Ministry of Health & Family Welfare
Government of India

World Health Organization
India

Guidelines for Programmatic Management of **Tuberculosis Preventive Treatment in India**

July 2021

National TB Elimination Programme
Central TB Division, Ministry of Health & Family Welfare
Government of India, New Delhi

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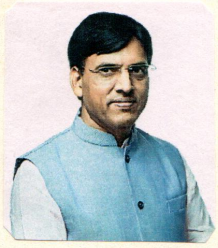
Message

मनसुख मांडविया
MANSUKH MANDAVIYA



सत्यमेव जयते

स्वास्थ्य एवं परिवार कल्याण
व रसायन एवं उर्वरक मंत्री
भारत सरकार
Minister for Health & Family Welfare
and Chemicals & Fertilizers
Government of India

Message

India has the highest estimated burden of tuberculosis infection (TBI) globally, with nearly 35–40 crore individuals having latent TBI, of which, an estimated 26 lakh are likely to develop active TB disease annually.

The likelihood of adults, adolescents, children and infants developing active TB disease is high, especially by virtue of their living in close contact with TB patients or with any of the high-risk groups that comprise of people living with HIV, those suffering from silicosis, receiving dialysis or preparing for organ transplant.

While this is a decisive moment to eliminate the disease once and for all, ending TB is just one half of the battle. It is equally important to ensure sustainability since people successfully completing treatment for TB remain at an elevated risk for recurrent disease, either from relapse or reinfection. This makes it critical to address this huge reservoir of potential disease that lurks within our communities.

We are committed to End TB by 2025. But much more needs to be done if we are to achieve this ambitious goal, five years ahead of the SDG targets. Even though the National Tuberculosis Elimination Programme has made significant strides in recent years, realizing the End TB targets would be impossible without considering TB Preventive Treatment (TPT). TPT is one of the most efficient ways to prevent TB disease after exposure to the TB bacteria.

To address this, the country will be implementing TPT in a phased manner. Treating TBI even in healthy people is equally important to protect them from potential infection. Contact tracing is a systematic way to reach suspects as evidenced during the COVID-19 pandemic and the TB programme shall leverage this for reaching people with TBI.

TB Preventive Treatment will be a game changer in TB elimination efforts. I am confident that with the current strategy that is prioritizing contact tracing and treatment on a war footing, the Government along with its partners, will be able to bridge the gap of missing cases and make India TB-free by the year 2030.

(Mansukh Mandaviya)

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Message

NATIONAL HEALTH MISSION
राष्ट्रीय स्वास्थ्य मिशन

डॉ. भारती प्रविण पवार
Dr. Bharati Pravin Pawar

सत्यमेव जयते

सर्वेसन्तु निरामया

स्वच्छ भारत
एक कदम स्वच्छता की ओर

स्वास्थ्य एवं परिवार कल्याण राज्य मंत्री
भारत सरकार
MINISTER OF STATE FOR
HEALTH & FAMILY WELFARE
GOVERNMENT OF INDIA

MESSAGE

Since Prime Minister, Shri Narendra Modi Ji's clarion call to end TB by 2025, efforts to eliminate TB has been accelerated to rapidly expand access of screening, diagnosis and treatment for people with tuberculosis infection. "Prevention" is one of the core pillars in the National Strategic Plan (2017-25) and outlines strategies and plans for preventing the emergence of TB in susceptible populations

I sincerely appreciate the efforts put forth by the National TB Elimination Programme in coming out with these Guidelines for Programmatic Management of TB Preventive Treatment following review of national and international evidences, recommendations made by WHO and though deliberations with subject experts. I am confident that this guideline will not only provide direction to programme managers but will be invaluable for private healthcare providers too.

I convey my best wishes to the Programme and look forward to the effective implementation of these Guidelines.

(Dr. Bharati Pravin Pawar)

"दो गज की दूरी, मास्क है जरूरी"

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Message

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सचिव

RAJESH BHUSHAN, IAS
SECRETARY

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स्वास्थ्य एवं परिवार कल्याण विभाग
स्वास्थ्य एवं परिवार कल्याण मंत्रालय
Government of India
Department of Health and Family Welfare
Ministry of Health and Family Welfare

MESSAGE

Early diagnosis and treatment of active TB remains a top priority for the National Tuberculosis Elimination Programme. Rigorous and expansive TB contact tracing and investigation among high-risk groups along with TB Preventive Treatment (TPT) are extremely important steps towards ending this disease. Different studies show that there has been almost 60% reduction in the risk of developing TB disease after TPT. This reduction can go up to 90% among People Living with HIV (PLHIV).

2. The current policy of treating eligible children <6 years of age who are contacts of TB patients and TB-HIV co-infected is now being expanded to cover all household contacts of confirmed pulmonary TB patients. The new policy will also cover other high-risk groups, including individuals on immunosuppressive therapy, those suffering from silicosis, people on anti-Tumor Necrosis Factor (TNF) treatment, on dialysis and those preparing for organ or hematologic transplantation. All such people will now be tested and treated for TB infection (TBI), given their increased risk for progression to active TB disease.

3. The implementation would be carried out by the States in the expanded target population for TPT as per this guideline in a phased manner. Universal Health Coverage envisaged through Health and Wellness Centres and Sub-Centers would be leveraged as focal point for TPT service delivery in their respective catchment areas with funding support through the national health mission (NHM) and the annual programme implementation plan (PIP) process.

4. Prevention of TB disease by treatment of TBI is a critical component of the National Strategic Plan (NSP) 2020–25 for Ending TB in India by 2025. As the NSP proposes a Detect-Treat-Prevent-Build approach, scaling-up TPT would be the key to hasten the decline in TB incidence from the present 2.5% annually to the required 10%.

Date : 18th May 2021
Place : New Delhi

(RAJESH BHUSHAN)

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Message

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सत्यमेव जयते

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स्वास्थ्य सेवा महानिदेशालय
Government of India
Ministry of Health & Family Welfare
Directorate General of Health Services

Message

Early diagnosis and treatment of active TB remains a top priority in India. To achieve the goal of TB elimination, the national programme has been focusing on preventing cases by finding and treating latent tuberculosis infection (LTBI) and active case finding amongst high-risk individuals. Several studies have shown on average, 5–10% of those infected will develop active TB disease over the course of their lives, usually within the first five years after initial infection.

Prevention of active TB disease by treatment of LTBI is a critical component of the WHO End TB Strategy. Therefore, the diagnosis and treatment of LTBI in India is essential, especially amongst high-risk groups.

The risk for active TB disease after infection depends on several factors, the most important being immunological status. This risk is increased by 16–21 times in case of HIV co-infection and 3–4 times in other immune-compromised states like diabetes etc. The risk of developing TB disease after TB preventive therapy decreases 90% from 11.1% for those not taking LTBI treatment to 1.2% for those taken the same.

"LTBI Management" is one of the key activities under the "Prevent" component of the National Strategic Plan 2017–25 for TB Elimination by 2025. The National Strategic Plan for India 2017–25 proposes a Detect-Treat-Prevent-Build approach and scaling-up TB preventive therapy would be key to hasten the decline in TB incidence from 2.5% at present to the desired 10% annually.

My best wishes for the programme and to the team that is dedicatedly navigating on-ground challenges to implement the same in line with the End TB targets. Despite the COVID-19 pandemic our collective effort is on track and we are confident of adding India to the TB free nations globally.

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Message

WHO Representative to India

Tuberculosis (TB) Preventive Treatment (TPT) is one of the key interventions recommended by World Health Organization (WHO) to achieve the #EndTB Strategy goals, as upheld by the UN High Level Meeting on TB in September 2018. TPT services complement screening for active TB, infection control, prevention and care of HIV and other co-morbidities and health risks, access to universal health care, social protection, and poverty alleviation.

In high-burden settings, the usual public health strategy is to focus on early diagnosis and treatment of persons with TB disease. However, preventing the development of the disease and its spread is vital to fast-track reductions in TB incidence in both high- and low-burden settings.

Programmatic Management of TPT (PMTPT) has been traditionally limited in extent and less emphasized under NTEP until now due to other competing priorities. However, in view of the ambitious target to #EndTB in India by 2025, expanding the scope and management options under PMTPT as a priority intervention has become critical to accelerate the decline in TB incidence.

India's has reiterated its commitment to End TB by 2025 by launching 'TB Mukt Bharat', a people's movement. It is crucial to adopt an integrated and comprehensive 'cascade of care' approach as a core strategy to deliver TPT services across the country to systematically reach out and screen all target populations (PLHIV, household contacts, and other groups at risk of developing TB disease) and after ruling out TB, provide TPT as a part of the continuum of care.

The goal is to have a significant impact on an individual's health while reducing TB transmission in the community. No one is safe until everyone is screened and treated to stop the spread of TB infection and #EndTB.

Message

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May 13, 2021

MESSAGE

The National TB Elimination Programme extends its services to all TB patients irrespective of the patient seeking care from the public or private sector. With the implementation of the Guidelines for Programme Management of Drug-Resistant Tuberculosis in India, NTEP intends to expand the target population for TB Preventive Treatment in a phased manner. Planned intensified active and passive case finding activities in mapped vulnerable groups, high-risk co-morbid conditions and among the general population will result in an increased notification of index TB patients.

Over the past few years, rigorous efforts have been made to engage private health-care providers such as establishing Patient Provider Support Agencies (PPSA) who were tasked with making private health-care providers aware of the services available under NTEP and increasing their participation and role in the management of TB patients. These efforts have translated to a significant rise in TB notification from the private sector. Going forward, this will provide the NTEP with a good opportunity for tracing contacts of index cases and administering TPT to them in a timely and efficient manner.

The complete range of health facilities providing care to the patients from both sectors, together with community volunteers will synergize their efforts in the effective implementation of the TPT strategy. This will go a long way in ensuring accessibility, acceptability, complete coverage, efficient service delivery, real-time monitoring and long-term follow-up to protect all vulnerable groups as well as contacts of TB patients from breakdown to active TB.

As all PLHIV, contacts of confirmed pulmonary TB patients and other at-risk groups will be screened for TB, diagnostic tests too may be outsourced through PPSAs and other partnership mechanisms to identified private facilities. People in the target population who are themselves detected with any form of TB or found eligible for TPT can be offered TPT from the facility of their choice, public or private.

The programmatic implementation and scale-up of TPT would require the strengthening of each element in the cascade of care, right from the identification of the target population to provision and continuation of TPT. Hence as we move forward, we will need to ensure that all individuals who are most at risk of developing TB are systematically identified as a first critical step. Once TB disease is excluded, the next critical step would be to offer them TPT, so that they can improve their own individual health as well as the health of their communities.

(Arti Ahuja)

Message

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MESSAGE

Prevention of TB disease by treatment of TB infection is a critical component of the National Strategic Plan (2017–25) for Ending TB in India by 2025. To expand implementation of TB Preventive Treatment in a programmatic mode beyond the existing policy (children less than 5 years and PLHIV) to cover all adolescent and adult household contacts of pulmonary TB, prioritizing bacteriologically confirmed pulmonary TB, is a bold step being taken by the national programme.

The scaling-up of TB Preventive Treatment would be an excellent strategy to accelerate the rate of decline in TB incidence (from 2.5% currently to an expected 10% annually). Rigorous TB contact tracing and investigation for TB among household contacts, coupled with active screening for TB among high-risk groups and TB Preventive Treatment is a critical and significant component under the "Prevent" component of the National Strategic Plan.

The National Health Mission undoubtedly plays a pivotal role in implementation of the TB programme including TB Preventive Treatment within the state/district health machinery. Here I would like to emphasize the extremely critical role played by the Medical Officers and Community Health Officers who are engaged in implementing the same at the Health & Wellness Centers (HWC).

The Community Health Officers and the peripheral health workers like ANMs and ASHAs in Health & Wellness Centres would be responsible for contact tracing/investigation and identifying those eligible for TB preventive treatment and ensure continuum of care for those initiated on TB Preventive Treatment by the Medical Officers at PHC or above level.

With the support of the entire NHM machinery, I am confident that the country would accelerate its efforts towards achieving the End TB targets by 2025.

(**Vandana Gurnani**)

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Message

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It is estimated that nearly 40 crore Indians suffer from latent TB infection. This large reservoir of infected but asymptomatic people will contribute to future TB patients. The risk is increased multifold in contacts of bacteriologically confirmed TB patients, in TB-HIV co-infected and in other immune-compromised co-morbid population groups. Moreover, 71% household contacts of pulmonary TB patients have been found to have baseline TBI.

Preventing TB by finding and treating the infected through active case finding amongst high-risk populations is extremely important to end TB. The programmatic management of TPT must be scaled rapidly as a priority intervention to achieve an accelerated decline in TB incidence rates. It is critical to adopt an integrated and comprehensive 'cascade of care' approach as a core strategy for delivering TPT services where all target population who are at-risk of developing TB disease are systematically reached out, screened for TB disease and accordingly provided TPT as part of the continuum of care.

The biggest challenge would be to monitor TPT in individuals and the prompt identification of interrupters. As most people enrolled on TPT would be relatively healthy and may not feel the need to take medication regularly, they may choose not taking/ or miss taking TPT doses or in a worst case scenario, stop the treatment altogether. All efforts must be made by the health-care providers; the family and community members to ensure that TPT is regularly monitored and interrupters are identified and brought back into the ambit of treatment and care.

Community engagement is central to all public health interventions and involves those affected in understanding the risks they face and response actions that are acceptable. Communities will play a major role in preventing TBI progressing to TB disease. Community engagement and health education will play the most vital role in ascertaining that individuals and communities make informed choices about TPT and policies must be evaluated based on views and experiences of affected populations in an equitable manner based on consent and confidentiality.

The community collectives that have been formed as support groups, notable being the TB survivor group and the PLHIV networks, can definitely be leveraged to mobilize community members for TPT. This will help bring issues to the notice of the health system directly or through platforms such as community meetings, TB forums, etc. Community and civil society organizations will continue to facilitate demand generation and appropriate health-seeking behaviour of the target populations.

More such innovative ways have to be found to ensure stigma around TB is removed and those carrying the infection are put on treatment without delay. The goal of having a TB-free India must lie, not just at the altar of the Ministry of Health but be a shared responsibility of all partners and stakeholders. Only then can we aspire to reach the desired targets and to sustain the momentum that has been achieved this far.

Message

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I feel honoured to introduce guidelines on TB Preventive Treatment (TPT). The overall structure of these guidelines and the recommendations follow the logical cascade of management of TB Infection (TBI) - identification of at-risk populations including adults and children living with HIV, HIV-negative adult and child contacts of TB cases and other HIV-negative at-risk groups, ruling out active TB disease, testing for TBI, providing treatment, monitoring adverse events, adherence to and completion of treatment and monitoring & evaluation.

Studies have shown that, on an average, 5–10% of those infected with TB bacilli will develop TB disease over the course of their lives. This usually manifests within the first 2 years after initial infection. Therefore, it is important to identify those at highest risk of progression to active TB and manage TBI in them, as not all individuals infected with M. tuberculosis develop active TB. As currently there are no predictive tests to identify individuals who will progress to disease a targeted approach would be an appropriate public health response.

Adherence to the TPT regimen throughout the course and treatment completion, are important determinants of clinical benefit. Poor adherence and/or early cessation of TPT can potentially increase the risk of the individuals developing active TB disease, including drug-resistant TB. Since the success of the TPT strategy is based on adherence to the treatment, meticulous monitoring and apt management of any adverse events is quintessential.

Prevention of TB through TPT begins with the diagnosis of TBI and exclusion of active TB among high-risk individuals. Prevention of TB disease by treatment of TBI is a critical component of the National Strategic Plan (NSP) 2020-25 for Ending TB in India. The NSP proposes a Detect-Treat-Prevent-Build approach and scaling up TPT would be the key to smart decline in TB incidence annually.

(Dr. Sudarsan Mandal)

Contents

Abbreviations

3HP	three months of weekly rifapentine plus isoniazid
4R	four months of daily rifampicin
6H	six months of daily isoniazid
6Lfx	six months of daily levofloxacin
1HP	one month of daily rifapentine plus isoniazid
ACF	active TB case finding
AIDS	acquired immunodeficiency syndrome
ALT	alanine aminotransferase
ART	antiretroviral therapy
ARV	antiretroviral drugs
AST	aspartate aminotransferase
BCG	bacille Calmette-Guérin (vaccine)
CAD	computer aided detection
CFP-10	culture filtrate protein 10
CLHIV	children living with HIV
CMSS	Central Medical Services Society stores
DMPA	depot medroxyprogesterone acetate
DSD	differentiated HIV service delivery
DS-TB	drug sensitive TB
ELISA	enzyme-linked immunosorbent assay
ESAT-6	early secretory antigenic target-6
FDC	fixed-dose combination
GMSD	Government Medical Store Depot (GMSD)
HCV	hepatitis C virus
HWC	health and wellness centre
HF	health facility
HHC	household contact
HBV	hepatitis B virus
HCV	hepatitis C virus
HIV	human immunodeficiency virus
Hr-TB	isoniazid-resistant, rifampicin susceptible TB disease

IGRA	interferon-gamma release assay
INSTIs	integrase strand transfer inhibitors
IPT	isoniazid preventive treatment
LFT	liver function test
Lfx	levofloxacin
MDR-TB	multidrug-resistant tuberculosis
NGO	non-governmental organization
NNRTI	non-nucleoside reverse transcriptase inhibitor
OST	opiate substitution therapy
PDE-5	phosphodiesterase-5
PIs	protease inhibitors
PLHIV	people living with HIV
PMTPT	programmatic management of tuberculosis preventive treatment
PPD	purified protein derivative
PPSA	patient provider support agency
PHC	primary health centre
PWUD	people who use drugs
RCT	randomized controlled trial
RR	relative risk
SSRI	selective serotonin reuptake inhibitor
TDF	tenofovir-disoproxil fumarate
TDF-DP	tenofovir diphosphate
TNF	tumour necrosis factor
TPT	tuberculosis preventive treatment
TST	tuberculin skin test
TB	tuberculosis
TBI	tuberculosis infection
UNHLM	United Nations High Level Meeting on Tuberculosis (2018)
WHO	World Health Organization

Acknowledgements

The Guidelines on Programmatic Management of TB Preventive Treatment (PMTPT) in India (2021) have been developed as the end-product of a series of meetings and deliberations with national experts from the Government of India (GoI), WHO Country Office for India (WHO India) and key technical and developmental partners. These meetings and deliberations were organized by the Central TB Division (CTD), Ministry of Health and Family Welfare (MoHFW), GoI with technical and organizational support from WHO India over 2019 and 2020. These involved discussions with several stakeholders, extensive review of literature and aligning with current and emerging evidence to address the prevailing epidemiology of TB in India. In May 2020, the National Technical Working Group (NTWG) & National Task Force on TB infection (TBI) recommended adoption of the updated WHO consolidated guidelines and operational handbook on tuberculosis Module 1: Prevention – Tuberculosis preventive treatment (2020) as per country requirements along with introduction of shorter TB preventive treatment regimen among all house hold contacts of pulmonary (*bacteriologically confirmed) TB patients and expanded high risk groups in India.

We express our gratitude to Shri Rajesh Bhushan, Union Secretary, MoHFW, GoI; Dr. Sunil Kumar, Director General Health Services (DGHS), GoI; Ms. Arti Ahuja, Additional Secretary (Health) & Director General (NTEP), MoHFW, GoI; Ms. Vandana Gurnani, Additional Secretary & Mission Director, National Health Mission (NHM), MoHFW, GoI; Shri Vikas Sheel, Additional Secretary (Policy), MoHFW, GoI; Dr V G Somani, Drug Controller General of India (DCGI), DGHS, GoI; Dr. Ofrin Roderico, WHO Representative to India; Ms. Payden, Deputy WHO Representative to India; Dr. Alexandra Vokaty, Team Leader – Communicable Diseases, WHO Country Office for India; Dr. Randeep Guleria, Director All India Institute of Medical Sciences, New Delhi; Dr. Kuldeep Singh Sachdeva, Regional Director, The Union South East Asia and Dr. Sudarsan Mandal, Deputy Director General TB, Central TB Division, GoI for providing leadership, encouragement and support to the core team as they developed the Guidelines for PMTPT in India (2021). This will play a major role in contributing to the rapid and effective decline in TB incidence to end TB in the country. We would like to place on record efforts of the core team from the Central TB Division and WHO India who took the lead in this process.

Eminent experts from the WHO Global TB Programme (GTB), Geneva; WHO South East Asia Region Office (SEARO); WHO Country Office for India; All India Institute of Medical Sciences (AIIMS), New Delhi; National Institute for Research in Tuberculosis (NIRT), Chennai; National Institute for TB and Respiratory Diseases (NITRD), New Delhi and Centre for Disease Control India (CDC) provided technical inputs in developing this document. The valuable contribution of prominent experts and officials from the above organizations and those experts who reviewed this document, providing inputs for its finalization are well acknowledged. Special appreciation is due for the medical consultants of WHO–NTEP technical assistance network

for their inputs, particularly in aligning the content with the WHO consolidated guidelines and operational handbook on tuberculosis Module 1: Prevention – Tuberculosis preventive treatment (2020) with knowledge, emerging evidence, national and global guidelines and the National Strategic Plan for ending TB (2020-25). Special thanks to the communications team at WHO India for their crucial support in editing, formatting and designing this document.

Overall coordination for developing this document was done by Dr. Malik Parmar, National Professional Officer – Drug Resistant and Latent TB, WHO Country Office for India and Dr. Ravinder Kumar, TB Specialist, Central TB Division, GoI. The team who worked on writing these guidelines comprised of Dr. M Parmar, Dr. R Kumar, Dr. R Ramachandran, Dr. L Mehandru, Dr. S Anand, Dr. D Balasubramanian, Dr. T Quazi, Dr. S Balakrishnan, Dr. K Khaparde, Dr A Shamim, Ms. K Nair, Mr. M Kumar, Dr. S Chauhan, Dr H Solanki, Dr R Taralekar, Ms. S Khumukcham, Ms. S Chalil Dr M Mathew, Dr K Suma, Dr B Bishnu and Dr V Shah.

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These guidelines are consistent with the WHO consolidated guidelines and operational handbook on tuberculosis Module 1: Prevention – Tuberculosis preventive treatment (2020). The technical and operational aspects listed herein are intended to complement the existing NTEP technical and operational guidelines and the National Strategic Plan for ending TB (2017-25) in India. These guidelines will now be implemented across India to gain and document experiences on feasibility, safety monitoring and enhancement in treatment outcomes of TB preventive treatment to further guide the country in its refinement as national and global evidence emerges in future.

Definitions

Active case finding (ACF): It is defined programmatically as systematic screening for TB disease through outreach activities outside health facility settings.

Adult: For programmatic purpose in India, adult is a person over 19 years of age.

At-risk group: is any group of people in whom the prevalence or incidence of TB is significantly higher than in the general population.

Bacteriologically confirmed TB: is TB diagnosed in a biological specimen by smear microscopy, culture or a WHO-endorsed rapid molecular test and adopted by NTEP such as Xpert MTB/RIF®/TrueNat®.

Child: For programmatic purpose in India, child is a person up to and including 18 years of age. [This include adolescents aged 10-18 years.]

Contact: is any individual who was exposed to a person with active TB disease.

Contact investigation: is a systematic process for identifying previously undiagnosed people with TB disease and TB infection among the contacts of an index TB patient and/or other comparable settings where transmission occurs. [Contact investigation consists of identification, clinical evaluation and/or testing and provision of appropriate anti-TB treatment (for people with confirmed TB) or TB preventive treatment (for those without TB disease)].

Close contact: is a person who is not in the household but shared an enclosed space, such as at a social gathering, workplace or facility, for extended periods during the day with the index TB patient during the three months before commencement of the current TB treatment episode. This group will be included for all intervention as applicable for house-hold contacts in this guidelines.

High TB transmission setting: is a setting with a high frequency of individuals with undetected or undiagnosed TB disease, or where infectious TB patients are present and there is a high risk of TB transmission. [TB patients are most infectious when they are untreated or inadequately treated. Transmission will be increased by aerosol-generating procedures and by the presence of susceptible individuals. These settings (health care workers, prisons, mines, slums, tribal, migrant laborer's etc.) could be mapped out as part of vulnerability mapping exercise done for and prioritized by states for specific TPT interventions guided by differential TB epidemiology in the respective state.]

Household contact (HHC): is a person who shared the same enclosed living space as the index TB patient for one or more nights or for frequent or extended daytime periods during

the three months before the start of current TB treatment. [For simplicity, close contacts may be considered inclusive in this term throughout the guidelines.]

Index patient of TB: is the initially identified person of any age with new or recurrent TB in a specific household or other comparable setting in which others may have been exposed. [An index TB patient is the person on whom a contact investigation is centered but is not necessarily the source.]

Infant: is a child under one year (12 months) of age.

Tuberculosis infection (TBI): is a state of persistent immune response to stimulation by *M. tuberculosis* antigens with no evidence of clinically manifest TB disease. [There is no gold standard test for direct identification of *M. tuberculosis* infection in humans. Most infected people have no signs or symptoms of TB but are at risk for developing TB disease. TB infection is also known as "latent TB infection" (LTBI), although this term is being discarded given that infection cannot always be considered latent.]

People who use drugs (PWUD): are those who engage in the harmful or hazardous use of psychoactive substances, which could impact negatively on the user's health, social life, resources and legal situation.

Programmatic Management of TB preventive treatment (PMTPT): includes all coordinated activities by public and private health caregivers and the community aimed at scaling up TB preventive treatment to people who need it.

Systematic screening for TB disease: is a systematic identification of people with presumed TB disease, in a predetermined target population, using tests, examinations or other procedures that can be applied rapidly. [Among those screened positive, the diagnosis needs to be established by one or several diagnostic tests and additional clinical assessments, which together have high accuracy.]

TB preventive treatment (TPT): Treatment offered to individuals who are considered to be at risk of developing TB disease, in order to reduce that risk. [Also referred to as treatment of TB infection.]

Tuberculosis (TB): is the disease that occurs in someone infected with *M. tuberculosis*. [It is characterized by signs or symptoms of TB disease, or both, and is distinct from TB infection, which occurs without signs or symptoms of TB. In this document, it is commonly referred to as "active" TB or TB "disease" to distinguish it from TB infection.]

Underweight: in adults and adolescents usually refers to a body mass index <18.5 kg/m2 and in children < 10 years to a weight-for-age < –2 z-scores.

CHAPTER 1:
OVERVIEW OF TB INFECTION

Learning Objectives

In this chapter we will learn about:

- Burden of TB infection
- Cascade of care approach

1.1 Burden of TB infection

India has the highest estimated burden of tuberculosis infection (TBI) globally, with nearly 35-40 crores Indian population having TBI, of which 26 lakhs people (18-36 lakh) are estimated to develop tuberculosis (TB) disease annually. This may change after the ongoing national TB prevalence survey data becomes available.

From this large pool of infected but asymptomatic persons, most patients of TB disease will arise. Several studies have shown that, on average, 5–10% of those infected will develop TB disease over the course of their lives, usually within the first 2 years after initial infection. The risk for TB disease after infection depends on several factors, the most important being immunological status. This risk is increased >25 times among contacts of bacteriologically confirmed TB patients compared to general populations, 16-21 times in case of HIV co-infection and 3-4 times in other immune-compromised status like diabetes, etc. Risk versus benefit assessment is critical with plans to expand active case finding (ACF) and programmatic management of TB preventive treatment (PMTPT) to populations beyond those currently recommended by WHO e.g. health care workers, migrants, people having diabetes mellitus and other vulnerabilities mapped by states for ACF.

