fund investments in TB prevention would have required that information on outcomes and impact of TB prevention on TB morbidity (incidence), mortality and catastrophic costs be available. This information is currently unavailable. Modelling work, however, suggests that TB prevention may contribute significantly to reductions in TB incidence, mortality, and costs[37]. The current design of the Global Fund module and Global Fund cost category modules were challenging to navigate and limited the evaluation team's ability to carry out spending analysis on IPC and TPT.

In relation to the outputs, outcomes, and impact of Global Fund investments in TB prevention, this evaluation confirmed what is already known about both TB-IPC and TPT. Both these interventions are poorly implemented and have therefore not contributed much to the epidemiological situation of TB. The situation is, however, not overwhelmingly gloomy with good progress made in the provision of TPT to PLHIV. In the period covered by this intervention (2018 to 2021), there was a significant jump in the number of PLHIV placed on TPT between 2018 and 2020, with coverage figures exceeding targets set at the UNHLM in 2018. This is notwithstanding the damper that the expansion of the pool of people eligible for TPT while retaining the same UNHLM targets may have artificially increased coverage performance. It remains a major

[37] Mandal S et al BMC Med 2020; 18(1):163

achievement that between 2018 and 2020, the number of PLHIV who were placed on TPT in the 20 Global Fund supported countries that were selected for this evaluation increased threefold from 682,138 to 2,234,712. A smaller increase in TPT uptake was seen in HH contacts below the age of 5.

In the 20 countries selected for this evaluation, the number of HH under 5 who were treated for TB infection increased from 70,059 to 100,491. There was hardly any uptake of TPT among HH contacts older than 5 years, based on reports to the Global Fund and WHO. This is not surprising. Up to 2018 when the UNHLM was held, HH contacts over the age 5 were not prioritized at all levels, including by the WHO, the Stop TB Partnership, the Global Fund, and countries**.** Global Funds grants signed in this period therefore did not include TPT for HH contacts over age 5 and the appropriate indicator was not included in the countries' performance frameworks. For the Global Fund, TPT in older persons over the age of 5 will probably have to wait until the next funding cycle (NFM4) to see progress. While the progress was good for TPT in PLHIV, the same cannot be said about TPT uptake and coverage in child contacts below the age 5. The fact that only 100,491 or 10% of those eligible for this intervention actually received it in 2020 is cause for concern. Admittedly, the COVID-19 pandemic likely contributed to the poor TPT uptake and coverage performance in 2020, however the trends in the performance of this intervention was not satisfactory even in the pre-COVID period.

Notably this evaluation found very limited data on TPT uptake and coverage for other high-risk groups for whom TPT may be beneficial such as prisoners, immigrants, health care workers, and those with existing medical conditions such chronic kidney disease on dialysis. Only Azerbaijan is providing TPT to prisoners and other at-risk populations and had apparent high coverage of TPT among HH contacts over 5 years.

While some visible progress is being made with TPT, for TB –IPC, there is no data. Only 2 of the 20 countries that were selected for this evaluation reported to the WHO, the number of health care workers who were notified to have had TB in 2020. There are no other metrics that are used to track and monitor TB-IPC, yet of the two TB prevention interventions that have been supported by the Global Fund, TB-IPC is the one that receives more funding.

The evaluation team observed a major challenge with availability of data for TB prevention. In this evaluation data completeness is defined as the proportion of the 20 selected countries that had TB prevention (TPT/IPC) data. The evaluation team expected that all countries would have TB prevention data and were surprised that 15% of these countries did not have data on TPT uptake in HH contacts under the age of 5 and 50% of them had no data on TPT uptake in PLHIV. It was also expected that the data reported to WHO and the Global Fund would be concordant because it is derived from the same source which is the national health information system. Thus, it is surprising to observe that data concordance was only about 36% for HH contacts below 5 years and 44% for TPT in PLHIV.

The underperformance and inadequate tracking of TB prevention is not due to a lack of guidance. The policy to provide TPT in PLHIV has been in place since 2004[38] but implementation of this policy has been poor, until in the last few years. Similarly, the policy to provide TPT for young children below the age of 5 who are HH contacts of people with infectious TB has been in place for decades yet by 2020, uptake and implementation of this policy remained low, which is disheartening.

The technical Information Note and guidance produced by the Global Fund has been helpful. We observed that the Global Fund TB technical Information Note of July 2019 includes TPT and IPC in the list of high impact interventions and encourages applicants to include these interventions in their funding requests. The technical Information Note, which operationalizes the WHO normative guidance on TB prevention, prioritizes HH contacts and PLHIV for TPT and advises countries to include TPT as a continuum of the interventions for early identification of people with TB in these population groups. This is sound advice which, it is noted, countries have adopted. Thus, all the 9 CCs in this evaluation prioritized PLHIV and HH contacts below the age of 5, however, most countries have not prioritized HH contacts over the age of 5. Azerbaijan, Thailand, Ethiopia, Kazakhstan, and Zimbabwe have included HH contacts over the age of 5 in their national policies with Ethiopia and Thailand limiting the age bracket to those between 5 to 15 and 5 to 18 years, respectively.

While multiple factors present barriers to the implementation of TB preventive therapy underfunding (as highlighted above), provider and individual/community hesitancy, lack of access to sensitive screening tools to exclude active TB and lack of access to tests for TB infection probably pose the biggest challenges. Barriers to implementation of TB-IPC are equally many but the major hurdles include inadequate leadership at the level of Ministries of Health, a focus on physical infrastructure for IPC, rather than basic easily implementable and non- costly administrative measures and the striking lack of suitable indicators to monitor and track progress.

There are, however, opportunities that could be used to accelerate uptake and scale up TB prevention. These include the political momentum that was created by the UNHLM and the targets that came from that meeting, the potential to set aside funding for TB prevention through the catalytic investment mechanism, the lessons learnt and opportunities that came out of the COVID-19 response and a new Global Fund Strategy that has proactively prioritized TB prevention.

Public health programming for TPT should not be underrated in terms of its complexity. There are multiple issues to consider when developing PMTPT. These include the populations to be prioritized for TPT, the screening approaches and algorithms to exclude active TB before initiating TPT, to or not to test for TB infection before initiating TPT for those found to be eligible for this intervention and the regimens to be used. The global guidance on all these issues allows for a wide array of choices, a menu of options, that requires careful and thoughtful considerations of resource needs and capacity. The evaluation team considers that TPT should not be made to compete with interventions to find missing people with TB but rather be complementary and synergistic to these efforts. It has been observed that if high coverage of vulnerable populations with high quality TB screening services is carried out repeatedly as

[38] Interim policy on collaborative TB/HIV activities WHO/HTM/TB 2004.330

happened in clinical trial settings in Vietnam[39] and the slums of Harare in Zimbabwe[40], TB rates come down and therefore it may be argued that active TB case finding alone is adequate to address the burden of TB. While the application of TPT to whole populations, as was done in the Thibela study[41] may not have the desired effect, clinical trial data suggests that focused TPT on at least HH contacts may have a significant effect on TB incidence[42]. The evaluation team strongly believes that greater gains on the burden of TB will be made if TPT is an integral component of these active case finding initiatives. It may be that ending TB will need to happen vulnerable population after vulnerable population, in district after district using comprehensive coverage of screening, testing and treatment services that include TBI testing and treatment. The Global Fund is in a unique position to spur movement in this area.

As for TB-IPC, the challenges for the robust implementation of TB-IPC programs may be even bigger but the funding needed to solve these challenges is not necessarily more costly. It is the evaluation team's opinion that the overwhelming focus on environmental controls and personal protection as evidenced by the budgets requested by countries for facility refurbishments and Personal Protective Equipment (PPEs) may be inappropriate. There are low hanging fruits in less costly administrative controls that unfortunately are mostly ignored. A huge focus on personal protection while ignoring administrative controls may be likened to mopping the floor without turning off the tap. To effectively work, TB-IPC needs to be a component of the overall national and facility IPC program. The bigger challenge therefore is how to ensure there are coordination mechanisms among the multiple players that need to develop, implement, monitor, and report on IPC. There are no easy answers for this challenge, however, the Global Fund may want to use its RSSH platform to push the agenda of IPC and to ensure that there is IPC cross talk among the RSSH, HIV and TB components. As with TPT, a comprehensive information/data system for IPC needs to be developed with appropriate indicators on IPC processes as well as on HAI including TB among health staff.

In this evaluation it was not possible to assess the level of engagement of communities in TB prevention. None of the selected evaluation countries had data on community engagement in TB prevention. Communities will be critical for the delivery of TB prevention services. The TB interventions that can be delivered at the community level span the entire spectrum from actions to address social determinants of TB to the provision of TPT and adherence support. Because TPT is targeted at healthy people, it is likely that both uptake and coverage are likely to be better if a community approach to the delivery of this intervention is pursued.

Suffice it to say that significant level of TPT implementation will not happen if: a) funding for the TB response in general does not increase; b) the proportion of available TB funding that is budgeted for TB prevention is not increased (the increase that occurred between NFM2 and NFM3 is far from sufficient); c) TPT is not included as

[39] Marks GB, Nguyen NV, Nguyen PTB, Nguyen TA, Nguyen HB, et al. Community-wide Screening for Tuberculosis in a High-Prevalence Setting. *N Engl J Med.* 2019; 381: 1347-1357

[40] Corbett EL, Bandason T, Duong T, Dauya E, Makamure B, Churchyard GJ, et al. Comparison of two active case-finding strategies for community-based diagnosis of symptomatic smear-positive tuberculosis and control of infectious tuberculosis in Harare, Zimbabwe (DETECTB): a cluster-randomised trial. Lancet. 2010 Oct 9;376(9748):1244-53

[41] Gavin J. Churchyard et al. NEJM 2014; 370(4): 3011-10

[42] Cavalcante SC et al. Int J Tuberc Lung Dis 2010; 14:203-209

an integral component of the TB care cascade and continues to be pursued in a siloed manner, d) TPT is not an integral component of the package of interventions delivered at the PHC level and in the community; e) TPT hesitancy by both health care service providers and the targeted individuals and communities is not comprehensively addressed; f) it is not recognised that PMTPT requires a system approach related to all the six WHO elements of the health care system; and g) appropriate implementation and or operations research is not undertaken to help define the most effective approaches to delivering a PMTPT intervention that reaches all the relevant populations (high coverage ) with a high quality program.

