

TB REACH Wave 10
Technical Brief on Theme and Focus Areas
*Innovations in Integrated Service Delivery and
Tuberculosis Preventive Treatment Expansion
to Strengthen Health Systems*

Tuberculosis (TB) remains one of the leading causes of death globally. The COVID-19 pandemic has set back the global TB response by more than a decade. The pandemic has led to unprecedented disruptions in health care services and many people with TB have remained undiagnosed, untreated, and have had challenges accessing care. Many people with TB also have other comorbidities and addressing multiple conditions can increase effectiveness and efficiency for both the person seeking care and the health system. To regain the momentum towards meeting the global targets to end TB, innovative approaches are needed to (1) find the people with TB who are missed and ensure they receive proper diagnosis and care and to (2) increase efforts to prevent TB through the expanding access to and provision of TB preventive treatment (TPT).

For TB REACH's Wave 10 funding round the overarching theme is *health systems strengthening (HSS)* and applications can be submitted under the following two focus areas*:

- **Integrated Service Delivery (ISD)**
- **Expansion of TB Preventive Treatment (TPT)**

Applicants can submit an application that **combines both ISD and the provision of TPT.*

For either of these focus areas, proposals overall should aim to

- improve detection or treatment of TB disease *OR* TB infection
- be innovative
- contribute to health systems strengthening (HSS), and
- achieve sustainability beyond the lifecycle of the grant.

All proposed projects will need to describe how their interventions can contribute to HSS (see section below and [Wave 10 Logic Model Framework](#) document for more information).

To help ensure sustainability of successful projects, applicants are expected to engage with different government structures and departments, the Global Fund country coordinating mechanism (CCM), and other donors and partners throughout the grant period.

This document further includes details and technical considerations for the Wave 10 theme and focus areas.

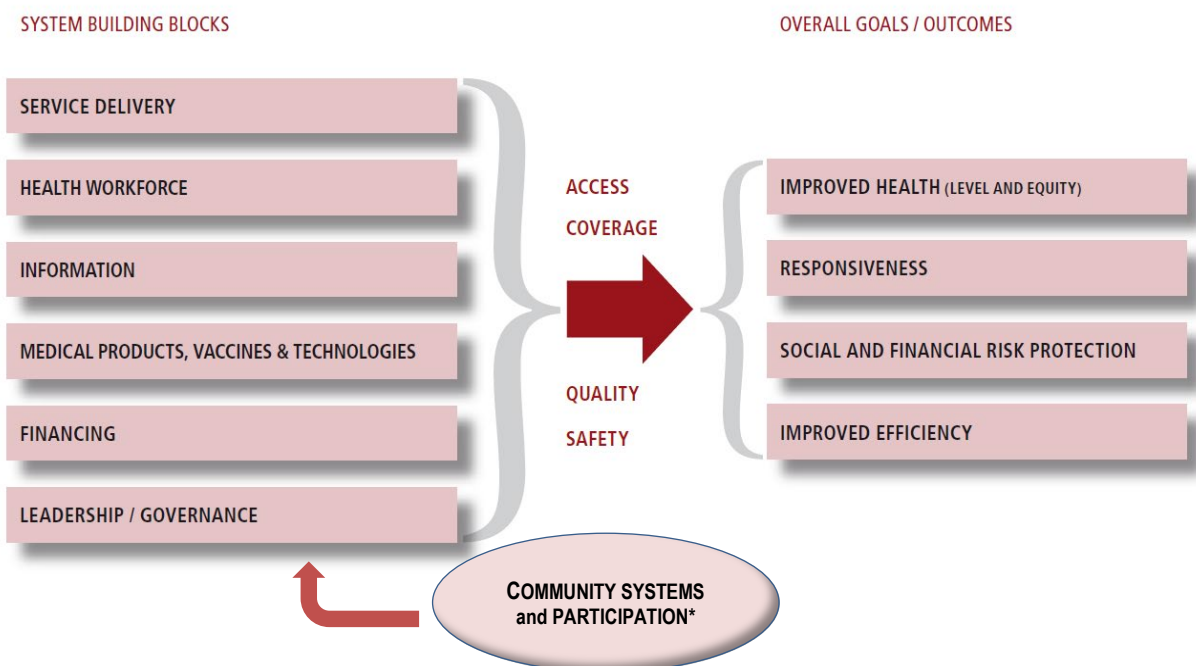
**Wave 10 Overarching Theme
Health Systems Strengthening**

