

A multigroup model for HIV transmission in the sex working community of Kibera

by

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BSc, University of British Columbia, 2010

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ABSTRACT

The informal settlement of Kibera in Nairobi has a significantly higher prevalence of HIV than the Kenyan average. Sex workers and their male clients from Kibera were recently surveyed; their responses indicate a population that is well mixed with large variance in individual number of sexual contacts. Hence, a multigroup two-sex model is created to study HIV spread in the sex working population of Kibera. This model is parameterized to the Kibera data, and the effects of various parameters on the prevalence of HIV and the risk of infection to individuals are studied by an elasticity analysis. The probability of infection from males to females per sexual act has the greatest implications for HIV control. A simplified model is presented and a theoretical analysis gives the reproduction number and proves global stability of the endemic equilibrium.

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Cheers.

Chapter 1

Introduction

Mathematical models for the spread of disease through a population have been developed for decades [3]. New models for disease spread continue to be developed as there are innumerable situations for disease to occur; new diseases are discovered, and diseases spread via various means of infection, and spread through different populations in varying environments. Additionally, mathematicians are continually thinking of new techniques to use to model disease.

In this thesis the goal is to utilize data collected in Nairobi, Kenya to model the spread of HIV in a population of sex workers and their clients. Sex work has been determined to be an important driver of the HIV epidemic in sub-Saharan Africa as sex workers have a high number of sexual contacts and many customers are willing to pay more to avoid using a condom [11, 26].

1.1 HIV in sub-Saharan Africa

Though the HIV outbreak likely began in Western Africa, once HIV spread to Eastern sub-Saharan countries the epidemic began to take hold [27]. Eastern African countries had high male to female ratios in urban centres, and large migrational workforces [6]; this imbalance of men and women in urban centres led to widespread sex work [26]. High levels of sexually transmitted disease allowed for easy transmission of HIV, and during the 1980s the prevalence of HIV skyrocketed in these Eastern African

countries [18].

Throughout the 1980s, as HIV continued to spread, investigators found some sub-populations with significantly higher than average prevalence; these included sex workers, truck drivers, and other workforces that often had high male to female ratios or were required to travel long distances [6, 18]. Many of the male dominated workforces with high prevalence of HIV were assumed to have high prevalence due to the frequent interaction with sex workers [6].

By the mid 1990s many sub-Saharan countries' governments were deeply concerned by the continued spread of HIV, as prevention campaigns were having little effect, and large, effective treatment programs seemed unattainable [18, 43]. Sex work (among many other factors) continued to drive the infection; in Nairobi, it is thought that 85% of sex workers were infected with HIV by the late 1980s [29]. Sub-Saharan Africa continued to play a strong role in driving the worldwide spread of HIV, with 70% of new worldwide HIV infections in 1998 occurring there [31]. Daniel Arap Moi, the president of Kenya, declared the HIV epidemic a national disaster in 1999 [10].

In 1996, highly active antiretroviral therapy (HAART) became available to those in countries that could afford it; however, a combination of high HIV prevalence and high cost of HAART made the drugs incredibly unaffordable for many African nations [1, 18]. After numerous years of lobbying by sub-Saharan countries, some pharmaceutical companies agreed to allow generic versions of HAART to be made available [1]. Once cheaper drugs became more widely available many African nations were able to provide treatment to their infected citizens; however, limited access to health resources and stigma around the drugs' effectiveness meant a large proportion of infected individuals were still without treatment [45].

The UNAIDS 2006 report indicated that prevalence was levelling off in many countries, and dropping in some others, including Kenya [32]; this change in prevalence indicated a behavioural change in Africans. In Kenya, data indicated a trend in reduction of high risk behaviour for young people; however, many high risk groups, like sex workers and drug injection users, continued to have high prevalence [32].

Even though much work has been done in the fight against HIV in sub-Saharan Africa, there remains a lot of progress to be made. In 2009, 1.3 million individuals died of HIV/AIDS in sub-Saharan Africa, bringing the estimated total African lives lost from

the disease to more than 15 million [33].

This thesis uses data collected in Kibera, Kenya to inspire a model for HIV transmission amongst individuals involved in the sex trade there. The model is analyzed in an effort to determine factors which can be used to control driving HIV in the population.

1.2 Thesis Outline

Chapter 2 introduces the Kibera data; the population that was surveyed is described and some of the qualities of the data are discussed.

In Chapter 3 different types of epidemiological models that could represent the Kibera data are reviewed. They range from traditional ordinary differential equation (ODE) models to more recently developed network models.

Chapter 4 explores the data and one of the models from the previous chapter is chosen to be built upon; the chosen model is then extended to more accurately represent those involved in the sex trade of Kibera.

Chapter 5 presents the parameterization and sensitivity analysis of the model with the data. A recent method of maximizing likelihood at an equilibrium is presented. The additional methods and results of both parameterization and sensitivity are described.

Chapter 6 presents a simplification of the model developed in Chapter 4. The reduced model is analyzed theoretically and various model properties are discussed; the basic reproduction number is calculated, and equilibria stability conditions are proved.

Chapter 7 relates the results of Chapters 5 and 6 to Kibera. Specifically the implications of the sensitivity analysis on control measures are discussed.

Chapter 2

The Kibera Data

2.1 Data Collection

The data used in this thesis were collected in 2009 and 2010 from a survey of female sex workers, women who have never engaged in sex work, and men in bars (who are occasional clients of sex workers). All individuals interviewed for this study resided in a region of Nairobi called Kibera, an urban slum, or informal settlement.

Kibera is approximately 5km from the city centre, but has never been properly developed [26]; as such, access to potable water, electricity, plumbing and health services are almost non-existent [26]. Most homes are constructed of mud and sheet metal, and built where space is available [26]. Though relatively small (approximately 2.5 square kilometres), the population of Kibera is estimated at up to 800,000 [26].

Prevalence of HIV in Kibera is estimated to be 12%, more than double the national Kenyan average of 5.1% [26, 29]. Prevalence among female sex workers is expected to be much higher as sex work is an important factor in the transmission of HIV in Kenya [11, 26, 30].

Data were collected for A Kenya Free of AIDS: Harnessing interdisciplinary science for HIV prevention, a National Institutes of Health funded grant bringing together individuals from the University of Victoria, the University of Washington, and the University of Nairobi [26]. Exploration of Kenyan Female Commercial Sex Workers and Their Male Partners - Life Course and Harm Reduction Approaches was one of

many projects carried out, and led to the survey used to collect these data. In 2009, 320 women were interviewed, 161 sex workers, and 159 non-sex workers. During 2010 220 men were interviewed. The project used random and respondent-driven sampling.

This study was carried out as a social epidemiological study, and asked questions regarding numerous aspects of the respondents' lives. Individuals were questioned about their family, upbringing, and history of alcohol or drug use. The aim of the survey was to ascertain what type of factors in early life made females and males more likely to become involved in sex work.

When it comes to modelling, however, the HIV status of individuals and the number of sexual partners in the past week and month are particularly interesting. This information allows us to create a distribution of the number of partners for sex workers and clients, along with calculating prevalence of HIV in the population. Information regarding number of sexual partners over different periods of time allows the type of contact, whether they are repeated or random, to be determined (see Section 4.1).

2.2 HIV Status and Recent Partners

Individuals were questioned about many aspects of their lives, including HIV status and number of recent sexual partners (see Figure 2.1).

The HIV status of the surveyed population is given in Table 2.1, where prevalence is the percentage of people who reported being HIV+ out of those who knew their HIV status.

Group	HIV+	HIV-	Unknown	Prevalence
Female sex workers	24.6%	64.2%	11.2%	27.2%
Females uninvolved in sex work	11.6%	76.6%	11.8%	13.2%
Males who go to sex workers	11.6%	61.1%	27.3%	16.0%
Males who do not go to sex workers	7.6%	64.3%	28.1%	10.6%

Table 2.1: HIV status of interviewed individuals

The prevalence of HIV in women is higher than that in men for both the sex working population and for those not involved in sex work; however, a larger proportion of men report not knowing their current HIV status.

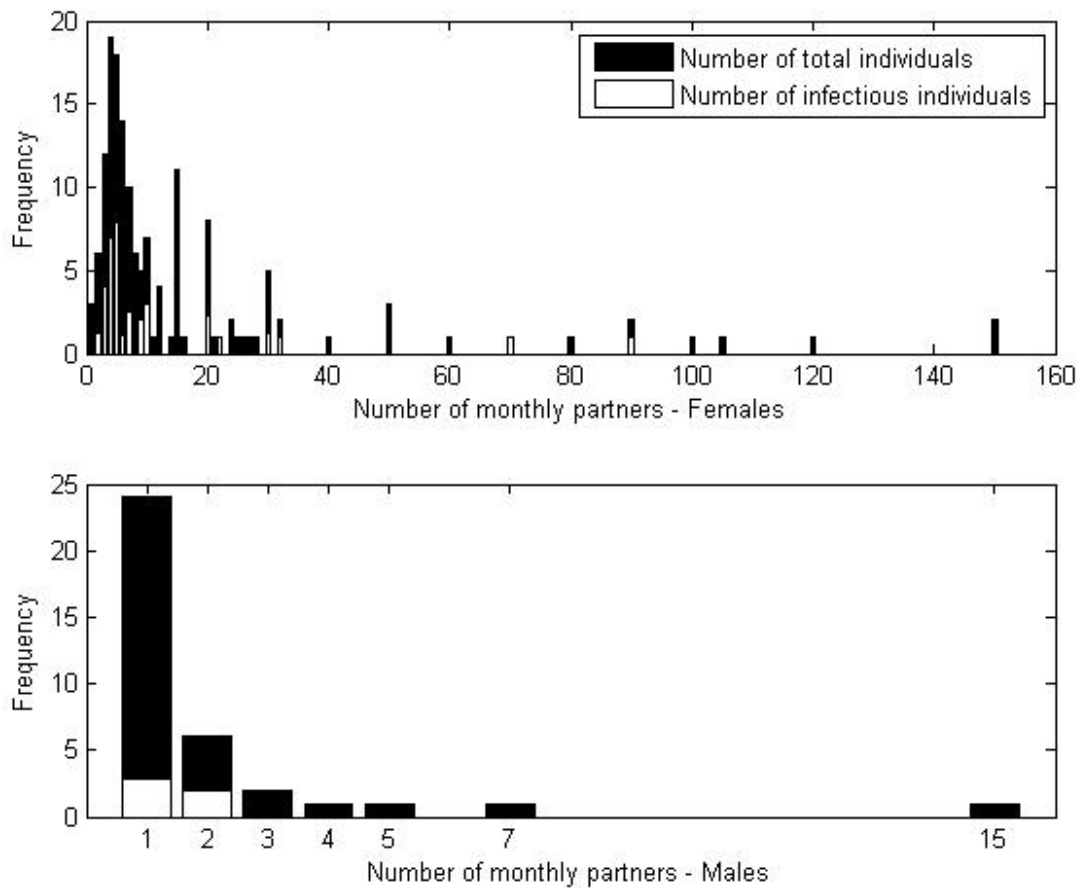


Figure 2.1: Distribution of individuals by number of sexual partners in the past month and HIV status.

Questions regarding number of recent sexual partners were asked of individuals both involved and uninvolved in sex work, but only those involved in sex work are being modelled. Prevalence of the outside population gives the prevalence of individuals who become involved in sex work, while the distribution of monthly partners among those involved in sex work dictates the number of monthly partners for individuals who join the sex working population.

The distribution of number of sexual partners in the last month for sex workers and men who go to sex workers shows that there need to be many more males in the population than females, as the males generally have fewer partners in a month. Both sexes follow approximate power law distributions (see Figure 2.2 that displays the power law of best fit); females following an exponent of -0.760 , and males an

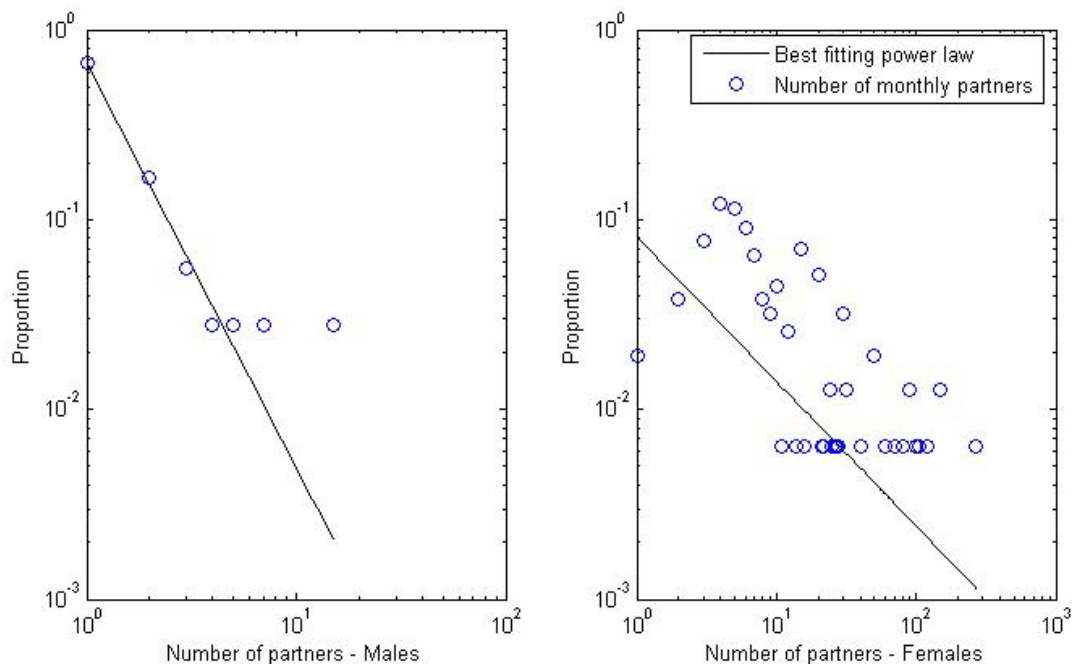


Figure 2.2: The male and female distribution for number of contacts in last month.

exponent of -2.127 . Interviewed sex workers have a mean of 18.2 partners, and a maximum of 270; men who go to sex workers have a mean of 2.1 partners per month, with a maximum of 15 among those interviewed. It is apparent that the number of monthly contacts varies largely within each sex, with most having few contacts, but a significant portion having many.

An important aspect of modelling disease transmission is to know whether the method of transmission (in this case, heterosexual sex) is repeated between pairs of individuals or whether it occurs between random individuals [12]. In the Chapter 4 the number of sex workers' sexual partners in the past week and past month are compared to determine what fraction of partners are repeated.

Chapter 3

Review of Relevant Epidemiological Models

Many existing options for modelling spread of disease are available. Some models that are well suited specifically to HIV spread are outlined in this chapter. Then, in the next chapter, the Kibera data are analyzed to determine which model type is best suited to the studied population.

When modelling diseases spread primarily through heterosexual contact, two-sex models need to be considered. HIV can, of course, be spread by other methods; however, our data do not include any information on these other types of contact, and so they are ignored here.

A traditional two-sex model would not be appropriate as the large spread of contact numbers (see previous chapter) would not be represented well with a traditional ODE model (that would assume the same average contact rate for all individuals of the same sex) [5, 12]. A traditional ODE model is presented in the next section for context, and then more appropriate models for the Kibera data are presented in the order of least to most individualistic.

3.1 Ordinary Differential Equation Models

The classical ODE model is the Susceptible-Infectious-Recovered (SIR) model developed by Kermack and McKendrick in 1927 [20]. Ignoring population dynamics, a simple version of their model takes the form

$$\begin{aligned}\frac{dS}{dt} &= -\lambda IS, \\ \frac{dI}{dt} &= \lambda IS - \gamma I, \\ \frac{dR}{dt} &= \mu I,\end{aligned}$$

where S , I , and R are the number of susceptible, infectious, and recovered people in the population, respectively. This model is appropriate for diseases that convey immunity once individuals recover; individuals who are susceptible can become infected by infectious individuals, moving them from the susceptible to infectious class; this process happens at rate λ per individual and is dependent upon the product of the susceptible and infectious populations. This type of transmission term is commonly called "mass action" [5]. Finally, individuals are removed from the infectious class at rate γ ; in this model that means moved to the recovered class; i.e. $1/\gamma$ is the mean time that individuals remain infectious before moving to the recovered class.

Epidemiological ODE models can take on many forms, and apply to many different situations [12]. Some of these variations include the susceptible-infectious model, where individuals do not recover from infection, the susceptible-exposed-infectious-recovered model, where there is a latent period in which individuals are infected, but not infectious, and many more [5]. Another aspect important for some models is population dynamics; this accounts for birth and death, and immigration into and emigration out of the population. Population dynamics are often important to include when the effect of a disease takes place over a long time period. HIV is a lifetime disease, and so a model with population dynamics and only susceptible and infectious individuals is appropriate.