# 10. Recommendations

To operationalize and adequately implement sub-objective 2 of the new Global Fund Strategy, 2023-2028, and taking into account the findings and conclusions of this evaluation, the evaluation team provides recommendations to the Global Fund and partners in the following areas:(1) Financing for TB prevention;(2) TB prevention data availability and quality (3) Provision of high-quality TB prevention Services, (4) Community engagement and empowerment and 5) Operations and implementation research for TB prevention. If the recommendation is policy or operational in orientation, the responsibility for its implementation and the timelines for its implementation, are highlighted.

## 10.1. Financing for TB Prevention

**The Global Fund and partners are urged to continue mobilizing additional financial resources to support robust programming of TB prevention in TB endemic settings.**

i. To catalyse implementation of TB prevention interventions and activities, the Global Fund and partners are urged to consider including TB prevention in the priority list of interventions to benefit from catalytic investments (SI and MF). It is recommended that the focus of catalytic investments on TB preventive treatment be expanded to include other high-risk groups beyond PLHIV.

**Recommendation orientation**: policy, high priority.

**Rationale:** A concerted effort by the Global Fund and partners appears to have stimulated action at the country level that led to a marked increase in TPT uptake and coverage in PLHIV within a relatively short period of time after many years of stagnation. A similar approach should be used for other targeted at-risk populations. It is currently estimated that over 230, 000 children die every year from TB. The Global Fund has a public health mandate to prevent these deaths with TB preventive treatment being one of the tools the Global Fund could use to reduce and eventually eliminate these deaths. In view of the limited resources, it is suggested that in HH contacts, TPT be sequentially prioritized to cover PLHIV, all HH contacts under the age of 5, HH contacts with additional risk factors for progression to active TB (e.g., HH contacts who are HIV infected, diabetics, malnourished, over the age of 65 or have another clinical risk factor for progression to active TB if infected with Mycobacterium tuberculosis). Screening HH contacts for additional risk factors for progression to active TB implies that contact management will need to go beyond TB screening to allow for national TB programs to provide targeted TPT. This would cost more money of course but would have significant return on investment in the form of fewer TB deaths and possibly a faster decline in TB incidence.

Responsibility: The Global Fund Secretariat in consultation as relevant, with the Strategy Committee, the Global Fund Board and partners

Timeline: During preparations for NFM4.

ii. The Global Fund is encouraged to collaborate and partner with TB financing partners and technical partners as relevant to develop and support countries to implement

comprehensive budget templates to estimate the cost of interventions for TB prevention, both IPC and TPT.

Recommendation orientation: operational, medium priority.

**Rationale:** The development of budget templates will assist applicants to the Global Fund to comprehensively budget for TB prevention and be better able to define budget gaps for TB prevention and thus better prioritize interventions and activities for TB prevention. The costs for TB prevention should include costs for Human Resources for Health (HRH), developing and/or improving the TB prevention information system, Procurement and Supply Chain Management (PSM), Behaviour Change and Communication among other budget items. Applicants to the Global Fund should be encouraged to use the budget templates or costing tools when developing their national strategic plans, annual work plans and in funding requests to the Global Fund.

Responsibility: The Global Fund Secretariat in consultation as relevant, with TB financing partners, technical partners

Timelines: During preparations for NFM4

iii. The Global Fund is encouraged to continue collaborating with other stakeholders such as UNITAID and the Global Drug Facility as they undertake market shaping activities to address the challenge of cost, affordability, and availability of newer shorter rifapentine based TPT regimens.

Recommendation orientation: operational, medium priority.

Rationale: The treatment of TB infection using a fixed dose combination formulation of rifapentine, and isoniazid (3HP) currently costs USD 15 based on current Global Drug Facility prizes. This cost is nearly three times the cost of treatment of TB infection using a course of 6 months of isoniazid (less than USD 4). The shorter course of treatment using 3HP is not only likely to be associated with better adherence to treatment and higher treatment completion rates, but also may address TPT hesitancy among health care workers who have the fear of inducing drug resistance by using a single drug in people who may have sub-clinical TB. While market shaping activities for anti-TB medicines may be better carried out by the GDF, the Global Fund is a critical partner in these activities.

Responsibility: The Global Fund Secretariat in consultation as relevant, with partners

Timelines: During preparations for and implementation of NFM4.

## 10.2. TB prevention data availability and quality

The Global Fund and partners are encouraged to develop and fund a mechanism to provide technical support to countries to develop (if not existing) and enhance TB prevention health information systems that capture the entire cascade of processes, outputs, outcomes and impact of TB prevention.

i. The Global Fund and partners are encouraged to define and elaborate key indicators for TB-IPC and TPT to enable target setting and assessment of cost efficiency and cost effectiveness of these interventions. Additionally, the Global Fund is encouraged

to include TPT uptake and coverage among selected at-risk populations (we suggest PLHIV and HH contacts under age 5) among its Key Performance Indicators (KPIs).

Recommendation orientation: operational, high priority.

**Rationale:** This recommendation is based on the principle of "what is measured gets done". By elaborating key indicators for TB prevention and tracking these indicators the Global Fund will be able to link investments in TB prevention to TB outcomes and eventually to impact.

Responsibility: The Global Fund Secretariat in consultation as relevant, with partners

Timelines: During preparations for and implementation of NFM4.

ii. The Global Fund and partners are encouraged to provide technical support to Global Fund recipient countries to set high but realistic targets for TB prevention in addition to having a monitoring and evaluation framework that allows the Global Fund, partners, and the countries to monitor and track TPT and IPC uptake, coverage, and outcomes. For TPT the monitoring and evaluation should be able to provide TPT initiation and completion rates, rate of adverse events and rates of breakthrough TB during or within a specific period after completion of TPT. It is suggested that the Global Fund uses the Strategic Initiative mechanism to support the provision of technical assistance to applicants to the Global Fund.

iii.

Recommendation orientation: operational, medium priority.

Responsibility: Global Fund Secretariat in consultation as relevant, with partners, and countries

Timeline: during preparations for NFM4 and implementation of NFM4

## 10.3. Quality of TB prevention Services

The Global Fund and partners are encouraged to develop mechanisms to support countries to provide high quality TB prevention services.

i. The Global Fund and partners are encouraged to collaboratively define and publish program essentials for TB prevention that recipient countries should strive to achieve. This recommendation includes a request to the Global Fund and partners to clarify how countries should implement global recommendations on TPT, and to guide countries, through the development and publication of a practical handbook for example, on how to navigate common implementation bottlenecks so that the TB prevention services that emerge are of the highest possible quality. The Global Fund is encouraged to continue to clearly and strongly communicate to countries that the provision of TB prevention, especially TPT, should be an integral component of approaches to find people with TB, an intervention that should also be based on clarified program essentials.

Recommendation orientation: operational; high priority.

Rationale: The focus of TB preventive treatment has been on a limited number of outputs and outcomes including number of people placed on TPT (uptake) and proportion of those eligible to receive TPT that are treated (coverage). TPT completion rates have been sub-optimal and therefore a focus on TPT uptake and coverage alone is inadequate. For TB-IPC, surveillance of TB among health care workers is inadequate to assess the full breath of IPC measures for the Global Fund to be confident that resources it provides are used to provide care and treatment in safe environments.

Responsibility: Global Fund Secretariat in consultation as relevant, with partners and countries

Timeline: during preparations for NFM4 and implementation of NFM4

ii. To address provider hesitancy, the Global Fund is requested to: a) encourage and support countries to adopt and scale up more sensitive and specific TB screening approaches such as digital chest x-ray with artificial intelligence; b) encourage and support countries to adopt more sensitive, specific and probably easier to deploy tests for TB infection such as the newly approved antigen-based skin tests; and c) support countries to develop and implement targeted educational activities for health care service providers. This would support linkages between the TB prevention sub-objective and sub-objective 4 (Adapt TB programming to respond to the evolving situation, including through rapid deployment of new tools and innovations) of the 2023-2028 Global Fund Strategy.

Recommendation orientation: operational; high priority.

Responsibility: Global Fund Secretariat in consultation as relevant, with partners and countries

Timeline: during preparations for NFM4 and implementation of NFM4

iii. The Global Fund is requested to reinforce messaging, through the TB information note, to countries to emphasize that the development and implementation of TB-IPC programs should be part of the wider health system effort to prevent transmission of infections at the health facility level and the community level. These efforts should be part of the effort to ensure safety of health care workers and to combat AMR.

Recommendation orientation: operational; medium priority.

Responsibility: Global Fund Secretariat in consultation as relevant, with partners, and countries

Timeline: during preparations for NFM4 and implementation of NFM4

## 10.4. Community engagement

i. The Global Fund is strongly urged to encourage and push countries to include and engage communities fully in the development, implementation, and monitoring of interventions for TB prevention. Community engagement measures should include BCC and support for community led monitoring**.** This would support the linkage of the TB prevention sub-objective 2 to sub-objective 5 (Promote enabling environments, in

collaboration with partners and affected communities, to reduce TB-related stigma, discrimination, human rights and gender-related barriers to care; and advance approaches to address catastrophic cost due to TB) of the 2023-2028 Global Fund Strategy

Recommendation orientation: operational; high priority.

Rationale: Community Engagement (CE) and Community Led Responses (CLR) will be essential to deliver community level TB –IPC and TPT. TPT is directed at well people in the community and is likely to better taken up by eligible people in the community when the community is fully engaged and drives activities.

