

TB REACH Wave 6 **Treatment of TB Infection**

Background

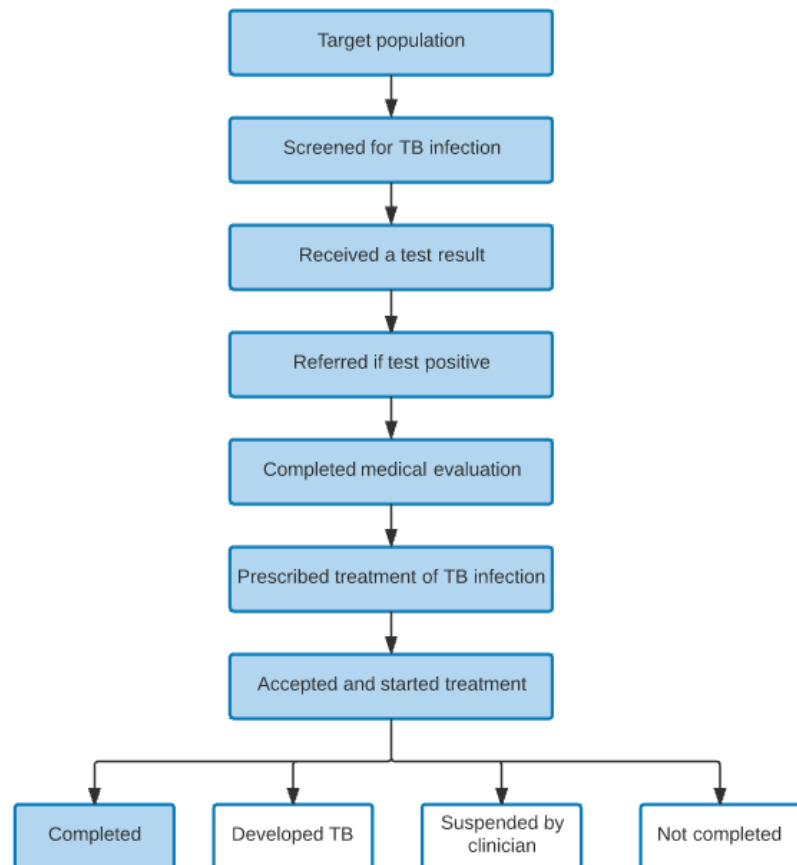
Around one quarter of the world population harbor tuberculosis (TB) infection [1], an asymptomatic state in which individuals demonstrate an immunological response to *Mycobacterium tuberculosis*. Individuals with TB infection are at increased risk for developing active disease, representing a substantial hidden reservoir for future disease [2]. Mathematical modeling, as well as programmatic experience from settings that have brought TB under control, suggests that treatment of TB infection is vital to curbing the TB epidemic [3]. However, the uptake of TB infection screening and treatment has been poor despite conservative international guidelines that only contacts younger than 5 years or patients with specific immunosuppressive conditions, notably HIV, should receive treatment of TB infection – only 7% child contacts and 38% PLHIV who were newly enrolled on HIV care were started on treatment of TB infection in 2015 [4]. With the 90-(90)-90 targets set up in the Global Plan and the new End TB Strategy, there has been increased recognition of the importance to enhance the programmatic management of TB infection.

In TB REACH Wave 6 call for proposals, treatment of TB infection can be a stand-alone intervention under the ‘improving treatment adherence and outcomes’ Category in the TB REACH’s [‘Transition to Scale Up’ grants framework](#), or one of the interventions under ‘improving detection, linkage to treatment and reporting of TB’ Category.

Monitoring and Evaluation (M&E)

[The standard TB REACH’s M&E framework](#) will also apply to projects focusing on the treatment of TB infection. Individuals are first screened and evaluated to determine if they are eligible for treatment of TB infection. People who are eligible should be prescribed treatment of TB infection and then start the treatment. For those who start treatment of TB infection, generally speaking, four outcomes are possible: (1) the person completes treatment of TB infection (completed); (2) the person develops TB while on treatment of TB infection (developed TB); (3) the treatment was stopped by clinician before completion for a medical reason such as side effects (suspended by clinician), or (4) the person stops taking treatment of TB infection before completion for some other reason (not completed). (figure 1).

Figure 1 Care Cascade of TB Infection



For applicants applying under the ‘improving detection, linkage to treatment and reporting of TB’

Category, basic impact measures would include the additional number of people started on treatment of TB

infection during intervention period compared to the pre-intervention period. For the ‘improving treatment adherence and outcomes’ project category, the main impact measures would also include the improvement in the proportion of people completing treatment among those who started.

Areas of consideration

The below sections provide some areas of consideration when preparing a TB REACH proposal on treatment of TB infection. The sequence or inclusion of an area of consideration / strategy does not imply any prioritization by TB REACH. Similarly, there may be other area of consideration that are not included in this concept note and their lack of inclusion does not mean TB REACH will not fund them.