As a result the models considered further in this chapter are SI models with population dynamics. New terms need to be added for population dynamics, a birth (or

immigration) term, b , and natural death (or emigration) with rate μ . The most basic SI ODE model with population dynamics takes the form

$$\begin{aligned}\frac{dS}{dt} &= b - \lambda IS - \mu S, \\ \frac{dI}{dt} &= \lambda IS - (\mu + \gamma)I,\end{aligned}$$

where the parameters are positive, and γ is the death rate due to disease. Note that this is a one-sex model; the next step is to create a two-sex model.

The two-sex model for a disease spread by heterosexual contact differs from a one-sex model in that the population is split into two sexes, with each sex only able to contract infection from the other; males can only infect females and vice versa. This attribute is the key to the two-sex model and is commonly used in models of diseases spread by heterosexual contact [12]. The resulting model has the form

$$\begin{aligned}\frac{dS_F}{dt} &= b - \lambda_{MF}I_M S_F - \mu S_F, & \frac{dS_M}{dt} &= b - \lambda_{FM}I_F S_M - \mu S_M, \\ \frac{dI_F}{dt} &= \lambda_{MF}I_M S_F - (\mu + \gamma)I_F, & \frac{dI_M}{dt} &= \lambda_{FM}I_F S_M - (\mu + \gamma)I_M,\end{aligned}$$

where subscripts F and M stand for female and male, respectively; additionally, subscripts FM and MF are for processes (such as infection) from females to males, and males to females, respectively. There are now two λ s, one that represents the rate at which males infect females, λ_{MF} , and the other the rate at which females infect males, λ_{FM} . The birth and death terms are unchanged from the last model, and assumed equal for each sex.

Now that a simple, deterministic, two-sex SI ODE model has been demonstrated, we move on to models that are more appropriate for populations with large variance in contact numbers.

3.2 Core Group Models

The core group was originally modelled by Yorke, Hethcote and Nold in 1978 for gonorrhoea transmission [44]. The core group model is fairly simple to understand; the two-sex model is expanded again to include a group that is different from the main population in some way; core groups often have higher contact rates or larger infection probability [12]. This change can be expressed in many forms in the model, but can be taken care of simply by multiplying λ with a constant.

An interesting feature with the two-sex core group model is that the core group can belong to either or both sexes. Two-sex models can have a core group added to determine the effect of sex-work on the population [12]; this typically means the core group is a subpopulation of females. If this is the case, the two-sex core group model can take the form

$$\begin{aligned}\frac{dS_F}{dt} &= b - \lambda_{MF}I_M S_F - \mu S_F, \\ \frac{dI_F}{dt} &= \lambda_{MF}I_M S_F - (\mu + \gamma)I_F,\end{aligned}$$

$$\begin{aligned}\frac{dS_C}{dt} &= b - \nu\lambda_{MF}I_M S_C - \mu S_C, \\ \frac{dI_C}{dt} &= \nu\lambda_{MF}I_M S_C - (\mu + \gamma)I_C,\end{aligned}$$

$$\begin{aligned}\frac{dS_M}{dt} &= b - \lambda_{FM}I_F S_M - \nu\lambda_{FM}I_C S_M - \mu S_M, \\ \frac{dI_M}{dt} &= \lambda_{FM}I_F S_M + \nu\lambda_{FM}I_C S_M - (\mu + \gamma)I_M.\end{aligned}$$

The female core group has been added (with subscript C); the rate at which it becomes infectious (and at which it infects males) is multiplied by a constant, $\nu > 1$. Males can be infected by any females, and thus have two infection terms. Note that the core group of females can only influence the non-core group females indirectly through the males, and vice-versa. The immigration and emigration terms are written as equal between groups in this model, but could be separated to differ between the sexes or

core group.

The key to the core group model is that it is, at heart, an ODE model, with a homogeneously mixing population of each sex. The core group has different properties, that warrant more detail and separate equations. Variations of this model are useful when the population can be separated into a small number of distinct groups.

3.3 Multi-Group Models

A multigroup model separates the population into multiple groups with different characteristics [5]; two-sex and core group models are specific instances of multigroup models, but multigroup models could have many groups and be very general. In practice, the number of groups is restricted only by the information in the data. In the example used above, there may be highly sexually active sex-workers, less sexually active sex-workers in addition to females not involved in sex-work. Males could also be split into a group of males that see sex-workers, and a group that does not. This would result in a 5 group model. All these groups could have different infection and recovery rates, and could grow and shrink at different rates as well.

The next model is a multigroup model that could be modified to be well suited to the Kibera data.

3.4 Pastor-Satorras and Vespignani Model

The Pastor-Satorras and Vespignani (PS&V) model is an SIS (susceptible-infectious-susceptible) model that was published in 2001 [28]. An SIS model is used for diseases that do not convey immunity to past infectious individuals; individuals pass directly from the infectious class back to the susceptible class. The population is held constant for this model, so only the infectious population needs to be modelled (the number of susceptibles is equal to the infectious population subtracted from the total population).

The PS&V model is a specific multigroup model that is potentially suited to the type of data being modelled here; groups are separated by the number of contacts

they have per time unit (for example, number of contacts per day, week, or month). This means there can be *many* groups; in the Kibera data the number of contacts (per unit time) ranges from zero to dozens (see Section 2.2). The rate of contact is dependent on the number of contacts each group makes per unit time. This results in a complicated set of equations; for a group with k contacts per unit time, the SIS PS&V equation for the number of infectious individuals with k contacts per unit time is

$$\frac{dI_k}{dt} = \beta k \theta S_k - \gamma I_k. \quad (3.5)$$

Here β is the probability of infection given contact occurs, thus βk is the number of contacts per unit time multiplied by the probability one of those contacts leads to infection. Therefore θ needs to be the probability that a random connection leads to an infectious individual. This is calculated by counting the total number of connections and the number of connections that lead to infectious individuals, namely

$$\theta = \frac{\sum_k k I_k}{\sum_k k N_k},$$

where $\sum_k = \sum_{k=1}^K$ and K is the maximum number of contacts per unit time. In order to use the PS&V model with data, plenty of information about the distribution of number of contacts is required [28]. Splitting the population up into so many varied groups needs to be inspired by the data; the Kibera data do include the number of monthly and weekly partners, and as such could potentially fit a PS&V model if it were generalized to two sexes.

3.5 Network Models

Network models are used when the goal is to model the individual [25]. All of the previously described models use ODEs, and model groups of the population. When the population is well mixed (or data at an individual level are not available) these models can be acceptable approximations [12]; however, when data are available at an individual level, and the data are varied and detailed enough to suggest homogeneous

mixing is too simplistic, a network model can be employed as it is much more specific. This is especially useful when the nature of connections between individuals is known.

A common way of modelling networks is to use percolation theory where the population is assumed arbitrarily large and degree distributions (generating functions that give the probability of different contact numbers) are used. Modelling in this way can be used to determine the final size of an outbreak [24] and find the epidemic threshold, a variable based on degree distribution and transmissibility of disease, above which the disease can invade the population [24]. This form of network model keeps track of individuals based on their degree.

Another approach to network models is to model the contacts between individuals [37]. This method keeps track of how the different types of contacts change throughout an infection; for example, as the number of infectious individuals increases the number of connections between two susceptibles will go down as the number of connections between susceptible and infectious individuals increases.

Network models capture data at an individual level, and are often used for sexual networks [25]. However, most current models keep networks static, or evolve them in an algorithmic way [23]; additionally, even this simplistic evolution is complicated to carry out and analyze. If the data suggest that partners are not often repeated and are generally random, then a dynamic network model is needed.

In the next chapter the Kibera data are analyzed to determine which type of model is best suited to the data.

Chapter 4

Model Development

In this chapter the Kibera data are analysed to determine which type of model will best approximate how the questioned individuals are connected. The amount of population mixing, that is whether a population is well mixed (that would cause us to choose an ODE model) or exposure to individuals is lasting and repeated (indicating that a network model is a good choice) assists in the choice of model type as these are some of the large differences between possible models. Our data focus on sex-workers and their partners, which may have many repeated partners, or could be largely random.

Once the data have been discussed, the type of model is determined in Section 4.1. In Section 4.2 the generic model is specified to be appropriate for the Kibera data. The resulting model is complicated, and some simple analysis is performed in Section 4.3 before numerical results are presented in Chapter 5.

4.1 Model Selection

This section determines which type of model will be used. The amount of mixing in the population, and the individualization in the data will determine which model is chosen.

4.1.1 Repeated Partners

To determine the amount of mixing, we examine the number of partners a sex-worker had during the past week, and compare that number to partners in the past month (see Figure 4.1). The assumption with this type of data (HIV status and number of recent contacts of many individuals) is that a network model should be used; however, the data fall nicely around a line with a slope of four in the figure. This implies that the number of partners in the last month is nearly four times the number of partners in the last week. This suggests the population may indeed be well mixed; if there were many repeated partners then the number of monthly partners would be less than four times the number of weekly partners. Therefore, further examination of what proportion of partners are repeated, and what proportion are random is required.

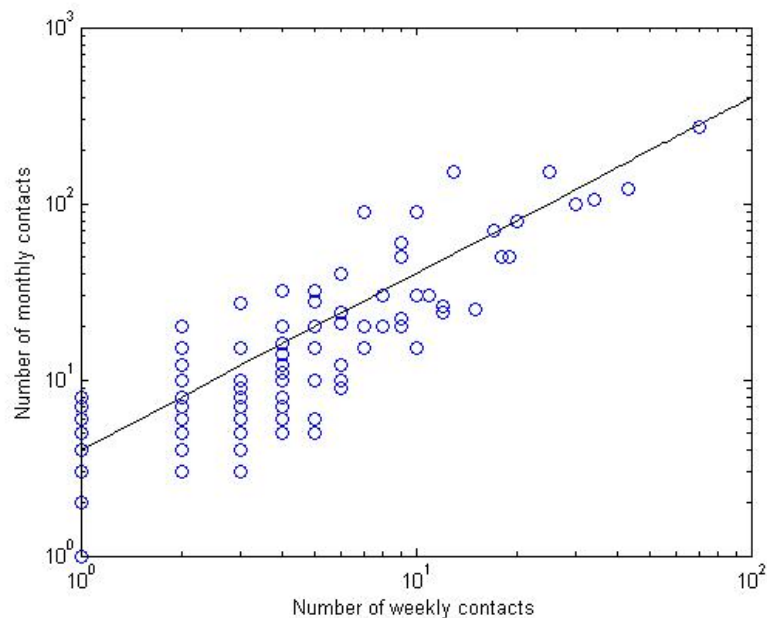


Figure 4.1: Number of monthly partners is approximately four times the weekly number of partners for sex-workers. The line has slope four and intersects the origin.

To find the proportion of partners that are repeated, assume that for each i th individual the number of weekly contacts is a Poisson distribution with mean λ_i , where i is an index. Assume another Poisson process with mean $f(\lambda_i)$ of these partners are repeated partners, with the rest of the partners randomly selected. It is assumed that the expected number of weekly partners has some impact on the number of repeated partners; thus, the function $f(\lambda_i)$ is assumed the same for all individuals with the

same number of expected weekly contacts. The function $f(\lambda_i)$ is assumed to be linear, such that

$$f(\lambda_i) = a_1 + a_2\lambda_i$$

With these assumptions the number of partners in the rest of the month for the i th individual is a Poisson distribution with mean

$$M_i(\lambda_i) = 3.35(\lambda_i - f(\lambda_i)). \quad (4.1)$$

The average number of weeks in a month is 4.35, so there are 3.35 weeks of new partners after that first week.

These distributions and the function $f(\lambda_i)$ allow the use of two likelihood functions to determine the number of repeated partners. For each individual, the number of reported contacts in the last week is compared to the estimate λ_i using log-likelihood function

$$\ell_{\lambda_i} = \bar{k}_i \ln(\lambda_i) - \lambda_i, \quad (4.2)$$

where \bar{k}_i is the reported number of contacts in the last week by the i th individual, and a constant has been dropped.

Similarly, we compare M_i to the data using log-likelihood function

$$\ell_{M_i} = (k_i - \bar{k}_i) \ln(M_i(\lambda_i)) - M_i(\lambda_i), \quad (4.3)$$

where k_i is the reported number of monthly contacts by the i th individual, and a constant has been dropped.

Thus the sum of the (4.2) and (4.3) for all individuals gives the overall log-likelihood, which is maximized by varying λ_i and the values of a_1 and a_2 in function $f(\lambda_i)$. The number of reported weekly contacts versus the expected number of weekly contacts

(λ_i) can be seen in Figure 4.2; the figure indicates that the two quantities are usually close.

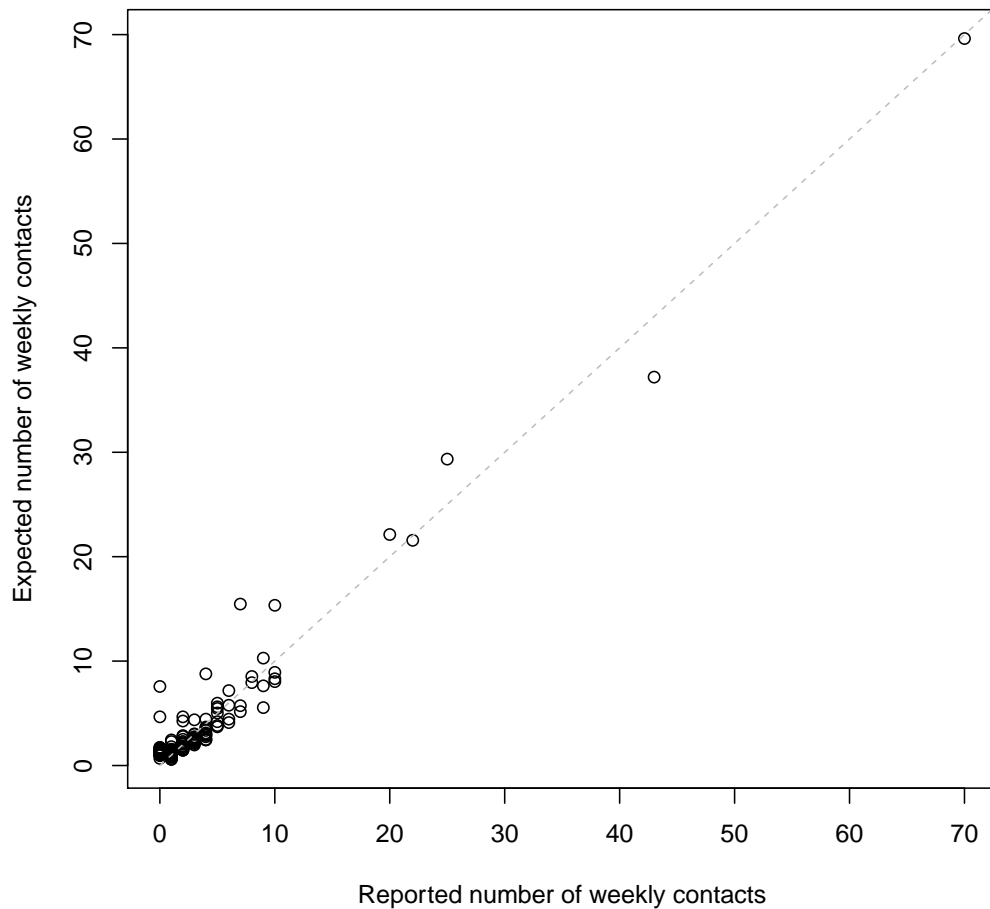


Figure 4.2: The reported number of weekly partners compared to the expected number of repeated partners λ_i for each female sex worker.

The parameters that maximize the likelihood give $f(\lambda_i) = 0.579 + 0.027\lambda_i$. The number of expected weekly partners including the expected number of repeated partners can be seen in Figure 4.3. The figure implies the number of contacts that are repeated is quite low, especially given that the average number of monthly contacts for sex workers is 18.2, where the expected number of repeated partners is just 1.07. Therefore an ODE model with homogeneous mixing is most appropriate.

