Effects of assortative mixing and differing sex-traits on male-bias in Tuberculosis:

A modelling study

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**Study narrative**: Infectious diseases often affect males and females differently. Reasons why include different social mixing patterns and sex-traits of males and females. We wanted to understand the potential impact of social mixing (assortativity) and sex-traits on the male-bias of cases in TB. We wanted to learn this because it’s interesting to think about how social and biological factors combine at the individual-level to produce widespread differences in infection at the population-level. Also, the relative potentials for previous explanations for sex-bias have never been systematically assessed alongside each other in a model. Finally, understanding drivers of male-bias might inform treatment/vaccine research and public health control strategies. To determine the relative effects of mixing patterns and sex-traits, we conducted a comparative simulation study of pathogen scenarios spreading on networks that varied from random to extremely sex-assortative. Sex-traits investigated were sex-specific susceptibility, transmissibility, and infectious period. We found no evidence that assortativity by sex can drive male-bias in TB alone, even at extreme levels. Instead, sex-traits alone or combined with sex-assortativity can lead to realistic levels of male-bias observed globally. Overall epidemic dynamics were mostly unchanged by the presence of sex-traits.

**Introduction:**

Tuberculosis (TB) is now the leading cause of death due to infectious diseases globally, and notification data show that, on average, 1.8 male cases are reported for every female case (World Health Organization 2018). This pattern is strikingly consistent across all regions of the world with male:female ratios below 1 being extremely rare (Neyrolles and Quintana-Murci 2009). Male-bias is also seen in adults of all ages but does not seem to apply to children (Guerra-Silveira and Abad-Franch 2013). Differences in access to healthcare are not associated with this pattern as male-bias is observed in surveys using active case-finding (Salim et al. 2004; Borgdorff et al. 2000). Moreover, male-bias is observed in developing and developed countries alike (Neyrolles and Quintana-Murci 2009), further reducing the likelihood that male-bias is primarily driven by differences in access to healthcare since access to healthcare should be more equal in developed countries. In fact, TB is not unique in being male-biased (among adults, 9 out of 11 infectious diseases were found to be male-biased (Guerra-Silveira and Abad-Franch 2013)). Understanding how sex-bias happens, both in TB and other infectious diseases, has widespread applications including for basic research on sex-differences in disease and treatments (Clayton 2016), public health (World Health Organization 2007), and more realistic models and predictions of disease burden.

What causes male-bias in infectious diseases, and in TB, specifically? Proposed mechanisms are often categorized into “biological” or “social” (World Health Organization 2007) (Guerra-Silveira and Abad-Franch 2013). Biological mechanisms for male-bias in TB typically suggest higher male susceptibility to infection. For instance, female cells have two X chromosomes, which encode genes involved with both the innate and adaptive immune system and are thought to reduce susceptibility of females to a number of pathogens. In addition, the female hormone estradiol enhances, while testosterone downregulates, macrophage activation which is an important pathway for initiating the innate immune response and consequently detecting *M. tuberculosis* (reviewed in (Schurz et al. 2019)). Another common explanation for increased male susceptibility to TB is smoking, which is more common among men (Islami, Torre, and Jemal 2015) and can lead to damaged lung tissues (reviewed in (Centers for Disease Control and Prevention (US), National Center for Chronic Disease Prevention and Health Promotion (US), Office on Smoking and Health (US) 2010)). Indeed at the country-level, adult smoking rates explain up to one-third of variation in male-bias (Watkins and Plant 2006). Other than susceptibility, lesser studied biological mechanisms could plausibly lead to male-bias. For instance, males are more likely to spread infection to their household contacts (Hector et al. 2017) and therefore be more transmissible. Males also aerosolize 25% higher particle volume during coughing, measured in a study of influenza patients (Lindsley et al. 2012), also potentially causing higher infectiousness of men. Finally, the rate of progression from infection to disease can vary by sex, with females generally progressing faster than males (up to 30% faster), leaving open the possibility of differing latent and infectious periods in men (reviewed in (Holmes, Hausler, and Nunn 1998)). These different sex-traits, susceptibility, transmissibility, and infectious periods, could all plausibly lead to male-bias in TB.

