The Impact of Random Screening and Contact Tracing in Reducing the Spread of HIV *

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November 16, 2000

Abstract

Mathematical models can help predict the effectiveness of control measures on the spread of HIV and other sexually transmitted diseases by reducing the uncertainty in assessing the impact of intervention strategies such as random screening and contact tracing. Even though contact tracing is one of the most effective methods used for controlling treatable sexually transmitted diseases, it is still a controversial strategy for controlling HIV because of cost and confidentiality issues. To help estimate the effectiveness of these control measures, we formulate two models with random screening and contact tracing based on

*This research was supported by the Department of Energy under contracts W-7405-ENG-36 and the Applied Mathematical Sciences Program KC-07-01-01.

the differential infectivity model and the staged-progression model. We derive formulas for the reproductive numbers and the endemic equilibria and compare the impact that random screening and contact tracing have in slowing the epidemic in the two models. In the differential infectivity model the infected population is divided into groups according to their infectiousness, and HIV is largely spread by a small, highly infectious, group of superspreaders. In this model contact tracing is an effective approach to identifying the superspreaders and has a large effect in slowing the epidemic. In the staged-progression model every infected individual goes through a series of infection stages and the virus is primarily spread by individuals in an initial highly infectious stage or in the late stages of the disease. In this model contact tracing is only slightly more effective than random screening. Thus the effectiveness of the intervention strategy strongly depends on the underlying etiology of the disease transmission.

1 Introduction

Mathematical models based on the underlying transmission mechanisms of the disease can help the medical/scientific community understand and anticipate the spread of an epidemic and evaluate the potential effectiveness of different approaches for bringing an epidemic under control. Models can be used to improve our understanding of the essential relationships between the social and biological mechanisms that influence the spread of a disease. The relative influence of various factors on the spread of the epidemic, as well as the sensitivity to parameter variation, can be ascertained. Because the transmission dynamics form a complex nonlinear dynamical system, the behavior of the epidemic is a highly nonlinear function of the parameter values and levels of intervention strategies. This at times may even lead to changes in infection spread that are counter to both intuition and simple extrapolated predictions. We can use the knowledge gained from studying models to help set priorities in research, saving time, resources, and lives.

Screening is one of the most common strategies used to control the spread of HIV infection. State health services provide anonymous or confidential screening to individuals who come in on a voluntary basis, perhaps because they believe they may have been exposed to HIV by a particular behavior, or they are part of a higher risk group. Infected individuals are identified through the testing of all blood donations or as a regular part of a blood test, and pregnant women are often screened for HIV infection. Models can be used to study the impact of such screening programs. They can also be applied to study more costly contact tracing programs.

Contact tracing, also known as “partner notification by provider referral” is one of the most effective strategies for controlling treatable sexually transmitted diseases (STDs) such as syphilis and gonhorrhea. These programs ask infected individuals to identify other people whom they may have infected or been infected by. Trained personnel then attempt to contact the named partners, inform them that they had an infected partner, educate them, and provide them with opportunities to be themselves tested for the infection. If they are infected, they can begin treatment and stop unknowingly spreading infection.

Although contact tracing has been used for years as a method for controlling curable STDs, and has been very effective for them, it remains controversial and hotly-debated as a strategy for controlling HIV. The advantages of identifying partners of those infected with HIV are not as clear as they are with easily treated infections, but the gravity of HIV infection and the epidemic itself, cause many to argue that it needs to be done.

Some of the reasons people argue against contact tracing are confidentiality issues, the cost of the program, and the likelihood that fewer people will come in for testing. Some specialists in the field argue that the cost and the risks of putting people at serious risk of ostracization and even physical harm from others are not worth it. People are less likely to voluntarily be tested when they will be asked, or even required by law, to name their sexual partners. This is of particular concern when there is the possibility of domestic violence [1, 26, 31]. There are also many other reasons people do not wish to name their partners. Until recently, very little could be done for HIV-infected people, and thus informing them of their infection was like handing them a death sentence. Many health service workers were reluctant to do this.

Other specialists in the field have argued that contact tracing is more effective than screening programs, which often attract mostly the worried well who are not at much risk [5,18]. It is also argued that the rights of those who have been exposed to know about their exposure, and the need to stop the chain of infection, should supersede the rights of the infected to privacy [28]. Many studies have found that contact tracing is an effective strategy for finding and counseling infected people [14,21,29,31]. Another argument in favor of contact tracing is that it can “delineate the risk networks hosting transmission and provide empiric estimates for mathematical model parameters [23].”

With today’s new treatments for HIV infection, some of the earlier arguments against contact tracing are less valid, since there are more and more reasons to attempt to identify infected people as early in the course of infection as possible to allow them to be promptly treated and to reduce the chance that they will unknowingly transmit the disease to other susceptibles.

