

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

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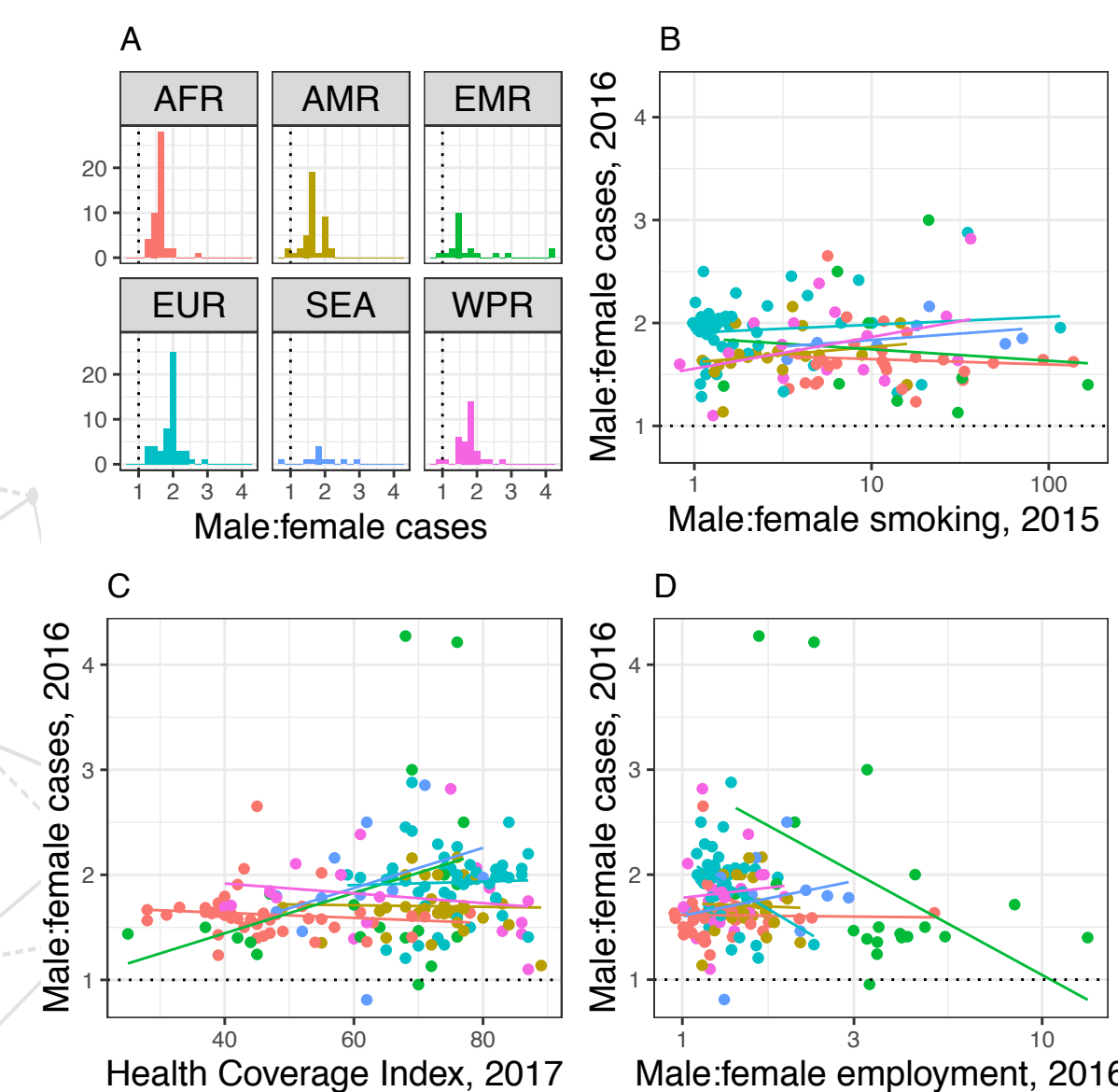
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## Background

