Serological Testing versus Other Strategies for Diagnosis of Active Tuberculosis in India: A Cost-Effectiveness Analysis

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Background: TB Diagnosis in India

• 2 million cases of active TB per year in India
  – 39% of cases go undiagnosed.
• WHO-recommended diagnostics include sputum smear microscopy and TB culture.
  – Sputum smear: Cheap, but low sensitivity
  – TB culture: Expensive, slow, but high sensitivity
• Serological testing is widely available through the private sector.
  – Cost-effectiveness of serological testing uncertain

Serological Testing for TB

• Based on detection of TB antibodies in serum
  – Should not be specific for active (vs. latent) TB
• Not approved for use in the U.S. or Europe
  – Often produced in Europe for export to countries where regulatory framework is weaker.
• Quality of supporting evidence is very poor.
  – Small studies, industry-funded, hand-selected populations, inconsistent results
  – No randomized data

Methods

• Decision-analytic cost-effectiveness model

• Two analyses:
  – Analysis I: Smear vs. serology as initial test
  – Analysis II: Serology vs. culture as add-on to smear

• Population: 1.5 million TB suspects in India
  – Current annual volume of TB serological tests
  – 10-15% of total TB suspects in India
## Key Assumptions

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
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</thead>
<tbody>
<tr>
<td><strong>Sensitivity/Specificity:</strong></td>
<td></td>
</tr>
<tr>
<td>Sputum smear</td>
<td>0.53/0.97</td>
</tr>
<tr>
<td>Serology</td>
<td>0.68/0.87</td>
</tr>
<tr>
<td>TB Culture</td>
<td>0.87/0.99</td>
</tr>
<tr>
<td><strong>Time to diagnosis:</strong></td>
<td></td>
</tr>
<tr>
<td>Smear or Serology</td>
<td>1 week</td>
</tr>
<tr>
<td>TB Culture</td>
<td>8 weeks</td>
</tr>
<tr>
<td><strong>Cost:</strong></td>
<td></td>
</tr>
<tr>
<td>Sputum smear x2</td>
<td>$3.62</td>
</tr>
<tr>
<td>Serology or TB Culture</td>
<td>$20</td>
</tr>
<tr>
<td><strong>Prevalence of TB Among TB Suspects</strong></td>
<td>14%</td>
</tr>
<tr>
<td><strong>Cost to Treat One TB Case</strong></td>
<td>$82</td>
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</table>
# Cost-Effectiveness

<table>
<thead>
<tr>
<th>Diagnostic Test</th>
<th>Cost (US$)</th>
<th>Additional TB Cases</th>
<th>Additional False-Positives</th>
<th>DALYs Averted</th>
<th>Incremental Cost per DALY Averted</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Performed Alone, Relative to No Microbiological Testing</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sputum smear microscopy</td>
<td>$11.9 million</td>
<td>44,000</td>
<td>36,000</td>
<td>623,000</td>
<td>$19</td>
</tr>
<tr>
<td>Serology</td>
<td>$47.5 million</td>
<td>58,000</td>
<td>157,000</td>
<td>520,000</td>
<td>(dominated)</td>
</tr>
<tr>
<td><strong>Performed on Smear-Negative Specimens Only, Relative to Sputum Smear Alone</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TB culture</td>
<td>$27.6 million</td>
<td>26,000</td>
<td>12,000</td>
<td>130,000</td>
<td>$213</td>
</tr>
<tr>
<td>Serology</td>
<td>$39.0 million</td>
<td>24,000</td>
<td>152,000</td>
<td>110,000</td>
<td>(dominated)</td>
</tr>
</tbody>
</table>

DALY = disability-adjusted life year; dominated = more costly and less effective
Sensitivity Analysis: Smear vs. Serology

- Serology more effective than sputum smear
- Serology less effective than sputum smear

Estimate from published literature
Sensitivity Analysis:
TB Culture vs. Serology
Discussion

• Sputum smear is preferred to serology as an initial test.

• TB culture is preferred to serology as an “add-on” test to sputum smear.

• This is true despite conducting an analysis that is the “best-case scenario” for serology.
  – Published estimates overestimate actual accuracy.
  – Minimal “cost” for false-positives
  – High TB prevalence biases in favor of serology.
Limitations

• Unable to adopt societal perspective
• No accounting for drug resistance testing
• Urban population with access to serology not representative of entire Indian population
• Does not fully account for secondary TB transmission
Conclusions

These data were presented to the WHO Expert Group on TB Serodiagnosis (Geneva, 2010).

Strategic & Technical Advisory Group on TB and WHO have factored these data into their recent decision to make a negative recommendation on serological tests for TB (July 19, 2011)