On the social side, gender-roles and preferences in social contacts may prime males and females to have different exposure patterns (Nhamoyebonde and Leslie 2014; Dodd et al. 2016; Horton et al. 2020). For example, one study found adult males travelled 75% more often outside their village than women and more than one-quarter of women identified as housewives, although there was no difference in the total number of contacts by sex (le Polain de Waroux et al. 2018) which suggests if social networks play a role in male-bias, it’s not the number of social contacts but the traits of social contacts that matter for transmission. Assortative mixing by sex is a marked trait across many cultures and because males are a higher incident demographic than females, this social network structure may be important to understanding the basis for male-bias of TB (Dodd et al. 2016; Horton et al. 2020). Whether biological sex-traits or assortative-mixing by sex, have an outsized effect on male-bias at the population-level is the focus of this modeling study.

Infectious disease transmission models can help sort out the importance of various biological and social factors on sex-bias in infection. In this study, we use mathematical models of disease spread on social networks to examine the relative differences in sex-traits and preferential mixing by sex (i.e., assortativity), independently and in combination, required to give rise to observed levels of male-bias as seen in TB. We were also interested in whether the unique life history of human TB, with its long and variable latent period and endemic levels of infection in some regions, changed the effects of sex-traits and assortative mixing on male-bias. To investigate these questions, we conducted a comparative simulation study of multiple pathogen scenarios (SIR, SLIR, SIRS, and SLIRS) spreading on contact networks that varied from random to extremely sex-assortative. Sex-traits investigated were sex-specific susceptibility, transmissibility, and infectious period.

**Methods:**

*Network simulation*

In simulated social networks, nodes represent individuals and edges between them represent repeated interactions between nodes on which infection can spread. To measure assortativity of simulated networks, we used Newman’s discrete assortativity coefficient, **,** where is the matrix with entries describing the fraction of edges of each sex. is the fraction of edges that are within-sex. is the fraction of edges that would be within-sex if the edges were random. Modularity, , is another common statistic to measure within-group mixing. In the context of two equal-sized groups (i.e., sexes) .

To simulate social networks with varying levels of sex-assortativity, we used an algorithm presented in (Sah et al. 2014). The Sah algorithm is designed to simulate assorted networks that maintain network structures which alter epidemic dynamics including average clustering, path length, and degree assortativity (Anderson:1991ta; Badham and Stocker 2010). We simulated Sah networks with geometric degree distributions because other degree distributions listed as options (e.g., Poisson and power law) often did not converge with two modules (i.e. sexes) which was the focus of this study. As sensitivity analyses, we developed a simple rewiring scheme whereby we rewired between-sex edges of small-world and scale-free networks until desired levels of assortativity were reached (within 0.05) and made sure the resulting networks were simple (i.e., no multiple edges or self-loops) and connected (i.e., only one component). Additional details on the rewiring algorithm are given in the Supplement. We chose these networks because they represent realistic human interaction networks (Eubank et al. 2004). All networks were initialized with 1000 nodes (500 male, 500 female) and had a final mean degree of 10. We established how the rewiring algorithm affected network structural characteristics as we increased sex-assortativity, and compared changes to the Sah algorithm.

*Disease model*

To study disease processes affecting sex-bias in TB, we varied parameters within a Susceptible-Latent-Infectious-Recovered-Susceptible (SLIRS) model corresponding to different assumptions about disease transmission (Table 1). For example, we turned on/off latent infection by changing the parameter. Similarly, to represent endemic levels of infection where “new” susceptibles reenter contact networks over longer time periods, we varied the parameter. Finally, to understand how overall pathogen transmissibility and corresponding affects results, we varied the overall τ. In SIR models, the analytical solution for when an outbreak is possible (i.e., when is given by where K is the set of all node degree values in a network, is the set of all node degree values squared, and brackets indicate the mean of values in the set. We chose three values of corresponding to low, medium, and high estimates for active tuberculosis 1.5, 2.5, and 3.4 (CITE) and confirmed these values for epidemic simulations on Sah networks numerically (Figure R0). Thus, sensitivity analyses investigate different pathogen life histories and transmission rates.

**Table 1.** Transitions and parameter values for disease model.

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| **Transition** | **Parameters** | **Average values** |
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To study how sex-bias could be generated though differences in male and female sex traits we varied the ratio of male to female susceptibility, transmissibility, and infectious period (, , and ). For susceptibility, we changed the rates of and depending on the sex of the *target* node in the S-I edge pair. Specifically, for the male:female susceptibility ratio, we solved the following set of equations:

This results in susceptibility of male and female nodes to be:

So that when and when , the average susceptibility is still . Sex differences in transmissibility were modeled in the exact same way; except we changed the rates depending on the sex of the *source* node in the S-I edge pair. Sex differences in the duration of the infectious period were modeled by changing the male and female parameters. Specifically, we wanted the average infectious period to remain so we solved the same types of equations, except holding the average infectious period () rather than the average recovery rate () constant.