Responsibility: Global Fund Secretariat in consultation as relevant, with partners and countries

Timeline: during preparations for NFM4 and implementation of NFM4

## 10.5. Operations and implementation research for TB prevention

The Global Fund and partners are encouraged to support appropriate research, including operations, implementations/health system research to better define how TB-IPC and PMTPT should be implemented and or delivered.

i. The Global Fund and partners are encouraged to define and elaborate implementation level TB prevention knowledge gaps tor questions that can best be addressed through well designed operations, implementation or health system research.

Recommendation orientation: Operational; medium priority

Responsibility: Global Fund Secretariat in consultation as relevant, with partners, the Strategy Committee, the Global Fund Board

Timeline: during preparations for NFM4.

ii. It is suggested that, in addition to supporting country level operations research through country grants, the Global Fund should consider developing a mechanism for funding essential implementation or health system research to provide answers to major knowledge gaps affecting delivery of TB prevention services at multi- country, regional or global level. The Global Fund may use approaches such as “request for proposal”, which was used recently by the USAID in its SMART4TB initiative to identify groups of researchers to undertake this research. All research supported by the Global Fund should engage countries and communities in the design, development, implementation, dissemination, and translation of research results into policy.

Recommendation orientation: Policy; medium priority

Responsibility: Global Fund Secretariat in consultation as relevant, with partners, the Strategy Committee, the Global Fund Board

Timeline: during preparations for NFM4.

iii. The Global Fund should encourage countries to prioritize their target groups for TPT based on their epidemiological and funding context. For example:

- group 1- Household contacts of bacteriologically positive people who are below 5 years old and PLHIV - highest priority.
- group 2: Household contacts of bacteriologically positive people > 5 years with additional risk factors for progression to active TB such as those who are malnourished, diabetics, older than 65 and alcohol use disorders – high priority.
- group 3: Non HH contacts with high rates of TB such as persons older than age 65, health care workers, prisoners, etc - medium priority

Recommendation orientation: Policy; medium and high priority

Rationale: A concerted effort by the Global Fund and partners appears to have stimulated action at the country level that led to a marked increase in TPT uptake and coverage in PLHIV within a relatively short period of time after many years of stagnation. Prioritizing efforts should focus on household contacts below 5 years for all countries firstly and other risk-groups such as household contacts over 5 years, and then non-household contacts on a country-based approach.

Responsibility: Global Fund Secretariat in consultation as relevant, with partners, the Strategy Committee, the Global Fund Board

Timeline: during preparations for NFM4.

# 11. Annexes

## Annex 1: Evaluation Questions (EQs)

The five main EQs, which were adapted from the evaluation's ToRs, guided all data collection and analysis as detailed below. These EQs, which were finalized in consultation with the TERG, and the Global Fund Secretariat are:

1. How relevant have Global Fund's TB prevention investments and activities been in addressing needs at both country and global levels, and how effectively have these activities aligned with IPC and TPT interventions conducted by TB and HIV programs? It is worth noting that the target to provide TPT to 6 million PLHIV between 2018 and 2022 had been achieved and exceeded by 2020 (WHO, Global TB Report 2021), thus providing an excellent opportunity to learn lessons to support the roll out of TPT to other TB at risk populations, in addition to identifying and describing Global Fund TPT and IPC investments for other groups outside the setting of HIV infection. The investment period covered planning and implementation period of NFM2 and planning (without implementation) of NFM3 with timeline variation by country.
2. How effectively are TB prevention investments meeting their objectives and how effectively are partnerships functioning to achieve these for NFM2 grants already implemented?
3. How efficiently have TB prevention activities been implemented and how cost effective have they been for NFM2 grant already implemented?
4. How impactful have Global Fund TB prevention investments been on influencing national, country, and global strategies and policies for NFM2 grants already implemented?
5. What specific gaps can be identified to be addressed by future Global Fund TPT and IPC investments?

The EQs were mapped onto the TB prevention Theory of Change (ToC) to provide the overall framing for this evaluation.

The evaluation was operationalized through four complementary modules:

1. **Global policy and norms on IPC and TPT**.
   In this module, the evaluation team examined, through document reviews and key informant interviews, existing norms and policies, tools and mechanisms to critically assess the coherence and relevance in promoting and supporting IPC and TPT with the Global Fund and partners. Key sources of information and key informants included those from the Global Fund, WHO (HQ and five of its 6 regions), Stop TB Partnership (STP) and main technical and donor partners including United States Agency for International Development (USAID), the United States Centres for Disease Control and Prevention (CDC), the International Union Against Tuberculosis and Lung Disease (the Union) , KNCV Tuberculosis Foundation (KNCV), Clinton Health Access Initiative (CHAI), and Program for Appropriate Technology in Healt (PATH). .
2. **Process assessment**
   In this module the evaluation team explored the Global Fund processes, procedures, and tools to determine their fitness for purpose in supporting TB prevention efforts. The focus was on Global Fund guidance to countries, reviews by the Technical Review Panel (TRP) and grant making and management in the

current and previous funding cycles. The evaluation team also assessed the coherence and relevance of these processes, procedures, guidance, and tools to support investments in TB prevention (IPC-TPT) interventions in accordance with global norms and policies. A major output of the process assessment was to determine the level of investment by the Global Fund in TB prevention.

3. **Country level assessment**
   At the country level the evaluation team reviewed the relevance, coherence, efficiency, effectiveness and impact of TB prevention investments in IPC and TPT in 9 countries through document review, country visits and key informant interviews. The evaluation team also carried out portfolio data analysis in an additional 11 countries. With these approaches the evaluation was able to assess country level policies, strategies and interventions on TB prevention, level of financial investment in TB prevention from all sources including national funding sources and outcomes of TB prevention interventions and activities.
4. **Learning and synthesis**
   In this module the evaluation team synthesized the information and evidence gained from across modules 1-3 to answer the four main EQs to inform this draft report with initial findings and lessons learnt against the ToC and to identify areas of synergy, overlap and gaps.

## Annex 2: Questionnaires used at global level among KII, Global Fund Country Team, country level

**Introduction** (of those taking part in the interview) **Background** of the review (for the benefit of the interviewee):
The Global Fund has developed a new Strategy that will cover the period 2023-2028. Among the TB sub-objectives in the new Global Fund Strategy is TB prevention with an emphasis on Infection Prevention and Control (IPC) and TB Preventive Treatment (TPT). This sub-objective is in sync with the global push to enhance TB prevention and will support TB endemic countries to achieve the ambitious TPT targets that were set at the UNHLM on TB in 2018.
A joint TERG/Secretariat evaluation on TB prevention focusing on IPC and TPT is being undertaken as a learning opportunity for the Global Fund as it seeks to assess its role in and the support it provides to TB prevention efforts. It is anticipated that the results of this evaluation will assist the Global Fund as it invests in future policies, processes, and programming to support TB prevention.
The evaluation has four objectives:

1. Review policies, processes, and guidance to shape and enhance the inclusion of IPC and TPT TB prevention programs in the next funding allocation cycle (NFM 4) and the 2023-2028 Strategy period.
2. Outline the Global Fund's role (alone or with partners) in supporting IPC and TPT TB prevention.
3. Assess the scope, scale, and results of Global Fund investments in IPC and TPT TB prevention.
4. Identify recommendations to inform the Global Fund's role and investment in IPC and TPT TB prevention.

The primary intended users of the evaluation will be Global Fund's Board and its Strategy Committee (SC), the TERG, and key Secretariat staff involved in IPC and TPT TB prevention. Secondary intended users will include Principal Recipients, National TB program managers, Country Coordinating Mechanisms (CCMs) and Country Teams.
**Confidentiality** (no information will be attributed to an individual or organisation)

### Questionnaire 1. for Key Informant Interview (KII) at global level – list in Annex 6

Permission to record (request of the interviewee)
Interviewee details: Name:
Organisation/type:
Date interviewed:
Interviewed by: PY Norval and Chakaya

**Questions**

1. Are there gaps in global policies for IPC and TPT? If so, what are these gaps and how may they be addressed?
2. In your view what are the major barriers to IPC and TPT implementation? how may they be addressed?
3. In your view what are the enablers /opportunities for IPC and TPT implementation?

Include in new/ending NSP: prioritize IPC and TPT

4. In your view, what is the effect of COVID19 on TPT, on IPC? how potential gap may be addressed?
5. Who are the other partners involved in IPC and TPT? What mechanisms are there to enhance coordination of IPC and TPT efforts at the global level?
6. Are there levers that the GF could apply to stimulate implementation of IPC and TPT?
7. In the context of current state of the global epidemic of TB, and in the context of competing needs, what is your view on the level of financing for TB for IPC and TPT by the GF? Is this level of financing appropriate? What changes need to be made in global financing for TB prevention?
8. Are IPC and TPT interventions/activities supported by the Global Fund synergistic with those supported by other TB financing partners? If they are not, what are the major gaps and how could these gaps be addressed?
9. Is the Global Fund receiving the right information on IPC and TPT from Global Fund recipient countries to allow assessment and tracking of performance in this area of the TB response?
10. Does the Global Fund Modular Framework should include a module on TB prevention for IPC and TPT interventions?
11. Does the GF should do anything to address TB prevention beyond IPC and TPT such as actions on social determinants, TB vaccine development and deployment? If yes, what role GF should take? Please describe.

## Questionnaire 2: Country interview questionnaire on TB Infection Prevention and Control (IPC) and TB Preventive Treatment (TPT)

| | |
|---|---|
| Country | |
| Job Title | Text Response |
| Gender | Male / Female / Non-binary |
| Years of work experience inTB | Numeric answer |

### IPC TPT questionnaire at country level

### Planning

1. Do IPC and TPT interventions rely on programmatic information sources? (Yes/No)
2. Please describe those sources (NSP -indicators-budget, policy and guidelines, Operational plans, NFM, PF, program review, other).
3. Are IPC and TPT prioritized enough by the country? Describe any gap in NSP, NFM3 for IPC and TPT
4. Are IPC and TPT interventions streamlined and easy to understand? (Yes/No) If no, please describe the key constraints.
5. Do IPC and TPT interventions define precisely what activities will be implemented? (Yes/No) If No, state the gap

**Implementation of TPT**

6. Has TPT implementation been successful i.e. have the TPT indicators been achieved?
7. What have been the successes of TPT implementation?
8. In your view what are the enablers /opportunities TPT implementation?
9. What in your view have been the 3 key gaps or challenges to the uptake of TB preventive treatment? What is your proposal on how these challenges can be addressed?

| Challenge | Solution |
|---|---|
| | |
| | |

10. Are there some stakeholders who have been missed and what role do you think the stakeholders you have mentioned will play in TB Preventive treatment?
11. How has the community and clients been involved in the TPT roll out? Can TB patients cite positive effects of TPT implementation activities on their daily lives? How in your view can the patients be engaged more in the process?
12. Is there confusion or any misleading messages about the duration and scope of the primary TB prevention interventions?
13. What indicators been used to measure TPT? Describe Any challenges to report these indicators
14. Are the country targets for TPT in line with UNHLM targets for TPT? (Yes/No) *(*Probe for the targets)* If not, why?

