Tuberculosis transmission and social network structure: A case study in Kampala, Uganda and simulations on structured networks

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Background

- Although tuberculosis (TB) is a treatable and preventable disease, it remains a leading cause of death worldwide.
- The prevalence of TB disease is greater in men than women, with 1.8 cases notified among men for each woman in 2017.
- Drivers of male-bias of tuberculosis (TB) are poorly understood. Biological factors including hormones, immunology, and genetics likely enhance susceptibility to M. tuberculosis (Mtb) among men¹.
- Alternatively, men could have higher exposure to Mtb than women, possibly due to different social roles men play which

Social network structure in Kampala, Uganda

- We determined the social network from egocentric surveys of 247 index individuals and merged networks by common contacts.
- Observed network consisted of 11,840 unique individuals (123 index cases, 124 index controls, 2,418 first-level, and 9,175 second-level contacts)
 - 14,307 total edges,
 - 10.4, index mean degree = $\{8.2, \text{first} - \text{level}\}$ 2.4, overall
 - 247 egocentric networks linked together in 47 components by common contacts

Factors leading to male-bias

We measured male-bias as the total number infected male nodes/total number of infected female nodes for SLIR (or at the end of the simulation or 200 timesteps for SLIRS).



• Endemic disease models (SLIRS) resulted in male-bias under a broader range of parameters Male SUS and IP more associated with male-bias than TRA Assortativity magnified the effects of α on male-bias

influence social mixing with others in their community².

- Given that the current paradigm for TB control depends on case detection, understanding how and why TB disease differs by sex is important to informing control programs.
- Here, we analyze the structure of a large social network from Kampala, Uganda to see if male position or patterns of mixing could lead to higher exposure rates among men.

Global male-bias of tuberculosis

Male-bias is similar around the world (A). This pattern not wellexplained by rates of smoking (B), health coverage (C), or employment (D). Data from WHO³ and ILO⁴.



Kampala network study

Questions

influenced

sampling

(high

- Clustering coeff. was 0.12
- Degree distrib. resembled a power-law but we could not distinguish it others (e.g., lognormal)⁵.

TB disease is not associated with node position

We compared the network position of index cases and controls.

- There was little variation in estimates of node position.
- Men tended to be slightly more clustered with TB cases than females but this difference was small (3.2 vs. 3.7 network links; F_{1,183}=2.78, p=0.096).



We assessed mixing patterns overall and by index type.

Sensitivity analyses (not shown): faster spreading pathogens generated less malebias. Similar results in small-world and scale-free networks.

Effects of assortativity on epidemic size

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Network assortativity was slightly associated with larger epidemics for slow demic spreading pathogens, and slightly smaller epidemics spreading faster 800 tor pathogens 600 400 0.04 0.15 200

Are men and TB cases more central in their social networks?

Do men and TB cases have different mixing patterns in their social networks?

Methods

- From 2012-2016, we performed a cross-sectional, social network survey in Rubaga Division of Kampala, Uganda.
- We recruited index cases (sputum-smear positive or cultureconfirmed) and index controls without TB and then delineated their social networks with data from interviews.
- Index cases presented to the National Mulago Hospital Complex or were found through active case-finding. Index controls were recruited by frequency-matching index cases according to age, sex, and parish. Inclusion procedures for index individuals were identical (had to be >15 years old and reside primarily in Rubaga).



Closeness

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- Networks were sampled in a hybrid snowballegocentric fashion such that index individuals and their contacts were asked to list their contacts.
- Contacts were defined as having been in talking distance for 4 hours during the past week.

Statistic	Definition
Node degree	Number of adjacent edges
Betweenness	Number of times node is on shortest path between

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- Same-sex edges were almost twice as common as different-sex ! edges (9,079 vs. 5,228), $r = 0.26 (\pm 0.01)$
- Men had a slightly higher proportion of contacts with adults and ! within-sex than women (0.49 vs. 0.43).



Questions

- Can sex-assortativity drive male-bias alone or in combination with biological sex-traits?
- What are the effects of sex-assortativity on epidemic sizes and equilibriums?

Methods

- We generated networks of varying assortativity (r = 0 to 0.9) by re-wiring edges to the desired value (within 0.035).
- We simulated disease transmission with variations of a **S**usceptible-Latent-Infected-Recovered (-**S**usceptible) model⁶.



not shown).

750 **(**) 500рі**д** В 250-Sensitivity analyses (not shown): epidemic size was probably affected by changes in 8,3,5,1,9 8,3,5,1,9 network structure due to re-wiring (results Assortativity (r)

Conclusions

- In our Kampala network study, we investigated whether men could have higher exposure to Mtb than women due to social network structure.
- We found no evidence that male position in social networks is associated with TB disease. However, stark contrasts in assortative mixing patterns between men and women led us to perform a simulation study investigating the effects of assortative mixing patterns on male-bias of TB.
- Our simulation study revealed a combination of factors that could lead to observed male-bias worldwide. Assortativity tends to magnify the effects of biological factors on malebias.
- For applied purposes, these findings could be used to inform estimation of transmission trees and development of targeted intervention strategies.

pairs of other nodes

Inverse of the average length of shortest path to all other nodes

Network distance to a TB case **Distance to TB**

case Assortativity proportion expected if edges drawn at random coefficient

Proportion of within-group edges relative to the

We modeled sex-traits by varying the male: female ratio (α) of susceptibility (SUS), transmissibility (TRA), and infectious periods (IP). Overall transmission and recovery rates were held constant. Each sex-trait was modeled separately. 50

replicates for each parameter combination.

Sensitivity analyses: transmission rate (τ) and network type (scale-free, SF; small-world, SW).

References

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