Latent tuberculosis infection (LTBI) is a state of persistent immune response to stimulation by *Mycobacterium tuberculosis* antigens without evidence of clinically manifested active TB.

A direct measurement tool for *M. tuberculosis* infection in humans is currently unavailable. We need more research to achieve accurate diagnosis of LTBI.

**KEY FACTS**

- About one-third of the world's population has latent TB, which means people have been infected by TB bacteria but are not (yet) ill with the disease and cannot transmit the disease.
- Persons with LTBI do not have active TB disease but may develop it in the near or in the remote future, a process called TB reactivation.
- The lifetime risk of reactivation TB for a person with documented LTBI is estimated to be 5–10%, with the majority developing TB disease within the first five years after initial infection. However, the risk is considerably higher in the presence of predisposing factors, such as HIV infection.

**LTBI DIAGNOSIS**

Persons with LTBI have negative bacteriological tests: the diagnosis is based on a positive result of either a skin (tuberculin skin test, TST) or blood (Interferon-gamma release assay, IGRA) test indicating an immune response to *M. tuberculosis*. However, these tests have limitations as they cannot distinguish between latent infection with viable microorganisms and healed/treated infections; they also do not predict who will progress to active TB.

**WHO recommendations for the management of LTBI, by country group**

<table>
<thead>
<tr>
<th>COUNTRY GROUP</th>
<th>AT RISK POPULATIONS</th>
<th>TESTING ALGORITHM</th>
<th>TREATMENT OPTIONS</th>
</tr>
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<tbody>
<tr>
<td>High-income and upper middle-income countries with an estimated TB incidence rate of less than 100 per 100,000 population (Low TB burden countries)</td>
<td>Strongly recommended for the following risk groups: 1) People living with HIV; 2) Adults and children who are household or close contacts of pulmonary TB cases; 3) Clinical indications—patients with silicosis; patients initiating anti-TNF treatment; patients on dialysis; transplant patients.</td>
<td>Exclude active TB using TB investigations. A positive IGRA or TST test result is required to diagnose LTBI.</td>
<td>6 months daily isoniazid 9 months daily isoniazid 3 months weekly rifampentine plus isoniazid 3 to 4 months daily isoniazid plus rifampicin 3 to 4 months daily rifampicin</td>
</tr>
<tr>
<td>Resource-limited and other middle-income countries with an estimated TB incidence rate of more than 100 per 100,000 population (High TB burden countries)</td>
<td>1) People living with HIV; 2) Children under 5 years of age who are household contacts of a TB case.</td>
<td>Exclude active TB using TB investigations. An LTBI test is not required prior to LTBI treatment, but is encouraged for people living with HIV. IGRA should not replace TST.</td>
<td>6 months daily isoniazid</td>
</tr>
</tbody>
</table>
**LTBI TREATMENT**
LTBI can be effectively treated to prevent progression to active TB, thus resulting in a substantial benefit for the individual. Currently available treatment options can reduce the risk of developing active TB by 60-90%. However, safety concerns exist, mainly related to the development of hepatotoxicity. Hence, regular clinical monitoring of individuals receiving treatment for LTBI through a monthly visit to the health-care provider is advised.

**CONTACTS OF MDR-TB CASES**
Strict clinical observation and close monitoring for the development of active TB disease for at least two years is preferred over the provision of preventive treatment for contacts with MDR-TB cases.

*Algorithm for diagnosis and treatment of LTBI among high risk individuals*

**SCALE-UP**
Systematic diagnosis and treatment of LTBI is part of the new End TB strategy and achieving ≥90% LTBI treatment coverage among people living with HIV and child contacts of TB cases is one of the global priority targets. LTBI management can also contribute to TB elimination, particularly in low TB incidence countries where a large proportion of cases are due to reactivation of latent infection. Therefore, WHO recommends a two-pronged approach, in which: (1) treatment for LTBI is provided in all countries to people living with HIV and children aged less than 5 years old who are household or close contacts of a TB case; and (2) treatment for LTBI is provided to additional risk groups in low TB burden countries.

The key role of this intervention should be recognized and financial resources should be adequately allocated in order to establish a programmatic approach focused on population risk groups. Cost-effectiveness needs to be assessed in each specific context in order to develop tailored strategies based on local epidemiology.

Systematic recording and reporting and surveillance should be established and improved within the national health information system to allow effective monitoring of LTBI diagnosis, treatment and outcome.

**RESEARCH GAPS**
Research gaps include the development of diagnostic tests with improved performance and predictive value for reactivation TB and drug regimens that can be provided for short duration and with less adverse events.

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* Any symptoms of TB include any one of: cough, haemoptysis, fever, night sweats, weight loss, chest pain, shortness of breath, fatigue. HIV test could be offered based on national or local guidelines or clinical judgment. Similarly chest radiographs can be done if efforts are intended also for active TB case finding.

** Clients for whom LTBI treatment is not indicated should be provided information about TB including on the importance of seeking care if symptoms of TB developed.

*** National TB guidelines should be followed while investigating for TB. In addition, those individuals in whom TB is excluded after investigations (including individuals with fibrotic radiologic lesions) can be considered for LTBI treatment.

Please access www.who.int/tb/areas-of-work/preventive-care/ltbi/en/