Guidelines for Programmatic Management of TB Preventive Treatment in India - 2021

Frequently Asked Questions

Que 1. Does the definition of close contacts include both household contacts as well as workplace contacts?

Yes, it includes both household contacts and workplace contacts

Que 2. What are the common side effects of using 3HP or 6H regimen?

- Common side effects of Isoniazid are- Asymptomatic elevation of serum liver enzyme concentrations, Hepatitis, Peripheral neuropathy (paresthesia, numbness, and limb pain), Skin rash, Sleepiness, and lethargy
- Common side effects of Rifapentine are- Gastrointestinal reactions (abdominal pain, nausea, vomiting), Hypersensitivity reactions (flu-like symptoms), Hepatitis & Discoloration of body fluids

Ques 3. Under NTEP, is paediatric age group upto 14 years or upto 18 years?

For programmatic purpose in India, child is a person up to and including 18 years of age.

Que 4. What is the difference between household contacts and close contact?

Household contact is a person who shared the same enclosed living space as the index TB patient for one or more nights or for frequent or extended daytime periods during the three months before the start of current TB treatment.

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

Que 5. Should TPT services be expanded to the high TB transmission settings?

Yes. High TB transmission setting refers to a setting with a high frequency of individuals with undetected or undiagnosed TB disease or where infectious TB patients are present and there is a high risk of TB transmission. TB patients are most infectious when they are untreated or inadequately treated. Transmission rates are higher in settings where aerosol-generating procedures are carried out and/or by the presence of susceptible individuals.

The high-risk settings/individuals include health-care workers, prisons, mines, slums, tribals, migrants etc., They should be mapped out as part of a vulnerability mapping and prioritized for specific TPT interventions guided by differential TB epidemiology by the state TPT committee if the risk of active TB among them is higher than that of the general population in the respective states.

Que 6. Which are the target group for TPT interventions?

The programme has prioritized the following target population for TPT based on elevated risk of progression from infection to TB disease or increased likelihood of exposure to TB disease:

1. People living with HIV (+ ART)
    a. Adults and children >12 months
    b. Infants <12 months with HIV in contact with active TB
2. Household contacts (HHC) of pulmonary* TB patients notified in Nikshay from public and private sector (*bacteriologically confirmed pulmonary TB patients will be prioritized for enumeration of TPT target population)
    a. HHC below 5 years
    b. Expanded eligible group[#] including children >5 years, adolescents and adult household contacts
3. Expanded to other risk groups: Individuals who are:
    a. Initiated on immunosuppressive therapy
    b. having silicosis
    c. Initiated on anti-TNF treatment
    d. on dialysis
    e. preparing for organ or hematologic transplantation

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

Que 7. Who should be initiated on TPT - contacts of pulmonary TB patients or contacts of bacteriologically confirmed pulmonary TB patients?

The programme prioritises the TPT intervention among the household contacts of bacteriologically confirmed pulmonary TB patients in whom active TB has been ruled out. This is because the risk of transmission is the highest in these patients.

Que 8. If the household contact is not offered TPT since the index patient is not bacteriologically confirmed but clinically diagnosed, should TPT be provided later when the index patient turns to be bacteriologically confirmed during universal DST?

Yes. Once the index patient is bacteriologically confirmed, the contact should be evaluated for eligibility and TPT regimen should be provided after ruling out of active TB.

Que 9. Should TBI testing be carried out for child contacts <5 years before administering TPT?

No. TPT in child below 5 years who are contacts of pulmonary* TB (prioritized in *bacteriologically confirmed pulmonary TB) patients should be given after ruling out active TB disease. Testing for TBI is not mandatory.

Que 10. Is there any necessity of repeating the TPT in an individual from any of the target population who have received TPT in the past?

No. Currently, there is no evidence to date on the utility of repeated courses of TPT. WHO 2020 TPT guidelines as well as Guidelines for PMTPT in India 2021 do not specifically recommend a repeat course of TPT. However, restarting the full course of TPT may be necessary if there has been significant interruption in the current TPT course given.

Que 11. Should TPT be given to PLHIVs who have already taken TPT in the past? Or Should PLHIV be considered for repeat TPT?

No. Guidelines for PMTPT in India 2021 do not recommend repeating the TPT course in any individual from any of the target population if a TPT course is successfully completed in the past. However, restarting the full course of TPT may be necessary if there has been significant interruption in the current TPT course given.

Que 12. If a person has been treated previously for TB disease with anti-TB treatment, should the person be offered TPT?

Post TB treatment TPT is considered ONLY for the people living with HIV/AIDS.