We implemented the model as a continuous-time Markovian model using the Epidemics on Networks (Miller and TIng 2020) and Networkx packages (https://networkx. github.io/) in Python (Version 2.7.17).

*Analysis*

To measure male-bias, we calculated the number of males infected over the course of the epidemic for SIR and SLIR model structures and as the equilibrium ratio of male to female infecteds in the SIRS and SLIRS model structures. For the SIR and SLIR models, simulations were run until there were no infected individuals left. For the SIRS and SLIRS models, simulations were run until there were no infected individuals left or for 250 timesteps (whichever came first). For the SIRS, SLIRS models, we performed preliminary analyses to determine when simulations reached endemic levels of infection and parameters required to lead to 25% of the population having latent infection at equilibrium (Houben and Dodd 2016).

To compare the effects of assortativity and heterogeneity in individual-level infection on epidemic dynamics, we calculated the final size, epidemic duration, equilibrium latent and infected prevalence for each simulation. From the prevalence of latent infection at endemic equilibrium in the SLIRS model given different parameter combinations, we assessed parameter ranges for the transmission rate that approximate TB. In 2017, 1.7 billion people (23% of the world’s population) were estimated to have latent TB infection (2018 WHO TB Report).

We used R Version 4.xxx for analyses and visualizations. All Python and R scripts are available at github.com/drakelab/miller-tb-assortativity.

**Results:**

In simulated networks, the proportion of within-sex contact increases with increasing r, from 45% when r=0 to 77% when r=0.6 (Figure 1). Results from a meta-analysis of the proportion of within-sex mixing among adults (Horton et al. 2020), correspond to values of sex-assortativity from r=0.2 to 0.3 which matches an estimation of sex-assortativity for a social network in Uganda (Miller et al. 2020).

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| **Figure 1**. The proportion of contacts within-sex tracks with Newman’s r. For context, the range of proportional within-sex mixing from a meta-analysis by Horton et al. (2020) is shown in horizontal grey-dashed lines and the sex-assortativity coefficient from a social network in Uganda in a horizontal dashed line. Boxplots show calculated proportional within-sex mixing from 250 simulated networks at each assortativity level. |

In the absence of sex-traits, sex-assortativity did not lead to male-bias. This result was not sensitive to model type (SIR, SLIR, SIRS, SLIRS), overall transmission rate, or network type (Sah networks, rewired small-world, rewired scale-free) (Figure 2, Figure 3, Figure NET\_TYPE).

Combined with sex-traits, however, assortativity amplified male-bias (Figure 2), especially for slower spreading pathogens relative to faster spreading pathogens (Figure 3). Amplification of male-bias was especially notable in the case of increased male transmissibility (TRA). Without sex-assortativity, even when males had three-fold higher transmissibility, male and female infections were equally common and this was true across model types and network types (Figure 2, Figure NET\_TYPE). Also, higher male transmissibility rarely resulted in high ratios of male-bias and median values of male-bias were always below 1.8, the global ratio of male:female case notifications.

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| **Figure 2**. Sex-assortativity (measured by Newman’s r, shown in colors) can amplify the effects of sex-traits on the mean value of M:F case bias (shown in color). Sex-traits (vertical columns) are infectious period (IP), susceptibility (SUS), and transmissibility (TRA). M:F case bias is measured as the ratio of male to female recoveries (SIR, SLIR) or infections at equilibrium (SIRS, SLIRS). Only parameter combinations leading to mean M:F case bias greater than 1.1 are colored (the brightest blue corresponds to M:F case bias of 1.8). Sex-traits are incorporated by holding respective overall parameter rates constant but increasing the male parameter by the value on the x-axis relative to the female trait. Figure generated with 250 simulations of epidemics on Sah networks with |

Similarly, epidemics with longer male infectious periods (IP) did not lead to male-bias in SIR and SLIR epidemics unless taking place on sex-assorted networks (Figure 2). In contrast, longer male infectious periods can result in male-bias without assortativity in SIRS and SLIRS epidemics. In the parameter ranges investigated here, median values of male-bias for simulations of longer male infectious periods were all below 1.8. These results were not sensitive to network type (Figure NET\_TYPE).