- 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 men<sup>1</sup>.
- Alternatively, men could have higher exposure to Mtb than women, possibly due to different social roles men play which influence social mixing with others in their community<sup>2</sup>.
- 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

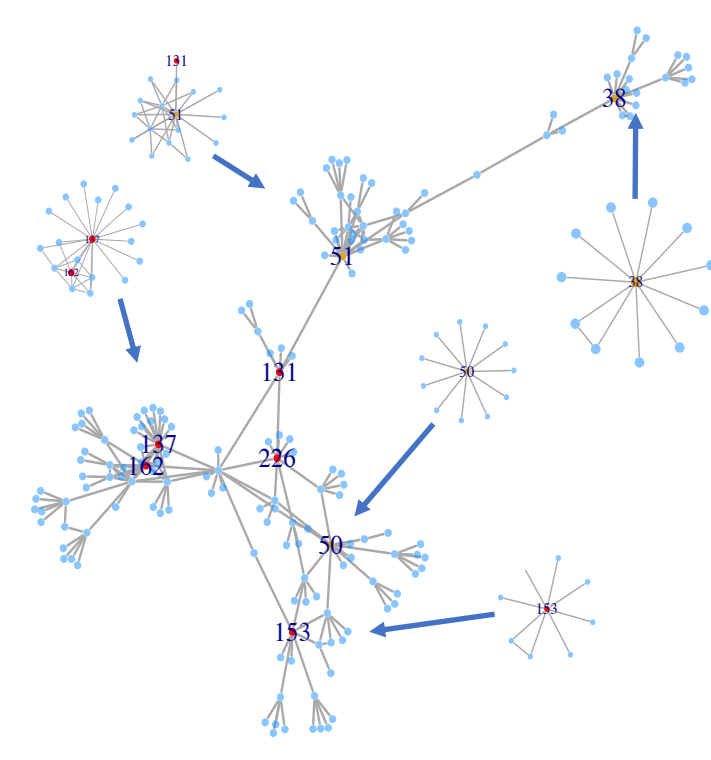
**Male-bias is similar around the world (A).** This pattern not well-explained by rates of smoking (B), health coverage (C), or employment (D). Data from WHO<sup>3</sup> and ILO<sup>4</sup>.