However, if a TB patient who had been initiated on anti-TB treatment but did not complete the treatment course in the past, is now in contact of bacteriologically confirmed pulmonary TB patients, such contact should be thoroughly evaluated for active TB disease and considered for TPT after ruling out active TB.

Que 13. Should we test health care workers for TB infection at regular intervals and treat them with an appropriate regimen if found positive for TB infection?

Guidelines for PMTPT in India 2021 is clearly articulated that high TB transmission settings (health-care workers, prisons, mines, slums, tribal, migrant laborers etc.) should be mapped out as a part of the vulnerability mapping exercise carried out for ACF for TB disease. These populations can then be prioritized for specific TPT interventions basis the differential TB epidemiology and the probability of higher risk of active TB among identified risk groups or population. This should be state specific and can be decided by respective state TPT committees. Hence, testing and treating TB infection with an appropriate TPT regimen among health care workers need to be a state specific policy. Any decision to implement periodic screening for TB infection and/or TB disease among health care workers should always be based on high quality evidence of the risk of transmission, and the benefit to both health care workers and others potentially affected.

Que 14. Are the health care providers and medical doctors included in close contact of TB patients?

As per the definition, a close contact is a person who is not a part of the household but shares an enclosed space, such as at a social gathering, workplace or facility, for extended periods during the day with the index TB patient during the three months before commencement of

the current TB treatment episode are considered as close contacts. Thus, health care providers and medical doctors do not qualify as close contact of TB patients unless they are directly serving active TB patients and at increased risk of acquiring TB infection and/or disease when infection control measures are not effective. Hence, health care providers and medical doctors will be considered as those in high TB transmission settings.

Que 15. What are the chances of development of resistance to the drugs given as a part of TPT regimen(s)?

One of the concerns commonly expressed about the large-scale use of TPT is the potential risk of propagating drug resistance. These concerns have not been supported by high quality evidence to date. Multiple trials have failed to find scientific evidence of a significant association between emergence of drug-resistance and the use of isoniazid or rifamycin for TPT. An increase in drug resistance is unlikely if good TPT practices are observed i.e., TPT is used in people without active TB disease. Individuals with TB infection have a small number of slowly and sporadically replicating bacteria in their body, and hence there is a low risk for TPT leading to drug-resistance.

Reference studies:

1. TPT implementation tools. IMPAACT4TB [website] 2019 (https://www.impaact4tb.org/3hp-documents/, accessed 16 March 2020).

2. Balcells ME, Thomas SL, Godfrey-Faussett P, Grant AD. Isoniazid preventive therapy and risk for resistant tuberculosis. Emerg Infect Dis. 2006;12(5):744–51.

3. den Boon S, Matteelli A, Getahun H. Rifampicin resistance after treatment for latent tuberculous infection: a systematic review and meta-analysis. Int J Tuberc Lung Dis. 2016;20(8): 1065–1071.

Que 16. Should we conduct follow up IGRA or TST?

No. The guidelines do not recommend follow-up IGRA or TST.

Que 17. What does "ruling out of active TB disease" mean in a person considered for TPT? Does the assessment include bacteriological confirmation or is it clinical?

TPT should be considered only after ruling out active TB disease among the eligible target population by screening them thoroughly for clinical evaluation, radiology and bacteriological confirmation in consultation with treating physician and accordance to the algorithm for TB screening and TPT in India.

Que 18. Is there any relation between sensitivity of IGRA and duration of contact with index TB patients?

No. The sensitivity of the test is dependent on the amount of interferon gamma released in response to stimulus with *M. tb* specific antigens and not proportional to the duration of exposure with the index TB patient.

Que 19. Are there any formal specifications available for IGRA testing?

Central TB Division, Ministry of Health & Family Welfare has issued a detailed specifications of IGRA wide DO letter no. Z-28015/232/2021-TB dated 6th September 2021. The specifications for IGRA testing are as under:

- Interferon Gamma Release Assays for TB Infection testing should be WHO approved/ endorsed and licensed by the Drug Controller General of India. Manufacturer of test kits should also have certification of international standards/ WHO GMP Certification.
- IGRAs are only to be performed using the latest version of the currently endorsed tests which include QuantiFERON-TB Gold Plus (QFT- Plus) manufactured by QIAGEN and T-SPOT.TB manufactured by IMMUNOTEC. The states could choose any of these depending on the laboratory capacity and feasibility.
- If the tests are outsourced, it should be ensured that they are performed only by laboratories accredited by NABL for the purpose. Standard SOPs and Quality assurance practices must be followed and documented. Turn Around Time from sample collection to result availability must be monitored.