The final sex-trait that we investigated, increased male susceptibility (SUS), led to male-bias in the absence of sex-assortativity across all model types but we note that epidemics on assorted networks had higher male-bias than networks without sex-assortativity (Figure 2). The amplification effect of sex-assortativity on male-bias grew

with the strength of male:female susceptibility. This was observed across all model types: without sex-assortativity median values of male-bias are below 1.8 while median values of male-bias with sex-assortativity can exceed 1.8. The amplification effect of sex-assortativity on male-bias was not as pronounced in rewired scale-free networks as rewired small-world networks or Sah networks (Figure NET\_TYPE).

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| **Figure 3.** Sex-assortativity increases M:F case bias more for pathogens with lower overall infection rates compared with higher overall infection rates (horizontal facets). The M:F case bias, sex-traits, and relative male:female values of sex-traits are the same as in Figure 1. Figure generated with 250 SLIR simulations of epidemics on Sah networks |

This paragraph describes characteristics of epidemics given parameters tested here.

In general, epidemic dynamics were not affected by sex-assortativity and the presence of sex-traits (infectious periods, susceptibility, and transmissibility) including the peak size, final size, and duration for SLIR epidemics on Sah networks (Figure 4). One notable exception was that higher male susceptibility reduced the final size of epidemics. As for rewired networks, assortativity was associated with changes in peak size, final size, and duration (Figure EPI\_STR). We note, however, that while networks generated with the Sah algorithm had stable values of clustering, average network path length, and degree assortativity as sex-assortativity increased, rewired networks did not (Figure NET\_STR). Rewired networks had diverging network structures as assortativity increased. As assortativity increased from r=0 to r=0.6, clustering increased by approximately 10% in scale-free networks and decreased by approximately 60% in small-world networks. With increasing assortativity, average network path length increased by about 10% in scale-free networks and decreased by approximately 25% in small-world networks. In both small-world and scale-free networks, degree-assortativity increased as sex-assortativity increased.

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| **Figure 4.** Sex-assortativity has negligible effects on peak size, final epidemic size, and epidemic duration. Sex-traits and relative male:female values are the same as in Figure 1. Figure generated with 250 SLIR simulations of epidemics with and on Sah networks |

**Discussion:**

This paragraph highlights the main findings about assortativity and heterogeneity in infection.

* Sex-assortativity cannot be a sole driver of male-bias but can contribute to amplifying the effects of other sex-traits on male-bias.
* Lower levels of assortativity, such as sex-assortativity, don’t have an effect on epidemic dynamics such as final size across a number of different model types.

This paragraph reviews assortativity in other studies to determine whether it is strong enough to increase effects of sex-traits.

* There are few studies that calculate assortativity by sex (or report both respondent and contact sex in social mixing surveys) making it difficult to know the range of assortativity across human populations. Horton study found sex-assortative patterns in many populations. In Uganda, previous work estimated the sex-assortativity coefficient was 0.26 (which amounted to 65% of edges within-sex). A similar proportion of within-sex contacts was found in South Africa (62%). In general, we don’t expect sex-assortativity to be much higher than these studies. However, some sub-populations (mining, fishing communities may have higher sex-assortativity) and some regions with fewer differences in gender roles sex-assortativity could be lower. This is an area for future human social network research.

This paragraph reviews evidence for individual-level differences in TB susceptibility, infectious periods, and transmission by sex and emphasizes the importance of new research looking into the nature of TB infectious period.

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| There is no evidence that heterogeneities in individual-level infection dynamics exist to the magnitudes in this analysis | There is so much about TB that we don’t know. For example, just now people are starting to think there may be transmission during latent period. If this is true, is it possible that men are more likely to be infectious during the latent period? Future research needed. Overall, it’s likely that real-world is compound of many differences in epidemic rates. |

This paragraph compares results about epidemic dynamics on assorted networks to previous studies.

* The effects of assortativity on epidemic dynamics are not sensitive to lower levels of assortativity (as has been found in other studies). The conclusions reached can depend, however, on the technique used to simulate assorted networks, as simple techniques can also change fundamental network structures such as clustering, which is well-known to limit the final size of outbreaks.

This paragraph discusses remaining limitations of this study: rewiring changed some potentially important network structural properties, simplistic TB models, unclear what levels of assortativity are across human populations, model parameterization.