**Implementation of IPC**

15. Are there national implementation plans for IPC?
16. What forms of IPC interventions are currently in use? *Tick what IPC interventions are available and for what level of facilities The facility levels we can include is (a)community, b)primary health care, c) hospitals, d) referral or national hospitals)*
    a. Administrative controls

i. IPC plans
i. Triaging coughers
i. Prompt Treatment initiation
i. Cough etiquette

a. Environmental controls
i. Upper-room germicidal ultraviolet (GUV) systems
i. Ventilation systems (including natural, mixed-mode, mechanical ventilation and recirculated air through high-efficiency particulate air [HEPA] filters)

a. Respiratory protection
i. Cloth masks
i. Surgical masks
i. Particulate respirators

17. What are the successes of IPC implementation?
18. What are the major barriers you are facing for IPC implementation?
19. What indicators been used to measure IPC? Any target was set? If No- Describe reasons why?

**Effect of COVID-19**

20. How did the COVID-19 pandemic affect IPC and TPT TB prevention implementation?

**Financing**

21. Who are the major donors engaged in the implementation of TB prevention interventions and activities in your country? *(This is already in the online survey but you can prompt for more information if necessary)*
22. In the context of current state of the epidemic of TB, and in the context of competing needs, what is your view on the level of financing for IPC and TPT by the GF? please describe
23. What changes need to be made in global and national financing for IPC and TPT?
24. Are IPC and TPT interventions/activities supported by the Global Fund synergistic with those supported by other TB financing partners? Please comment

**Partners**

25. Who are the stakeholders engaged in the implementation of IPC and TPT interventions and activities in your country? Please describe
26. What were the strategies for identifying and involving CSOs and other partners during the Global Fund application process (NFM2 and NFM3)??
    26.1. What lessons were learned?
27. Has the NTP regularly communicated decisions and activities on TPT TB prevention and IPC, including any changes to partners and direct and indirect beneficiaries? Please describe

**Next steps**

28. What, in your view, should be the main TB prevention interventions/activities that should be included your next country GF request (NFM4)?
29. What, in your view, should be changed in the NFM4 GF Modular Framework and indicators re IPC and TPT? Please describe
30. Does the GF should do anything to address TB prevention beyond IPC and TPT such as actions on social determinants, TB vaccine development and deployment? If yes what role GF should take ? Please describe

## Annex 3: Online Survey at country level

# Survey Tool

### Consent Note

As part of the evaluation, we are carrying out a survey to gather feedback on the status of IPC and TPT across 20 countries. You have been identified as a key stakeholder in IPC and TPT in your country and the evaluation team would greatly appreciate your perspective and views on the successes, challenges, barriers and lessons learned from your experience.
The survey should take no longer than 10 minutes to complete.

**Background Information**

| | |
|---|---|
| Country | |
| Type of Implementing Partner | Country Coordinating Mechanism<br>Principle Recipient<br>Ministry of Health<br>NGO, CSO<br>Private sector<br>National Health Expert/Advisor<br>Other (Specify) |
| Job Title | Text Response |
| Gender | Male / Female / Non-binary |
| Years of work experience inTB | Numeric answer |

**Main Questions**

| Question | Response options |
|---|---|
| 1a. Has the country developed TB Preventive Treatment interventions in their current NSP TB and NFM3 ? | Yes<br>No<br>Don't know |
| 1b. Has the country developed Infection Prevention and Control interventions in their current NSP TB and NFM3 ? | Yes<br>No<br>Don't know |
| If 1a=Yes<br>2a. what were the bases for developing these TB Preventive Treatment interventions? Were these based on Global Guidelines (eg. WHO, GF, CDC) or national plan/guidelines/data/research? (eg. National Health plan-guidelines, C19 mitigation plan …) | WHO Guidelines<br>GF Guidelines<br>CDC Guidelines<br>Other Global Guidelines<br>TB National Strategic Plan<br>TB National Guidelines<br>Other (please specify) |
| If 1b=Yes<br>2b. What were the bases for developing these Infection Prevention and Control interventions? Were these based on Global Guidelines (eg. WHO, GF, CDC) or national data/research? Other (eg. National Health plan-guidelines, C19 mitigation plan …) | WHO Guidelines<br>GF Guidelines<br>CDC Guidelines<br>Other Global Guidelines<br>TB National Strategic Plan<br>C19 Mitigation Plan<br>TB National Guidelines<br>Other (please specify) |
| 3. In your opinion, are there gaps in national policies for<br>- IPC<br>- TPT | Yes – Significant gaps<br>Yes – Minor gaps<br>No<br>Don't know |
| If 3=Yes | Yes – to a large extent |

| | |
|---|---|
| 3a. Are these gaps impacting national level policies on TPT or IPC? | Yes – to a small extent<br>No<br>Don't know |
| If 3=Yes<br>3b. What are these gaps? | Text Response |
| If 4=Yes<br>3c. How may they be addressed? | Text response |
| 4a. What are the major barriers you are facing for IPC implementation? | Funding<br>Policy<br>Commodity<br>Human resource related<br>Reporting and monitoring of IPC<br>IEC<br>Others-specify |
| 4b. What are the major barriers you are facing for TPT implementation? | Funding<br>Policy<br>Commodity<br>Human resource related<br>Reporting and monitoring of TPT<br>IEC<br>Others-specify |
| 5. Do you agree/disagree that IPC and TPT are appropriately prioritised by the country?<br>IPC<br>TPT | Strongly agree<br>Agree<br>Neither<br>Disagree<br>Strongly disagree |
| 6a. Who are the major donors engaged in the implementation of IPC and TPT interventions and activities in your country? | Global Fund<br>WHO<br>BMGF<br>Bilateral Funds<br>Other Multilateral Orgs<br>Other Foundations<br>National Government<br>USAID<br>CDC<br>PEPFAR<br>Others-specify |
| 6b. Who are the major stakeholders engaged in the implementation of IPC and TPT interventions and activities in your country? | Text response<br>Ministry<br>Funders/Technical agencies<br>NGOs<br>CSOs<br>Patient representatives<br>Private sector<br>Universities/research institutions<br>Health related associations |
| 6c. Are there any stakeholders who are not engaged in the implementation of IPC and TPT interventions and activities in your country, but that you feel should be? Who? | Text Response |
| 7a. In your view what are the enablers /opportunities for IPC implementation? | |
| 7b. In your view what are the enablers /opportunities for TPT implementation? | |

| | |
|---|---|
| 8. In the context of current state of the epidemic of TB, and in the context of competing needs, what is your view on the level of financing for TPT and IPC by the Global Fund? | Very good<br>Good<br>Neither good/bad<br>Poor<br>Very poor |
| 8a. What changes need to be made in global and national financing for IPC and TPT ? | Increase funding<br>Increase ownership<br>Redistribution |
| 9a. Do you agree/disagree that TPT interventions/activities supported by the Global Fund are synergistic with those supported by other TB financing partners? | Strongly agree<br>Agree<br>Neither<br>Disagree<br>Strongly disagree |
| 9b. If (strongly) disagree → what are the major gaps on TPT | Supplies and equipment (TB drugs, Igra/TST, digital Xray equipment, CAD etc);<br>IEC on TPT<br>HR training<br>Community engagement<br>Private sector engagement<br>Health Information System (HIS) on TPT<br>Data analysis on impact of TPT<br>Other (specify)<br>Other TB prevention interventions |
| 9c. how could these gaps on TPT be addressed? | Text response |
| 10a. Do you agree/disagree that IPC interventions/activities supported by the Global Fund are synergistic with those supported by other TB financing partners? | Strongly agree<br>Agree<br>Neither<br>Disagree<br>Strongly disagree |
| 10b. If (strongly) disagree → what are the major gaps on IPC | Supplies and equipment (GUV, health facility building, PPM);<br>HR training<br>Community engagement<br>Private sector engagement<br>Health Information System (HIS) on IPC<br>Data analysis on impact of IPC<br>Other (specify)<br>other TB prevention interventions |
| 10c. how could these gaps on IPC be addressed? | Text response |
| 11. Is the country information system for TPT and IPC appropriate for the assessment and tracking of performance in this area of the TB response? | Strongly agree<br>Agree<br>Neither<br>Disagree<br>Strongly disagree |
| 12. Are the country targets for TPT in line with UNHLM targets for TPT? | Strongly aligned<br>Aligned<br>Neither<br>Poorly aligned<br>Very poorly aligned |
| 12a. If not, why? | Text response |

**Web Survey Analysis**

A web survey was sent to approximately 70 key informants across the case study countries. 31 survey responses were been received across seven countries, representing a response rate of 44%. This is comparable to, and indeed exceeds, the response rates in comparable web-based surveys, particularly considering the entirely voluntary nature of participation.

The small sample size means that it is not possible to generate robust findings or recommendations based solely on the survey data. However, the survey responses do provide interesting areas for discussion, which can be triangulated with data from other sources to provide more reliable conclusions.

Despite the relatively low number of respondents, a good level of variation was acquired in terms of the background and demographic characteristics of the survey respondents. For example, respondents came from a variety of types of organisations and roles, with a range of experience in TB prevention, and a good balance between males and females. Further details on these characteristics are displayed in Table 13.

