

National Guidelines for the Programmatic Management of Tuberculosis Preventive Treatment (PM-TPT)

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Foreword

Tuberculosis is a formidable public health challenge in Pakistan, placing us 5th amongst high burden countries globally. While most high burden TB countries are seeing falls in incidence of TB, in Pakistan, the estimated TB incidence has not fallen in two decades and a third of TB cases are not notified. This is a matter of serious concern.



It is encouraging to see collaborative work between the National and Provincial TB Control Programmes; this work is via a well-designed policy and includes private sector engagement.

There is strong evidence that preventive therapy is effective in reducing the incidence of TB and the Government of Pakistan has committed to provide preventive therapy (at UNHLM, September 2018) to eligible persons in the country. We are some distance from targets, but it is heartening to see that National TB Control Program (NTP) is on the right track in the provision of preventive treatment where needed.

The ministry of National Health Services, Regulations and Coordination (NHSRC) appreciates the efforts of the NTP regarding finalizing the policy guidelines for Programmatic Management of Tuberculosis (TB) preventive treatment (PM-TPT). The contributions of the National Coordinator, Deputy National Coordinator, technical and programmatic experts from federal and provincial teams, academia, Pakistan Chest Society and Pakistan Paediatric Association, for putting this together is commendable.

The NHSRC acknowledges support from Global Funds (ATM), WHO and USAID for their contribution to initiate, implement and scaling up efforts for TPT implementation.



Dr Faisal Sultan
Special Assistant to
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Message from the National Coordinator Common Management Unit (CMU), National Health Services, Regulations and Coordination (NHSRC)



Based on the global recommendations and World Health Organization (WHO) guidelines 2020, National TB Control Program (NTP), with the support of national and international experts, has adapted and developed National guidelines for the programmatic management of Latent Tuberculosis Infection (LTBI) through a broad based consultative process, recommending TB preventive treatment (TPT).

These guidelines cover every aspect of management of LTBI & TPT. The target audience of these guidelines are health care professionals providing care and treatment to TB patients.

I am pleased to acknowledge the efforts made by Strategic Technical Advisory Group (STAG) members, composed of esteemed members of Academia, National and Provincial TB Control program for participating in the endorsements of the TPT policy guidelines.

I also acknowledge the contribution of the WHO representatives, Dr Dennis Falzon and Dr Matrin Van Den Boom and others in reviewing and approving the guidelines ahead of their publication.

Mr Mohammad Bashir Khan
National Coordinator, CMU/ NHSRC





Message from Deputy National Coordinator Common Management Unit (CMU), National Health Services, Regulations and Coordination (NHSRC)



Pakistan ranks fifth among 30 high-burden countries worldwide for tuberculosis. As per WHO estimated incidence (@ 259 per 100,000), around 570,000 new TB cases emerge annually in the country. National Tuberculosis Control Programme (NTP) has taken effective measures to impact incidence and mortality of TB in Pakistan.

High prevalence, operational challenges in the health system especially private sector engagement were the key areas of concern.

Based on the global recommendations and World Health Organization (WHO) guidelines 2020 and as envisaged in National Strategic Plan (NSP) 2020-2023. NTP, with the support of national and international experts, has adapted and developed National guidelines for the management of Latent Tuberculosis Infection (LTBI) through a broad based consultative process, recommending TB preventive treatment (TPT) to around 1.9 million eligible people by 2023.

These guidelines cover every aspect of management of LTBI & TPT. The target audience of these guidelines are health care professionals providing care and treatment to TB patients including doctors, paramedics, nurses, pharmacists, laboratory technologists, and program management staff. I hope these guidelines will go a long way in providing preventive treatment to all those who are eligible.

I would also like to offer my gratitude to the WHO and USAID for financial and technical support, and looking forward to working together in a participating environment to End TB from Pakistan.

Dr Abdul Wali Khan

Deputy National Coordinator
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Abbreviations and Acronyms

ART	Antiretroviral Treatment	MDR-TB	Multidrug–Resistant
BCG	Bacille Calmette–Guérin		Tuberculosis
BMI	Body Mass Index	MUAC	Middle Upper–Arm
CRP	C – Reactive Protein		Circumference
CXR	Chest X-Ray	NSP	National Strategic Plan
CBC	Complete Blood Count	PMTPT	Programmatic Management of
DS-TB	Drug Susceptible Tuberculosis		Tuberculosis Preventive
DST	Drug Susceptibility Testing		Treatment
IGRA	Interferon–Gamma Release	PLHIV	People Living with Human
Assay			Immunodeficiency Virus
INH	Isoniazid; Isonicotinic acid	PTB	Pulmonary Tuberculosis
	hydrazide; C ₆ H ₇ N ₃ O	TB	Tuberculosis
IPT	Isoniazid Preventive Therapy or	TNF	Tumour Necrosis Factor
	Isoniazid Preventive Treatment	TPT	Tuberculosis Preventive
LFTs	Liver Function Tests		Treatment
LTBI	Latent Tuberculosis Infection	TST	Tuberculin Skin Test





Definitions*

- **Infant:** a child under 1 year of age.
- **Child:** a person under 10 years.
- **Adolescent:** a person aged 10–18 years.
- **Adult:** a person over 18 years of age.
- **Bacteriologically confirmed TB:** TB diagnosed in a biological specimen by smear microscopy, culture or a WHO-approved molecular test such as Gene X-pert.
- **Contact:** any person who was exposed to a case of TB.
- **Household contact:** a person who shared the same enclosed living space for one or more nights or frequent or extended periods during the day with the index case during the 3 months before the commencement of the current treatment episode (once effective treatment is started; index case is less likely to transmit the infection to contacts).
- **Close contact:** a person who is not in the household but shared an enclosed space, such as a social gathering place, workplace or facility, for extended periods during the day with the index case during the 3 months before the commencement of the current treatment episode.
- **Contact investigation:** a systematic process for identifying previously undiagnosed cases of TB among the contacts of an index case. Contact investigation consists of identification and prioritization and clinical evaluation.
- **The index case (index patient) of TB:** the initially identified case of new or previously treated TB in a person of any age, in a specific household or another comparable setting in which others may have been exposed. An index case is a case on which a contact investigation is centred but is not necessarily the source case.
- **Tuberculosis (TB) disease:** an illness in which TB bacteria are multiplying and attacking a part of the body, usually the lungs. The symptoms of TB disease include weakness, weight loss, fever, no appetite, chills, and sweating at night. Other symptoms of TB disease depend on where in the body the bacteria are growing. If TB disease is in the lungs (pulmonary TB), the symptoms may include cough, pain in the chest, or coughing up blood. A person with TB disease may be infectious and spread TB bacteria to others.





- **Latent Tuberculosis Infection (LTBI):** a state of persistent immune response to stimulation by *Mycobacterium Tuberculosis* antigens with no evidence of clinically manifest active TB. There is no gold standard test for the direct identification of *Mycobacterium Tuberculosis* infection in humans. The vast majority of infected people have no signs or symptoms of TB, but are at risk of developing active TB disease in their lifetime.
- **Tuberculosis Preventive Treatment (TPT):** the treatment offered to individuals who are considered to be at risk of TB disease to reduce that risk. It is also referred as LTBI treatment or TB preventive therapy.

**The definitions listed above apply to the terms that are used in these guidelines. They may have different meanings in other contexts.*





Target Audience

The target audience of these guidelines is health care professionals providing prevention and care in National TB and HIV Control Programmes. The guidelines specifically target doctors, clinical officers, nurses, pharmacists, service providers, laboratory technologists, and programme management staff. They are also appropriate for officials in other line ministries who work in the areas of health, including prison services, social services and immigration (such as Ministries of Law and Justice) and clinicians and public health practitioners working on TB, HIV, infectious diseases, prevention, child health and non-communicable diseases such as chronic kidney disease and cancer.





Executive Summary

Latent Tuberculosis Infection (LTBI) is defined as a state of a persistent immune response to stimulation by *Mycobacterium tuberculosis* antigens with no evidence of clinically manifest active TB. There is no gold standard test for LTBI. The WHO guidelines on LTBI consider the probability of progression to active TB disease in a specific risk group, epidemiology, and burden of TB, availability of resources, and the likelihood of a broad public health impact.

These guidelines are adapted from WHO recommendations for programmatic management of LTBI issued in 2020. Recommendations are presented logically according to the “cascade of prevention” for managing LTBI: identification of at-risk populations (adults and children living with HIV, HIV-negative adult and child contacts, and other HIV negative at-risk groups), ruling out active TB disease, testing for LTBI, providing treatment, monitoring adverse events, adherence, and completion of treatment and monitoring and evaluation.

The guiding principle that individual benefit outweighs risk is the mainstay of recommendations on LTBI testing and treatment. The benefit of systematic testing and treatment of LTBI for people living with HIV and children under 5 years of age who are household contacts of bacteriologically confirmed pulmonary TB (PTB) patients is effective. Similarly, there is evidence that HIV-negative groups at clinical risk, such as patients initiating anti-TNF treatment, receiving dialysis, preparing for organ or haematological transplantation, and those with silicosis could also benefit from testing and treatment of LTBI, because of their increased risk of progression to active TB disease.

Key Points 1

The LTBI treatment through systematic testing targets people living with HIV, children under 5 years of age who are household contacts of bacteriologically confirmed pulmonary TB (PTB) patients is effective.

HIV-negative groups at clinical risk, which include patients initiating anti-TNF treatment, receiving dialysis, preparing for organ or haematological transplantation and those with silicosis could also benefit from testing and treatment of LTBI because of their increased risk of progression to active TB disease.





Background

Pakistan ranks fifth among 30 high-burden countries for TB and fifth for drug-resistant TB (DRTB). The estimated TB incidence is 259 per 100,000 with an estimated 570,000 new TB cases each year. TB mortality is showing a decline and currently is at 44,000 deaths (2021).¹ In 2019, the National Tuberculosis Control Programme (NTP) notified 334,800 incident TB cases, which accounts for 68% of the estimated cases. Among the notified cases, 80% are PTB. Among PTB cases, 50% are bacteriologically confirmed. Most of the population have their first contact with a private provider for health care therefore, it is important to involve private practitioners in TB care services.

The NTP, working under the Ministry of National Health Services, Regulation and Coordination, Government of Pakistan implements, after adaptation, the World Health Organization (WHO) recommended End-TB Strategy for effective control of TB. In agreement with the strategy, the NTP endorses the adoption of a strategy for the identification and treatment of latent tuberculosis infection (LTBI) in high-risk populations.

In addition, Pakistan adopted the Sustainable Development Goals (SDGs) 2030 agenda providing a comprehensive long-term strategy for achieving inclusive growth and sustainable development. It is a signatory to the Moscow Declaration to End TB. Pakistan also endorsed the Political Declaration on the Fight against Tuberculosis at the United Nation's (UN) first High-Level Meeting for TB held on 26th September 2018. By that declaration, the UN and Pakistan committed to global prevention of tuberculosis through preventive treatment by 2022 in at least 30 million people, including 4 million children under five years of age, 20 million other household contacts of people affected by tuberculosis, and 6 million people living with HIV and AIDS.