### 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)

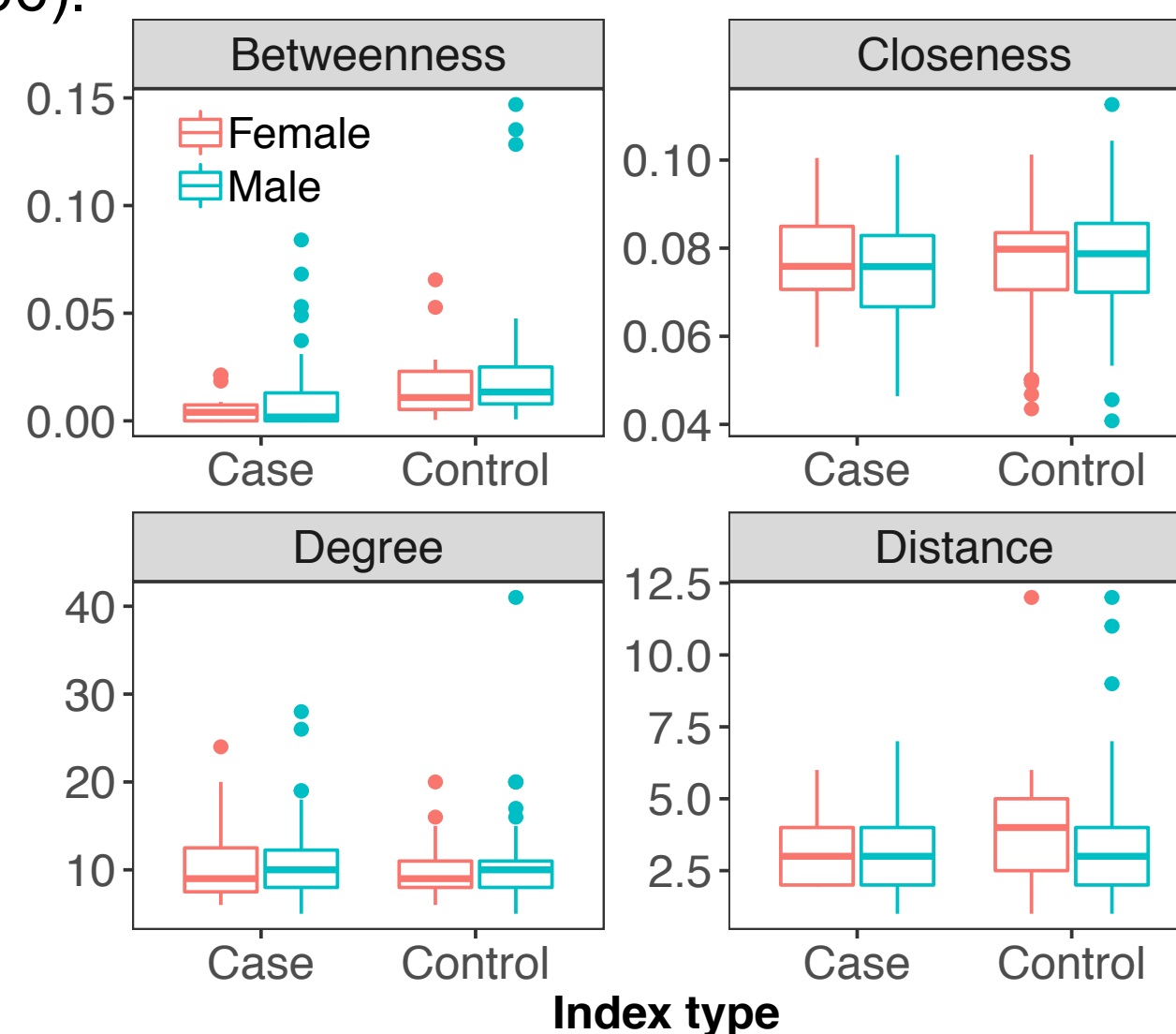


- 14,307 total edges,
- mean degree =  $\begin{cases} 10.4, \text{ index} \\ 8.2, \text{ first-level} \\ 2.4, \text{ overall} \end{cases}$
- 247 egocentric networks linked together in 47 components by common contacts
- Clustering coeff. was 0.12
- Degree distrib. resembled a power-law but we could not distinguish it from others (e.g., log-normal)<sup>5</sup>.

