Tuberculosis Transmission in Households and Communities

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Model for *M. Tuberculosis* Transmission

Partition transmission by social constructs

Universe of *M. tuberculosis* Transmission

- Community
  - Health Care Institutions
  - Households
Model for *M. Tuberculosis* Transmission

Assortment of susceptible individuals within social constructs
Kawempe Community Health Study

• Household Contact Study
  – Kawempe Division, Kampala Uganda
  – 1996 – 2010

• Research Aims
  – Estimate household transmission
    • *M. tuberculosis* infection
    • Tuberculosis disease
  – Stratify by HIV serostatus
Household Contact Study Design

Index Cases → Household Contacts → Community Households

- Cure
- Relapse
- Death

Baseline Evaluation
- Tuberculin Skin Testing
- Active Tuberculosis
- HIV Testing

3, 12, 24 Months
- TST Conversion
- Incident Tuberculosis

Creates a cohort of household contacts exposed to an infectious index case
## Effect of HIV Serostatus on TB

| Contact Characteristic | HIV Serostatus of Index Case | | | |
|------------------------|-----------------------------|---|---|
|                        | Seropositive (n = 249)      | Seronegative (n = 251) | P Value |
|                        | - - - - - n (%) - - - - -   | | |
| No. contacts           | 962                         | 960                        | - |
| HIV seropositive       | 157 (16)                    | 46 (5)                     | 0.000 |
| Latent TB Infection    | 685 (71)                    | 769 (80)                   | 0.000 |
| Active TB              | 35 (3.6)                    | 41 (4.3)                   | NS |

### HIV Serostatus of Contacts

<table>
<thead>
<tr>
<th>Latent TB Infection</th>
<th>Seropositives (n = 203)</th>
<th>Seronegatives (n = 1459)</th>
<th>NS</th>
</tr>
</thead>
</table>
Age-Specific Prevalence of TB Infection
Household Contacts vs. Community Members

## Secondary Attack Rates

<table>
<thead>
<tr>
<th></th>
<th>SAR TB</th>
<th>SAR Infection</th>
<th>Risk of TB after new Infection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>3.0</td>
<td>47.4</td>
<td>6.33</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;= 5</td>
<td>5.1</td>
<td>50.3</td>
<td>10.1</td>
</tr>
<tr>
<td>&gt;5</td>
<td>2.2</td>
<td>48.5</td>
<td>4.5</td>
</tr>
<tr>
<td>HIV serostatus</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HIV+</td>
<td>8.8</td>
<td>47.4</td>
<td>18.6</td>
</tr>
<tr>
<td>HIV-</td>
<td>2.5</td>
<td>47.4</td>
<td>5.3</td>
</tr>
</tbody>
</table>

# DNA Fingerprinting

## Household Contacts with Active TB by HIV Sero-Status

<table>
<thead>
<tr>
<th>HIV Status</th>
<th>n</th>
<th>RFLP Pattern Compared with Index Case Isolate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Match</td>
</tr>
<tr>
<td></td>
<td></td>
<td>--- n (%)</td>
</tr>
<tr>
<td>HIV negative</td>
<td>39</td>
<td>33 (84)</td>
</tr>
<tr>
<td>HIV positive</td>
<td>22</td>
<td>13 (59)</td>
</tr>
<tr>
<td>Total</td>
<td>61</td>
<td>46 (75)</td>
</tr>
</tbody>
</table>
CART Analysis of MTB Transmission

BMI > 20 (n = 12)

HIV - (n = 7)

HIV + (n = 5)

BMI ≤ 20 (n = 49)

HIV - (n = 30)

Age ≤ 5 (n = 10)

Age > 5 (n = 20)

HIV + (n = 19)

Age ≤ 5 (n = 5)

Age > 5 (n = 14)

Care: No (n = 5)

Care: Yes (n = 9)

RFLP Pattern

<table>
<thead>
<tr>
<th>Same</th>
<th>Different</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>10</td>
<td>0</td>
</tr>
<tr>
<td>18</td>
<td>2</td>
</tr>
<tr>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>5</td>
<td>4</td>
</tr>
</tbody>
</table>
TB Transmission in Community

