Heterogeneities in individual-level infection are more important than social mixing patterns in determining male-bias for human TB

**Story**: Across the world, more cases of TB are reported among men than women. Hypotheses for this pattern encompass population- and individual-level differences in the social networks and infections of men and women. We wanted to learn the relative impact of social mixing patterns (assortativity) and heterogeneity in the infection process (susceptibility, transmissibility, and infectious period) on sex-bias in TB cases. We wanted to learn this because previous explanations for sex-bias have never been systematically assessed in a model. Additionally, understanding drivers of male-bias might improve case-finding or other public health control strategies. To determine the relative effects of mixing patterns and individual-level differences in infection, we conducted a comparative simulation study of three pathogen scenarios spreading on networks that varied from random to extremely sex-assortative. Pathogen scenarios included heterogeneities in susceptibility, transmissibility, and infectious period by sex. We found no evidence that preferential-mixing by sex can drive male-bias in TB alone, even with extreme levels of sex-assortativity. Instead, heterogeneities in infection and transmission by sex alone or combined with sex-assortativity can lead to realistic levels of male-bias observed globally. While individual infection and transmission affect who gets infected, how many infections and overall epidemic dynamics were mostly unchanged by the presence of these sex-specific differences.

**Methods:**

1. To generate networks with varying assortativity levels, scale-free networks were first created and edges occurring between-sex were randomly replaced with edges occurring within-sex until the desired level of assortativity was reached within a small range of error.
2. To simulate the spread of TB under different assumptions about infection and recovery, four distinct modeling structures based on a Susceptible-Latent-Infectious-Recovered model were parameterized.
3. To further compare the relative effects of hypothesized individual-level heterogeneity in infection with assortativity, the ratio of male to female susceptibility, transmissibility, and infectious period was varied from 1 to 2.
4. To measure male-bias, we calculated the number of males infected over the course of the epidemic for SIR and SLIR models and as the equilibrium ratio of male to female cases in the SIRS and SLIRS models.
5. To compare the effects of assortativity and heterogeneity in individual-level infection on epidemic dynamics, we calculated the total outbreak size, epidemic duration, equilibrium latent and infected prevalence for each simulation.
6. To understand model output in relationship to WHO estimates, simulated values of male-bias and prevalence of latent infection were plotted against WHO estimates from Uganda.

**Results:**

1. Network assortativity