While it seems likely that contact tracing could be as effective in controlling the spread of HIV as it has been for other STDs, there are few analytical studies to estimate what fraction of the population should be screened, what fraction of their partners should be contacted in order for the program to have a significant effect on the spread of the epidemic, or how much the behavior of this tested population needs to change. Modelers are beginning, however, to develop models which are capable of studying these questions. Kretzchmar et al. [13] used simulations of the spread of gonorrhea and chlamydia to study random screening and contact tracing, finding that, for their model, treatment of even a small fraction of the partners of those with symptoms could completely halt the epidemic, whereas screening of even large fractions of the population had little effect. Müller et al. [20] analytically studied contact tracing and screening in a stochastic model of a simple SIRS (susceptible-infected-removed-susceptible) epidemic in a population of fixed size. They derived formulas for the reproductive number under different assumptions, and, using the reproductive number from their stochastic model, created a deterministic model with the same reproductive number. Both of these models neglect “snowballing”, the situation where not only the partners of the originally screened infecteds, but also the the partners of those partners, and so on, are traced, until no more infected individuals are found. These models also neglect the situation where a past partner of an infected individual was infected by someone else either before or after their partnership.

Here we use a different methodology to develop two models for HIV spread which includes contact tracing and random screening in populations which do not have a constant size. We develop the models directly as differential equations, using approximations to estimate terms in our equations, rather than attempting to derive them from a stochastic or simulation model. Differential equations allow us to quickly obtain insights into the dynamics of the two models. Like Müller et al. [20], we neglect snowballing, but we do account for the possibility that partners of infecteds were infected by someone other than the index case.

These models are extensions of the two models developed in detail in [8, 9]. We have chosen them specifically to address questions about whether or not contact tracing can be effective given that viral loads vary so much between individuals and within individuals over the course of their infection. The differential infectivity (DI) model divides the infected population into groups according to their infectiousness, and accounts for differences in rates of developing AIDS. In contrast with this model, we also studied a simple version of a staged-progression (SP) model, in which every infected individual goes through the same series of stages. This model has a short early highly infectious stage equivalent to the acute phase of infection, a middle period of low infectiousness, and a late chronic stage with higher infectiousness. Thus the DI model captures individual differences and the SP model captures differences in time within the same individual.

In [8, 9] we simulated the transient dynamics and studied the sensitivity of both models using parameters that we derived from the literature. We also developed a robust method for initializing multigroup epidemic models. For the SP model, these studies provided further insight into the observations in [11, 12] that when partner acquisition rates are high the bulk of the infections early in the epidemic are caused by those in the acute infectious stage. For the DI model, we showed that a small number of individuals who are highly infectious during the chronic stage have a disproportionate impact on the epidemic, even though they have a short life expectancy. Both models were found to be very sensitive to the probability of transmission per contact and the sexually active removal rate.

In this paper we first review the mathematical formulation of the original DI and SP models, and then reformulate them to include random screening and contact tracing. We find reproductive numbers for both models, and show that they have a unique endemic equilibrium which exists if and only if the epidemics are above threshold. Then we analyze the models to assess the impact of intervention strategies. We use numerical simulations to compare the impact of the strategies on the epidemic. Random screening does slow the epidemic, but not a great deal for either model. For the DI model, contact tracing is an effective approach to identifying the superspreaders and has a large effect in slowing the epidemic. However, for the SP model contact tracing is only slightly more effective than random screening. We use our analytical formulas for the reproductive numbers and the endemic equilibria to examine in more detail the sensitivity of both models to the level of intervention strategy. If the SP model holds, then it would appear that contact tracing will primarily identify individuals after they are past the infectious stage, and thus public health will not be served by an expensive contact tracing program. However, if the DI model is closer to the underlying disease etiology, then the epidemic can be significantly slowed if the superspreader group can be identified and removed from the transmission network.

2 The DI and SP Models

Here we briefly describe the DI and SP models without random screening or contact tracing and review the analysis for R_0 and the endemic equilibrium [8, 9]. The intervention strategies will be added to these basic models in the next section.