As the data contain the contact distribution for sex-workers and their clients, a natural

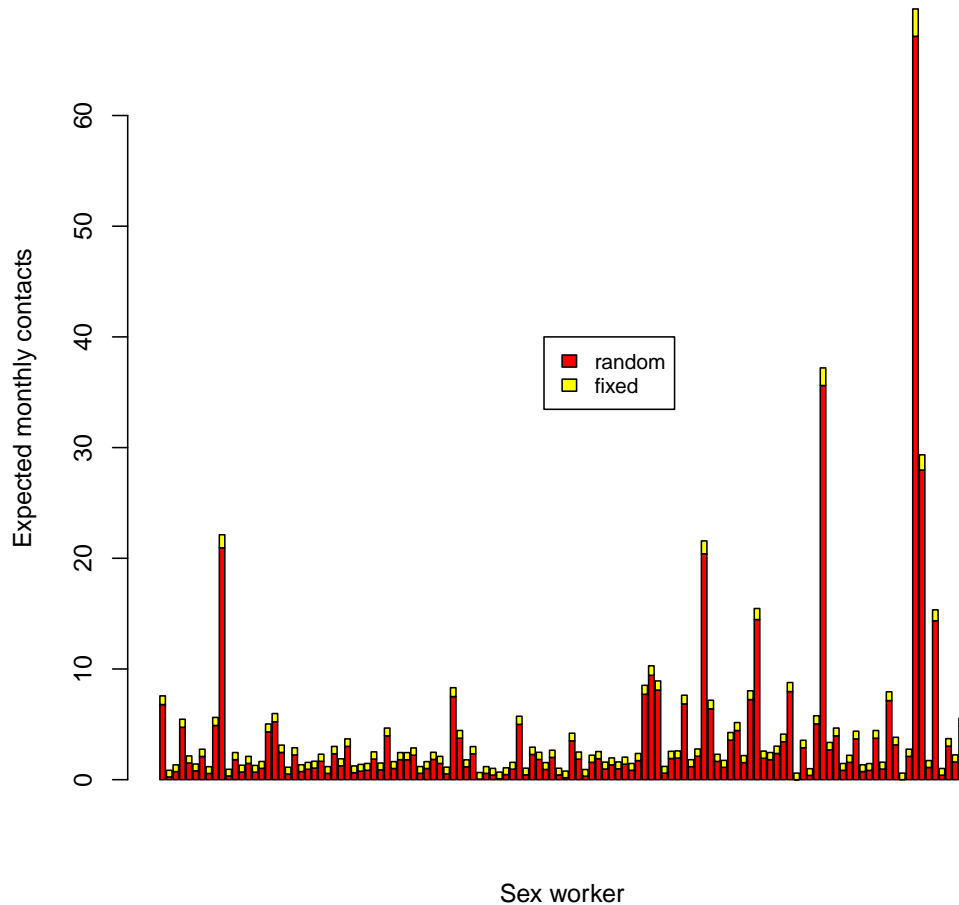


Figure 4.3: The expected number of weekly partners, per individual, and the number of those partners expected to be repeated for each female sex worker.

model choice is a modified version of Pastor-Satorras and Vespignani’s model [28]. This model development takes place in the next section.

4.2 Modified Pastor-Satorras & Vespignani Model

We modify the disease model by Pastor-Satorras and Vespignani [28] as described in Section 3.4.

The Kibera data involve heterosexual activity between sex workers and males who go

to sex workers, so it is necessary to differentiate between the sexes in the model. As the Kibera data have no information on other forms of HIV transmission, the only form of transmission in the model is through heterosexual intercourse.

For each sex the total number of individuals with k contacts per month is denoted by N_k^F and N_k^M for females and males, respectively, and the number of infected (\equiv infectious) individuals with k contacts per month by I_k^F and I_k^M , respectively. Introducing two sexes means the number of contacts between sexes needs to be matched, such that $\sum_i i N_i^F = \sum_j j N_j^M$ (see Theorem 4.2.1).

As HIV is a lifetime disease, we need to modify the original PS&V model (equation (3.5)), which is an SIS model, to an SI (susceptible-infected) model where individuals cannot go back to the susceptible population once infected. Additionally, population of individuals involved in the sex trade is dynamic; individuals immigrate into the population ($\sigma_F, \sigma_M > 0$ individuals per month), and emigrate out of the population at rate $\mu_F, \mu_M > 0$. Depending on their sex, immigrating individuals have k monthly contacts with probability P_k^F or P_k^M ; these distributions are assumed constant in time, and are set to the best fitting power law (see Section 2.2). The source of the immigrating individuals is Kibera, so the prevalence of HIV is positive in the immigrating population, $p_F > 0$ for females, and $p_M > 0$ for males. Even though the immigration and emigration rates vary between the sexes, the removal rate γ due to HIV remains the same for both sexes as there is no indication that HIV dynamics differ between sexes.

Adding immigration and emigration to the model means that the total populations are no longer constant; it is now necessary to have equations for the change in group populations, N_k^F and N_k^M , for all $k = 1, \dots, K$, as opposed to just equations for the infectious classes, as in the original PS&V model (3.5). Additionally, the number of individuals joining and leaving the population are not equal for males and females as the supply and demand for contact between sexes is constantly changing. For example, if 5 females with 5 monthly contacts enter the population then twenty-five monthly contacts with males have been added, and some males from the population will increase their number of monthly contacts such that those twenty-five contacts are matched. Sex workers and males are continually shifting the number of partners they have in a month to match this supply and demand. In order to follow this shifting (and keep the number of male-female and female-male contacts equal, recall

$\sum_i iN_i^F = \sum_j jN_j^M$), terms are introduced reflecting the rates of migration that accomodate the shifting of individuals to have fewer or more monthly contacts.

These terms rely on the immigrating and emigrating terms of the opposite sex. To compensate for immigration of the opposite sex, a group with k monthly contacts gains individuals from the group with $k - 1$ contacts, and loses individuals to the group with $k + 1$ contacts; the group similarly gains individuals from the group above it and loses individuals to the group below it to compensate for emigration of the opposite sex.

For example, females with k monthly contacts respond to male immigration and emigration (as all females do). How each group responds to immigration and emigration depends on the number of monthly contacts; individuals with more contacts are more likely to change their behaviour. Females with k contacts per month have, as a group, a total of kN_k^F contacts per month, out of a total $\sum'_k kN_k^F$ contacts for *all* females per month (where $\sum'_k = \sum_{k=1}^{K-1}$, as sex workers with the maximum number of contacts cannot move to have more). The total number of contacts that males add per month is $\sigma_M \sum_i iP_i^M$. Thus, we introduce a term

$$Y_k^F = \sigma_M \sum_i iP_i^M \left(\frac{k}{\sum'_i iN_i^F} \right) \quad (4.4)$$

that is the proportion of females with k monthly contacts that move to have $k + 1$ monthly contacts per month in response to male immigration. The number of females with $k - 1$ contacts that shift to have k monthly contacts is calculated similarly, $Y_{k-1}^F N_{k-1}^F$. Over a month males remove $\mu_M \sum_i iN_i^M$ contacts due to emigration and $\gamma \sum_i iI_i^M$ contacts due to advanced HIV; in response the proportion of females with k contacts per month that shift to have $k - 1$ contacts per month is calculated using

$$Z_k^F = (\mu_M \sum_i iN_i^M + \gamma \sum_i iI_i^M) \left(\frac{k}{\sum''_i iN_i^F} \right). \quad (4.5)$$

Here $\sum''_k = \sum_{k=2}^K$ as sex workers with only one contact cannot have less. Similarly, females with $k + 1$ contacts shift to have k contacts. Males respond to female immigration and emigration similarly with equivalent terms Y_k^M and Z_k^M .

The probability that an individual becomes infected is the product of three quantities,

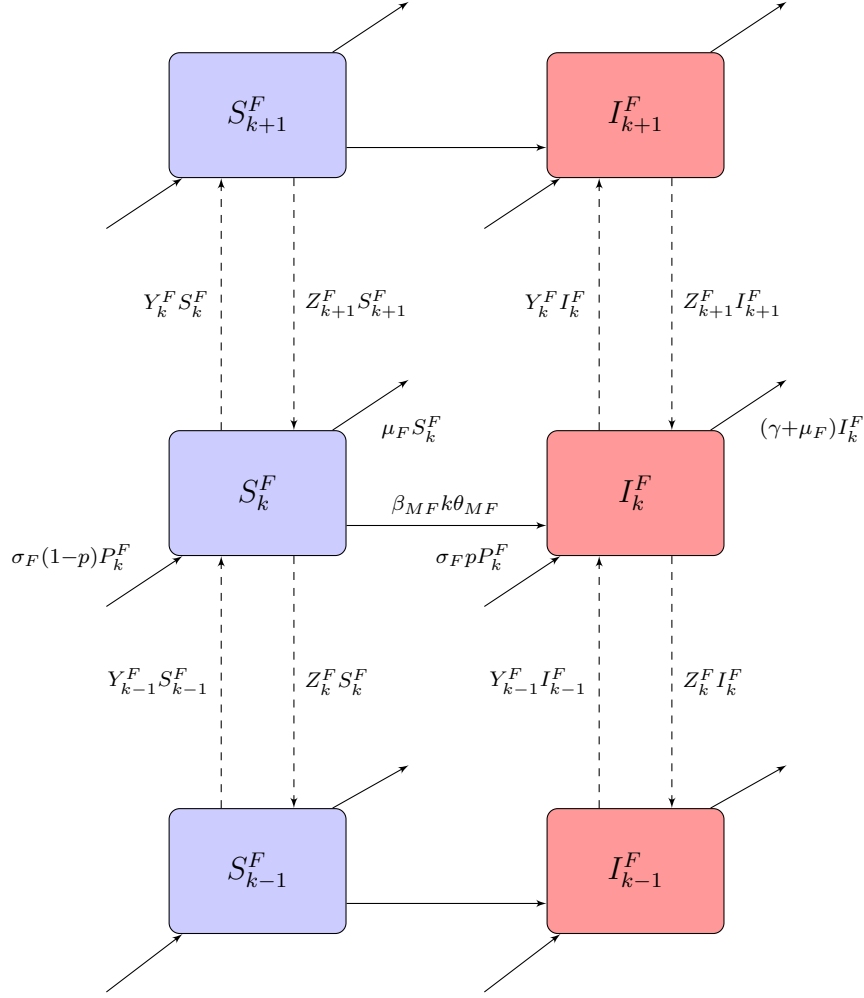


Figure 4.4: Flow diagram for females with k monthly contacts, where Y_k^F and Z_k^F are as defined in (4.4) and (4.5), respectively.

the probability of infection per sexual act, the number of sexual acts per month, and the probability that a random sexual act is with an infectious individual. Numerous studies indicate the probability of HIV infection per sexual act is different for each sex, and thus there are two infectious probabilities: β_{MF} for infection from males to females, and β_{FM} for infection from females to males. The number of contacts per month is dictated by the subscript on terms, for example S_k^F has k contacts per month. The probability that a random sexual act takes place with an infected individual is calculated by determining the proportion of all sexual acts per month that involve an HIV positive person; thus two terms are introduced: $\theta_{MF} = \frac{\sum_i I_i^M}{\sum_i N_i^M}$ and similarly $\theta_{FM} = \frac{\sum_i I_i^F}{\sum_i N_i^F}$ calculate the probability that a random contact of the

opposite sex is infected with HIV, θ_{MF} for male-to-female infections, and θ_{FM} for female-to-male infections. Thus, as an example, the probability that a susceptible female with k contacts becomes infected during any given month is $\beta_{MF}k\theta_{MF}$.

The resulting interactions for females with k monthly contacts are shown in a flow diagram in Figure 4.4. Males with k monthly contacts are similar, with F and M exchanged.

The resulting equations for the model are thus:

$$\begin{aligned} \frac{dN_k^F}{dt} = & -\mu_F N_k^F - \gamma I_k^F + \sigma_F P_k^F + \sigma_M \Sigma i P_i^M \left(\frac{(k-1)N_{k-1}^F - kN_k^F}{\Sigma' i N_i^F} \right) \\ & + (\mu_M \Sigma i N_i^M + \gamma \Sigma i I_i^M) \left(\frac{(k+1)N_{k+1}^F - kN_k^F}{\Sigma'' i N_i^F} \right), \end{aligned} \quad (4.6a)$$

$$\begin{aligned} \frac{dI_k^F}{dt} = & \beta_{MF} k \theta_{MF} (N_k^F - I_k^F) - (\gamma + \mu_F) I_k^F + \sigma_F p_F P_k^F \\ & + \sigma_M \Sigma i P_i^M \left(\frac{(k-1)I_{k-1}^F - kI_k^F}{\Sigma' i N_i^F} \right) \\ & + (\mu_M \Sigma i N_i^M + \gamma \Sigma i I_i^M) \left(\frac{(k+1)I_{k+1}^F - kI_k^F}{\Sigma'' i N_i^F} \right), \end{aligned} \quad (4.6b)$$

$$\begin{aligned} \frac{dN_k^M}{dt} = & -\mu_M N_k^M - \gamma I_k^M + \sigma_M P_k^M + \sigma_F \Sigma i P_i^F \left(\frac{(k-1)N_{k-1}^M - kN_k^M}{\Sigma' i N_i^M} \right) \\ & + (\mu_F \Sigma i N_i^F + \gamma \Sigma i I_i^F) \left(\frac{(k+1)N_{k+1}^M - kN_k^M}{\Sigma'' i N_i^M} \right), \end{aligned} \quad (4.6c)$$

$$\begin{aligned} \frac{dI_k^M}{dt} = & \beta_{FM} k \theta_{FM} (N_k^M - I_k^M) - (\gamma + \mu_M) I_k^M + \sigma_M p_M P_k^M \\ & + \sigma_F \Sigma i P_i^F \left(\frac{(k-1)I_{k-1}^M - kI_k^M}{\Sigma' i N_i^M} \right) \\ & + (\mu_F \Sigma i N_i^F + \gamma \Sigma i I_i^F) \left(\frac{(k+1)I_{k+1}^M - kI_k^M}{\Sigma'' i N_i^M} \right), \end{aligned} \quad (4.6d)$$

with

$$\theta_{MF} = \frac{\sum i I_i^M}{\sum i N_i^M}, \quad \theta_{FM} = \frac{\sum i I_k^F}{\sum i N_i^F}.$$

The number of monthly contacts is $k = 1, \dots, K$ and $\sum = \sum_{i=1}^K$, $\sum' = \sum_{i=1}^{K-1}$, and $\sum'' = \sum_{i=2}^K$. Note that the terms that accomodate switching are written for a general k ; if $k = 1$ then individuals cannot move to have zero monthly contacts, and there is no group with zero monthly contacts to move up to $k = 1$. Similarly when $k = K$ there is no term for switching up to have $K + 1$ contacts, and no individuals shifting to have K contacts from above.

The parameters used in this model are defined in Table 4.1, and all are assumed to be positive.

Parameter	Male	Female
Probability of infection	β_{FM}	β_{MF}
Number of new individuals per month	σ_M	σ_F
Proportion of individuals leaving per month	μ_M	μ_F
Prevalence of incoming population	p_M	p_F
Removal rate per month due to HIV/AIDS	γ	γ
Probability of having k partners	P_k^M	P_k^F

Table 4.1: Meaning of parameters in the model

The initial conditions for the model are $0 \leq I_k^F(0) \leq N_k^F(0)$ and $0 \leq I_k^M(0) \leq N_k^M(0)$. As shown in Theorem 4.2.2, this means solutions are invariant to $\mathbb{R}_{\geq 0}^{2K}$.

As mentioned previously, the balance of connections between sexes must be satisfied. The condition must be satisfied initially ($\sum k N_k^F(0) = \sum k N_k^M(0)$), but continues to be satisfied as time progresses.