LTBI is defined as a state of a persistent immune response to stimulation by *Mycobacterium tuberculosis* antigens with no evidence of clinically manifest active TB.² Internationally, Tuberculin Skin Test (TST) and Interferon-Gamma Release Assays (IGRA) are used to test for LTBI. However, neither provide the “gold standard” to identify the global burden of LTBI. Research indicates that up to one-fourth of the world's population is estimated to be infected with *M. tuberculosis*,³ and the vast majority have no signs or symptoms of TB disease and are not infectious, although they are at risk for active TB disease and for becoming infectious. Several studies specify that approximately 5–10% of those infected with LTBI will develop active TB disease throughout their lives, usually within the first 5 years after initial infection.⁴ The risk is particularly high among children under the age of 5 years and people with compromised immunity.⁵





People with LTBI do not have symptoms, and they cannot spread TB bacteria to others. However, if M. Tuberculosis reactivates in the body and multiply, the person will go from having LTBI to being sick with TB disease. There is strong evidence that preventive therapy is effective in reducing the incidence of TB and death from TB in infected people, the main evidence coming from PLHIV. Prevention of active TB disease by treatment of LTBI is a critical component of the WHO End TB Strategy.⁶ The efficacy of currently available treatment regimens ranges from 60% to 90%.

LTBI testing to cover the entire population is infeasible because there is no gold standard to tests for LTBI. Cost of the existing methodologies: TST and IGRA, is high, for an unproven public health impact. Moreover, there may be risks of serious and fatal side effects of the treatment used to treat LTBI. Nonetheless, for individuals infected with LTBI among population groups in which the risk for progression to active disease significantly exceeds that of the general population, the benefits are expected to be greater than the harms.

There is no evidence that the provision of one or two drug regimens for preventive therapy for people infected with LTBI increases the risk of developing drug-resistant TB. LTBI is characterized by a limited number of M. Tuberculosis bacilli, whereas the probability of finding naturally resistant M. Tuberculosis bacteria, which can be selected under drug pressure, is insignificant. Henceforth, LTBI treatment is unsupervised, yet it should start only after cautiously excluding the possibility of active TB disease.

Historically, Pakistan limited dissemination of Tuberculosis Preventive Treatment (TPT) to children < 5 years of age and PLHIV, who were the household contacts of bacteriologically confirmed TB cases.⁷ Still, TPT implementation has been at a low level - 5.7% (C.I. 5.2% - 6.3%).¹ For comparison, the coverage of LTBI diagnosis and treatment in high-risk groups is 23% in EMRO and 27% globally. Since the UN High-Level Meeting on TB in 2018, the recommendations by the WHO now advocate tuberculosis preventive therapy (TPT) for contacts of any age. The country target set in the National Strategic Plan (NSP) 2020-2023 for preventive treatment is 1.6 million.

In a recent experience, among 215 household contacts of MDR-TB who were eligible for infection treatment in Pakistan, 172 (80.0%) initiated a fluoroquinolone regimen and 121 (70.3%) completed it. No TB disease or significant adverse events were observed during 12 months of follow-up.⁸ The authors concluded that fluoroquinolone-based treatment for contacts with presumed DR-TB infection is feasible and well-tolerated in Pakistan. In another publication from Malik AA et al on data from preventive therapy of MDR-TB contacts in Pakistan, the incidence of adverse events over 6 months of treatment was 7.9 per 100 person-months (p-m); 16 per 100 p-m with a fluoroquinolone and ethionamide and 4.4 per 100 p-m with a fluoroquinolone and ethambutol.⁹





Key Points 2

There is no evidence that the provision of one or two-drug regimens for preventive therapy to infected people increases the risk of developing DRTB.

As there is no “gold standard” test for LTBI, with the uncertain global burden of LTBI. However, treatment of LTBI should start only after having carefully excluded the possibility of TB disease.

Several studies indicate that, on average, 5–10% of those infected will develop active TB disease over the course of their lives, usually within the first 5 years after initial infection.

Mass population-wide LTBI testing and treatment is not feasible because the tests are imperfect, there are risks of serious and fatal side effects, and the cost would be high, for an unproven public health impact.

A limited number of bacilli characterizes the state of infection and the probability of finding naturally resistant bacteria that can be selected under drug pressure is insignificant.

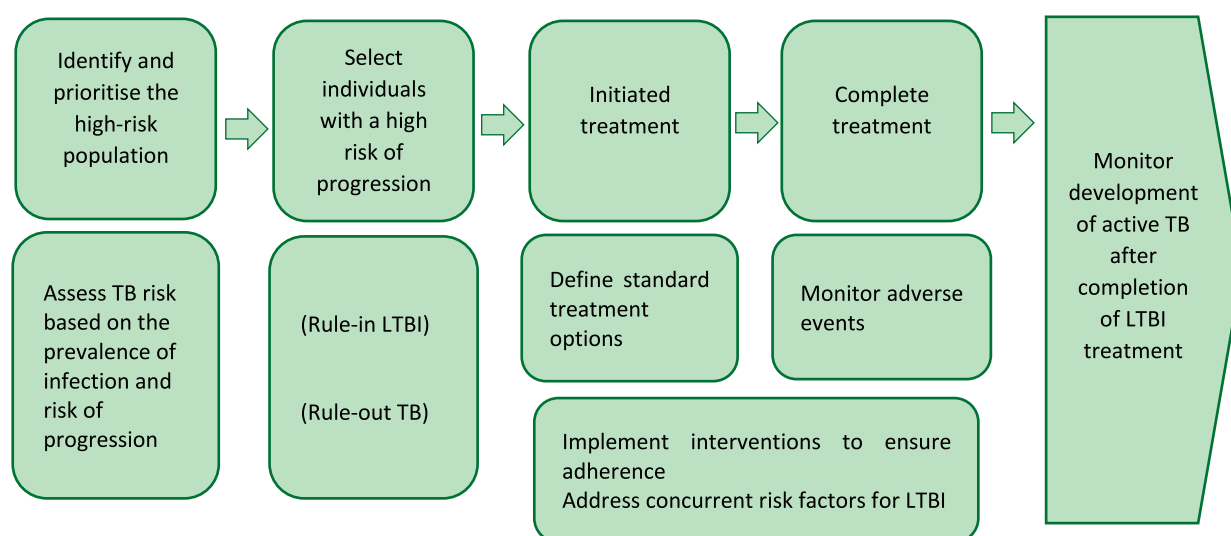
Pakistan has reserved preventive treatment for children under 5 years of age who are household contacts of bacteriologically confirmed TB cases and PLHIV.

The Cascade of Prevention

Among the urgent steps to take towards ending the TB epidemic,⁶ major investments are required towards health systems strengthening and specifically developing a comprehensive ‘cascade of prevention’ approach to scale up the programmatic management of tuberculosis preventive treatment (PMTPT).¹⁰ This involves a comprehensive package of interventions: identifying and testing those individuals who should be tested, delivering effective, safe treatment in such a way that the majority of those starting a treatment regimen will complete it with no or minimal risk of adverse events, and monitoring and evaluation of the process (Figure 1).



Figure 1 Schematic approach to the programmatic management of tuberculosis infection



It is important to ensure systematic identification of all individuals, who are at increased risk of developing TB and should have access to a full course of TPT. This is challenging because losses in the cascade of care before starting TPT are significant.

Programmatic implementation and scale-up of TPT services require strengthening of each element in the cascade of prevention starting from identification of the target population to the provision of preventive treatment. Better retention and referral of individuals evaluated for TB, identification of those eligible for TPT and development of more person-friendly and accessible services will ensure that a substantial proportion of people with LTBI are initiated on TPT and complete the treatment, thereby reducing the reservoir of LTBI from which TB disease develops.

Key Points 3

Losses in the cascade of care before starting TPT are significant. Henceforth, ensuring systematic identification and providing access to a full course of TPT of all individuals, who are at increased risk of developing TB becomes challenging.

These challenges are even greater than the losses that occur due to lost to follow-up from treatment.



Global Recommendations





Global Recommendations for Managing LTBI

The importance of the management of LTBI was reaffirmed at the United Nations General Assembly, first-ever high-level meeting on tuberculosis held in 2018. The declaration posed the basis to accelerate efforts in ending TB and reach all affected people with prevention and care.¹¹ Targets on the number of people to be started on preventive therapy by 2022 were established, including a contribution of 1.6 million people in Pakistan.

In 2020, the WHO issued an updated version of the Consolidated Guidelines on Tuberculosis Preventive Treatment^{12(p1)} and the first version of the Operational Handbook on Tuberculosis Preventive Treatment¹³. This document was developed in light of the aforementioned guiding documents, with adaptation to the epidemiology and health infrastructure of tuberculosis in Pakistan.

1) Target Populations

The LTBI treatment through systematic testing targets people living with HIV, children under 5 years of age who are household contacts of bacteriologically confirmed pulmonary TB (PTB) patients is evidently effective. Moreover, HIV-negative groups at clinical risk, which include patients initiating anti-TNF treatment, receiving dialysis, preparing for organ or haematological transplantation and those with silicosis could also benefit from testing and treatment of LTBI because of their increased risk of progression to active TB disease.

Several studies specify that approximately 5–10% of those infected with LTBI will develop active TB disease over the course of their lives, usually within the first 5 years after initial infection.⁴ LTBI testing to cover the entire population is infeasible because there is no gold standard to tests for LTBI. Cost of intervention through existing methodologies: TST and IGRA, is high, for an unproven public health impact. Moreover, there may be risks of serious and fatal side effects of the treatment used to treat LTBI. Nonetheless, for individuals infected with LTBI among population groups in which the risk for progression to active disease significantly exceeds that of the general population, the benefits are expected to be greater than the harms.

1.1. Identifying Populations for LTBI Testing and TPT

The criteria for the selection of the target populations listed in the recommendations below include:

- High risk of progression to TB disease.
- High prevalence of LTBI.
- High incidence of TB disease compared to the general population, indicating high TB transmission setting.
- Benefits of TPT outweighing the potential risk of drug toxicity.





1.1.1. Household Contact

Household contacts are the people who share the similar and enclosed living space for one or more nights or frequent or extended periods during the day with the index case during the 3 months before the commencement of the current treatment episode (once effective treatment is started, index case is less likely to transmit the TB infection to contacts). It is essential to target the following groups for TPT, who are the household contacts of people with bacteriologically confirmed PTB, with no symptoms of active TB on an appropriate clinical evaluation:

1. Children aged < 5 years should be given TPT (Strong Recommendation),
2. Children aged ≥ 5 years, adolescents and adults should be considered for TPT (Conditional Recommendation).

In selected high-risk household contacts of patients with multidrug-resistant tuberculosis, preventive treatment may be considered based on individualized risk assessment and a sound clinical justification (Conditional Recommendation).

1.1.2. People Living with HIV

Adults and adolescents living with HIV with no symptoms of active TB on an appropriate clinical evaluation should receive TPT as part of a comprehensive package of HIV care. TPT should also be given to those on antiretroviral treatment, to pregnant women and to those who have previously been treated for TB, irrespective of the degree of immunosuppression (Strong Recommendation). Moreover, infants aged < 12 months living with HIV who are in contact with a bacteriologically confirmed PTB person with no symptoms of active TB on an appropriate clinical evaluation should receive TPT (Strong Recommendation). Children aged ≥ 12 months living with HIV with no symptoms of active TB on an appropriate clinical evaluation should be offered TPT as part of a comprehensive package of HIV prevention and care if they live in a setting with high TB transmission, regardless of contact with TB (Strong Recommendation). All children living with HIV who have completed treatment for TB disease and are not symptomatic for active TB on an appropriate clinical evaluation may receive TPT (Conditional Recommendation).