*Table 13 Web Survey Respondent Characteristics*

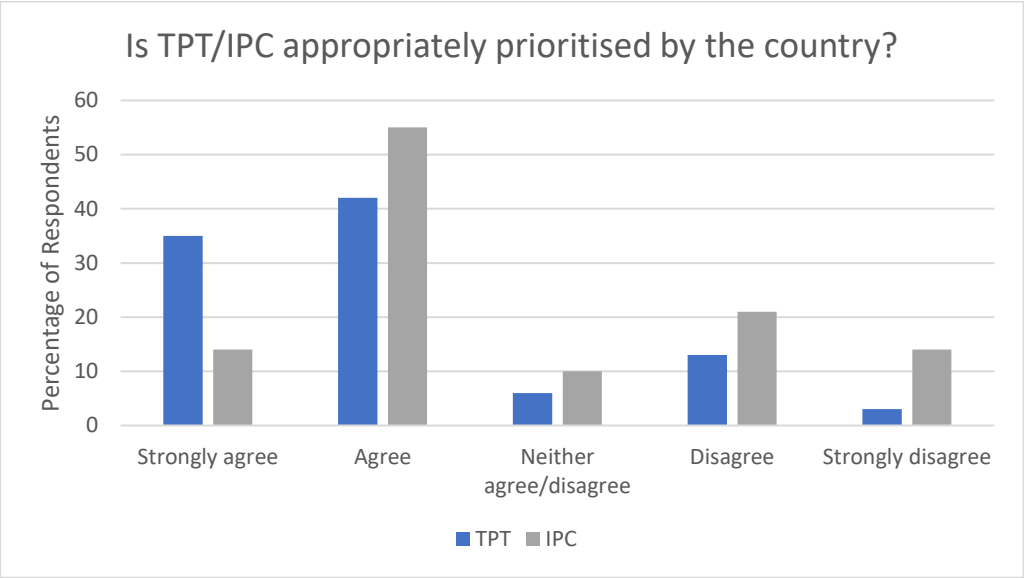
| Characteristic of Respondent | Number of Responses |
|---|---|
| **Country** | |
| Azerbaijan | 7 |
| Ethiopia | 5 |
| Gabon | 3 |
| Kazakhstan | 1 |
| Nepal | 5 |
| South Africa | 6 |
| Tanzania | 1 |
| Thailand | 1 |
| Zimbabwe | 2 |
| | |
| **Gender** | |
| Male | 15 |
| Female | 16 |

| Characteristic of Respondent | Number of Responses |
|---|---|
| **Years of Experience in TB Prevention** | |
| 0-5 years | 4 |
| 6-10 years | 2 |
| 11-15 years | 5 |
| 16-20 years | 6 |
| >20 years | 8 |
| | |
| **Type of Organisation** | |
| Ministry of Health | 4 |
| NGO, CSO | 11 |
| National Health Expert / Advisor | 2 |
| Principal Recipient | 4 |
| Other | 10 |
| | |

Below we present some of the key findings from the survey data. Where possible we include comparisons between county level TPT and IPC.

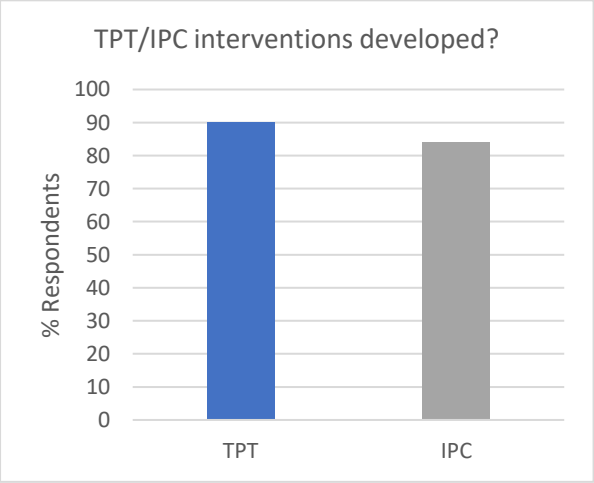
Respondents generally agreed that TPT and IPC were prioritised by their country, but this feeling was slightly stronger in relation to TPT (figure 26). Across both TPT and IPC, over two-thirds of respondents agreed or strongly agreed that TPT/IPC was appropriately prioritised by their country.

*Figure 26 Is TPT/IPC appropriately prioritised by the country?*



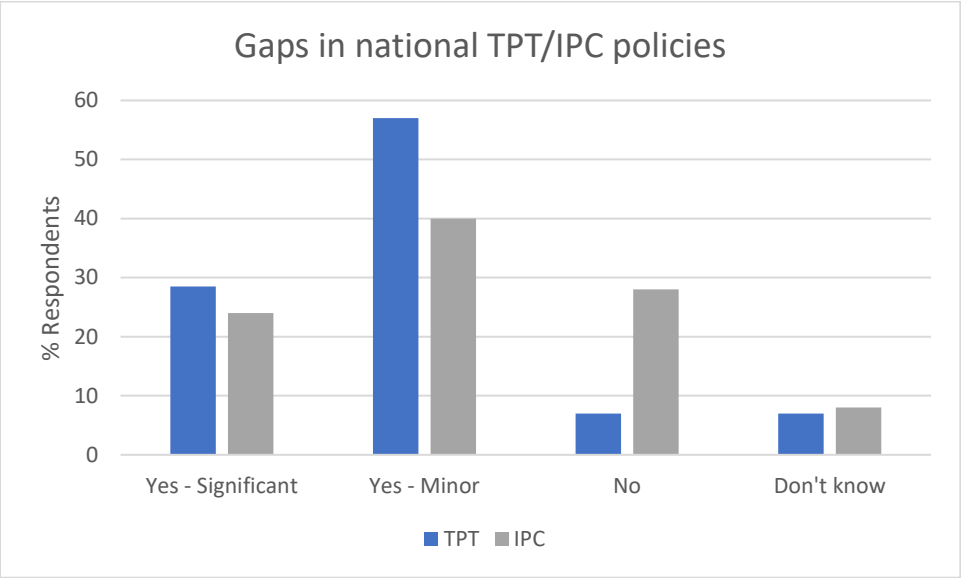

There was also clarity among respondents in relation to the development of national strategic plans, with over 80% of respondents stating that TPT and IPC interventions had been developed as part of the NSP TB and NFM3 (figure 27). For TPT these were most commonly based on WHO guidelines (81% of respondents) and national TB plans (61%), whereas for IPC the most common bases were WHO and CDC guidelines (61% and 48% respectively). Kazakhstan was the only country for which the majority of respondents said there was not a plan, which was the case for both TPT and IPC.

*Figure 27 Has the country developed TPT/IPC interventions in their current NSP TB and NFM3?*



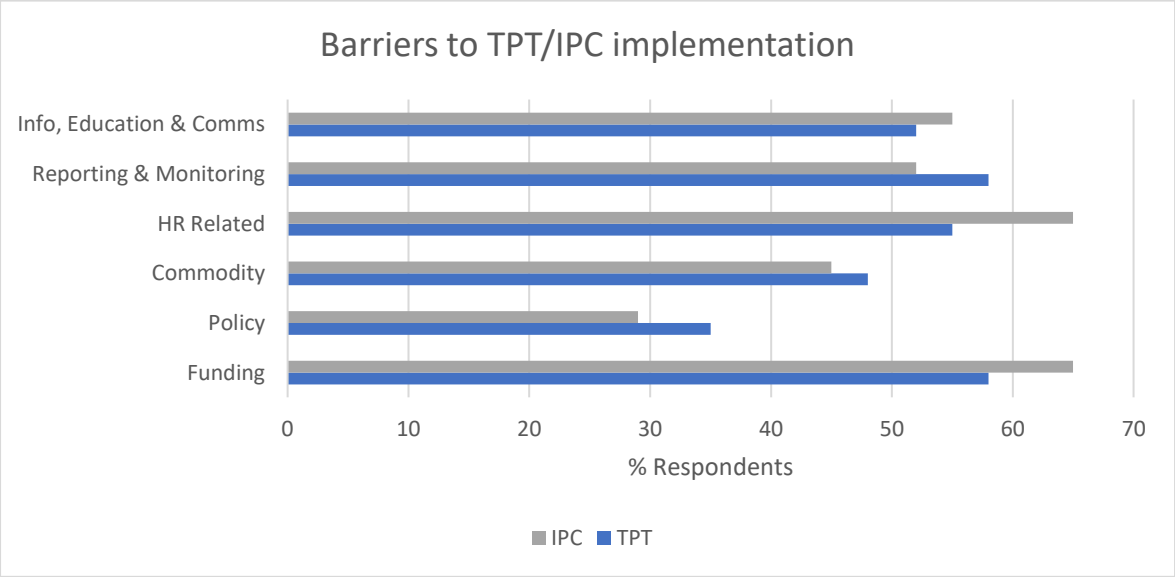

Despite good coverage in terms of national strategic plans and use of best practice guidelines, the majority of respondents also reported that there were gaps in national policies (86% of respondents for TPT and 64% for IPC) (figure 28) and that these gaps were significantly impacting national level policies on TPT (92% agree) and IPC (76% agree). Across all countries the majority of respondents reported that gaps in national policies existed for TPT.

*Figure 28 In your opinion, are there gaps in national policies for TPT/IPC interventions?*




Respondents reported the existence of a range of barriers they face in implementing TPT/IPC policies. Each of the six barriers asked about was faced by at least a quarter of respondents with regard to both TPT and IPC (figure 29).