Theorem 4.2.1. *Given system (4.6), satisfying the initial condition $\sum k N_k^F(0) = \sum k N_k^M(0)$, the condition $\sum k N_k^F = \sum k N_k^M$ is satisfied for all time.*

Proof. Consider

$$\begin{aligned} & \frac{d}{dt}(\sum k N_k^F) - \frac{d}{dt}(\sum k N_k^M) \\ &= \sum k \frac{d}{dt}(N_k^F) - \sum k \frac{d}{dt}(N_k^M). \end{aligned}$$

Before moving to substitute $\frac{d}{dt}(N_k^F)$ and $\frac{d}{dt}(N_k^M)$ from (4.6) into the above equation, notice that the derivative of N_k^F from (4.6) can be written as

$$\frac{d}{dt}(N_k^F) = -\mu_F N_k^F - \gamma I_k^F + \sigma_F P_k^F + \left(Y_{k-1}^F N_{k-1}^F - Y_k^F N_k^F \right) + \left(Z_{k+1}^F N_{k-1}^F - Z_k^F N_k^F \right)$$

where Y_k^F and Z_k^F are as defined previously in this section. It is simpler to deal with these complicated terms $Y_k^F, Z_k^F, Y_k^M, Z_k^M$ first. Recall that individuals cannot shift to or from having zero or $K+1$ contacts, so these terms are cut off for the derivatives of N_1^F and N_K^F , i.e., there are no terms Y_1^F, Y_K^F or Z_1^F, Z_K^F . For example, the term for females adding contacts in response to male immigration sums in the following manner:

$$\begin{aligned} \sum_{k=2}^K k Y_{k-1}^F N_{k-1}^F - \sum_{k=1}^{K-1} k Y_k^F N_k^F &= \sum_{k=1}^{K-1} (k+1) Y_k^F N_k^F - \sum_{k=1}^{K-1} k Y_k^F N_k^F \\ &= \sum_{k=1}^{K-1} Y_k^F N_k^F \\ &= \sum_{k=1}^{K-1} \sigma_M \sum_{i=1}^K i P_i^M \left(\frac{k N_k^F}{\sum_{j=1}^{K-1} j N_j^F} \right) \\ &= \frac{\sigma_M \sum_{i=1}^K i P_i^M}{\sum_{j=1}^{K-1} j N_j^F} \sum_{k=1}^{K-1} k N_k^F \\ &= \sigma_M \sum_{i=1}^K i P_i^M \end{aligned}$$

Similarly, the terms for moving to have fewer contacts sum as follows:

$$\sum_{k=1}^{K-1} k Z_{k+1}^F N_{k+1}^F - \sum_{k=2}^K k Z_k^F N_k^F = -(\mu_M \sum_i i N_i^M + \gamma \sum_i i I_i^M).$$

All the switching terms, when summed in this way, have similar results. Thus, substitution of $\frac{d}{dt} N_k^F$ and $\frac{d}{dt} N_k^M$ from system (4.6) yields

$$\begin{aligned}
& \left(-\mu_F \sum k N_k^F - \gamma \sum k I_k^F + \sigma_F \sum k P_k^F \right. \\
& \quad \left. + \sigma_M \sum k P_k^M - \mu_M \sum k N_k^M - \gamma \sum k I_k^M \right) \\
& - \left(-\mu_M \sum k N_k^M - \gamma \sum k I_k^M + \sigma_M \sum k P_k^M \right. \\
& \quad \left. + \sigma_F \sum k P_k^F - \mu_F \sum k N_k^F - \gamma \sum k I_k^F \right) = 0.
\end{aligned}$$

So the difference of the derivatives, $\sum_k k \frac{d}{dt}(N_k^F) - \sum_k k \frac{d}{dt}(N_k^M)$, is zero, and thus when the condition is satisfied initially, $\sum_k k N_k^F = \sum_k k N_k^M$ is satisfied for all time.

□

Theorem 4.2.2. *Given system of equations (4.6) with positive parameters and non-negative initial conditions satisfying $0 \leq I_k^F(0) \leq N_k^F(0)$ and $0 \leq I_k^M(0) \leq N_k^M(0)$, the solutions to (4.6) are invariant to the region $\mathbb{R}_{\geq 0}^{2K}$.*

Proof. Before moving to the main section of the proof, it is necessary to show, given the initial conditions, that $I_k^F \leq N_k^F$ and $I_k^M \leq N_k^M$ for all time, for all $k = 1, \dots, K$. To do this we require the equation for susceptible individuals, matching with (4.6).

As with all SI models, the susceptible population is the difference between the total population and infected population ($S_k^F = N_k^F - I_k^F$, and similarly for males). Thus, the equation for susceptible females with k monthly contacts is

$$\begin{aligned}
\frac{dS_k^F}{dt} = & -\beta_{MF} k \theta_{MF} S_k^F - \mu_F S_k^F + \sigma_F (1 - p_F) P_k^F + \sigma_M \sum i P_i^M \left(\frac{(k-1)S_{k-1}^F - kS_k^F}{\sum i N_i^F} \right) \\
& + (\mu_M \sum i N_i^M + \gamma \sum i I_i^M) \left(\frac{(k+1)S_{k+1}^F - kS_k^F}{\sum i N_i^F} \right).
\end{aligned}$$

The equation for susceptible males is similar.

To show the infectious classes are constrained by the total group populations, assume there exists some time t_1 , when first $I_k^F = N_k^F$ and thus $S_k^F = 0$. The derivative of the susceptible population at zero is

$$\begin{aligned} \left. \frac{dS_k^F}{dt} \right|_{S_k^F=0} &= \sigma_F(1 - p_F)P_k^F + \sigma_M \Sigma i P_i^M \left(\frac{(k-1)S_{k-1}^F}{\Sigma' i N_i^F} \right) \\ &\quad + (\mu_M \Sigma i N_i^M + \gamma \Sigma i I_i^M) \left(\frac{(k+1)S_{k+1}^F}{\Sigma'' i N_i^F} \right) \geq 0. \end{aligned}$$

As $N_k^F = S_k^F + I_k^F$ it follows that

$$\frac{dN_k^F}{dt} = \frac{dS_k^F}{dt} + \frac{dI_k^F}{dt}$$

and thus

$$\left. \frac{dN_k^F}{dt} \right|_{N_k^F=I_k^F} \geq \left. \frac{dI_k^F}{dt} \right|_{N_k^F=I_k^F}$$

as $dS_k^F/dt \geq 0$.

Thus, when the entire population is infectious, $\frac{dI_k^F}{dt} \leq \frac{dN_k^F}{dt}$ at t_1 for every $k = 1, \dots, K$ and $I_k^F \leq N_k^F$. The same is true for males and is shown similarly.

Now, given the initial conditions, solutions must pass through a zero value to leave the region $\mathbb{R}_{\geq 0}^{2K}$; thus, in order to falsify the theorem, there must exist a group with a negative derivative when the group is at zero.

First, check I_k^F (note that I_k^M is similar). Let $I_k^F = 0$ at shortest time t_2 and recall $I_k^F \leq N_k^F$ for every $k = 1, \dots, K$. Examination of (4.6) shows

$$\begin{aligned} \left. \frac{dI_k^F}{dt} \right|_{I_k^F=0} &= \beta_{MF} k \theta_{MF} N_k^F + \sigma_F p_F P_k^F + \sigma_M \Sigma i P_i^M \left(\frac{(k-1)I_{k-1}^F}{\Sigma' i N_i^F} \right) \\ &\quad + (\mu_M \Sigma i N_i^M + \gamma \Sigma i I_i^M) \left(\frac{(k+1)I_{k+1}^F}{\Sigma'' i N_i^F} \right) \geq 0. \end{aligned}$$

Clearly the infectious population cannot become negative with non-negative initial

conditions. Additionally, as we showed $\frac{dI_k^F}{dt} \leq \frac{dN_k^F}{dt}$ when $I_k^F = N_k^F$, it must also be true that the total population must remain non-negative.

Thus, with positive parameters and non-negative initial conditions, solutions to (4.6) are invariant to the region $\mathbb{R}_{\geq 0}^{2K}$. \square

Even with initial conditions of zero for all groups, the solutions are invariant to $\mathbb{R}_{\geq 0}^{2K}$ (and do not just stay zero) as $\sum_k P_k^F = \sum_k P_k^M = 1$ and $p_F, p_M > 0$, meaning there must exist susceptible and infectious groups with positive immigration.

In the next section we prove an endemic equilibrium must exist.

4.3 Equilibrium of the Model

The existence of an endemic equilibrium can be shown analytically. It is clear that when prevalence of HIV in the source community is positive ($p_F, p_M > 0$) that no disease free equilibrium can exist. In order for an endemic equilibrium to exist solutions must be bounded and equilibria can not lie on the boundary of the bounded region.

Theorem 4.3.1. *Given system of equations (4.6) with positive parameters and non-negative initial conditions satisfying $0 \leq I_k^F(0) \leq N_k^F(0)$ and $0 \leq I_k^M(0) \leq N_k^M(0)$, there exists an endemic equilibrium, such that $0 \leq I_k^{F*} < N_k^{F*}$ and $0 \leq I_k^{M*} < N_k^{M*}$, for all $k = 1, \dots, K$, and there exist k, j such that $0 < I_k^{F*} < N_k^{F*}$ and $0 < I_j^{M*} < N_j^{M*}$.*

Proof. To prove this, we first show the solutions are bounded.

The dynamics of the total female or male population can be studied by summing the equations for $\frac{dN_k^F}{dt}$ or $\frac{dN_k^M}{dt}$, respectively. Summing over all k for $\frac{dN_k^F}{dt}$ yields

$$\sum_k \frac{dN_k^F}{dt} = \frac{dN^F}{dt} = -\mu_F N^F - \gamma I^F + \sigma_F, \quad (4.12)$$

where $\sum N_k^F = N^F$ and $\sum I_k^F = I^F$; the equation for $\frac{dN_k^M}{dt}$ is similar. It is clear that total female (and male) populations are bounded above by σ_F/μ_F (and σ_M/μ_M), given

initial conditions are below this threshold; if solutions begin above these bounds, they will decay down to the bounds. Thus N_k^F and N_k^M are bounded above for each k by σ_F/μ_F and σ_M/μ_M , respectively.

This, in addition to the result of the previous theorem, implies solutions are invariant to a bounded, non-negative region. It must be shown that there exist k, j such that a positive equilibrium exists $(I_k^{F*}, I_k^{M*}, N_k^{F*}, N_k^{M*})$ that satisfies $I_k^{F*} < N_k^{F*}$ and $I_j^{M*} < N_j^{M*}$.

The infected groups are bounded above by the respective total group population (as shown in Theorem 4.2.2)). That no equilibrium can lie on the boundary of the region can be shown by contradiction. Assume there exists a k such that $I_k^{F*} = 0$. This can clearly only be true if $P_k^F = 0$; assume such a k exists. In order for the derivative to be zero (required for equilibrium) it must also be true that $I_{k-1} = I_{k+1} = N_k^F = 0$, as if these quantities are positive immigration into I_k^F will occur. However, to guarantee that neighbouring infectious groups have equilibria at zero, the groups neighbouring them (N_{k-2}, N_{k+2}) must also have zero equilibria; this carries on for all of the groups. Thus, for $I_k^{F*} = 0$ to be an equilibrium, *all* groups must have a zero equilibrium. This, however, is a contradiction, as there *must* be groups with no equilibrium at zero, as $\sum_k P_k^F = \sum_k P_k^M = 1$ and $p_F, p_M > 0$.

Thus, the domain of solutions lies within a convex, compact and positively invariant set that maps into itself; therefore, by Brouwer's Fixed Point Theorem, there must exist at least one equilibrium within the set (see [35], Theorem 4.7); however, as no equilibrium lie entirely on the boundary of the solution, an equilibrium must exist in the interior of the domain. Thus an endemic equilibrium must exist. \square

Note that the above result does not imply that the endemic equilibrium is unique, only that there must exist at least one endemic equilibrium. Further analysis of this model is complicated and thus carried out numerically in the next chapter, in which the model is parameterized and sensitivity analysis is performed.

Chapter 5

Parameterization and Sensitivity Analysis

5.1 Parameterization

While careful development of a mechanistic model is important, the model can be more useful when it is properly parameterized; the use of data to parameterize the model means that the model can determine features intrinsic to the studied population. Proper parameterization also allows study of the sensitivity of the equilibrium to model parameters. How the equilibrium shifts in response to parameter changes can help determine which changes in the studied population can reduce characteristics, for example prevalence and risk.

For these reasons the data are utilized to parameterize the model (4.6) developed in the previous chapter; this allows us to compare our calculated values with those found in the literature. Additionally, once the model is properly parameterized for this system, we can predict how behaviour changes affect prevalence, risk, and other social factors (see Section 5.2).

We assume that the system is at equilibrium, as HIV has been in the sex-working population of Nairobi since the middle of the 1980s [21]. Additionally, the Kibera data are the result of a single survey, and so the data give no information on the dynamics of HIV prevalence. Though the existence of at least one endemic equilibrium is proven

in Section 4.3, uniqueness could not be shown; however, numerical results indicate that each set of parameters yields only one endemic equilibrium.

To match the model output to the data the maximum log-likelihood method is used, comparing expected prevalence for each number of monthly contacts with the observed data. All parameters (except γ , the removal rate due to HIV/AIDS) are potentially different for each sex; we estimate those parameters separately.

When parameterizing the model, the immigration distributions P_k^F and P_k^M need to be fit to curves (for both sexes). Using the data directly as input causes a heavy bias towards high immigration, as the input data are then the same as the data that are being fit. This means that strong immigration parameters easily match the model output to the data (and thus, large immigration values are likely). This is unrealistic, and thus both P_k^F and P_k^M from (4.6) are fit to power law distributions for parameterization (as found in Section 2.2).

When initially attempting to parameterize (4.6), it became apparent that confidence intervals on parameter estimations were very wide. Wide intervals for possible parameter values were the result of compensating by other parameters; for example, both high and low values were acceptable for σ_F and σ_M , as these could be compensated with low and high values of other parameters.

The Kibera data can give a few parameters directly that do not need to be estimated; this can reduce the number of parameters to estimate, and control the back and forth effect the parameters can have. Prevalence of HIV in incoming populations is known as individuals not involved with the sex trade were interviewed. Prevalence among incoming females is $p_F = 13.2\%$, and prevalence among incoming males is $p_M = 10.6\%$. Additionally, HIV causes AIDS about 10 years after infection, meaning that removal rate (per month) $\gamma = 0.008$, as it is the reciprocal of the average numbers of months an individual remains in the infectious population before developing AIDS [5, 12].

The remaining parameters to fit are then the probability of infection upon a sexual encounter with an HIV positive individual (β_{MF} and β_{FM}), the immigration numbers for each sex (σ_F and σ_M), and the emigration rate for each sex (μ_F and μ_M).

5.1.1 Method of Parameterization

As the population is assumed to be at equilibrium, it is natural to use the multinomial distribution for the maximum likelihood estimate. Based on the multinomial distribution of infection status and number of monthly contacts, the likelihood function for females is as follows (the likelihood function for males takes the same form)

$$L^F = \frac{\tilde{N}^F!}{\tilde{I}_1^F! \dots \tilde{I}_K^F! \tilde{S}_1^F! \dots \tilde{S}_K^F!} (I_1^{F*})^{\tilde{I}_1^F} \dots (I_K^{F*})^{\tilde{I}_K^F} (S_1^{F*})^{\tilde{S}_1^F} \dots (S_K^{F*})^{\tilde{S}_K^F}, \quad (5.1)$$

where \tilde{N}^F , \tilde{I}_k^F , and \tilde{S}_k^F are the assumed equilibrium values from the data: the total number of observed females, the number of infected females with k monthly contacts, and the number of susceptible females with k monthly contacts. Similarly, I_k^{F*} and S_k^{F*} are obtained from the model at an equilibrium of the system (which is shown to exist in Theorem 4.3.1), and are the proportion of females with k monthly contacts that are infected and susceptible, respectively. A similar likelihood function, L^M exists for the male population. To maximize the likelihood for the whole population (for both sexes), we multiply the two likelihood functions together, such that the likelihood function is $L = L^F L^M$.

Calculations were done using negative log-likelihood; the function being minimized is thus $\ell = -\ln(L)$. Minimizing the negative log-likelihood function is equivalent to maximizing the likelihood function; see [4], Theorem 9.2.2. The negative log-likelihood function (for the whole population) takes the form

$$\begin{aligned} -\ell &= \ln(L^F) + \ln(L^M) \\ &= \sum_{k=1}^K \tilde{I}_k^F \ln(I_k^{F*}) + \sum_{k=1}^K \tilde{S}_k^F \ln(S_k^{F*}) + \sum_{k=1}^K \tilde{I}_k^M \ln(I_k^{M*}) + \sum_{k=1}^K \tilde{S}_k^M \ln(S_k^{M*}), \end{aligned} \quad (5.2)$$

where the factorials from (5.1) have been dropped as they become constants in the above equation.

Parameterization is done using the Matlab minimizing optimization routine, `fmincon`; the routine minimizes (5.2) from an initial estimate of parameters. The common

practice of parameterization is to solve the system of non-linear ODEs at every iteration of minimization. This method can be highly inefficient and computationally time consuming; as our system of ODEs is large, this is certainly the case here. The assumption that the system is at equilibrium (see above) lends itself to the utilization of another, more efficient method of parameterization.

Instead of repeatedly numerically solving the large ODE system, the system (4.6) can be set equal to zero, and become part of the constraints [42]. In this way, the optimizer solves the system while maximizing log-likelihood.

5.1.2 Parameterization

Point estimates and confidence intervals for the parameters are given in Table 5.1, with time unit of one month.

Parameter	Estimate (95% Confidence Interval)
β_{MF}	1.750×10^{-3} ($1.746 \times 10^{-3}, 1.754 \times 10^{-3}$)
β_{FM}	4.60×10^{-4} ($4.57 \times 10^{-4}, 4.94 \times 10^{-4}$)
μ_F	$7.50 \times 10^{-4}/\text{month}$ ($0, 7.51 \times 10^{-4}$)
μ_M	$9.20 \times 10^{-4}/\text{month}$ ($9.04 \times 10^{-4}, 9.44 \times 10^{-4}$)
σ_F	15.95/month (15.88, 16.02)
σ_M	31.29/month (29.26, 32.30)

Table 5.1: Parameter estimates.