Studies show 75% of people who develop TB disease after contact with a patient of active TB are estimated to do so within one year of TB diagnosis of the index patient and 97% within two years. Molecular fingerprinting studies further confirmed the probabilities of developing disease within one, two, and five years as 45%, 62%, and 83% respectively. Unfortunately, biomarkers that distinguish newly acquired infection from remote infection are not available at present. The eligibility for TB preventive treatment (TPT) relies on ruling out active TB among individuals and groups who are known to have high risk of acquiring TB, using the tests as an aide in decision making in people when available.

In a recent study published in July 2020 from India, 71% household contacts (HHC) of pulmonary TB (PTB) patients had baseline TBI (tuberculin skin test [TST] ≥ 5 mm or Quantiferon®- Gold-in-Tube [QGIT] ≥ 0.35 IU/ml). Overall, 2% HHC developed incident TB disease (12 cases/1000 person-years, 95%CI: 8–19). HIV infection (aIRR = 29.08, 95% CI: 2.38–355.77, p = 0.01) and undernutrition (aIRR = 6.16, 95% CI: 1.89–20.03, p = 0.003)

were independently associated with incident TB disease while age, diabetes mellitus, smoking, alcohol, and baseline TBI, regardless of TST (≥ 5 mm, ≥ 10 mm, ≥ 6 mm increase) or QGIT (≥ 0.35 IU/ml, ≥ 0.7 IU/ml) cut-offs were not associated. Given the high overall risk of incident TB disease among recently exposed HHCs and the lack of association between TBI status and incident TB disease, the study supports the new WHO recommendation to offer TPT to all HHC of PTB patients residing in a high TB burden country such as India. They do not suggest any benefit of TBI testing at baseline or during follow-up to risk stratify recently-exposed HHC for TPT *(7)*.

Although early diagnosis and treatment of active TB remains a top priority in India, preventing TB by finding and treating TBI and active case finding (ACF) amongst high-risk groups (HRGs) are extremely important steps towards ending TB. The risk of developing TB disease after TPT decreases by approximately 60% and the reduction can be up to 90% among people living with HIV (PLHIV) *(8)*. Epidemiological modelling studies show that effective implementation of TPT alone in South-East Asia (SEA) region would result in an annual TB incidence decline of 8.3%, independent of other background interventions *(9)*.

Prevention of TB disease by treatment of TBI is a critical component of the National Strategic Plan 2017-25 for Ending TB (NSP) in India by 2025. The NSP proposes a Detect-Treat-Prevent-Build approach and scaling up TPT would be key to hasten the rate of decline in TB incidence from 2.5% at present to 10% required annually. Rigorous, expansive and accountable "TB contact tracing and investigation" for secondary TB patient detection and treatment coupled with active screening for TB among HRGs and TPT is one of the key activities under the "Prevent" component of the NSP.

1.2 Cascade of care approach

Programmatic Management of TPT (PMTPT) has been traditionally limited in extent and given low priority under National Tuberculosis Elimination Programme (NTEP) until now, due to other competing and important priorities. It is crucial to adopt an integrated and comprehensive 'cascade of care' approach as a core strategy for delivering TPT services across India. This is so because despite ambitious targets of ending TB by 2025 in India, there is need to expand the scope and management options under PMTPT as a priority intervention to accelerate decline in TB incidence.

In the cascade of care approach, all target population who are at-risk of developing TB disease are systematically reached out, screened for TB disease and after ruling out TB disease provided TPT as a part of continuum of care. The aim is to have significant impact on an individual's health as well as to reduce TB burden and transmission. The cascade of care approach among TPT target population is detailed in Figure 1.1.

Globally, there are significant losses in the cascade of care prior to initiation of PMTPT, in addition to patient non-adherence following initiation of treatment. Research studies from all over the world show that among those estimated to be eligible for PMTPT, less than 20% completed the entire cascade of care (Figure 1.2) *(10).* Strengthening the cascade of care would require interventions along the entire cascade of care to optimize the impact of TPT on accelerating decline in TB incidence nationwide.

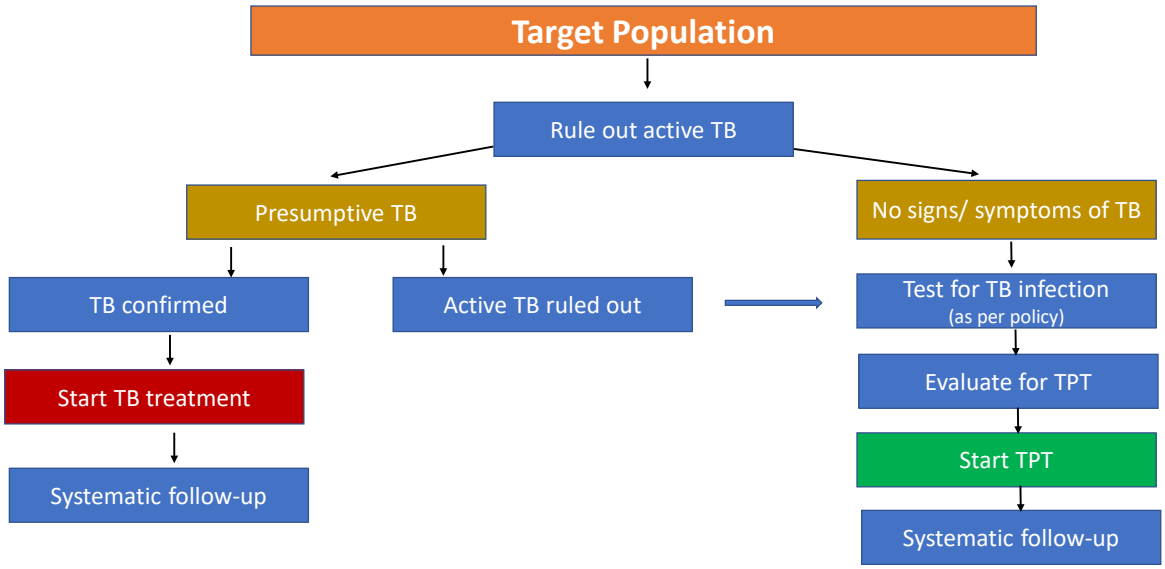


Figure 1.1 Cascade of TB case finding and preventive treatment

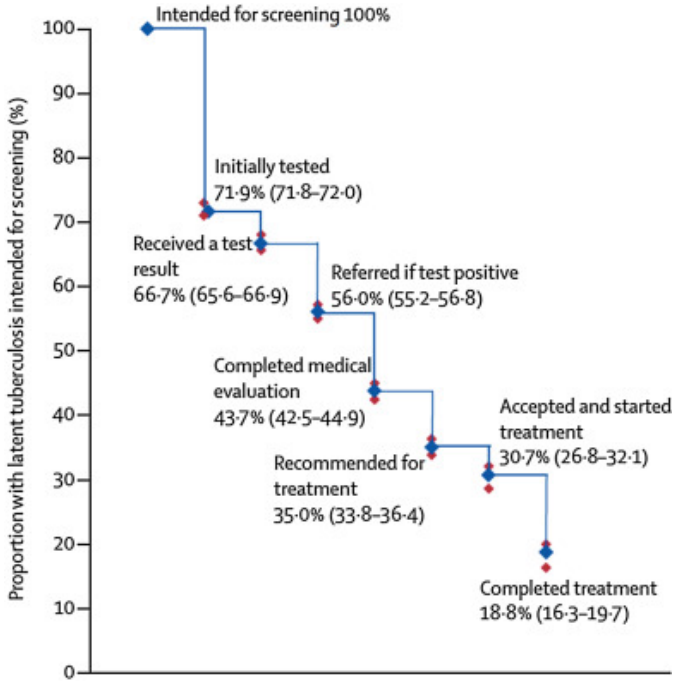


Figure 1.2 Losses and drop-outs at each stage of the cascade of care in latent TB

KEY POINTS TO REMEMBER

- ✓ India has the highest burden of TB infection (TBI) globally.
- ✓ 5–10% of those infected will develop active TB disease over the course of their lives, usually within the first 2 years after initial infection.
- ✓ In India, 71% HHC of pulmonary TB patients had baseline TBI.
- ✓ Risk of TBI increases 16-21 times in case of HIV co-infection with or without ART.

- ✓ Eligibility for TPT relies on ruling out active TB and risk versus benefit assessment.
- ✓ Prevention is one of the four strategic priorities of National Strategic Plan to end TB in India.
- ✓ Strengthening cascade of care for TPT would require interventions along the entire cascade of care to optimize impact of TPT on accelerating decline in its incidence nationwide.

CHAPTER 2:
TARGET POPULATION FOR TB PREVENTIVE TREATMENT

Learning Objectives

In this chapter we will learn about:

- Identifying at-risk population
- Target population for TPT
- Policy on TPT in India

2.1 Identifying at-risk population

It is important to identify those at highest risk of progression to active TB, to manage TBI in them, as not all individuals infected with *M. tuberculosis* develop active TB and currently there are no predictive tests to identify individuals who will progress to disease. Hence a targeted approach is considered as an appropriate public health response. Prevention of TB through TPT begins with exclusion of active TB among HRG and the diagnosis of TBI.

In the typical screening process, asymptomatic and early active TB cases are also found, and case detection rates vary by the TB prevalence of the population targeted. Active TB case finding (ACF) process also offers an opportunity to simultaneously rule out active TB among HRG and identify the target population for TPT, wherein PMTPT services can be integrated within existing ACF interventions. Hence, TPT is a continuum of care for routine programme activities including ACF. Some countries like Vietnam are contemplating community-wide screening at frequent intervals and population level TPT provision which may be the route once reliable tests and shorter TPT are widely available. The programme has prioritized the following target population for TPT based on elevated risk of progression from infection to TB disease or increased likelihood of exposure to TB disease:

a. Expanded eligible group including children >5 years, adolescents and adult HHC of pulmonary* TB patients notified in Nikshay from public and private sector (**bacteriologically confirmed pulmonary TB patients will be prioritized for enumeration of the target population for TPT*)

Target population	Strategy
• People living with HIV (+ ART) ▸ Adults and children >12 months ▸ Infants <12 months with HIV in contact with active TB • HHC below 5 years of pulmonary* TB patients	TPT to all after ruling out active TB disease
• HHC 5 years and above of pulmonary* TB patients#	TPT among TBI positive# after ruling out TB disease

#Chest X Ray (CXR) and TBI testing would be offered wherever available, but TPT must not be deferred in their absence

b. Expanded to other risk groups

Target population	Strategy
Individuals who are: • on immunosuppressive therapy • having silicosis • on anti-TNF treatment • on dialysis • preparing for organ or hematologic transplantation	TPT after ruling out TB disease among TBI positive

2.1.1 People Living with HIV (Adults, Adolescents and Children)

TPT reduces the overall risk for TB by 60-90% among PLHIV. Following are the recommended actions:

- Adults and children (>12 months) living with HIV should be screened for TB using a four-symptom complex and TPT can be provided to those without symptoms or after ruling out active TB in those with TB symptoms. TPT should be given to all these individuals irrespective of the degree of immunosuppression, whether they are on antiretroviral treatment (ART), previous TB treatment, and/or pregnancy in women.
- Infants aged < 12 months living with HIV who are in contact with a patient of pulmonary TB and are investigated for TB should receive TPT with 6 months of isoniazid (6H) after active TB is ruled out.

2.1.2 All household contacts of pulmonary* TB patients

All HHC of pulmonary* TB patients notified in Nikshay from public and private sector, regardless of their age or TBI status, are at substantially higher risk for progression to active TB than the general population. Hence contact tracing is of paramount importance. Following are the recommended actions:

- All HHC of pulmonary* TB patients, regardless of their age, should be given TPT after ruling out TB. In children HHC under 5 years of age, TPT will be offered after ruling out active TB, without TBI testing. In children HHC >5 years and adults, chest X Ray and TBI testing would be offered wherever available. All efforts need to be made to ensure that CXR & TBI testing is made available. However, TPT must not be deferred in their absence. [This includes close contacts of pulmonary* TB patients at workplace and other settings, regardless of their age].

2.1.3 Expansion to other risk groups

Individuals with clinical risk factors who are on immunosuppressive therapy, having silicosis, on anti-TNF treatment, on dialysis, preparing for organ or hematologic transplantation should be tested and treated for TBI because of their increased risk for progression to active TB disease.

Systematic TBI testing and treatment is not recommended for people with diabetes mellitus, malnutrition, smoking, harmful alcohol abuse unless they have other risk factors for TB, such as HIV infection or history of contact with TB patient within their household.

High TB transmission settings (health-care workers, prisons, mines, slums, tribal, migrant laborer's etc.) could be mapped out as part of a vulnerability mapping exercise done for ACF. This can be prioritized for specific TPT interventions guided by differential TB epidemiology by the state TPT committee (Annexure 1) if the risk of active TB among them is higher than that of the general population in the respective states.

KEY POINTS TO REMEMBER

- ✓ Target population for TPT after ruling out active TB includes PLHIV, all HHC of pulmonary* TB patients notified in Nikshay from public and private sector, individuals who are on immunosuppressive therapy, having silicosis, on anti-TNF treatment, on dialysis and preparing for organ or hematologic transplantation.
- ✓ In adults and children (>12 months) living with HIV, TPT can be provided to those without symptoms or after ruling out active TB in those with TB symptoms. TPT should be given to all these individuals irrespective of the degree of immunosuppression, whether they are on antiretroviral treatment (ART), previous TB treatment, and pregnancy in women.
- ✓ Infants aged < 12 months living with HIV who are in contact with a patient of pulmonary TB and are investigated for TB should receive TPT with 6 months of isoniazid (6H) after TB is ruled out.
- ✓ In children HHC under 5 years of age, TPT will be offered without testing for TBI.
- ✓ In children HHC >5 years and adults, chest X Ray and TBI testing would be offered wherever available. All efforts need to be made to ensure that CXR & TBI testing is made available. However, TPT must not be deferred in their absence.
- ✓ In individuals who are on immunosuppressive therapy, having silicosis, on anti-TNF treatment, on dialysis, preparing for organ or hematologic transplantation or other vulnerable risk groups, treatment would always be preceded by testing.
- ✓ High TB transmission settings (health-care workers, prisons, mines, slums, tribal, migrant labourer's etc.) could be mapped out as part of a vulnerability mapping exercise done for ACF and prioritized by states for specific TPT interventions guided by differential TB epidemiology by the state TPT expert groups if the extent of TB among them is higher than that of the general population in the respective state.

CHAPTER 3:
DIAGNOSIS OF TB INFECTION

Learning Objectives

In this chapter we will learn about:

- Introduction to lab diagnostics for TBI
- Tests for TBI
- Implementation considerations for testing services for TBI
- Newer tests in pipeline

3.1 Introduction to lab diagnostics for TB infection

Excluding TB disease is a critical step before starting TPT, and confirming TBI before starting TPT may increase the certainty that individuals targeted for TPT would benefit from it. Tests also enhance confidence of providers as well as recipients to start TPT. However, there is no gold standard test to diagnose TBI or predict progression to TB disease among those infected. Currently, available tests are indirect and measure the immune response following TB exposure and hence require the person to mount an adequate immune response to provide reliable results.

3.2 Tests for TB infection

The currently recommended and available tests for TBI are Tuberculin Skin Test (TST) and Interferon-Gamma Release Assay (IGRA). Both tests measure immune sensitization (type IV or delayed-type II hypersensitivity) to mycobacterial protein antigens that occurs following infection by *M. tuberculosis*. TST detects the reaction to purified protein derivative (PPD) of the mycobacterium. IGRAs measure the amount of interferon-gamma released in vitro by white blood cells when mixed with *M. tuberculosis* antigens or the number of T-lymphocytes producing interferon-gamma. A diagnosis of TBI needs to be complemented by a negative test outcome for TB disease, through clinical evaluation, chest radiography and examination of sputum or another suitable specimen if symptomatic, as per NTEP diagnostic algorithm.

Testing for TBI by TST or IGRA is not a requirement for initiating TPT in PLHIV or children aged < 5 years in contact with pulmonary* TB patients. In children HHC >5 years and adults, TST or IGRA testing would be offered wherever available. All efforts need to be made to ensure that TST or IGRA testing is made available. However, TPT must not be deferred in their absence. In other risk groups, TST or IGRA are to be performed for considering TPT after ruling out active TB, especially if the prevalence of TB among these risk groups is low. A positive test result by either of the two methods available is not by itself a reliable indicator that the person will progress to TB disease as the possibility of false positive results cannot be ruled out. Conversely, a negative test result does not rule out TBI, given the possibility of

a false-negative test result among at-risk groups, such as young children or among those recently infected.

3.3 Implementation considerations for testing services for TB infection

3.3.1 Tuberculin Skin Test (TST)

- Ensure availability and supply of tuberculin in cold chain as well as syringes, needles and consumables up to the health and wellness centre (HWC) and primary health centre level (PHC).
- Train health personnel in intradermal injections as well as reading and interpretation and provide ongoing capacity building and supportive supervision to maintain skill levels.
- Develop mechanisms to ensure standardized application of test procedures, mentoring and supervision and periodic standardized reliability testing for quality assurance.
- Establish mechanisms to call people who have been tested to return for the test reading within 48–72 hours of tuberculin administration, or alternatively ensure test reading at the person's residence.
- Update test request and results in the Prevent TB India app (later on TBI module of Nikshay whenever available) to enable documentation and reporting of TST results.

3.3.2 Interferon-Gamma Release Assay (IGRA)

- Develop capacity of the laboratory system and technicians to conduct IGRA (phlebotomy, processing of blood specimen, incubation and automated enzyme-linked immunosorbent assay (ELISA) reading).
- Establish mechanisms to ensure rapid transportation of blood specimens from peripheral centres to the IGRA testing laboratory (within 8–30 hours to allow incubation depending on type of IGRA test used).
- Ensure functioning of laboratory equipment and establish a mechanism for regular equipment maintenance for optimal functioning of the laboratory.
- Map out IGRA testing facilities available both in public and private sector in the state.
- The biggest potential for expansion of IGRA testing across India may be in collaboration with private sector labs, which may have blood collection facilities through their network of collection centres up to block levels and transportation arrangement for IGRA testing. This can be considered under the partnership options with funding through the national health mission (NHM) using established mechanisms of annual project implementation planning (PIP).
- Update test request and results in the Prevent TB India app (later on TBI module of Nikshay whenever available) to enable documentation and reporting of TST results.

States need to forecast requirements and procure requisite quantities of equipment and test kits with funding through the NHM annual PIP process either directly under the programme or preferably through rate contract mechanism or outsourced through the NTEP partnership options to purchase end to end services. This includes cost of specimen collection and tests leveraging their availability in the private laboratories across India.

Table 3.1 Comparison between TST and IGRA test

	TST	IGRA
Specificity	Low in BCG vaccinated	High also in BCG vaccinated
Sensitivity	High	High
Ease of use	Field friendly, complex test interpretation	Require labs and infrastructure
Cost of test	Low	High
Manufacturing	Complex old product	Complex, multiple components*
Special populations		
Children	Affected by young age	Affected by young age
PLHIV	Requires info on HIV status for correct interpretation	Affected by HIV and low CD4 count

* It may be suitable under partnership options where services are purchased from private labs

KEY POINTS TO REMEMBER

- ✓ The currently recommended and available tests for TBI are TST and IGRA. Either of these tests can be used for assessing TBI.
- ✓ Both TST & IGRA measure immune sensitization (type IV or delayed-type hypersensitivity) to mycobacterial protein antigens.
- ✓ States need to forecast the requirements and procure requisite quantities of equipment and test kits with funding through NHM annual PIP process, either directly under the programme or preferably through rate contract mechanism or outsourced through NTEP partnership options for purchase of end to end services. This includes cost of specimen collection and tests leveraging their availability in private laboratories across India.

CHAPTER 4:
ENUMERATING TARGET POPULATION, RULING OUT ACTIVE TB DISEASE & INITIATING TB PREVENTIVE TREATMENT

Learning Objectives

In this chapter we will learn about:

- Enumerating target population and contact tracing
- Algorithm for TB screening to rule out active TB
- Assessing eligibility, contraindications and providing TPT
- Counselling of TPT eligible persons and their families
- Pre-treatment assessment and TPT initiation

4.1 Enumerating target population and contact tracing

Enumerating and contact tracing/investigation of the target population is the first and most critical step for universal access and success of PMTPT. The complete list of PLHIV, HHC and other risk groups need to be available on a weekly basis with the concerned health-care provider at health facility (HF) (including health and wellness centres [HWC] & private providers [PPs]), TB Units(TU), integrated counselling and testing centres (ICTC) and anti-retroviral treatment (ART) centres and those health facility providers caring for other risk groups.

PLHIV detected and enrolled for ART can be enumerated at the ICTC and ART centres where screening and eligibility for TPT would be ascertained for this group of patients. The data for the enumeration and TPT coverage in PLHIV need to be updated on Prevent TB India app (detailed later) by the respective staff at the ICTC and ART centers. The TB Unit team (senior treatment supervisors [STS], TB health visitors [TBHVs]) is expected to regularly supervise and monitor this. Further, the DTO/DNO (district TB officer/district nodal officer) must regularly review the uptake and analyze the data to guide corrective actions.

Index TB patients are the pulmonary* TB patients detected through passive, intensified or ACF approaches and notified in Nikshay from the public and private sector. For enumerating the HHC of index pulmonary* TB patients, the first step is to enlist the index patients at every HWC and HF level. The index pulmonary* TB patients list must be downloaded from Nikshay for all notified pulmonary* TB patients including those notified from private sector and uploaded on the Prevent TB India app where the index patients data gets auto-populated and information for all HHC is entered and monitored by the concerned HWC and HF staff using Nikshay HF logins. However, this download and upload process would not be necessary once TBI module in Nikshay is developed and fully functional.

Contact tracing must be done during the initial home visit or virtual interaction through tele/video calls by health workers with family/close contacts for enumeration, counselling, screening and encouraging eligible HHC for TPT initiation at HWC or HF.

ACF rounds are an add-on to complement the contact tracing detailed above. During ACF rounds, mapping of these target populations must be an integral part of the vulnerability mapping for ACF activities already undertaken. Vulnerable groups considered for TPT in the state would be enumerated and entered into Prevent TB India app. Also, the HHC of pulmonary* TB patients detected during ACF rounds must be enumerated, traced, counselled and screened. As the index pulmonary* TB patients from ACF rounds are notified in Nikshay, their data management would follow the same steps as above for entering the information of the target population.

To enumerate the target population for other risk groups, the institutions providing care to the specific risk groups considered eligible for TPT within the states need to be mapped out and engaged systematically by every district and TB unit. The providers need to be trained in Guidelines for TPT and enumeration of the target population as well as their counselling, screening, TPT initiation, follow up and information management as well as monitoring of the TPT care cascade. All this should be done through the Prevent TB India app till TBI module in Nikshay is available and fully functional.

Enumeration and contact tracing/investigation of the target population needs to be proactively undertaken by the health-care workers at every HF (HWC, primary health centre [PHC]/ community health centre [CHC], private clinic, ICTC/ART centres and institutions providing care to the specific risk groups considered eligible for TPT) using the Prevent TB India app for information management and monitoring of the TPT care cascade.

4.2 Algorithm for TB screening and providing TPT in India

The following algorithmic approach would be used for PMTPT under the existing programmatic framework (Figure 4.1).

4.3 Assessing eligibility and providing TPT

Once the target population is enumerated and traced by the health-care worker either through home visit or virtually (tele/video call) or at the facility level, screening for the HRGs is initiated by first ascertaining their eligibility, contraindications and provision of TPT as per the algorithm given below.

4.3.1 People Living with HIV (Adults, Adolescents and Children)

All PLHIV/CLHIV should be screened for TB according to clinical algorithm. Those who do not report any of the symptoms of current cough, fever, weight loss or night sweats are unlikely to have active TB and should be offered preventive treatment, regardless of ART status. In addition to four symptom screening (current cough, fever, weight loss or night sweats), CXR need to be done to exclude any abnormal radiological findings suggestive of TB; CXR is however not mandatory and lack of CXR should not be a barrier for giving TPT. However, all efforts must be taken by the provider to get a CXR done including from the private sector.

Adults and adolescents living with HIV who are screened for TB according to a clinical algorithm and who report any of the four symptoms may have active TB and should be evaluated for TB and other diseases. TPT can be offered to those in whom TB disease is ruled out.

Infants (< 12 months) living with HIV who have poor weight gain, fever or current cough or who have a history of contact with a pulmonary* TB patient should be evaluated for TB and

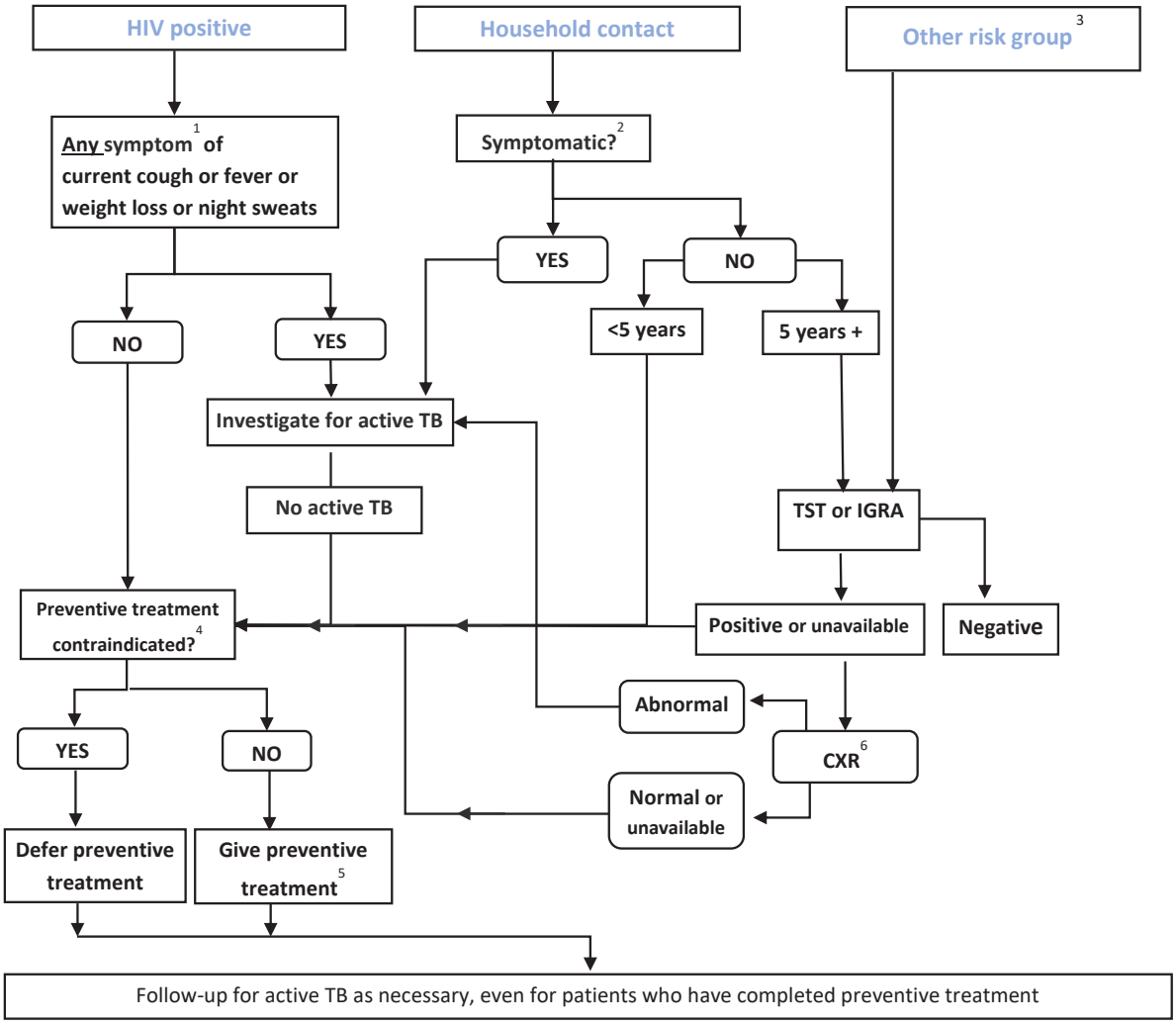


Figure 4.1 Algorithm for TB screening and TPT in India

1. *If <10 years, any one of current cough or fever or history of contact with TB or reported weight loss or confirmed weight loss >5% since last visit or growth curve flattening or weight for age <-2 Z-scores.*

   Asymptomatic infants <1 year with HIV are only treated for TBI if they are household contacts of TB. TST or IGRA may identify PLHIV who will benefit most from preventive treatment. Chest radiography (CXR) may be used in PLHIV on ART, before starting TPT.
2. *Any one of cough or fever or night sweats or haemoptysis or weight loss or chest pain or shortness of breath or fatigue. In children <5 years, they should also be free of anorexia, failure to thrive, not eating well, decreased activity or playfulness to be considered asymptomatic.*
3. *Including silicosis, dialysis, anti-TNF agent treatment, preparation for transplantation or other vulnerable risk groups where testing must precede before TPT.*
4. *Including acute or chronic hepatitis; peripheral neuropathy (if isoniazid is used); regular and heavy alcohol consumption. Pregnancy or a previous history of TB are not contraindications.*
5. *Regimen chosen based on considerations of age, strain (drug susceptible or otherwise), risk of toxicity, availability and preferences.*
6. *CXR may have been carried out earlier as part of intensified case finding.*

other diseases that cause such symptoms. If the evaluation shows no TB, these children should be offered TPT, irrespective of age.