*Figure 29 What are the major barriers you are facing for TPT/IPC implementation?*

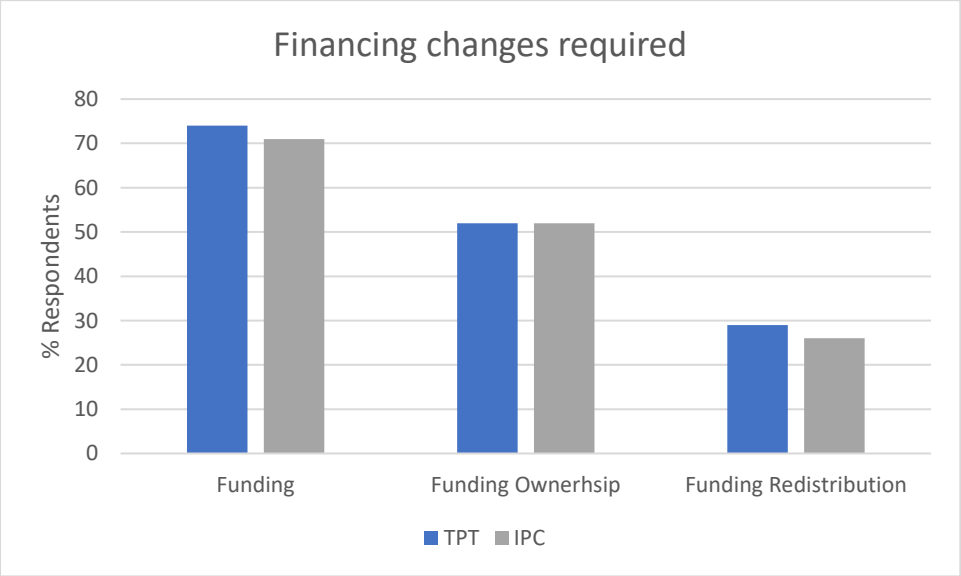



Encouragingly, the Global Fund was mentioned by 84% of respondents as one of the most engaged donors in the implementation of TPT and IPC interventions and activities, the most of any stakeholder, followed by national governments at 48% and USAID at 29%. In terms of national stakeholders, government ministries (84%), NGOs (61%) and funders/technical agencies (45%) were seen as the most engaged. Respondents were also asked about any groups of stakeholders who were not currently involved in TPT/IPC interventions and activities, but should be, with private sector actors being mentioned by multiple respondents.
Respondents also felt that Global Fund TPT/IPC interventions were well synergised with other TB financing partners, with 73% stating that it was “good” or “very good” for both. Furthermore,

73% of respondents stated that the country targets for TPT are “aligned” or “strongly aligned” with current UNHLM targets for TPT. Indeed, all countries provided more positive than negative responses to this question, with the exceptions of Kazakhstan and Tanzania where the response was neutral.

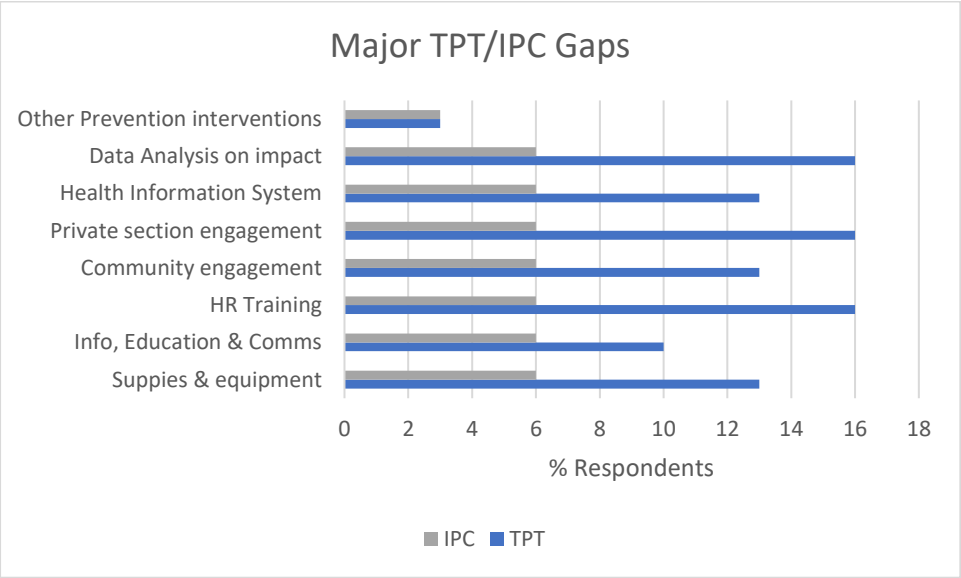
There were mixed responses on the level of financing available from the Global Fund to countries, with 55% of respondents stating that it was “good” or “very good”. However, respondents were consistent in what changes they felt were needed in global and national financing for both TPT and IPC (figure 30). Increased funding was the most important factor, followed by increased ownership of funds. Increased funding was the most popular answer for both TPT and IPC across all countries, with the exception of Nepal where increased ownership was selected most often.

*Figure 30 What changes need to be made in global and national financing for TPT/IPC?*



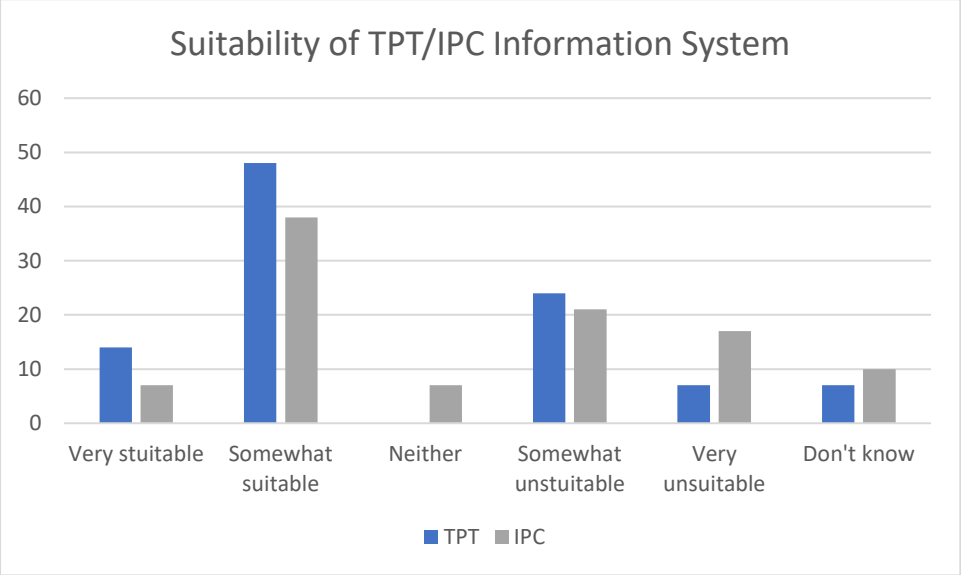

Respondents were not very forthcoming when it came to discussion gaps in TPT/IPC, with only a small proportion of respondents mentioning any gaps, and with a relatively even spread across the options, though with consistently more gaps identified for TPT than IPC (figure 31).

*Figure 31 What are the major gaps on TPT/IPC?*




The suitability of the information system for TPT/IPC varied between countries, with no common aggregate trend (figure 32). South Africa reported the lowest suitability scores, with Ethiopia and Nepal the highest.

*Figure 32 Is the country information system for TPT/IPC suitable?*



## Annex 4: Countries case study and portfolio analysis among countries of the global lists of high burden countries for TB, HIV-associated TB and MDR/RR TB for 2021-2025

| Country | High TB | High TB/HIV | high MDR | WHO Region | Incom | TPT child | TPT PLH | TB HCW | Tot HCW | % tot HCW |
|---|---|---|---|---|---|---|---|---|---|---|
| Angola | 1 | | 1 | AFRO | LMIC | NA | NA | 92 | NA | |
| Azerbaijan | | | 1 | EURO | UMIC | | | | | |
| Bangladesh | 1 | | 1 | SEARO | LMIC | 49% | | | | |
| Belarus | | | 1 | EURO | | | | | | |
| Botswana | | 1 | | AFRO | UMIC | | | | | |
| Brazil | 1 | 1 | | AMRO | UMIC | 59% | | 1269 | | |
| Cameroon | | 1 | | AFRO | LMIC | | 52% | | | |
| CAR | 1 | 1 | | AFRO | LIC | | | | | |
| China | 1 | 1 | 1 | WPRO | HIC | | | 210 | | |
| Congo | 1 | 1 | | AFR | LMIC | | | | | |
| DPR Korea | 1 | | 1 | WPRO | LIC | 95% | | | | |
| DR Congo | 1 | 1 | 1 | AFRO | LIC | 42% | | | | |
| Eswatini | | 1 | | AFRO | LMIC | 32% | | 9 | 4500 | 0.20% |
| Ethiopia | 1 | 1 | | AFRO | LIC | 31% | 42% | | | |
| Gabon | 1 | 1 | | AFRO | UMIC | | | | | |
| Guinea | | 1 | | AFRO | LIC | 100% | | | | |
| Guinea B. | | 1 | | AFRO | LIC | 20% | | | | |
| India | 1 | 1 | 1 | SEARO | LMIC | 42% | 39% | 5167 | 1115198 | 0.46% |
| Indonesia | 1 | 1 | 1 | SEARO | LMIC | 4% | | 868 | 1024271 | 0.08% |
| Kazakhstan | | | 1 | EURO | UMIC | | | | | |
| Kenya | 1 | 1 | | AFRO | LMIC | 46% | 78% | 167 | | |
| Kyrgyzstan | | | 1 | EURO | LMIC | | | | | |
| Lesotho | 1 | 1 | | AFR | LMIC | 33% | | 24 | | |
| Liberia | 1 | 1 | | AFRO | LIC | 4% | | | | |
| Malawi | | 1 | | AFR | LIC | 59% | | | | |
| Mongolia | 1 | | 1 | WPRO | LMIC | 8% | | 50 | 56502 | 0.09% |
| Mozambique | 1 | 1 | 1 | AFRO | LIC | 100% | 84% | 337 | 59264 | 0.57% |
| Myanmar | 1 | 1 | 1 | SEARO | LMIC | 15% | | 28 | | |
| Namibia | 1 | 1 | | AFRO | UMIC | 71% | | 30 | 15883 | 0.19% |
| Nepal | | | 1 | SEARO | LMIC | 38% | | | 67227 | |
| Nigeria | 1 | 1 | 1 | AFRO | LMIC | 12% | | 669 | 464720 | 0.14% |
| Pakistan | 1 | | 1 | EMRO | LMIC | 5% | | | | |
| PNG | 1 | | 1 | WPRO | LMIC | 23% | 11% | | | |
| Peru | | | 1 | AMRO | UMIC | 36% | | 207 | 265460 | 0.08% |
| Philippines | 1 | 1 | 1 | WPRO | LMIC | 6% | 49% | 64 | | |
| Rep Moldova | | | 1 | EURO | UMIC | 46% | 27% | 3 | 60005 | 0.00% |
| Russian | | 1 | 1 | EURO | UMIC | 100% | | 10 | 23873 | 0.04% |
| Sierra Leone | 1 | | | AFRO | LIC | | | | | |
| Somalia | | | 1 | AFRO | LIC | 10% | | 0 | 735 | 0.00% |
| South Africa | 1 | 1 | 1 | AFRO | UMIC | 51% | 93% | | | |
| Tajikistan | | | 1 | EURO | | 100% | 93% | 53 | | |
| Thailand | 1 | 1 | | SEARO | UMIC | 84% | | 325 | 507013 | 0.06% |
| Uganda | 1 | 1 | | AFRO | LIC | 34% | 39% | 198 | 150000 | 0.13% |
| Ukraine | | | 1 | EUR | LMIC | 100% | 73% | | | |
| UR Tanzania | 1 | 1 | | AFRO | LMIC | 62% | | 484 | 102469 | 0.47% |
| Uzbekistan | | | 1 | EURO | | 85% | | 53 | 391253 | 0.01% |
| Viet Nam | 1 | | 1 | WPRO | LMIC | 5% | | | | |
| Zambia | 1 | 1 | 1 | AFRO | LMIC | 28% | | 76 | | |
| Zimbabwe | | 1 | 1 | AFR | LMIC | 42% | | | | |
| 9 Case study | 11 Portfolio analysis | | | | | | | | | |