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| **Problem** | **Response** |
| TB models make too many simplifying assumptions, especially the structure of the latent class and lack of age-structure, to accurately make inferences about biological mechanisms. | Our main results (about the relative effects of assortativity and heterogeneity in infection by sex) were consistent across model structures and transmission rates suggesting some generalizability. Overall, we believe these results suggest relative, rather than absolute, effect sizes of the different drivers of male-bias. |
| Model parameterization is very arbitrary. Why these transmission rates, recovery parameters, etc. | While our simulations tested broad parameter ranges, and results were not sensitive to parameters chosen in the main text, we acknowledge that these math models do not fully capture the complexities of TB. |

Closing paragraph restates main findings, new questions raised by study, and potential applications of research.

These results provide insight into how behavior can amplify the consequences of evolutionary trade-offs between sex and immunity to infection. While focusing on TB, many infectious diseases are male-biased and most populations have social mixing patterns marked by sex-assortativity. We conclude that heterogeneity in sex rates, especially differing susceptibility, is more important to sex-bias in infectious diseases than social mixing patterns but mixing patterns can amplify the effects of sex-traits in some cases. For TB, important questions arise about whether differences in susceptibility and other sex-traits, are similar to levels analyzed here or if there are remaining factors driving sex-bias in TB. For practical purposes, results from this study shed light on when it could be inappropriate or misleading to extrapolate infection risk or rates across genders for different models.

**Supplement:**

Rewired networks were initialized as small-world or scale-free networks because these networks resemble patterns of clustering and high-degree network hubs found in real-world social networks. Small world networks were initialized with \_\_\_ parameters and scale free networks were initialized with \_\_\_ parameters.

**Table S1.** Network rewiring algorithm.

1. Simulate a network
2. Randomly assign node sex
3. Rewire a proportion of edges occurring between-sex
4. Check that the network is still a single component, if not, reject rewiring and return to step 3
5. Check for multiple edges or self-edges, and randomly rewire those edges
6. Continue process until the desired level of assortativity was reached within a small range of error

**References:**

Badham, Jennifer, and Rob Stocker. 2010. “The Impact of Network Clustering and Assortativity on Epidemic Behaviour.” *Theoretical Population Biology* 77 (1). Academic Press: 71–75. doi:10.1016/j.tpb.2009.11.003.

Borgdorff, M W, N J Nagelkerke, C Dye, and P Nunn. 2000. “Gender and Tuberculosis: a Comparison of Prevalence Surveys with Notification Data to Explore Sex Differences in Case Detection..” *Int. J. Tuberc. Lung Dis.* 4 (2): 123–32.

Centers for Disease Control and Prevention (US), National Center for Chronic Disease Prevention and Health Promotion (US), Office on Smoking and Health (US). 2010. “How Tobacco Smoke Causes Disease: the Biology and Behavioral Basis for Smoking-Attributable Disease: a Report of the Surgeon General.” Atlanta (GA): Centers for Disease Control and Prevention (US).

Clayton, Janine Austin. 2016. “Studying Both Sexes: a Guiding Principle for Biomedicine..” *FASEB Journal : Official Publication of the Federation of American Societies for Experimental Biology* 30 (2). John Wiley & Sons, Ltd: 519–24. doi:10.1096/fj.15-279554.

Dodd, Peter J, Clare Looker, Ian D Plumb, Virginia Bond, Ab Schaap, Kwame Shanaube, Monde Muyoyeta, et al. 2016. “Age- and Sex-Specific Social Contact Patterns and Incidence of Mycobacterium Tuberculosis Infection.” *American Journal of Epidemiology* 183 (2): 156–66. doi:10.1093/aje/kwv160.

Eubank, S, H Guclu, VSA Kumar, M V Marathe, A Srinivasan, Z Toroczkai, and N Wang. 2004. “Modelling Disease Outbreaks in Realistic Urban Social Networks.” *Nature* 429 (6988). Nature Publishing Group: 180–84. doi:10.1038/nature02541.

Guerra-Silveira, Felipe, and Fernando Abad-Franch. 2013. “Sex Bias in Infectious Disease Epidemiology: Patterns and Processes.” Edited by Hiroshi Nishiura. *PLoS ONE* 8 (4). Public Library of Science: e62390. doi:10.1371/journal.pone.0062390.

Hector, Jonas, Suzanne T Anderson, Gertrude Banda, Mercy Kamdolozi, Laura F Jefferys, Doris Shani, Natalie J Garton, et al. 2017. “TST Positivity in Household Contacts of Tuberculosis Patients: a Case-Contact Study in Malawi..” *BMC Infectious Diseases* 17 (1): 259. doi:10.1186/s12879-017-2348-2.