A country's health system is comprised of organizations, human and financial resources, and activities focused on promoting and sustaining health. Health Systems Strengthening (HSS) refers to strategies and activities designed to improve the performance of a health system. Strong, resilient health systems are critical for achieving Universal Health Coverage (UHC) and Global Health Security (GHS). UHC includes ensuring that all people have access to quality health services without suffering from financial hardship. GHS focuses on preparing, preventing, detecting, and responding to existing, emerging, or new public health threats. Routine surveillance, health information, laboratory, and procurement and supply chain management are all necessary activities for GHS.

In the World Health Organization's (WHO's) framework, the overall goals for HSS are to improve health and health equity, responsiveness, social and financial risk protection, and efficiency. The overall goals are achieved through the intermediates goals of improving access and coverage of effective health interventions and safe, quality care. Strengthening health systems can be complex, but progress to HSS goals can be made by focusing on the six operational “building blocks” that are essential for a functioning and effective health system. The building blocks include: 1) leadership, governance, and accountability; 2) health and financing; 3) access to essential medicines and supplies; 4) health information systems; 5) health workforce; and 6) service delivery. Community systems and participation are also essential for an effective health system and thus have been included as an additional health system component (Figure 1). The building blocks are interlinked and can interact with each other. These building blocks can be used to help identify and understand health system facilitators and barriers to design your TB REACH interventions and for achieving the HSS goals.(1,2)

Figure 1: [WHO Health System Framework adapted* from FCDO Position Paper: Health Systems Strengthening for Global Health Security and Universal Health Coverage\(1,2\)](#)

THE WHO HEALTH SYSTEM FRAMEWORK



*Community systems and participation is added as a component in the WHO model adapted by FCDO to underscore the essential role they play in HSS

For Wave 10, applicants will need to describe how their projects contribute to HSS goals using the building blocks framework. It is not expected that TB REACH projects will be able to impact/change all HSS building blocks, however applicants will need to describe which building blocks their intervention activities aim to impact and how. A [Wave 10 Logic Model Framework](#) that includes components of the WHO HSS framework is described in the document. It is intended to help applicants develop their interventions and understand how they will be evaluated if their proposal is awarded.

Partner Engagement for HSS and Sustainability

Wave 10 applicants should aim for sustainability if their projects are successful.

This requires early and continued engagement of local and international partners and donors. Applicants will need to briefly describe their engagement plans with the National TB Program (NTP) and other relevant Ministry of Health (MOH) units and programs. Engagement with government entities is important to ensure that projects are contributing to country health system and are not seen as a parallel effort. Early and continued engagement with the MOHs, NTPs, and other governmental programs/organizations throughout the lifecycle of the project is important for promoting the uptake of successful interventions.

Applicants are also expected to actively engage with other implementing partners, the Global Fund CCM, and other funding agencies to build awareness of their approaches.

The linkage to and involvement of the CCM will help ensure that the TB REACH projects are based on need, complement existing Global Fund-supported interventions, and are considered for scale-up if proven to be impactful. Participation in country dialogues, National Strategic Plan (NSP) development and national policy meetings is also encouraged. For more information refer to the [Wave 10 Application Information Document](#).

Wave 10 Application Focus Area

A. Integrated Service Delivery

Integrated service delivery (ISD), combines multiple interrelated healthcare services, allows for the offering of people-centered care, and the maximization of resources to increase efficiencies in the health system. ISD can contribute to HSS, help progress towards UHC, and is compatible with the global move towards *One Health*, a multidisciplinary approach to improve GHS through collaborative, multisectoral, and transdisciplinary initiatives to combat diseases.

