World Health Organization

www.who.int/tb

TUBERCULOSIS DIAGNOSTICS

KEY MESSAGES

- Diagnostic algorithms should start with appropriate screening policies to identify persons at risk.
- Recommended diagnostics are not mutually exclusive and should be combined based on country epidemiology, the existing laboratory network (see Figure 1), and available resources.
- Implementation of any recommended diagnostic requires all core laboratory components to be in place (see box below).
- Culture-based, drug susceptibility testing (DST) is accurate and reproducible for detection of resistance to isoniazid and rifampicin, i.e. multidrug-resistant (MDR-TB) and fluoroquinolones and second-line injectable drugs, i.e. extensively drug-resistant (XDR) TB. For other drugs DST is problematic and the clinical relevance of results are unclear.
- In 2015-2016 WHO issued recommendations on use of new tests to diagnose TB: LF-LAM (diagnostic aid in HIV positive patients with low CD4 count or seriously ill HIV positive patients) and TB-LAMP (manual molecular assay to replace microscopy in settings where Xpert® MTB/RIF assay cannot be used)
- In 2016 WHO issued recommendations on use of rapid molecular tests to detect MTBC, resistance to isoniazid and rifampicin (LPA), as well as resistance to fluoroquinolones and second-line injectable drugs (SL-LPA),
- Even with new, rapid molecular diagnostics, conventional laboratory capacity (microscopy, culture and DST) must be maintained for monitoring patient response to treatment and detecting resistance to drugs other than rifampicin.
- Scale-up of diagnostic capacity must be matched with access to appropriate treatment and care.

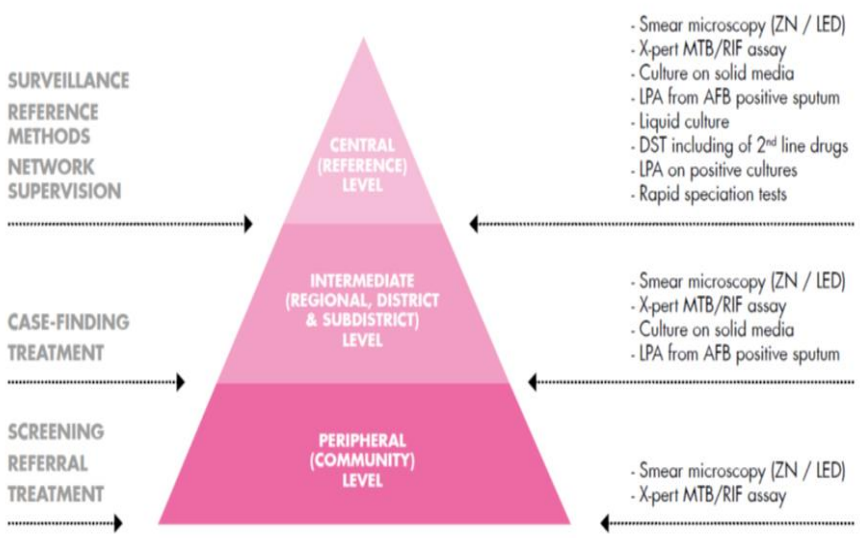
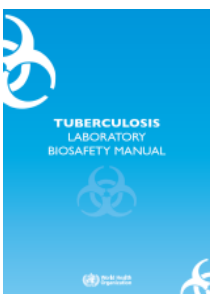


Figure 1: Currently recommended TB diagnostics require different levels of laboratory sophistication due to technical complexity and biosafety concerns

BOX: CORE LABORATORY COMPONENTS FOR UPTAKE OF DIAGNOSTICS

- Sufficient funding.
- Adequate human resources and training.
- Country-specific diagnostic algorithms.
- Appropriate infrastructure and biosafety.
- Specimen transport and referral mechanisms.
- Equipment validation and maintenance.
- Management of laboratory commodities.
- Laboratory information management systems.
- Laboratory quality management systems.



