Xpert MTB/RIF Implementation Manual: selection of patients to test and interpretation of results

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Evidence synthesis for utility of Xpert MTB/RIF assay

- Expert Group Meeting – Veyrier-du-Lac, France 20-21 May 2013
- WHO commissioned three systematic reviews
  - Xpert for the diagnosis of pulmonary TB and rifampicin resistance in adults
  - Xpert for the diagnosis of extrapulmonary TB
  - Xpert for the diagnosis of TB in children
- Review of affordability and cost-effectiveness of Xpert
Using Xpert MTB/RIF to diagnose pulmonary TB and rifampicin resistance in adults and children

- Xpert MTB/RIF should be used rather than conventional microscopy, culture and DST as the initial diagnostic test in adults suspected of having MDR-TB or HIV-associated TB (strong recommendation, high-quality evidence).
- Xpert MTB/RIF should be used rather than conventional microscopy, culture and DST as the initial diagnostic test in children suspected of having MDR-TB or HIV-associated TB (strong recommendation, very low-quality evidence).
- Xpert MTB/RIF may be used rather than conventional microscopy and culture as the initial diagnostic test in all adults suspected of having TB (conditional recommendation acknowledging resource implications, high-quality evidence).
- Xpert MTB/RIF may be used rather than conventional microscopy and culture as the initial diagnostic test in all children suspected of having TB (conditional recommendation acknowledging resource implications, very low-quality evidence).
- Xpert MTB/RIF may be used as a follow-on test to microscopy in adults suspected of having TB but not at risk of MDR-TB or HIV associated TB, especially in further testing of smear-negative specimens (conditional recommendation acknowledging resource implications, high-quality evidence).
Xpert MTB/RIF implementation manual

Technical and operational ‘how-to’: practical considerations

- First edition was based on the outcomes of a Global consultation on implementation and scale-up of the Xpert MTB/RIF assay convened by WHO in December 2010. First edition served a basis for the update.
- Draft reviewed by the large group of experts from Centers for Disease Control and Prevention, United States, TB Supranational Reference Laboratories of Australia, Belgium and Italy, Office of the United States Global AIDS Coordinator, United States, KNCV, FIND, MSF, South Africa’s National Health Laboratory Service, Indian National Institute of TB & Respiratory Diseases, Stop TB Partnership and WHO.
Topics included in the Implementation Manual

- Evidence base
- Positioning the test
- Testing and managing patients
  - Selection of individuals to be tested
  - Interpreting results of Xpert
- Case definitions and patient registration
- Practical considerations
  - Key prerequisites and actions
  - Testing capacity
  - Operation and storage conditions
  - Biosafety
  - Calibration and maintenance
  - Quality assurance
  - Budgeting guidance
- Monitoring and evaluation
- SOPs for EP specimens
**Selection of individuals to test**

- Xpert MTB/RIF should be used rather than conventional microscopy, culture and DST as the initial diagnostic test in adults suspected of having MDR-TB or HIV-associated TB *(strong recommendation, high-quality evidence).*
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- Xpert MTB/RIF may be used rather than conventional microscopy and culture as the initial diagnostic test in all adults suspected of having TB *(conditional recommendation acknowledging resource implications, high-quality evidence).*
- Xpert MTB/RIF may be used rather than conventional microscopy and culture as the initial diagnostic test in all children suspected of having TB *(conditional recommendation acknowledging resource implications, very low-quality evidence).*
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Interpretation of test results

- **MTB not detected**
  - If TB still suspected
    - Further investigation (CXR, repeat Xpert MTB/RIF, culture, etc.)

- **MTB detected**
  - **R resistant**
    - Repeat Xpert MTB/RIF*
    - DST to at least R; H; Quinolones; SL injectable
  - **R sensitive**
    - WHO recommended first-line treatment;
    - Registration as bacteriologically confirmed TB

- **MTB detected**
  - **R resistant**
    - DST to at least R; H; Quinolones; SL injectable
  - **R sensitive**
    - WHO recommended regimen for MDR-TB with H;
    - Registration as RR-TB

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- **Modify MDR-TB treatment based on the DST results;**
  - Update registration

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  - Update registration

- **In case of discordance on R result, refer sample for sequencing**

- Done on a fresh sample. If LPA is available at the site and sample is smear positive, LPA can be used for the repeated testing.
Linking parts of the algorithm

- Should be decided by Ministries of Health (MoH) within the context of national plans for appropriate management of TB, MDR-TB and HIV associated TB, including the:
  - development of country-specific screening strategies,
  - timely access to quality-assured first- and second-line anti-tuberculosis drugs, and
  - appropriate care delivery mechanisms.

- The settings and algorithms for using Xpert MTB/RIF should be guided by:
  - country or region specific epidemiology (TB, HIV and MDR-TB),
  - available resources,
  - diagnostic tools available in the country and their characteristics and
  - anticipated cost-effectiveness.

- Adoption of Xpert MTB/RIF does not eliminate the need for conventional TB microscopy, culture and DST capacity.

- Microscopy and/or culture remain necessary for monitoring of treatment.
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