1.1.3. Other People at Risk

Population of this group includes people who are initiating anti-TNF treatment, receiving dialysis, preparing for an organ or haematological transplant, or who have silicosis should be systematically tested and treated for LTBI (Strong Recommendation). Systematic LTBI testing and treatment may be considered for health workers, prisoners, homeless people, immigrants and long-term visitors from countries with a high TB incidence (above 100/100,000), people living in congregate settings, and people who use drugs (Conditional Recommendation). Systematic LTBI testing and treatment is not recommended for people with diabetes, people who engage in the harmful use of alcohol, tobacco smokers and underweight people unless they also belong to other risk groups included in the above recommendations (Strong Recommendation).





1.2. Algorithms to Rule out Active TB Disease

Giving TPT to someone who has active TB can delay the resolution of the disease and favour the emergence of drug resistance. Therefore, all candidates for preventive therapy must be preliminarily evaluated to exclude active TB disease. Asymptomatic TB and normal chest radiographic findings may be used to rule out active TB disease among household contacts; henceforth, to confirm their eligibility for preventive therapy.

Moreover, asymptomatic TB and normal chest radiographic findings may be used to rule out active TB disease among HIV-negative household contacts aged ≥ 5 years and other risk groups, prior the initiation of TPT (Conditional Recommendation). Adults and adolescents living with HIV should be screened for TB according to the 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 their ART status (Strong Recommendation). Chest radiography may be offered to people living with HIV on ART and TPT given to those with normal radiographic finding (Conditional Recommendation). Adults and adolescents living with HIV who are screened for TB according to a clinical algorithm and who report any of the symptoms of current cough, fever, weight loss or night sweats may have active TB and should be evaluated for TB and other diseases, and offered preventive treatment if active TB is excluded (Strong Recommendation). Infants and children living with HIV who have poor weight gain, fever or current cough; or who have a history of contact with a person with bacteriologically confirmed TB, should be evaluated for active TB and other diseases that cause such symptoms. After an appropriate clinical evaluation, if active TB disease is excluded, these children should be offered TPT, regardless of their age (Strong Recommendation).

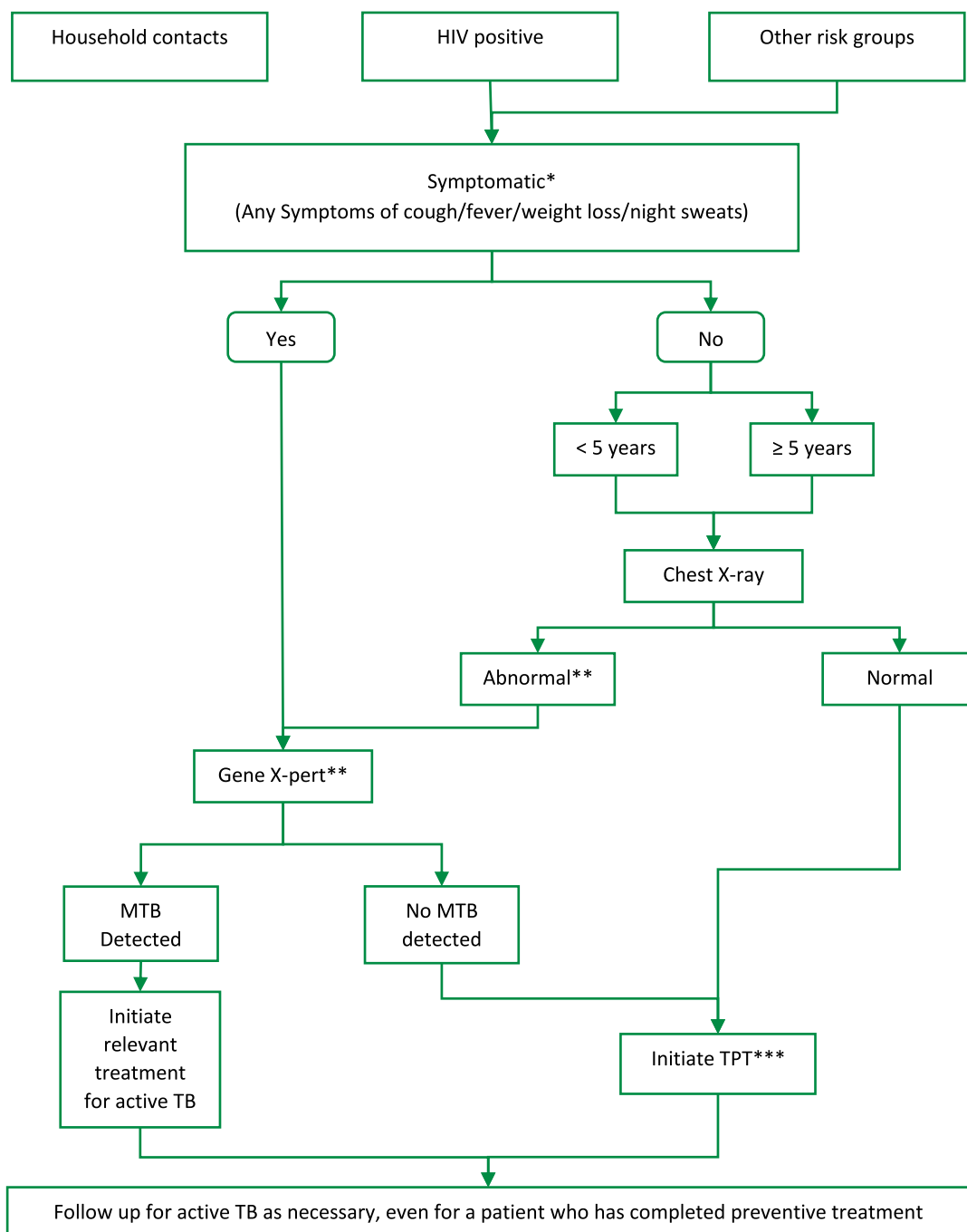
Adults, adolescents, and children living with HIV should be screened for TB according to a clinical algorithm shown in Figure 3. Briefly, adults and adolescents living with HIV presenting fever, cough, weight loss or night sweats, and infants and children presenting poor weight gain, or who have a history of contact with a case of TB should be evaluated for active TB and other diseases that cause such symptoms. If the clinical evaluation shows no TB, these contracts should be offered preventive treatment, regardless of their age. The same algorithm applies to contacts of a bacteriologically confirmed pulmonary TB case. In order to assess reactivation of LTBI in other risk groups, they should be screened with both: questionnaire and chest radiography, to exclude symptoms of active TB disease. If neither of those is suggestive of active TB disease, the subject should be offered preventive therapy (Figure 3).

In case of finding abnormal chest radiography (not just those suggestive of TB), a detailed investigation for TB disease and other diseases should take place. These investigations should be based on microbiological investigations, primarily through Gene X-pert MTB/RIF as the initial diagnostic test. Detailed algorithms for people living with HIV suspected of having TB have been proposed by the WHO¹⁴.





Figure 2 Algorithm for TB screening and TPT



* Any Symptoms of cough/fever/weight loss/night sweats

** Investigate for active TB through Gene X-pert; it will also specify TB sensitivity/resistance (if any) in the population

*** Initiate appropriate daily dosage of INH for 6 months



*Key Points 4*

There are risks of serious and fatal side effects from the preventive treatment; henceforth, selectively targeting the population groups at highest risk for progression to active TB disease.

Children aged ≥ 5 years, adolescents and adults who are household contacts of people with bacteriologically confirmed pulmonary TB who are found not to have active TB by an appropriate clinical evaluation should be considered for TB preventive treatment.

Adults and adolescents living with HIV who are unlikely to have active TB should receive TB preventive treatment as part of a comprehensive package of HIV care.

All children living with HIV who have completed treatment for TB disease may receive TB preventive treatment.

The absence of any symptoms of TB and of abnormal chest radiographic findings may be used to rule out active TB disease among candidates put on preventive therapy.

The absence of any symptoms of TB and the absence of abnormal chest radiographic findings may be used to rule out active TB disease among HIV-negative household contacts aged ≥ 5 years and other risk groups before preventive treatment.

Chest radiography may be offered to people living with HIV on ART and preventive treatment given to those with no abnormal radiographic findings.

Infants and children living with HIV who have poor weight gain, fever, or current cough or who have a history of contact with a person with TB should be evaluated for TB and other diseases that cause such symptoms.

Adults and adolescents living with HIV and TB presumptive should be offered preventive treatment after ruling out TB disease, regardless of their age.

People belonging to the other risk groups for reactivation of LTBI should be screened with both the questionnaire to elicit symptoms of TB and a chest X-ray.

In case of abnormal chest radiographic findings (TB presumptive or otherwise), undertake a detailed investigation for TB and other diseases through microbiological investigations that primarily include X-pert MTB/RIF as the initial diagnostic test.





2) Diagnosis of LTBI

TB screening tools are designed to distinguish people with a higher probability of having TB disease from those with a low probability and can be assumed to be free of TB disease. They are not intended to provide a definitive diagnosis. In general, they need to be able to be implemented easily and relay results rapidly in order to be informative in a screening context. Screening tests need to be followed by a diagnostic test, offered as part of a comprehensive clinical evaluation, to confirm or rule out TB disease in individuals who screen positive.

Either a tuberculin skin test (TST) or interferon-gamma release assay (IGRA) should be used to test for LTBI (Strong Recommendation). Although, LTBI testing through TST or IGRA is not a prerequisite to initiating TPT in PLHIV, household contacts of age > 5 years, and household contacts of age ≤ 5 years (Strong Recommendation).

There is no gold standard test to diagnose LTBI. Currently, available tests are indirect and require the person to mount an immune response to work properly. The currently recommended tests for LTBI are TST and IGRA. Both tests measure immune sensitization (type IV or delayed-type hypersensitivity) to mycobacterial protein antigens that occur following infection by *M. tuberculosis*. There is evidence that people who tested positive for LTBI benefit more from TPT than those who have a negative test. However, logistic difficulties to procure and implement testing should also be considered while developing policy for TPT.

There is no significant difference between TST and IGRA in predicting future TB disease. In a systematic review performed by the WHO in 2018 to compare the predictive utility of the two tests five prospective cohort studies were identified, that included PLHIV, pregnant women, adolescents, healthcare workers and household contacts. The pooled risk ratio estimate for TST was 1.49 (95% CI, 0.79; 2.80), and that for IGRA was 2.03 (95% CI, 1.18; 3.50). Although the estimated risk ratio for IGRA was slightly higher than that for TST, the 95% CIs for risk ratio estimates of TST and IGRA overlapped and were imprecise. Therefore, the choice of test for national programmatic use of LTBI testing tool depends on cost, availability, human resources, and infrastructure to provide testing services in the country.





Key Points 5

LTBI testing by TST or IGRA is not a prerequisite to start TB preventive treatment in PLHIV and household contacts of age > 5 years.

LTBI testing by TST or IGRA is not recommended in household contacts of age < 5 years.

There is evidence that persons with a positive test for LTBI benefit more from TB preventive treatment than those who have a negative test.