The final list of 20 countries that was provided by TERG after internal processes within the Global Fund had been carried out includes India, Pakistan, Bangladesh,

Philippines Mozambique, DR Congo, Uganda, Lesotho, Zambia, Guinea, Nigeria South Africa, Nepal, Thailand, Azerbaijan, Gabon, Ethiopia, Kazakhstan, Tanzania and Zimbabwe.

Of these 20 countries, the evaluation team carried out portfolio analysis alone in all of them and undertook 9 in-depth country case studies with country visits in 8 countries (South Africa, Nepal, Thailand, Azerbaijan, Gabon, Ethiopia, Tanzania and Zimbabwe) and remote engagement for Kazakhstan.

All 20 countries satisfied the criteria that had been proposed by the evaluation team: high burden/incidence of TB, TB/HIV and or MDRTB with 14 of these countries being high TB burden countries, 15 high TB/HIV burden countries and 13 high MDR TB burden countries. The countries span 5 of the six WHO regions: 12 countries from AFRO (both French and English-speaking countries), 4 from SEARO, 1 from WPRO, 1 from EMRO and 2 from EURO. The Americas were not represented in this evaluation. Five countries are categorized as Low-Income Countries (LIC), 10 as Low Middle-Income Countries (LMIC) and 5 as Upper Middle-Income Countries (UMIC) by the World Bank. Collectively the twenty countries are estimated to carry 61% of global TB burden (6 out of 10 million people estimated to have had TB in 2020), 69% of global TB/ HIV burden (539,000 people with TB/HIV) and 51% of notified MDR-TB. In terms of size of the Global Fund grants, the 9 countries for case study represent US$ 2.5 billion (15%) out of US$16.4 billion signed TB and TB/HIV grants to countries and with the addition of the 11 countries selected for portfolio data analysis, the grant size in these countries rises to 45% of the total Global Fund funding for TB to countries.

## Annex 5: Quality assurance approach

The evaluation team structure and evaluation methodology were designed to ensure that this evaluation meets the highest standards, and provide rigorous, credible, relevant and useful evidence for the benefit of all stakeholders and beneficiaries.
Thus, the evaluation team integrated strong quality assurance mechanisms into the team structure through the dual team leader roles and the backstopping and technical support of quality assurance specialists. Below is a layout of the evaluation team's quality assurance mechanisms that were used during data collection, analysis, and reporting for this evaluation. The evaluation was also carried out under a robust management and risk mitigation procedures, to ensure that quality runs through all processes of the evaluation.

To ensure quality across all activities, this evaluation closely adhered to the OECD-DAC quality standards for development of the evaluation, compliance of deliverables with evaluation standards and ensuring that all comments from stakeholders and partners were appropriately addressed. In line with the technical team's principle of delivering high-quality outputs, a rigorous and comprehensive quality assurance regime was implemented at each stage of data collection, analysis, and reporting. The key measures included:

- Design of the data collection tools was carried out by technical experts.
- The design stage included review and testing by both technical and survey experts to ensure that the data collection tools met all required functionalities and that the data management process works appropriately.
- Data collection tools were standardised across locations and languages to ensure consistency and comparability of results. However, in the qualitative tools flexibility was allowed to ensure that questions were contextually appropriate and that interviewers could focus in on key areas of interest or expertise.
- Setting up the survey using an electronic software with automatic skip patterns and response validation, with configuration performed by an experienced survey manager.
- During data collection, the team implemented a set of quality-assurance procedures to ensure that the data was accurate, timely, complete, and had integrity. This includes monitoring of incoming data and providing feedback where appropriate.
- Data collected from the survey was cleaned thoroughly to prepare it for efficient analysis.
- The evaluation team has extensive experience of implementing the methodology and ensuring that all technical analysis were of the highest quality. This was complemented by additional quality reviews of all technical reports by the QA function and technical experts.
- All deliverables went through a robust quality assurance process, including rounds of review and feedback by the QA leads.

## Annex 6: Global KII performed as of 20th May

| Position | Organization |
|---|---|
| Senior Fund Portfolio Manager of Thailand | The Global Fund |
| Fund Portfolio Manager | |
| Program Officer, Azerbaijan | |
| Disease Advisor, TB/HIV, Technical Advice and Partnerships,SI HIV/TB -TB Preventive Treatment | |
| Senior Specialist - Strategic Delivery Initiative | |
| IPC expert from the US CDC | |
| Senior Program Officer | |
| Head of TB | |
| Public Health and M & E Specialist, Eastern Europe and Central Africa Team (Azerbaijan) | |
| Senior Disease Advisor, TB | |
| Fund Portfolio Manager of Gabon | |
| Specialist, Public Health and M&E, Central African Team | |
| Senior Fund Portfolio Manager for Tanzania | |
| Tuberculosis Advisor, World Health Organization | |
| Regional Manager, EECA | |
| Senior Disease Advisor, Technical Advice and Partnerships | |
| Senior Fund Portfolio Manager, Zimbabwe | |
| Senior Program Officer, Zimbabwe | |
| Senior Disease Advisor, Technical Advice and Partnerships | |
| Specialist, Public Health and M&E, High Impact Africa 1 Department | |
| Senior Program Officer, High Impact Africa 2 Department | |
| Disease Advisor, TB Strategic Initiative, TAP Department, SI TB - Finding Missing People with TB | |
| Senior Fund Portfolio Manager for Kazakhstan | |
| Fund Portfolio Manager for Kazakhstan | |
| Specialist, Public Health and M&E, EECA | |
| Head, High Impact Asia Department | |
| Senior Fund Portfolio Manager, Nepal | |
| Senior Program Officer, Nepal | |
| Senior Specialist, Impact & Evaluation, ME&CAT and Manager, TRP | |
| Specialist, Impact and Evaluation, Monitoring Evaluation & Country Analysis Team | |
| Senior Specialist, Public Health Monitoring & Evaluation, High Impact Asia Department | |
| Regional Advisor for TB/HIV/STI/Hepatitis SEARO, WHO | WHO |
| Medical Officer at WHO (TB Focal Poiint) | |
| Medical Officer, SEARO World Health Organization | |
| Unit Head, Prevention, Care and Innovation, Global TB Programme, World Health Organization · World Health Organization | |
| Team Lead, Prevention, Research and Innovations, WHO/GTB | |
| Medical Officer, TB/HIV and Community Engagement Unit, Global TB Programme of the World Health Organization. | |
| Regional Advisor for TB/HIV/STI/Hepatitis SEARO, WHO | |
| Medical Officer at WHO (TB Focal Point) | |
| Medical Officer, SEARO World Health Organization | |

| | |
|---|---|
| Coordinator of The End TB and Leprosy Elimination unit for the WHO, WPRO | |
| WPRO, WHO | |
| WPRO, WHO | |
| WPRO, WHO | |
| TB diagnostics and Infection prevention and control, EURO Regional office, WHO | |
| TB Team Leader, Joint Tuberculosis, HIV/AIDS & Hepatitis Programme (JTH) EURO, WHO | |
| WHO EURO TPT Focal point and surveillance, monitoring and evaluation of TB programmes, R&R, digital Health. | |
| Regional Advisor, TB EMRO, WHO | |
| Medical Officer (Tuberculosis) EMRO, WHO | |
| Deputy Executive Director | Stop TB Partnership |
| Regional Advisor, Asia and the Pacific at Stop TB | |
| Chief, Global Drug Facility at Stop TB atUNOPS | |
| Prinicpal Investigator (USAID) THE ROLE OF NEW PUBLIC DIPLOMACY IN GLOBAL TUBERCULOSIS CONTROL | USAID |
| Senior Technical Advisor/ TB/HIV, Prevention, and M&E Team Lead at USAID/GH/TB | |
| Technical Advisor /Medical Officer, Tuberculosis Division/Infectious Disease Office, Global Health Bureau | |
| Branch Chief, Global TB Branch - CENTERS FOR DISEASE CONTROL AND PREVENTION, (CDC) | CDC |
| TB Program Manager, South Africa, (CHAI), Program Manager, TB Access · Clinton Health Access Initiative, Inc. | CHAI |
| Associate Director, Global Tuberculosis Team, Infectious Diseases, Research, & Laboratories Division · Clinton Health Access Initiative | |
| Global TB Technical Director at PATH. | PATH |
| MD PhD,Head of Emerging Bacterial Pathogens Unit, WHO collaborating Centre and TB Supranational Reference laboratory, | San Raffaele Institute, Milan |
| Senior Project Manager WP5 EU - PEARL, Responsible of WHO Collaborating Centre and PI TB REACH Wave 6 presso | |
| DIRECTOR, HEALTH, Palladium | TRP Chair |
| Medical Officer (TB, HIV) · Medical Officer (Global Health, Infectious Diseases Specialist) · Medical Officer (HIV/AIDS, TB/HIV Specialist). Technical Adviser (Infectious Disease Control and Laboratory Services: AMR, TB and HIV) | JICA |
| President of the Union | The Union |
| DMCH, MPH Director of the Department of Tuberculosis and HIV. | The Union |
| Executive Director/ KNCV Country Representative for KNCV and Challenge TB Country Director Nigeria. | KNCV |