Among PLHIV, all the above steps should be incorporated if differentiated HIV service delivery models are implemented. TPT should be an integral part of the care package for PLHIV.

4.3.2 All household contacts of pulmonary* TB patients

a. If they are symptomatic - investigate for TB and manage appropriately. Absence of any symptoms of TB and the absence of abnormal chest X-ray findings may be used to rule out active TB disease among HIV-negative HHC aged ≥ 5 years and other at-risk groups before considering TPT.
b. If they are not having any signs/ symptoms of TB, there are two scenarios
    i. Age <5 years. Rule out active TB and provide TPT; and
    ii. Age 5 years and more. Rule out active TB and provide TPT if TBI test (IGRA/TST) is positive or not available and if chest X-ray is normal or not available.

Screening for children and pregnant or breastfeeding women may be integrated into various entry points for care (such as maternal and child health, immunization, well baby clinics and nutrition clinics).

4.3.3 Expansion to other risk groups

In this group, testing with IGRA/TST must precede TPT and treatment given accordingly. The following need to be considered for ruling out TB:

a. All individuals should have active TB ruled out prior to considering TPT. A positive TBI test does not diagnose active TB;
b. All other HRGs should have a negative symptom screening to rule out active TB followed by appropriate diagnostic test for TBI and only receive TPT if TBI test is positive and CXR, if available, is normal and
c. If symptomatic or with an abnormal CXR, the patient should be evaluated for active TB as per existing guidelines and algorithms.

In all of the above situations, symptom screening among target population should be done at every visit to a health facility or contact with health worker. Chest X-ray wherever available must be done at baseline and as and when indicated during follow-up visits.

4.4 Contraindications for TPT

TPT is contraindicated in the following situations:

- Active TB disease
- Acute or chronic hepatitis
- Concurrent use of other hepatotoxic medications (such as nevirapine)
- Regular and heavy alcohol consumption
- Signs and symptoms of peripheral neuropathy like persistent tingling, numbness and burning sensation in the limbs
- Allergy or known hypersensitivity to any drugs being considered for TPT

Note

- Pregnancy or a previous history of TB are not contraindications for TPT; and
- Contact with drug resistant TB (DR-TB) cases have been dealt with in detail later in the corresponding chapter.

4.5 Counselling of TPT eligible persons and their family

Counselling is of paramount importance for TPT initiation and completion as most of the target population screened and found eligible would know that they do not have TB disease, would be symptom-free or otherwise healthy and would not feel the need to take any treatment, especially the HHC. The PLHIV and other risk groups do have some medical condition with counselling and medical advice for TPT being part of the routine service package for their existing conditions. However, counselling for TPT initiation and completion would be critical in all target populations, tailored to the target populations (PLHIV, HHC, other risk groups), for success of PMTPT as the information on TBI, need for TPT, schedule of medication collection, medication adherence support and follow-up visits, benefits from completing the course, adverse events, actions on development of TB symptoms need to be transparently shared with the eligible people and their families.

Counselling will be the prerogative of the health care workers (HWC & PHC staff for HHC, ICTC & ART counsellors for PLHIV, treating doctors/staff attending other risk groups and private providers/staff of private facilities for any of these target populations). The index TB patients and their family members would play an important role in synergizing with the efforts of the health-care workers to counsel and convince eligible people to initiate and complete the course of TPT. Similarly, community strengths need to be leveraged through the engagement of TB champions/survivors, community representatives, members of village health and sanitation (VHS) committees, peer groups of TB survivors and youth volunteers to synergize with the efforts of the health system to ensure TPT is accepted and completed under monitoring of the health system by the eligible people. The NTEP national call centre (NIKSHAY SAMPARK – Toll free number 1800116666) may be provided to index TB patients, those initiated on TPT and family members to serve as a resource for any time information, counselling and trouble-shooting as required to enable TPT initiation, follow-up monitoring and completion.

While counselling the person and family members, the treating doctors/staff must follow the steps below for an effective outcome of the counselling session:

- Ensure confidentiality when seeking a person's commitment to complete the course before initiating TPT;
- Ensure that the person understands the role of TPT regimen options and the duration required to complete for maximizing protection;
- Provide information materials in the local language and at the appropriate literacy level of the person concerned;
- Involve family members and caregivers in health education when possible. As children often move between households and health facilities; it may be helpful to include additional family members and caregivers in adherence support;
- Reinforce supportive educational messages at each contact during treatment;
- Give clear information regarding adverse drug reactions ("side-effects") and triggers on when to stop treatment and contact the health-care worker;
- Invite clarification questions and provide clear and simple answers; and
- Provide a telephone number of the HCW staff/TBHV and STS concerned to call for other queries or a need to contact health services for advice.

The following are the components of counselling for TPT:

- Explain to the individual that (s)he is eligible for TPT and provide key messages to the individual and her/his family/treatment supporter on:
  - rationale for TPT and protective benefits to the individual, the household and the wider community;
  - TPT being available free of charge under NTEP;
  - TPT regimen prescribed, including the duration, directions for intake of medicines and follow-up schedule;
  - potential side effects and adverse events involved and what to do in the event of various side effects;
  - the importance of completing the full course of TPT;
  - reasons and schedule of regular clinical and laboratory follow-up for treatment monitoring; and
  - signs and symptoms of TB and advise on steps if they develop them.
- Agree on the best approach to support treatment adherence, including the most suitable location for drug intake and treatment support based on each individual preference. Options may include:
  - Location. Home, community or health facility (with counselling support); and
  - Treatment supporter. Assess if a treatment supporter is needed or self-administration is possible. If a treatment supporter is needed, options may include a trained family member/ community volunteer/ workplace treatment partner or health-care workers. For a weekly regimen, it is preferable that intake of each dose is directly observed by the trained family member, community member, workplace treatment partner, or health-care workers (either in person or through a digital tool like tele/video calls and 99DOTS/ MERM).
- Explain the disease process and rationale for medication in the absence of symptoms or radiographic abnormalities.
- Review the importance of completing TPT.
- Discuss possible side effects of TPT medications that may include:
  - Fever, unexplained anorexia, brown urine (colour of coffee or cola), Icterus (yellowish discoloration of skin and eyes), rash, persistent paresthesia (abnormal sensations, numbness, pins and needle pricks) of hands and feet, persistent fatigue or weakness lasting 3 or more days, abdominal tenderness, especially in right upper quadrant, easy bruising or bleeding, arthralgia (joint pains), nausea & vomiting; and
  - Phone/mobile number of the HCW to be shared to enable urgent contact in case of any adverse event.
- Discuss Management of common side effects and need for self-monitoring and report to the concerned health-care provider.
  - The person on TPT should be educated about the likely adverse events and urged to contact the health-care provider if they develop events suggestive of drug toxicity in between visits;
  - Common ADRs are loss of appetite, persistent fatigue or weakness, abdominal discomfort, nausea, vomiting, dark-coloured urine, pale stools, rash or itching, yellowing skin or eyes, tingling or numbness in hands or feet).

- If a health worker cannot be consulted at the onset of such symptoms, the person on TPT should immediately call the community health officer (CHO) or HF doctor or Nikshay Sampark to seek advice; and
- People treated with rifamycins should be alerted in advance about the pink discoloration of secretions due to this medicine.

4.6 Pre-treatment assessment and TPT initiation

Once TB disease is ruled out, and decision to consider TPT is made, baseline assessment to determine the eligibility of an individual for TPT should be undertaken. The baseline assessment includes personal and medication history and investigations as per NTEP guidelines.

- **Personal history.** Elicit information relevant for TPT initiation and continuation, such as
  - allergy or known hypersensitivity to TB drugs (isoniazid, rifampicin, rifabutin or rifapentine).
  - HIV status and ART regimen;
  - pregnancy status or birth control method used; and
  - assess presence of co-morbidities (such as malnutrition, diabetes, liver disease and record medications being taken.
- **History of medication.** Elicit medication history to guide the choice of TPT regimen or determine the need for modification of treatment of co-morbid conditions. Certain drug classes – ARVs, opioids, antimalarials – often affect TPT.
- **Liver function test (LFT):** There is insufficient evidence to support mandatory or routine LFT at baseline, and perhaps the benefit of TPT without LFT would likely outweigh harms, particularly with less hepatotoxic regimen. However, where feasible, baseline testing is strongly encouraged for individuals having risk factors – such as history of liver disease, regular use of alcohol, chronic liver disease, HIV infection and pregnancy or immediate postpartum period (within 3 months of delivery). In individuals having abnormal baseline LFT results (ALT/AST is ≥ 3 times upper limit of normal [ULN] in the presence of symptoms or ≥ 5 times the ULN in the absence of symptoms), sound clinical judgement is required to determine that benefit of TPT outweighs the risks of adverse events related to the therapy. These individuals should be guided to report early signs of hepatic dysfunction like yellowish discoloration of skin/eyes and tested routinely at subsequent visits.
- **Social and financial situation.** Due assessment must be made of the person and the family along with the kind of support that would be required to overcome the barriers for TPT completion.

The doctor at the HF (including CHO) with support of their staff will assess every individual for their eligibility and contraindication for TPT based on the algorithm and pre-treatment evaluation above and have the prerogative of initiating the TPT regimen that suits the eligible individuals identified from the target population as well as their monitoring, management of any adverse events, declaring treatment outcomes and long-term follow up.

KEY POINTS TO REMEMBER

- ✓ Enumeration and contact tracing of target population needs to be proactively undertaken by the health-care providers at HWC, HF, ICTC/ART centres and the institutions providing care to the specific risk groups considered eligible for TPT using the Prevent TB India app for information management and monitoring of the TPT care cascade.
- ✓ Index TB patients are the pulmonary* TB patients detected through passive, intensified or ACF approaches and notified in Nikshay from the public and private sector.
- ✓ Asymptomatic infants <1 year with HIV are only treated for TBI if they are HHC of TB. The four symptoms used for screening of PLHIV consist of cough, fever, night sweat and weight loss. PLHIV who do not report any of the symptoms of current cough, fever, weight loss or night sweats are unlikely to have active TB and should be offered TPT, regardless of ART status.
- ✓ Frequency of symptom screening for the person on TPT is at every visit to health facility or contact with a health worker.
- ✓ Test for TBI is not required among PLHIV and contacts < 5 years of age.
- ✓ TPT should be offered irrespective of availability of TBI tests (IGRA/TST) or CXR.
- ✓ Contraindication to TPT includes, active TB disease, active hepatitis, peripheral neuropathy and regular and heavy alcohol consumption.
- ✓ Counselling for TPT includes Information on TBI, need for TPT, schedule of medication collection, medication adherence support and follow-up visits, benefits from importance of completing the course, adverse events, actions on development of TB symptoms or adverse events.
- ✓ Pre-treatment assessment for TPT initiation includes personal, social, financial and medication history as well as investigation as per the NTEP guidelines.
- ✓ TPT initiation, monitoring, management of ADRs, declaring treatment outcomes and long-term follow-up will be the responsibility of the doctor at HF (including CHO) with support of their staff.

CHAPTER 5:
TB PREVENTIVE TREATMENT

Learning Objectives

In this chapter we will learn about:

- Evidence on TPT
- TPT regimen with dosages
- Role of pyridoxine (Vitamin B6)
- Emergence of drug resistance following TPT

Over the past decades, Isoniazid preventive treatment (IPT) and chemoprophylaxis for six months (6H) has been the most widely used regimen under programmatic conditions among PLHIV and children < 5 years in contact with pulmonary* TB patients respectively. Several systematic reviews have consistently demonstrated the efficacy of IPT in preventing TB disease among those infected with *M. tuberculosis.* In recent years, globally the evidence on efficacy and safety of newer shorter TPT regimen has been growing and WHO has recommended multiple TPT options that are equivalent and increasingly the programme needs to move to shorter, safer and more effective regimens. Isoniazid based regimen will continue to have a role when rifamycins cannot be used e.g. in CLHIV.

5.1 Evidence on TPT regimen

5.1.1 Evidences for 3HP

- Clinical trial based evidence generated over the past two decades shows similar preventive efficacy with shorter rifamycin-based TPT regimen, both in HIV-positive and HIV-negative individuals, as monotherapy or in combination with isoniazid. The 3HP regimen was also associated with a higher completion rate in all subgroups (adults with HIV: RR 1.25, 95% CI 1.01; 1.55; adults without HIV: RR 1.19, 95% CI 1.16; 1.22; children and adolescents: RR 1.09, 95% CI 1.03; 1.15) *(11)*.
- Two of the RCTs involved adults with HIV from South Africa, Peru and a number of countries with a TB incidence <100/100,000 population. One RCT included a comparison between 3HP and continuous isoniazid monotherapy in adult PLHIV *(12).* No significant difference was found in the incidence of active TB between participants given a 3HP and 6H or 9H (RR 0.73, 95% CI 0.23; 2.30). Furthermore, the risk for hepatotoxicity was significantly lower with 3HP in adult PLHIV (RR 0.26, 95% CI 0.12; 0.55) and in those without HIV (RR 0.16, 95% CI 0.10; 0.27) *(12,13)*.
- Compared to 9H, it was observed that the 3HP has a better completion rate in a multicentre randomized controlled study in Taiwan *(14,15)*.

- A systematic review of adverse events of rifapentine and isoniazid compared to other treatments for latent tuberculosis infection (23 RCTs & 55 non-randomised studies) shows lower rate of AEs with 3HP *(16).*
- No significant difference in TB incidence was found in an intention-to-treat analysis; however, a per-protocol analysis showed a lower rate of TB infection or death in participants given continuous isoniazid. In all the studies, 3HP was given under direct observation *(17*).
- In a study of 3HP in 112 pregnant women, the rates of spontaneous abortion and birth defects were similar to those in the general population in the US *(18).*
- The clear advantages of these regimens are better adherence due to the shorter duration and fewer adverse events. The use of shorter rifamycin-based regimens is associated with at least 20% greater treatment completion rate (82% vs 61%). WHO recently assessed and recommended several shorter rifamycin-based regimens as alternatives to six months of isoniazid *(10*).

5.1.2 Evidence for 6H

- A systematic review of randomized control trials (RCTs) involving PLHIV in 2009 showed that IPT reduces overall risk for TB by 33% (RR 0.67; 95% CI 0.51;0.87), and the preventive efficacy reached 64% for people with a positive TST (RR 0.36; 95% CI 0.22;0.61). This review also demonstrated that the efficacy of the six-month regimen was not significantly different from that of a 12-month daily isoniazid monotherapy (RR 0.58; 95% CI 0.3;1.12) *(19).*
- A recent systematic review of RCTs showed a significantly greater reduction in TB incidence among participants given the six-month regimen than in those given a placebo (odds ratio 0.65; 95% CI 0.50;0.83) *(20).*

5.2 TB preventive treatment

The following TPT treatment options are recommended under NTEP once active TB has been ruled-out:

a. Expanded eligible group which includes children >5 years, adolescents and adult HHC of pulmonary* TB patients notified in Nikshay from public and private sector and regimen of choice for contacts of drug sensitive (DS) TB patients.

Target population	Treatment option
• People living with HIV (adults and children >12 months) • Infants <12 months in contact with active TB • HHC below 5 years of pulmonary* TB patients	• 6-months daily isoniazid (6H) • 3-month weekly Isoniazid and Rifapentine (3HP) in persons older than 2 years
• HHC 5 years and above of pulmonary* TB patients (testing would be offered whenever available)	• 3-month weekly Isoniazid and Rifapentine (3HP) • 6-months daily isoniazid (6H)

b. Other risk groups expansion

• Children/adult on immunosuppressive therapy, silicosis, anti-TNF treatment, dialysis, transplantation	• 3-month weekly Isoniazid and Rifapentine (3HP) • 6-months daily isoniazid (6H)

Until 3HP is widely available under the programme, all states must intensify the monitoring to saturate the TPT coverage in PLHIV and children < 5 years who are in contact with an index TB patient using 6H and move to 3HP whenever available. The states planning to roll-out TPT to the expanded risk groups in the immediate future, while awaiting 3HP availability under NTEP, 6H may be considered for use in the respective patient groups in consultation with NTEP. The choice of regimen will be guided by the availability of the drugs and tolerability profile of the eligible people.

Table 5.1: TPT regimen options and recommended dosages of medicines

Regimen	Dose by age and weight band					
6 months of daily isoniazid monotherapy (6H)	Age 10 years & older: 5 mg/kg/day[d] Age <10 years: 10 mg/kg/day (range, 7–15 mg)					
Three months of weekly rifapentine plus isoniazid (12 doses) (3HP)	**Age 2-14 years[c]**					
	Medicine, formulation	10–15 kg	16–23 kg	24–30 kg	31–34 kg	>34 kg
	Isoniazid, 100 mg[a]	3	5	6	7	7
	Rifapentine, 150 mg	2	3	4	5	5
	Isoniazid + rifapentine FDC (150 mg/150 mg)[b]	2	3	4	5	5
	Age >14 years[c]					
	Medicine, formulation	30–35 kg	36–45 kg	46–55 kg	56–70 kg	>70 kg
	Isoniazid, 300 mg	3	3	3	3	3
	Rifapentine, 150 mg	6	6	6	6	6
	Isoniazid + rifapentine FDC (300 mg/300 mg)[b]	3	3	3	3	3

a. 300 mg formulation can be used to reduce the pill burden

b. Expected to become available in the near future

c. Dosage may differ among adults and children in overlapping weight-bands

d. Maximum dose of H if given daily would be 300 mg/day

Table 5.2 Comparison of TB preventive treatment options

	6H	3HP
Medicines	Isoniazid	Isoniazid + rifapentine
Duration (months)	6	3
Interval	Daily	Weekly
Doses	182	12
Pill burden per dose (total number of pills for an average adult)	1 (182 pills)	9 pills with loose drugs (108 pills) 3 pills of FDC (36 pills)
Pregnant women	Safe for use	Not known
Interaction with ART	No restriction	Contraindicated: All PIs, NVP/NNRTIs, TAF Use: TDF, EFV (600 mg), DTG, RAL (without dose adjustment)

Toxicity	Hepatotoxicity (more), peripheral neuropathy, rash, gastrointestinal (GI) upset	Flu-like syndrome, hypersensitivity reactions, GI upset, orange dis-coloration of body fluids, rash, hepatotoxicity (less)
Absorption	Best absorbed on an empty stomach; up to 50% reduction in peak concentration with a fatty meal	Oral rifapentine bioavailability is 70% (not HP); peak concentration increased if given with a meal

5.2.1 Post-treatment TPT for PLHIV

In patients previously treated for TB, post-treatment TPT has been considered in view of the 5-7 times higher risk of recurrence of TB among PLHIV and nearly 90% of these due to re-infection *(11).* In addition to post-treatment TPT, ensuring completion of the initial course of TB treatment and effective infection control measures in clinical and community settings frequently visited by PLHIV would reduce recurrence of TB. Thus, all CLHIV/PLHIV who had successfully completed treatment for TB disease earlier should receive a course of TPT after completing treatment of TB.

5.3 Role of pyridoxine and its availability

Peripheral neuropathy that develops secondary to a deficiency of vitamin B6 (pyridoxine) during TB treatment, occurs infrequently among patients taking standard doses of H for TPT. It is easily recognized (as symmetrical numbness and tingling of the extremities) and usually easily reversible upon withdrawal of H and giving high-dose pyridoxine therapeutic dose (100–200mg/day).

Individuals at risk for peripheral neuropathy, such as those with malnutrition, chronic alcohol dependence, HIV infection, renal failure or diabetes, or who are pregnant or breastfeeding, should receive vitamin B6 supplements when taking H-containing regimen. The standard dose of pyridoxine when used prophylactically for prevention of neuropathy among patients taking isoniazid is 10 mg/day in children and 25 mg/day in adults. In adult PLHIV, the dose would be 50 mg/day (17).

TPT should not be withheld if pyridoxine is not available. Alternatively, the multi-vitamin/B-complex formulations with the requisite prophylactic dose of pyridoxin available within the general health system may be considered. If pyridoxine/multi-vitamins/B-complex are in short supply it may be restricted to those at highest risk, like the severely malnourished and people with problem alcohol use. Close monitoring for peripheral neuropathy during treatment would be important to start treatment early at the appropriate dose.

5.4 Emergence of drug resistance following TPT

There is no evidence of significant association between development of resistance to H or R with use of these drugs for TPT. However, TB disease must be ruled out before TPT is initiated, along with regular follow-up to rule out development of active TB disease. Rapid molecular DST must be offered to all patients if TB disease is detected before, during or any time post TPT.

KEY POINTS TO REMEMBER

- ✓ Preventive efficacy with shorter rifamycin-based TPT regimen, both in HIV-positive and HIV-negative individuals are similar as monotherapy or in combination with isoniazid with clear advantages of better adherence due to the shorter duration, fewer adverse events and at least 20% greater treatment completion rate.
- ✓ Isoniazid based regimen will continue to have a role when rifamycins cannot be used e.g. in CLHIV
- ✓ Treatment options recommended for TPT once active TB has been excluded under NTEP include 6H and 3HP with weight band wise doses suggested with specific applicability to various target populations.
- ✓ All CLHIV/PLHIV who had successfully completed treatment for TB disease earlier should receive a course of post-treatment TPT.
- ✓ The standard dose of pyridoxine when used prophylactically for prevention of neuropathy among patients taking isoniazid is 10 mg/day in children and 25 mg/day in adults. In adult PLHIV, the dose would be 50 mg/day.
- ✓ TPT should not be withheld if pyridoxine is not available. Alternatively, multi-vitamins/ B-complex formulations with the requisite prophylactic dose of pyridoxin available within the general health system may be considered.
- ✓ There is no evidence of significant association between development of bacterial resistance to TB drugs and use of isoniazid or rifamycin for TPT.

CHAPTER 6:
ADVERSE EVENTS

Learning Objectives

In this chapter we will learn about:

- Possible adverse events
- ADRs of Isoniazid & Rifamycins
- Managing adverse events
- Drug–drug interactions

It is critical to identify any sign of drug toxicity early on and manage it vigorously, particularly among people who are usually healthy. As with any preventive action, the health-care provider must weigh the risks and benefits of TPT for every individual. Obtaining a detailed and accurate medical history (inclusive of medicines being taken and known past adverse drug reactions) and keeping up-to-date information at every contact with the person on TPT, can help identify persons who require close monitoring and the most appropriate course of action if an adverse event emerges. Individuals receiving TPT should also be monitored regularly through scheduled visits and active drug safety management and monitoring (aDSM) system existing under NTEP.

6.1 Potential adverse event

As part of initial counselling, the health worker should explain the rationale for TPT, importance of completing the course and re-emphasize the risk associated with TB disease. The person on TPT should also be educated about the likely adverse events and urged to contact the health-care provider if they develop events suggestive of drug toxicity in between visits (such as loss of appetite, persistent fatigue or weakness, abdominal discomfort, nausea, vomiting, dark-coloured urine, pale stools, rash or itching, yellowing skin or eyes, tingling or numbness in hands or feet). If a health worker cannot be consulted at the onset of such symptoms, the person on TPT should immediately call the doctor (or CHO) or Nikshay Sampark to seek advice. People treated with rifamycins should be alerted in advance about the pink discoloration of secretions due to this medicine. Table 6.1 summarizes known adverse events associated with currently used TPT drugs.

Table 6.1 Possible adverse events associated with TPT drugs

Drug	Known adverse events	Rare adverse events
Isoniazid	• Asymptomatic elevation of serum liver enzyme concentrations • Hepatitis • Peripheral neuropathy (paraesthesia, numbness and limb pain) • Skin rash • Sleepiness and lethargy	• Convulsions • Pellagra • Arthralgia • Anaemia • Lupoid reactions
Rifampicin	• Gastrointestinal reactions (abdominal pain, nausea, vomiting) • Hepatitis • Generalized cutaneous reactions • Thrombocytopenic purpura • Discoloration of body fluids	• Osteomalacia • Pseudomembranous colitis • Pseudoadrenal crisis • Acute renal failure • Shock • Haemolytic anaemia • Flu-like syndrome
Rifapentine	• Gastrointestinal reactions (abdominal pain, nausea, vomiting) • Hypersensitivity reactions (flu-like symptoms) • Hepatitis • Discoloration of body fluids	• Hypotension/syncope • Decrease in white blood cell and red blood cell count • Decreased appetite • Hyperbilirubinemia

6.2 Management of adverse events

Individuals receiving TPT are otherwise healthy, and therefore adverse events during TPT must be minimized and promptly managed. If a severe adverse reaction is encountered, TPT must be immediately discontinued, and supportive medical care provided. Conservative management and continuation under observation can be considered in the presence of mild-to-moderate adverse events as determined by the health care provider.

People experiencing adverse events may need medical attention and doctor's discretion should be exercised for management. A complete history, including concomitant medication and supplements, must be taken. The following questions may help in the assessment and in deciding actions for management of adverse events:

1. How severe is the adverse event (mild, moderate, severe)?
2. How serious is the event (i.e. hospitalization or prolongation of hospitalization; persistent significant disability; congenital anomaly, a life-threatening experience or likely to lead to death)?
3. What is the immediate management (reassurance, symptomatic relief, hold/discontinue TPT, or requires a medical intervention to avert severe outcomes)?
4. What is the underlying cause (drug related, other factors)?
5. How will the adverse event affect future adherence (tolerability, consideration of substitution with an alternative regimen)?
6. What is the next step (continue or restart, substitute, follow up and reassess)?

The management of the adverse drug reactions depends on the type of drugs being used.