Que 20. Do we need any certification or proficiency required under NTEP for performing IGRA test?

No. Currently, programme does not provide any certification or proficiency procedure required by any laboratory to perform IGRA test. However, the Central TB Division, MoHFW has issued standard specification for IGRA test which should be referred while procuring the test from private sector.

Que 21. Can we start TPT based on TST, if IGRA is not available?

Yes, provided standard TST (PPD-RT 23 with Tween 80 of strength 2 TU is available for the use.

Que 22. Are there any cross-reacting antigens in IGRA test?

No. Mycobacterium tuberculosis specific antigens such as ESAT 6, CFP 10 and Tb7.7 are used in IGRA. These antigens are absent in BCG and most NTMs, hence cross reaction is unlikely.

Que 23. Is there any implication in TST results in a person with previous history of TST?

History of previous TST should be elicited as a previous test can boost the reaction size to the subsequent test. This boosting has been found to take place up to one and half years. Therefore, the test should be repeated preferably within 2-3 days of the first test in case of leakage or sub cutaneous injection of the first test. To declare this as a new infection, there should be an increase of at least 10 mm from the 1st test if done within 1.5 years, provided the first test result was <10 mm.

Que 24. What are the possible reports of IGRA?

Possible IGRA report	Positive
	Negative

	Indeterminate

Que 25. If a health worker presumes a false negative result of IGRA/TST, should the test be repeated?

Given the high sensitivity of the test, false negative results are highly unlikely, hence repeat testing is not recommended.

Que 26. Can both the tests (IGRA and TST) be done simultaneously to rule out false positive or false negative?

No. Either IGRA or TST should be used to determined TB infection as per algorithm.

Que 27. Why are EPTB symptoms not included in symptom screening to rule out active TB?

Meta-analysis of 12 studies and 8148 PLHIV with all forms of TB observed 98.5% NPV (Negative Predictive Value) with four symptoms complex. *(Reference: Getahun H et al. Development of a standardized screening rule for tuberculosis in people living with HIV in resource constrained settings: individual participant data meta-analysis of observational studies. PLoS Medicine, 2011, 8(1): e1000391. doi:10.1371/journal.pmed.1000391.)* EP TB symptoms may vary according to the site of involvement. Many of the patients suffering from EP TB may also have one of the 4 symptoms along with site specific symptoms. Further, EP TB may coexist with an underlying clinical/sub-clinical pulmonary involvement. Hence, the health worker should also elicit the history of EP TB symptoms and ruling out of active TB before initiating the TPT.

Que 28. If a household contact >5 years of age was symptomatic and active TB has been ruled out by microbiological and clinical evaluation, should this person be offered TST or IGRA for diagnosing TB infection to offer TPT? What if TST or IGRA is not available?

Yes. As per policy in household contact >5years should be offer TPT after ruling out of active TB and positive for TB infection by TST or IGRA. In situation of TST or IGRA is not available, TPT should not be deferred and ruling out of active TB is the most important

Que 29. Should a person with other risks (like individual on immunosuppressive therapy, anti-TNF treatment, silicosis, on dialysis or preparing for organ/haematological transplantation) with history of current symptoms be offered TST/IGRA without ruling out of active TB?

No. TB should be ruled out in an individual with TB symptoms with bacteriological, radiological and clinical evaluation before offering tests for TBI or TPT.

Que 30. Is it possible to examine the role of community engagement in contact tracing, like through community structures apart from health care workers?

Yes. Community engagement is central to all public health interventions and is viewed as involving those affected in understanding the risks they face and involving them in response actions that are acceptable.

Informed and empowered communities can play a very important role in ascertaining that individuals and communities make informed choices regarding TPT and adhere to the same, sensitization of community, advocacy and demand generation.
Further details can be referred in Chapter 15: Community engagement in Guidelines for PMTPT in India 2021

Que 31. What are the contraindications for initiating TPT?
Only absolute contraindication is active TB disease. Apart from this, relative contraindications are acute or chronic hepatitis, concurrent use of other hepatotoxic medications (such as nevirapine), signs and symptoms of peripheral neuropathy like persistent tingling, numbness and burning sensation in the limbs and allergy or known hypersensitivity to any drugs being considered for TPT.

Que 32. What is the mode of action by which TPT provides protection against TB after completion of treatment and for how much duration?