WHO-RECOMMENDED DIAGNOSTIC TOOLS

RECOMMENDED FOR USE (detailed policy guidance: http://www.who.int/tb/areas-of-work/laboratory/policy_statements/en)

- **LED microscopy:** For use at all laboratory levels as replacement of conventional fluorochrome and light microscopy.
- **Commercial liquid culture and DST systems**: For use at central/regional reference laboratory level, as current reference standard.
- **Rapid speciation strip technology**: For use with conventional culture and DST at central/regional reference laboratory level, to identify *Mycobacterium tuberculosis.*
- **Automated real-time nucleic acid amplification - Xpert MTB/RIF system**: For rapid detection of pulmonary and extrapulmonary TB and rifampicin resistance in both adults and children at decentralised laboratory and health care centres.
- **Lateral flow urine lipoarabinomannan (LF-LAM) assay** may be used to assist in the diagnosis of TB in HIV positive patients with signs and symptoms of TB (pulmonary and/or extrapulmonary) who have a CD4 cell count less than or equal to 100 cells/µL, or HIV positive patients who are seriously ill regardless of CD4 count or with unknown CD4 count.
- **Loop-mediated isothermal amplification test kit for TB (TB-LAMP) -** manual molecular assay to replace microscopy to diagnose TB in settings where automated molecular tests cannot be used.
- **Line probe assay (LPA)** as a rapid diagnostic test for detection of rifampicin and isoniazid resistance. The WHO recommended commercially available tests include GenoType MTBDRplus VER 1 and 2 (Hain Lifescience, Germany), Nipro NTM+MDRTB detection kit 2 (Nipro, Japan). Suitable for use on smear-positive specimens or culture isolates.
- **Second-line line probe assay (SL-LPA)** as a rapid diagnostic test in patients with confirmed rifampicin-resistant TB or MDR-TB to detect resistance to fluoroquinolones and the second-line injectable drugs.

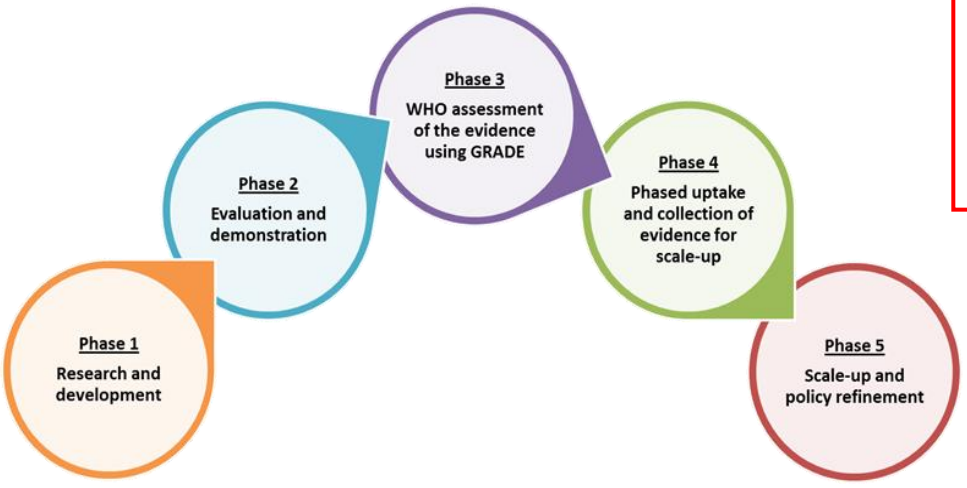
NOT RECOMMENDED DUE TO CURRENT INSUFFICIENT EVIDENCE

- Phage-plaque technology for rapid rifampicin resistance.
- Thin-layer agar methods for rapid culture and DST.
- Interferon-gamma release assays as replacement for the tuberculin skin test for detection of latent TB in low- and middle-income (typically high TB and/or HIV) settings.

RECOMMENDED NOT TO USE (detailed policy guidance: http://www.who.int/tb/areas-of-work/laboratory/policy_statements/en)

- Commercial TB serodiagnostic tests.
- Interferon-gamma release assays for detection of active TB (all settings).

THE PHASES OF TB DIAGNOSTICS DEVELOPMENT AND ASSESSMENT FOR WHO RECOMMENDATIONS



TARGET PRODUCT PROFILES

Consensus on the minimal and optimal specifications of four different types of TB diagnostic tests has been reached. Full report is available at http://www.who.int/tb/publications/tpp_report/en/

For more information please visit: http://www.who.int/tb