### 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;  $F_{1,183}=2.78, p=0.096$ ).

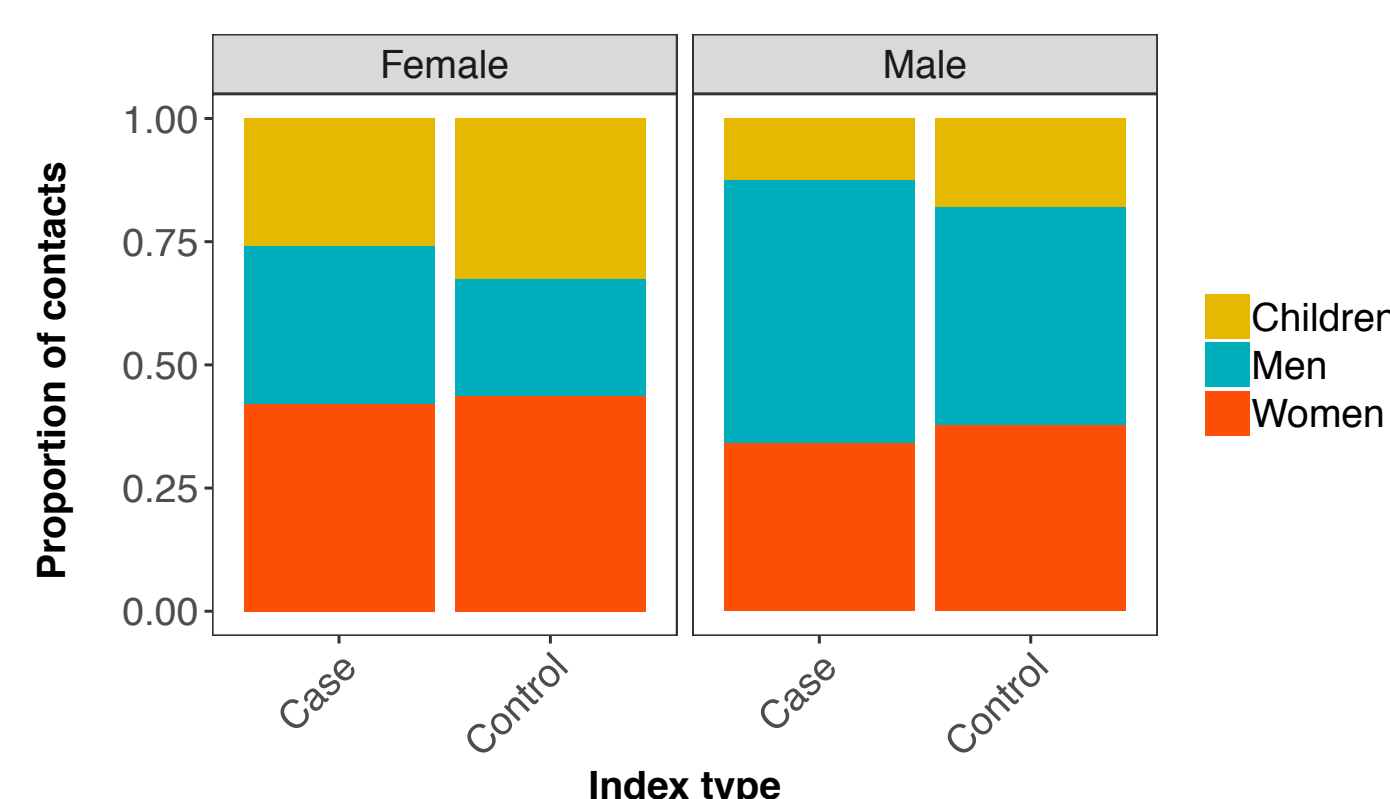


Sensitivity analyses (not shown): estimates of node position could be influenced by network sampling if the true network resembled a small-world structure (high clustering, long path length).

### Assortative mixing by sex.

We assessed mixing patterns overall and by index type.

- 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).



Sensitivity analyses (not shown): estimates of assortativity not sensitive to network sampling.

## Simulation study

### Questions

Can sex-assortativity drive male-bias alone or in combination with biological sex-traits?

