Secondary considerations: where MDR or HIV-associated TB is of lesser concern

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Where is MDR or HIV-associated TB of lesser concern?

Proportion of global estimated TB cases

- With HIV infection: 12%
- With MDR (no HIV): 4%
- With no HIV or MDR: 84%
Case detection gap remains large

Incidence 137/100,000
Notification 86/100,000

37% gap
Longer delay – more transmission

Hypothetical benefit of early case detection

"Implementation and roll-out of the Xpert MTB/RIF system for rapid diagnosis of tuberculosis and multidrug-resistance"

- Rapid from the time of identification of a TB suspect? (90 minutes)

- Or, from the time of onset of active TB disease? (90 days, weeks, months?)

- Patient and health system delays are still long

- "Symptom delay": Five recent prevalence surveys show that:
  - 15-38% of infectious cases experience no symptoms
  - 50-75% of infectious cases do not fulfil suspect criteria

- More active case finding requires:
  - More inclusive suspect definition
  - TB screening in risk groups, regardless of symptoms
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

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

Follow TB/HIV algorithm

Follow DR-TB algorithm

? •Not enough resources to do Xpert for all suspects
•Use Xpert in high risk groups only?
•Add screening step before confirmation with Xpert?
Absolute Increases in bacteriologically identified Case Detection Assuming 15% C+ in Population of 10,000 TB Suspects (1,500 cases)

<table>
<thead>
<tr>
<th>Algorithm</th>
<th>Number of Xpert tests</th>
<th>TB Cases detected</th>
<th>Absolute True Positives</th>
<th>Bacteriologically confirmed cases</th>
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<tbody>
<tr>
<td>Standard (SS only)</td>
<td>1070</td>
<td>1000</td>
<td>8930</td>
<td>1170</td>
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<td>Xpert</td>
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<td>SS Xpert</td>
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<td>1380</td>
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<td>CXR, Xpert</td>
<td>1378</td>
<td></td>
<td>1352</td>
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</table>

PPV = Positive Predictive Value
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

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

### TB Cases detected
- **Standard (Smear only):** 490
- **Xpert:** 650
- **SS Xpert:** 826
- **CXR, Xpert:** 508

### Number of Xpert tests done
- **Standard (Smear only):** 300
- **Xpert:** 10,000
- **SS Xpert:** 9,510
- **CXR, Xpert:** 3,340

### PPV (Positive Predictive Value)
- **Standard (Smear only):** PPV = 61%
- **Xpert:** PPV = 71%
- **SS Xpert:** PPV = 54%
- **CXR, Xpert:** PPV = 89%

**Note:** PPV = Positive Predictive Value
People with suspected TB

Follow TB/HIV algorithm

1. HIV status
   2. DR-TB risk

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

Quality CXR and result available and accessible?

Yes

CXR

Result

CXR Normal

Further Clinical Management**

No TB

TB+

Treat with FLD

SLD/confirm DST result

TB+ No Rif Res

No

CXR abnormal

XPERT MTB/RIF

Result

TB+ Rif Res

1. Xpert MTB/Rif available in the facility where the patient seeks care

**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.
People with suspected TB

Microscopy

Result

SS-

Prioritize high risk groups (symptoms and risk factors) for Xpert MTB/RIF

Send sputum or patient

SS+

In high MDR settings or in patients with high risk of MDR-TB

XPERT MTB/RIF

TB+ No Rif Res

Treat with FLD

TB+ No Rif Res

Treat w/SLD

Repeat Xpert or other DST in cases of low MDR prevalence

Further Clinical Management

No TB

Legend/Guide

Start

Process/Action

Decision

Endpoint

1 TB suspect definition will be different for HIV+ and HIV- patients – see section on HIV algorithm.

2 HIV should always be referred to receive the Xpert MTB/RIF test, and other groups should be based on national and local profiles and epidemiology.

3 Some SS+ patients may receive the Xpert MTB/RIF test if DR is suspected after screening the patients for risk factors.

4 For HIV+ patients, follow HIV guidelines. 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.
Pending questions

• In what epidemiological situations, and for what target groups (other than people at risk of HIV or MDR) is it relevant, feasible and cost-effective to use Xpert?

• What is sensitivity, specificity, cost-effectiveness and feasibility of the proposed CXR plus Xpert algorithm in field conditions?

• Capacity strengthening needs for Xpert, X-ray, smear microscopy, R&R, etc?

• Health systems implications of strengthening imaging and lab services: both Xpert and X-ray are "multi-disease platforms"

• What role of Xpert in TB screening, including community screening?