Cost-Effectiveness of a Lateral-Flow Urine Lipoarabinomannan Test for TB diagnosis in HIV-infected South African Adults

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TB and HIV in South Africa
- TB is the leading cause of non-injury death in South Africa with the rise in TB rates largely driven by the HIV epidemic.
- Standard diagnostics for TB (chest X-ray, sputum smear microscopy) perform poorly in people living with HIV/AIDS (PLWHA).
- Novel modalities required to rapidly diagnose and treat these patients to prevent early mortality.

Lateral Flow Urine LAM Assay
- Lipoarabinomannan (LAM) is an immunogenic glycolipid found in the cell wall of Mycobacterium tuberculosis that can be detected in urine.
- Lateral-flow urine LAM assay is an immunochromatographic point-of-care test requiring minimal training and equipment.

Purpose
Evaluate the cost-effectiveness of lateral-flow urine LAM assay in HIV-infected South African adults and the economic conditions under which it is most likely to be preferred

Methods
- We used a cohort study of hospitalized HIV-infected South African adults and iterative data to populate a decision-analytic cost-effectiveness model.
- Primary outcome: Incremental cost-effectiveness ratio (ICER) expressed in 2010 USD per disability-adjusted life year (DALY) averted.
- Perspective: Public-sector TB control program.
- Lifetime time horizon with 3% discounting
- Sensitivity and uncertainty analyses performed on all parameters

RESULTS
- Cost-effectiveness of urine lateral-flow LAM averts 58 DALYs at a cost of $1370 per DALY averted (95% uncertainty range: $710-3396).
- This is cost-effective when compared to the per capita GDP of South Africa ($7275). This is a standard WHO accepted cost-effectiveness threshold.

Decision Analytic Model
Decision-analytic cost-utility model (TB arm expanded below) of adding lateral-flow urine LAM to the existing array of standard TB diagnostics (sputum smear, clinical judgment, etc.).

Cost-effectiveness model.

Parameter Values

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
<th>Range</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>TB Dynamics</td>
<td>0.28</td>
<td>0.12-0.5</td>
<td>Study data</td>
</tr>
<tr>
<td>Probability of death among patients without TB</td>
<td>0.53</td>
<td>0.0-0.75</td>
<td>Field et al.</td>
</tr>
<tr>
<td>LAM Specificity</td>
<td>0.95</td>
<td>0.7-1</td>
<td>Study data</td>
</tr>
<tr>
<td>LAM Sensitivity</td>
<td>0.66</td>
<td>0.3-1</td>
<td>Study data</td>
</tr>
<tr>
<td>Probability of empiric treatment among HIV on ART (WHO Clinical Stage IV)</td>
<td>0.17-0.33</td>
<td>Study data</td>
<td></td>
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<tr>
<td>Probability of empiric treatment among CD4 &lt;100</td>
<td>0.21-0.5</td>
<td>Study data</td>
<td></td>
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<tr>
<td>LAM Specificity</td>
<td>0.95</td>
<td>0.7-1</td>
<td>Study data</td>
</tr>
<tr>
<td>LAM Sensitivity</td>
<td>0.66</td>
<td>0.3-1</td>
<td>Study data</td>
</tr>
<tr>
<td>Life Expectancy (yrs)</td>
<td>1.45</td>
<td>1-10</td>
<td>Study data</td>
</tr>
</tbody>
</table>

Willingness-to-Pay
- The probability that lateral-flow LAM would cost less than the per capita GDP of South Africa ($7275) is 98.3%.

Limitations
- Study outcomes: Sensitivity and Specificity
  - No empirical evidence that addition of urine LAM improves survival
  - Did not model transmission
  - Transmission time unlikely to be reduced with addition of urine LAM due to advanced disease
  - May not be generalizable to other populations
  - Outpatient setting
  - Other high-burden settings

CONCLUSIONS
- Lateral-flow urine LAM is a feasible point-of-care test in hospitalized South African adults
- Urine LAM is a cost-effective diagnostic strategy
  - ICER: $1370/DALY averted, South Africa GDP: $7275
  - Robust across wide range of sensitivity and uncertainty analysis
- Cost-effectiveness depends most strongly on LAM specificity, life expectancy, and TB prevalence
- Highly cost-effective if treated patients live 5 years post-diagnosis

ACKNOWLEDGEMENTS

Diagnosis of TB
- Decision Analytic Model
  - Existing Diagnostics
  - TB diagnosed by existing test
  - TB treated by existing test
  - Treat
  - LAM + LAM treated
  - LAM treated
  - Do Not Treat

Three-way Sensitivity Analysis
- Life Expectancy after TB cure 5 yrs
- Life Expectancy after TB cure 1 yrs
- Time horizon 8 yrs
- DALYs averted 58
- Cost $1370

One-way Sensitivity Analysis
- Cost-effectiveness of urine lateral-flow LAM is most sensitive to assay specificity, cost of TB treatment, life expectancy after TB cure, and cohort TB prevalence.

Appendix
- Table of Parameter Values
- Table of Cost-Effectiveness Results
- Table of Limitations
- Table of Conclusions
- Table of Acknowledgements