The GDG stated that LTBI testing by TST or IGRA should not be a prerequisite to start TB preventive treatment in PLHIV and household contacts of any age, given that benefits outweigh the risks.

Considerations of logistic difficulties to procure and implement testing through TST and IGRA towards the development of this policy are essential.

The estimate for IGRA was slightly higher than that for TST, the 95% CIs for the estimates for TST and IGRA overlapped and were imprecise.

The choice of test for programmatic use depends on cost, availability, human resources, and infrastructure to provide testing services in the country.

3) Treatment of LTBI

The following options are recommended for the treatment of LTBI regardless of HIV status (Strong Recommendation):

- 6 months of daily isoniazid
- 12 weeks of weekly rifapentine plus isoniazid
- 3 months of daily isoniazid plus rifampicin

Clinical trial evidence generated over the past two decades shows similar preventive efficacy with shorter rifamycin-based TPT regimens, both in HIV-positive and HIV-negative individuals, as monotherapy or in combination with isoniazid.^{15–18} 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 a 20% greater treatment completion rate (82% vs 61%).¹⁰

Isoniazid preventive treatment (IPT) for six months has been the most widely used regimen under programmatic conditions and has emerged as a standard for TPT for both HIV-positive and HIV-negative adults and children. 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 that preventive efficacy reaches 64% for people with a positive TST (RR 0.36; 95% CI 0.22; 0.61).¹⁹ The choice of the preventive regimen may also depend on the availability of drugs, fixed-dose combinations (FDCs), child-friendly formulations, concomitant medications for PLHIV, such as antiretroviral drugs (ARVs), opioid substitution therapy, oral contraception), as well as acceptability to recipients in the country context. Details on duration, interval, doses, pill burden, costs, use in children and pregnant women, toxicity and interaction with ART are presented in Table 1, whereas the recommended weight-based dosages of TPT regimens are described in Table 3 under section 3.2.

Table 1 Recommended regimens for preventive therapy*

	6H	3HP	3HR	H+B6+CPT
Medicines	Isoniazid	Isoniazid + Rifapentine	Isoniazid + Rifampicin	Isoniazid + Pyridoxine + Co-trimoxazole
Duration (months)	6	3	3	6
Interval	Daily	Weekly	Daily	Daily
Doses	182	12	84	182
Pill burden per dose	1	9 singles 3 FDC	3	1
Total number of pills	182	108 (singles) 36 (FDC)	252	182
Children	All ages. Child-friendly formulations available	>2 years. No child-friendly formulations available	All ages. Child-friendly formulations available	All ages. No child-friendly formulations available
Pregnant women	Safe for use	No data	Safe for use	Safe for use
Interaction with ART	No restriction	Contraindicated: All PIs; Nevirapine ; TAF	Contraindicated: All PIs; Nevirapine ; TAF	No restriction
Toxicity	Hepatotoxicity, rash, peripheral neuropathy, GI upset	Flu-like syndrome, hypersensitivity reactions, rash, GI upset, hepatotoxicity	Ras, GI upset, hepatotoxicity, thrombocytopenia	Hepatotoxicity, rash, GI upset

* These regimens for TPT are recommended by the WHO

3.1. Treatment Considerations

Preventive therapy with recommended regimens requires careful consideration if the candidate presents one of the following: active hepatitis (acute or chronic), regular and heavy alcohol consumption, and symptoms of peripheral neuropathy. History of TB and current pregnancy do not represent a contraindication for starting preventive treatment.





3.1.1 Use of pyridoxine (vitamin B6)

Individuals at risk for peripheral neuropathy that include those with malnutrition, chronic alcohol dependency, HIV infection, renal failure, diabetes, pregnant or breastfeeding women, should receive vitamin B6 supplements when taking isoniazid preventive therapy. The long-term treatment with high-dose isoniazid presents an undesirable side effect of peripheral neuropathy that develops secondary to a deficiency of vitamin B6 (pyridoxine) during therapies inclusive of isoniazid. Additionally, exclusively breastfed infants should receive vitamin B6 while taking isoniazid. The standard dose of pyridoxine when used prophylactically for prevention of neuropathy among patients taking isoniazid is 10–25 mg/day. Peripheral neuropathy is infrequent among other patients taking standard doses of isoniazid, which is easily recognized as symmetrical numbness and tingling of the extremities and usually easily reversible upon withdrawal of isoniazid and institution of high-dose pyridoxine therapy (100–200 mg/day).

However, routine pyridoxine supplementation with isoniazid to all individuals undergoing preventive therapy is not necessary. Table 3 reports recommended doses of pyridoxine in children below the age of 15.

Table 2 Recommended dose of pyridoxine in children, by age.

Vitamin B6 dosage for Children (0-15 years)	
0-1 year	5mg/day
2-10 years	10-15mg/day
11-15 years	25mg/day

3.2. Preventive Treatment for Contact of Patients with Multidrug-Resistant TB

In selected high-risk household contacts of patients with multidrug-resistant tuberculosis, preventive treatment may be considered based on individualized risk assessment and a sound clinical justification (Conditional Recommendation). The criteria to recommend TPT regimen among contacts exposed to MDR-TB patients include:

- Consideration of intensity of exposure,
- Confirming the source patient and her/his drug resistance pattern (i.e. MDR-TB confirmed bacteriologically and susceptibility to a fluoroquinolone established), and
- Ascertaining LTBI using IGRA or TST.

NTP recommends that each TPT regimen for respective MDR-TB contacts will be conducted under operational research conditions. Data on treated and untreated contacts of MDR-TB patients will be





collected and analysed by the NTP. The guidelines will be further updated in due time according to the results of the analysis. The NTP will coordinate and supervise the collection of data on preventive therapy for MDR-TB contacts. The analysis of the results will allow, in the next few years, to update the current guidelines based on collected evidence.

The recommended regimen for preventive therapy of MDR-TB contacts is levofloxacin for six months (paediatric formulation for child contacts) (see dosages in Table 3). Regardless of initiating TPT regimen among household contacts of MDR-TB patients, clinical follow-up should be performed for two years after exposure to MDR-TB. Any emergent signs and symptoms suggestive of TB in this duration should be actively investigated and appropriate curative regimens should start. Contacts of individuals with rifampicin-resistant TB may be treated similarly to those for MDR-TB, but if isoniazid susceptibility is confirmed in index patients, contacts may be given 6H.

Table 3 Recommended doses for preventive treatment regimens

Regimen	Dose by age and weight band					
6 or 9 months of daily Isoniazid monotherapy (6H, 9H)*	Age < 10 years = 10 mg/kg/day (range 7 – 15 mg) Age 10 years and older = 5 mg/kg/day 1 pill daily for adults, half pill for children 5 years and older of age and quarter for children < 5 years of age					
Four months of daily Rifampicin (4R)	Age < 10 years = 15 mg/kg/day (range 10 – 20 mg) Age 10 years and older = 10 mg/kg/day					
Three months of daily Rifampicin + Isoniazid (3HR)	Isoniazid: Age < 10 years = 10 mg/kg/day (range 7 – 15 mg) Age 10 years and older = 5 mg/kg/day					
	Rifampicin: Age < 10 years = 15 mg/kg/day (range 10 – 20 mg)					
	Weight Band	4 – 7 kg	8 – 11 kg	12 – 15 kg	16 – 24 kg	> 25 kg
	RH 75/50 mg (FDC)	1	2	3	4	Use Adult Formulation
Three months of Rifapentine and a high dose of Isoniazid weekly (12 doses) (3HP)	Age 10 years and older = 10 mg/kg/day					
	Age 2 – 14 years**					
	Medicine; Formulation	10 – 15 kg	16 – 23 kg	24 – 30 kg	31 – to 34 kg	> 34 kg
	Isoniazid 100 mg***	3	5	6	7	7
	Rifapentine 150 mg	2	3	4	5	5
	Isoniazid + Rifapentine FDC (150 mg/150 mg)****	2	3	4	5	5
	Age > 14 years**					
	Medicine; Formulation	30 – 35 kg	36 – 45 kg	46 – 55 kg	56 – 70 kg	> 70 kg





Regimen	Dose by age and weight band					
	Isoniazid 300 mg***	3	3	3	3	3
	Rifapentine 150 mg	6	6	6	6	6
	Isoniazid + Rifapentine FDC (300 mg/300 mg)****	3	3	3	3	3
Six months of levofloxacin daily (preventive treatment of MDR-TB)	Age > 14 years, by body weight: < 46 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					

* A triple pill combination containing isoniazid 300 mg + pyridoxine 25 mg + sulfamethoxazole 800 mg + trimethoprim 160 mg is the preferred alternative regimen for PLHIV being considered for isoniazid monotherapy.

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

*** Expected to become available in a near future.

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

***** Levofloxacin 100 mg dispersible tablets are available for children.

3.3. Adverse events monitoring

The risk of adverse events should be minimized during preventive treatment because recipients do not have a current sign or symptom of the disease. Health care providers should monitor individuals receiving treatment for LTBI routinely at monthly visits.

Haematochemical investigation to check for drug toxicity is not routinely recommended. Scheduling routine visits to the health care providers are mandatory for people receiving TPT. The health care provider will monitor symptoms of active TB between visits, such as anorexia, nausea, vomiting, abdominal discomfort, persistent fatigue or weakness, dark-coloured urine, pale stools or jaundice. If a health care provider cannot be consulted at the onset of such symptoms, the patient should immediately stop treatment.

Haematochemical investigations may also be performed at baseline in individuals with concomitant diseases (i.e. chronic hepatitis).

3.4. Adherence and Completion of TPT

Adherence to the full course and completion of treatment are important determinants of clinical benefit to the individual and the program success. The efficacy of TPT is greatest if at least 80% of doses are taken within the duration of the regimen. As expected, shorter regimens are associated with better adherence and higher treatment completion. The number of doses recommended for each of the treatment regimens is shown in Table 4.





Table 4 TB Preventive Treatment Completion

	Total duration (months)	Expected number of dosed	80% of recommended doses (days)	Extended time for treatment completion (days) (treatment duration + 33% additional time)
6H (daily)	6	182	146	239
3HR (daily)	3	84	68	120
3HP (weekly)	3	12	11*	120
4R (daily)	4	120	96	150

* 90% of the recommended number of doses.

TPT regimens can be effectively self-administered and routinely monitored by the health care provider following DOTS protocol. The responsibility for evaluation of candidates to TPT, the prescription of therapy, and ensuring adherence and completion of treatment lays to the specific services (TB clinic for contacts, HIV clinic for PLHIV, nephrological services for patients with end-stage renal diseases, etc.) either through centralized care or through home-based care. Recommendations for the management of missed doses are presented in Table 5.

The modality for treatment provision and adherence support should be determined considering the individual's preference. Interventions to support adherence to TPT include peer support networks, coaching and educational interventions including quality counselling and video observed therapy (VOT). National programmes should dedicate necessary financial and human resources to strengthen adherence mechanisms for TPT, to prevent the negative impact of poor adherence on scale-up of TPT services. Interventions should be tailored to the specific needs of risk groups and the local context.