Isoniazid protects against progression of TB infection to active disease (against endogenous reactivation). It also prevents TB re-infection post exposure to an open case of TB (against exogenous re-infection / super infection / nosocomial transmission) during IPT. Currently recommended TPT regimens offer a durable protection following one course of TPT among PLHIV, HIV-negative contacts and other at-risk populations. The protection is shown to range between 6 to 19 years with IPT.

Que 33. In other high-risk group individual with any of the cardinal symptoms of TB like fever, night sweat etc., if the biological sample was not available for TB testing, should this individual be considered for TPT?
The symptomatic individuals from other high-risk groups may be considered for TPT only after ruling out active TB disease. In case of non-availability of sample for TB testing, TPT should be offered only after ruling out TB disease thoroughly for clinical evaluation, radiology and bacteriological confirmation in consultation with treating physician.

Que 34. When should we start TPT for PLHIV who have completed the TB treatment with anti-TB drugs?
There is no time lag suggested for initiating TPT post TB treatment in PLHIV. The TPT can be started from the next day of the completed TB treatment.

Que 35. Is a written consent required before starting TPT?
No. The individual eligible for TPT should be counselled and well informed by the health worker before initiating the TPT. This being an established national public health policy, a written consent is not required.

Que 36. Is HIV or random blood sugar test mandatory before initiating TPT?

No. Once TB disease is ruled out, and decision to consider TPT is made, baseline assessment to determine the eligibility of an individual for TPT should be undertaken. The baseline assessment includes personal and medication history and investigations as per NTEP guidelines. The history of person should be elicited for HIV and Diabetes, but it is not mandatory to test before initiating TPT.

Que 37. Is treatment supporter of TPT be eligible for incentives?

No. Currently there is no provision of incentive for the treatment supporter of patients initiated on TPT. However, states may propose in their annual budget with justification to NHM for consideration.

Que 38. If an individual on TPT develop TB disease, it will be invariably DR-TB?

No. However, the person on TPT breakdown to TB disease should be subjected to rapid molecular DST as per guidelines.

Que 39. How will the treatment outcome of an individual on TPT be determined?

Please refer to chapter 9 - Monitoring and treatment outcome in the Guidelines for Programmatic Management of TB Preventive Treatment

Que 40. Is the provision of DBT-Nikshay Poshan Yojana applicable for individual on TPT?

No. Currently there is no DBT scheme for individual on TPT.

Que 41. How can we design TPT for household contacts with DR-TB index patient?

Index TB patient	**Regimen**
MDR/RR-TB with FQ sensitive	6 months of daily levofloxacin (6LfX) for contacts
Isoniazid mono-	4 months of daily rifampicin (4R) for contacts

Que 42. Should the contact tracing and TPT for DR-TB contacts be applicable for pulmonary DR-TB only?

Yes. As per guidelines, TPT should be initiated in a household contact of pulmonary* TB (prioritizing in *bacteriologically confirmed pulmonary TB) after ruling out of TB disease. This would invariably be applicable as bacteriological confirmation to determine the DR-TB pattern in the index DR-TB patients required to decide the TPT regimen will be possible mostly in pulmonary DR-TB patients and transmission is mainly through airborne route.

Que 43. Is TPT regimen available in Fixed Dose Combination?

Yes. Isoniazid + Rifapentine (HP) combination is available as fixed dose combination.

Que 44. What is the role of private medical colleges and private practitioners in the detection and management of TB infection?

There is no difference in role between private sector and public sector related to programmatic management of TPT. Private sector is an integral part of PMTPT. The eligible contacts of index patient either from public or private sector must offer TPT. Refer the chapter 13 on private sector engagement in Guidelines for PMTPT in India 2021 for detailed understanding.

Que 45. What is the recommendation for 3RH as TPT regimen?

3RH is not prioritized in the Guidelines for PMTPT in India 2021. However, National Technical Expert Group for LTBI recommended that 3RH can be utilized in limited geography under operational research settings. This is being introducted in the state of Kerala. Policy guidance may be updated based on learnings and experience of implementation in Kerala.

Que 46. How to manage an individual eligible for TPT with contraindication for any TPT regimen?

In case of absolute contraindication such as active TB disease, anti-TB treatment should be initiated. In case of relative contraindication, an individual should thoroughly be investigated by a medical officer and advised TPT based on beneficial effect versus harm that may be caused by TPT.

Que 47. When an index TB patient is detected as DR-TB during DS-TB treatment and the household contact is already initiated on 6H/3HP TPT regimen; how should be proceed?

Beneficiary should be re-evaluated for active TB disease and initiated on the TPT after ruling out active TB on an appropriate TPT regimen in accordance to the DR-TB pattern of the index patient.