While TB and human immunodeficiency virus (HIV) programs have been supported to integrate for over a decade, and WHO guidance has been issued on TB and diabetes, there are many more opportunities for improving TB care with other health and service programs. A recent systematic review provides a framework for integration of TB and non-communicable diseases (NCDs) services in low- and middle-income countries (LMICs) and suggests integration has the potential to improve health service delivery.(3) Another recent systematic review on integration of HIV services with other health services including TB found that ISD strategies can lead to improved health and health system outcomes.(4)

ISD models and approaches have the potential to accelerate the finding of missing persons with TB (both pulmonary and extrapulmonary TB) while simultaneously addressing other health conditions or diseases that may contribute to TB morbidity (i.e., HIV, diabetes, malnutrition, cancer, and COVID-19). ISD can also integrate TB with other health conditions or non-medical services (i.e., financial, social, or mental health support) that do not necessarily contribute to TB incidence but are common concerns for persons affected by TB disease and can impact treatment outcomes.

Joint delivery of services can increase health coverage and reduce costs, while promoting person centered care. For persons seeking and receiving health care, ISD can potentially improve their experience by being more convenient, removing access barriers, saving time and costs by allowing for access to multiple services at once and improving continuity of care and coordination of treatments for multiple health conditions. From a program perspective, integration could potentially maximize resources and processes.

However, it is important to note that ISD may come with risks if not carefully planned and implemented. Joint delivery of health services may lead to inadequate care due to the loss of specialization and the overburdening of health care workers if they are asked to take on additional duties without additional support. (5–8)

Considerations for ISD Proposals

Wave 10, applicants are encouraged to propose innovative approaches that integrate TB care and services with other health areas based on country context, feasibility, and local epidemiology.

Integration efforts should aim to improve TB case detection and/or treatment outcomes while maximizing resources and providing health service users convenient, safe, and quality care.

Interventions that combine multiple disease areas to maximize convenience to persons seeking care are highly encouraged. Innovations in screening, diagnosis, or treatment approaches (i.e., artificial intelligence (AI), specimen pooling, new treatment regimens, and digital treatment support) are also encouraged.

Organizations applying for TB REACH funds can propose different models of ISD to improve TB case detection

or treatment outcomes and contribute to health systems strengthening. There are multiple services that can be integrated with TB and multiple ways that ISD can be envisioned.

TB services can be integrated with existing programs focusing on other health services targeting other diseases or conditions; or vice versa, other health services can be integrated with existing TB services.

For example, TB services can be integrated with other activities such as COVID-19 screening, testing, or contact tracing; lung cancer and other lung ailments screening; maternal and child health programs, immunization campaigns, diabetes, and other NCDs.

Services can be at different levels of integration (screening, testing, and/or treatment) and can be either in *private or public sector facilities or community-based programs*.

ISD interventions can also be combined with *active case finding (ACF)* activities such as the use of mobile vans and ultraportable x-ray units, spirometers, pulse oximeters, and other portable tools to bring health care access to communities and key populations.

Below are some brief examples of what and how to integrate TB with other services; this list is by far not exhaustive, and applicants are encouraged to propose additional ideas which might include vaccination, smoking cessation, antimicrobial resistance or any other area that can be addressed. References at the end of this document further describe the link between TB and other health conditions and lessons learned from other ISD projects.

Examples of ISD integration Opportunities

COVID-19

While many resources have been diverted to address COVID-19, there are opportunities to leverage the pandemic response to simultaneously address TB and COVID-19. Both infectious diseases share some similarities such as airborne transmission, common symptoms (fever and cough), shared social risk factors (e.g., crowding), and co-morbidities (diabetes, immune-compromising conditions, chronic lung conditions, and under and malnutrition) that can increase chances of infection and disease complications. (9) Moreover, persons with TB who are co-infected with SARS-CoV-2 are at an increased risk for death from COVID-19 compared to those without TB. Persons with (latent) TB infection co-infected with SARS-CoV-2 may also be at an increased risk for progressing to TB disease due to lung damage, a weakened immune system, and if any corticosteroids were used in the treatment of COVID-19. Additionally, control efforts for both diseases are similar and include contact tracing and infection control (masking, ventilation, and air filtration).(10–13)