Confidence intervals are estimated using Likelihood Ratio Profiles; variance for the parameters are estimated using the Hessian produced by the optimizer. The absolute value of the square root of the diagonal of the inverse of the Hessian are variance estimates on the optimization [13]. Using the estimated variance, parameters are shifted, one by one with other parameters free, along this estimated range and the log-likelihood values of the output taken. These likelihood estimates are compared to the best likelihood estimate (when all parameters were free). The ratio of the two likelihoods follows an approximate χ^2 distribution, with one degree of freedom, as the difference in the number of free parameters between the two estimates is one. Therefore,

$$2 \log\text{-likelihood of shifted output} - 2 \log\text{-likelihood of best output} \sim \chi^2.$$

When the shifting of a parameter from its optimal value causes the above equation to be larger than 5, the difference in likelihood is significant and the confidence that the difference is due to the parameter is 95%; this value, therefore, is the 95% confidence interval.

5.1.3 Parameter Validation

Using these estimated parameter values the endemic equilibrium can be found numerically (for example, see Figure 5.1).

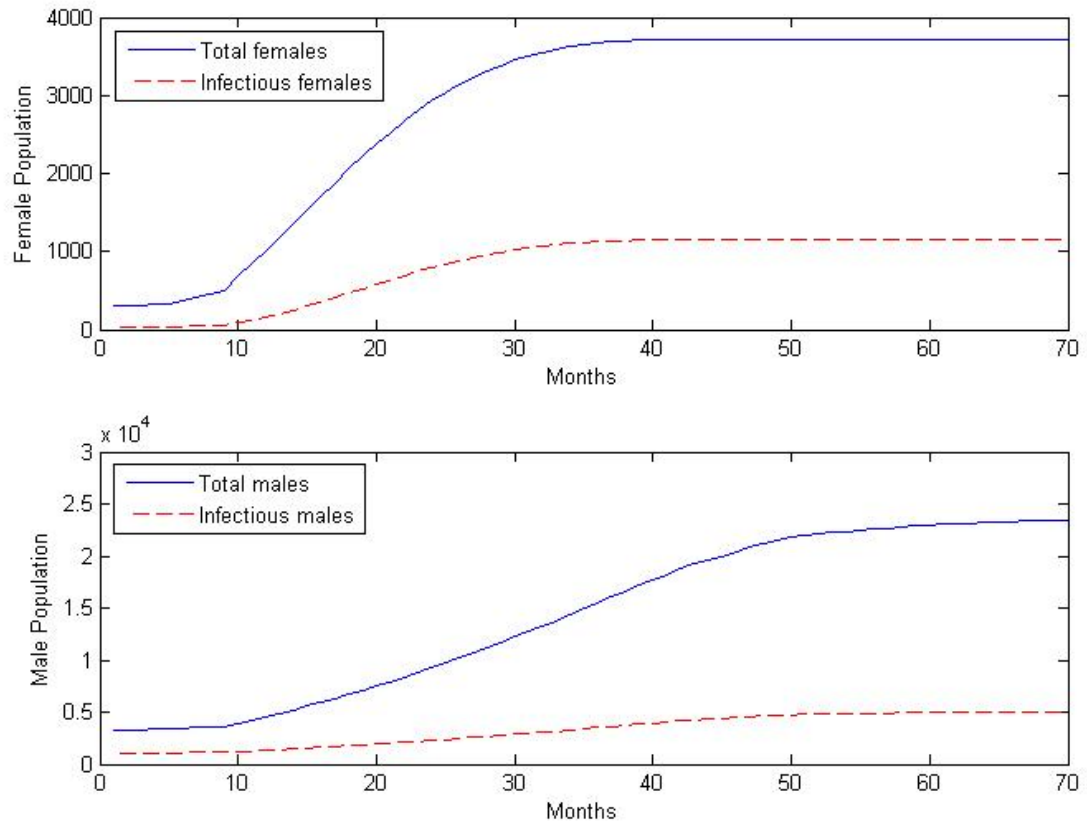


Figure 5.1: A numerical simulation of (4.6) using the estimated parameter values (see Table 5.1).

The results of the numerical simulation can be used to gather more information about the population and model. We first compare parameter estimates with those estimated in previous studies.

The probability of infection per sexual act has been estimated in some other studies. Some of these do not separate the probability between males and females, but use just one infection probability for both sexes. In sub-Saharan Africa, previous estimates for probability of infection per sexual act range from 6×10^{-4} to 3.7×10^{-3} [14, 15, 17]. In other countries, estimates of 7×10^{-4} to 9.2×10^{-3} (USA) have been made [36]. The estimates from our model fall within these ranges.

When separate estimates have been made for probability from males to females, and from females to males, the probability of infection from males to females has consistently been estimated as larger than that of from females to males [15, 17]; our estimate of β_{MF} is approximately 3.8 times larger than for β_{FM} .

Note that estimate of the probability of infection per sexual act is an average for the whole population as individuals in Kibera may use condoms or be receiving treatment for HIV (which may reduce the transmission probability).

The emigration rate is the reciprocal of the average time healthy individuals spend in the sex-working population. This seems not to have been estimated for male clients, and estimates in previous studies for female clients range from three months to sixteen years, with most estimates less than seven years [2, 16, 30]; however, estimates of this parameter are made by interviewing current sex-workers, and therefore it is difficult to estimate directly from the data.

The emigration rates that are estimated here seem comparatively low, as they indicate individuals remain involved with sex work for decades. No question of this type was asked during the collection of the Kibera data, and so there is no direct data to contradict this estimate by the model; however, anecdotally, these estimates seem to indicate that individuals remain in the population an order of magnitude too long. Conversation with researchers in Kibera indicate that individuals (particularly men) leave the population quickly, and then may re-enter it at a later date (after more than a month out of the population). The data also indicated this directly, as 70% of men said they had visited a sex worker during their lifetime, while only 16% said the same of the last month.

The number of males and females that become involved in the sex trade in Kibera has not been estimated directly in the data, and previous studies indicate these numbers differ largely between populations [2, 16]. Though no estimates for these quantities

exist in Africa, the ratio of the parameters (1.96 males join for every female) is larger than one, as expected, because females have, on average, higher numbers of monthly contacts than males. This imbalance in immigration means that the males have a higher population than females. The parameterization and model indicate the size of the sex working population of Kibera to be approximately 3500 sex workers and 25 000 males. This population has never been estimated before.

5.1.4 Model Predictions

The model, with this set of parameters, indicates an endemic equilibrium with an HIV prevalence of 31.8% in females, and 21.4% in males, where prevalence for females is calculated using $\sum_{k=1}^K I_k^F / \sum_{k=1}^K N_k^F$, and similarly for males. According to the Kibera data the prevalence of the population involved in the sex trade is 27.2% in females, and 16.0% in males. This discrepancy in prevalence is interesting, especially considering the above comments regarding low emigration being necessary to achieve higher prevalence values. However, recall that the model is parameterized to maximize the likelihood it would produce the number of total and infectious individuals at each number of monthly contacts in the Kibera data. As one can see in Figure 5.2 (which shows the equilibrium distribution of individuals found by the model), the resulting best fit appears to underestimate the total number of females when the number of monthly contacts is low. However, the best fitting parameters do not seem to similarly underestimate the number of infectious females in the same classes. This discrepancy has the effect that the model overestimates the prevalence of HIV in sex workers.

Additionally, the average number of monthly contacts for females is found, from the model, to be 15.7, while the Kibera data showed the average number of monthly contacts for sex workers is 18.2. Similarly, for males, the model indicated just 1.44 contacts per month for the average male, while the data showed an average number of contacts of 2.03.

Another interesting quantity the model can give (though, it cannot be collected explicitly from the data) is the risk of contracting HIV to the average male or female; as we know the probability of infection per sexual act, the average number of monthly contacts, and the probability a random contact is infectious, we can calculate the risk as the product of these three quantities. Thus, the model indicates the risk of

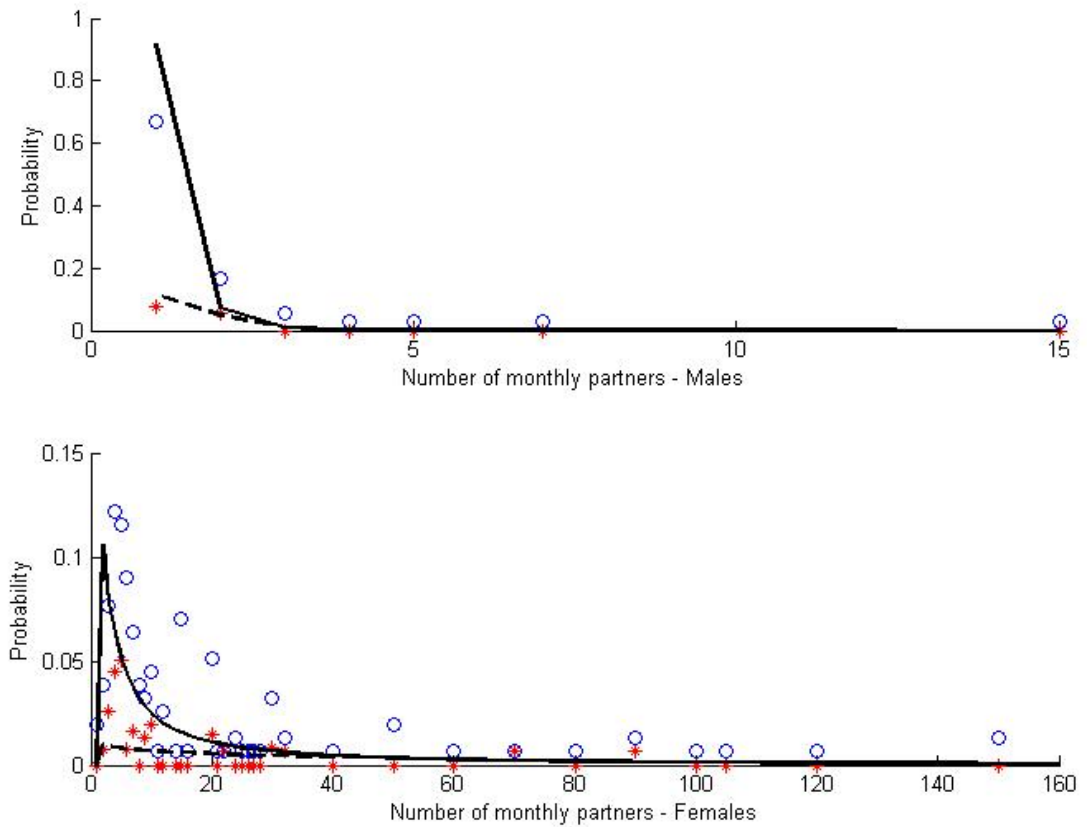


Figure 5.2: The distribution of the population at equilibrium. One female with a higher number of monthly contacts (270) is not shown in the figure.

contracting HIV in the population is

$$\beta_{MF}\langle k \rangle_F \frac{\sum_k k I_k^M}{\sum_k k N_k^M} = 6.12 \times 10^{-3}$$

per month for females and

$$\beta_{FM}\langle k \rangle_M \frac{\sum_k k I_k^F}{\sum_k k N_k^F} = 4.30 \times 10^{-4}$$

per month for males. The large differences of infection probabilities and average monthly contacts between the sexes lead to the higher prevalence of HIV in females. These two properties are what greatly increase the risk of infection for females over

the risk for males; the risk for an average female is 14.2 times the risk for an average male. This, inevitably, means the prevalence for females is higher at the endemic equilibrium.

In the next section we do an elasticity analysis to determine the effect of parameter change on these quantities.

5.2 Sensitivity Analysis

Sensitivity analysis of the model can assist modellers in determining which parameters play the most important roles on model dynamics [9]. With this model, some key aspects of output to examine are changes to prevalence and risk; risk here is the average probability that a susceptible individual will contract HIV during a month. Ultimately, this sensitivity analysis can inform public health workers about the areas where resources should be focused to help control HIV in the Kibera sex-working population.

Sensitivity analysis is done by deviating parameters slightly from their estimated value (found in the previous section), and measuring the change in the desired output. With prevalence and risk, both sexes can be examined separately, or the prevalence of the whole population can be examined. When conducting sensitivity analysis for the prevalence of the whole population the prevalence of each sex is weighted such that the effect of female prevalence on total prevalence is equal to the fraction of the total population that is female.

Here we do an elasticity analysis, a specific form of sensitivity analysis, where the elasticity of a with respect to b is

$$\frac{d \ln(a)}{d \ln(b)} = \frac{da}{db} \frac{b}{a}. \quad (5.3)$$

Use of this measure allows us to compare the different effects of parameters on the population's properties [7]. Table 5.2 gives the elasticity of these population properties with respect to the parameters.

Property	Init. Value	Elasticity of population properties to:					
		β_{MF}	β_{FM}	μ_F	μ_M	σ_F	σ_M
Prev _F	0.32	0.52	0.23	-0.02	-0.05	-0.19	0.51
Risk _F	6.1e-3	5.85	3.55	-0.00	-0.52	-4.28	6.66
Prev _M	0.21	0.01	0.00	-0.01	-0.01	-0.00	0.01
Risk _M	4.3e-4	0.64	0.84	-0.00	-0.04	-0.20	0.51
Prev _{Tot}	0.22	0.29	0.15	-0.02	-0.03	-0.15	0.31

Table 5.2: Elasticity of prevalence and risk in the population with respect to parameters

The probability of infection from males to females (β_{MF}) has a large effect on female prevalence, and average female risk. Not surprisingly, the infection probability from females to males also plays a large role in the average risk for males; recall that infection probability is directly involved in the calculation of risk.

As the two sexes are linked, logically when one sex has increased prevalence that effect carries over to increase the prevalence of the other sex; this can be seen for changes in all the parameters as all columns in Table 5.2 are of one sign.

A very interesting result from the analysis is the large effect of immigration; male immigration is the parameter with the largest effect on female risk, male prevalence, and prevalence of the total population. The immigration of females actually has a reverse relationship, with increases in female immigration causing decreases in prevalence and risk.

The repercussions and impact of these results will be further discussed in Chapter 7.

Chapter 6

Simpler Model

Theoretical analysis of the full system of equations (4.6) is complicated to pursue. In this chapter system (4.6) is simplified to a model with constant population (in total, and such that every N_k^F and N_k^M are positive constants) and this simpler model is analysed theoretically. The new model is a two-sex SI Pastor-Satorras and Vespignani model with constant populations and balanced birth and death, thus, since $S_k^F = N_k^F - I_k^F$ and $S_k^M = N_k^M - I_k^M$, only the I_k^F and I_k^M equations need to be considered. The model examined in this chapter is

$$\frac{dI_k^F}{dt} = \beta_{MF} k \theta_{MF} (N_k^F - I_k^F) - \gamma I_k^F, \quad (6.1a)$$

$$\frac{dI_j^M}{dt} = \beta_{FM} j \theta_{FM} (N_j^M - I_j^M) - \gamma I_j^M, \quad (6.1b)$$

where $k \in K_F$ and $j \in K_M$. Here K_F and K_M are the sets of classes containing only positive populations. This means, for example, that if there are no males with nine monthly contacts, then $9 \notin K_M$. This differs from (4.6) where no group can remain empty as individuals can shift into it from a group above or below. Additionally, parameters β_{MF} , β_{FM} and γ are positive. As in Section 4.2,

$$\theta_{MF} = \frac{\sum_{j \in K_M} j I_j^M}{\sum_{j \in K_M} j N_j^M}, \theta_{FM} = \frac{\sum_{k \in K_F} k I_k^F}{\sum_{k \in K_F} k N_k^F}. \quad (6.2)$$

The model is a special case of (4.6), without degree changes and no immigration or emigration ($\mu_F = \mu_M = \sigma_F = \sigma_M = 0$). Removing degree changes means the population, and thus the distributions of N_k^F and N_k^M , remain constant, and the total female and male populations, $\sum_{k \in K_F} N_k^F = N^F$ and $\sum_{k \in K_M} N_k^M = N^M$, respectively, are also constant. Additionally, so that the contacts between each sex match, it is necessary that

$$\sum_{k \in K_F} k N_k^F = \sum_{j \in K_M} j N_j^M. \quad (6.3)$$

This condition, when satisfied for the initial condition, is satisfied for all time following, as the populations are constant. Initially the infectious classes are assumed non-negative and are such that (6.3) is satisfied. Solutions remain in the non-negative invariant region bounded by N_k^F and N_j^M for $k \in K_F$ and $j \in K_M$; this will be shown in Proposition 6.0.1, but first the model is written in matrix form.

