Cost-effectiveness of the Xpert MTB/RIF

Preliminary findings

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Objectives

Estimate the cost-effectiveness of the Xpert MTB/RIF system by decision-analytic simulation modeling

- comparing various diagnostic scenarios to current practice,
- evaluate them for a range of epidemiological and health service settings,
- health service perspective
Methods

- **Setting**
  - low HIV prevalence, low MDR prevalence: India
  - high HIV prevalence, low MDR prevalence: Uganda
  - high HIV prevalence, high MDR prevalence: South Africa

- Applying standard practices to local settings
  - Epidemiological conditions
  - Estimated local health service and measured test costs
  - Protocols
  - Data on effectiveness from the FIND demonstration study ("field trial") and literature
  - Treatment outcomes from literature
Diagnostic scenarios

**Current practice**
*Base case*

- **TB suspect**
  - 2 sputum smears
  - [+] → **TB treatment**
  - [-] → Clinical diagnosis (X-ray, antibiotics)
    - [+] → **TB treatment**
    - [-] → No treatment

**Xpert in addition to smear examination**

- **TB suspect**
  - 2 sputum smears
  - [+] → **TB treatment**
  - [-] → **Xpert MTB/RIF**
    - [+] → **TB treatment**
    - [-] → No treatment

**Xpert instead of smear examination**

- **TB suspect**
  - **Xpert MTB/RIF**
    - [+] → **TB treatment**
    - [-] → No treatment

+ Conventional DST of all diagnosed retreatment patients

+ Xpert screening for all smear-positive retreatment patients
Model

- 10,000 *TB suspects* including patients with S+ and S- pulmonary TB
  - Presenting with prolonged cough with or without systemic or other symptoms suggestive of pulmonary TB – as in field trial

- Separately for:
  - new and previously treated patients
  - HIV- and HIV+ patients
  - RIF-resistance/MDR

- Apply costs for testing and treatment to each step
- Estimate numbers of patients, deaths averted and DALYs gained for each pathway
Cohort assumptions

<table>
<thead>
<tr>
<th></th>
<th>India</th>
<th>South Africa</th>
<th>Uganda</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>% TB suspects</td>
<td>10%</td>
<td>10%</td>
<td>10%</td>
<td></td>
</tr>
<tr>
<td>% previously treated</td>
<td>19.2%</td>
<td>16.8%</td>
<td>7.3%</td>
<td>WHO Global TB Report 2009 update</td>
</tr>
<tr>
<td>% MDR new patients</td>
<td>2.3%¹</td>
<td>6.6%¹²</td>
<td>1.1%³</td>
<td>¹WHO 2010 DR Report</td>
</tr>
<tr>
<td>% MDR PrevTx patients</td>
<td>17.2%¹</td>
<td>24.5%¹²</td>
<td>11.7%³</td>
<td>²Interpolation ³Unpublished data</td>
</tr>
<tr>
<td>% HIV</td>
<td>0.63%¹</td>
<td>24.8%¹</td>
<td>31.9%²</td>
<td>¹WHO Global TB Report 2009 update ²Unpublished data</td>
</tr>
<tr>
<td>% S+ among HIV- patients</td>
<td>65%</td>
<td>65%</td>
<td>65%</td>
<td>Demonstration study</td>
</tr>
<tr>
<td>% S+ among HIV+ patients</td>
<td>47%</td>
<td>47%</td>
<td>47%</td>
<td>Demonstration study</td>
</tr>
</tbody>
</table>

Probability of HIV is independent of retreatment/ treatment status
Probability of RIF-resistance/MDR is independent of HIV status
Treatment assumptions

- Treatment follows diagnosis:
  - Patients are treated correctly following diagnosis
  - New patients are treated with 2HREZ/4HR
  - Retreatment patients with no RIF-resistance are treated with 2HRZES/1HRZE/5HRE
  - Patients with RIF-resistance/MDR are treated with the standard second-line treatment regimen currently used in PMDT (Uganda = India)
  - Patients can only have cure, failure and death as treatment outcomes
  - All HIV+ patients get HAART
  - Xpert showing RIF resistance are started in second-line treatment, then followed by conventional DST
  - Patients treatment awaiting conventional DST results are started on first-line treatment, and switched to second-line treatment if RIF-resistant/MDR
Other key assumptions

**Follow-up**
- Undiagnosed suspects with TB return after 3 months
- 10% of smear-negative TB patients will after 3 months be smear-positive

**DALYs** (*Disability Adjusted Life Years*)
- Disability weights GBD 2004
- All HIV+ patients get lifelong HAART
- Survival on HAART estimated using results of published Markov model (Cleary 2009)
- Untreated smear patients probably of death (0.085) much lower than Sm+ (0.213). For HIV+ patients (0.5)
- Spontaneous recovery also included
The model does NOT take into account...

- Repeated treatment episodes
  - A patient who fails on treatment is assumed to remain untreated
  - Relapses

- Effects of diagnostic delay on treatment outcomes

- Transmission effects

- Patient costs
Diagnostic costs
- All costs measured through *direct observations*
  - Specific for each country
  - In different *routine* settings
- Ingredient costing approach
- Incremental costs includes all assay costs, labour, equipment and building space, all processes (facility based average costs).