Que 48. What to do if there is a breakdown to active TB disease (either clinically or bacteriologically confirmed TB) while an individual is on TPT regimen?

TPT should be stopped immediately, universal DST undertaken as part of the evaluation and the patient should be treated with anti-TB treatment as per the DST pattern.

Que 49. If any household/close contact of pulmonary TB patient could not be provided TPT services for any reasons during the treatment phase of the index TB patient, can the contact be still provided TPT services after the index TB patient has completed treatment i.e. during the post-treatment follow up phase. If yes, for how long after the index TB patient's treatment completion it is advisable to provide TPT services to the household contacts?

Yes, such contacts of pulmonary TB patients who missed receiving TPT for any reasons during the treatment phase of the index TB patients can still be provided TPT services (repeat screening, ruling out active TB, evaluation and provision of TPT) up to at least 2 years (i.e. during the post-treatment follow up of index TB patient) post TB exposure.

- Studies have shown around 5-10% of those infected will develop TB disease over the course of lives usually within the first 2 years after initial infection. *(reference: Comstock GW, Livesay VT, Woolpert SF. The prognosis of a positive tuberculin reaction in childhood and adolescence. Am J Epidemiol. 1974;99(2):131–8.)*
- Studies have also shown that 75% of people who develop TB disease after contact with a patient of active TB are estimated to do so within one year of TB diagnosis of the index patient and 97% within two years. *(reference: Behr MA, Edelstein PH, Ramakrishnan L. Revisiting the timetable of tuberculosis. BMJ. 2018;362:k2738.)*
- Molecular fingerprinting studies further confirmed the probabilities of developing disease within one, two, and five years as 45%, 62%, and 83% respectively. *(reference: Borgdorff MW, Sebek M, Geskus RB, Kremer K, Kalisvaart N, van Soolingen D. The incubation period distribution of tuberculosis estimated with a molecular epidemiological approach. Int J Epidemiol. 2011;40(4):964–70.)*

The substantial incidence of TB disease during the 5 years after exposure, and particularly within the first 12 months, highlights the potential importance of serial screening for TB infection and TB disease in contacts that do not receive treatment for TBI in the past.

Que 50. Provide the weight band wise dosage for 6H regimen

Weight band wise dosage for 6H regimen:

<table>
<tr><th>Regimen</th><th colspan="6">Dosage by age and weight band</th></tr>
<tr><td rowspan="11">6 months of daily isoniazid monotherapy (6H)</td><td colspan="6">Age < 10 years (dosage: 10 mg/kg/day; range: 7 - 15 mg) [d]</td></tr>
<tr><td></td><td><7</td><td>8-11 kg</td><td>12-15 kg</td><td>16-25 kg</td><td>≥25 kg*</td></tr>
<tr><td>Isoniazid 100mg</td><td>0.5</td><td>1</td><td>1.5</td><td>2.5</td><td>3</td></tr>
<tr><td colspan="6">Or</td></tr>
<tr><td>Isoniazid 300mg</td><td>-</td><td>-</td><td>0.5</td><td>1</td><td>1</td></tr>
<tr><td colspan="6">Age >= 10 years (dosage: 5 mg/kg/day) [d]</td></tr>
<tr><td>Isoniazid 100mg</td><td>< 25 kg</td><td>25-34 kg</td><td>35-49 kg</td><td>>50 kg*</td><td></td></tr>
<tr><td></td><td>1</td><td>1.5</td><td>2</td><td>2.5</td><td></td></tr>
<tr><td colspan="6">Or</td></tr>
<tr><td>Isoniazid 300mg</td><td>0.5</td><td>0.5</td><td>1</td><td>1</td><td></td></tr>
<tr><td colspan="7">[d] Maximum dose of H if given daily would be 300 mg/day
* 300 mg formulation is preferrable to use if available to reduce the pill burden</td></tr>
</table>

Que 51. If any individual has been tested with IGRA/TST and detected positive for TB infection during survey, research or clinical practice from private and public sector and individual is not falling under any of the high-risk settings considered eligible for TPT in the national guidelines, should such an individual be provided TPT?

Yes, Such an individual should be thoroughly evaluated to rule out active TB on priority and once active TB is ruled out, TPT services must be offered to him/her to treat the TB infection detected.

Que 52. If any adult or child living in shelter-home or orphanage and diagnosed with TB, should the TB screening and TPT be offered to the contacts?

Yes, If any adult or child living in shelter-home or orphanage and diagnosed with TB, TB screening should be offered to all the contacts and fellow habitant of shelter-home or orphanage and TPT should be provided to eligible as per guideline.