Positioning of Xpert MTB/RIF to diagnose TB among people living with HIV

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Outline of presentation

• The WHO 12 point policy package and progress

• WHO recommendations on Xpert

• TB screening rule & new WHO ICF/IPT guidelines

• Revised TB/HIV algorithms

• Conclusions
The WHO 12 points TB/HIV policy package

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<th>A. Establish the mechanism for collaboration</th>
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<td>1. TB/HIV coordinating bodies</td>
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<td>2. HIV surveillance among TB patient</td>
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<td>3. TB/HIV planning</td>
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<td>4. TB/HIV monitoring and evaluation</td>
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<th>B. Decrease the burden of TB among PLHIV</th>
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<td>6. Isoniazid preventive therapy</td>
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<td>7. Infection control for TB</td>
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<td><strong>Three Is and earlier ART</strong></td>
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<th>C. Decrease burden of HIV among TB patient</th>
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<td>8. HIV testing and counselling</td>
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<td>9. HIV preventive methods</td>
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<td>11. HIV/AIDS care and support</td>
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<td>12. Antiretroviral therapy to TB patients.</td>
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WHO recommendations on Xpert 2010

- Xpert MTB/RIF should be used as the initial diagnostic test in individuals suspected of having MDR-TB or HIV-associated TB  
  (Strong recommendation)

- Xpert MTB/RIF may be considered as a follow-on test to microscopy in settings where MDR-TB or HIV is of lesser concern, especially in further testing of smear-negative specimens.  
  (Conditional recommendation)

Children are included in the recommendations  
Suitable for district and sub-district levels
How to use Xpert?

Figure 1. Selection of individuals to test with Xpert MTB/RIF based on risk assessment:

- A. Individuals at risk of MDR-TB
  - Diagnosed with TB or
  - Suspected of having TB

- B. HIV (+) individuals (or HIV unknown in high HIV settings) suspected of having TB

Primary considerations:

- HIV (-) individuals not at risk of MDR-TB with either:
  - Abnormal CXR
  - Sputum smear (-) but still suspected of having TB

Secondary considerations:

- Xpert MTB/RIF

Outcomes:

- TB, Rif resistance
  - Enrol on MDR-TB regimen
    - DST FID and SIT
    - ART if HIV +

- TB, no Rif resistance

- No TB detected
  - Treatment regimen based on patient history
    - ART if HIV +

  - Appropriately further clinical management
    - IPT if HIV +
Definition of TB suspicion in those known to be HIV positive

• **Adults and adolescents**: anyone who reports any one of current cough, fever, weight loss, or night sweats;

• **Children**: anyone who reports any one of poor weight gain, fever, current cough, or history of contact with a TB case.
When HIV status is unknown

- **HIV testing** should be performed according to national guidelines in all persons with suspicion of TB.

- In **HIV prevalent settings**, a person with unknown HIV status can still be classified as HIV-positive if there is strong clinical evidence of HIV infection.
Inclusion criteria for studies

• Collected sputum specimens from PLHIV regardless of signs or symptoms;

• Used mycobacterial culture of at least one specimen to diagnose TB and;

• Collected data about signs and symptoms.
## Top five best performing rules (1 of m) in all subjects (n = 8173)

<table>
<thead>
<tr>
<th>Combination rule</th>
<th>Sen (%)</th>
<th>Spe (%)</th>
<th>LR-</th>
<th>NPV (95% CI) 5% TB prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>CC, F, NS, WL</td>
<td>79</td>
<td>49</td>
<td>0.42</td>
<td>97.7 (97.4-98.0)</td>
</tr>
<tr>
<td>H, F, NS, WL</td>
<td>76</td>
<td>53</td>
<td>0.46</td>
<td>97.6 (97.2-98.0)</td>
</tr>
<tr>
<td>CC, F, WL</td>
<td>74</td>
<td>54</td>
<td>0.48</td>
<td>97.5 (97.1-97.9)</td>
</tr>
<tr>
<td>CC, NS, WL</td>
<td>73</td>
<td>59</td>
<td>0.49</td>
<td>97.5 (97.1-97.8)</td>
</tr>
<tr>
<td>CC, F, NS</td>
<td>73</td>
<td>61</td>
<td>0.44</td>
<td>97.7 (97.4-98.0)</td>
</tr>
</tbody>
</table>