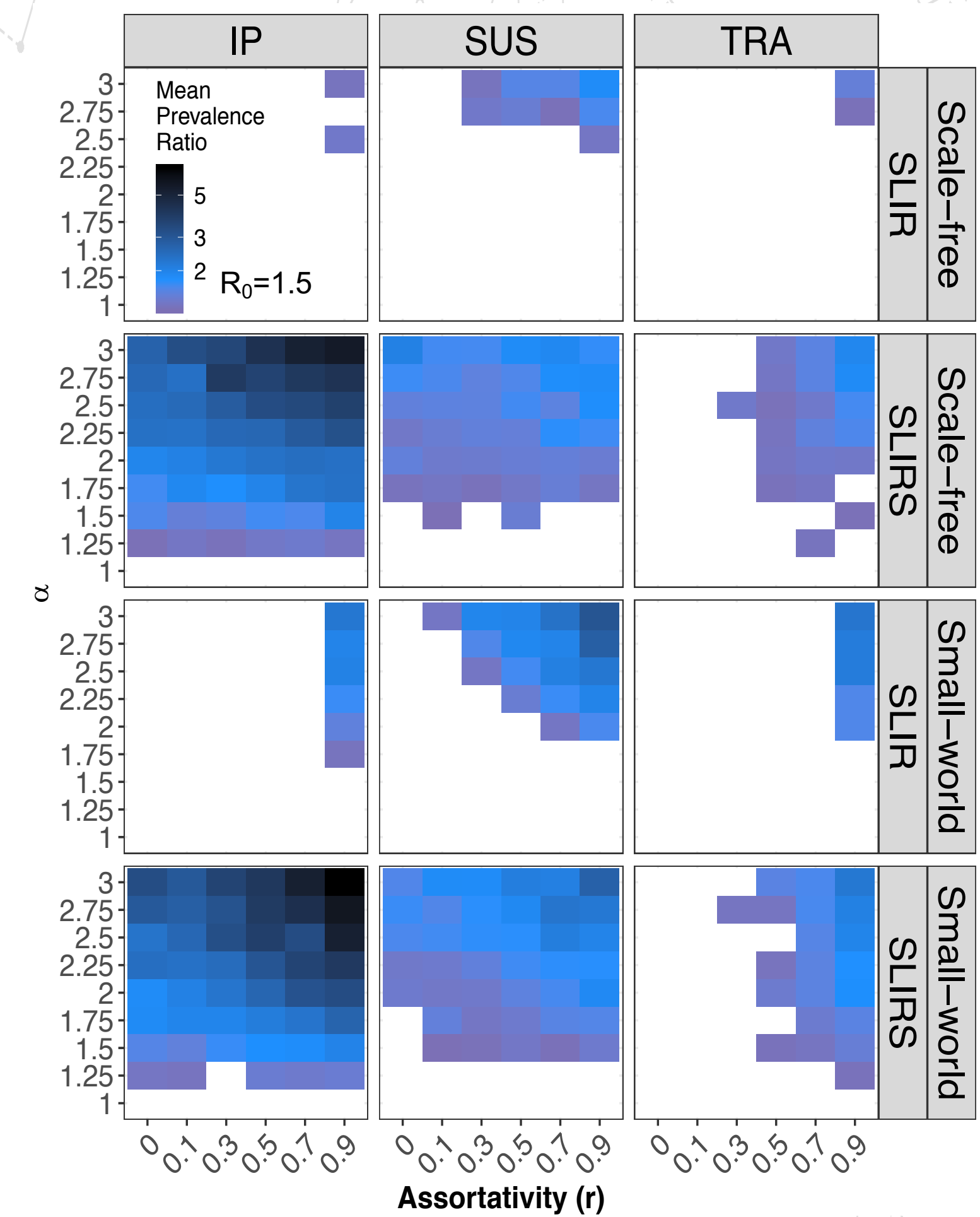
What are the effects of sex-assortativity on epidemic sizes and equilibriums?

### 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 Susceptible-Latent-Infected-Recovered (-Susceptible) model<sup>6</sup>.
- We modeled sex-traits by varying the male:female ratio ( $\alpha$ ) 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 ( $\tau$ ) and network type (scale-free, SF; small-world, SW).