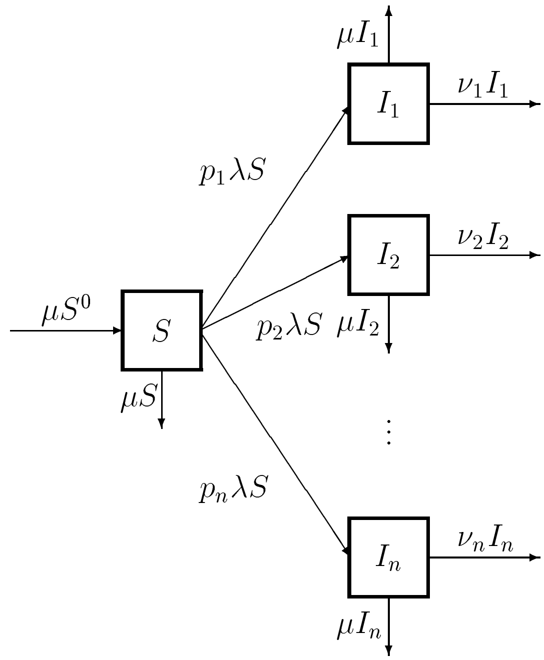

Figure 2.1: The DI model divides the infected population into groups according to their infectiousness or differences in rates of developing AIDS. In this model HIV is primarily spread by a small, highly infectious, group of superspreaders.

2.1 The DI model

During the chronic stage of infection, viral levels differ by many orders of magnitude between individuals. Those with high viral loads in the chronic phase tend to progress rapidly to AIDS, while those with low loads tend to progress slowly to AIDS [3, 4, 22, 30]. The DI model accounts for the distribution of times from infection to AIDS by assuming variations between individuals in their duration of infection, dividing the infected population into n groups.

The equations for the DI model illustrated in Fig. 2.1 are:

$$\begin{aligned}
\frac{dS}{dt} &= \mu(S^0 - S) - \lambda S, \\
\frac{dI_i}{dt} &= p_i \lambda S - (\mu + \nu_i) I_i, \qquad i = 1, \cdots, n, \\
\frac{dA}{dt} &= \sum_{j=1}^{n} \nu_j I_j - \delta A. \\
\lambda(t) &= \sum_{i=1}^{n} \lambda_i(t), \quad \lambda_i(t) = r\beta_i \frac{I_i(t)}{N(t)},
\end{aligned} \tag{2.1}$$

where $N(t) = S(t) + \sum_{j=1}^{n} I_j(t)$. Here S denotes the susceptibles, I_i denotes the number of infected individuals in group i, and A denotes the number of infected individuals no longer transmitting the disease. S^0 is the constant steady state population maintained by the inflow and outflow when no virus is present in the population. The total removal rate μ accounts for both natural death in the absence of HIV infection and people moving in and out of the sexually active susceptible population due to behavior changes or physical migration. $\lambda(t)$ is the rate of infection per susceptible, r is the partner acquisition rate, and β_i is the probability of transmission per partner from infected individuals in group i. Upon infection, an individual enters subgroup i with probability p_i, where $\sum_{i=1}^{n} p_i = 1$, and stays in this group until becoming inactive in transmission. Finally, ν_i is the rate at which infected individuals in group i enter group A, and δ is the death rate of people in group A. All infected individuals are assumed to eventually enter group A prior to death due to their infection.

2.2 The SP model

The viral burden during HIV infection varies as a function of time within an individual. Initially, the HIV-1 RNA levels in plasma and serum can become extremely high during the first weeks of acute primary infection, even before there is a detectable immune response [24, 25]. These levels are higher than at any other time during infection. Acute primary infection is followed by a chronic phase during which the HIV RNA levels drop several orders of magnitude and remain at a nearly constant level

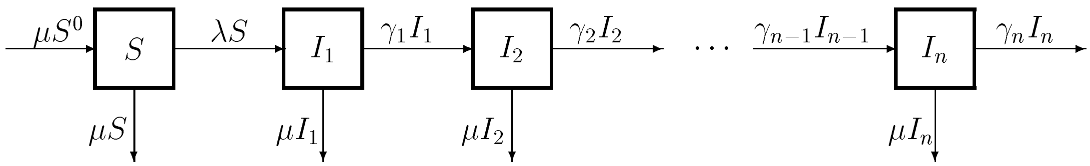

Figure 2.2: In the SP model every infected individual goes through the same series of stages. This model can account for a short early highly infectious stage equivalent to the acute phase of infection, a middle period of low infectiousness, and a late chronic stage with higher infectiousness.

for years [7, 22, 30]. In the late chronic stages of an infection the HIV-1 RNA levels may increase as much as ten fold [7] over what they have been during the rest of the chronic stage. The SP model accounts for the temporal changes in the infectiousness of an individual by a staged Markov process of n infected stages progressing from the initial infection to AIDS.