Table 5 Management of interruptions in TB preventive treatment

TPT regimen	Duration of treatment interruption	Next step	Suggested actions
3HR, 4R, 6H	Less than 2 weeks	<p>Resume preventive treatment immediately upon return and add the number of days of missed doses to the total treatment duration.</p> <p>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 3HR missed 3 days of treatment, continue preventive treatment for a total duration of 3 months + 3 days from the date of start).</p>	<p>Address the reason for interruption. Counsel the person on TPT and the caregiver on the importance of adherence to preventive treatment. Review and agree with the person on TPT and the caregiver about the best ways to improve adherence.</p>
	More than 2 weeks	<p>If treatment interruption occurred after more than 80% of doses expected in the regimen were taken, no action is required. Continue and complete the remaining treatment as per the original plan.</p> <p>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, no action is required. Continue and complete the remaining treatment as per the original plan.</p> <p>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.</p>	
3HP	Weekly schedule of one dose missed	<p>If the missed dose is remembered within the next 2 days, the person can take the dose immediately. Continue the schedule as originally planned (i.e. continue to take remaining doses following the same schedule).</p> <p>If the missed dose is remembered more than 2 days later, 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 2 weekly doses being taken less than 4 days apart.</p>	
	More than 1 weekly doses of 3HP missed	<p>If between 1 and 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.</p> <p>If, however, 4 or more weekly doses are missed, consider restarting the full TPT course.</p> <p>If adherence to a weekly routine is not possible, consider discontinuing 3HP and offering an alternative (daily) regimen.</p>	



4) Ethical considerations

LTBI testing and treatment raise a range of ethical issues.^{19, 20} First, LTBI is by definition an asymptomatic state. This alters the ethical obligations that would be imposed by active TB. For example, the absence of an immediate risk of transmission makes it unethical to restrict movements based on the LTBI status of an individual. Secondly, the difficulty of accurate assessment of individual risk for the development of active TB poses a communication challenge. Informed consent requires effective and adequate communication about the unreliability of LTBI testing tools, the importance of excluding active TB, the risk for development of active TB, possible side-effects of treatment and their protective benefits. Risks and uncertainties must be communicated in culturally and linguistically appropriate forms and feedback obtained after screening programs. Thirdly, LTBI disproportionately affects individuals and groups that are already socially and medically vulnerable. Therefore, efforts must be made to ensure equity, human rights and elimination of stigma, so that the vulnerability of target groups do not preclude their access to screening and treatment. Policies should be evaluated from an ethical perspective after implementation, both to consider possible unexpected effects and to ensure that the evidence on which they are based remains current and relevant.²²





Key Points 6

The choice of the preventive regimen may also depend on the availability of drugs, fixed-dose combinations (FDCs), child-friendly formulations, concomitant medications (such as antiretroviral drugs (ARVs), opioid substitution therapy, oral contraception), as well as acceptability to recipients in the country context.

Refer to Table 1 for recommended regimens and Table 2 for recommended doses for preventive therapy.

One of the undesirable side effects of long-term treatment with high-dose isoniazid is peripheral neuropathy that develops secondary to a deficiency of vitamin B6 (pyridoxine) during therapy.

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 isoniazid.

Peripheral neuropathy occurs infrequently among other patients taking standard doses of isoniazid, which is easily recognised, such as symmetrical numbness and tingling of the extremities.

The unavailability of vitamin B6 should not represent a barrier to TPT initiation.

The criteria to recommend TPT among contacts exposed to MDR-TB patients include consideration of intensity of exposure, confirming the source patient and her/his drug resistance pattern (i.e., MDR-TB confirmed bacteriologically and susceptibility to a fluoroquinolone established), and ascertaining TB infection using IGRA or TST.

NTP recommends that any TPT for MDR TB contacts will be conducted under operational research conditions.

The recommended regimen for preventive therapy of MDR-TB contacts is levofloxacin for six months.

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.

People receiving TPT should be urged to contact their health care providers if they develop symptoms between visits, such as anorexia, nausea, vomiting, abdominal discomfort, persistent fatigue or weakness, dark-coloured urine, pale stools or jaundice.

TPT regimens can be effectively self-administered.

Informed consent requires effective, adequate communication of the uncertainty in TBI testing, the risk for development of active TB, possible side effects of treatment and their protective benefits.

Efforts must be made to ensure equity, human rights and elimination of stigma so that the vulnerability of target groups does not preclude their access to screening and treatment.





Operational Considerations





Operational Considerations

Purpose

This is an operational manual for the diagnosis and treatment of LTBI in Pakistan

Scope

It is intended to guide all individuals and organizations involved in the screening and treatment of LTBI in at-risk populations in Pakistan by providing step-by-step guidelines for its management.

Goal

The goal for national implementation of these guidelines is to reach people who were not reached previously and to detect TB disease early, thereby improving outcomes for individuals and reducing transmission and incidence of LTBI and active TB at the population level.

1) Target populations and implementation approach

Appropriate implementation of TPT on a national scale requires identifying and targeting risk groups in the population. These groups are at the highest risk of contracting tuberculosis.

1.1. Risk Groups

The risk groups include groups at high risk of exposure to TB or of progression to TB disease or who have limited access to TB services,²³ and are among the populous that is infected by LTBI. The following risk groups should always be systematically screened for TB:

- Household and close contacts of bacteriologically confirmed TB patients – those who are currently on TB treatment or have previously been treated for TB in their lifetime,
- People living with HIV,
- Other risk groups include persons undergoing organ transplants, TNF and anti-cancer treatments.





1.1.1. Household Contacts

A strong contact investigation programme is essential to pave the way for the achievement of commitments made by the Member States to provide TPT to 24 million household contacts by 2022.

The occurrence of TB in the family has serious social and economic effects including catastrophic costs due to loss of income or cost of health care. Screening of household contacts for TB disease is a very high yield and cost-effective active case finding strategy (ACF).²⁴ Since Pakistan has high TB incidence, screening and treatment of household contacts for LTBI has high significance and the probability of progression to active disease is particularly high in the first two years after infection. Therefore, in compliance with the National Policy Guidelines for TPT, the target population for TPT has extended from paediatrics and PLHIV to all household contacts of bacteriologically confirmed TB patients.

Investigation and treatment of all household contacts have important advantages and can provide important health and financial benefits to the family and the community. By investigating, detecting, and treating both TB disease and LTBI, transmission in the household can be stopped and catastrophic costs and dire health outcomes due to TB disease can be prevented.

Although the household contacts are provided with a huge resource allocation as a support to avoid OOP, it significantly contributes to contact tracing activities under the coordination of TB services by the private sector and NGOs.

1.1.2. PLHIV

PLHIV who have LTBI have the highest risk of progression to active disease. The risk increases as the degree of immunosuppression (measured by the CD4 cell count) worsen. Conversely, highly active antiretroviral therapy decreases the risk of reactivating TB although it does not revert the risk to the same level of the uninfected population (a 10-fold increase in the risk does persist). To decrease the risk of TB among PLHIV the WHO recommends systematic screening and treatment of LTBI for all those who attend HIV services.

All PLHIV should be screened for TB symptoms at every opportunity or when in contact with a health worker. Those with TB symptoms should be referred for a diagnostic procedure, and those without symptoms should be evaluated for eligibility and started on TPT, if appropriate (General recommendation). Whereas, those who have completed TPT should be monitored by their respective health care providers.

The TB and HIV programmes should provide resources and undertake site monitoring to ensure implementation and quality improvement measures when gaps are noted (such as lack of screening, cursory screening, lack of linking to TPT).





1.2. Key implementation elements in contact investigation

The standard model of care for contact investigation is facility-based. However, community-based models of care, which ensure a higher yield of contacts and TB cases should be preferred, whenever feasible.

The role and responsibilities of programme personnel, health care workers and community health workers, in reaching the contacts, symptom screening, and referral for testing and clinical evaluation should be clearly defined. If the community-based model is implemented, health care workers responsible for the supervision of personnel conducting contact investigations should be identified.

Specific recording and reporting forms for contact investigations should be available. In case of adoption of the community-based model, tools/referral slips should be used to record TB screening and referral of identified contacts for further care. The level of service delivery points for systematic recording and reporting should be well described, as well as frequency. Messages for demand generation and patient education should be in place.

1.2.1. Key steps

Following are 10 key steps, which need the systematic following for appropriate implementation of the National Guidelines for TPT.

1.2.1.1. Index Tuberculosis Case Form

The DOTS facilitator should compile the “Index TB case form” of all bacteriologically confirmed pulmonary TB cases (Annex 4). This form allows the collection of information of all close contacts of the respective index case.

1.2.1.2. Counselling of the Index Patient

The index patient should be interviewed as soon as possible after diagnosis, preferably within one week, to elicit details about the household and other close contacts. Health providers should explain clearly and sensitively the urgency of initiating contact investigations to the index patient, considering the increased risks of progression to TB disease with recent exposure. The DOTS facilitator may speak to the head of the family and ask them to bring all the contacts to the health care facility for eligibility evaluation and LTBI screening. A second interview may be required to elicit additional contacts as well as complete any missing information.

1.2.1.2. Education of the Index Patient

All index patients and household members should be educated regarding the benefits of taking TPT and the risks of NOT taking it. The overall aim should be to enable informed decisions by the individuals to receive a complete course of TPT.





1.2.1.4. Follow-up with the Index Patient

- i. If the household contacts fail to visit the facility within 5-7 days after the first contact, the family will be reminded over the phone for the visit.
- ii. If the family fails to visit the facility after the second contact, they will be reminded over the phone again.
- iii. 3 days after the second reminder, health facility staff or field staff of the private sector or health workers will visit the index patient's house.

In addition, contact investigations should also be conducted for people who died of TB by gathering information from family members and service providers.

1.2.1.5. Consent for Screening for Family Members

- i. DOTS facilitators will take written informed consent from the head of the household to screen all family members for TB symptoms and ask them to visit the clinic for further investigations. A copy of the consent form should be given to the family (Annex 1).
- ii. At the facility, all contacts should be evaluated by a clinician and data should be recorded on the TB Contact Register (Annex 2).
- iii. Verbal screening for TB symptoms and using CXR as a diagnostic tool to rule out active TB disease.

1.2.1.6. Home Visits

Preferably, the public or private health care provider conducting the contact investigation should visit the home/workplace of the index patient. They should conduct interviews and underscore the importance of identifying and evaluating contacts. Also, they shall perform symptom screening and document it. Afterward, they will gather accurate information about the likely intensity and duration of exposure; and ensure that all relevant contacts are referred for further evaluation and treatment decisions. Home visits may need to be done outside of normal working hours since contacts may be at work or school during these hours; these activities may therefore require incentives.

1.2.1.7. Child and PLHIV Contacts

During the home visit, the health care provider should assess the presence of child contacts and PLHIV, in whom TB could progress rapidly. HIV testing and counselling should be offered as part of this process, including biological children of any adults living with HIV.

1.2.1.8. Other Referrals

Home visits by health providers also allow identifying the needs for social support, nutrition, and education on infection control measures. After the visit, the health provider may refer to the index patient and contacts relevant social and nutritional support programmes.





1.2.1.9. Patient Confidentiality

Maintaining confidentiality during contact investigation is a challenge because of the social connections between index patients and their contacts. All persons should be treated with respect, and confidentiality should be maintained as much as possible. When the index patient is reluctant to give information regarding both household and social contacts, counselling efforts should continue over time to gain the trust of the patient. The index patient should not be coerced, nor should her/his TB treatment be linked with the success of the contact investigation.

