

Frequently Asked Questions

Updated and consolidated guidelines for programmatic management of LTBI: *a critical action to achieve the WHO End TB Strategy targets*

1) What is latent TB?

Latent tuberculosis infection (LTBI) is a state of persistent immune response to stimulation by *Mycobacterium tuberculosis* antigens without evidence of clinically manifested active TB. Someone has latent TB if they are infected with the TB bacteria but do not have signs of active TB disease and do not feel ill. However, they can develop active TB disease in the future.

2) Why should I take pills to treat latent TB when I do not feel ill?

You have been asked to take treatment for latent TB because your health-care worker or clinician believes you have an increased chance of developing active TB disease from the infection. Effective drugs are available for the treatment of latent TB and taking a complete course of treatment can prevent the infection from becoming active disease.

3) Do I need to take TB preventive treatment if I am living with HIV and receiving ART, and have a high CD4 cell count?

All adults and adolescents living with HIV should take TB preventive treatment as part of a comprehensive package of care for HIV, regardless of their CD4 cell count. Although regular ART reduces the overall risk of developing TB among PLHIV, the risk remains very high compared to HIV-negative people. Combined use of TB preventive treatment and ART significantly reduces the risk of TB.

4) Should I receive TB preventive treatment if a person in my family has multidrug-resistant TB?

Please consult your health-care worker or clinician. The health-care worker or clinician will make the decision to provide preventive treatment in selected household contacts of patients with multidrug-resistant tuberculosis, if they are regarded as high-risk for developing drug-resistant TB.

5) What should I do if I develop drug-related adverse events?

If you are receiving treatment for latent TB, and become aware of symptoms such as anorexia, nausea, vomiting, abdominal discomfort, persistent fatigue or weakness, dark-coloured urine, pale stools or jaundice you should immediately contact your health care provider. If a health care provider cannot be consulted at the onset of such symptoms, you should stop treatment immediately and continue to seek help from your health care provider.

6) Who should receive testing and treatment for latent TB?

Adults, adolescents, children and infants living with HIV, infants and children < 5 years who are contacts of TB patients, and HIV-negative clinical risk groups, such as patients initiating anti-TNF treatment, receiving dialysis, preparing for organ or haematological transplantation have the highest likelihood of developing active TB disease and should be prioritized for systematic testing and treatment of LTBI, regardless of setting or the background TB epidemiology. Additional groups for LTBI testing and treatment are: HIV-negative children >5 years, adolescents and adults who are contacts of patients with pulmonary TB and contacts of patients with multidrug-resistant TB. Systematic testing and treatment of LTBI may be considered for HIV-negative prisoners, health-workers, immigrants from high TB burden countries, homeless persons and people who use illicit drugs, if living in low TB burden settings.

7) Should pregnant women living with HIV take TB preventive treatment?

Pregnant women living with HIV are at risk for TB, which can have severe consequences for both the mother and their unborn child. Pregnancy should not disqualify them from receiving preventive treatment. Sound clinical judgement is required to determine the best time to provide treatment.

8) How can we rule-out active TB in PLHIV prior to TB preventive therapy?

Adults and adolescents living with HIV should be screened for TB according to a clinical algorithm and those who report any of the symptoms of current cough, fever, weight loss or night sweats may have active TB and

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should be evaluated for TB. Those with a negative symptoms screen are unlikely to have active TB and should be offered preventive treatment, regardless of their ART status. Chest radiography may be offered to people living with HIV who are receiving ART. If no abnormal radiographic findings are observed, preventive treatment can be given. However, chest radiography should not be considered a mandatory requirement or be a barrier to initiating TB preventive treatment in people living with HIV.

9) Which tests can be used to test for latent TB infection?