6.0.1 The Simplified Model in Matrix Form

Many of the propositions and theorems in this chapter are more straightforward when done with the model written in matrix form, instead of addressing each equation individually. Define a vector of all the infectious classes

$$\mathcal{X} = [I_{K_F(1)}^F \ I_{K_F(2)}^F \ \cdots \ I_{K_F(|K_F|)}^F \ I_{K_M(1)}^M \ I_{K_M(2)}^M \ \cdots \ I_{K_M(|K_M|)}^M]^T.$$

Next define a $(|K_F| + |K_M|) \times (|K_F| + |K_M|)$ matrix

$$F = \begin{bmatrix} 0 & F_1 \\ F_2 & 0 \end{bmatrix} \quad (6.4)$$

where $F_1 = \left[\beta_{MF} \frac{K_M(j)K_F(i)N_{K_F(i)}^F}{\sum_{k \in K_M} k N_k^M} \right]$ is a $|K_F| \times |K_M|$ matrix, and similarly

$F_2 = \left[\beta_{FM} \frac{K_M(i)K_F(j)N_{K_M(i)}^M}{\sum_{k \in K_F} kN_k^F} \right]$ is a $|K_M| \times |K_F|$ matrix. Defined as such, $F\mathcal{X}$ gives a vector of the first terms from the right hand side of (6.1), $\beta_{MF}k\theta_{MF}N_k^F$ and $\beta_{FM}j\theta_{FM}N_j^M$. To write the last term in matrix form create a $(|K_F| + |K_M|) \times (|K_F| + |K_M|)$ matrix, $V = \text{diag}(\gamma)$; thus the last term of (6.1) can be written $V\mathcal{X}$. The middle term is more complicated to write; it requires defining a vector $\bar{N} = [N_{K_F(1)}^F \ N_{K_F(2)}^F \ \cdots \ N_{K_F(|K_F|)}^F \ N_{K_M(1)}^M \ N_{K_M(2)}^M \ \cdots \ N_{K_M(|K_M|)}^M]^T$. Using this vector the middle term of (6.1) is written $\text{diag}(\mathcal{X}) \text{diag}(1/\bar{N})F\mathcal{X}$. With all the terms in place equation (6.1) can be rewritten in matrix form as

$$\frac{d\mathcal{X}}{dt} = F\mathcal{X} - V\mathcal{X} - \text{diag}(\mathcal{X}) \text{diag}(1/\bar{N})F\mathcal{X}. \quad (6.5)$$

This form of the equation will be used for some of the proofs in this chapter.

The following proposition gives the region in which solutions are invariant.

Proposition 6.0.1. *Given a non-negative initial number of infected individuals ($0 \leq I_k^F(0) \leq N_k^F$, $0 \leq I_j^M(0) \leq N_j^M$ for $k \in K_F, j \in K_M$) then the solution to (6.1) is invariant to a region such that $I_k^F \in [0, N_k^F] \forall k \in K_F$ and $I_k^M \in [0, N_k^M] \forall k \in K_M$.*

Proof. Given the initial conditions, solutions for individual infectious classes are bounded to $\mathbb{R}_{\geq 0}$, as $I_k^F \rightarrow 0^+$ implies $\frac{dI_k^F}{dt} \geq 0$, and similarly for males. The right-hand side of the system (6.1) is negative when $I_k^F = N_k^F$ and $I_j^M = N_j^M$. Along with the initial conditions, this keeps the infectious population below the total population. Thus $0 \leq I_k^F < N_k^F$ and $0 \leq I_j^M < N_j^M$. \square

By the definitions of θ_{MF} and θ_{FM} above, and the bounds on the infectious classes, it follows that $0 \leq \theta_{MF}, \theta_{FM} \leq 1$.

6.1 Disease Free Equilibrium

The model analyzed in this chapter, namely (6.1) and (6.5), has no immigration of infected individuals (unlike (4.6)), and thus there exists a disease free equilibrium (DFE), with $I_k^F = I_j^M = 0$, $S_k^F = N_k^F$, $S_j^M = N_j^M$, for all $k \in K_F, j \in K_M$, and $\theta_{MF} = \theta_{FM} = 0$.

6.1.1 Local Stability of DFE

To determine a local stability condition for the DFE, the basic reproduction number \mathcal{R}_0 is calculated using the next generation matrix method of [12, 34]. When $\mathcal{R}_0 < 1$ the DFE is locally asymptotically stable [12, 34].

Theorem 6.1.1. *If $\mathcal{R}_0 < 1$, then the DFE of (6.1) is locally asymptotically stable where*

$$\mathcal{R}_0 = \sqrt{\frac{\beta_{MF}\beta_{FM} \sum_{k \in K_F} k^2 N_k^F \sum_{j \in K_M} j^2 N_j^M}{\gamma^2 \sum_{k \in K_F} k N_k^F \sum_{j \in K_M} j N_j^M}}. \quad (6.6)$$

If $\mathcal{R}_0 > 1$, then the DFE is unstable.

Proof. Separate (6.1) into two parts, new infections \mathcal{F}_k and movement between compartments \mathcal{V}_k , giving $\mathcal{F}_k = \beta_{MF} k \theta_{MF} (N_k^F - I_k^F)$, and $\mathcal{V}_k = \gamma I_k^F$ for $k \in K_F$ and similarly for the male equations, such that

$$\begin{aligned} \frac{dI_k^F}{dt} &= \mathcal{F}_k - \mathcal{V}_k, & k \in K_F \\ \frac{dI_j^M}{dt} &= \mathcal{F}_{j+|K_F|} - \mathcal{V}_{j+|K_F|}, & j \in K_M. \end{aligned}$$

As per [12, 34], to find \mathcal{R}_0 , define two matrices, $F = \left[\frac{d\mathcal{F}_i}{d\mathcal{X}(j)} \right]$, and $V = \left[\frac{d\mathcal{V}_i}{d\mathcal{X}(j)} \right]$ where \mathcal{X} is as defined for the matrix model in Section 6.0.1; the derivatives are evaluated at the DFE. Thus F and V are as in the matrix model in Section 6.0.1.

With this notation \mathcal{R}_0 is the spectral radius of FV^{-1} [12, 34]. It is easy to determine that

$$G = FV^{-1} = \begin{bmatrix} 0 & G_1 \\ G_2 & 0 \end{bmatrix}$$

where $G_1 = \left[\beta_{MF} \frac{K_M(j)K_F(i)N_{K_F(i)}^F}{\gamma \sum_{k \in K_M} k N_k^M} \right]$, and $G_2 = \left[\beta_{FM} \frac{K_M(i)K_F(j)N_{K_M(i)}^M}{\gamma \sum_{k \in K_F} k N_k^F} \right]$, thus FV^{-1} has rank 2 and trace 0. The characteristic polynomial of the $(|K_F| + |K_M|) \times (|K_F| + |K_M|)$

matrix G can be simplified to $\lambda^{(|K_F|+|K_M|)-2}(\lambda^2 + \sum 2 \times 2 \text{minors}) = 0$. Finding the constant term of the quadratic gives:

$$\lambda^2 = \frac{\beta_{MF}\beta_{FM}}{\gamma^2} \frac{\sum_{k \in K_F} k^2 N_k^F \sum_{j \in K_M} j^2 N_j^M}{\sum_{k \in K_F} k N_k^F \sum_{j \in K_M} j N_j^M} \quad (6.8)$$

and so $\mathcal{R}_0 = \sqrt{\frac{\beta_{MF}\beta_{FM}}{\gamma^2} \frac{\sum_{k \in K_F} k^2 N_k^F \sum_{j \in K_M} j^2 N_j^M}{\sum_{k \in K_F} k N_k^F \sum_{j \in K_M} j N_j^M}}$. Therefore, by the results of [12, 34], the DFE is locally asymptotically stable when $\mathcal{R}_0 < 1$; whereas it is unstable when $\mathcal{R}_0 > 1$. \square

The \mathcal{R}_0 here is somewhat intuitive and analogous to that of the single sex SIS model; in the one sex model, $\mathcal{R}_0 = \frac{\beta}{\gamma} \left(\frac{\sum_k k^2 N_k}{\sum_k k N_k} \right)$. As calculated here, \mathcal{R}_0 is the geometric mean of an \mathcal{R}_0 for males and an \mathcal{R}_0 for females, where the geometric mean is the square root of the product. The reason for the geometric mean here is that the cycle for infection for each sex must go through the opposite sex: female-male-female and male-female-male. Often vector-host models (like those for Malaria or West-Nile virus) give a similar geometric mean, as each generation of disease must pass through another organism before coming back to the source [41].

Increasing β_{MF} , β_{FM} , or shifting the number of contacts of the male or female population higher increases \mathcal{R}_0 , and makes the spread of infection through the population easier. These results are intuitive, as greater infectivity and higher contact numbers will clearly lead to a greater number of infections.

6.1.2 Global Stability of DFE

In addition to showing local stability of the DFE of system (6.1), it is desirable to show the DFE is globally asymptotically stable when $\mathcal{R}_0 < 1$, as global stability indicates the disease can be controlled from any prevalence level (by reducing \mathcal{R}_0 to less than one).

Theorem 6.1.2. *Given equation (6.5), and $\mathcal{R}_0 < 1$, the disease free equilibrium ($\mathcal{X} = 0$) is globally asymptotically stable.*

Proof. Recall F, V and \mathcal{X} as defined in Subsection 6.0.1. By ignoring the nonpositive non-linear terms of (6.5)

$$\frac{d\mathcal{X}}{dt} \leq (F - V)\mathcal{X}, \quad (6.9)$$

Define a Lyapunov function, $L = \omega^T V^{-1} \mathcal{X} \geq 0$, where ω^T is the positive left-eigenvector of $V^{-1}F$ associated with \mathcal{R}_0 . To show global stability, in addition to L being positive definite, it is required that the time derivative of L along solutions of (6.5) be negative definite; see [35, Theorem 8.2]. Utilizing (6.9), taking the time derivative of L along a solution of (6.5) gives:

$$\frac{dL}{dt} = \omega^T V^{-1} \frac{d\mathcal{X}}{dt} \quad (6.10a)$$

$$\leq \omega^T V^{-1} (F - V) \mathcal{X} \quad (6.10b)$$

$$= \omega^T (V^{-1}F - \mathcal{I}) \mathcal{X} \quad (6.10c)$$

where \mathcal{I} is the $(|K_F| + |K_M|) \times (|K_F| + |K_M|)$ identity matrix. Since $\mathcal{R}_0 = \rho(FV^{-1}) = \rho(V^{-1}F)$ and FV^{-1} is irreducible, it follows that $\omega > 0$ and

$$\omega^T (V^{-1}F) = \mathcal{R}_0 \omega^T.$$

Thus $\frac{dL}{dt} \leq (\mathcal{R}_0 - 1)\omega^T \mathcal{X} \leq 0$ if and only if $\mathcal{R}_0 < 1$, with equality only occurring at $\mathcal{X} = 0$. Thus, when $\mathcal{R}_0 < 1$, the Lyapunov function is positive definite, $\frac{dL}{dt}$ is negative definite, and both are zero only at the DFE, resulting in global stability of the DFE when $\mathcal{R}_0 < 1$; see [35]. \square

6.2 Existence and Uniqueness of an Endemic Equilibrium

In addition to the disease free equilibrium, the existence and stability of possible endemic equilibria should be explored. Any equilibrium of the two-sex SIS model

must satisfy the following equations:

$$\begin{aligned}\beta_{MF}k\theta_{MF}(N_k^F - I_k^F) - \gamma I_k^F &= 0, & k \in K_F \\ \beta_{FM}j\theta_{FM}(N_j^M - I_j^M) - \gamma I_j^M &= 0, & j \in K_M.\end{aligned}$$

The equilibrium points for this system must then satisfy:

$$I_k^{F*} = \frac{\beta_{MF}k\theta_{MF}N_k^F}{\beta_{MF}k\theta_{MF} + \gamma}, \quad (6.12a)$$

$$I_j^{M*} = \frac{\beta_{FM}j\theta_{FM}N_j^M}{\beta_{FM}j\theta_{FM} + \gamma}. \quad (6.12b)$$

The solution of I_k^{F*} is dependent on $\theta_{MF} = \frac{\sum_{k \in K_M} k I_k^{M*}}{\sum_{k \in K_M} k N_k^M}$, and the solution of the male equation for I_j^{M*} is dependent on θ_{FM} . Substituting I_j^{M*} from (6.12) into the equation for θ_{MF} in (6.2) yields:

$$\theta_{MF} = \frac{\sum_{k \in K_M} k N_k^M \frac{\beta_{FM}k\theta_{FM}}{\beta_{FM}k\theta_{FM} + \gamma}}{\sum_{k \in K_M} k N_k^M} \quad (6.13)$$

Clearly, θ_{MF} and θ_{FM} can be expressed as functions of each other. It can be shown easily that $0 \leq \theta_{MF}, \theta_{FM} < 1$, as, for example,

$$\theta_{MF} \leq \sum \frac{\beta_{FM}k\theta_{FM}}{(\beta_{FM}k\theta_{FM} + \gamma)} \frac{\sum_{k \in K_M} k N_k^M}{\sum_{k \in K_M} k N_k^M} < 1$$

since $\gamma > 0$, and $\sum_k f(k)g(k) \leq \sum_k f(k) \sum_k g(k)$, for $f(k)$ and $g(k)$ positive. Further exploring of the relationship between θ_{MF} and θ_{FM} reveals the conditions for existence of an endemic equilibrium. The first and second derivatives of θ_{MF} and θ_{FM} , as calculated below, demonstrate that only one value for θ_{MF} and θ_{FM} can satisfy the existence condition for the endemic equilibrium.

Theorem 6.2.1. *When $\mathcal{R}_0 > 1$ a unique endemic equilibrium exists (along with the DFE), and when $\mathcal{R}_0 < 1$ only the DFE exists.*

Proof. From equation (6.13), the derivative $\frac{d\theta_{MF}}{d\theta_{FM}}$ takes the form:

$$\frac{d\theta_{MF}}{d\theta_{FM}} = \frac{1}{\sum_{k \in K_M} k N_k^M} \sum_{k \in K_M} k \frac{\beta_{FM} k N_k^M \gamma}{(\beta_{FM} k \theta_{FM} + \gamma)^2} \quad (6.14)$$

while $\frac{d\theta_{FM}}{d\theta_{MF}}$ is similar. Clearly, these values are positive, as all parameters are positive. A further derivative indicates the concavity of θ_{MF} and θ_{FM} , for example:

$$\frac{d^2\theta_{MF}}{d\theta_{FM}^2} = \frac{-2}{\sum_{k \in K_M} k N_k^M} \sum_{k \in K_M} k \frac{\beta_{FM}^2 k^2 N_k^M \gamma}{(\beta_{FM} k \theta_{FM} + \gamma)^3}. \quad (6.15)$$

Again, it is obvious these values are negative and so θ_{MF} is concave down with respect to θ_{FM} , and similarly θ_{FM} is concave down with respect to θ_{MF} . Figure 6.1 shows there exists an equilibrium at the DFE, and *at most* one other equilibrium: the endemic equilibrium. The existence of the second equilibrium is dependent on the derivatives of θ_{MF} and θ_{FM} at the origin. In order for an endemic equilibrium to exist, it is required that:

$$\left. \frac{d\theta_{MF}}{d\theta_{FM}} \right|_{\theta_{MF}=0} = \frac{\beta_{FM} \sum_{j \in K_M} j^2 N_j^M}{\gamma \sum_{j \in K_M} j N_j^M} > \frac{\gamma \sum_{k \in K_F} k N_k^F}{\beta_{MF} \sum_{k \in K_F} k^2 N_k^F} = \left(\left. \frac{d\theta_{FM}}{d\theta_{MF}} \right|_{\theta_{FM}=0} \right)^{-1} \quad (6.16)$$

When this condition is satisfied, θ_{MF} is originally below θ_{FM} ; as a result of the monotonicity and negative concavity, the two curves must then intersect in the region $(0, 1) \times (0, 1)$. Additionally, by (6.12) each infectious population can be determined; therefore a unique endemic equilibrium exists. A comparison of (6.8) and (6.16) reveals (6.16) is equivalent to $\mathcal{R}_0^2 > 1$.

□

In the next section, it is shown that when the endemic equilibrium exists, it is globally asymptotically stable.

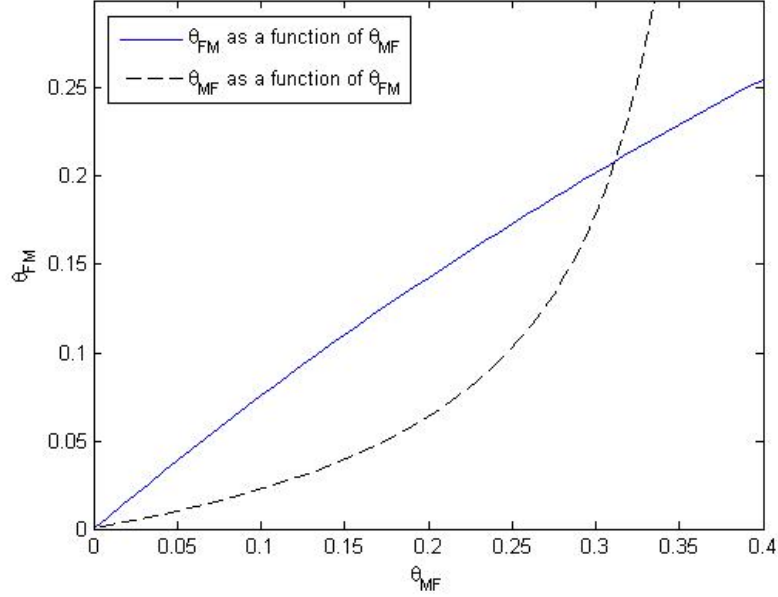


Figure 6.1: θ_{MF} and θ_{FM} are functions of each other, monotonically increasing, and concave down, thus they intersect with positive values exactly once if $\mathcal{R}_0 > 1$.