Simultaneous (bi-directional) integrated testing for both TB and COVID-19 at the community or primary health care level can optimize the use of resources and tackle both diseases at the same time. People with a cough and fever should be tested for both TB and COVID-19, using laboratory tests and imaging techniques. Because of COVID-19, many countries have scaled-up their molecular-testing capacity using multiplex testing platforms, this scale-up can also be leveraged for TB testing. (14–17) This approach has been implemented in a few countries including India, Indonesia, Nigeria, Pakistan, Peru, and South Africa, Peru. (14,15,18) One project in India is evaluating the use of rapid, onsite molecular testing for persons who have signs and symptoms of TB but have tested negative for SARS-CoV-2 on rapid antigen tests (RAT). (15) Another project in India, the Joint Effort for Elimination of Tuberculosis (JEET), is working to sensitize private sector health care providers to simultaneously test patients for TB and COVID-19. While these projects are ongoing, there is still much to learn about this feasibility and effectiveness of this approach.(13,15) Stop TB Partnership, in conjunction with USAID, and the Global Fund have issued separate guidance documents on implementing integrated COVID-19 and TB testing.(16,17)

TB and Non-Communicable Diseases

With aging populations, LMICs are seeing an increase in the prevalence of NCDs. Annually, 41 million people die from NCDs with 85% of these deaths occurring in LMICs. NCDs are chronic diseases that can last a year or more, limit activities, and often require ongoing medical attention. Common NCDs include diabetes mellitus (DM); cardiovascular disease (CVD); mental health illnesses (MHI), lung ailments (further described below).(4,19)

NCDs can be risk factors for progressing to TB disease and may impact treatment and management of TB. TB can also serve as a risk factor for some NCDs and complicate the treatment and management of other conditions.(4) For some NCDs, such as DM, the link between TB is well-established. About 15% of TB cases may be linked to DM. DM can increase the risk of progressing to TB disease and has implications for the management and treatment of TB. Moreover, TB can also increase risk of DM as it may impair glucose tolerance. Several examples of TB and diabetes integration already exist and the WHO and the International Union Against Tuberculosis and Lung Disease have developed a collaborative framework which can guide ISD activities to address both conditions synergistically and simultaneously.(20–22) Because of the current existence of multiple TB and diabetes integration programs, applicants submitting proposals solely on TB and diabetes must demonstrate that their proposed interventions are innovative and based on need or they should seriously consider including additional health conditions in their proposal for integration.

Many NCDs share common social and behavioral risk factors with TB, including smoking, alcohol, and other drug use. Smoking has been established to be associated with TB infection and disease and can affect treatment. (23) Alcohol and drug use can impact the immune system, delay sputum conversion, and make adherence to treatment challenging. (24) MHIs are also particularly important to address during TB treatment. TB treatment can be more challenging for those suffering MHI or substance abuse and can also contribute to these conditions as well due to the social and financial stresses that often result from the long course of treatment, particularly for drug-resistant TB (DR-TB).(4)

Tackling TB and NCDs together presents an opportunity to provide better people-centered care through integrated case-detection activities, linkages to care, and better clinical management.

Lung Cancer and Other Chronic Respiratory Diseases and the use of Artificial Intelligence

Lung cancers and chronic respiratory diseases (CRDs), similar to TB, primarily affect the lungs and airways. TB is associated with CRD in adults. It has been established that along with cigarette smoking, silica dust exposure increases the risk of developing both CRDs and TB disease. Conversely TB may also increase the chances of developing CRD, in particular bronchiectasis and chronic obstructive pulmonary disease (COPD).(25,26)

Lung cancer is the leading cause of all cancer deaths worldwide, contributing to 18% of all cancer deaths in 2020. Early diagnosis and treatment of lung cancer can improve outcomes while delayed diagnosis can result in poorer survival. However, lung cancer is often asymptomatic until later stages and can be difficult to diagnosis in the presence of other co-existing respiratory diseases. In LMICs there are gaps in screening and detection due to lack of resources and technical capacity.(26)