1.2.1.10. Monitoring

The TB Programme should monitor the yield of contact investigations and the proportion of TB disease and LTBI detected.

Key Points 7

The National Policy Guidelines for TPT prioritises the household contacts of bacteriologically confirmed TB patients – those who are currently on TB treatment or have previously been treated for TB in their lifetime.

Those with TB symptoms should be referred for a diagnostic procedure, and those without symptoms should be evaluated for eligibility and started on TPT.

DOTS facilitator may speak to the head of the family and ask them to bring all the contacts to the health care facility for eligibility evaluation and LTBI screening.

Contact investigation for people who died of TB by gathering information from family members and service providers.

Verbal screening for symptoms is adequate with CXR to rule out active disease.

The public or private health care provider conducting the contact investigation should visit the home/workplace of the index patient.

During the home visit, the health care provider should assess the presence of child contacts and PLHIV, in whom TB could progress rapidly.



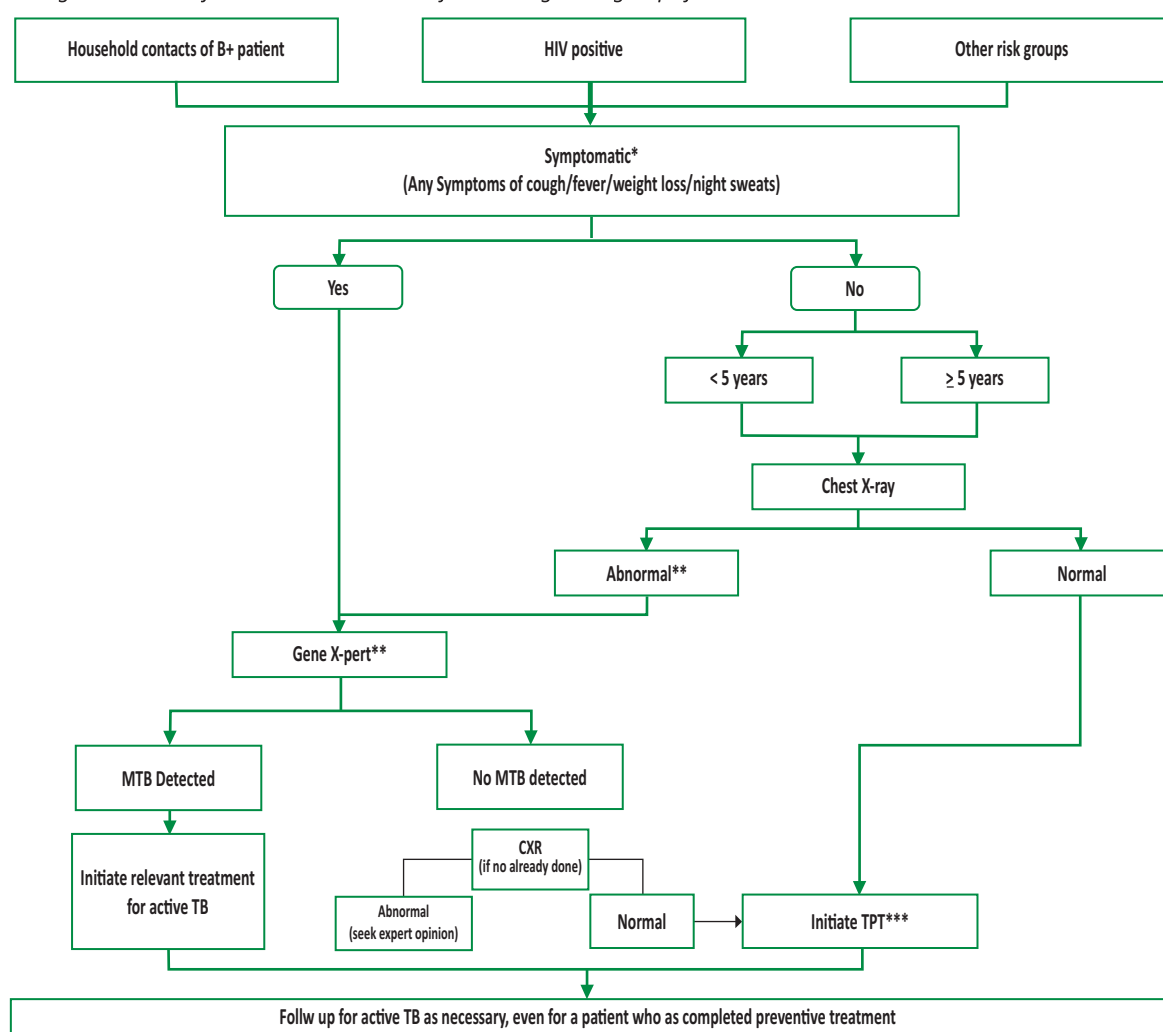


2) Algorithms to rule out active TB disease

Offering TPT to someone who has TB disease can delay the resolution of the disease and favour the emergence of drug resistance. Thus, excluding TB disease before initiating TPT is one of the critical steps in the preventive TB care pathway.

Using a standard set of signs and symptoms to screen for TB disease has high sensitivity and a high negative predictive value, meaning that it can reliably rule out TB if none of the clinical manifestations is present (Figure 3). Secondly, it is a straightforward intervention inherent to any clinical encounter and can be repeated as often as necessary without special equipment.

Figure 3 Algorithm: Identification and treatment of LTBI in high-risk groups for tuberculosis



* Any Symptoms of cough/fever/weight loss/night sweats

** Investigate for active TB through Gene X-pert; it will also specify TB sensitivity/resistance (if any) in the population

*** Initiate appropriate TPT





Additional tests such as chest radiography can be combined with a symptom screen to improve its accuracy and should be considered whenever radiological facilities are available. However, their absence should not represent a barrier to access LTBI screening and treatment.

Chest radiography is known to have high sensitivity but low specificity for TB. This means that persons with an abnormal chest X-ray should undergo additional investigations to confirm or rule out TB, and diagnose alternative causes of pulmonary disease. Chest X-ray should be offered with no costs to the individual, costs being beard by the TB Programme/Department of Health. The use of chest radiography in addition to TB symptom screening is likely to increase the confidence of health providers given the very high sensitivity of the combination (less chance of missing TB disease). This may conceivably reduce provider concerns around the development of drug resistant-TB resulting from the inadvertent treatment of TB disease with a TPT regimen. This is particularly important among HIV-negative household contacts who are adolescents and adults, other close contacts and clinically at-risk populations. Similarly, the use of chest radiography may increase provider confidence among PLHIV who are receiving ART. The key steps in ruling out active TB cases are summarized in table 6.

Table 6 Key steps in ruling out TB and considering TPT

	Adults and adolescents living with HIV**	Children living with HIV*	HIV-negative household/close contacts of TB patients	Clinical at-risk populations
Clinical symptom-based screening*	Current cough, fever, weight loss or night sweats	Absence or poor weight gain, fever or current cough or history of contact with a case of TB, reduced playfulness, night sweats	Cough of any duration, haemoptysis, fever, night sweats, weight loss, chest pain, shortness of breath, fatigue	
Frequency of symptom screening	At every visit to a health care facility or contact with a health worker			
Chest radiography	Not mandatory although desirable. May be considered among PLHIV on ART; among asymptomatic adolescent and adult contacts and clinical at-risk groups where facilities are available and human resources and health system capacity permits			
Diagnostic testing for TB if screen test is positive	WHO recommends rapid diagnostics (such as X-pert MTB/Rif, urine lipoarabinomannan assay*** among seriously ill PLHIV) or as per national guidelines			





Test for LTBI (TST or IGRA)	Not required among PLHIV and contacts below five years of age. In other populations, these tests limit unnecessary treatment of uninfected individuals (such as settings with a low prevalence of LTBI) Unavailability of tests should not be a barrier to the provision of TPT to those in need
Contradictions to TPT	Active hepatitis (acute or chronic), regular and heavy alcohol consumption and symptoms of peripheral neuropathy Concurrent use of other hepatotoxic medications (such as nevirapine) History of hypersensitivity to TPT
Counselling	Information on LTBI, need for TPT, schedule of medication collection, medication adherence support and follow-up visits, benefits from completing the course, adverse events, actions on the development of TB symptoms or adverse events

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

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

*** Tests based on the detection of mycobacterial lipoarabinomannan (LAM) antigen in urine have emerged as potential point-of-care tests for TB

2.1. Digital Technology for Radiology

With the increase in the availability of digital radiography, the use of Computer-Aided Detection (CAD) to interpret films, and the engagement of private health facilities to purchase radiography services is expected to increase access to radiography in TB screening and diagnostic algorithms. CAD software can analyse digital CXR images for abnormalities and the likelihood of TB being present. Such technology could help reduce inter-reader variability and delays in reading radiographs when skilled personnel is not available. At this time, there is not enough evidence to define the role of CAD for chest radiograph reading as part of screening algorithms.

2.2. Testing for LTBI

Although they are imprecise, tests for the detection of LTBI, both TST and IGRA, are useful to predict who will benefit more from the treatment of LTBI. A positive test for LTBI is not a mandatory prerequisite for treatment of LTBI in PLHIV and in children of age < 5 years that are a contact of bacteriologically confirmed TB cases. In these population groups, the benefits of treatment largely exceed the risks, so that all those who are included in the population group, which does not have the active disease should receive an LTBI regimen.

Either a TST or IGRA can be used to test for LTBI. There is no strong evidence that one test should be preferred over the other in terms of predicting progression from LTBI to active TB disease. The choice of test for programmatic use depends on cost, availability, human resources and infrastructure to provide testing services in the clinical context.





2.3. General Requirements

At all TB clinics providing treatment of LTBI, the following elements should be in place:

- Health care workers responsible for LTBI testing identified and trained on different components of testing (such as administration of TST and test reading, collection and processing of blood specimen for IGRAs, specimen collection and transport).
- SOPs available for administration of TST, collection and processing of a blood specimen for IGRA and interpretation of test results.
- SOPs available for appropriate follow-up after testing including access to clinical evaluation, chest radiography and other TB investigations to decide the eligibility of individuals for TPT.
- SOP available for job-aide to assist providers in educating the test recipient and to respond to frequently asked questions regarding the utility and procedure of TST/IGRA.
- Tools available for systematic recording and reporting of test results and linkage to care and treatment.
- Mechanisms are available for supportive supervision and monitoring of accurate implementation.

2.4. TST

The following are requirements for the adoption of TST for the detection of LTBI:

- Ensure availability and supply of tuberculin in a cold chain as well as syringes, needles and consumables.
- Train 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.
- Develop and provide job-aides for health care workers showing the correct technique for TST administration and measurement of induration.
- Establish mechanisms to call people tested to return for the test reading within 48–72 hours of tuberculin administration, or ensure test reading at the person's residence.
- Provide funding support for travel to test recipients and/or health care workers to administer and read test results.
- Develop and supply TST request forms and update the HMIS to enable documentation and reporting of TST results.

2.5. IGRA

The following are requirements for the adoption of IGRAs for the detection of LTBI

- Develop the capacity of the laboratory system to conduct IGRA (phlebotomy, processing of blood specimen, incubation and enzyme-linked immunosorbent assay (ELISA) reading).
- Ensure availability of trained laboratory technicians in laboratories performing IGRA tests.
- Establish mechanisms to ensure rapid transportation of blood specimens from peripheral centers to the IGRA testing laboratory (within 8–30 hours to allow incubation depending on the type of IGRA).