- **Drug-induced hepatitis.** Features that indicate the need to stop medication include transient, asymptomatic increase in serum liver transaminases (≥3 times ULN that occur during the early weeks of treatment. There is no need to interrupt or change treatment unless there is anorexia, malaise, vomiting or clinically evident jaundice.
- **Clinical features of concern include protracted vomiting, mental changes and signs of bleeding.** All of this suggest impending acute liver failure and require immediate discontinuation of medication and referral to a health facility for further management.
- **Management of jaundice and other severe features.** If jaundice or any of the clinical features like yellowish discoloration of skin and eyes, pale stools, dark urine suggestive of acute liver failure develop or elevation of serum transaminases (e.g. ALT/AST ≥5 times ULN or ≥3 times ULN with symptoms), all drugs must be stopped until jaundice or hepatic symptoms have resolved, and liver enzymes have returned to baseline levels. If liver enzymes cannot be measured, it is advisable to wait for two weeks after the jaundice has disappeared before starting TPT. Other causes of hepatitis must be explored.

  Where reintroduction is concerned, once hepatitis has resolved, the same drug regimen can be reintroduced, either gradually or all at once ("re-challenge"). However, if hepatitis has been life-threatening and was unlikely to have been caused by something else (such as alcohol, viral infection), it is probably safer to switch to an alternative regimen.
- **Skin reactions itching with no rash or with a mild rash.** Symptomatic treatment with antihistamines may be tried and TPT continued.
  - Itching with moderate/severe rash. If the rash is severe, or there is evidence of mucosal involvement, hypotension or severe illness, corticosteroid treatment should be considered. Oral prednisolone (40–60 mg) should be given daily until there is a response and the dose should then be reduced gradually in the following days according to the clinical response. TPT should be withheld until the reaction has completely subsided. If the initial cutaneous reaction was severe, the full dose may be ramped up with smaller initial challenge doses. If a severe reaction occurs, the suspected medicine should not be given again and an alternative regimen may be considered.
  - Isoniazid-associated pellagra. Persons with isoniazid-associated pellagra who discontinue isoniazid and receive high-dose nicotinamide (a form of vitamin B3) treatment can fully recover, however pellagra may result in severe illness or death if untreated. The recommended treatment for pellagra is 300 mg of nicotinamide daily for three to four weeks. Good dietary sources of vitamin B3 are similar to those for vitamin B6 in consultation with a dietician.
- **Peripheral neuropathy.** To prevent peripheral neuropathy, administer daily dose of vitamin B6 (pyridoxine), or multi-vitamins/B complex to people at risk at a dose of 10 mg/day in children and 25 mg/day in adults. In adult PLHIV, the dose would be 50 mg/day. For established peripheral neuropathy, pyridoxine should be given at a larger dose of 100–200 mg daily.
- **Gastrointestinal reactions with rifampicin (abdominal pain, nausea, vomiting).** If symptoms are mild, the episode is usually self-limiting and reassurance may suffice. If gastrointestinal intolerance is severe enough to risk interruption of treatment, suspend rifampicin for three or four doses, use medications that provide symptomatic relief (such as metoclopramide to counteract vomiting), or as a last resort give rifampicin with small amounts of food to allow continued use of the medicine. Although concomitant ingestion of food reduces the absorption of rifampicin slightly, this is preferable over the risk of complete discontinuation of rifampicin.

- **Lethargy.** Reassure the person.
- **Discoloration of body secretions (urine, tears, semen and sweat) red or orange.** Reassurance.

Table 6.2 below explains the methodology to be adopted for the management of potential adverse reactions with 3HP. Most adverse drug events associated with HP regimens are mild, self-resolving and without sequelae.

Table 6.2 Reintroduction of TPT drugs while managing AE

Adverse event	Stop and consider reintroduction with caution	Stop and do not reintroduce
Flu-like syndrome (attacks of fever, chills and malaise, sometimes with headache, dizziness or bone pain)	If mild and not increasing, continue treatment and observe closely	If moderate to severe symptoms, consider alternative TPT options without a rifamycin (such as 6H)
Drug-associated fever only	Consider reintroduction if fever settles below 39°C, but stop permanently if fever recurs	If fever > 39°C after previous episode of drug-associated fever
Persistent nausea, frequent vomiting and/or persistent episodes of unformed watery stools	Administer antiemetic or anti diarrhoeal medication Consider reintroducing 3HP with caution once the symptoms have resolved	If there is nausea, vomiting or diarrhoea which requires aggressive rehydration
Cutaneous reactions	Diffuse rash (no vesicles) Diffuse rash with limited vesicles	If there are extensive bullous lesions/ulceration of mucous membranes/Stevens Johnson or toxic epidermal necrolysis, contact a specialist and use steroids
Other hypersensitivity reactions (hypotension, acute bronchospasm, conjunctivitis, thrombocytopenia)	Assess the clinical severity of the symptoms and if severe consider alternative TPT options without a rifamycin (6H)	
Hepatitis (early symptoms weakness, fatigue, loss of appetite, persistent nausea)	Alanine aminotransferase (ALT)/ aspartate aminotransferase (AST) < 5 times the upper limits of normal and absence of symptoms	ALT/AST >5 times (Upper limit of normal in the absence of symptoms) ALT/AST is ≥ 3 times (the upper limit of normal in the presence of symptoms)
Psychosis	Psychiatric evaluation, antipsychotic therapy, pyridoxine	Attributable to isoniazid
Seizures	Withhold isoniazid pending resolution of seizures, evaluate possible causes of seizures	Attributable to isoniazid

Note-

- Rifamycins are potent enzyme inducers and any side-effects should be assessed and managed together with potential drug–drug interactions
- LFTs prior to initiating TPT are not routinely indicated. Baseline and follow-up LFTs are only needed when there is a defined risk, such as pre-existing liver dysfunction, liver cirrhosis or other indications.

6.3 Drug-drug interactions with TPT drugs

The potential drug-drug interactions with drugs in TPT regimen are detailed in table 6.3

Table 6.3 Common drug–drug interactions of isoniazid and rifamycins (17)

Medication class	Drugs	Isoniazid inhibits metabolism and increases blood levels	Rifamycins accelerate metabolism and decrease blood levels
Antiarrhythmics	Disopyramide/ mexiletine/ quinidine/ tocainide		↓
Antibiotics	Chloramphenicol/ clarithromycin/ dapsone/ doxycycline/ fluoroquinolones		↓
Anticoagulants	Warfarin	↑	↓
Anticonvulsants	Phenytoin	↑ (Phenytoin, carbamazepine, primidone, valproic acid)	↓
Antidepressants	Amitriptyline/ nortriptyline	↑Some SSRI (selective serotonin reuptake inhibitors)	↓
Antimalarials		↑Halofantrine	↓Quinine
Antipsychotics	Haloperidol	↑	↓
Antivirals		↑Ritonavir (ARV) ↑Efavirenz	↓PI, INSTI ↓Nevirapine with rifampicin
Azole antifungals	Fluconazole/ itraconazole/ ketoconazole	↑	↓
Barbiturates	Phenobarbital		↓
Benzodiazepines	Diazepam	↑Diazepam, triazolam	↓
Beta-blockers	Propranolol		↓
Cardiac glycoside preparations	Digoxin		↓
Corticosteroids	Prednisone		↓
Fibrates	Clofibrate		↓
Oral hypoglycaemic agents	Sulfonylureas		↓
Hormonal contraceptives/ progestins	Ethinyl oestradiol/ levonorgestrel		↓ (Rifapentine)
immunosuppressants	Cyclosporine/ tacrolimus		↓

Medication class	Drugs	Isoniazid inhibits metabolism and increases blood levels	Rifamycins accelerate metabolism and decrease blood levels
Methylxanthines	Theophylline	↑	↓
Narcotic analgesics	Methadone	↑Levomethyldate acetate	↓
Phosphodiesterase-5 (PDE-5) Inhibitors	Sildenafil		↓
Thyroid preparations	Levothyroxine		↓

Rifampicin is contraindicated, or should be used with caution, in HIV-infected individuals being treated with certain antiretroviral medications. Substitution of rifabutin for rifampicin in the 4-month regimen many be considered for such patients. Rifapentine should not be used in HIV-infected persons taking antiretroviral medications that have clinically significant or unknown drug interactions with it.

KEY POINTS TO REMEMBER

- ✓ Most adverse drug events associated with HP regimens are mild, self-resolving and without sequelae.
- ✓ Co-administration of commonly used ARVs with TPT regimens 6H and 3HP is safe, and alternatives are available when low ARV exposure is suspected due to drug–drug interaction.
- ✓ Caution is required when an individual receiving TPT is also on treatment for a co-morbidity.
- ✓ Rifamycins are potent enzyme inducers and any side-effects should be assessed and managed together with potential drug–drug interactions. Women on hormonal contraceptives should use an additional barrier contraceptive to avoid pregnancy when using rifamycin-based TPT.
- ✓ LFTs prior to initiating TPT are not routinely indicated. Baseline and follow-up LFTs are only needed when there is a defined risk, such as pre-existing liver disease, regular use of alcohol, HIV infection and pregnancy or immediate postpartum period (within 3 months of delivery) or if a patients reports with signs and symptoms (e.g. yellowish discoloration) of hepatic dysfunction while on TPT.

CHAPTER 7:
SPECIAL SITUATIONS

Learning Objectives

In this chapter we will learn about:

- Women
- Liver disease
- Renal failure
- People living with HIV
- Babies born to mothers with TB disease
- People who use drugs

7.1 Women

Pregnancy should not disqualify women living with or without HIV who are eligible for receiving TPT. TPT can be started during antenatal and postnatal periods taking due care. Pregnant women living with HIV are at higher risk for TB during pregnancy and postpartum period and can have worse prognosis for both mother and child. Isoniazid and Rifampicin, are considered safe for use in pregnancy. There is no evidence to show an association of TPT (6H) with adverse pregnancy outcomes like foetal/neonatal death, prematurity, low birth weight or any congenital anomaly. Statistically, no significant risks for maternal hepatotoxicity, grade 3 or 4 events or deaths were reported. Therefore, routine LFT can be done as per advice of the treating physician. Pyridoxine (Vitamin B6) supplementation should be given routinely to all pregnant and breastfeeding women on TPT. There is limited data on the efficacy and safety of rifapentine in pregnancy and therefore 1HP and 3HP should not be used in pregnancy until more safety data is available.

Rifampicin and rifapentine interact with oral and hormonal contraceptive medications with a potential risk of decreased contraceptive efficacy. Women receiving oral contraceptives while on rifampicin or rifapentine should use an alternative (such as depot medroxyprogesterone acetate (DMPA) every eighth week or higher dose oestrogen (50µ)) in consultation with a clinician; or use another form of contraception, a barrier contraceptive or intrauterine device. In women having hormonal contraceptive implants, the interval for replacing the implants may need to be shortened from 12 weeks to eight weeks *(23)*.

7.2 Liver disease

Isoniazid and rifampicin/rifapentine are associated with liver damage. TPT should be initiated with caution among individuals whose baseline liver transaminase values are available and ≥3 times the ULN. TPT should not be given to individuals with end-stage liver disease.

However, it is known that 6H is well-tolerated among individuals with chronic hepatitis B virus (HBV) or hepatitis C virus (HCV) infections. In acute hepatitis (including acute viral hepatitis), defer TPT until the acute hepatitis has resolved.

Rifamycins including rifapentine, are not recommended for use together with many of the direct-acting ARV drugs used to treat HCV, since rifamycins can decrease the concentration of HCV drugs to subtherapeutic levels. People with HCV infection should consult with their health-care providers and start rifamycin-based TPT either before or after completing treatment for HCV.

7.3 Renal failure

Isoniazid and rifampicin/rifapentine are eliminated by biliary excretion. These drugs, therefore, can be given in standard dosages to individuals with renal failure. Persons with severe renal failure should receive isoniazid with pyridoxine (vitamin B6) to prevent peripheral neuropathy.

7.4 People living with HIV

A key challenge in TPT with rifamycin-based regimen among PLHIV is drug–drug interaction. While rifampicin and rifapentine can be co-administered with efavirenz without dose adjustment, in PLHIV receiving raltegravir and rifampicin, a higher dosage of raltegravir (800 mg twice daily) should be used. Rifampicin or rifapentine TPT regimens should not be co-administered with protease inhibitors (atazanavir/ ritonavir, lopinavir /ritonavir) or nevirapine.

7.5 Babies born to mothers with TB disease

If a newborn is not well, it is important to refer him/her to a specialist/pediatrician. It is critical that the mother receives effective TB treatment so that she is no longer infectious. Also, ensure that infection control measures are in place in the facility, especially if the baby is in an inpatient facility for care when preterm or small at birth. If the newborn is well (absence of any signs or symptoms presumptive of TB) TPT must be provided. Experts in India recommend that the Bacille Calmette-Guérin (BCG) vaccination should not be delayed even if TPT is administered. Further, it is advised to administer pyridoxine at 5–10 mg/day. If the infant is HIV-exposed (mother is HIV infected) and on nevirapine, 6H should be started. TPT with 4R and 3HP cannot be given along with nevirapine prophylaxis since rifamycins decrease nevirapine levels and may result in increased mother-to-child transmission of HIV. If the mother is taking anti-TB drugs, she can safely continue to breastfeed with appropriate practice like using a mask and cough etiquette. Mother and baby should stay together and the baby may be breastfed while on TPT. Infant breastfeeding from a mother on either TB treatment or TPT should receive pyridoxine for the duration of the mother's treatment.

7.6 TPT among people who use drugs

People who use drugs (PWUD) have a higher prevalence of TBI and incidence of TB disease. Rifapentine has not been systematically studied among people who use drugs. However, rifampicin is known to reduce exposure to opioid substitution therapies (OST) such as methadone and buprenorphine. In some people, this results in opiate withdrawal. For this reason, people taking 3HP or 4R with OST should be closely monitored for signs of opiate withdrawal and other adverse events. Increasing the dose of methadone or buprenorphine

when taking rifamycins can lessen the risk of withdrawal. 6H is safe to use among PWUD, although careful monitoring for liver toxicity is important. Drug use should never be taken as a blanket rationale for denying someone TPT. It is the responsibility of health-care providers to proactively manage drug–drug interactions for PWUD safely.

KEY POINTS TO REMEMBER

- ✓ Pregnancy should not disqualify women living with or without HIV who are eligible for receiving TPT.
- ✓ Isoniazid and Rifampicin, are considered safe for use in pregnancy.
- ✓ There is limited data on the efficacy and safety of rifapentine in pregnancy and therefore 1HP and 3HP should not be used in pregnancy until more safety data is available.
- ✓ Rifampicin and rifapentine interact with oral and hormonal contraceptive medications with a potential risk of decreased contraceptive efficacy.
- ✓ Isoniazid and rifampicin/rifapentine are associated with liver damage.
- ✓ Rifampicin or rifapentine TPT regimens should not be co-administered with protease inhibitors or nevirapine.
- ✓ The Bacille Calmette-Guérin (BCG) vaccination should not be delayed even if TPT is administered.
- ✓ Rifamycins can decrease the concentration of HCV drugs to subtherapeutic levels.
- ✓ People taking Rifamycin based regimen with OST should be closely monitored for signs of opiate withdrawal and other adverse events.

CHAPTER 8: PREVENTIVE TREATMENT IN DR-TB CONTACTS

Learning Objectives

In this chapter we will learn about:

- Rationale and evidence
- Integrated algorithm for screening and ruling out active TB among HHC of DR-TB patients
- Policy on TPT for DR-TB contacts in India
- Treatment, drug dosages, adherence and follow-up
- Managing ADRs and referring to DR-TB centres

8.1 Rationale & evidences

Multidrug-resistant TB (MDR-TB) is a serious form of TB and is less easy to treat than other types of TB disease. Mathematical modelling suggests 3 in every 1000 people globally carry MDR tuberculosis infection. Also, prevalence of MDR *M tuberculosis* in those with TBI is more than double among those younger than 15 years *(24)*.

HHC of patients with MDR/RR-TB or H mono-resistance are at higher risk of TBI than contacts exposed to drug-sensitive TB, however the risk of progression to TB disease does not differ among contacts in both groups *(17).*

Recent evidence from systematic review & meta-analysis, and cost-effectiveness of treatment of latent tuberculosis to reduce progression to multidrug-resistant tuberculosis *(25)* revealed

- a reduced risk of TB incidence with treatment for MDR-TBI, suggesting effectiveness in prevention of progression to MDR-TB, and confirmed cost-effectiveness;
- estimated MDR-TB incidence reduction was 90% (9%-99%) using data from five comparison studies;
- high treatment discontinuation rates due to adverse effects in persons taking pyrazinamide-containing regimens; and
- cost-effectiveness was greatest using a fluoroquinolone/ethambutol combination regimen.

The rationale for four-month daily rifampicin (4R) in contacts of H resistant R sensitive DR-TB patients is that R has an excellent efficacy and safety profile compared to H and the cost is lower than rifapentine. This regimen is useful to give to contacts of people with bacteriologically confirmed isoniazid-resistant, rifampicin-sensitive TB disease (Hr-TB). One of the main challenges with 4R however may be to deal with the perception that R needs to be protected for use as a first-line TB medicine and concerns that its use in TPT may increase levels of R resistance in the community or promote misuse of the agent as monotherapy for TB disease. There is however no evidence till date demonstrating the significant increase in R

resistance levels due to scale-up of TPT services *(17)*. Other challenges to consider are: drug–drug interactions with ARVs (refer to the section on drug–drug interactions). Child-friendly formulations are not available currently, and the supply of single dose formulations may be limited due to widespread availability of FDCs of first-line TB treatment. However, studies have shown that in adults, 4R has been shown to be safer (lower frequency of grade 3 or 4 hepatotoxicity) and to have better adherence rate than 9H. Also, inadequately powered TB prevention trials involving adults, 3R was found to be non-inferior to 6H and 3HP was found to be noninferior to 9H. In the study (26), 829 children were randomly assigned to receive 9H or 4R, with drugs administered by the participants or their caretakers. Of these children, 79 were under the age of 2 years, an age group with the highest risk of life-threatening TB disease. No significant safety concerns were identified with either regimen, but the R group had better treatment-completion rates.

8.1.1 WHO recommendations on TPT among contacts of DR-TB patients

WHO recommends TPT among contacts exposed to MDR-TB with FQ sensitive or H resistant with R sensitive DR-TB patients following consideration of intensity of exposure; confirming the source patient and her/his drug resistance pattern confirmed bacteriologically and ascertaining TBI using IGRA or TST.

Among contacts exposed to patients with known MDR-TB with FQ sensitive, WHO suggests the use of levofloxacin for six months (paediatric formulation for child contacts) if tolerated. If H susceptibility is confirmed in RR-TB index patients, contacts may be given 6H. Among contacts exposed to individuals with known H-resistant TB with R sensitive, the use of rifampicin for four months is proposed. Regardless of whether treatment is given or not, clinical follow-up should be done for two years and any emergent signs and symptoms suggestive of TB should be actively investigated and curative regimens started as needed.

8.1.2 Studies in the pipeline

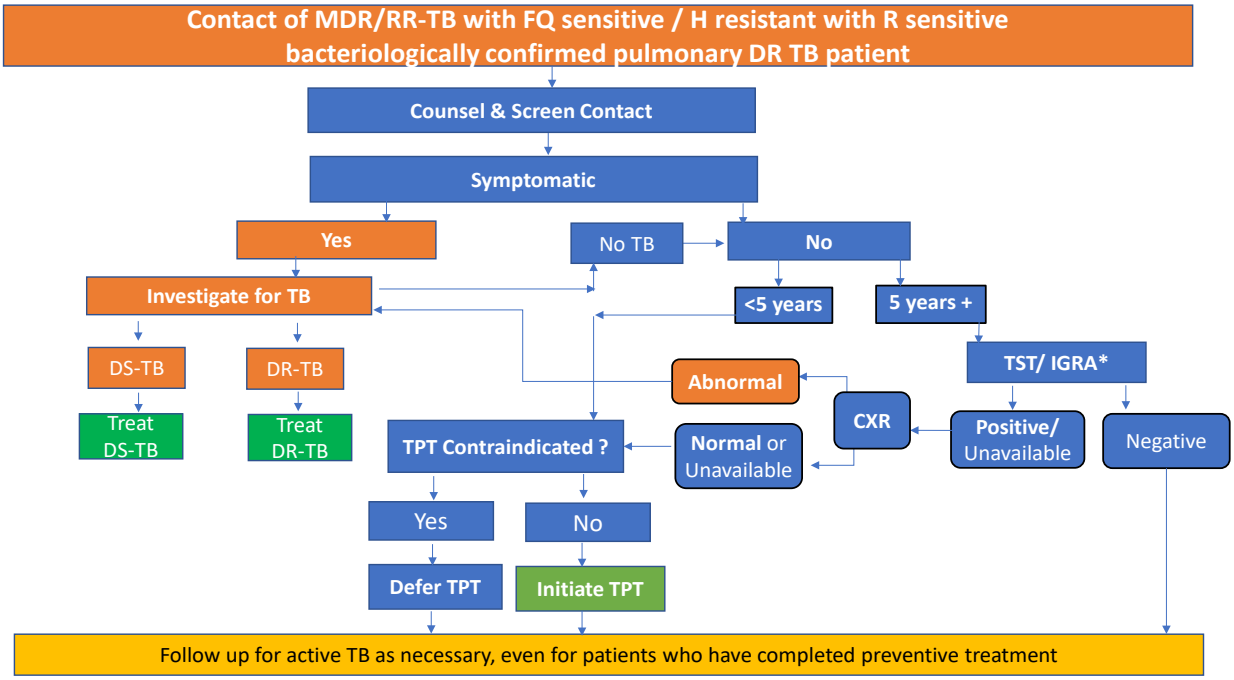
Randomized controlled trials on MDR-TB preventive treatment are urgently needed to improve the evidence base. Results from following three RCTs of TPT among HHC of MDR-TB patients are expected to become available in the next few years:

- **TB CHAMP.** Testing six months of levofloxacin (Lfx) vs placebo in infants and young children less than five years of age exposed to MDR-TB (South Africa; ongoing recruitment and intending to publish by end 2021);
- **V-QUIN.** Testing 24 weeks of Lfx vs placebo in all ages with evidence of infection (Viet Nam; recruitment completed; date of ending data collection is March 2022); and
- **PHOENIx.** Testing 26 weeks of delamanid vs isoniazid in all ages (11 countries; estimated completion in mid-2025).

8.2 Integrated algorithm for screening and ruling out active TB among household contacts of DR-TB patients

The integrated algorithm for screening and ruling out active TB among HHC of DR-TB patients is detailed in Figure 8.1 below. It is critical to know the DST pattern of the index DR-TB patients to guide the TPT regimen choice in those found eligible to received TPT for among DR-TB contacts.

Footnotes for the algorithm for TB screening and TPT in India for DS-TB (Figure 4.1) would apply.



*whenever available

Figure 8.1 Integrated algorithm for screening and ruling out active TB among HHC of DR-TB patients

The following are the salient features of the integrated algorithm:

- Once a DR-TB patient has been identified, all household contacts are counselled, screened and evaluated to rule out active TB;
- NAAT is used upfront among contacts with symptoms or abnormal chest X-ray to diagnose TB;
- If the result is MTB detected with no resistance, the treatment for DS-TB is initiated;
- If the result is MTB detected with H and/or R resistance, manage as per DR-TB guidelines;
- If the result is MTB not detected, in HHC <5 years, assess for TPT and check for any contraindications;
- If the result is MTB not detected, in HHC >5 years of age with TBI test positive or unavailable and chest X-ray is normal or unavailable check for any contraindications;
- If contraindications to TPT drugs exists, defer TPT and if no contraindication exists, offer TPT regimen as appropriated based on DST pattern of the index patient; and
- Follow-up for active TB as necessary, even for patients who have completed preventive treatment irrespective of TPT offer.

8.3 Policy for TPT in DR-TB contacts in India

Preventive treatment among HHC of MDR-TB index patients (in whom FQ resistance has been ruled out) and among HHC of H resistant index patients (in whom R resistance has been ruled out), the target population, using 6Lfx and 4R respectively to be introduced in a phased manner for all age groups to gain programmatic experience to guide future expansion while awaiting results of ongoing studies. This recommendation may be considered for children given their special needs pan India.

8.4 Treatment, drug dosages, adherence and follow-up

The recommended dosages of medicines for TB preventive treatment among contacts of DR-TB index patients after ruling out active TB and testing for TBI by age and weight are given in table 8.1 below.

Table 8.1: TPT regimen options and recommended dosages of medicines for contacts of DR-TB index patients

Regimen	Dose by age and weight band
Six months of daily levofloxacin (6Lfx) for contacts of R resistant FQ sensitive patients[#]	Age > 14 years, by body weight: < 45 kg, 750 mg/day; ≥ 45 kg, 1g/day Age < 15 years (range approx. 15–20 mg/kg/day), by body weight: 5–9 kg: 150 mg/day 10–15 kg: 200–300mg/day 16–23 kg: 300–400mg/day 24–34 kg: 500–750mg/day
Four months of rifampicin daily (4R) for contacts of H resistant R sensitive patients*	Age 10 years & older: 10 mg/kg/day[@] Age <10 years: 15 mg/kg/day (range, 10–20 mg)

[#] Levofloxacin 100 mg dispersible tablets available for children. Children receiving 6Lfx should be watched for joint abnormalities.

* In children from 0-14 years, 4R should only be used after ruling out active TB in limited geographies/ populations for evidence generation to guide future scale up for country wide implementation.

[@] *Maximum dose of R would be 600 mg/day.*

Note: 6H can be considered as the TPT regimen option for contacts of index patients with RR-TB with FQ and H sensitive, after ruling out active TB in them.

Once TPT is initiated, the individuals will be monitored by the medical officer for clinical and laboratory parameters as below.

- Screening with 4S symptoms (cough, fever, night sweats and weight loss);
- Any side effects;
- If any of the sign/ symptoms of TB emerge, the person may be referred to the DR-TB centre for further evaluation for active TB/DR-TB disease; and
- In the above case the person may be subjected to NAAT & LPA for diagnosis of TB & DR-TB and appropriately managed if found to have developed active TB/DR-TB disease.

Develop a personal adherence plan with the support of a family member, caregiver or health worker as per treatment regimen being provided. Give first preference to the family member to be the treatment provider in consultation with the person. Use of digital platforms (tele/ video calls, 99DOTS/MERM), counting empty blisters, refill monitoring etc., to strengthen adherence monitoring.

Adherence to the TPT course and treatment completion are important determinants of clinical benefit, both at individual and population levels. Irregular or inadequate treatment reduces the protective efficacy of the TPT regimen. Poor adherence or early cessation of TPT can potentially increase the risk of the individual developing TB including drug-resistant TB (although not supported by existing evidence from research settings). It is known that

the efficacy of TPT is greatest if at least 80% of the doses are taken within the duration of the regimen. The total number of doses taken is also a key determinant of the extent of TB prevention. For details on effective person-centered strategy to promote adherence, refer to section 4.5 and 9.2.1.

The criteria for completion of TPT among DR-TB contracts is given in table 8.2 below.