• Cough Survey
  – Rubaga Division, Kampala, Uganda, 2007 - 2012
  – Random community sample
  – Cough > 2 weeks -> sputum microscopy and culture

<table>
<thead>
<tr>
<th>Total Screened</th>
<th>5088</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
</tr>
<tr>
<td>Chronic Cough</td>
<td>195</td>
</tr>
<tr>
<td>Active TB</td>
<td></td>
</tr>
<tr>
<td>HIV+</td>
<td>53</td>
</tr>
<tr>
<td>HIV-</td>
<td>22</td>
</tr>
<tr>
<td></td>
<td>31</td>
</tr>
</tbody>
</table>

Active Case Finding for TB
Rubaga Division, Kampala, Uganda

<table>
<thead>
<tr>
<th></th>
<th>HIV Seropositive</th>
<th>HIV Seronegative</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACF 13%</td>
<td>9</td>
<td>26 P = 0.05</td>
</tr>
<tr>
<td>PCF 9%</td>
<td>5</td>
<td></td>
</tr>
</tbody>
</table>

ACF – Active Case Finding
PCF – Passive Case Finding

P = 0.05
Mathematical Model of TB Dynamics

TB Epidemic driven by HIV seronegative TB cases when HIV prevalence is less than 30%

Relative steady-state prevalence of tuberculosis according to HIV prevalence in population
TB Contact Networks
Rubaga Division, Kampala, Uganda

Network Size = 16
Density = 0.88
Degree mean = 13

Network Size = 15
Density = 0.34
Degree mean = 4
TB Contact Networks
Kampala Uganda

Connections between TB networks
Local Bars
Hospitals and clinics

Partition contact networks by location and time
Relate to TB infection and disease
Summary

• HIV seropositive index TB cases
  – More frequent HIV+ contacts
  – Possibly less infectious

• HIV seropositive contacts
  – Similar likelihood for infection as other contacts
  – Increased risk (3-fold) for disease

• HIV seropositive co-prevalent TB cases
  – Different strains imply additional contact networks besides the household

• HIV seronegative TB cases appear to drive the TB epidemic until HIV prevalence is very high
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Estimation of Secondary Attack Rates

\[ \text{SAR}_D = \text{SAR}_I^* \ p_D \]

\[ \text{SAR}_D = \frac{\text{Cases with same strain}}{\text{Total number of contacts}} \]

\[ \text{SAR infection} \approx \ P_{H \in h} - P_{C \in c} \]
\[ P_{H \in h} - P_{C \in c} = \text{ARI}^t \text{SAR} \]

\[ p_D = \frac{\text{SAR disease}}{\text{SAR infection}} \]
<table>
<thead>
<tr>
<th>Latent TB Infection in Contacts (%)</th>
<th>HIV +</th>
<th>HIV -</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤ 5</td>
<td>62</td>
<td>66</td>
</tr>
<tr>
<td>&gt; 5</td>
<td>76</td>
<td>80</td>
</tr>
<tr>
<td>Total</td>
<td>74</td>
<td>75</td>
</tr>
</tbody>
</table>
Replacement Principle

As long as one case of tuberculosis is replaced by another, elimination of tuberculosis cannot be achieved
Replacement Principle of TB Control

- Interrupt Transmission
- Prevent Infection
- Prevent Disease

Infectious Tuberculosis Index Case → Transmission of *M. tuberculosis* → Active Tuberculosis In Contact → Latent Tuberculosis Infection → Active Tuberculosis In Contact

→ Prevent Relapse

→ Tuberculosis Relapse

→ Index Case Replaced
Platform for Global Public Health Action

Comprehensive Plan for TB Elimination

- DOTS
- Treat LTBI
- Active Case Finding
- Environmental Controls
- Vaccination
- HIV Care

- Scientific Research
- New Drugs
- New Vaccines
- New Diagnostics
- New Surveillance

- Sustainable Development
- Poverty Mitigation
- Affordable Modern Housing
- Medical and Public Health Care Systems
- Competent TB Control Programs

Stable and Supportive Government Commitment to TB Elimination

Regional TB Control Alliances between Industrialized and Developing Countries