6.3 Global Stability of the Endemic Equilibrium

Following the method of Wang and Dai [38], we use a comparison theorem to show that if an endemic equilibrium exists, then it is globally asymptotically stable; however, before proving the main theorem, a few propositions are given since the proof requires a series of inequalities to demonstrate that solutions become squeezed to the endemic equilibrium. The decreasing sequences are straight-forward, however, in order to utilize the increasing sequences it must be shown that, with positive initial conditions, solutions remain positive and have a positive infimum.

The first proposition proves that given an initial supremum (or infimum) for each infectious class, we can find a smaller supremum (or larger infimum) for the same class. The inequalities found in the proposition are used to define the inequalities for the comparison theorem.

Proposition 6.3.1. *Given an infimum, $\underline{I}_k^F \geq 0$, and supremum, $\overline{I}_k^F \geq 0$, to the solution, $I_k^F(t)$, of (6.1) such that $\liminf_{t \rightarrow \infty} I_k^F(t) \geq \underline{I}_k^F$ and $\limsup_{t \rightarrow \infty} I_k^F(t) \leq \overline{I}_k^F$; with similar values for men, \underline{I}_k^M and \overline{I}_k^M , respectively, then new supremums and infimums of the form*

$$\limsup_{t \rightarrow \infty} I_k^F(t) \leq N_k^F \frac{\beta_{MF} k \overline{\theta_{MF}}}{\beta_{MF} k \overline{\theta_{MF}} + \gamma}, \text{ and} \quad (6.17a)$$

$$\liminf_{t \rightarrow \infty} I_k^F(t) \geq N_k^F \frac{\beta_{MF} k \underline{\theta_{MF}}}{\beta_{MF} k \underline{\theta_{MF}} + \gamma} \quad (6.17b)$$

can be found, where $\overline{\theta_{MF}} = \frac{\sum_{k \in K_F} k \overline{I_k^M}}{\sum_{k \in K_F} k N_k^M}$ and $\underline{\theta_{MF}} = \frac{\sum_{k \in K_M} k I_k^F}{\sum_{k \in K_M} k N_k^F}$. There are similar inequalities for males.

Proof. As $\limsup_{t \rightarrow \infty} I_k^M(t) \leq \overline{I_k^M}$, then $\forall \epsilon > 0$, there exists τ such that $\forall t \geq \tau$, $I_k^M(t) \leq \overline{I_k^M} + \epsilon$. From (6.1) it follows that:

$$\frac{dI_k^F}{dt} \leq \beta_{MF} k \frac{\sum_j j (\overline{I_j^M} + \epsilon)}{\sum_j j N_j^M} (N_k^F - I_k^F) - \gamma I_k^F \quad (6.18a)$$

$$= - [\beta_{MF} k \frac{\sum_j j (\overline{I_j^M} + \epsilon)}{\sum_j j N_j^M} + \gamma] I_k^F + \beta_{MF} k \frac{\sum_j j (\overline{I_j^M} + \epsilon)}{\sum_j j N_j^M} N_k^F \quad (6.18b)$$

Integration of (6.18b) gives:

$$I_k^F(t) \leq I_k^F(\tau) \left/ \exp \left(\left(\beta_{MF} k \frac{\sum_j j (\overline{I_j^M} + \epsilon)}{\sum_j j N_j^M} + \gamma \right) (t - \tau) \right) \right. \quad (6.19)$$

$$\left. + N_k^F \left(\beta_{MF} k \frac{\sum_j j (\overline{I_j^M} + \epsilon)}{\sum_j j N_j^M} \right) \left(\beta_{MF} k \frac{\sum_j j (\overline{I_j^M} + \epsilon)}{\sum_j j N_j^M} + \gamma \right)^{-1}$$

for $t \geq \tau$. Taking the limit as $\epsilon \rightarrow 0$, and $t \rightarrow \infty$ and using the definition of $\overline{\theta_{MF}}$ gives the desired inequality (6.17a). A parallel proof applies to the inequality (6.17b). \square

Note this technique is similar to that of Wang and Dai [38]; however, a result of modifying the model for two sexes is that these inequalities are functions of the limit

for the opposite sex. The inequalities found in the proposition are used to define the sequences in Theorem 6.3.1, the comparison theorem.

Solutions are bounded above as N_k^F, N_j^M are constant for all $k \in K_F, j \in K_M$. Thus supremums for the infectious classes exist; the next proposition is a required first step towards showing a positive infimum exists for the infectious classes.

Proposition 6.3.2. *Given a positive initial number of infectious individuals (with $\sum_{k \in K_F} I_k^F(0) + \sum_{k \in K_M} I_k^M(0) > 0$, $0 \leq I_k^F(0) \leq N_k^F$, $0 \leq I_j^M(0) \leq N_j^M$ for $k \in K_F, j \in K_M$) then for finite $t > 0$, the solution to (6.1) satisfies $I_k^F(t) > 0$, $I_j(t)^M > 0$, for $k \in K_F, j \in K_M$, $\theta_{MF} > 0$, and $\theta_{FM} > 0$.*

Proof. Given $\sum_{k \in K_F} I_k^F(0) + \sum_{k \in K_M} I_k^M(0) > 0$, either $\sum_{k \in K_F} I_k^F(0) > 0$ or $\sum_{k \in K_M} I_k^M(0) > 0$; arbitrarily assume $\sum_{k \in K_F} I_k^F(0) > 0$, implying $\theta_{FM} > 0$ at $t = 0$.

By a summation of (6.1a), it can be shown that θ_{FM} satisfies:

$$\begin{aligned} \frac{d}{dt} \left(\frac{\sum_{i \in K_F} i I_i^F}{\sum_{i \in K_F} i N_i^F} \right) &= \beta_{MF} \frac{\sum_{i \in K_F} i^2 (N_i^F - I_i^F)}{\sum_{i \in K_F} i N_i^F} \theta_{MF} - \gamma \frac{\sum_{i \in K_F} i I_i^F}{\sum_{i \in K_F} i N_i^F} \\ \frac{d\theta_{FM}}{dt} &= -\gamma \theta_{FM} + \beta_{MF} \frac{\sum_{i \in K_F} i^2 (N_i^F - I_i^F)}{\sum_{i \in K_F} i N_i^F} \theta_{MF}, \end{aligned} \quad (6.20a)$$

while θ_{MF} can be differentiated similarly. As the rightmost term is non-negative, (6.20) implies

$$\frac{d\theta_{FM}}{dt} \geq -\gamma \theta_{FM}$$

that, with the given initial conditions ($\theta_{FM}(0) > 0$), implies $\theta_{FM} > 0$ for finite $t > 0$. To show, similarly, that every I_k^M with $k \in K_M$ is positive, examine (6.1). By using the above property that $\theta_{FM} > 0$, (6.1b) can be rewritten as:

$$\frac{dI_k^M}{dt} + (\gamma + \beta_{FM} k \theta_{FM}) I_k^M > 0,$$

that can be integrated using an integrating factor of $\exp(\gamma t + \beta_{FM} k \int_0^t \theta_{FM}(\tau) d\tau)$. This integration yields

$$I_k^M(t) > I_k^M(0) \exp\left(-\gamma t - \beta_{FM} k \int_0^t \theta_{FM}(\tau) d\tau\right) \geq 0.$$

As such, for finite $t > 0$, $I_k^M > 0$. Based on the definition of θ_{MF} , it is clear that $I_k^M > 0$ implies $\theta_{MF} > 0$. The proof that $I_k^F > 0$ for $t > 0$ is as above for I_k^M , by using (6.1a). \square

The next proposition uses the matrix form of the model (equation (6.5)) and the result of the last proposition to show that I_k^F and I_j^M have a positive liminf when $\mathcal{R}_0 > 1$ for all $k \in K_F$ and $j \in K_M$, a requirement for the comparison theorem.

Proposition 6.3.3. *Assume $\mathcal{R}_0 > 1$. Given a positive initial infectious population (such that $\sum_{k \in K_F} I_k^F(0) + \sum_{k \in K_M} I_k^M(0) > 0$, $0 \leq I_k^F(0) \leq N_k^F$, $0 \leq I_j^M(0) \leq N_j^M$ for $k \in K_F, j \in K_M$) then the solution of (6.5) satisfies $\liminf_{t \rightarrow \infty} \theta_{MF}(t) > 0$, $\liminf_{t \rightarrow \infty} \theta_{FM}(t) > 0$, and for $k \in K_F, j \in K_M$, both $\liminf_{t \rightarrow \infty} I_k^F(t) > 0$ and $\liminf_{t \rightarrow \infty} I_j^M(t) > 0$.*

Proof. The same Lyapunov function used in the proof of Theorem 6.1.2 is used here: $L = \omega^T V^{-1} \mathcal{X}$. The function is positive definite, and we aim to show the derivative of L along a solution of (6.5) is positive definite in a neighbourhood of the origin (if $\mathcal{R}_0 > 1$). Recall from Section 6.0.1 that $V = \text{diag}(\gamma)$, and let $\Omega = \text{diag}(\omega)$. Using the matrix model (6.5), the time derivative of L is

$$\begin{aligned} \frac{dL}{dt} &= \omega^T V^{-1} [F \mathcal{X}(t) - V \mathcal{X}(t)] - \omega^T V^{-1} \text{diag}(\mathcal{X}(t)) \text{diag}(1/\bar{N}) F \mathcal{X}(t) \\ &\geq (\mathcal{R}_0 - 1) \omega^T \mathcal{X}(t) - (1/\gamma) (\Omega \mathcal{X}(t))^T \text{diag}(1/\bar{N}) F \Omega^{-1} \Omega \mathcal{X}(t), \end{aligned}$$

as $\omega^T \text{diag}(\mathcal{X}(t)) \text{diag}(1/\bar{N}) F \mathcal{X}(t) = (\Omega \mathcal{X}(t))^T \text{diag}(1/\bar{N}) F \mathcal{X}(t)$, and $\omega^T V^{-1} F = \mathcal{R}_0 \omega^T$. Examining the right hand term of the above expression it can be determined that

$$(1/\gamma)(\Omega\mathcal{X}(t))^T \text{diag}(1/\bar{N})F\Omega^{-1}\Omega\mathcal{X}(t) \leq (1/\gamma) \left\| \text{diag}(1/\bar{N})F\Omega^{-1} \right\| (\omega^T \mathcal{X}(t))^2$$

as $|(\Omega\mathcal{X}(t))^T \text{diag}(1/\bar{N})F\Omega^{-1}(\Omega\mathcal{X}(t))| \leq \left\| \text{diag}(1/\bar{N})F\Omega^{-1} \right\| \|\Omega\mathcal{X}\|^2$, and $\|\Omega\mathcal{X}\| = \omega^T \mathcal{X}$ (as $\omega, \mathcal{X} \geq 0$ when $\mathcal{R}_0 > 1$), where $\|A\| = \max_j \sum_i |a_{ij}|$ is the matrix 1-norm. Using this information, the time derivative of L satisfies the inequality

$$\frac{dL}{dt} \geq (\mathcal{R}_0 - 1)\omega^T \mathcal{X}(t) - (1/\gamma) \left\| \text{diag}(1/\bar{N})F\Omega^{-1} \right\| (\omega^T \mathcal{X}(t))^2 > 0$$

when $\mathcal{R}_0 > 1$, and $0 < \omega^T \mathcal{X}(t) \ll 1$. Thus for $\mathcal{R}_0 > 1$, with initial condition $\sum_{k \in K_F} I_k^F(0) + \sum_{k \in K_M} I_k^M(0) > 0$ the Lyapunov function prevents the system from approaching the DFE ($\mathcal{X}(t) = 0$), and so $\omega^T \mathcal{X}(t) > 0$; additionally, when the system is near the DFE, $\omega^T \mathcal{X}(t) \ll 1$. As such, there exists $\epsilon > 0$ such that $\omega^T \mathcal{X}(t) > \epsilon > 0$ for all $t > 0$.

Given $\omega^T \mathcal{X}(t) > \epsilon$, there exists $\epsilon^* > 0$ such that either $\theta_{FM}(t) > \epsilon^*$, or $\theta_{MF}(t) > \epsilon^*$ for all $t > 0$; arbitrarily, assume $\theta_{MF} > \epsilon^*$. Examining the equation for dI_k^F/dt from (6.1a) gives

$$\begin{aligned} \frac{dI_k^F(t)}{dt} &= \beta_{MF}k\theta_{MF}(t)(N_k^F - I_k^F(t)) - \gamma I_k^F(t) \\ &\geq \beta_{MF}k\epsilon^*(N_k^F - I_k^F(t)) - \gamma I_k^F(t) \\ &= -(\beta_{MF}k\epsilon^* + \gamma)I_k^F(t) + \beta_{MF}k\epsilon^*N_k^F. \end{aligned}$$

Solving the above ODE, there exists a t^* such that for $t > t^*$, and for all $k \in K_F$

$$I_k^F(t) \geq \frac{1}{2} \frac{\beta_{MF}k\epsilon^*N_k^F}{\beta_{MF}k\epsilon^* + \gamma} \geq \hat{\epsilon} > 0 \quad (6.23)$$

Thus, there exists $\bar{\epsilon} > 0$ such that

$$\begin{aligned}\theta_{FM}(t) &= \frac{\sum_{k \in K_F} k I_k^F(t)}{\sum_{k \in K_F} k N_k^F} \\ &\geq \frac{\sum_{k \in K_F} k \hat{\epsilon}}{\sum_{k \in K_F} k N_k^F} \geq \bar{\epsilon} > 0\end{aligned}$$

for all $t > 0$. Since $\theta_{FM}(t) \geq \bar{\epsilon} > 0$ it follows by the above argument that $I_k^M(t) \geq \tilde{\epsilon} > 0$ for all $t > 0$, $k \in K_M$.

Thus a vector $\underline{\mathcal{X}} = [\epsilon_{K_F(1)}^F \epsilon_{K_F(2)}^F \cdots \epsilon_{|K_F|}^F \epsilon_{K_M(1)}^M \epsilon_{K_M(2)}^M \cdots \epsilon_{|K_M|}^M]^T$ can be defined with $\epsilon_k^F, \epsilon_j^M > 0$ for all $k \in K_F, j \in K_M$, such that $\liminf_{t \rightarrow \infty} \mathcal{X}(t) \geq \underline{\mathcal{X}}$ \square

The final proposition guarantees that there is an initial infimum vector such that, when $\mathcal{R}_0 > 1$, solutions grow and a new, larger infimum vector can be determined. This condition will be necessary for the induction basis in the proof of global asymptotic stability (Theorem 6.3.1).

Proposition 6.3.4. *Given $\mathcal{R}_0 > 1$, $\epsilon > 0$, and initial vector $\underline{\mathcal{X}}^{(1)} = \nu \epsilon$, where ν is the right-eigenvector of $V^{-1}F$ associated to \mathcal{R}_0 (F and V as defined in Theorem 6.1.2), a second, componentwise larger vector $\underline{\mathcal{X}}^{(2)}$ can be found in terms of $\underline{\mathcal{X}}^{(1)}$.*

Proof. Given $\mathcal{R}_0 > 1$, let $\underline{\mathcal{X}}^{(1)}$ be a small multiple of the right-eigenvector of $V^{-1}F$ associated with \mathcal{R}_0 ; thus let $\underline{\mathcal{X}}^{(1)} = \nu \epsilon$.