Chest x-rays (CXRs) are being increasingly used as an initial screening tool for TB given their high sensitivity. But the CXR is an incredibly useful tool to identify other lung conditions as part of an integrated screening processes. Furthermore, using AI to read CXR provides an opportunity to screen for multiple lung conditions such as TB, lung cancer, and other lung diseases in areas where human readers might not be available or could take a long time to provide a thorough reading. Additionally, AI tools can scan large numbers of images

in a short time. Primary care clinics conducting routine health screenings or mobile vans conducting ACF can leverage AI-CXR to screen for additional lung conditions.(27)

HIV

The links between HIV and TB and examples of TB/HIV ISD activities are well-documented. Lessons from these efforts can be applied to other opportunities for ISD. For persons with the co-morbidity, efforts include improving TB diagnosis and treatment among people living with HIV (PLHIV) and vice versa with the aims to improve clinical outcomes. ISD also provides an opportunity to prevent TB among PLHIV through the provision of TPT. **However, because of the existence of other funding for TB/HIV collaborative programs, projects proposing TB/HIV integration would have to provide justification that their proposed intervention fulfills an unmet need and is innovative compared to existing programs.(28,29)**

Family and Community-Centered Strategies to Find Pediatric TB and Other Childhood Illnesses

Pediatric TB remains to be a major problem. According to the WHO 2021 Global TB Report, 1.2 million children fall ill with TB in 2020, and TB deaths have increased for the first time in over a decade to 700 children every day. Only 44% of children estimated to have TB were detected in 2020.(9) There are multiple opportunities along a child's pathway that can be targeted to identify missing children with TB and other childhood illnesses. Maternal and child health clinics, immunization programs, antenatal and postnatal care, growth monitoring and nutrition programs, and other family and community-centered programs can provide opportunities to find and treat both children and mothers with TB along with contact tracing and TB prevention for their family members.(30)

Nutrition and Social Protection Programs

The association between TB and under and malnutrition is well documented. Undernutrition weakens immunity and increases the likelihood of latent TB infection progressing to active TB disease. An estimated 2.2 million TB cases globally are attributed to undernutrition. TB can also worsen malnutrition as it can affect protein metabolism and a person's nutritional status through multiple mechanisms. Persons with TB often have a lower body mass index (BMI) and can develop wasting which is associated with severe disease and increased mortality. The nutrition status of persons-affected by TB can improve while on TB treatment; however adequate nutritional intake is also important during treatment for improved treatment outcomes.(9,31)

Persons with TB should receive a nutritional assessment of their nutritional status, and appropriate counselling throughout treatment. While undernutrition is recognized as an important risk factor, supplementary feeding programs delivered by TB programs are often expensive and difficult to implement. Multisectoral opportunities for collaboration and coordination of nutritional programs through other existing health programs, such as MCH, immunizations, HIV, and social protection programs may optimize efficiencies and resources.(32)

Wave 10 Application Focus Area

B. Expansion of TB Prevention Treatment(TPT)

A quarter of the world's population is estimated to have TB infection and is at risk for developing TB disease. Although some progress has been made towards scaling up access to TPT; efforts need to be accelerated in order to achieve the ambitious 2018 UN high-level meeting targets of reaching at least 30 million people with TPT including 24 million contacts of people with active TB and 6 million PLHIV. Specifically, progress among children under five years of age and household contacts (five years and above) are among the poorest performing indicators with 29% and 1.6% of the 2022 target being met according to the latest WHO Global TB Report. Offering TPT to people at highest risk for infection and for developing TB disease will protect them from becoming sick; reduce the risk of continued TB transmission in the community; and is a critical part of the Global Plan to End TB.(9,33,34).

To help accelerate these efforts, Wave 10 applicants should propose innovative solutions that can be implemented and sustained to improve the identification, testing, and treatment of individuals at high risk for infection and development of TB disease. Interventions can be facility-based (private or public) or community-based. Proposals using innovative approaches to overcome barriers to scale-up, newer diagnostic tools, or shorter treatment regimens are encouraged.