CC: cough in the last 24 hours; F: Fever; H: Haemoptysis; NS: Night sweats; WL: Weight loss
Top five best performing rules (1 of m) in all subjects with abnormal CXR (n = 2805)

<table>
<thead>
<tr>
<th>Combination rule</th>
<th>Sen (%)</th>
<th>Spe (%)</th>
<th>LR-</th>
<th>NPV (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CC, F, NS, WL, X</td>
<td>91</td>
<td>39</td>
<td>0.24</td>
<td>98.7 (97.1-99.5)</td>
</tr>
<tr>
<td>CC, F, NS, X</td>
<td>89</td>
<td>52</td>
<td>0.21</td>
<td>98.9 (97.6-99.5)</td>
</tr>
<tr>
<td>CC, F, WL, X</td>
<td>88</td>
<td>42</td>
<td>0.28</td>
<td>98.5 (96.9-99.3)</td>
</tr>
<tr>
<td>H, F, NS, WL, X</td>
<td>87</td>
<td>43</td>
<td>0.29</td>
<td>98.1 (97.3-98.6)</td>
</tr>
<tr>
<td>CC, NS, W, L X</td>
<td>87</td>
<td>45</td>
<td>0.29</td>
<td>98.6 (97.5-99.3)</td>
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CC: cough in the last 24 hours; F: Fever; H: Haemoptysis; NS: Night sweats; WL: Weight loss
## Performance of the best rule (one of current cough, fever, night sweats or weight loss)

<table>
<thead>
<tr>
<th>Setting</th>
<th>Sen (%)</th>
<th>Spe (%)</th>
<th>LR- (%)</th>
<th>NPV (95% CI) 5% TB prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Community</td>
<td>76</td>
<td>61</td>
<td>0.39</td>
<td>97.3 (96.9-97.7)</td>
</tr>
<tr>
<td>Clinical</td>
<td>89</td>
<td>30</td>
<td>0.38</td>
<td>98.3 (97.5-98.8)</td>
</tr>
<tr>
<td>CD4 &lt; 200</td>
<td>94</td>
<td>22</td>
<td>0.29</td>
<td>98.9 (95.8-99.5)</td>
</tr>
<tr>
<td>CD4 ≥ 200</td>
<td>83</td>
<td>34</td>
<td>0.49</td>
<td>96.9 (95.1-98.0)</td>
</tr>
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CC: cough in the last 24 hours; F: Fever; H: Haemoptysis; NS: Night sweats; WL: Weight loss
Guidelines for intensified tuberculosis case-finding and isoniazid preventive therapy for people living with HIV in resource-constrained settings
Recommendation 1: TB screening

Adults and adolescents living with HIV* should be screened with a clinical algorithm and those who do not report any one of;

– current cough,
– fever,
– weight loss or
– night sweats

are unlikely to have active TB and should be offered IPT.

(Strong recommendation, moderate quality evidence)

* Irrespective of degree of immunosuppression, also to those on ART, those previously been treated for TB and pregnant women
Recommendation 2: TB screening

Adults and adolescents living with HIV screened with a clinical algorithm and reported one of the following;

- current cough,
- fever,
- weight loss or
- night sweats

may have active TB and should be evaluated to TB and other diseases.

*(Strong recommendation, moderate quality evidence)*
Recommendation 3: duration of IPT

Adults and adolescents who are living with HIV and:
   – have unknown or positive TST status and;
   – unlikely to have active TB
should receive IPT for at least 6 months

(Strong recommendation, high quality evidence)
Recommendation 4: duration of IPT

Adults and adolescents who are living with HIV in settings with higher TB transmission and:

– have unknown or positive TST status and;
– unlikely to have active TB

should receive IPT for at least 36 months

(Conditional recommendation, moderate quality evidence)
Adults TB screening and IPT algorithm

Adults and adolescents living with HIV

Screen for TB with any one of the following symptoms:
- Current cough
- Fever
- Weight loss
- Night sweats

No

Assess for contraindications to IPT
- No
  - Give IPT
- Yes
  - Defer IPT

Yes

Investigate for TB and other diseases
- Other diagnosis
- Not TB
  - Follow up and consider IPT
- TB
  - Treat for TB