## Annex 7: WHO recommendations on TPT and IPC

### WHO Recommendations for TB preventive therapy

**A: People who should be provided with TPT even when testing for TB infection is not available and after exclusion of active tuberculosis:**

i) People living with HIV of all ages (infants under 12 months, children over 12 months, adolescents and adults including those who are pregnant)
ii) Children of age 5 and below who are household contacts of people with TB.

**B: People who should be routinely tested for TB infection and provided with TPT after active TB has been excluded:**

i) People beginning treatment with anti-TNF.
ii) People undergoing dialysis.
iii) People preparing for solid organ or hematological transplantation.

**C: People who may be tested for TB infection and provided with TPT after active TB has been excluded:**

i) People over the age of 5, including children, adolescents and adults who are HH contacts people with TB.
ii) People at risk or vulnerable to develop active TB following TB infection: prisoners, health care workers, immigrant from countries with a high prevalence of TB, the homeless and those who use drugs.

**D: Population groups in whom TPT is not recommended**

i) Diabetes mellitus.
ii) Harmful users of alcohol.
iii) Tobacco smokers.
iv) People who are underweight.

**E: The recommendations for TB screening to exclude TB** prior to initiation of TPT include symptom screening (cough, fever, night sweating, loss of weight or failure to gain weight) and or a chest x-ray.

**F: Testing for TB infection** may be carried out using the tuberculin skin test, antigen-based skin test (which is a new recommendation) or interferon gamma release assay (IGRA).

G: **Regimens for TB preventive therapy**: National TB control programs, clinicians and individuals may choose any of the following regimens for the treatment of TB infection: 6-9H, 3HP, 3RH, 4R and 1HP. In settings of high TB transmission, adolescents and adults living with HIV may be treated for TB infection using 36H. Contacts of persons with multi – drug resistant TB may be treated with 6Lfx to prevent MDRTB.

### WHO Recommendations for TB IPC

For TB infection transmission prevention and control (IPC), the latest WHO guidelines[43] came out in 2019. These guidelines advise that IPC interventions should include administrative, environmental, and respiratory protection measures and the associated core components which should be developed and implemented as an integrated package of IPC interventions. Additionally, the guidelines advocate for building an integrated well-coordinated, multi-sectoral actions that go beyond TB IPC

[43] WHO guidelines on tuberculosis infection prevention and control, 2019 update, Geneva: World Health Organization; 2019. License: CC BY-NC-SA 3.0 IGO.

alone and are part of the effort to build resilient systems for health service delivery, prevention of Health care Associated Infections (HAI) and control of Anti-Microbial Resistance (AMR). The recommendations for TB -IPC include:

**A: Administrative controls** which include triaging of people with TB symptoms and signs, respiratory separation and isolation of people with presumed or demonstrated infectious TB, prompt initiation of effective TB treatment for people identified to have TB and respiratory hygiene including cough etiquette.
**B: Environmental controls** which include upper room germicidal ultra-violet systems and ventilation systems (natural, mixed mode, mechanical, and air recirculation through high efficiency particulate air filters) in health care settings with high risk of TB transmission.
**C: Respiratory protection** which involves the use of particulate respirators
These measures should be implemented under core components which include: a) the presence of a dedicated IPC program at national and health facility level, guided by national and health facility IPC guidelines, and with training and education of health care staff; b) Health care infection surveillance; c) multi-modal strategies for implementing infection prevention and control at facility and national level; d) monitoring and audit of IPC practices and feedback; e) ensuring workload, staffing and bed occupancy norms at health facility level are adhered to; and f) building a health care environment, with materials and equipment that ensures care is provided in a clean and hygienic environment.

In line with the Grading of Recommendations, Assessment Development and Evaluations (GRADE) approach which has been adopted by WHO for the development of global policies, the use of the words “should” and “may” in these recommendations is important. A recommendation in which the word “should” is used denotes a strong recommendation implying that most people with the condition would want the recommended course of action and would request a discussion if the action is not offered. The recommendation can be adopted as policy in most situations. The use of the word “may” on the other hand denotes a conditional recommendation, implying that many people with the condition can choose not to have the recommended action, clinical judgement needs to be balanced with values and preferences of the affected individual and substantial debate is required at the policy making level among stakeholders.

## Annex 8: TB prevention data by source in 2020 and coverage in 9 countries case study

| | TPT among HH <5 | | | TPT among PLH | | | TPT HH >5 | | TB among Health staff | |
|---|---|---|---|---|---|---|---|---|---|---|
| | WHO | GF | NTP | WHO | GF | NTP | WH | NTP | WH | NTP |
| Az | 291 | NA | 291 | NA | NA | NA | NA | 4,114 | NA | NA |
| Eth | 8,771 | NA | NA | 10,723 | NA | 12,913 | NA | 8,769 | NA | NA |
| Gab | NA | NA | NA | 677 | NA | NA | NA | NA | NA | NA |
| Kaz | 997 | NA | NA | 1,209 | NA | NA | NA | NA | 5 | NA |
| Nep | 1,995 | 2,105 | 1,995 | NA | - | NA | NA | NA | NA | NA |
| SA | 15,392 | 7,190 | NA | 356,872 | 193,279 | NA | NA | NA | NA | NA |
| Thai | 6,501 | NA | NA | NA | 410 | NA | NA | 5,434 | 325 | NA |
| Tanz | NA | NA | 12,986 | NA | 1,265,268 | 411,084 | NA | NA | NA | 485 |
| Zim | 1,808 | 1,703 | 519 | 156,512 | NA | 156,512 | NA | NA | 388 | 329 |

| country | year | Stop TB P.UNHLM target | | | NTP coverage | | | GF coverage | |
|---|---|---|---|---|---|---|---|---|---|
| | | PLHIV target | < 5 target | >5 target | PLHIV Cov NTP | <5 Cov NTP | > 5 Cov NTP | PLHIV Cov GF | <5 Cov GF |
| Azerbaijan | 2018 | 742 | 254 | 3 835 | NA | 100% | 119% | NA | NA |
| | 2019 | 1 151 | 432 | 3 886 | NA | 100% | 146% | NA | NA |
| | 2020 | 1 529 | 602 | 3 903 | NA | 48% | 105% | NA | NA |
| Ethiopia | 2018 | 25 158 | 6 470 | 7 932 | 0% | 99% | 0% | NA | NA |
| | 2019 | 30 854 | 15 150 | 14 526 | 0% | 46% | 0% | NA | NA |
| | 2020 | 31 933 | 22 760 | 31 916 | 40% | 0% | 27% | NA | NA |
| Gabon | 2018 | 1 653 | 331 | 402 | NA | NA | NA | NA | NA |
| | 2019 | 2 018 | 754 | 716 | NA | NA | NA | NA | NA |
| | 2020 | 2 082 | 1 480 | 2 050 | NA | NA | NA | NA | NA |
| Kazakhstan | 2018 | 1 954 | 700 | 1 569 | NA | NA | NA | NA | NA |
| | 2019 | 1 052 | 1 310 | 2 372 | NA | NA | NA | NA | NA |
| | 2020 | 1 152 | 1 930 | 5 171 | NA | NA | NA | NA | NA |
| Nepal | 2018 | 2 026 | 1 650 | 2 885 | 100% | 37% | NA | 9% | 113% |
| | 2019 | 1 029 | 3 490 | 4 780 | 0% | 69% | NA | 0% | 66% |
| | 2020 | 1 037 | 5 700 | 11 405 | 0% | 35% | NA | 0% | 37% |
| South Africa | 2018 | 453 149 | 25 360 | 21 831 | 100% | 100% | NA | 0% | 0% |
| | 2019 | 367 294 | 36 420 | 36 091 | 140% | 62% | NA | 35% | 14% |
| | 2020 | 421 583 | 43 950 | 76 152 | 0% | 0% | NA | 46% | 16% |
| Thailand | 2018 | 14 651 | 6 090 | 7 890 | 37% | 8% | 2% | 0% | 0% |
| | 2019 | 16 919 | 13 780 | 13 959 | 33% | 33% | 40% | 1% | NA |
| | 2020 | 15 219 | 20 540 | 30 429 | 35% | 32% | 18% | 3% | NA |
| Tanzania | 2018 | 291 813 | 5 440 | 5 895 | 102% | 87% | NA | 100% | NA |
| | 2019 | 77 924 | 14 370 | 12 171 | 750% | 54% | NA | 742% | NA |
| | 2020 | 88 237 | 26 770 | 33 149 | 466% | 49% | NA | 1434% | NA |
| Zimbabwe | 2018 | 55 969 | 1 970 | 2 036 | 130% | 19% | NA | 0% | 98% |
| | 2019 | 71 664 | 3 430 | 3 101 | 147% | 14% | NA | 0% | 76% |
| | 2020 | 79 567 | 4 920 | 6 776 | 197% | 11% | NA | 0% | 35% |