Step 1: Target Populations and Settings

The TPT proposals should describe the population or setting for their intervention. Interventions should focus on the identification, testing, and treatment of individuals at high risk for infection and development of TB disease. Because there are other global initiatives to expand TPT among PLHIV, proposals for TB REACH Wave 10 should focus mainly/solely on providing TPT to children under the age of five, household contacts, or other groups who are exposed, infected and high risk for progression to TB disease. The following criteria can be used to determine target populations for TB REACH TPT proposals (35):

- Persons at high risk for progressing to TB disease
- Persons at high risk for TB infection
- High transmission settings (high incidence of TB disease compared to the general population)

Persons at a High Risk for Progressing to TB Disease

Persons with immune-compromising conditions

Other than PLHIV, other people at high risk for progressing to TB diseases include those who have silicosis, are on anti-tumor necrosis factor (TNF) treatment, are receiving dialysis, and those who are preparing for an organ or hematologic transplant. TB REACH applicants can propose a systematic approach to identifying and treating these and other immune-compromised populations at risk for TB in public or private clinics.

Children aged < 5 years

Children aged < 5 years who are contacts of people with TB disease have a higher risk for rapidly progressing to TB disease if they are infected. Children < two years of age are also at a high risk for morbidity and mortality from severe and disseminated forms of TB. Therefore, TPT should be initiated once TB disease is ruled out even in the absence of a TB infection test. Proposals targeting children, for example, can focus on household contact investigations, integration with maternal and child health services, or other community-based interventions.

Persons at High Risk for TB Infection

Household Contacts

Household contacts of person with TB are considered a high-risk group for TB infection and TB disease compared to the general population. Systematic reviews suggest that the prevalence of TB disease among household contacts in LMICs ranges from 3% to 5%. Screening of household contacts for TB disease has shown to be a high yield and cost-effective ACF strategy.(36–39). Contact investigations and treatment of all eligible household contacts, including children ≥5 years, adolescents, and adults, can be beneficial for family members by preventing the development of TB disease and further reducing future transmission of the disease. Applicants planning to target household contacts should describe their systematic approach to conducting contact investigations and ensure that TB treatment and TPT are provided to those eligible.

Other Populations at High Risk for Infection

Other persons who are at high risk for infection include those who live or work in congregate or crowded settings, such as prisons; health workers; recent immigrants and refugees from countries with a high TB burden, homeless people; and people who use drugs. Systematic testing of these populations may be considered based on the country context and local epidemiology.

High Transmission Settings

Active Case Finding in High Incidence Populations and Settings

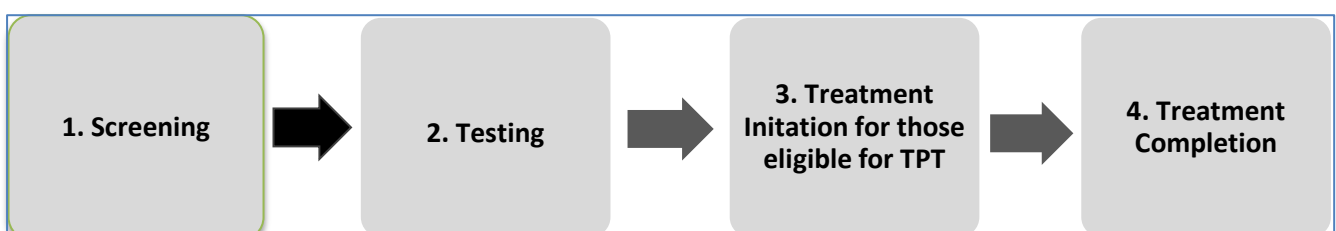
TB REACH applicants can propose the integration of TPT with community based ACF among populations and settings with high incidence (hotspots) based on epidemiology. This approach can increase coverage while maximizing resources and has the potential to drive down community transmission. (40–42) Applicants planning on submitting an ACF proposal that includes TPT with the screening of other health conditions can apply under the category of *ISD with TPT* in the application.

Step 2: TB Infection Cascade of Care

After selecting the intervention target population, Wave 10 TPT proposals should describe approaches and entry points for the TPT cascade, e.g., how individuals in the target population will be screened, those at high-risk identified, tested for infection if applicable, and excluded for active TB. Applicants should also describe plans for recording and reporting data along the care cascade.