Screen for TB regularly at each encounter with a health worker or visit to a health facility
Recommendation 8: TB screening in children

- Children living with HIV who do not have poor weight gain*, fever or current cough are unlikely to have active tuberculosis TB.  
  (Strong recommendation, low quality evidence)

*Poor weight gain is defined as reported weight loss, or very low weight (weight-for-age less than -3 z-score), or underweight (weight-for-age less than -2 z-score), or confirmed weight loss (>5%) since the last visit, or growth curve flattening
Recommendation 9: IPT in children

- Children living with HIV who have any one of poor weight gain*, fever, current cough or contact history with a TB case may have TB and should be evaluated for TB and other conditions.
- If the evaluation shows no TB, children should be offered IPT regardless of their age.

Strong recommendation, low quality evidence

*Poor weight gain is defined as reported weight loss, or very low weight (weight-for-age less than -3 z-score), or underweight (weight-for-age less than -2 z-score), or confirmed weight loss (>5%) since the last visit, or growth curve flattening
Children TB screening and IPT algorithm

1. Child more than 12 months of age and living with HIV
   - Screen for TB with any one of the following symptoms:
     - Poor weight gain
     - Fever
     - Current cough
     - Contact history with a TB case

2. Assess for contraindications to IPT
   - No
     - Give IPT
   - Yes
     - Defer IPT

3. Investigate for TB and other diseases
   - Other diagnosis
     - Give appropriate treatment and consider IPT
   - Not TB
     - Follow up and consider IPT
   - TB
     - Treat for TB

Screen regularly for TB
Investigate for TB with Xpert MTB/RIF: Revised TB/HIV algorithms – ambulatory patients

Figure 1

Ambulatory TB suspect¹ HIV positive² No danger signs

- Xpert MTB+/RIF+
  - Treat for MDR-TB
  - CPT³
  - ART⁵
  - DST FLD+SLD⁵

- Xpert MTB+/RIF-
  - Treat for TB
  - CPT³
  - ART⁵

- Xpert MTB-/RIF- PTB unlikely
  - Clinical assessment for EPTB or other diseases
  - Chest x-ray⁷

EPTB likely
  - Refer to 2007 algorithms for Rx and management

EPTB unlikely
  - Treat for bacterial infection³
  - HIV Rx assessment⁹
  - CPT³

- No or partial response
  - Reassess for TB
  - Repeat Xpert MTB/RIF

- Response
Investigate for TB with Xpert MTB/RIF: Revised TB/HIV algorithms – seriously ill patients

Figure 2

- Seriously ill TB suspect HIV positive with danger signs
  - Immediate referral to a higher level facility, if possible

- Immediate referral to a higher level facility was not possible
  - Parenteral antibiotics for empiric treatment of bacterial infection
  - Consider treatment for PCP
  - Xpert MTB/RIF

- Xpert MTB+/RIF+
  - Treat for MDR-TB
  - CPT
  - ART
  - DST FLD+SLD

- Xpert MTB+/RIF-
  - Treat for TB
  - CPT
  - ART

- Xpert MTB-/RIF-
  - Immediate referral was not possible
  - Immediate referral was possible

- Clinical worsening or no improvement after 3 days
  - Start empirical TB treatment
  - Complete antibiotics
  - CPT
  - Refer for HIV and TB care

- Improvement after 3 days
  - Reassess for other HIV related diseases
  - HIV Rx assessment
  - CPT

- Clinical worsening or no improvement after 3 days
  - Repeat Xpert MTB/RIF
  - Additional investigations for EPTB or other diseases
  - Consider empirical TB treatment
  - Complete antibiotics
  - HIV treatment assessment
  - CPT
Where do the revised algorithms apply?

- If Xpert MTB/RIF is available on site (incl. HIV facilities), then Xpert MTB/RIF should be the first diagnostic test.

- If Xpert MTB/RIF is not available, the 2007 WHO guidelines still apply. Refer sputum/patient to facilities with Xpert MTB/RIF if possible.
Conclusions

- Routine HIV testing in all those with presumptive TB;
- Use of simplified four-symptom TB screening algorithm in PLHIV;
- IPT for those unlikely to have active TB;
- Xpert MTB/RIF as initial TB diagnostic test in those with presumptive TB.