Treatment costs
- Includes costs for drugs, clinic visits, follow-up tests, treatment supervision
- Based on WHO Choice estimates, published drug prices and literature
Results

Costing results diagnostics
Model predictions
Incremental cost-effectiveness ratios
Sensitivity analyses
## Costing

<table>
<thead>
<tr>
<th>Lab test</th>
<th>Setting</th>
<th>Costs per patient (US$)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>India</td>
</tr>
<tr>
<td>AFB Smear (one smear)</td>
<td>Peripheral lab</td>
<td>1.25</td>
</tr>
<tr>
<td>Xpert (current pricing)</td>
<td>Peripheral lab</td>
<td>25.15</td>
</tr>
<tr>
<td>Xpert (Vol. &gt; 1.5 Mil / Yr)</td>
<td>Peripheral lab</td>
<td>21.15</td>
</tr>
<tr>
<td>Xpert (Vol. &gt; 3.0 Mil / Yr)</td>
<td>Peripheral lab</td>
<td>17.25</td>
</tr>
<tr>
<td>Culture (LJ)</td>
<td>Reference lab</td>
<td>21.62</td>
</tr>
<tr>
<td>Culture (MGIT)</td>
<td>Reference lab</td>
<td></td>
</tr>
<tr>
<td>DST (LJ)</td>
<td>Reference lab</td>
<td>30.39</td>
</tr>
<tr>
<td>DST (MGIT)</td>
<td>Reference lab</td>
<td></td>
</tr>
<tr>
<td>Antibiotic trial</td>
<td>Routine clinic</td>
<td>3.66</td>
</tr>
<tr>
<td>Chest X-ray</td>
<td>Routine clinic</td>
<td>11.88</td>
</tr>
</tbody>
</table>
Model predictions: case detection

India

Uganda

South Africa

All TB

MDR TB
Diagnostic cost per TB case detected (US$2010)

India

Uganda

South Africa

Diagnostic cost

Treatment cost
### Cost per DALY
(Diagnosis and Treatment)(US$2010)

<table>
<thead>
<tr>
<th>Country</th>
<th>Baseline</th>
<th></th>
<th></th>
<th>In addition to Smear</th>
<th></th>
<th></th>
<th>Instead of Smear</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean (2.5)</td>
<td>(0.975)</td>
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<td>(0.975)</td>
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<td>(0.975)</td>
<td>Mean (2.5)</td>
<td>(0.975)</td>
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<tr>
<td></td>
<td>21.65</td>
<td>28.68</td>
<td>26.77</td>
<td>23.27</td>
<td>30.35</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>South Africa</td>
<td>78.05</td>
<td>65.65</td>
<td>90.53</td>
<td>80.60</td>
<td>67.65</td>
<td>93.67</td>
<td>88.76</td>
<td>74.52</td>
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<tr>
<td></td>
<td>80.60</td>
<td>67.65</td>
<td>93.67</td>
<td>74.52</td>
<td>103.16</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>India</td>
<td>31.96</td>
<td>24.72</td>
<td>39.14</td>
<td>34.96</td>
<td>28.08</td>
<td>41.81</td>
<td>37.44</td>
<td>30.53</td>
</tr>
<tr>
<td></td>
<td>34.96</td>
<td>28.08</td>
<td>41.81</td>
<td>30.53</td>
<td>44.34</td>
<td></td>
<td></td>
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</tbody>
</table>

Confidence intervals generated through Monte Carlo analysis 10,000 iterations
Incremental Cost Effectiveness Ratio (Cost per DALY) (US$2010)

<table>
<thead>
<tr>
<th>Country</th>
<th>Xpert in addition to smear (US$2010)</th>
<th>Xpert instead of smear (US$2010)</th>
</tr>
</thead>
<tbody>
<tr>
<td>India</td>
<td>€56</td>
<td>€74</td>
</tr>
<tr>
<td>Uganda</td>
<td>€58</td>
<td>€67</td>
</tr>
<tr>
<td>South Africa</td>
<td>€93</td>
<td>€133</td>
</tr>
</tbody>
</table>

Both compared to base case.
If ‘instead of’ compared to ‘in addition to’ then ICER very high
Eg. Uganda 1077 US$2010 (but no transmission effect)
South Africa; in addition to example
Sensitivity analyses – prevalence of sm+ TB among suspects

India

South Africa
Sensitivity analyses – cartridge cost

India

South Africa
Incremental cost-effectiveness ratios (ICERs) for Xpert scenarios compared to base case
SOUTH AFRICA

ICER vs specificity of clinical diagnosis

- Xpert in addition to smear
- Xpert instead of smear
Conclusion

In this simulation model including treatment effects and full costs:

1. Diagnostic scenarios in which XPERT is used in addition to or instead of smear examination strongly and equally increase TB case finding in all three epidemiological settings.

2. Both these scenarios yield more DALYs than the baseline scenario.

3. The “Xpert instead of” scenario has higher cost per DALY gained than the “Xpert in-addition-to” scenario, partly due to the higher detection rate of MDR-TB cases and treatment costs involved.

4. Both these scenarios are cost-effective cf. WHO criteria compared to the base case.
But...

- WHO threshold for acceptance may be higher than feasible budgetary reallocation constraints
  - Affordability/ funding streams
- Treatment costs
- Real gains in countries dependant on:
  - Suspect population
  - Current practices (in terms of the base case)
  - Number of people on ART
  - True incremental costs
  - HIV testing

→ requires careful further assessment and evaluation