Modelling the Impact of TB Transmission in Households and Communities

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Background: Heterogeneity in TB Transmission

- TB transmission is heterogeneous across space and time.
  - Seattle (5.9 per 100,000/yr) vs. Khayelitsha (1600)
  - USA: 1955 (52.6) vs. 2011 (3.6)

- In many other infectious diseases, “core groups” or spatial “hotspots” have become the focus of control efforts.
  - “80/20 rule” Woolhouse ME et al, Proc Natl Acad Sci 1997; 94:338
  - “Core groups” in STIs Thomas JC, JID 1996; 174:S134
  - “Hitting hotspots” in malaria Bousema T, PLoS Med 2012; e1001165

- The degree to which spatial “hotspots” contribute to community-wide TB transmission remains uncertain.
  - Is there an “80/20 rule” for TB?
Research Objectives

• To investigate the degree of ongoing community-wide TB transmission in Rio de Janeiro, Brazil, that originates from spatial hotspots

• To project 5- and 50-year reductions in community-wide TB incidence if those hotspots could be “normalized”
  – Bringing TB incidence in the hotspots to current levels in the community
TB in Rio de Janeiro

- Slums (*favelas*) integrated into low-incidence areas
- Surveillance data available at the sub-district level
- Active attempts to “pacify” the *favelas* in advance of World Cup/Olympics
TB Incidence City-Wide: 95 per 100,000 (pop. 6.3 mil)
3 Hotspots: 6.0% of Population, 16.5% of TB Incidence

- Manguinhos: 313/100k (55,600)
- Rocinha: 382/100k (70,600)
- Botafogo: 62/100k (234,700)

AP 1.0: 219/100k (250,000)
Model Diagram

General Community

- Susceptible
  - TB infection
  - Latent TB, Recently Infected
    - Reinfecition
    - Persistent Latency
    - Rapid Progression
  - Latent TB, Remotely Infected
    - Slow Progression
  - Active TB
    - Treatment/Self-Cure
    - Relapse
  - Treated/Recovered

TB Hotspot

- 6% of population size
- 16% of TB incidence
- RR of HIV = 2.1

Indexed by:
- Smear status
- HIV status

TB Transmission
## Model Fitting

<table>
<thead>
<tr>
<th>Epidemiological Data</th>
<th>Value, Rio de Janeiro</th>
<th>Value, Model</th>
</tr>
</thead>
<tbody>
<tr>
<td>TB incidence, per 100,000/yr</td>
<td>95.3</td>
<td>95.3</td>
</tr>
<tr>
<td>Proportion of TB incidence in the hotspot</td>
<td>16.5%</td>
<td>16.5%</td>
</tr>
<tr>
<td>HIV/TB incidence, per 100,000/yr</td>
<td>10.7</td>
<td>10.7</td>
</tr>
<tr>
<td>TB mortality, per 100,000/yr</td>
<td>5.0</td>
<td>5.0</td>
</tr>
<tr>
<td>HIV/TB mortality, per 100,000/yr</td>
<td>0.7</td>
<td>0.7</td>
</tr>
<tr>
<td>TB prevalence, per 100,000</td>
<td>103.1</td>
<td>103.1</td>
</tr>
<tr>
<td>HIV prevalence, per 100,000</td>
<td>390</td>
<td>390</td>
</tr>
<tr>
<td>HIV mortality, per 100,000/yr</td>
<td>16.0</td>
<td>16.0</td>
</tr>
<tr>
<td>Proportion of retreatment cases</td>
<td>27.4%</td>
<td>27.4%</td>
</tr>
</tbody>
</table>
From a Modeling Perspective:

Key parameter is the relative transmission rate:
\[ \beta_{HC}/\beta_{HH} \]

<table>
<thead>
<tr>
<th>FROM:</th>
<th>TO:</th>
<th>Community</th>
<th>Hotspot</th>
</tr>
</thead>
<tbody>
<tr>
<td>Community</td>
<td></td>
<td>(\beta_{CC})</td>
<td>(\beta_{CH})</td>
</tr>
<tr>
<td>Hotspot</td>
<td></td>
<td>(\beta_{HC})</td>
<td>(\beta_{HH})</td>
</tr>
</tbody>
</table>
Quantifying Transmission Heterogeneity

“Hotspot”
11 people:
1 TB case
10 susceptible

Community
190 people
Quantifying Transmission Heterogeneity

\[ \frac{\beta_{HC}}{\beta_{HH}} = \frac{(\text{Probability of infecting someone in the hotspot})}{(\text{Probability of infecting someone in the general population})} \]

1.0 = homogeneous transmission = unreasonable

1/19 = heterogeneous transmission = more reasonable

The baseline assumption in our model will be that one hotspot case causes 2 transmission events in the hotspot for every event in the general population.

\[ \frac{\beta_{HC}}{\beta_{HH}} \approx 0.03 \]
Results: Proportion of TB Transmission ARISING FROM HOTSPOT CASES

If a hotspot case infects 1 person in the community for every 2 people in the hotspot:

- 35% of all transmission originates in the hotspot (6% of population)

0.5 Hotspot-to-Community Transmission for Each Hotspot-to-Hotspot Transmission (Baseline Scenario): 35.3%

Complete Geographic Isolation: 19.4%

Eliminating Hotspots Extinguishes the City’s TB Epidemic (R0 Outside Hotspots <1.0)

One Hotspot-to-Community Transmission for Each Hotspot-to-Hotspot Transmission: 51.3%

Transmission from Hotspot Resident to General Resident: 15.8% as Likely as from Hotspot Resident to Hotspot Resident: 100%
Results: Impact of TB Control Interventions

- Baseline (Equilibrium)
- Reduce Time to Treatment by 50% in Non-Hotspots
- Reduce Time to Treatment by 50% in Hotspots
- Reduce Transmissibility by 50% in Non-Hotspots
- Reduce TB Transmissibility in Hotspots to Non-Hotspot Level

9.8% reduction
29.7% reduction
Summary Points

• Small geographic hotspots are likely responsible for large proportions of TB transmission.
  – “35/6 rule”
  – 80/20 probably unreasonable

• Achieving TB control targets in a 6% hotspot vs. the 94% general population may have similar long-term impact.
  – Hotspot-targeted interventions may be appropriate, even if it costs 10x as much per person.

• Relative transmission rate ($\beta_{HC}/\beta_{HH}$) is critical to estimate.
  • Foci of cross-transmission: public transit, hospitals, occupational, prison
  • We need innovative methods to evaluate this parameter
Limitations/Additional Considerations

- Combining geographically-disparate groups into 1 hotspot
  - No change in results when split into 3 hotspots
- Rio de Janeiro: relatively unique epidemiological laboratory
  - Other hotspots may be more geographically and culturally isolated.
  - Most countries have no real intention of “normalizing” those areas.
- “Early saturation” of transmission in hotspots
  - Need more complex models (e.g., agent-based network) to study
Conclusions

- Under realistic conditions, 6% of a city’s population could account for 35% of ongoing TB transmission.
  - Achieving TB control targets in a 6% hotspot vs. the 94% general population may have similar long-term impact.
- To better estimate the impact of TB transmission in households and communities, we need to better understand the relative transmission rate ($\beta_{HC}/\beta_{HH}$).
  - Hotspot-to-community vs. hotspot-to-hotspot
Acknowledgments

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