- Ensure the functioning of laboratory equipment and establish a mechanism for regular equipment maintenance for optimal functioning of the laboratory.
- Ensure the supply of updated laboratory request forms, registers, update laboratory information systems to document, and report IGRA test results.

2.6. Treatment of LTBI

Following are key points to consider whilst disseminating treatment of LTBI:

2.6.1. Organization of Services for TPT

- Trained doctors, nurses and peripheral health care workers can evaluate and start TPT once TB disease is reliably ruled out following a national protocol. TPT should be initiated by doctors through prescriptions. Whereas, nurses and frontline health care workers, such as screeners, in the periphery health care facilities, will monitor persons on TPT and make decisions about whether TPT should be suspended or modified (e.g. in the case of adverse events) or restarted (e.g. after an interruption by the person on treatment) after appropriate training. In most instances there is no need to seek the opinion of a medical doctor or a specialist for such decisions, however, there should be a provision to solicit such support in case it becomes necessary.
- TPT should be prescribed by a doctor. Nurses and peripheral health care workers, in addition to doctors, can provide for drug replenishment and monitor adherence and drug toxicity.
- Each TB clinic providing TPT should develop SOPs for TPT initiation and follow up to:
 - Maintain the flow of persons considered for TPT in various health facilities and across different service points within those facilities.
 - Ascertain the role and responsibilities of health providers, community health care workers and key stakeholders (such as malnutrition care services, prisons, correctional facilities, refugee camps and mining communities) in the evaluation of eligibility and start of TPT.
 - Provide adherence support for TPT.
 - Manage TPT interruptions.
 - Identify, document and manage adverse drug events – support supervision.
- Establish TPT services in all relevant service delivery sites (such as TB treatment site, ART centres, maternal and child health services centres, community health centre) decentralizing the service as much as possible.
- Leverage existing TB, HIV and general health services to provide specialized care as needed for people receiving TPT (such as management of adverse events, drug-drug interactions, special situations (pregnancy)).
- Evaluate the availability and capacity of community health workers and other networks (such as former TB patients) that can contribute to TPT service delivery and support to individuals.





- Build capacity:
 - Build capacity through initial training and sensitization of staff.
 - Build capacity of primary care doctors, nurses and other health care workers in history taking, symptom screening and referral for investigations, assessment of eligibility for TPT and starting TPT.
 - Build the capacity of community health workers in the provision of TPT and follow up.
- Undertake phase-in/phase-out planning for TPT medications (from a procurement perspective) as the national programme transitions to shorter TPT regimens. This is important during the introduction of new regimens.
- Review and strengthen the mechanism for quantification, and ordering an uninterrupted supply of commodities (such as TPT medications, pyridoxine).
- Address specific issues regarding TPT for children to:
 - Coordinate TPT with multiple family member households (parents/grandparents) as children may receive care at multiple service delivery sites (such as maternal and child health services, TB or HIV centres).
 - Build capacity on counselling and actions on post-dose emesis and indications for re-dosing.
 - Provide food information to mask the taste of medication.
- Strengthen systematic recording and reporting, including information from the case form or capture data on electronic platforms. Key data variables should be integrated into the HMIS for monitoring and evaluation of performance.

2.6.2. TPT initiation and pre-TPT baseline assessment

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

- 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
 - Co-morbidity: assess the presence of co-morbidities (such as malnutrition, diabetes, viral hepatitis) and record medications being taken
 - Contacts of drug-resistant TB patients (isoniazid, rifampicin only or MDR-TB)
 - Potential contraindications to TPT: such as active hepatitis (acute or chronic) or known elevation in transaminases (>3x Upper Limit of Normal), regular and heavy alcohol consumption and symptoms of peripheral neuropathy. These conditions should prompt detailed investigations and application of clinical judgement to weigh harms versus the benefits of TPT, and timing to start TPT if benefits outweigh harms. History of past TB treatment or current pregnancy should not be considered as contraindications for starting TPT.





- 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, antimalarial medication – often affect TPT.
- Routine LFT is not necessary before starting TPT. Available evidence suggests that close clinical monitoring of signs and symptoms of liver disease is sufficient for early detection and management of adverse events, more so with shorter rifamycin containing TPT regimen. However, LFT is encouraged for individuals having additional risk factors.
- However, where feasible, baseline testing is strongly encouraged for individuals having risk factors – such as a history of liver disease, regular use of alcohol, chronic liver disease, HIV infection, age more than 35 years and pregnancy or immediate postpartum period (within 3 months of delivery). In individuals having abnormal baseline LFT results, sound clinical judgement is required to determine if the benefit of TPT outweighs the risk of adverse events. These individuals should be tested routinely at subsequent visits.
- The social and financial situation of the person and the family should be assessed and support required overcoming the barriers for TPT completion identified.
- Counselling:
 - 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:
 - The rationale for TPT and benefits to the individual, the household and the wider community
 - TPT is available free of charge through the national program
 - TPT regimen prescribed, including the duration, directions for the 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
 - Signs and symptoms of TB and advice 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 preference. Options may include:
 - Location: Home, community or health facility (with counselling support)
 - Treatment supporter: Assess if a treatment supporter is needed or self-administration is possible. If a treatment supporter is needed, options may include an oriented family member/ community volunteer/workplace treatment partner or health care workers. For a weekly regimen, intake of each dose should be directly observed by the oriented family member, community member, workplace treatment partner, or health care workers (either in person or through a digital tool)
 - Digital tools: include video observed treatment (VOT)/phone missed call/SMS reminders
 - After the investigations and clinical evaluation, the clinician will fill the Preventive Treatment register (Annex 2)





2.6.3. Initiation of Preventive Treatment

- Once contact is considered eligible for preventive treatment by the clinician, a preventive treatment regimen will be initiated within 7 days of documenting eligibility for preventive treatment.
- Weight-based dosages for TPT have been summarized in table 2.
- The final TPT regimen is based on the clinician's discretion, also at the light of the drug susceptibility pattern of the strain, whenever known (such as during contact tracing activities).
- The clinician will explain all the side effects and benefits of preventive treatment to the patient.
- Counselling of the head of the family can have very successful outcomes.

2.6.3. Follow-up Treatment Support and Clinical Monitoring

- The treatment supporter and DOTS facilitator will be trained on the recognition of treatment adverse effects.
- After 2 weeks of treatment initiation, DOTS facilitator will call the contact and get information about treatment adherence and adverse effects and will record all the information in the Preventive Treatment register.
- Field workers will visit the household monthly to quantify adherence, ask about adverse events, and record the data on the Preventive treatment register.
- If adherence to the treatment is low as shown by the monthly follow-up, contact/guardian will be counselled, either over the phone or in person.
- If either the treatment supporter or DOTS facilitator identifies a participant with a possible adverse event, the treatment supporter or DOTS facilitator will immediately refer the participant to the clinician for evaluation.
- Persons receiving an LTBI regimen will be asked to visit the health facility every month for follow up evaluation by a physician.
- The Preventive treatment register will be filled at each clinic visit.
- A TB helpline number 0800-88000 for questions and queries will be provided.
- Ancillary medicines, if required, will be provided free of cost for any adverse events.
- If a person stops taking preventive treatment before completion, the DOTS facilitator will counsel this person/guardian on the benefits of completing preventive treatment as well as its proven safety, and attempt to ensure completion.
- If a person takes LTBI treatment for less than 2 weeks, it will be considered as treatment refusal for those who take it for over 2 weeks and then refuse, they will be declared lost to follow-up.
- For patients who succeed in taking over 80% of medication, TPT will be considered as completed.





2.7. Recording and Reporting

The National TB control program uses TB Preventive Treatment cards (Annex 3) that is assigned against each contact of bacteriologically positive TB patients, as sources for information on LTBI. From the contact card, this information is transferred to the TB Preventive Treatment Register (Annex 2). These are paper-based tools, containing lists of contacts investigated in a household, contacts put on TPT and HIV positive patients put on TPT. These tools are reviewed periodically to derive indicators, usually requiring manual computation.

The National AIDS control program has revised treatment registers and included a provision to record information related to TPT. This information is collected on monthly basis from ART centres and is reported to the National AIDS and TB control programmes.

Currently, the data from the TB programme is increasingly being recorded electronically for people with TB disease who need treatment including ART. These databases are used to generate M&E indicators as well as to follow up patient treatment responses. NTP is upgrading the existing electronic systems to capture data elements that are needed for PMTPT monitoring to generate indicators automatically.

Programmatic implementation and scale-up of TPT require strengthening of each element in the cascade of care starting from identification of the target population to provision and continuation of TPT. To this aim, a monitoring and evaluation system must be established that is aligned with national systems. Appropriate recording and reporting tools should be developed, with standardized indicators. The M&E system for TPT should be integrated into the existing national HMIS.

Data on TPT activities are collected at the TB clinics (whether the person receives care at the clinic or home) using the specific data collection form presented in Annexes 1, 2 and 3.

The indicators generated by the recording and reporting system are analysed every quarter at regional and national levels. Data on TPT services are aggregated and reported to higher levels to monitor progress. The case-based data system is available in an electronic version with nationwide access.

2.8. Monitoring and Evaluation

A comprehensive programme for monitoring and evaluation activities should be developed, under the responsibility of the NTP. The minimum set of indicators recommended to be measured consists of the following:

- Assessment of high-risk population eligible for screening.
- The high-risk population that was screened for TPT
- Among the high-risk population screened, the number who are eligible for TPT.



- Among the high-risk population eligible for TPT, the number who initiated treatment.
- Assessment of the proportion of people who initiated TPT, the number/proportion of people who completed TPT.
- Among the population that completed TPT, the number/proportion that developed active TB. Among the population that completed TPT, the number/proportion that was diagnosed with active TB, after appropriate follow-up and monitoring.

Also, the following indicator is optional to measure:

- Assessment of the proportion of the screened high-risk population that is eligible for TPT.

The description of the three major monitoring indicators (Table 7). The data source is the *TB treatment register*, the *Index Tuberculosis Case Forms* and the *Contact Register*.