Holmes, C B, H Hausler, and P Nunn. 1998. “A Review of Sex Differences in the Epidemiology of Tuberculosis.” International Union Against Tuberculosis and Lung Disease.

Horton, Katherine C, Anne L Hoey, Guillaume Béraud, Elizabeth L Corbett, and Richard G White. 2020. “Systematic Review and Meta-Analysis of Sex Differences in Social Contact Patterns and Implications for Tuberculosis Transmission and Control..” *Emerging Infectious Diseases* 26 (5): 910–19. doi:10.3201/eid2605.190574.

Houben, Rein M G J, and Peter J Dodd. 2016. “The Global Burden of Latent Tuberculosis Infection: a Re-Estimation Using Mathematical Modelling..” Edited by John Z Metcalfe. *PLoS Med* 13 (10): e1002152. doi:10.1371/journal.pmed.1002152.

Islami, Farhad, Lindsey A Torre, and Ahmedin Jemal. 2015. “Global Trends of Lung Cancer Mortality and Smoking Prevalence..” *Translational Lung Cancer Research* 4 (4). AME Publications: 327–38. doi:10.3978/j.issn.2218-6751.2015.08.04.

le Polain de Waroux, O, S Cohuet, D Ndazima, A J Kucharski, A Juan-Giner, S Flasche, E Tumwesigye, et al. 2018. “Characteristics of Human Encounters and Social Mixing Patterns Relevant to Infectious Diseases Spread by Close Contact: a Survey in Southwest Uganda..” *BMC Infectious Diseases* 18 (1). BioMed Central: 172. doi:10.1186/s12879-018-3073-1.

Lindsley, William G, Terri A Pearce, Judith B Hudnall, Kristina A Davis, Stephen M Davis, Melanie A Fisher, Rashida Khakoo, et al. 2012. “Quantity and Size Distribution of Cough-Generated Aerosol Particles Produced by Influenza Patients During and After Illness.” *Journal of Occupational and Environmental Hygiene* 9 (7). Taylor & Francis Group: 443–49. doi:10.1080/15459624.2012.684582.

Miller, Joel C, and Tony TIng. 2020. “EoN (Epidemics on Networks): a Fast, Flexible Python Package for Simulation, Analytic Approximation, and Analysis of Epidemics on Networks.” *Journal of Open Source Software*. doi:10.21105/joss.01731.

Neyrolles, Olivier, and Lluis Quintana-Murci. 2009. “Sexual Inequality in Tuberculosis.” *PLoS Med* 6 (12). Public Library of Science: e1000199. doi:10.1371/journal.pmed.1000199.

Nhamoyebonde, Shepherd, and Alasdair Leslie. 2014. “Biological Differences Between the Sexes and Susceptibility to Tuberculosis.” *Journal of Infectious Diseases* 209 (suppl 3): S100–S106. doi:10.1093/infdis/jiu147.

Sah, Pratha, Lisa O Singh, Aaron Clauset, and Shweta Bansal. 2014. “Exploring Community Structure in Biological Networks with Random Graphs.” *BMC Bioinformatics* 15 (220). BioMed Central. doi:10.1186/1471-2105-15-220.

Salim, MAH, E Declercq, A Van Deun, and KAR Saki. 2004. “Gender Differences in Tuberculosis: a Prevalence Survey Done in Bangladesh.” *Int. J. Tuberc. Lung Dis.* 8 (8): 952–57.

Schurz, Haiko, Muneeb Salie, Gerard Tromp, Eileen G Hoal, Craig J Kinnear, and Marlo Möller. 2019. “The X Chromosome and Sex-Specific Effects in Infectious Disease Susceptibility.” *Human Genomics* 13 (1). BioMed Central: 1–12. doi:10.1186/s40246-018-0185-z.

Watkins, R E, and A J Plant. 2006. “Does Smoking Explain Sex Differences in the Global Tuberculosis Epidemic?.” *Epidemiology and Infection* 134 (2): 333–39. doi:10.1017/S0950268805005042.

World Health Organization. 2007. “Addressing Sex and Gender in Epidemic-Prone Infectious Diseases.”

World Health Organization. 2018. *Global Tuberculosis Report*. https://www.who.int/tb/publications/global\_report/en/.