Either a tuberculin skin test (TST) or interferon gamma release assays (IGRA) can be used to test for LTBI. There is no strong evidence that one test should be preferred over the other to predict progression to active TB disease. The choice will depend on test availability, cost and the health infrastructure. However, neither the TST nor IGRA can be used to diagnose *active TB disease* nor for the diagnostic workup of adults suspected of having active TB. LTBI testing by TST or IGRA is not a requirement for initiating preventive treatment in people living with HIV or children aged < 5 years who are household contacts with a pulmonary TB patient. The evidence reviewed and the recommendations in the 2018 consolidated guidelines apply to the use of QuantiFERON®-TB Gold In-Tube and T-SPOT®.TB only. Any new or generic test should be subjected to proper validation according to WHO guidelines.

10) What TB preventive treatment options are available?

Isoniazid or INH has been the standard treatment for LTBI. It works very well to prevent TB but it has to be taken daily for 6 to 9 months. It is usually given with vitamin B6 or pyridoxine. Rifapentine combined with isoniazid, also known as 3HP, is another regimen that is recommended as an alternative to INH monotherapy for both adults and children. 3HP is taken once a week for 12 weeks. Isoniazid plus rifampicin for 3 months (3RH), is recommended for children and adolescents < 15 as alternative to isoniazid in countries with a high TB incidence.

11) Should people living with HIV on ART receive rifapentine?

Regimens containing rifamycins such as rifampicin and rifapentine should be prescribed with caution to people living with HIV who are on ART because of potential drug-drug interactions. These regimens should not be administered to people receiving protease inhibitors or nevirapine. The 3-month regimen of weekly rifapentine plus isoniazid can be administered to patients receiving efavirenz-based antiretroviral regimens without dose adjustment. Administration of rifapentine with raltegravir was found to be safe and well tolerated. Rifapentine-containing regimens should not be administered with dolutegravir until more information becomes available from ongoing studies.

12) Should TB preventive treatment be provided by direct observation of treatment (DOT)?

All TB preventive treatment options can be self-administered. The selection of treatment options by programmes and clinicians should consider the best modality for treatment provision and monitoring, considering client preference and to ensure that treatment is not only initiated but also completed.

13) Should the course of TB preventive treatment be repeated?

There is no evidence about repeated courses of preventive treatment, and hence no recommendation is made in the present guidelines. However, in settings with high TB transmission (as defined by local authorities), isoniazid for 36 months (as a proxy for life long therapy) is recommended for PLHIV.

14) What can be done to encourage treatment adherence and support completion of TB preventive treatment?

Interventions should be tailored to the specific needs of the risk groups and to the local context to ensure adherence and completion of treatment. Such interventions could include peer support, coaching and educational interventions. Further interventions to support adherence are mentioned in the WHO Guidelines

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on the treatment of drug susceptible TB, which could be applied to the treatment of LTBI. Shorter latent TB treatment regimens are associated with better adherence and higher treatment completion. Concerns about adherence should, however, not be a barrier to nationwide scale-up of TB preventive treatment.

15) Is it necessary to do testing of baseline liver function?

There is insufficient evidence to support mandatory or routine testing of baseline liver functions. However, where feasible, baseline testing is strongly encouraged for individuals with the following risk factors: history of liver disease, regular use of alcohol, chronic liver disease, HIV infection, age > 35 years, pregnancy or in the immediate postpartum period (within 3 months of delivery). For individuals with abnormal baseline test results, sound clinical judgement is required to ensure that the benefit of TB preventive treatment outweighs the risks. Moreover, these individuals should be tested routinely at subsequent visits. Appropriate laboratory testing should also be performed for patients who become symptomatic while on treatment (e.g. liver function tests for those with symptoms of hepatotoxicity).

16) Will implementation of TB preventive treatment worsen the TB drug-resistance problem?

There is no evidence of a significant association between TB drug-resistance and the use of INH or rifamycins for the treatment of LTBI. Nonetheless, active TB disease must be excluded before TB preventive treatment is prescribed, and regular follow-up is required to ensure that people who develop active TB while receiving TB preventive treatment could be identified early. It would be desirable for countries implementing programmatic management of LTBI to establish national surveillance systems for resistance to TB drugs.