Table 8.2: Criteria for completion of TPT with 6Lfx and 4R

	Total duration in months	Expected no. of doses	80% of recommended doses (days)	Extended time for treatment completion (days) (treatment duration +33% additional time)
6Lfx (daily)	6	180	144	239
4R (daily)	4	120	96	160

8.5 Managing adverse events

Levofloxacin

- Many people using this medication do not have serious side effects. Nausea, diarrhoea, headache, dizziness, light-headedness, or trouble sleeping may occur.
- If any of these effects last or get worse, the doctor may be consulted promptly.
- If any serious side effects are observed, including unusual bruising/bleeding, signs of kidney problems (such as change in the amount of urine), signs of liver problems (such as nausea/vomiting that doesn't stop, loss of appetite, stomach/abdominal pain, yellowing eyes/skin, dark urine), the treating physician should be consulted immediately
- Very serious side effects, includes chest pain, severe dizziness, fainting, fast/irregular heartbeat, signs of a tear/break in the main blood vessel called the aorta (sudden/severe pain in the stomach/chest/back, cough, shortness of breath).
- This medication may rarely cause a severe intestinal condition (Clostridium difficile-associated diarrhoea) due to a type of resistant bacteria. This condition may occur during treatment or weeks to months after the treatment has been stopped. Tell your doctor right away if you develop: diarrhoea that doesn't stop, abdominal or stomach pain/cramping, blood/mucus in your stool.
- Do not use anti-diarrhoea or opioid medications if you have any of these symptoms because these products may make them worse.
- Use of this medication for prolonged or repeated periods may result in oral thrush or a new yeast infection. The medical officer may be contacted if you notice white patches in your mouth, a change in vaginal discharge, or other new symptoms.
- A very serious allergic reaction to this drug is rare. However, get medical help right away if you notice any symptoms of a serious allergic reaction, including: rash, itching/swelling (especially of the face/tongue/throat), severe dizziness, trouble breathing.
- Patients with moderate and severe ADRs may be referred to the linked DR-TB centre with all necessary documents/ records.
- These cases may be referred to the N/DDR-TBC as appropriate for further management.

Rifampicin

For details on implementation strategy, effective person-centered strategy to promote adherence, adverse events and their management, drug supply chain management, recording & reporting using Prevent TB India app till Nikshay TPT module is developed, treatment outcomes, private sector engagement, supervision monitoring evaluation and community engagement, refer to the respective chapters.

KEY POINTS TO REMEMBER

- ✓ Preventive treatment among HHC of MDR-TB with FQ sensitive or H resistant R sensitive bacteriologically confirmed pulmonary index patients using 6Lfx or 4R respectively to be introduced in a phased manner for all age groups to gain programmatic experience to guide future expansion while awaiting results of ongoing studies.
- ✓ The person on TPT with 6 Lfx/4R may be referred to the DR-TB center in case he /she develops any of the sign/ symptoms of TB for further evaluation and management.

CHAPTER 9: MONITORING AND TREATMENT OUTCOMES

Learning Objectives

In this chapter we will learn about:

- Monitoring and support during TPT
- Monitoring TPT adherence
- Management of missed doses
- Follow up assessment and investigations
- Treatment outcomes of TPT regimen

To achieve high treatment completion rates and the desired epidemiological impact of TPT, monitoring treatment adherence including management of missed doses and adverse drug reactions is of paramount importance under NTEP.

9.1 Monitoring and support during TPT

Individuals receiving TPT should be monitored at every contact with the health-care providers. Every dose of the treatment must be preferably taken under direct supervision of the health-care worker, particularly the 3HP regimen that has weekly doses. Frontline health-care workers (including community health volunteers) need to be trained to monitor and identify adverse effects due to TPT. However, the decision to modify/stop TPT drugs due to adverse events or to restart (e.g. after an interruption by the person on treatment) must be taken by the treating doctor.

Alternatively, monitoring may be aligned with mechanisms under differentiated service delivery (DSD) model for PLHIV where implemented, or schedule for collection of other medication (such as ARV). As a principle, the schedule for follow-up visit should consider the individual's convenience. It is important that an informed decision to not take treatment by a person offered TPT, or to stop it after having started it, be respected; people should not feel forced to take treatment.

During every contact with the person receiving TPT, the provider should:

- reinforce the person's understanding of symptoms of TB disease, reasons for TPT, and the importance of completing the course;
- check for presence of signs or symptoms of TB disease; and if diagnosed with TB disease, TPT should be stopped and curative TB treatment started;
- measure weight, if possible, and adjust dosage accordingly. This is especially important for young children as rapid weight gain can normally occur in growing infants and young children over the period of TPT, thus requiring dosage adjustment. On the other hand, documented weight loss or failure to thrive is an early clinical indicator of TB disease;

- check for adverse drug reactions and manage any toxicity identified or refer to the treating doctor;
- persons on TPT should contact the health care worker/provider if they notice adverse events, such as anorexia, nausea, vomiting, abdominal discomfort, persistent fatigue or weakness, dark-coloured urine, pale stools or jaundice. These are suggestive of liver injury and require urgent evaluation under the treating doctor and relevant investigations need to be done as clinically indicated;
- elicit reasons for any missed dose and extend support to enable future adherence to TPT;
- continue the management of co-morbid conditions and consult with the treating doctor whenever necessary;
- ask about pregnancy, breastfeeding and contraceptive use; and
- make a record of the visit, drug intake and findings using information from individual case files or forms prescribed by the national programme.

9.2 Monitoring TPT adherence

Adherence to the TPT doses throughout the course and treatment completion are important determinants of clinical benefit, both at individual and population levels. Irregular or inadequate treatment reduces the protective efficacy of TPT regimen. Poor adherence or early cessation of TPT can potentially increase the risk of the individual developing TB disease including drug-resistant TB.

Efficacy of TPT is greatest if at least 80% of the doses are taken within 133% of the duration of the regimen. Total number of doses taken is a key determinant of the extent of TB prevention.

Success of the TPT strategy is based on adherence to the treatment. There should be strict monitoring for adverse events and their appropriate management. As expected, shorter regimens are associated with better adherence and higher treatment completion.

9.2.1 Effective person-centered strategies to promote adherence

- Effective counselling of the TPT eligible individuals and their family members is of utmost importance to ensure TPT initiation, adherence and completion. Refer to section 4.5 for further details on counselling.
- Develop a personal adherence plan with the support of family member, caregiver or health worker as per treatment regimen being provided. Give first preference to the family member to be the treatment provider in consultation with the person.
- Use of digital platforms (tele/video calls, 99DOTS/MERM), counting empty blisters, refill monitoring etc. at the level of treatment supporter to strengthen adherence monitoring.
- Engage the TB survivors/champions at the community level to create a peer support group for social support and continuous motivation of TPT eligible persons and their family to adhere and complete treatment as well as report any adverse events in time for resolution.

9.2.2 Suggested actions for improving TPT adherence

- Address the reason for interruption;
- Counsel the person on TPT and the caregiver on the importance of adherence to treatment; and
- Review and agree with the person on TPT and caregiver about the best way to improve adherence.

9.3 Management of missed doses

As most of the individuals enrolled on TPT would be relatively healthy and may not feel the need to take medications regularly or may choose to stop treatment due to an unaddressed adverse event, there could be instances these individuals may miss taking doses. All efforts must be made by the health-care providers, the family and community members to ensure that TPT is regularly monitored and the interrupters are promptly identified and brought back to treatment. The management of TPT interruptions are detailed in Table 9.1 below.

Table 9.1: Management of interruptions in TB preventive treatment

TPT regimen	Duration of interruption	Management steps
6H, 6Lfx, 4R	Less than 2 weeks	• Resume TPT immediately upon return and add the number of days of missed doses to the total treatment duration. • Do not change the scheduled date of the next follow-up visit but the last follow-up visit will be postponed by the number of extra-days to compensate for missed doses (e.g. If a child on 6H missed 3 days of treatment, continue TPT for a total duration of 6 months + 3 days from the date of start)
	More than 2 weeks	• If treatment interruption occurred after more than 80% of doses expected in the regimen were taken, continue and complete the remaining treatment doses in the course. • If less than 80% of doses expected in the regimen were taken, and the treatment course can still be completed within the expected time for completion, i.e. treatment duration + 33% additional time, continue and complete the remaining treatment doses in the course. • If less than 80% of doses expected in the regimen were taken, and the treatment course cannot be completed within the expected time for completion, consider restarting the full TPT course.
3HP	Weekly schedule of up to 3 doses missed	• If the missed dose is remembered within 2 days of scheduled day, the person can take the dose immediately and continue to take remaining doses following the same schedule to complete the course. • If the missed dose is remembered after 2 days, the person can take the missed dose immediately and change the schedule for weekly intake to the day the missed dose was taken until treatment completion. This will avoid two weekly doses being taken less than 4 days apart. • If between 1–3 weekly doses are missed, treatment is continued until all 12 doses are taken, thus prolonging the treatment duration to a maximum of 16 weeks.
	More than 3 weekly doses of 3HP missed	• If 4 or more weekly doses are missed, consider restarting the full TPT course. • If adherence to a weekly routine is not possible, consider discontinuing 3HP and offering an alternative (daily) regimen.

9.4 Follow-up assessment and investigations

To achieve the desired success rates among people receiving TPT, they need to be closely followed up to monitor regularity of TPT intake and address any potential challenges to

ensure uninterrupted treatment and completion of the TPT course. Routine monitoring should include tolerability and adherence.

9.4.1 Maintaining regular contact with persons on TPT and their family

The health worker of HF and TBHV/STS concerned are responsible to maintain regular contact and review the persons on TPT and their family along with the index TB patient on monthly basis either at HF or during home visits or tele/video call to ascertain the following:

i. Assess adherence of every dose of TPT using digital tools or counting empty blister or refill monitoring if treatment supporter is a family member;
ii. Check for any signs and symptoms of TB emerging while on TPT;
iii. Check for any adverse events of TPT drugs and arrange for its prompt management;
iv. Arrange for clinical assessment by the doctor at HF (including CHO) on a monthly basis;
v. Conduct biochemical assessments (LFT etc.), as indicated; and
vi. Undertake periodic counselling.

9.4.2 Clinical monitoring

- All patients receiving TPT should be evaluated at least monthly or at every contact by the doctor of HF (including CHO) with the person on TPT for the following:
  - Assess adherence and provide necessary support. Any interruption in treatment should be discussed with the person on treatment and her/his treatment supporter and interventions to address problems in adherence should be instituted;
  - Signs and symptoms of TB disease ("breakthrough" or missed diagnosis at start of TPT);
  - Adverse reactions (type, onset and duration, severity);
  - Other co-morbid diseases during TPT, such as COVID-19, malaria etc;
  - Check for any medication (including traditional cures) that may interact with TPT; and
  - Conduct relevant physical examination.
- Patients receiving TPT who experience possible adverse reactions should be advised to stop medication and consult their health-care provider immediately.

9.4.3 Follow-up investigations

- Urine Pregnancy Test among women in reproductive age:
  - As and when clinically indicated; and
  - Discontinue 3HP if pregnancy is detected and consider alternative TPT regimen (e.g. 6H).
- Liver function test:
  - LFTs may be done at periodic intervals as clinically indicated among individuals who had pre-existing liver conditions or regular and harmful alcohol use with raised enzyme levels at baseline or previous visit; and
  - Routine LFTs are not indicated when TPT with 6H is given in pregnancy unless there are other risk factors for liver toxicity.
- Monitoring breakdown to active TB/DR TB disease:
  - The monitoring for breakdown to active TB/DR-TB disease during TPT or post-TPT completion for long-term follow up at 6, 12, 18 & 24 months need to be done by the doctor/staff of HF.

9.5 Treatment outcomes

A number of endpoints are proposed that could be used to trigger a review of persons on TPT and in some instances, changes to treatment. Table 9.2 below summarizes all recommended regimens and suggested criteria to assess the completion of different TPT regimen.

Table 9.2: TB preventive treatment completion

TB preventive treatment completion				
	Total duration in months	**Expected number of doses**	**80% of recommended doses (days)**	**Extended time for treatment completion (days) (treatment duration +33% additional time)**
6H (daily)	6	180	144	239
3HP (weekly)	3	12	11*	120
6Lfx (daily)	6	180	144	239
4R (daily)	4	120	96	160

* 90% of recommended number of doses

Accordingly, the following definitions will be used for recording treatment outcomes of individuals treated with various TPT regimen:

- **Treatment completion.** A person initiated on TPT who completed at least:
  - 80% of recommended dose (144/180) consumed within 133% of planned TPT duration (239 days) for 6H or 6Lfx
  - 90% of recommended dose (11/12) consumed within 133% of planned TPT duration (120 days) for 3HP.
  - 80% of recommended dose (96/120) consumed within 133% of planned TPT duration (160 days) for 4R.
- **Treatment failed.** A person initiated on TPT who developed active TB disease any time while on TPT course.
- **Died.** A person initiated on TPT who died for any reason while on TPT course.
- **Lost to follow-up.** TPT interrupted by person for eight consecutive weeks (2 months) or more for 6H or 6Lfx, four consecutive weeks (1 month) or more for 3HP or 4R.
- **TPT discontinuation due to toxicity.** A person whose TPT is permanently discontinued by the doctor due to adverse events or drug–drug interactions.
- **Not evaluated.** Such as records lost, transfer to another health facility without record of TPT completion.

KEY POINTS TO REMEMBER

- ✓ To achieve high treatment completion rates and the desired epidemiological impact of TPT, monitoring treatment adherence including management of missed doses and adverse drug reactions is of paramount importance under NTEP.
- ✓ Poor adherence or early cessation of TPT can potentially increase the risk of the individual developing TB disease, including drug-resistant TB.

- ✓ Efficacy of TPT is greatest if at least 80% of the doses are taken within 133% of the duration of the regimen.
- ✓ Use of digital platforms (tele/video calls, 99DOTS/MERM), counting empty blisters, refill monitoring etc. at the level of treatment supporter will strengthen adherence monitoring.
- ✓ Engage the TB survivors/champions at the community level.
- ✓ If less than 80% doses expected in the regimen (6H, 6Lfx or 4R) were taken, and the treatment course cannot be completed within the extended time for completion, consider restarting the full TPT course. If 4 or more weekly doses of 3HP are missed, consider restarting the full TPT course.
- ✓ The health worker of HF and TBHV/STS concerned are responsible to maintain regular contact and review the persons on TPT and their family along with the index TB patient on monthly basis, either at HF or during home visits or tele/video call.
- ✓ All patients receiving TPT should be evaluated at least monthly or at every contact by the doctor of HF (including CHO) with the person on TPT.
- ✓ LFTs may be done at periodic intervals as clinically indicated among individuals who had pre-existing liver conditions or regular and harmful alcohol use with raised enzyme levels at baseline or previous visit.
- ✓ The monitoring for breakdown to active TB/DR-TB disease during TPT or post-TPT completion for long-term follow up at 6, 12, 18 & 24 months need to be done by the doctor/staff of HF.

CHAPTER 10: PROCUREMENT AND SUPPLY CHAIN MANAGEMENT

Learning Objectives

In this chapter we will learn about:

- Procurement
- Supply chain/inventory management
- Reconstitution

10.1 Procurement

The drugs for various regimen for TPT will be centrally procured and supplied through the NTEP in the same manner as other anti-TB drugs. However, the annual state specific planning to forecast the demand of the drug quantities in various TPT regimens would be necessary to contribute to the national level quantification forecasting for procurement. Further, procurement/outsourcing of laboratory tests and kits for TBI detection, silica gel desiccant, 99DOTS/MERM materials, poster printings etc. need to be undertaken by the states.

10.2 Overview of drug distribution flow

All drugs used in various TPT regimens detailed earlier shall be supplied through a centralized procurement system at the Central TB Division, MoHFW, GoI & will be stored at Government Medical Store Depot (GMSD)/ Central Medical Services Society (CMSS) stores. The drugs for TPT full courses will be supplied to the states from the respective GMSD/CMSS. An advance intimation of all drug supplies will be communicated to the states for state drug stores (SDS) to make available requisite space in the drug store. The SDS will be supplied only in loose drug form. On receipt of drugs, the SDS shall acknowledge the receipt through the Nikshay Aushadhi Software.

The SDS shall supply full courses of TPT per person with a buffer stock of 3 months to all the districts on a quarterly basis; the districts will supply further with a buffer stock of 2 months to all TUs on monthly basis; and TUs will supply further with a buffer stock of 1 month to all HF on a monthly basis. An entire course of TPT drugs per eligible individual will remain under the custody of the trained treatment supporter till the individual completes the TPT course for the respective regimen. The stocking norms for full TPT courses at various stocking points are given in Table 10.1 below.

For maintaining inventory of TPT drug courses and for its accountability, once a full patient course of TPT drugs is issued to the trained treatment supporter of TPT eligible person, this will be taken as issue/consumption for recording and reporting under Nikshay and Nikshay-Aushadi.

Table 10.1 Standards for stocking norms for full TPT courses at various stocking points

Level	Stock for utilization	Reserve stock in months of full TPT courses	Drug requirements
Treatment supporter	One full TPT course per beneficiary	0 month	Full TPT course under utilization
HF drug store	0 month	2 month	Reserve stock in HF at end of the month (2 x total TPT beneficiaries on Full TPT course for HF)
TU drug store	0 month	2 months	(Quarterly consumption/ 3) x 5 – (existing stock in TU including HF drug stores at end of the quarter)
DTC drug store	0 month	3 months	(Quarterly consumption/ 3) x 8 – (existing stock in DTC drug store including TU & HF drug stores at end of the quarter)
SDS	0 month	3 months	(Quarterly consumption/ 3) x 11 – (existing stock in SDS including stocks at all districts at end of the quarter)

10.3 Reconstitution

In the event of loss to follow-up or death or discontinuation of TPT for any reason, the leftover tablets will be returned back to the DDS. These drugs would be taken back in stock and used under the supervision as per batch no. and expiry. The batch number and expiry need to be labelled properly. These loose drugs will then be repacked as full treatment courses at DDS and resent to TUs and HF for further usage.

KEY POINTS TO REMEMBER

- ✓ The drugs for various regimen for TPT will be centrally procured and supplied through the NTEP.
- ✓ Procurement/outsourcing of laboratory tests and kits for TBI detection, silica gel desiccant, 99DOTS/MERM materials, poster printings etc. need to be undertaken by the states.
- ✓ The SDS shall supply full courses of TPT per person with a buffer stock of 3 months to all the districts on quarterly basis, districts will supply further with a buffer stock of 2 months to all TUs on monthly basis and TUs will supply further with a buffer stock of 2 months to all HF on a monthly basis.
- ✓ For maintaining inventory of TPT drug courses and for its accountability, once a full patient course of TPT drugs is issued to the trained treatment supporter of TPT eligible person, this will be taken as issue/consumption for recording and reporting under Nikshay and Nikshay-Aushadi.
- ✓ In case of treatment interruption due to any reason, the leftover tablets will be returned back to the DDS, taken back in stock and used under the supervision as per batch number and expiry, repacked as a full treatment courses at DDS and then resent to TUs and HF for further usage.

CHAPTER 11: IMPLEMENTATION STRATEGY

Learning Objectives

In this chapter we will learn about:

- Health and Wellness Centres (HWC) and Sub-centres (SC) for TPT service delivery under guidance of HF, TU and District TB officers.
- Integration of TPT services at community and facility levels
- Key strategies and checklist to assess preparedness for TPT scale-up under NTEP

With implementation of this guideline, NTEP will expand the target population for TPT detailed in Chapter 2 in a phased manner. The implementation would be carried out by the states as per this guideline and in accordance to the activities budgeted in the annual PIP and under the overall guidance of the Central TB Division.

Active, intensified and passive case finding activities for mapped vulnerable groups, high-risk co-morbid conditions and general population respectively under NTEP, all leading to notification of index TB patients with efficient linkages to TB treatment and integrated Infection Prevention Control (IPC) measures should be in-place for effective TPT implementation, especially in high-risk settings.

The complete range of health facilities providing care to patients in the public and private sector as well as community volunteers would require to synergize their efforts in the effective implementation of TB preventive treatment strategy to ensure accessibility, acceptability, complete coverage, efficient service delivery, real-time monitoring and long-term follow-up to protect all vulnerable groups as well as contacts of TB patients from breakdown to active TB with TB preventive treatment.

11.1 Health and Wellness Centres and Sub-centres for TPT service delivery under guidance of HF, TU and District TB officers

Universal Health Coverage envisaged through HWCs/Sub-centers would be leveraged for organizing effective implementation of this activity and these would be the focal point for TPT service delivery to the target population in their respective catchment areas.

Community health officers (CHO) in HWCs would be the key responsible officers for organizing contact tracing/investigation and provision of TPT. All staff at HWCs/ Sub-centre will be primarily responsible for TPT service delivery along the entire TPT care cascade that includes the following activities:

- mapping out facilities managing HRGs and the households/workplaces of all index TB/ DR-TB patients where target population can be traced;

- enumerating and mapping out target population;
- contact tracing and investigation of target population at the level of households/workplaces/ ICTC-ART centres/facilities caring for all HRGs/mapped vulnerable groups;
- screening target population to rule out active-TB and ascertain eligibility for TPT;
- organizing investigations (whenever available) and facilitating TPT or TB treatment initiation through CHO or HF doctor;
- monitoring TPT adherence and observing for side effects. In case of any adverse reactions identify by the health care workers (including community volunteers) and referred to the doctor; and
- declaring TPT outcomes and long term follow-up.

Training to HF staff would be organized and facilitated by state/district/block health authorities. In Sub-centres which are not HWC, multi-purpose worker (MPW)/2nd auxiliary nurse midwife (ANM)/accredited social health activists (ASHA) would be given responsibility and trained.

TPT treatment supporter should be identified and trained by the CHO/ HF doctor and team at a point closest to beneficiary homes and where the index TB patient is receiving therapy by leveraging the existing health system. Regular home visits or tele/video contact should be undertaken by the health-care workers with the TPT beneficiaries to ensure adherence, adverse event identification/management, repeated counselling as necessary and follow-up for all TPT beneficiaries.

The responsibility to rule out active TB disease and evaluation of the individual for TPT eligibility lies on the doctor at the concerned HF (including CHO and PP) as per guidelines. Management for adverse events and decision to stop or change or restart the TPT regimen will be taken only by the treating doctor/CHO.

The CHO/ HF doctor is also responsible to lead the overall micro-planning and organization of TPT services in all HCWs/SCs of the HF catchment area to ascertain specific roles and responsibilities of health providers including community volunteers in coordination with HF staff. This is especially in target populations in the community where there is need to provide adherence support, manage therapy interruptions and identify, document and manage adverse drug events.

The block MO TU and DTO will be responsible to establish TPT service delivery for HRGs at key service delivery sites such as ART/DR-TB centres, all TB treatment centres (public and private) maternal and child health services centres, community health centres, private providers and facilities serving other HRGs etc. They will also review and strengthen the drug and logistics supply chain mechanism for an uninterrupted service delivery as well as strengthen digital recording and monitoring system.

11.2 Integration of TPT services at community & facility levels

Based on the TPT care cascade to rule out active TB and provide TPT as per the integrated algorithm for screening TB & TBI, following activities specific to PM TPT shall be integrated to the existing TB services at community and facility levels. The key officials and staff of the level of service delivery/facility will be responsible for undertaking the TPT activities/interventions detailed in table 11.1.

Table 11.1 TPT activities to be undertaken by various levels of service delivery/facility

TPT activities at various levels of services delivery/facility
1. Community volunteers (TB survivors/champions, ASHAs & AWWs)
• Awareness generation, peer education on TBI and TPT.
• Encourage families of TB patients to avail TPT services for protection of family/vulnerable individuals.
• Mobilization of target populations (contacts/vulnerable/high-risk groups) for TPT.
• ACF for TB among contacts/vulnerable groups mapped & referral for ruling out/diagnosis of TB or for screening for TBI eligibility to PHC/HWCs/Sub-centre in rural area and UPHC/health posts/ dispensaries in urban areas.
• Treatment support & adherence monitoring of individuals undergoing TPT including entry of daily doses taken in the Prevent TB India app/Nikshay TPT module.
• Early identification of adverse events and making the referrals to the doctor.
• Facilitating and ensuring follow-up examinations, as needed.
2. HWCs/Sub-centre/Urban health posts/Dispensaries (CHO, ANMs, MPWs & other field staff)
• Ensure ALL contacts of notified TB/DR TB patients are enlisted by HCW/SC staff.
• Screening of all target population (including all HHC and other vulnerable groups) in the Sub-centre area for symptoms of TB.
• Counsel and refer those with symptoms of TB for TB diagnosis to TB detection centres under intimation to HF doctor.
• Counsel and refer those not having symptoms of TB to HF doctor for assessment for TBI eligibility and necessary action.
• Gather and record medical history of the individual and make an assessment of alcohol/drug use etc. and share the same with HF doctor.
• Identify and train treatment supporters for each individual on TPT in consultation with the individual respecting their personal preferences.
• Regularly undertake home visit or tele/video calls to monitor all individuals on TPT for adherence, signs/symptoms of TB, adverse drug reactions and immediately refer them to HF doctor, if required.
• Identify treatment interruptions at the earliest (Dashboards of Prevent TB India app/Nikshay TPT module may be checked every week along with pill counting) and take necessary action to ensure that treatment is continued.
• Facilitate and ensure that required follow-up examinations like UPT or LFT are carried out including reporting treatment outcomes and post TPT follow ups.
• Review data updating in Prevent TB India app/Nikshay TPT module wherever available and quality of data regularly and provide feedback to TPT treatment supporters and for retrieval of TPT interrupters.
3. PHC/UPHC/Private clinic (MO, staff nurse, LT, pharmacist, DEO)
• Ensure ALL contacts of notified TB/DR TB patients are enlisted by HCW/SC staff, invited for evaluation, investigated for TB and eligibility for TPT, started TPT if eligible.
• Assess all eligible individuals for TPT following the Algorithm for TB screening & TPT provision.
• Conduct TBI tests (wherever available) either in the in-house lab/hub & spoke model/ outsourcing.
• Once eligible for TPT, conduct relevant pre-TPT assessment and investigations available either in-house or out-scoured.
• Start individuals eligible on TPT and educate them on the treatment schedule, need for adherence, follow-up schedule and need to contact doctor/health-care provider in case the TB symptoms/adverse events/adverse drug reactions develop.

- Identify & train TPT treatment supporters (health workers/ private providers/ community/ family members/ self) with the help of HCW/SC team in rural areas and ANM & ASHAs in urban areas.
- Issue full course of TPT drugs to the treatment supporter for all individuals on TPT.
- Monitor individuals on TPT with help of CHO/MPW, advice for management of side-effects, stop TPT and refer for higher facility in case of serious adverse events (tele/video call facilities shall be used for consultation with higher facilities, to the extent possible).
- Report AEs observed and development of TB symptoms to the HF doctor.
- Conduct follow-up examinations as prescribed.
- Ensure that all required information is updated on the Prevent TB India app/Nikshay TPT module.
- Review data updating in prevent TB India app/Nikshay TPT module wherever available and quality of data regularly and provide feedback to HCWs/SCs.

4. TB Unit (MO, LT, X-ray tech., staff nurse, pharmacist, counsellor (if available), STS, STLS, TBHV)

- Estimation of number of individuals requiring TPT in the TU area.
- Capacity building of PHC staff, Sub-centre staff, ASHAs, AWWs and community volunteers on TBI, screening for TBI, TPT care cascade monitoring, etc.
- Facilitation of access to necessary diagnostic facilities such as X-rays and lab investigations, including TBI testing (in-house or outsourced from private labs/facilities).
- Ensuring indenting, full course of TPT drugs constitution/reconstitution, DAT & supply of drugs for TPT in adequate quantity.
- Assessment of potentially eligible individuals directly accessing services from TU for TBI and initiation on TPT, if found eligible.
- Adherence support and clinical monitoring of these individuals to be done through the concerned PHC/Sub-centre.
- Supportive supervision and handholding support to field level facilities and frontline workers, ASHAs and community volunteers for conducting awareness initiatives, mobilization of target population, screening & assessment for initiation of TPT, starting, digital recording, using Prevent TB India app and monitoring TPT and follow-up examinations.
- Clinical management of adverse drug reactions referred to the TU as possible and referral to higher facilities if required (tele-medicine facilities to be used for consultation with higher facilities, to the extent possible).
- Ensure all required data is updated on the Prevent TB mobile application/Nikshay TPT module whenever available.
- Supervise and monitor coverage of screening, initiation and completion of TPT among eligible individuals under various PHCs under the TU.
- Review data updation in the prevent TB India app/Nikshay TPT module where available along with quality of data regularly and provide feedback to HCWs/SCs/PHCs/UPHCs.
- Address programme management and implementation gaps identified during real-time monitoring and flagging issues specific to districts/states to respective DTO/STO for resolution.