### Factors leading to male-bias

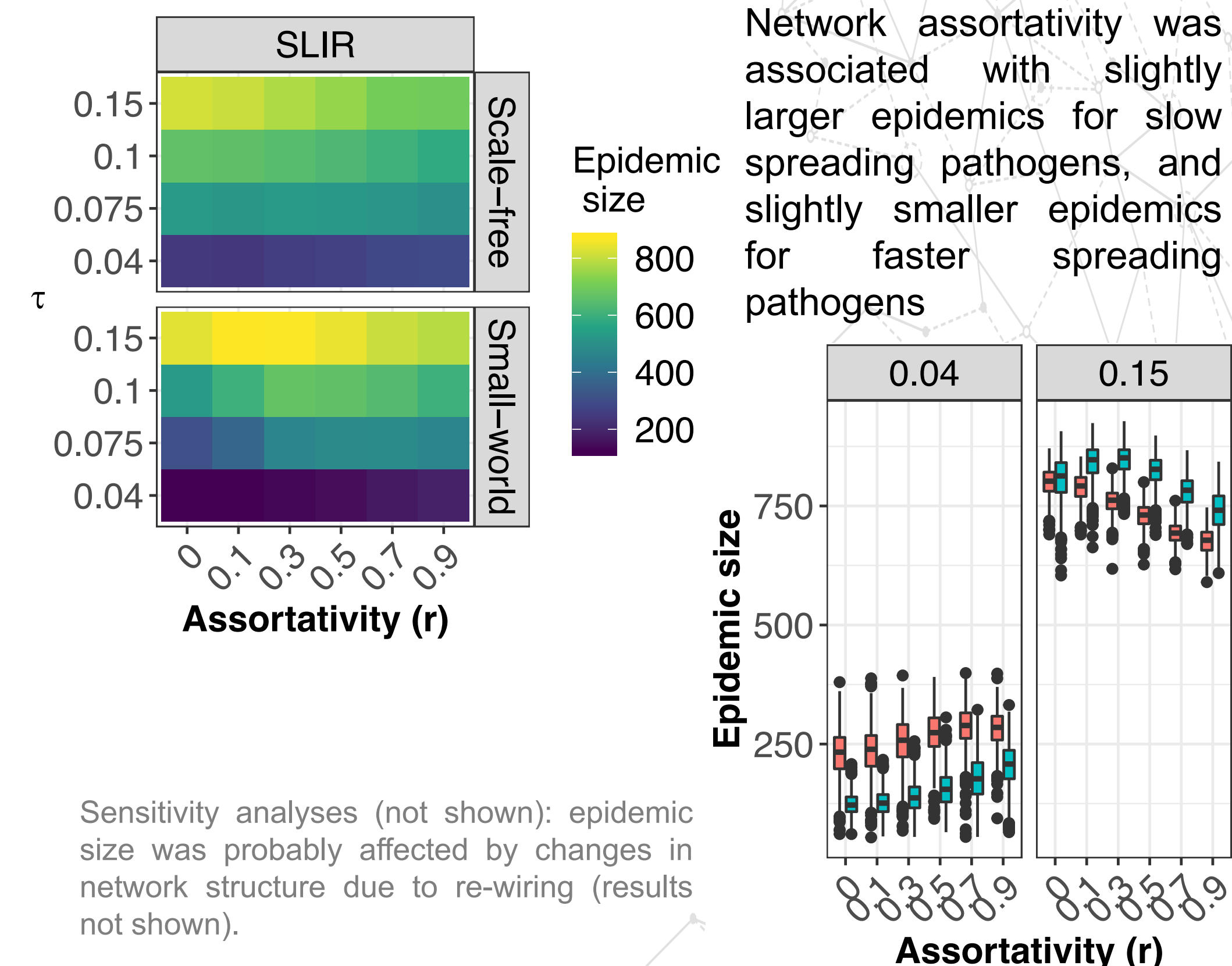
We measured **male-bias** as the total number infected male nodes/total number of infected female nodes for SLIR (or at the end of the simulation or 200 timesteps for SLIRS).



- 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  $\alpha$  on male-bias

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

### Effects of assortativity on epidemic size



Network assortativity was associated with slightly larger epidemics for slow spreading pathogens, and slightly smaller epidemics for faster spreading pathogens

Sensitivity analyses (not shown): epidemic size was probably affected by changes in network structure due to re-wiring (results not shown).

## 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 male-bias.
- For applied purposes, these findings could be used to inform estimation of transmission trees and development of targeted intervention strategies.

### References

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