Xpert MTB/RIF use for TB diagnosis in TB suspects with no significant risk of drug resistance or HIV infection

DOTS expansion and enhancement

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Assumptions and principles

• Intensified early case detection of *all TB cases* is essential for TB control.

• *Delays and patient costs* need to be substantially decreased.

• Beyond finding the appropriate place of Xpert in the current algorithms, we also need to *re-consider the whole algorithm*, including potentially changed role of microscopy and X-ray for screening, diagnosis and case categorization.

• X-ray is already widely used. It is a poor tool for diagnosis of TB, but a good TB screening tool, if used correctly.

• "Every effort must be made to identify the causative agent of the disease." (ISTC-2)

• "All persons with chest radiographic abnormalities should have sputum specimens submitted for TB laboratory examination." (ISTC-4)

• The diagnosis of TB should be provided free of cost to the patient (Patient Charter), this includes the cost of microscopy, CXR, Xpert MTB/RIF and culture.
People with suspected TB

Follow TB/HIV algorithm

1. HIV+
2. Unknown HIV in high HIV setting

Follow DR-TB algorithm

Risk of DR-TB (e.g. TB Rx history >1m, DR-TB suspect) irrespective of HIV status

1. HIV- or unknown HIV status in low HIV setting
2. Not significant risk for DR-TB
3. Not seriously ill

• Not enough resources to do Xpert for all suspects
• Use Xpert in high risk groups only?
• Add screening step before confirmation with Xpert?
**People with suspected TB**

1. HIV status
2. DR-TB risk

- Risk of DR-TB (e.g. TB Rx history >1m, DR-TB suspect) irrespective of HIV status
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**Microscopy center**

- CXR Normal
- CXR abnormal

**XPERT MTB/RIF**

- TB+ No Rif Res
- TB+ Rif Res
- No TB

**FLD**

**SLD**

**Further Clinical Management**

**Legend/Guide**

- Start
- Process/Action
- Decision
- Endpoint

**Quality CXR available and accessible (e.g. district level)**

**Follow TB/HIV algorithm**

**Follow DR-TB algorithm**

**TB diagnosis can not be totally ruled out, particularly for the TB suspects who have normal CXR and did not undergo any bacteriological examination. For this specific category of patients, a sputum smear examination may be needed.**
Absolute Increases in bacteriologically identified Case Detection Assuming 15% C+ in Population of 10,000 TB Suspects

**Algorithm**
- **Standard (SS only)**
- **Xpert**
- **SS Xpert**
- **CXR, Xpert**

**Positive Predictive Value (PPV)**
- **PPV = 84%**
- **PPV = 94%**
- **PPV = 84%**
- **PPV = 98%**

**Number of Xpert tests done**
- Standard (SS only): 1070
- Xpert: 1465
- SS Xpert: 1603
- CXR, Xpert: 1378

**Bacteriologically confirmed cases**
- Standard (SS only): 900
- Xpert: 1380
- SS Xpert: 1350
- CXR, Xpert: 1352

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**PPV = Positive Predictive Value**
Discussion points

• In what epidemiological situation, and for what target groups (other than people at risk of HIV or MDR) is it relevant and high priority to use Xpert?

• Ethical issues around MDR diagnosis. Consider other available and emerging tests that may be more appropriate when low MDR prevalence and/or no PMDT?

• What are the implications for use of smear and X-ray when Xpert is introduced?

• Where is the appropriate place of Xpert in the health system and what are the financial and logistic challenges and what are the capacity strengthening needs for Xpert, X-ray, smear microscopy, R&R, etc?

• What are the health systems strengthening implications, pros and cons of different algorithms?

• Strategy for Xpert use in the private sector:
  – Maintain global inventory of the sale of Xpert machines outside public sector TB programmes
  – Need to notify TB and manage TB according to Standards
  – NTPs to seek information on Xpert buyers in the country and proactively engage them
  – Offer Xpert at subsidized costs to NTP affiliated private providers offering free TB care?

• Should a generic operational research protocol be prepared and promoted in all settings implementing Xpert? What are the priority research questions?
Low TB prevalence in suspects, active case finding, etc: Absolute Increases in bacteriologically identified Case Detection Assuming 5% C+ in Population of 10,000 TB Suspects

<table>
<thead>
<tr>
<th>Algorithm</th>
<th>Absolute TB Cases</th>
<th>Absolute True Positives</th>
<th>Number of Xpert tests done</th>
</tr>
</thead>
<tbody>
<tr>
<td>Standard (Smear only)</td>
<td>490</td>
<td>300</td>
<td>10000</td>
</tr>
<tr>
<td>Xpert</td>
<td>650</td>
<td>10000</td>
<td>460</td>
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<td>SS Xpert</td>
<td>826</td>
<td>9510</td>
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<tr>
<td>CXR, Xpert</td>
<td>508</td>
<td>3340</td>
<td>451</td>
</tr>
</tbody>
</table>

PPV = Positive Predictive Value

PPV = 54%

PPV = 71%

PPV = 61%

PPV = 89%