5. ART centre/Link ART centre (MO, pharmacist, (institutional) staff nurse, counsellor, care coordinator, LT)

- Symptom screening of all PLHIV registered for ART during initial visit and monthly visits for active TB and contra-indications.
- Counselling and Initiation of all PLHIV not having active TB on TPT.
- Ensuring appropriate choice of TPT/ dose adjustment of ARV considering drug-drug interactions e.g. adjust dosing of DTG if 4R is used, or use of 6H if the person is on Nevirapine based ARV.
- Ensuring adherence support for PLHIV on TPT through mechanisms such as outreach workers, PLHIV networks, peer support groups etc.

- Monitoring of adverse drug reactions or development of symptoms of TB and its management.
- If symptoms of TB develop, stop TPT and investigate for bacteriological confirmation of TB/DR-TB.
- Ensure that all required information is updated on the Prevent TB India app/Nikshay TPT module.
- Review data updation in the Prevent TB India app/Nikshay TPT module, where available; ensure quality of data regularly; and provide feedback to ART centre staff.

6. Tertiary care/Medical colleges/Corporate hospitals/District hospitals/Dialysis/Cancer facility (doctors, staff nurses, LT, X-ray and dialysis technicians)

- Screen all patients on immunosuppressive therapy, silicosis patients, anti-TNF medicines, patients undergoing dialysis at regular intervals for symptoms of TB.
- Educate and refer patients not having symptoms of TB for TBI testing/assessment of their eligibility for TPT.
- Monitor and support adherence to TPT.
- Clinically monitor all patients on TPT for symptoms of TB, adverse drug reactions and ensure immediate management by doctors.
- If symptoms of TB develop, stop TPT and investigate for bacteriological confirmation of TB/DR-TB.
- Ensure that all required information is updated on the Prevent TB India app/Nikshay TPT module.
- Review data updation in the Prevent TB India app/Nikshay TPT module where available; ensure quality of data regularly and provide feedback to ART centre staff.

7. State/District TB cell (STO, DTO, State/District Programme Coordinator, etc)

- Include the TPT implementation plan and budget in the annual PIP process for funding approvals.
- Estimate the number of individuals requiring TPT in the district under guidance of CTD.
- Ensure establishment of mechanism for TBI screening & management at all HFs (including HWCs & private clinics), TUs, ART centres, tertiary hospitals, medical colleges, corporate hospitals, district, sub-district hospitals, dialysis facilities etc.
- Undertake capacity building of staff at levels listed above in national guidelines for TPT in India and the Prevent TB India app/Nikshay TPT module.
- Facilitate access to necessary diagnostic facilities such as X-ray and lab investigations including TBI testing.
- Ensure indenting & supply/outsourcing of IGRA, drugs for TPT and other logistics in adequate quantity through the PIP system.
- Review data updation in Prevent TB India app/Nikshay TPT module where available; ensure quality of data regularly; and provide feedback to PHCs/UPHCs.
- Carry out supportive supervision and monitoring of TPT care cascade and PMTPT activities in the district, including contact screening, TPT start and TPT completion data.
- Set-up mechanism for ADR management, including referral facilities.
- Ensure availability of necessary IEC activities on TBI and TPT for facilities as well as for community.

11.3 Key strategies for TPT scale-up under NTEP

The key strategies for TPT implementation scale-up under the programme are:

a) Building capacity of health-care workers at HWCs, Sub-centers and HFs (including private clinics) in the PMTPT guidelines for India.

b) Ensuring adequate human resources to provide TPT services at all of the above facilities as well as supervisory staff at the block, district and state level.

c) Implementing systematicaly active, intensified and passive case finding to detect and notify all index TB patients in the community.

d) Mapping out facilities managing HRGs and households/workplaces of all index TB patients where the target population can be traced.

e) Establishing diagnostic systems to rule out active TB and to detect TBI among contacts of index TB patients and HRGs

f) Providing TPT using newer and shorter regimens to eligible individuals who have been identified.

g) Strengthening treatment support systems for monitoring adherence and adverse events and ensuring high TPT completion rates in every centre.

h) Strengthening the monitoring system and establishing a robust surveillance system.

i) Designing effective communication strategies for TPT and initiating IEC campaign with community engagement to increase awareness among general population about TPT intervention to accelerate ending TB in India.

j) Following-up up to 2 years post TPT on a six-monthly basis to monitor individuals who completed TPT for breakdown to active-TB.

Every state, district and block level officer must clearly understand the requirements to organize TPT services in their respective catchment areas and prepare the health workforce and health system to be capable of effectively implementing the TPT services as an integral part of the universal health coverage (UHC) function of the health system. The checklist to assess preparedness for implementation of TPT services is given in table 11.2 below. This needs to be used to conduct an assessment of readiness of blocks, districts and states for rolling out TPT services in their respective catchment areas. All states must strive to complete state-wide expansion of their TPT coverage by the end of 2021 to reap its epidemiological impact on declining the TB incidence over the next 3-4 years.

Table 11.2 Checklist to assess preparedness for implementation of TPT services

Thematic area	Current Status	Next steps & timeline
State TB preventive treatment committee in place		
Advocacy for TPT		
Inclusion of TPT plan in PIP		
Expansion plan at State/ district level with timelines to complete expansion		
Human resources in place at HCW/SC, HF, Block, District and State as per existing NHM (Ayushman Bharat) and NTEP norms		
Training plan in place with timeline to complete training of all health workforce of HCW/SC, HF, Block, District and State		
Availability of necessary diagnostics (IGRA/TPT) and Chest X-ray for HRGs and HHC whenever available		
Mapping of TPT centres (HWCs, SCs, HFs including private providers) and updating directory of treatment supporters		
Identification of adherence mechanisms (trained TPT supporters/ 99DOTS/MERM/refill monitoring)		
TPT drug stocking and supply chain management for various regimen		
Upgradation of storage space at SDS/DDS/TUDS/HF/HWCs to store TPT drug quantities		

Thematic area	Current Status	Next steps & timeline
ADR management plan (from HF to DR-TB centres)		
Communication strategy, IEC and Community engagement plan		
Logistics/ trainings for recording & reporting (printing, digital platform readiness with peripheral devices and internet for use by HCW/SC staff etc)		
Any other preparedness		

KEY POINTS TO REMEMBER

- ✓ NTEP will expand TPT services in a phased manner to cover the entire country by 2022.
- ✓ Medical officer of the HF (including HWC) will be responsible for TPT implementation in the area.
- ✓ Community health officers (CHO) in HWC/SC level would be leveraged for contact investigation and TB preventive treatment organization and monitoring.
- ✓ Contact tracing will be done by ANM/ASHA/other HCWs including community health volunteers.
- ✓ ART centre and tertiary care institutes would be responsible for TPT services for PLHIV and other HRGs respectively.
- ✓ STO and DTO would be responsible for planning, capacity building, health system preparedness, human resources adequacy, procurement and supply chain management for TBI test (in-house/outsourced) and drugs for TPT, periodic supervision, digital data management, monitoring and course correction.

CHAPTER 12:
RECORDING AND REPORTING

Learning Objectives

In this chapter we will learn about:

- Information management in PMTPT
- TPT information workflow in Nikshay
- Operational aspects for using Prevent TB India app/Nikshay TPT module

The information system for PMTPT has been developed with the objectives to provide:

- Understanding in flow of information
- Variables to be recorded and entered in the information system
- Real-time access of the individual persons' details at all levels for appropriate services
- Tools for digital recording and reporting of TPT
- Real-time reports to monitor implementation of TPT care cascade using real-time dashboards

12.1 Information management in PMTPT in India

Nikshay is the real-time case-based information management and surveillance system for TB in India https://www.nikshay.in/. The information management for PMTPT will be built upon this system as a Nikshay TPT module in the near future.

12.1.1 Building TPT module in the existing Nikshay person's lifecycle approach

The existing approach under Nikshay is the person's lifecycle approach and TB treatment episode level as per the figure 12.1 given below. It means an individual notified for TB gets registered for the first episode of treatment following which the subsequent episodes of treatment are linked to the same Nikshay id for that individual. The information management for TPT will be built into the existing Nikshay person's lifecycle approach and the same will be strategically positioned as the entry point for information of individuals enumerated as the target population into the TPT care cascade of screening, testing, eligibility assessment, TPT initiation, adherence monitoring, follow-up till treatment completion. In the event of breakdown to active TB disease any time after TPT initiation or during long-term follow-up, the next episode for TB treatment will be linked to the same Nikshay id for that individual to ensure continuum of care in Nikshay.

Figure 12.1 TPT Information and related services integrated into a continuum of care

12.1.2 WHO Prevent TB mobile application customized for India as an interim solution

Since the TPT module is under development in Nikshay, as an interim arrangement, the WHO prevent TB mobile application with monitoring dashboards customized for India (Figure 12.2) is hosted on Nikshay and currently available on Google play store. This would be used for information management and monitoring of PM TPT implementation in India initially till Nikshay TPT module is available.

This real-time monitoring system for PMTPT is designed to help frontline health-care workers to screen and register target populations (PLHIV, HHC of pulmonary* TB patients, other risk groups), refer them for testing as per guidelines, and initiate them on appropriate TPT regimen.

The data as is recorded, is visualized on a dashboard in real-time to enable day-to-day performance monitoring of health-care workers, while also monitoring key indicators for the PMTPT. The existing WHO Prevent TB mobile application is customized for India, piloted in two districts in Chhattisgarh and rolled out in Kerala state, as per the guidelines and requirements of the programme. All beneficiary data will be captured through a mobile-based application. The detailed description of the Prevent TB India app along with screenshots is as under:

Link to the App on playstore:

https://play.google.com/store/apps/details?id=com.duretechnologies.apps.android.preventtbindia

Sign in & disclaimer page

After the app is installed the user will see a 'Splash Screen' & the 'Sign In' page with the default PREVENT TB logo. (Figure 12.2)

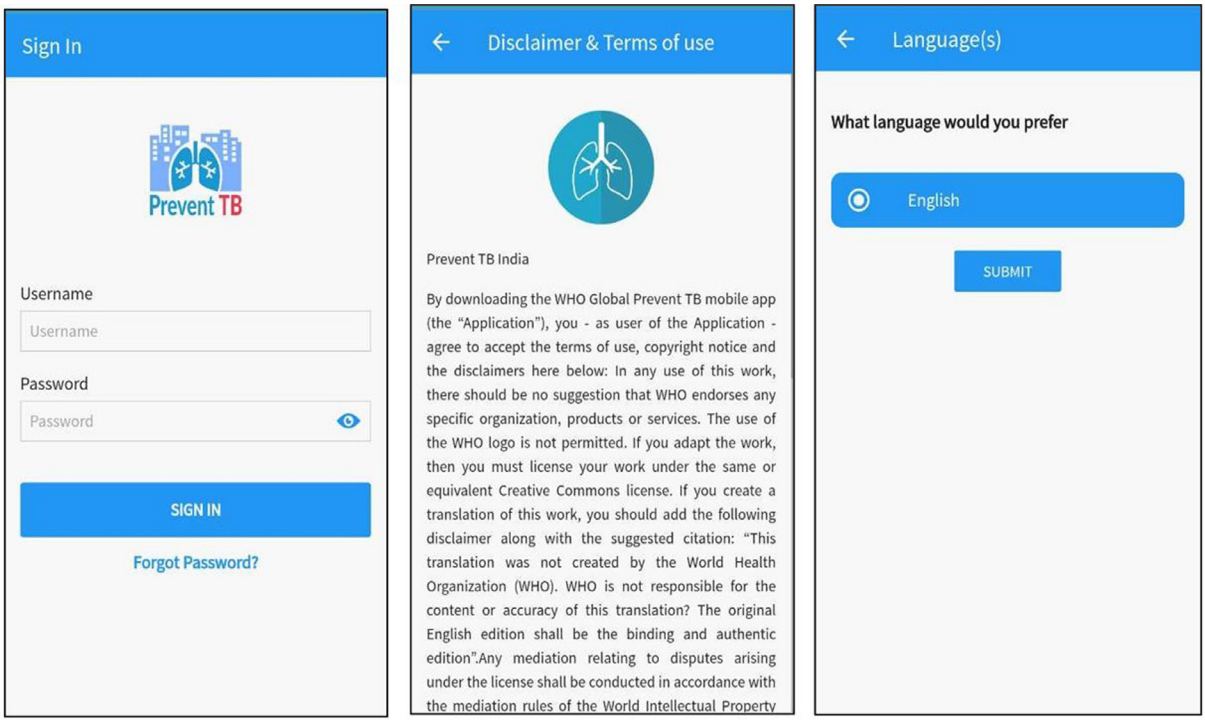


Figure 12.2 Sign in page on Prevent TB India app

Sign in page. The user can sign in with the Nikshay credentials. SSO (Single sign on) feature has been enabled, so all users on Nikshay including PHI users can use Nikshay credentials to sign into the Prevent TB India app. This will enable using the App by ASHA/ANM in the field level as well by assigning appropriate credentials to them via Nikshay.

Disclaimer & Terms of use page. After successful sign in, the user will see a 'Disclaimer & Terms of use' screen which will have a logo, programme description & disclaimer which were added during the programme details step in the Prevent TB smart set-up. On Clicking 'I Agree' the user will be directed to the home screen where s/he can access the different modules of the application. After the user logs in, there is an option to select the language (English) and proceed.

Home page & left menu

The Home page will have the app name on the top and 7 modules – Register, My Clients, Search, Alerts, Referral cases, Tutorials and Settings. On the left menu the user can see the app logo, user ID & other navigation buttons (Figure 12.3).

Register

The 'Register' module will allow the user to register a person/patient by capturing their basic personal details. Once the registration is completed and if the registered person/patient is not presently on TB medication then "refer to investigation" stage appears where the registered person/patient can be referred to TB/TBI testing based on the symptoms. If the registered person/patient is already on medication, then the flow stops there and there is an option to associate contacts with the registered person/patient at this stage. Registration includes registering 'Other risk groups' as per the TPT algorithm as well, which can be referred for TBI testing as required and can also be started on TPT given other criteria are met (Figure 12.4).

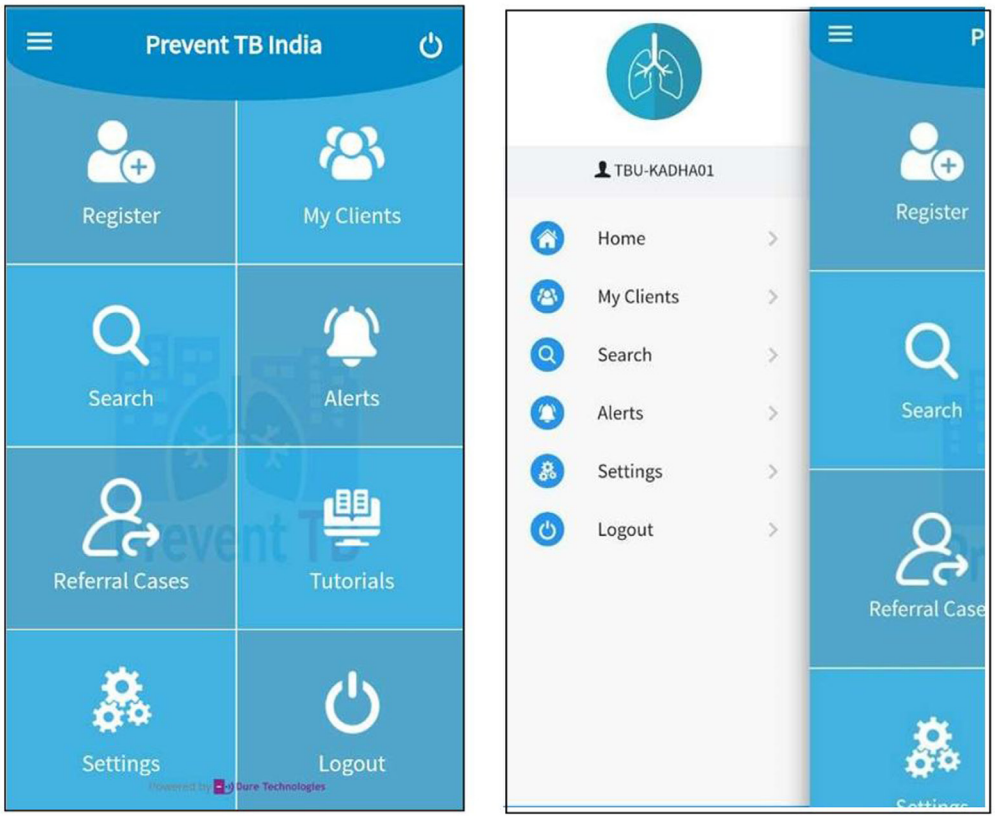


Figure 12.3 Home page and left menu on Prevent TB India app

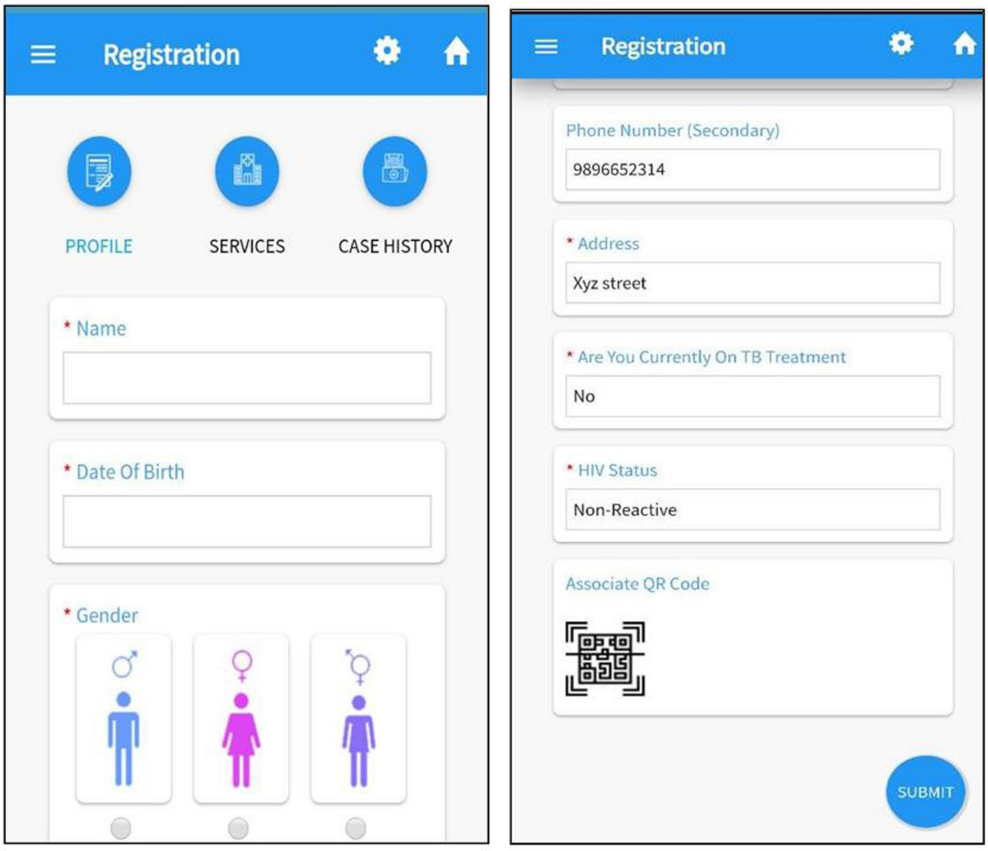


Figure 12.4 Registration on Prevent TB India app

My clients – registered persons/patients & associate contact

In this module the user can associate a contact person to the index TB patient. After clicking on the “Associate” button the contact registration form will open where contact details can be recorded and the contact will be registered in the system and will be assigned a Unique Identification Code (UIC). In this section, treatment initiation stage can be started. The user needs to go to the cases section, where the respective TB/TBI patients/persons can be seen, to whom the treatment initiation and treatment outcome services can be assigned (Figure 12.5).

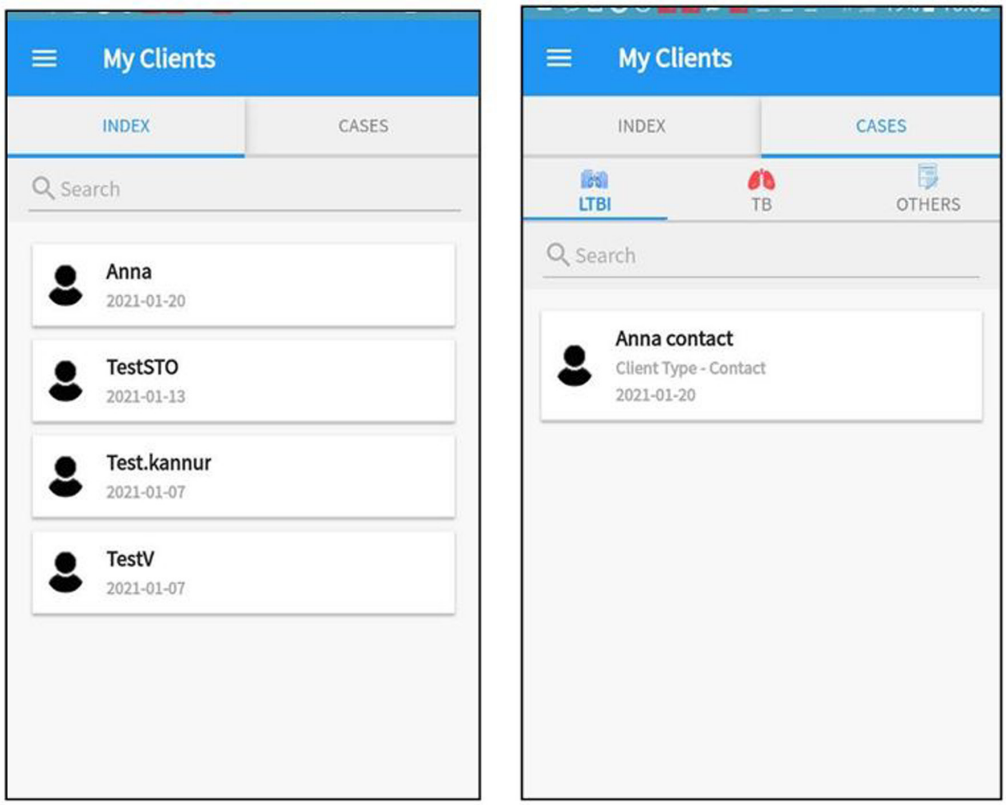


Figure 12.5 My clients – Registered person/patient and associate contact on Prevent TB India app

Refer to investigation

When an registered person/patient/contact is registered, there is a question that is asked ‘Presently on anti-TB medication’ & if the client has said ‘No’ then on submitting the form the user is directed to ‘Refer to investigation’ stage. Here, based on symptoms, the contact can either be referred for TB test or TBI test to a specific facility (Figure 12.6).

Referral cases

In this section, the user can assign the testing services to the client, who has been screened in the refer to investigation stage. Based on the presence or absence of symptoms, the client is assigned to either active TB or TB infection testing. The date, method and result of the test can be entered and then the case moves to the “My clients” section, where the treatment initiation stage can be completed (Figure 12.7).

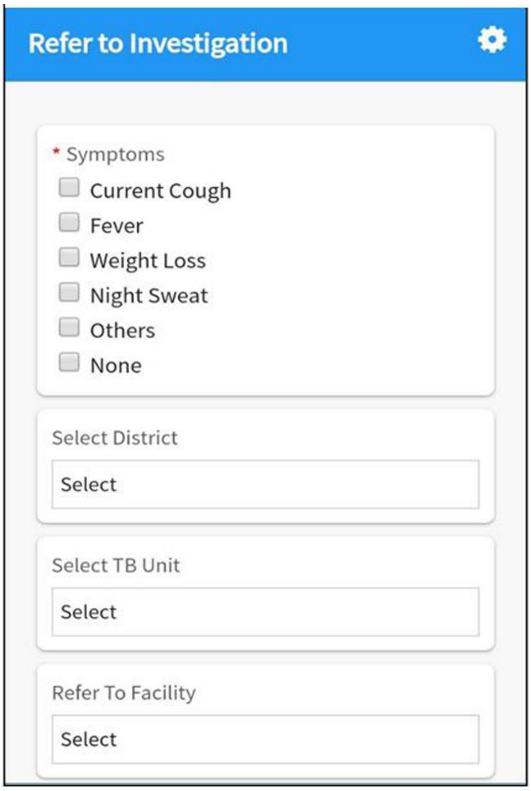


Figure 12.6 Refer for investigation on Prevent TB India app

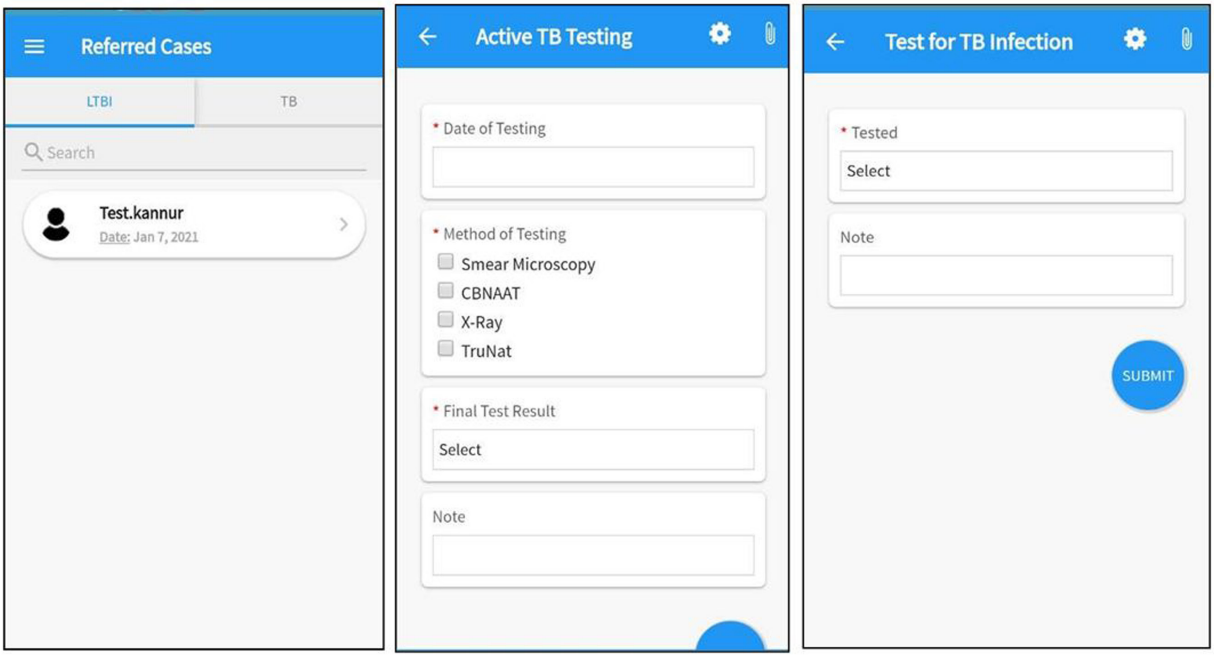


Figure 12.7 Referral for testing for active TB and TB infection

Treatment initiation

Under the "My clients" section, the registered persons/patients can be assigned the treatment initiation and the treatment outcome (for TPT persons only). These will appear under cases, where the treatment initiation can be started by clicking on add service (Figure 12.8).