When $\mathcal{R}_0 > 1$, the following holds

$$\begin{aligned}(\mathcal{R}_0 - 1)\underline{\mathcal{X}}^{(1)} - V^{-1} \text{diag}(\underline{\mathcal{X}}^{(1)}) \text{diag}(1/\bar{N})F\underline{\mathcal{X}}^{(1)} &> 0 \\ \text{equivalently, } (V^{-1}F - \mathcal{I})\underline{\mathcal{X}}^{(1)} - V^{-1} \text{diag}(\underline{\mathcal{X}}^{(1)}) \text{diag}(1/\bar{N})F\underline{\mathcal{X}}^{(1)} &> 0,\end{aligned}$$

as the left hand term dominates the right (recall, the vector $\underline{\mathcal{X}}^{(1)}$ is arbitrarily small). Left-multiplying the above with V gives

$$F\underline{\mathcal{X}}^{(1)} - V\underline{\mathcal{X}}^{(1)} - \text{diag}(\underline{\mathcal{X}}^{(1)}) \text{diag}(1/\bar{N})F\underline{\mathcal{X}}^{(1)} > 0.$$

The above inequality can be expressed as a series of equations instead of the current matrix form. This results in a series of inequalities; for example, a single equation from the female equations is shown

$$\beta_{MF} k \underline{\theta}_{MF}^{(1)} (N_k^F - \underline{I}_k^{F(1)}) - \gamma \underline{I}_k^{F(1)} > 0,$$

where $\underline{\theta}_{MF}^{(1)} = \frac{\sum_{k \in K_M} K I_k^{M(1)}}{\sum_{k \in K_M} K N_k^{M(1)}}$. Rearrangement of this inequality gives

$$\underline{I}_k^{F(2)} \equiv N_k^F \frac{\beta_{MF} k \underline{\theta}_{MF}^{(1)}}{\beta_{MF} k \underline{\theta}_{MF}^{(1)} + \gamma} > \underline{I}_k^{F(1)}.$$

This resulting right-hand side is the definition of $\underline{I}_k^{F(2)}$, for $k \in K_F$. The definition of $\underline{I}_j^{M(2)}$ for $j \in K_F$ is similar. As a result a vector $\underline{\mathcal{X}}^{(2)} > \underline{\mathcal{X}}^{(1)}$ exists. \square

The comparison theorem uses the previous four propositions to show that $\lim_{t \rightarrow \infty} I_k^F(t)$ exists and is non-zero. This is done by showing that $\liminf_{t \rightarrow \infty} I_k^F(t) = \limsup_{t \rightarrow \infty} I_k^F(t)$. This method works for the same way for I_k^M . The comparison theorem can now be proved; the increasing and decreasing sequences are defined in Proposition 6.3.1, and then the next three propositions set up the induction basis for the increasing sequences.

Theorem 6.3.1. *Given $\mathcal{R}_0 > 1$ and a positive initial number of infected individuals, the endemic equilibrium of (6.1) is globally asymptotically stable.*

Proof. This proof will be done using sequences and induction. The sequences defined in Proposition 6.3.1 will be shown to converge to the endemic equilibrium.

Let $\overline{I}_k^{F(1)} = N_k^F$, and define the sequence:

$$\overline{I}_k^{F(i+1)} = N_k^F \frac{\beta_{MF} k \overline{\theta}_{MF}^{(i)}}{\beta_{MF} k \overline{\theta}_{MF}^{(i)} + \gamma} \quad (6.26)$$

where $\overline{\theta}_{MF}^{(i)} = \frac{\sum_{k \in K_M} K \overline{I}_k^{M(i)}}{\sum_{k \in K_M} K N_k^{M(i)}}$. By the definition above in Proposition 6.3.4, it follows that $\overline{I}_k^{F(2)} = N_k^F \left(\frac{\beta_{MF} k \overline{\theta}_{MF}^{(1)}}{\beta_{MF} k \overline{\theta}_{MF}^{(1)} + \gamma} \right) < N_k^F = \overline{I}_k^{F(1)}$. Assuming the induction step (that

$\frac{\overline{I}_k^F(i)}{\overline{\theta}_{MF}^{(i)}} > \frac{\overline{I}_k^F(i+1)}{\overline{\theta}_{MF}^{(i+1)}}$) and using the fact that (6.26) is an increasing function of $\overline{\theta}_{MF}$, and $\frac{\overline{I}_k^F(i)}{\overline{\theta}_{MF}^{(i)}} > \frac{\overline{I}_k^F(i+1)}{\overline{\theta}_{MF}^{(i+1)}}$, it follows that

$$\frac{\overline{I}_k^F(i+2)}{\overline{\theta}_{MF}^{(i+2)}} \equiv N_k^F \frac{\beta_{MF} k \overline{\theta}_{MF}^{(i+1)}}{\beta_{MF} k \overline{\theta}_{MF}^{(i+1)} + \gamma} < N_k^F \frac{\beta_{MF} k \overline{\theta}_{MF}^{(i)}}{\beta_{MF} k \overline{\theta}_{MF}^{(i)} + \gamma} = \frac{\overline{I}_k^F(i+1)}{\overline{\theta}_{MF}^{(i+1)}} \quad (6.27)$$

So by induction the sequence of $\frac{\overline{I}_k^F(i)}{\overline{\theta}_{MF}^{(i)}}$, as defined above, is a decreasing sequence. By Proposition 6.3.1:

$$\limsup_{t \rightarrow \infty} I_k^F(t) \leq \frac{\overline{I}_k^F(i)}{\overline{\theta}_{MF}^{(i)}} \quad (6.28)$$

for all $k = 1, \dots, K$, and all $i \in \mathbb{Z}^+$. As the sequence is decreasing and $\frac{\overline{I}_k^F(i)}{\overline{\theta}_{MF}^{(i)}}$ is bounded below by $I_k^F > 0$, the sequence converges. Denote this by $\overline{I}_k^F = \lim_{i \rightarrow \infty} \frac{\overline{I}_k^F(i)}{\overline{\theta}_{MF}^{(i)}}$, and similarly by using the same method for males, $\overline{I}_k^M = \lim_{i \rightarrow \infty} \frac{\overline{I}_k^M(i)}{\overline{\theta}_{FM}^{(i)}}$.

By taking the limit of (6.26) as $i \rightarrow \infty$ and the male counterpart, \overline{I}_k^F and \overline{I}_k^M must satisfy:

$$\beta_{MF} k \overline{\theta}_{MF} (N_k^F - \overline{I}_k^F) - \gamma \overline{I}_k^F = 0 \quad (6.29a)$$

$$\beta_{FM} k \overline{\theta}_{FM} (N_k^M - \overline{I}_k^M) - \gamma \overline{I}_k^M = 0 \quad (6.29b)$$

where $\overline{\theta}_{MF} = \frac{\sum_k k \overline{I}_k^M}{\sum_k k N_k^M}$ and $\overline{\theta}_{FM}$ is similarly defined. The only available solution to (6.29), as shown in Section 6.2, is the endemic equilibrium.

Beginning from a lower bound requires more conditions. Utilizing Propositions 6.3.2, and 6.3.3 means that given initial conditions satisfying $\sum_{k \in K_F} I_k^F + \sum_{k \in K_M} I_k^M > 0$ and $\mathcal{R}_0 > 1$, positive lower bounds can be chosen such that $\underline{I}_k^{F(1)} = \epsilon_k^F > 0$ for $k \in K_F$, and $\underline{I}_k^{M(1)} = \epsilon_k^M > 0$ for $k \in K_M$. Define the sequence:

$$\underline{I}_k^{F(i+1)} = N_k^F \frac{\beta_{MF} k \underline{\theta}_{MF}^{(i)}}{\beta_{MF} k \underline{\theta}_{MF}^{(i)} + \gamma} \quad (6.30)$$

The induction basis is shown in Proposition 6.3.4, such that

$$\underline{I}_k^{F(2)} \equiv N_k^F \frac{\beta_{MF} k \theta_{MF}^{(1)}}{\beta_{MF} k \theta_{MF}^{(1)} + \gamma} > \underline{I}_k^{F(1)}.$$

Assuming the induction step,

$$\underline{I}_k^{F(i+2)} \equiv N_k^F \frac{\beta_{MF} k \theta_{MF}^{(i+1)}}{\beta_{MF} k \theta_{MF}^{(i+1)} + \gamma} > N_k^F \frac{\beta_{MF} k \theta_{MF}^{(i)}}{\beta_{MF} k \theta_{MF}^{(i)} + \gamma} = \underline{I}_k^{F(i+1)}. \quad (6.31)$$

By Proposition 6.3.1, $\limsup_{t \rightarrow \infty} I_k^F(t) \geq \underline{I}_k^{F(i)}$ for all $k \in K_F$, and all $i \in \mathbb{Z}^+$. Thus $\underline{I}_k^{F(i)}$ is a monotonic increasing sequence bounded above, that must converge. Defining these limits as $\underline{I}_k^F = \lim_{i \rightarrow \infty} \underline{I}_k^{F(i)}$ and $\underline{I}_k^M = \lim_{i \rightarrow \infty} \underline{I}_k^{M(i)}$, these limits must satisfy the equilibrium conditions.

As with the decreasing limit, the only solution is the endemic equilibrium. Therefore, $\liminf_{t \rightarrow \infty} I_k^F(t) = \limsup_{t \rightarrow \infty} I_k^F(t)$ and this occurs at the endemic equilibrium. Thus, if $\mathcal{R}_0 > 1$, the endemic equilibrium exists and must be globally asymptotically stable for the SI system. \square

This comparison method using a collection of converging sequences gives a new proof of the global stability of the endemic equilibrium of model (6.1) when $\mathcal{R}_0 > 1$. An alternative method using Lyapunov functions can be found in Lajmanovich and Yorke; see [22, 39]).

Chapter 7

Concluding Remarks

The modified Pastor-Satorras model is developed in response to the Kibera data (see Chapter 4). The model is appropriate for populations that have largely random contacts with individuals that immigrate to and emigrate from the population. Additionally, the model requires the disease to be a lifetime disease with transmission taking place through heterosexual activity. It is an especially good fit for the Kibera data due to the detail of contact frequency given by individuals.

Analytically, at least one endemic equilibrium exists (Theorem 4.3.1); however, numerical results of simulations imply that a unique endemic equilibrium exists. Recall that no disease free equilibrium exists for the modified Pastor-Satorras and Vespignani model, as there is constant immigration of infectious individuals.

If further data indicate that the Kibera population is largely static, and that individual's monthly change in number of contacts is negligible, then analytical results from Chapter 6 can be applied to the population. This simpler model allows for much more powerful analysis, with proven global asymptotic stability of the endemic equilibrium.

Parameterized to fit the Kibera data, the parameters that are most likely to produce the data are similar in magnitude to those that have been estimated in previous studies. Specifically, the probability of HIV transmission per sexual act agrees with previous estimates. These also indicate that, per sexual act, an infectious male is more likely to infect a susceptible female than a female is to infect a male. This result is

similar to those of previous studies, and is partly responsible for the higher risk and prevalence of HIV among females [14, 15, 17]. Note that, of course, some individuals involved in the sex trade of Kibera may currently use condoms or receive treatment for HIV (which lower transmission probability); thus, the estimated probability of infection per sexual act is an average covering all situations. Most previous studies that estimate probability of transmission are also of large groups of people engaging in different behaviour, and therefore are also average transmission probabilities, and not the basic probability of HIV transmission per sexual act where no measures to reduce transmission have been taken.

Immigration and emigration rates are difficult to estimate from the data collected; however, anecdotal estimates for emigration exist. These estimates tend to indicate that individuals remain involved with the sex trade for short periods of time, on the scale of a few months to a few years. In contrast, the estimates for emigration in Chapter 5 imply that individuals are involved in the sex trade for their entire lives. These small emigration rate estimates are, in part, due to the fact that in the Kibera data prevalence of HIV among those involved in the sex trade is higher than prevalence of those outside the population (27.2% versus 13.2% for females, and 16.0% versus 10.6% for males). This, and the fact that probability of infection per sex act is low, means that estimated emigration rates are lower than anticipated. If the emigration rates are higher then the prevalence in the population involved in the sex trade will drop as individuals will not have as much time to become infected. Thus, as an effect of maximizing the likelihood that the parameters produce the Kibera data, the estimated emigration rates are unexpectedly low.

The parameter estimates for immigration are difficult to verify, but as with the probability of HIV transfer, the estimates of these immigration parameters have the ratio expected, with more males than females becoming involved in the sex trade per month.

Due to transmission in the model relying entirely on heterosexual sex, parameters that greatly affect risk and prevalence in one sex also have large effects on the other. This result implies that a focus on reducing the probability of transmission for one sex benefits both sexes. This is useful knowledge because implementing harm reduction strategies with sex workers is more straightforward as there are many more males involved with the sex trade than females, and sex workers are often in contact with one another, allowing for flow of information.

This is especially useful when considering intervention practices which affect just one parameter. Condoms, for example, reduce HIV transmission probabilities for both sexes; however, highly active antiretroviral therapy (HAART) greatly reduces the transmission rate of the person being treated. Examining the elasticity of the total populations' prevalence to both infection probabilities would seem to indicate that men should be targeted for treatment (as infection from males to females has almost twice the effect on prevalence as infection from females to males). But when taking into account the estimated number of individuals involved in sex work, treating females with HAART could be 3.5 times as efficient as treating males.

The result that reducing risk and prevalence for one sex has similar results for the opposite sex is seen in the elasticity analysis. This analysis shows that in addition to transmission probability having a large effect on prevalence and risk in the population (as expected), the rates of immigration to and emigration from the population also affect these properties. Increasing male immigration causes the prevalence of HIV and the risk to individuals to increase for both sexes; this is a result of σ_M having a direct effect on the average number of contacts for females. If all other parameters remain constant, an increase in σ_M increases the demand for sex work, resulting in sex workers shifting to have more contacts; this shift results in an increased average number of monthly contacts for sex workers, thus increasing risk and HIV prevalence among sex workers.

Increasing female immigration causes an opposite effect, however, as there are many more males than females. Increased female immigration does cause the average number of male contacts to increase, however there are many more males than females, and so the average number of contacts for males increases only slightly. The more powerful effect of increased female immigration is that, as the prevalence of incoming females is 13.2% (much lower than that of the population involved in the sex trade), increasing female immigration flushes the population with low prevalence females. This effect overcomes the comparatively small effect of increased number of male contacts to actually reduce the risk for males. Similarly, reduced prevalence in females and reduced risk in males causes male prevalence to drop, thus reducing risk for females. This result, however, is also a consequence of modelling the population involved with the sex trade alone. If the model were of all of Kibera, increasing the number of people who become involved in sex work would decrease the prevalence of HIV in the population involved in sex work.

Additionally, methods to control HIV generally focus on reducing transmission and trying to assist sex workers in finding other income, as increasing the number of individuals involved in sex trade to lower the prevalence of HIV among sex workers is not ethical.

Increasing the rates at which males and females leave the sex trade caused decreases in risk and prevalence. This result is intuitive with the model, as increasing the emigration rate of either sex reduces demand for the other sex, which causes the average number of monthly contacts to decrease, which reduces risk. The proportional effect of emigration on these properties is small compared to other parameters, however, and this method of control is difficult to use as individuals are generally involved in sex work out of necessity.

Methods to reduce the probability of infection are much more commonly used as prevention for HIV. In particular, methods to reduce transmission generally include promoting condom use and increasing the number of individuals who receive treatment (HAART). It has been suggested that individuals who are on HAART not only have lower infectivity, but are also less likely to engage in risky behaviour [8, 19]. According to the sex workers interviewed for the Kibera data, condoms were not used with approximately 25% of their clients. This leaves the question open as to, not only, "what is the effect of reducing the probability of transmission?", but also, "what would happen if condom use decreased?" Condom use would have direct effect on the probability of infection per sex act while other parameters would remain largely the same. Thus the effect of condom use could be studied using the model as it currently exists.

For individuals involved in the sex trade of Kibera, the model results indicate that reducing the probability of transmission through condom use should be effective in reducing HIV prevalence and risk of infection. However, it predicts that these methods are effective at the current prevalence levels. The infection probability per sexual act should correlate linearly with changes in condom use; however, changes in infection probability will not necessarily correlate linearly with prevalence, i.e., decreases in infection probability will always cause prevalence to decrease but may not do so proportionally.

Reducing the probability of infection per sexual act is a current method being utilized through the promotion of condom use and HIV treatment to reduce the effect of HIV

in Kibera, especially among sex workers[26]; the results from the model support this action, as reducing infection probability for either sex significantly reduces the prevalence of HIV and the risk of infection for individuals of both sexes.

More complicated than modelling condom use is incorporating HAART into the model. Adding treatment reduces the probability of transmission, but also extends the length of time people can remain in the population while being HIV positive [40]; this increase of time in the population means that infectious individuals can have more sexual partners before developing AIDS. It is not clear whether the net effect causes an increase or decrease in prevalence, though further studies with an extension of this model could assist in that problem. New classes of infectious females and males receiving treatment would need to be created, where the probability of infection per sexual act would be reduced, and the removal rate γ due to HIV would be decreased to increase the length of time infectious individuals remain in the population.

The Kibera data were collected just once; thus the assumption is made that the data represents a static population. Ideally the survey should be collected again so the model could be fit to predict how the population is changing. This collection of data could also include questions that would assist in determining the immigration and emigration parameters directly from the data. Further data collection could allow for more in depth analysis and perhaps different parameterization for the immigration and emigration parameters. Future work to include treatment could assist in determining whether this is an effective measure to reduce HIV in the group of individuals involved in the sex trade of Kibera.

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