Executive summary

Latent tuberculosis infection (LTBI) is defined as 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. The vast majority of infected persons have no signs or symptoms of TB but are at risk for developing active tuberculosis (TB) disease. This can be averted by preventive treatment.

These *Guidelines on the management of latent tuberculosis infection* were developed in accordance to the requirements and recommended process of the WHO Guideline Review Committee, and provide public health approach guidance on evidence-based practices for testing, treating and managing LTBI in infected individuals with the highest likelihood of progression to active disease. The guidelines are also intended to provide the basis and rationale for the development of national guidelines. The guidelines are primarily targeted at high-income or upper middle-income countries with an estimated TB incidence rate of less than 100 per 100 000 population. Resource-limited and other middle-income countries that do not belong to the above category should implement the existing WHO guidelines on people living with HIV and child contacts below 5 years of age.

The following are the key recommendations of the guidelines:

- Systematic testing and treatment of LTBI should be performed in people living with HIV, adult and child contacts of pulmonary TB cases, patients initiating anti-tumour necrosis factor (TNF) treatment, patients receiving dialysis, patients preparing for organ or haematologic transplantation, and patients with silicosis. Either interferon-gamma release assays (IGRA) or Mantoux tuberculin skin test (TST) should be used to test for LTBI. *(Strong recommendation, low to very low quality of evidence)*

- Systematic testing and treatment of LTBI should be considered for prisoners, health-care workers, immigrants from high TB burden countries, homeless persons and illicit drug users. Either IGRA or TST should be used to test for LTBI. *(Conditional recommendation, low to very low quality of evidence)*

- Systematic testing for LTBI is not recommended in people with diabetes, people with harmful alcohol use, tobacco smokers, and underweight people provided they are not already included in the above recommendations. *(Conditional recommendation, very low quality of evidence)*

- Individuals should be asked about symptoms of TB before being tested for LTBI. Chest radiography can be done if efforts are intended also for active TB case finding. Individuals with TB symptoms or any radiological abnormality should be investigated further for active TB and other conditions. *(Strong recommendation, low quality of evidence)*