A web-based dashboard for desktops/laptops will visualize the data being collected through the mobile application in real-time. The dashboard can be used by programme staff for real-time progress monitoring of the TPT care cascade. All key staff at various levels would be trained in using this mobile app and dashboards (Figure 12.9).

The data entered in the Prevent TB India app would ultimately be migrated to Nikshay TPT module when it is ready for the field implementation with dashboards following which the Prevent TB India app would be phased out with necessary directions from NTEP.

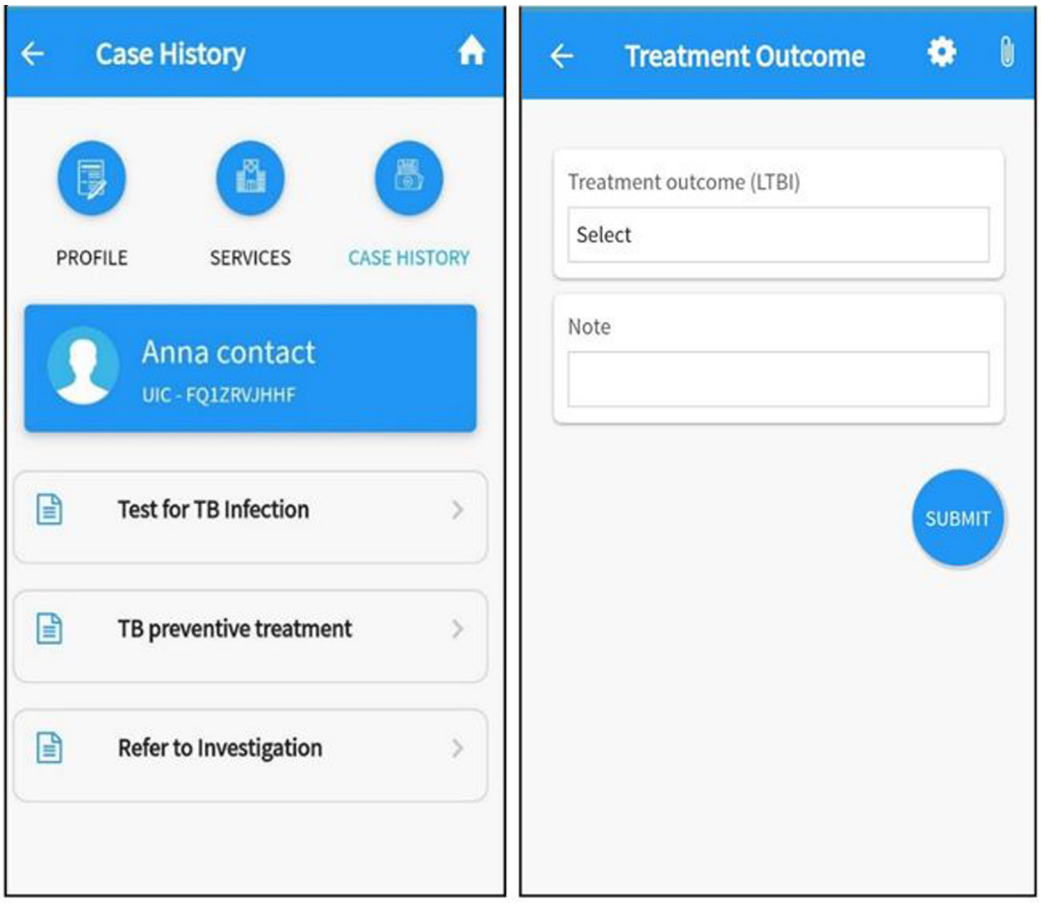


Figure 12.8 Treatment initiation and outcomes on Prevent TB India app

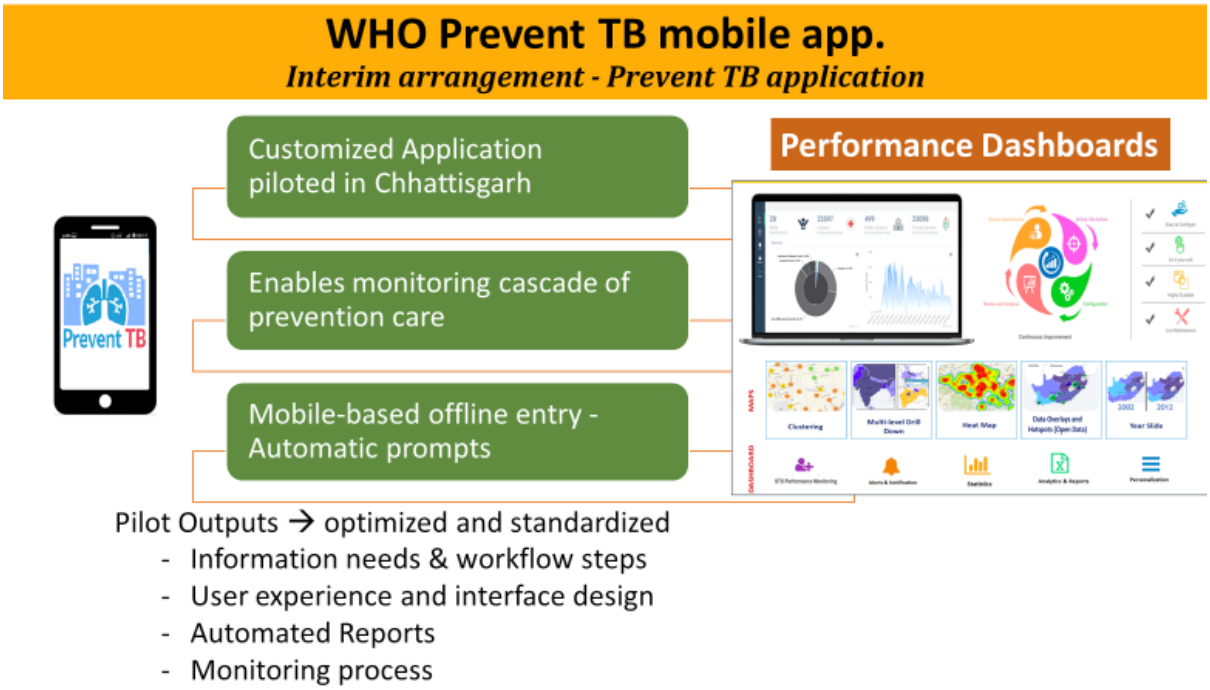


Figure 12.9 Prevent TB mobile application customized for India as an interim solution

12.2 TPT information workflow in Nikshay

The TPT information workflow is detailed in figure 12.2 above. This swim lane diagram illustrates four cardinal activities in the TPT workflow:

1. Enrolment/screening
2. Assessment and workflow for TPT criteria
3. Assessment and workflow for TBI test criteria
4. Assessment and workflow for TBI follow-up criteria

Each square in the diagram signifies a process and quadrangle signifies a decision point. There are data entry points associated with each process and decision point. Also, each of these four activities (swim lanes) are connected to other activities (swim lanes) in some way, which makes this flow an integrated workflow for TPT information management.

12.2.1 Enrolment/Screening

The first swim lane in the diagram illustrate the workflow around enrolment and screening of persons. At the first point of contact of the person, the process of enrolment begins. The person would be authenticated through primary details like gender, phone number and going forward Aadhar number (upcoming feature in Nikshay) and validated through Nikshay Deduplication module. On confirming the person as unique in Nikshay, further demographic details would be required to be entered, following which the process of screening begins. On entering symptom screening details, a decision point is reached. If the person has symptoms suggestive of TB then TB tests would be conducted as per the algorithm and if the TB tests are positive, the person becomes a diagnosed TB patient and exits the TPT workflow to enter the TB information workflow.

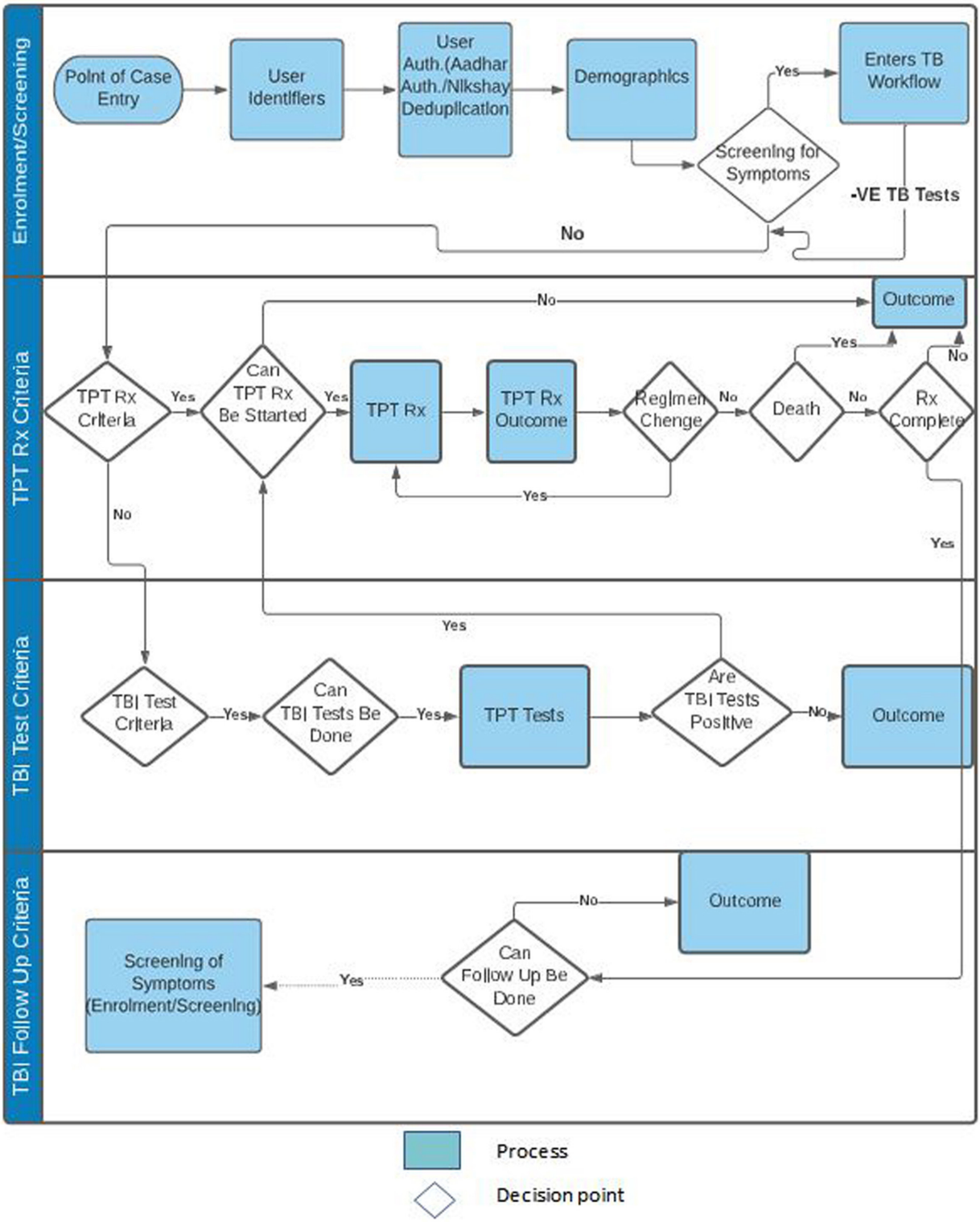


Figure 12.9 TPT information workflow – Swimlane diagram

If the person does not have symptoms suggestive of TB, then the second activity (swim lane) begins i.e. Assessment for TPT eligibility criteria. The field staff potentially assigned to the enrolment/screening activity and responsible for data entry are described in the table 12.1 below.

Table 12.1 Activity, workflow, level and responsible person for data entry in Prevent TB India app (Interim)/Nikshay

Activity/ Workflow Swim lane	Process/Decision	Point of contact of the person with the health system	Person responsible for data entry	Person responsible for ensuring data entry
Enrolment/ Screening	Entering patient demographic details and screening details in Nikshay, authentication of the person as unique in the system and making a decision if the person enters TBI workflow or TB workflow. The decision regarding the type of test to be conducted which is part of Diagnosis Workflow Swim lane is practically done simultaneously. Accordingly, Test Request should also be generated in Nikshay	Field	ASHA/ANM/ MPWs	STS/MO/CHO of HWC/PHC/ CHC/DTO
		HWC/PHC/CHC	MPWs/General health staff/ TBHV	
		District /Taluk hospital	General health staff/TBHV/ SA	STS/MO/DTO
		Medical college/N/ DDRTBC		
		ART centre		
		Pvt. health facility	PP/PPSA field coordinator/ DEO	STS/PPSA Partner/MO-DTC/DTO
Treatment-Workflow Swim lane	Taking a decision regarding treatment-start of treatment, type of treatment, etc… and updating the details of treatment	PHC/CHC/ District/Taluk Hospital/Medical College	TBHV/General health staff/SA	STS/MO-DTC/ MO-ART-centre/ DTO
Diagnosis/ Tests Workflow Swim lane	Decision regarding type of test to be conducted is taken in the first step along with enrolment/screening. And accordingly, once the person reaches a diagnostic facility the test request should ideally be already generated. Entering test details and updating test results is what is contemplated as data entry points in this stage.	IGRA LAB	LT/DEO	STLS/MO-DTC/ DTO
Follow-up-Workflow Swim lane	Taking a decision regarding follow-up, updating follow-up details including post TPT follow-up.	PHC/CHC/ District/Taluk hospital/Medical college/ N/DDR-TBC	TBHV/General health staff/SA	STS/MO-DTC/ MO-ART-centre/ DTO

12.2.2 Assessment for TPT eligibility criteria

If the person does not have symptoms suggestive of TB from the above screening activity then pursuing the workflow in the second activity, a decision point is reached. Assessment for TPT eligibility criteria would be conducted and if the person is eligible for receiving TPT and if TPT can be started (one more decision point) then the process of TPT would be initiated. If however, the TPT cannot be started inspite of the person being eligible as per TPT eligibility criteria, then an outcome would be assigned and the person would no longer remain in the TPT data management workflow.

Pursuing the persons for whom TPT has been initiated, the next process is assessment of treatment outcome across the following:

- For persons started on TPT and assessed for Regimen Change would re-enter the process of TPT initiation.
- For persons started on TPT and assessed as Died would end up with an outcome.
- For persons started on TPT and assessed as Treatment Completed would enter the next activity-Assessment for TBI follow-up criteria. However, if the patient is assessed as not belonging to any of these categories (Lost to follow-up/Not evaluated) would end up having an outcome assigned.

If the person after assessment for TPT eligibility criteria is found ineligible for treatment then the person enters the next activity (swim lane) - Assessment for TBI tests.

12.2.3 Assessment for TBI tests

In this activity the person is assessed for eligibility of TBI tests. If the person is found eligible for TBI tests and if the TBI tests are available, then the process of tests would be conducted. If the tests are positive for TBI, the person would be redirected for assessment of feasibility of initiating TPT and that workflow would be pursued further as above. However, if the TBI tests are not feasible to be conducted then an outcome would be assigned.

In events where the person is not eligible for TBI tests or if the TBI tests are negative or not available then the person would enter the next activity-Assessment for TBI follow-up criteria to monitor clinical progress of such persons, reassess for TBI or TB disease on a later date as long as the TB transmission and breakdown risk prevails.

12.2.4 Assessment for TPT follow-up criteria

In this activity (swim lane) the person would be assessed for TPT follow-up criteria and if eligible for follow-up the person would re-enter the screening activity. If the person is found ineligible for follow-up then an outcome would be assigned.

12.3 Operational aspects for using Prevent TB India app/Nikshay TPT module

In the context of the TPT workflow as described above, the operational aspects in terms of data entry points, health facility/field levels applicable and envisaged field staff expected to perform these activities including data entry are as described in the table 12.1 below:

KEY POINTS TO REMEMBER

- ✓ The WHO prevent TB mobile application with monitoring dashboards customized for India is hosted on Nikshay and currently available on Google play store. This would be used for information management and monitoring of PM TPT implementation in India as an interim arrangement.
- ✓ The dashboard can be used by programme staff for real-time progress monitoring of the TPT care cascade.
- ✓ The information management for PMTPT will be built upon this system as a Nikshay TPT module in the near future.
- ✓ The data entered in the Prevent TB India app would ultimately be migrated to Nikshay TPT module when it is ready for the field implementation following which the Prevent TB India app would be phased out with necessary directions from NTEP.

CHAPTER 13:
PRIVATE SECTOR ENGAGEMENT

Learning Objectives

In this chapter we will learn about:

- Private sector engagement
- Current scenario for TPT in the private sector
- Implementing TPT in contacts of private sector patients
- Opportunities for TB preventive treatment through the private sector

13.1 Private sector engagement

The National TB Elimination Programme extends its services to all TB patients irrespective of whether the patient seeks care from the public or the private sector. Hence, all diagnostics, drugs, treatment support, incentives and enablers, and public health action linked provisions that are available to patients in the public sector should also be ensured for patients in the private sector. Over the past few years rigorous efforts have been made by the States and Districts to 'engage' private health providers such as establishing Patient Provider Support Agency (PPSAs) who have the primary task of making private health providers aware of the services available under NTEP and increasing their participation and role in the management of TB patients. This has translated to a significant rise in TB notification from the private sector and provides good opportunity to extend part of public health action to all TB patients notified from the private sector, including contact tracing and TPT for their contacts.

13.2 Current scenario of TPT in the private sector

The following mechanisms exist under NTEP for engaging with private sector with respect to ending TB and TPT services:

a. Contact tracing and providing TPT is part of the public health action under the Mandatory TB Notification Gazette for all TB patients notified from public as well as private sector.

b. This will be extended to the expanded target populations for TPT now, enabling a policy for universal coverage and monitoring of contact tracing, focusing coverage and completion rates to cover contacts of pulmonary* TB patients notified from the private sector as well.

c. Data on contact tracing for children < 5 and ≥ 5 years to rule out/confirm active TB will also be captured in Prevent TB India app/NIKSHAY while TPT coverage and completion is monitored for PLHIV and children < 5 yrs for index TB patients notified from public as well as private sector.

d. The current PPSA for private sector engagement through the JEET Project (joint effort for elimination of TB) and domestic resources are focused on implementing the notification

gazette including facilitation of public health actions for private sector patients including contact tracing and TPT currently with 6H, 3HP, 6Lfx, 4R whichever is available and applicable.

e. The World Bank Project has private sector engagement as a major thrust area in the nine high priority states with private sector that would lead to further penetration with services for TB patients and their families seeking care in the private sector not only for TB but also for TPT.

13.3 Implementing TPT in contact of private sector patients

Private sector patients may come into the purview of the local public health authorities either through notification in Nikshay, or through referrals made by private practitioners themselves. In both these cases, the local public health authorities must ensure that complete details of the patients are entered into Nikshay and home visit of the patients conducted by the local public health staff (STS, TBHV, ASHA) or through PPSA staff, as may be the case in that specific area.

All PLHIV, contacts of pulmonary* TB patients, other risk groups must be screened for TB; diagnostic tests may be carried out through public sector services or outsourced through PPSA/other partnership options to a private facility of choice. People in the target population who are themselves detected with any form of TB will need to be linked for TB treatment which can be from the public or private sector facilities. All people in the target population found to be eligible for TPT should be offered TPT from the facility of their choice (public or private).

All attempts must be made to offer free TPT services to private persons either directly from the public sector health facilities or through purchasing of services from the private sector. The ultimate aim is to provide good quality TB services at minimal out-of-pocket expenditure for the private TB patients/TPT persons.

13.3.1 Staff responsibilities

The responsibility of providing TPT rests with the local public health facility either from their own public sector services through established linkages with private facility, or from purchased services from private service providers as per the Partnership Guidelines (2019). The decision to extend public health action from public sector or through purchased services would depend on the local context of accessibility of services, and also patient/provider willingness.

Partnership linkages should be established between the private health facility (from where the patient seeks care) and the facility providing the public health action (public or private) by the PPSA, if present, or the STS, TB/HV, District PPM Coordinator or whichever staff that has been given the responsibility of private sector engagement by the MO-TC and DTO.

The actual contact tracing through home visits would need context specific and locally developed action plans. Models to reach out to private sector patients which are locally available, within NTEP (TBHV) or through the general health system/other health programmes (ASHAs, ANMs, CHOs), may be leveraged through proper intersectoral and inter-departmental linkages.

13.4 Opportunities for TB preventive treatment through partnership options

A range of TB related services can be 'purchased' for private sector patients. These can also be purchased for public sector patients, if specifically needed in any particular geography.

Contact tracing and chemoprophylaxis (TPT) as a separate activity has been included in the "Public Health Action" option under the Guidance Document on Partnerships 2019. However, it must be noted that TPT as part of the range of public health action, can also be included as an activity for PPSAs, or can be bundled with any other service such as 'diagnostics'. Since TPT for expanded risk groups, including household/close contact and other risk groups is a new activity being introduced to strengthen the End TB efforts under NTEP, States and Districts may assess other aspects of this activity that need focus in their respective geographies.

Particularly for the private sector, additional efforts for engagement may require more targeted advocacy and communication material for the providers as well as the patients and their contacts. Likewise, additional channels for specimen management, X-rays, drug supply will have to be established for TPT in the private sector. States may assess their needs and purchase whole package of services as a bundle, or individual activities in the range of services needed for TPT. A summary of the various private services which can be adopted are listed in the table 13.1 below.

Table 13.1 TPT services that can be adopted by private sector through partnership options

Partnership option & TPT services
1. Patient Provider Support Agency (PPSA)
i. Private provider engagement
ii. Linkages for specimen transportation and diagnostics
iii. Patient management (public health action, counselling, adherence support) logistics of anti-TB drugs for TPT
The PPSA is an example of a "service bundle" that covers a whole range of activities for end-to-end management of private sector
2. Public Health Action
i. Counselling and adherence management
ii. Contact tracing and chemoprophylaxis (TPT)
iii. HIV counselling, testing and treatment linkage
iv. Drug susceptibility testing (DST) and linkage for DR-TB services
v. Blood sugar testing and linkages for diabetic care
vi. Linkages for Nikshay Poshan Yojana
3. Specimen Management
i. Collection of sputum samples, blood specimen for TBI tests
ii. Collection of respiratory (excluding sputum) and EP specimen
iii. Transportation of specimen
4. Diagnostics
i. X-ray centres
ii. Smear microscopy (ZN/FM)/molecular diagnostics
iii. Culture (standalone) / Line Probe Assay / Culture and Drug Susceptibility Testing
iv. Pre-treatment and follow-up investigation
v. TBI test (TBI)

5. Treatment Services
i. TB management centre
ii. DR-TB treatment centre (outdoor)
iii. DR-TB treatment centre (indoor)
iv. Specialist consultation for DR-TB patients
6. Drug Access and Delivery Services
i. Drug supply chain management
ii. Improving access to anti-TB drugs for TB patients notified by the private sector
7. Active TB Case Finding and TB Prevention
i. Active TB case finding
ii. TB prevention package for vulnerability mapping, TBI testing and TPT
8. Advocacy, Communication and Community Empowerment
i. Advocacy
ii. Communication
iii. Community empowerment
9. Innovations

The details of these partnership options as well as mechanisms for contracting private service providers are available in the Guidance Document on Partnerships 2019. If being included in PPSAs or through other partnership options, States/Districts must ensure to budget TPT as a separate activity since the overall engagement needed for reaching out to contacts of all private TB patients, would be much larger.

KEY POINTS TO REMEMBER

- ✓ A patient notified in the private sector must receive all services as a patient in the public sector does. As part of public health action, contact tracing of private sector patients must be conducted, and TPT should be initiated for eligible contacts after ruling out active TB.
- ✓ Linkages must be well established between the private sector health facility and the local public health authorities at the TU/District level to ensure smooth flow of information and services for the benefit of the patient.
- ✓ Services that cannot directly be provided by the public sector, if any, should be purchased from Private Sector Service Providers, to ensure minimal out-of-pocket expenditure.
- ✓ Access to Nikshay ID, recording & reporting formats, IEC materials, drugs and incentives for private providers must be ensured.
- ✓ Responsibility of establishing linkages with the private sector should be clearly established by the local public health authorities- a coordinated effort of all State/ District PPM coordinators, DR-TB coordinators, STS, TB-HV, and staff from PPSA (if present) is needed.

CHAPTER 14: SUPPORTIVE SUPERVISION, MONITORING, EVALUATION

Learning Objectives

In this chapter we will learn about:

- Supportive supervision
- Monitoring cascade of care for TPT
- Monitoring indicators
- Evaluation

14.1 Supportive supervision

Supportive supervision is a process of helping health-care providers and supervisors to improve their performance on a continuous basis to be able to provide high quality care along the TPT care cascade to the target population. It is carried out in a polite and non-authoritarian way with a focus on using supervisory visits as an opportunity to improve knowledge and skills of health staff. It is an essential element for routine monitoring & evaluation. It includes quality checks for data recording and reporting, including inspection and validation of a person's case files and data collection tools for validity and completeness of recording. The frequency of supportive supervision depends on resources and needs, but closer monitoring may be needed.

Supportive supervision encourages open communication and team building approaches to facilitate real time hand holding and problem-solving. It focuses on monitoring performance towards goals, and using data for decision-making, and depends upon regular follow-up with staff to ensure that assigned tasks are being implemented correctly. The objectives of supportive supervision are to:

1. Build capacity of health staff to implement TPT related activities as recommended
2. Ensure that the data recorded and reported is accurate and valid
3. Incorporate a system of analysis and review aimed at improving quality of programme implementation
4. Increase involvement and commitment of staff at different levels
5. Ensure that field staff responds to Nikshay tasks, lists activities and updates missing information promptly & provides actionable and timely feedback
6. Evaluate impact of training on performance of health staff & assess retraining needs
7. Assess stocks and replenishment of supplies
8. Supervisory visits by the programme and staff of the general health system may also gather data for reporting in the Nikshay/ Prevent TB India app. This should involve members of both TB HIV and other related programmes.

Supervision would be the responsibility of all cadres of supervisors from states, district, TB unit, PHC and HWC levels for their respective catchment area for the entire TPT care

cascade and the related programme management system. Standard checklist to assess TPT implementation across the cascade of care starting from identification of the target population for TPT initiation and completion is given as below.

Table 14.1 Checklist for supervision of TPT care cascade

Supervisory checklist for TPT case cascade			Supervisory notes
Advocacy material for TPT	○ Available ○ Not available		
Communication strategy for TPT	○ Available ○ Not available		
TPT implementation as per PIP	○ Yes ○ No		
Status on HR as per work load	○ Adequate ○ Inadequate		
Training status of			
• NTEP staff	○ Yes	○ No	
• Doctors (public & private)	○ Yes	○ No	
• PPSA staff	○ Yes	○ No	
• CHOs	○ Yes	○ No	
• Paramedical staff	○ Yes	○ No	
• Treatment providers	○ Yes	○ No	
• TB survivors/champions	○ Yes	○ No	
Contact tracing through line listing	○ Done ○ Not done		
Directory of Treatment supporters	○ Available ○ Not available		
Specimen transport system for sputum and blood in place	○ Yes ○ No		
Status on TBI tests	○ Available/ Linkages established ○ Not available/ Linkages not established		
Option of partnership options for diagnostics	○ Available ○ Not available		
Adherence mechanisms	○ Treatment supporter ○ Tele/video calls ○ 99DOTS/MERM		
Is the drug stocking and supply chain management adequate	○ Yes ○ No		
Number of months of stock available as per consumption and stocking norm ○ 6H ○ 3HP ○ 6Lfx ○ 4R	Months of stock _____ _____ _____ _____		

Is there a stock-out or low stocks for any TPT regimen courses	○ Yes ○ No	
aDSM system in place	○ Yes ○ No	
Community engagement done	○ Yes ○ No	
Logistics/ trainings for recording & reporting (printing, digital platform readiness with peripheral devices, internet etc)	○ Available ○ Not available	
Recommended actions:		
Name of the facility visited:		
Signature of supervisor	Designation of supervisor	Date of visit

14.2 Monitoring TPT care cascade

Monitoring and evaluation (M&E) play an important role in patient care and programme implementation. All individuals who are most at risk of developing TB are systematically identified and once TB disease is excluded, offered TPT.