The strategies to improve treatment of TB infection adherence are specific to the context and populations being served. Applicants must tailor their approaches to address to their local context.

Expand Access to Treatment of TB Infection

Due to financial constraints in high-burden countries, international guidelines generally recommend that only contacts younger than 5 years or patients with specific immunosuppressive conditions should receive treatment of TB infection [WHO]. However, modelling studies indicate that the substantial scale-up of the screening and treatment of TB infection will be essential if the global vision of TB elimination is to be realized [3]. WHO is currently in the process of revising and harmonizing guidance and it is expected to be more inclusive with the new recommendations. Expanding access to treatment of TB infection will require better identifying those in setting where the risk of TB acquisition and reactivation is substantial – including adult close contacts, health care workers, mine workers, homeless populations, and prisoners [5]. However, decisions about which populations should be tested should be informed by empirical and/or clinical evidence that demonstrates which group of people are at an increased risk of disease progression. For example, a scored screening algorithm was derived and validated to identify adult contacts that were at high risk of developing active TB in Peru. This simple algorithm successfully predicted 60% of TB identified during 10-year follow-up and can be helpful to prioritize TB control interventions for adult contacts [6].

Identify and Prevent Drop-outs in the Care Cascade of TB Infection

As the resources for treatment of TB infection are often limited in national TB programmes (NTPs) in high-burden countries, investments should be prioritized to areas where the drop outs from the care cascade of TB infection (figure 1) occur the most. This may be from identification of those intended for screening to those who completed treatment of TB infection. Applicants should identify the various interim steps where most patient attrition can occur in the specific population where activities will be implemented and tailored their patient retention and referral strategies. A greater public health gain if more resources are channeled to prevent drop outs earlier on in the care cascade of TB infection [7].

Enhance Uptake of Treatment of TB Infection

Unlike the treatment of active TB, the acceptance of screening for and treatment of TB infection is often low among providers and patients. Potential barriers to the uptake of TB infection screening and treatment include lack of information on TB infection and the risks if left untreated, reluctance of providers to prescribe treatment of TB infection (due to , for example, concern of hepatotoxicity, or fear of facilitating the development of drug resistance with monotherapy), reluctance of people infected with TB to undergo a prolonged course of treatment for an asymptomatic condition that may never progress to active disease, lack of trained and experienced medical staff, lack of perfect diagnosis of TB infection, lack of availability of patient friendly formulations for combination therapy, and lack of resources needed to address a large of pool of people, etc. Applicants should investigate the barriers that are specific to the population being served and design context-specific interventions to motivate buy-in from providers and patients.

Optimize Treatment Adherence

The adherence support strategies for treating active TB can be used in treatment TB infection, which include face-to-face direct observation of therapy (DOT – a recommended part of the 3HP regimen), regular patient review throughout treatment, mobile phone-based methods (including two-way SMS and staff phone contact), and even video DOT. Please read to the [concept note on treatment adherence](#) for details.

Scale-Up of Short-Course Treatment Regimens

Treatment with isoniazid for 9 month (9IHP) is the current the mainstay of treatment for TB infection in many countries [5]. However, due to its lengthy treatment duration, need for close follow-up, and risk of potentially fatal hepatotoxicity, physicians can be reluctant to recommend the treatment. People with TB infection are may be less likely to accept and adhere to a prolonged course of treatment for an asymptomatic condition that may never progress to active disease. Only 18.8% of those estimated to have TB infection completed treatment of TB infection [7]. Compared to 9IHP, there are shorter treatment regimens available. Three months of once-weekly isoniazid and rifapentine (3HP) has been shown to have higher completion rates with less hepatotoxicity. However, due to the current high costs of the regimen currently, it is unlikely TB REACH funding can support projects with heavy drug procurement. However, applicants are encouraged to seek co-financing to support the procurement of shorter treatment regimens.

Service Delivery

TB REACH's mandate is to improve service delivery and this implies any new diagnostics, adherence strategies, treatment regimens for TB infection must already exist and be available for use and evaluation. The focus of TB REACH project must be on the implementation of activities not evaluation nor development. TB REACH will NOT fund basic science and/or clinical trials on treatment of TB infection.

Conclusion

The Global Plan to End TB and the End TB Strategy to eliminate TB by 2035 underscore the needs to address the substantial reservoir of TB infection that will eventually develop into future diseases. There has been increased recognition of the importance of scaling-up the screening and treatment of TB infection. In the Wave 6 call for proposals, TB REACH provides a unique opportunity to test out new ideas and approaches that aim at increasing the uptake of testing in predefined high-risk populations and adherence to completion of treatment.

References

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