Table 7 Indicators adopted for monitoring and evaluation of programmatic management of TPT

Indicator	Definition	Numerator	Denominator	Remarks
Contact investigation coverage	Number of contacts of bacteriologically confirmed TB patients evaluated for TB disease and LTBI out of those eligible, expressed as a percentage	Total number of contacts of bacteriologically-confirmed TB patients who completed evaluation for TB disease and LTBI during the reporting period	Total number of contacts of bacteriologically-confirmed TB patients during the reporting period	Contact investigation identifies people recently exposed to TB with a high risk of developing TB disease. This activity is poorly implemented in many countries and needs urgent improvement to achieve the UNHLM targets. It is also one of the top 10 indicators of the WHO End TB strategy
TPT Coverage	Number of individuals initiated on TPT out of those eligible expressed as a percentage	Total number of individuals eligible for TPT who initiated treatment during the reporting period	Total number of individuals eligible for TPT during the reporting period	This indicator (also referred to as TPT initiation indicator) should include all people deemed to be at risk and eligible for TPT by the national policy. A time-trend analysis of the numerator provides information on the trajectory of TPT scale-up and help assess progress towards UNHLM targets



				<p>Disaggregation by PLHIV (newly or currently enrolled on ARV), contacts < 5 years of age and 5 years and older allows reporting to WHO for monitoring of UNHLM targets.</p> <p>Disaggregation by TPT regimen (e.g. 3HP, 3HR, 6H) helps assess the uptake of shorter rifamycin-containing regimen and inform the procurement and supply chain management</p>
TPT Completion	<p>Number of individuals completing TPT out of those initiating treatment expressed as a percentage</p>	<p>Total number of individuals who completed a course of TPT* during the reporting period</p>	<p>Total number of individuals who initiated a course of TPT during the reporting period</p>	<p>This indicator helps assess the quality of implementation of PMTPT given that the effectiveness of TPT depends upon its completion. When reported alongside the other two indicators above, the reporting period should be earlier (e.g. 6 months or 12 months preceding) to allow time for completion of the TPT</p> <p>Disaggregation by regimens lasting 6 months or more and others lasting less to handle TPT completion in “cohorts” within a practical time window</p>



*Key Points 8*

Offering TPT to someone who has TB disease can delay the resolution of the disease and favour the emergence of drug resistance. Thus, excluding TB disease before initiating TPT is one of the critical steps in the preventive TB care pathway.

CAD software can analyze digital CXR images for abnormalities and the likelihood of TB being present.

Chest radiography is known to have high sensitivity but low specificity for TB. This means that persons with an abnormal chest X-ray should undergo additional investigations to confirm or rule out TB, and to diagnose alternative causes of pulmonary disease.

Provide funding support for travel to test recipients and/or health care workers to administer and read test results.

In most instances there is no need to seek the opinion of a medical doctor or a specialist for such decisions, however, there should be a provision to solicit such support in case it becomes necessary.

TPT should be prescribed by a doctor. Nurses and peripheral health care workers, in addition to doctors, can provide for drug replenishment and monitor adherence and drug toxicity.

Undertake phase-in/phase-out planning for TPT medications (from a procurement perspective) as the national programme transitions to shorter TPT regimens.

Strengthen systematic recording and reporting, including information from the case form or capture data on electronic platforms.

Elicit information on personal history relevant for TPT initiation and continuation, as mentioned under 6.6.2.

The treatment supporter and DOTS facilitator will be trained on the recognition of treatment adverse effects.

The treatment supporter and DOTS facilitator will be trained on the recognition of treatment adverse effects.

If a person takes LTBI treatment for less than 2 weeks, it will be considered as treatment refusal for those who take it for over 2 weeks and then refuse, they will be declared lost to follow-up.

For patients who succeed in taking over 80% of medication, TPT will be considered as completed.

Assessment of people who were diagnosed with active TB after completion of the LTBI treatment.





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Annexures



Annexures

Annexe 1

Annexe 1 contains the consent form that is to be filled by contacts of the bacteriologically positive TB patients.

The Consent Form


Government of Pakistan
Ministry of National Health Services, Regulations & Coordination
National Tuberculosis Control Program


LTBI علاج کے لئے رضامندی

• میں سمجھتا ہوں کہ مجھے ٹی بی کی بیماری ہونے کی تشخیص نہیں کی گئی ہے، لیکن اس ITBL علاج کی تجویز کی گئی ہے کہ مستقبل میں ٹی بی ہونے کے امکانات کو کم کیا جائے۔

• مزید، میں پوری طرح سمجھتا ہوں کہ جب تک کہ کسی ڈاکٹر کے ذریعہ دوائیوں کو روکنے کی ہدایت نہ ہو اس وقت تک مجھے یہ دوائیں لینا جاری رکھیں۔

• مجھے ان دوائیوں سے وابستہ ضمنی اثرات کی وضاحت کی گئی ہے۔ مجھے آفس کے اوقات کے دوران، کسی مقامی ڈاکٹر یا کسی سرکاری اسپتال میں ڈاکٹر سے رابطہ کرنا چاہئے، اگر اس طرح کے کوئی ضمنی اثرات ہونے لگیں۔

• میں سمجھتا ہوں کہ مجھے کسی sDOT یا نیشنل ٹی بی کنٹرول پروگرام آفس سے رابطہ کرنا چاہئے جب میں سفر کرنے کا ارادہ کروں گا۔

• میں پوری طرح واقف ہوں کہ نیشنل ٹی بی کنٹرول پروگرام یا ڈسٹرکٹ ہیلتھ ڈائریکٹوریٹ کا ہیلتھ کیئر فراہم کرنے والا میری پیشرفت کی نگرانی کے لئے مستقل بنیاد پر مجھ سے رابطہ / ملاقات کرے گا۔

مجھے دوائیوں کے بارے میں سوالات پوچھنے کا موقع ملا۔ جو بھی سوال پوچھئے گئے ہیں ان کا جواب میرے اطمینان سے دیا گیا ہے۔ میں دوائیں لینے پر راضی ہوں اور میں مطمئن بھی ہوں

Consent

I consent to the administration of the treatment regimen for Latent Tuberculosis Infection.

Name of patient: _____ **S/O D/O W/O:** _____

Patient/Guardian CNIC: _____

Address: _____



Government of Pakistan

Ministry of National Health Services, Regulations & Coordination



National Tuberculosis Control Program

+++Continued+++

Facilitator Statement

I have given a verbal understanding of this consent form (and any other information given to the patient regarding LTBI) in a detail that the patient understands, which is:

Name of Facilitator & Designation: _____

Hospital: _____ **Signature & Date:** _____

TB Contact Register

PT Reg. No.	Registration Date	First Name	Last Name	Gender (M/F)	Age	Address	If the contact of TB case mentions Reg. No. of Index TB Case	All Contacts of B+ PLHIV Other (specify)	3HP 6INH Other (mention)	Tick and write the date of drug collection in Follow-ups Months 1 (Date) 2 (Date) 3 (Date) 4 (Date) 5 (Date) 6 (Date)	Date of Treatment Outcome	Treatment Completed Lost to Follow- Refused Died Diagnosed TB	Remarks
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PT Reg. No.	: Patient registration number for TPT Treatment
Index Case	: The TB patient in the family who is already on TB treatment
High Risk	: Select appropriate option. For others, specify why the person is high risk
PLHIV	: People living with HIV
Treatment Prescribed	: 3HP is Fixed Dose Combination (FDC) of Rifapentene and INH, given weekly for 12 weeks (3 months) : 6INH is Isoniazid daily dose given for 6 months : Others may include treatment for interrupted treatment or as advised by Physician



Annexe 3

TPT Card

Annexe 3 demonstrates the registration cards used for TB preventive treatment. The TPT cards keep a detailed record of the medication taken by the contacts of bacteriologically positive TB patients.

TB Prevention Treatment card

SECTION 1: Basic Details		
1	Date	<input type="text"/> <input type="text"/> - <input type="text"/> <input type="text"/> - <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>
2	Name of BMU	<input type="text"/>
3	Name of person	<input type="text"/>
4	CNIC #	<input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>
5	Name of doctor	<input type="text"/>
6	Index Patient TB No.	<input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>
7	Index Patient Name	<input type="text"/>
SECTION 2: LTBI Treatment Details		
1	Registration Date	<input type="text"/> <input type="text"/> - <input type="text"/> <input type="text"/> - <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>
2	TPT Registration #	<input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>
3	Weight (Kg)	<input type="text"/> <input type="text"/> . <input type="text"/> <input type="text"/>
4	Treatment Regimen	<input type="checkbox"/> INH <input type="checkbox"/> INH + Rifapentine <input type="checkbox"/> INH + Rifampicin <input type="text"/>
5	Drug Dose	<input type="text"/>



**SECTION 3: Daily marking of doses taken by the contact**

Mon th	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31
1																															
2																															
3																															
4																															
5																															
6																															

SECTION 4: Details of follow-up and drug collection

APPOINTMENTS FOR DRUG COLLECTION AND FOLLOW UP				Date Patients visited		Remark (General condition/adverse event)		Initial
	Next appointment date	Initial						
1								
2								
3								
4								
5								
6								

SECTION 5: Treatment end date and outcome (please circle only one):

Treatment end date	Treatment outcome			
	Complete	Lost to follow	Died	Refused
				Diagnosed as TB



Annexe 4 illustrates the Index Tuberculosis Case Form.

[illegible]

Annexe 5

STAG Notification Letter

F.1-6/2017-CMU (Admn)**Government of Pakistan****Ministry of NHR&C**

Coordination Unit to Manage Global Fund (AIDS, TB, Malaria)

Block F, EPI Building, Prime Minister Health Complex

Islamabad, the 03rd January 2022.**Notification of Strategic Technical Advisory Group for TB at CMU****Objectives:**

- To review, discuss and address technical issues pertaining to case management practices/protocols/processed (diagnostic and treatment) for both susceptible/drug resistant TB (DSTB and DRTB) and issue national advisories.
- To align the policies in line with global recommendations, adapt/endorse recommendations on national guidelines for TB case management.

Secretariat: The office of National Coordinator at CMU will serve as secretariat of TWG.**Meeting:** One-day meeting of technical working group will be held on quarterly basis OR as and when needed.**Composition:** Composition of the TWG will be as follows:

- Chairperson:** National Coordinator CMU
- Secretary:** Deputy National Coordinator TB
- Members:**

Office	Designated Member
Academia/ National Experts	a) Maj. Gen (R) Jawad, President Pakistan Chest Society. b) Dr. Naghman Bashir, Secretary General Pakistan Chest Society. c) Prof. Dr. Shehzad Munir, Dean FGPC, Head of Pediatrics. d) Prof. Nasim Salahuddin, Head of Department of Infectious Diseases, The Indus Hospital. e) Professor Arshad Javaid, Professor of Pulmonology, Member Health Task Force. f) Professor Rumina Hassan, Professor Pathology and Microbiology. g) Dr. Ejaz A. Khan, Consultant Pediatrician & Infectious Disease Specialist, Shifa International Hospital, Islamabad. h) Prof. Rai Asghar, Pediatric Association.
Ministry	a) Representative from DG (Health) / (DDPI), M/o NHR&C.
WHO	a) Dr. Khawaja Laeeq Ahmed, National Program Officer.
UNAIDS	a) Dr. Rajwal Khan, Strategic Information Advisor.
Stop Tb Partnership	a) Dr. Syed Karam Shah.
Pakistan Medical Association, Pakistan	a) Dr. Qaiser Sajjad, Secretary General Pakistan Medical Association Pakistan.
CMU	a) Dr. Basharat Javed Khan M&E and Surveillance Specialist. b) Dr. Sabira Tahseen, Advisor NRL. c) Dr. Abdul Ghafoor, Advisor MDR-TB. d) Dr. Razia Kaniz Fatima, Chief Research Coordinator.
Co-opted members	a) PTP Managers Balochistan, KP, Punjab, Sindh. b) Dr. Farah Naureen, Mercy Corps. c) Any other expert with approval of National Coordinator CMU.

(Muhammad Bashir Khan)
 National Coordinator,
 Common Unit to Manage Global Fund (AIDS, TB & Malaria)
 Islamabad

Copy To:

- SPS to SAPM, M/o NHR&C.
- PS to Secretary Health, M/o NHR&C.
- All concerned.



National Tuberculosis Control Program

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NTP Help line: 0800-8800, SMS Code: 9112