Several systematic reviews and meta-analyses have been conducted on TB infection testing and treatment programs and all have pointed to the wide ranging, and historically suboptimal testing, treatment initiation and completion rates. (43–46) Understanding where losses are occurring along the cascade can help identify challenges and potential solutions to improve interventions. Applicants should describe how their interventions intend to improve points along the care cascade to ultimately improve numbers of people completing treatment (Figure 2). For management of persons with TB infection and data collection for monitoring and evaluation purposes, several existing case finding or contact tracing apps exist, including WHO’s [Prevent TB app](#).

*Figure 2 TB Infection Cascade of Care**



**The TB Infection Cascade of Care can be adapted or modified to include more detailed steps based on the intervention and the target population*

Below are some considerations for the testing and treatment initiation and completion components of the cascade.

TB Infection Testing

Tests for TB infection are not required before starting TPT for high-priority groups such as PLHIV and household contacts <5 years of age. However, tests are recommended for people from other at-risk populations to identify those who would benefit from TPT and to avoid unnecessary treatment. WHO currently recommends a tuberculin skin test (TST) or an interferon- γ release assay (IGRA) (blood test) to test for TB infection.(35)

The tests for infection are not a gold standard method for diagnosing TB infection.

Currently available TB infection tests measure immune response to *M. tuberculosis* but cannot confirm or exclude the presence of bacteria or determine who with infection is most likely to progress to TB disease. Moreover, negative test results do not rule-out TB infection. Additionally, there have been operational challenges for implementing TB infection tests in high burden countries, which affect their feasibility. These include the need for training health care workers to place and read the TST, and the need to follow-up with persons to have their indurations interpreted. Challenges with the IGRAs have included the high costs and the need for laboratory capacity. New simpler tests are coming down the pipeline and could facilitate the scale-up of testing for TB. TB REACH encourages proposals that address barriers to testing. Proposals can include currently available tests or propose evaluating the performance and implementation of newer skin or blood tests that show promise.(47)

TPT Initiation and Completion

TPT should be considered after active TB disease is ruled out by a risk assessment and clinical evaluation. Below are currently available recommendations and options for the treatment of TB infection regardless of HIV status ([refer to WHO Guidelines on TPT](#) for more information on regimens):

- 6H or 9H, 6 or 9 months of daily isoniazid
- 3HP, 3-month regimen of weekly rifapentine plus isoniazid
- 3HR, a 3-month regimen of daily isoniazid plus rifampicin
- 1HP, a 1-month regimen of daily rifapentine plus isoniazid
- 4R, 4 months of daily rifampicin

While there are numerous regimens approved, availability of the drugs for many of the regimens has been extremely limited and applicants should ensure they will have access to procure proposed regimens. In settings with high TB transmission, adults and adolescents living with HIV who have an unknown or a positive LTBI test and excluded for active TB disease should receive at least 36 months of daily isoniazid preventive therapy (IPT). While evidence is still limited MDR TB contacts may be given alternative TPT regimens.(35)

Wave 10 applicants should provide information on which treatment regimens will be used and how adverse events will be managed, and how treatment will be supported to ensure completion.

Programs designed to address TB infection have often had low uptake in TPT initiation and low treatment completion rates. Low uptake and completion of TPT can be due to many factors.

Often both health care providers and community members may not understand the benefits of TPT, particularly since person with TB infection do not feel sick or exhibit symptoms. Shorter treatment regimens have been associated with higher treatment completion rates.(46,48)

Applicants will need to describe how they plan to improve treatment initiation, adherence, and completion for their target populations. Applicants should also describe how they will manage adverse reactions related to TPT regimens. Proposals using shorter TPT regimens will be encouraged as part of the TB REACH focus on driving innovation.

C. TB REACH Proposals Combining *ISD with TPT*.

Proposals that focus on *ISD* with the inclusion of the provision of TPT are encouraged. In the application, applicants will be asked to respond to questions that describe both their model of *ISD* and how their intervention aims to improve points along the TPT care cascade.

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