Programmatic implementation and scale-up of TPT requires strengthening of each of the following elements in the cascade of care starting from identification of the target population to provision and continuation of TPT.

14.2.1 Care cascade for TPT

Programmatic implementation and scale-up of TPT requires strengthening of each element in the cascade of care starting from identification of the target population to provision and continuation of TPT. It is important to ensure that all individuals who are most at risk of developing TB are systematically identified, and once TB disease is excluded, offered TPT to improve both their individual health as well as community level decline of TB disease.

Steps in TPT care cascade include:

- Identification of target population at risk will determine the overall denominator.
- Total number evaluated for TB disease will determine the number evaluated for TB disease out of the denominator of target population at risk. Ideally everybody should be evaluated to rule out active TB disease.

- Total number tested for TB infection will determine the number tested out of the number evaluated and ruled out of active TB disease.
- Total number eligible for TPT will determine the number eligible for TPT out of those tested for TB infection and found positive after ruling out active TB or screened and ruled out of active TB as per the eligible population.
- Total number initiated on TPT will determine the number initiated on TPT out of those tested positive for TB infection (includes children > 5yr, adults HHC and other risk groups) or screened and ruled out of active TB (includes children <5yrs & eligible PLHIV after ruling out TB).
- Total number completed TPT will determine the number who have completed the full course of TPT out of all who have started TPT as per eligible population and TPT regimen.

The cascade of care includes two critical sub-cascades as per the at-risk population as per table 14.1 and 14.2 below:

Table 14.1 Cascade of care for those with test & treat policy after ruling out TB

Steps of care cascade	Programmatic benchmarks
1. Total at-risk population	Includes all at-risk as per populations identified
2. Total no. screened for active TB disease	100%
3. Total no. tested for TB infection (excluding those with active TB)	>90% to be tested
4. Total no. eligible for TPT (excluding those with TBI test negative)	Includes children > 5yr and adults
5. Total started on TPT	>90% among eligible
6. Total completed TPT	>90% to complete TPT
7. Total post TPT follow-up for 6m, 12m, 18m, 24m	>90% individuals who completed TPT

Table 14.2 Cascade of care for those with screen and treat policy after ruling out TB

Steps of care cascade	Programmatic benchmarks
1. Total at-risk population	Includes all at-risk as per populations identified
2. Total no. evaluated for TB	100%
3. Total no. identified as TB disease	~10% as TB
4. Total no. eligible for TPT	>90%, includes children <5yrs & eligible PLHIV after ruling out TB
5. Total started on TPT	>90% among eligible
6. Total completed TPT	>90% to complete TPT
7. Total post TPT follow-up for 6m, 12m, 18m, 24m	>90% individuals who completed TPT

14.2.2 Tools for monitoring

Under NTEP, the electronic system (Nikshay) is being used to capture data elements that are needed for PMTPT care and monitoring to generate indicators automatically. The programme has adapted the WHO prevent TB India app, customized the same as per country requirements and hosted on Nikshay as an interim solution till the Nikshay TPT module is developed and fully functional. The entries will be done in the app by the health workers or the treatment supporters and the same will generate the line list of those beneficiaries enrolled for TPT. This will eventually be transitioned to the TPT module in Nikshay which will follow a life cycle approach for long-term follow-up of persons who complete TPT.

The monitoring tools include:

a. Line list for TPT

Line list of TPT beneficiaries enrolled will be generated as an output of the Prevent TB India app. It will have the details of all the beneficiaries who have been enrolled for TPT in the respective HF. The display of the line list is given in figure 14.1 below.

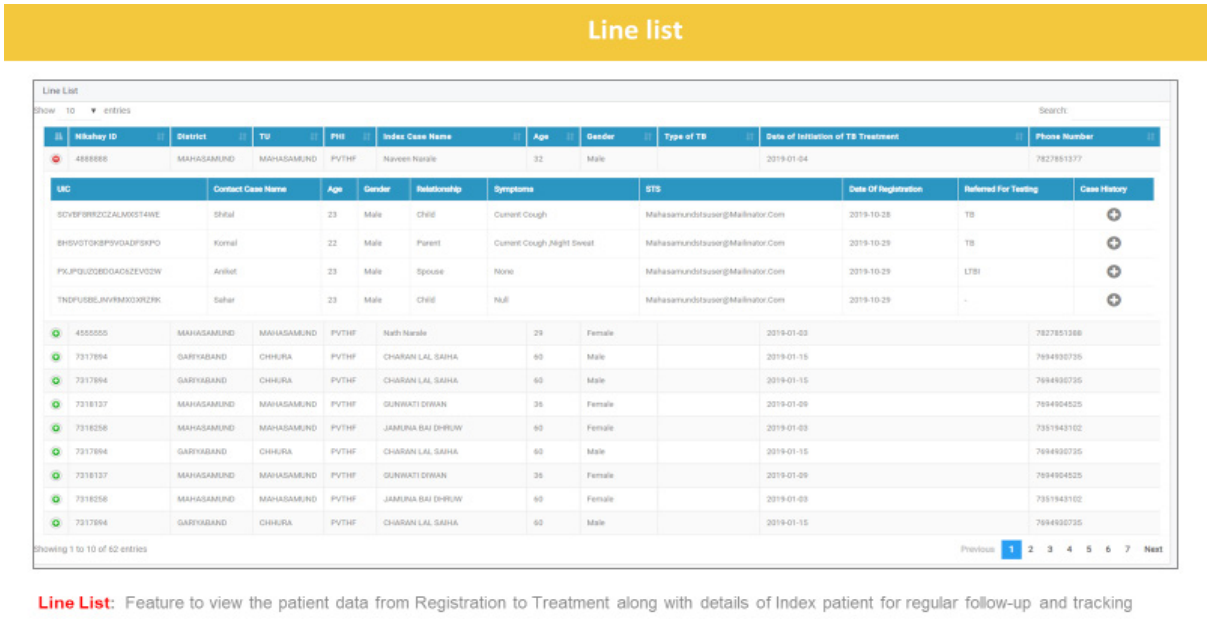


Figure 14.1 Display of line list of all TPT beneficiaries enrolled in Prevent TB India app.

b. Dashboard for TPT

Includes TPT cascade, screening overview, testing & evaluation overview, cascade analysis split by State and district level, prevalence of symptoms, age-wise distribution, regimen distribution, reason for non-initiation, treatment outcomes. These dashboards may be used for the monitoring of the activities at national, state, district, TB unit and HF level (figures 14.2 to 14.4). The TPT monitoring dashboard can be accessed by various levels of supervisors using their respective Nikshay login ids using a link provided in the Nikshay Reports section on TPT Reports.

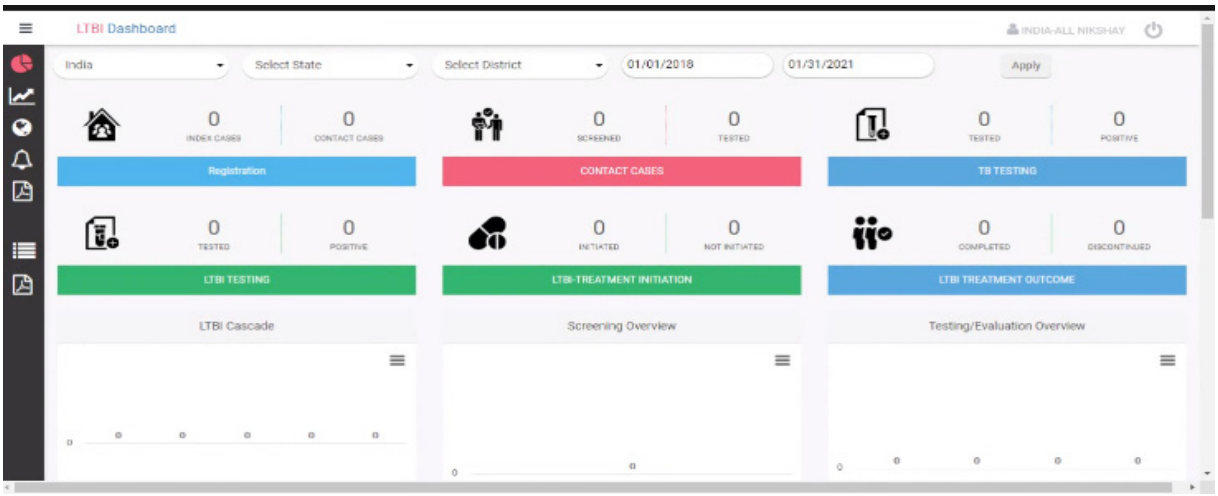


Figure 14.2 TPT dashboard overview in Prevent TB India app

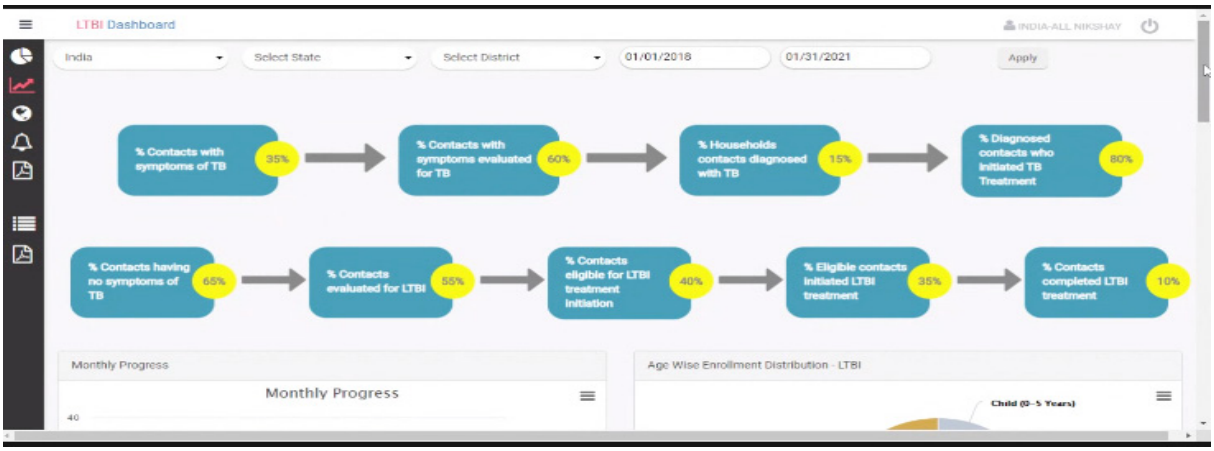


Figure 14.3 TPT care cascade analysis view on dashboard in Prevent TB India app/ desktop

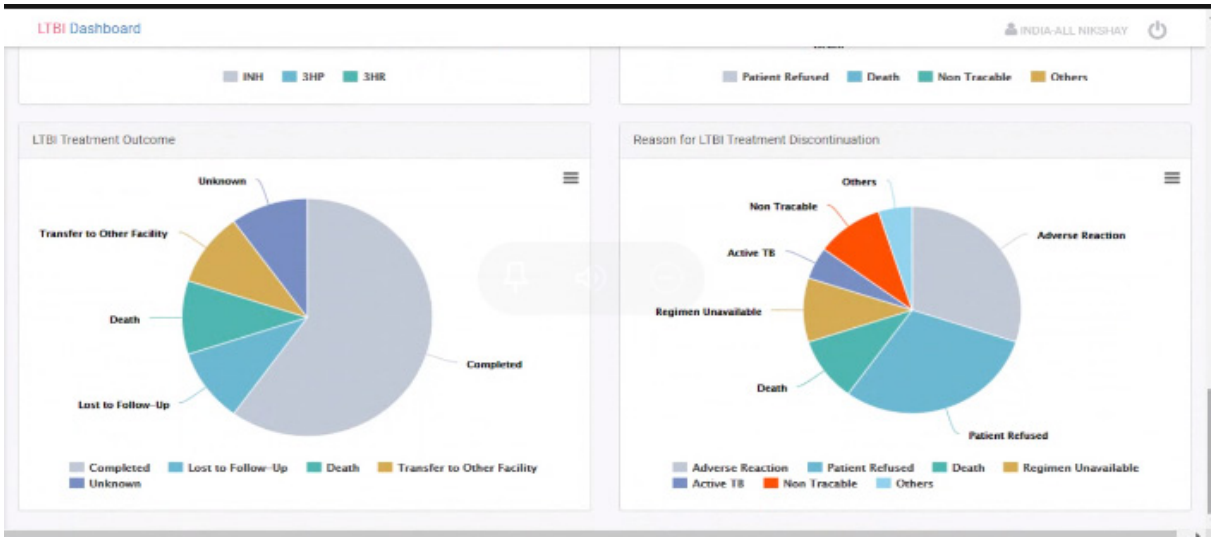


Figure 14.4 TPT Treatment outcome & reason for discontinuation on dashboard in Prevent TB India app/desktop

14.2.3 Monitoring indicators for TPT

The monitoring indicators for the TPT care cascade are enlisted and defined in table 14.3. The indicators would be automatically generated on the dashboard of the Prevent TB India app and can be used to monitor the care cascade by states, districts, TB units and HF levels for different time periods (monthly, quarterly, annual) even in real-time.

Table 14.3 Monitoring indicators for TPT care cascade

Indicator	Definition	Numerator	Denominator
Contact investigation coverage	Number of contacts of pulmonary* TB patients evaluated for TB disease and TB infection out of the target population, expressed as a percentage for total and for each age group (Children <5 yrs, Children 5-18 yrs & Adults >18yrs)	Total number of contacts of pulmonary* TB patients who completed evaluation for TB disease and TB infection during the specific period	Total number of contacts pulmonary* TB patients during the specific period

Indicator	Definition	Numerator	Denominator
TPT coverage	Number of individuals initiated on TPT out of those eligible (if tested – TPT positive or if only screened – ruled out of active TB), expressed as a percentage for total and for each of the risk groups (newly enrolled or all PLHIV, children <5 yrs, children 5-18 yrs & adults >18yrs, other risk groups)	Total number of individuals eligible for TPT who initiated treatment during the specific period	Total number of individuals eligible for TPT during the specj91 ific period
TPT completion	Number of individuals completing TPT out of those initiating treatment, expressed as a percentage for total and for each of the risk groups (newly enrolled or all PLHIV, children <5 yrs, children 5-18 yrs & adults >18yrs, other risk groups)	Total number of individuals who completed a course of TPT of those initiated on TPT during the specific period	Total number of individuals who were initiated on a course of TPT during the specific period
Breakdown rate to TB among all TPT beneficiaries	Proportion of beneficiaries on TPT, diagnosed as TB during the TPT course or during long term follow up at 6, 12, 18 & 24 months post-TPT completion	Total number of beneficiaries on TPT diagnosed as TB during the TPT course or during long term follow up at 6, 12, 18 & 24 months post-TPT completion	Total number of beneficiaries who were initiated on TPT during the specific period

14.2.4 Monitoring TPT completion

Monitoring TPT completion is required both for individual care and programme management. The electronic data capture tool should record details of treatment outcomes for each individual starting TPT. TPT may be considered completed when an individual takes 80% or more of the prescribed number of doses of treatment within 133% of the scheduled duration of the respective TPT regimen and remains well or asymptomatic during the entire period.

14.3 Evaluation

Periodic evaluation of the services under PM TPT and the performance of TPT care cascade implementation by various states and districts is a necessary requirement to enable continuous quality improvement. This will be integrated in the existing mechanisms of central and state internal evaluation protocols with inclusion of the above supervisory checklist and monitoring indicators in the existing evaluation protocols. PM TPT will thus be integral part of the NTEP central and state internal evaluation mechanism and would be carried out at the stipulated frequencies as per the NTEP guidelines.

KEY POINTS TO REMEMBER

- ✓ Supervision would be the responsibility of all cadres of supervisors from states, district, TB unit, PHC and HWC levels for their respective catchment area for the entire TPT care cascade and the related programme management system.
- ✓ Standard checklist to assess TPT implementation across the cascade of care starting from identification of the target population for TPT initiation and completion.
- ✓ It is important to ensure that all individuals who are most at risk of developing TB are systematically identified, and once TB disease is excluded, offered TPT to improve both their individual health as well as community level decline of TB disease.
- ✓ Line list of TPT beneficiaries enrolled will be generated as an output of the Prevent TB India app.
- ✓ The TPT monitoring dashboard can be accessed by various level of supervisors using their respective Nikshay login ids using a link provided in Nikshay Reports section on TPT Reports.
- ✓ PM TPT will thus be integral part of the NTEP central and state internal evaluation mechanism and would be carried out at the stipulated frequencies as per the NTEP guidelines.
- ✓ Programmatic implementation and scale-up of TPT requires strengthening of each element in the cascade of care starting from identification of the target population to provision and completion of TPT including monitoring breakdown to active TB during or post-TPT completion.

CHAPTER 15:
COMMUNITY ENGAGEMENT

Learning Objectives

In this chapter we will learn about:

- Community engagement
- Informing community
- Consulting community
- Collaborating with community
- Empowering community
- Role of community based organizations

Communities play a major role not only in treating the TB disease but also in preventing the TBI progressing to TB disease. Community engagement and health education play a very important role in ascertaining that individuals and communities can make informed choices regarding TPT and policies must be evaluated based on views and experiences of affected populations in an equitable manner while focusing on human rights aspects of it based on consent and confidentiality.

15.1 Community engagement

Community engagement is central to all public health interventions and is viewed as involving those affected in understanding the risks they face and involving them in response actions that are acceptable. Engaging with the community is essential to TPT in India as there is clear lack of knowledge among community members about the recognized benefits of TPT and actions are required from individuals, families and communities for the effective implementation of the same.

Informed and empowered communities can play a very important role in ascertaining that individuals and communities make informed choices regarding TPT and adhere to the same fully. This is important also because those infected with TB bacteria and at–risk of developing the disease may feel well and hence may not consider it necessary to take the medicine. Further, views, experiences and involvement of affected populations help in making policies and programmatic designs focus on human rights aspects of TPT and uphold privacy, dignity and autonomy of the individuals undergoing the TPT.

Following are the broad strategies for engaging community in TPT implementation and scaling up:

1. Inform
2. Consult

3. Collaborate
4. Empower

15.1.1 Inform community

Inform community about benefits of TPT to individuals, families, and community with emphasizing how TPT acts as prevention and how it can break the transmission chain of TB in the community. Interventions can include:

- Awareness & social mobilization drives/campaigns at community levels using multiple channels such as mass and mid media, inter-personal communication tools, etc.
- Sensitization and involvement of key community leaders, opinion leaders, celebrities, schools, etc in communication campaigns.
- Dissemination of user-friendly IEC materials on TPT which are easy to understand and help in making appropriate health-care decisions by individuals/families/community members (act on information). Such materials should cover information on prevention, myths and facts, nutrition, health-care facilities, co-morbidities, etc. Materials specific to TPT for those undergoing TPT shall also be developed in consultation with the communities.

15.1.2 Consult the community

Consult the community for planning, implementing, and monitoring the TPT intervention and scale-up. Community's opinion can be gathered through community meetings, patient provider meetings, involving community representatives in planning & monitoring meetings, etc. Such consultations will be done for developing tools and contents for communication on TPT, developing local plans for TPT implementation & scale-up, demand generation, gathering community feedback on TPT services, etc.

15.1.3 Collaborate with the community

Collaborate with the community through formal Civil Society Organizations (CSO) including NGOs, CBO, FBOs, etc. and informal groups for implementing TPT. Partnerships with CSOs at national, state, district/sub-district/town/village levels will be explored for various interventions, based on the need assessment and potential of individual organizations (The gap analysis tools given in NTEP Partnership Guidance 2019 shall be used for needs assessment). The areas of interventions could be, but not limited to, as follows:

- Awareness generation, behaviour change communication & social mobilization.
- Capacity building of health-care facilities and frontline health workers in TPT.
- Case finding through screening & referral and/or testing for TBI among contacts of TB patients & other target populations.
- Facilitating access to diagnostic services (e.g. sputum or blood specimen collection and transport, provisions for X-ray).
- Supporting TPT initiation & adherence through health education, counselling, follow-up support, etc.
- Developing TPT adherence support in community through identification and training of community treatment supporters, facilitation of treatment support groups, training of families/caregivers, implementation of Peer-support models, etc.
- Facilitate treatment completion & follow-up investigations.
- Facilitating community surveillance of TBI, TPT, ADRs, development of Active TB etc.
- Developing differential strategies for effective implementation of TPT among vulnerable populations such as PLHIV, tribal, urban slum population etc.

15.1.4 Empower the affected community

Empower the affected community as a partner in TPT response through capacity building and involvement of TB survivors, their contacts & others who are eligible for TPT and networks of TB survivors in various facets of the response across levels. Drawing from their experiences of going through the disease and potential to offer Peer Support, the TB champion's roles will cover the following areas:

- Encouraging contacts of TB patients and other eligible individuals for TBI screening and TPT.
- Providing peer counselling with psycho- social support, addressing of self- stigmatization, etc to the patient and family members.
- Ensuring supportive monitoring of those on TPT and providing of treatment education, suggestions on nutrition, healthy lifestyles and positive living, psychosocial support, addressing specific issues during home visits, etc.
- Preventing TPT treatment interruptions and promoting completion of TPT.
- Monitoring and early identification of adverse drug reactions and/or development of TB symptoms.
- Addressing stigma of TB in the community.
- Acting as a link between the community and health-care system and facilitating care seeking and feedback on health service delivery.

The community collectives such as TB survivor/PLHIV networks can also mobilize the community members for TPT and bring issues to the notice of the health system directly or through various platforms such as community meetings, TB forum, etc.

15.2 Role of community based organizations (CBOs) and civil society

CBOs, CSOs and affected communities are key stakeholders in the efforts for ending TB including TPT. While the TPT is primarily a responsibility of health services, it is acknowledged that the role of CSOs and communities is to facilitate demand generation and appropriate health seeking behaviour of target populations using a flexible user-centric model to meet users' needs and provide services to vulnerable and stigmatized members of society, whether as a faith group in the community, or as an organization. Therefore, models based on cross-sector collaboration are effective for improving access and quality of TB care including TPT.

Their major roles and responsibilities would include

- Integrating contact investigations into the roles and responsibilities of existing health and community workforce
- Ascertaining availability and capacity of community health workers and other networks (such as TB survivors, TB champions) that can contribute to TPT service delivery and support to individuals
- Training and capacity building of health-care workers, community workers and other implementers
- Building demand creation of TPT among vulnerable groups and community at large
- Ensuring community sensitization of TB survivors, PLHIV networks and others
- Identifying community volunteers as treatment supporters
- Undertaking training and on-the-job capacity building for health-care workers, community health workers and other service providers in systematic TB symptom screening

- Conducting regular supportive oversight at national, state, district, TB unit and community levels for TB screening activities, especially those carried out by community health workers to ensure good quality screening and adherence to national algorithms
- Ascertaining the role and responsibilities of health providers, community health workers and key stakeholders (such as Nutritional Rehabilitation Centres, ART Centres, MCH service delivery point etc.) in evaluation of eligibility, start and completion of TPT.

KEY POINTS TO REMEMBER

- ✓ Engaging with the community is essential to TPT in India as there is clear lack of knowledge among community members about the recognized benefits of TPT and actions are required from individuals, families and communities for the effective implementation of the same.
- ✓ Broad strategies for engaging community in TPT implementation and scaling up include Inform, Consult, Collaborate and Empower.
- ✓ Inform community about benefits of TPT to individuals, families, and community with emphasizing how TPT acts as prevention and how it can break the transmission chain of TB in the community.
- ✓ Consult the community for planning, implementing, and monitoring the TPT intervention and scale-up.
- ✓ Collaborate with the community through formal CSOs including NGOs, CBO, FBOs, etc. and informal groups for implementing TPT.
- ✓ Empower affected community as a partner in TPT response through capacity building and involvement of TB survivors, their contacts & others who are eligible for TPT and networks of TB survivors in various facets of the response at each level.
- ✓ The role of CSOs and communities is to facilitate demand generation and appropriate health seeking behaviour of target populations using a flexible user-centric model to meet users' needs and provide services to vulnerable and stigmatized members of society, whether as a faith group in the community, or as an organization.

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Annexure 1
STATE TB PREVENTIVE TREATMENT COMMITTEE

Constitution:

1. Chairperson – Principal Secretary Health
2. Vice Chairperson - Mission Director National Health Mission
3. Member – Project Director – State AIDS Control Society
4. Member Secretary – State TB Officer
5. Member – Joint Director (CST) - State AIDS Control Society
6. Members – Chairperson – State Task Force for Medical Colleges
7. Members – Heads of Department (Key institutions in the state)
    a. Pulmonary medicine
    b. General medicine
    c. Paediatric
    d. Microbiology
    e. Community medicine
    f. Obstetrics and Gynaecology
    g. Gastro-enterology
    h. Pharmacology
    i. Any other relevant departments
8. Members – Eminent specialists from private/corporate institutions
9. Members – Representative of State chapters of various medical associations
    a. Association of Physicians of India
    b. Indian Medical Association
    c. Indian Association of Paediatrics
    d. Any other relevant associations
10. Members – Eminent specialists from private/corporate institutions
11. Members – Representative from the community
12. Members – Representative from civil society organizations
13. Members – 1 District TB Officer
14. Members – 1 Block Medical Officer
15. Members – 1 Community Health Officer, Health & Wellness Centre
16. Members – Representatives from partner agencies
17. Member – WHO NTEP Regional Team Lead for the state
18. Member – WHO NTEP Medical Consultant – State Headquarters
19. Any other member with permission of Chairperson

Terms of Reference:

- Meet at monthly intervals initially and then quarterly after complete rollout in the state.
- Strategize activities for effective and rapid implementation of the national guidelines for programmatic management of TB preventive treatment (PM TPT) in the state.
- Develop plan of action for preparation (HR, training, testing, treatment centres, peripheral digital devices, prevent TB India app, drug supply chain management, community support etc.), implementation, expansion, and quality maintenance of TPT activities in all HWCs, blocks, districts of the state including private sector beneficiaries.
- Include TPT activities and budget in the State/ District PIP as per the NHM/NTEP norms.
- Map HFs providing care to the target populations eligible for TPT and organize the TPT care cascade of services in the blocks/districts.
- Map out high TB transmission settings (health-care workers, prisons, mines, slums, tribals, migrant labourers etc.) as part of a vulnerability mapping exercise done for ACF and undertake prioritization of state specific TPT risk groups guided by differential TB epidemiology if the risk of active TB among them is higher than that of the general population in the respective states.
- Periodically review implementation status of PM-TPT and address challenges in the respective state to ensure PM-TPT policies and guidelines are being followed.
- Periodically review adequacy status of testing, drugs & logistics related to PM-TPT activities
- Leverage partnership models for TPT activities as per NTEP Partnership Guidelines 2019
- Conduct periodic review & monitoring of PM-TPT activities at state level
- Use Prevent TB India app/Nikshay dashboards for real-time and periodic review of the TPT care cascade by districts, blocks, HFs to identify areas needing urgent intervention to improve access and quality of care.

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