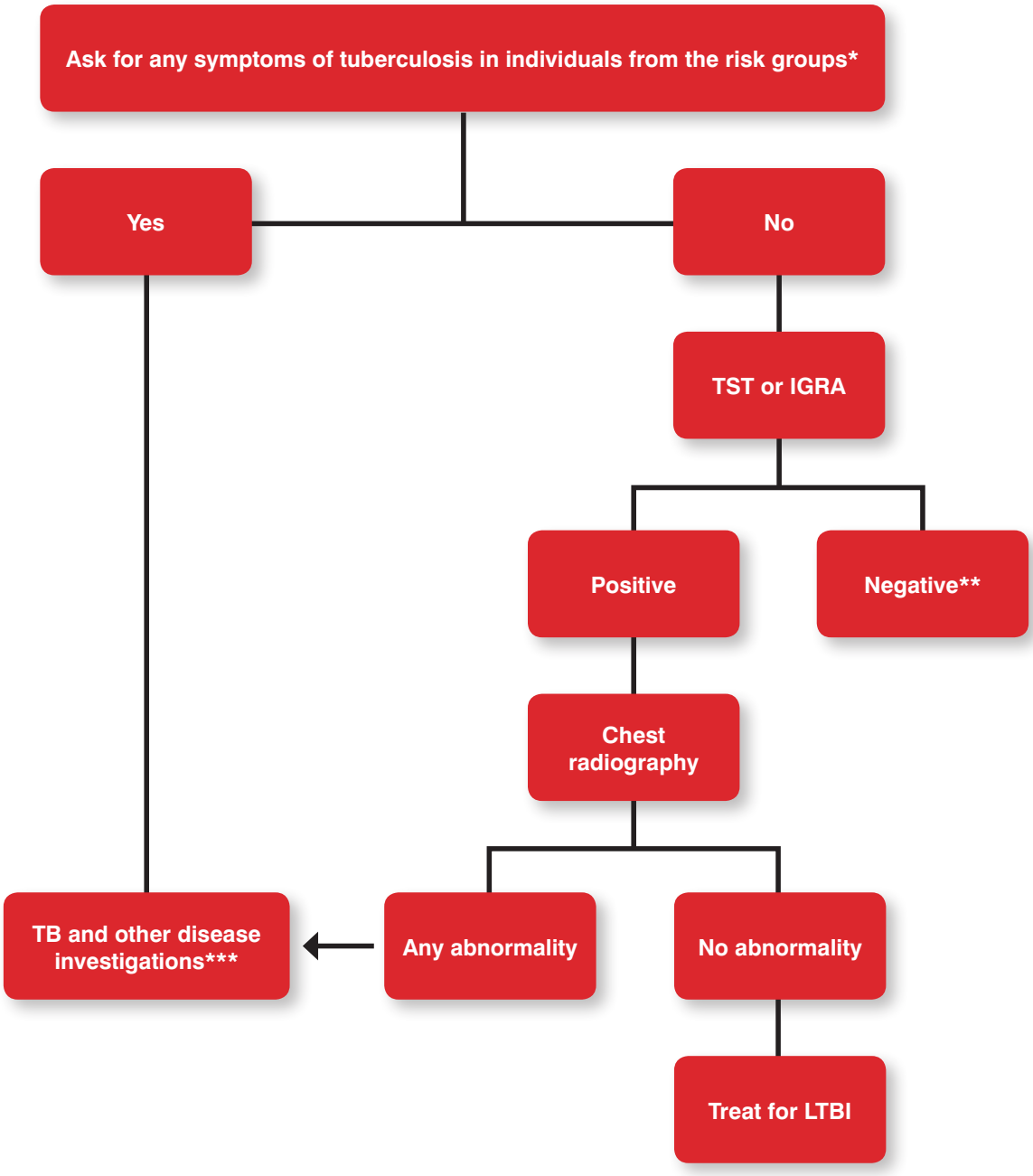
- Either TST or IGRA can be used to test for LTBI in high-income and upper middle-income countries with estimated TB incidence less than 100 per 100 000 *(Strong recommendation, low quality of evidence)*. IGRA should not replace TST in low-income and other middle-income countries. *(Strong recommendation, very low quality of evidence)*

- Treatment options recommended for LTBI include: 6-month isoniazid, or 9-month isoniazid, or 3-month regimen of weekly rifapentine plus isoniazid, or 3–4 months isoniazid plus rifampicin, or 3–4 months rifampicin alone. *(Strong recommendation, moderate to high quality of evidence).*

In addition, the Guidelines Development Panel noted the following critical issues for consideration in the implementation of the recommendations set out in these guidelines:

- Strict clinical observation and close monitoring for the development of active TB disease among contacts of multidrug-resistant TB (MDR-TB) cases preferably for at least two years over the provision of preventive treatment. Clinicians can consider individually tailored treatment regimens based on the drug susceptibility profile of the index case, particularly for child contacts below 5 years of age, when benefits can outweigh harms with reasonable confidence.
- Regular clinical monitoring of individuals receiving treatment for latent TB through a monthly visit to the health-care provider;
- Establishment of national TB drug resistance surveillance systems while implementing national latent TB management services;
- Introduction of flexible interventions and incentives by national TB programmes that are responsive to the specific needs of population groups at risk, as well as tailored to the local context and their needs to ensure acceptable initiation of, adherence to and completion of LTBI treatment.
- Documentation of treated individuals through a functional, routine monitoring and evaluation system that is aligned with national patient monitoring and surveillance systems.
- Creation of conducive policy and programmatic environment, including the promotion of universal health coverage, development of national and local policies, standard operating procedures, as well allocation of dedicated resources.

Figure 1. Algorithm for targeted diagnosis and treatment of LTBI in individuals from risk groups



* 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.