The equations for the SP model illustrated in Fig. 2.2 are:

$$\begin{aligned}
\frac{dS}{dt} &= \mu(S^0 - S) - \lambda S, \\
\frac{dI_1}{dt} &= \lambda S - (\gamma_1 + \mu) I_1, \\
\frac{dI_i}{dt} &= \gamma_{i-1} I_{i-1} - (\gamma_i + \mu) I_i, \qquad 2 \le i \le n, \\
\frac{dA}{dt} &= \gamma_n I_n - \delta A, \\
\lambda(t) &= \sum_{i=1}^{n} \lambda_i(t), \quad \lambda_i(t) = r\beta_i \frac{I_i(t)}{N(t)},
\end{aligned} \tag{2.2}$$

where now I_i is the number of infected individuals in each infected stage. Note that all individuals go into group 1 upon infection. γ_i is the rate at which individuals move from stage i of infection to stage $i+1$. The meanings of S^0, μ, r, and δ are the same as in the DI model, and β_i is the probability of transmission per partner from infected individuals in stage i. Previous studies of SP models can be found in [2,10–12,15–17].

2.3 Transmission Probability

The parameter r enters the model both as a multiplicative factor and through the dependence of the transmission probabilities per partner, β_i, on the average number of contacts per partner, c, which in turn depends on the number of contacts per partner ($c = c(r)$).

If ζ_i is the transmission probability per contact in group i, the probability that a susceptible individual will not be infected by a single contact with an infected individual is $1 - \zeta_i$. Hence the probability that a susceptible individual will avoid infection when they have $c(r)$ contacts with an infected partner is $(1 - \zeta_i)^{c(r)}$, and the probability of transmission per partner from an infected person in group i is

$$\beta_i = 1 - (1 - \zeta_i)^{c(r)}. \tag{2.3}$$

Our choice for $c(r) = 104r^{-\eta} + 1$ in Section 5 gives approximately two contacts per week for people with one partner per year, and decreases to about one contact per partner as r gets large [9]. The parameter η controls how fast this function decreases. In the simulations presented in Section 5, we set $\eta = 1$.

Let $\bar{\tau}_i$ be the mean duration of infection in group i. Then, for DI model, $\bar{\tau}_i = 1/(\mu + \nu_i)$, and for the SP model, $\bar{\tau}_i = 1/(\mu + \gamma_i)$. The mean duration of infection for the whole population for the DI model and SP model are given by $\bar{\tau} = \sum_{i=1}^{n} p_i \bar{\tau}_i$ and $\bar{\tau} = \sum_{i=1}^{n} q_i \bar{\tau}_i$, respectively. Based on these notations, the mean transmission probability per contact $\bar{\zeta}$ for the DI and SP models are

$$\bar{\zeta}^D = \sum_{i=1}^{n} p_i \frac{\bar{\tau}_i}{\bar{\tau}} \zeta_i, \quad \bar{\zeta}^S = \sum_{i=1}^{n} q_i \frac{\bar{\tau}_i}{\bar{\tau}} \zeta_i. \tag{2.4}$$

2.4 The Reproductive Number and Endemic Equilibrium

We proved in [8] that both of these models have two equilibria: the infection-free equilibrium given by ($S = S^0, I_i = 0$), and the endemic equilibrium given by ($S = S^* > 0, I_i = I_i^* > 0$). The endemic equilibrium is the asymptotic distribution of the infection in the population once the initial transients have settled down. Analyzing the stability of the infection-free equilibrium gives the reproductive number, which specifies the conditions under which the number of HIV infected individuals will initially increase or decrease when there are a small number of them at the start. The reproductive number, R_0 is defined such that if $R_0 < 1$ the modeled epidemic dies out and if $R_0 > 1$ the epidemic spreads for most models [6]. The reproductive number is obtained by investigating the stability of the infection-free equilibrium at which the components of infected groups are zero. If $R_0 < 1$, this infection-free equilibrium is the unique equilibrium. If $R_0 > 1$, the infection-free equilibrium becomes unstable and there appears, for both models, a unique endemic equilibrium at which the components of infected groups are positive.

The reproductive number can be written

$$R_0 = r\bar{\tau}\bar{\beta} \tag{2.5}$$

for both models. Here $\bar{\tau}$ is the mean duration of infection, and $\bar{\beta}$ is the mean probability of transmission per partner. We also found formulas for the endemic equilibrium, and proved that there exists a nontrivial equilibrium if and only if the reproductive number R_0 is greater than 1. If the endemic equilibrium exists, it is always locally asymptotically stable. The formulas for all of these quantities are given in Table 2.1.

The relative importance of each infection group in maintaining the chain of transmission is measured by the relative fraction of individuals being infected by each group. The *relative impact* of I_i on the rate of infection is

$$\rho_i(t) = \frac{\lambda_i(t)}{\lambda(t)} = \frac{\beta_i I_i(t)}{\sum_{j=1}^{n} \beta_j I_j(t)}. \tag{2.6}$$

Note that the formulas for the DI and SP models in Table 2.1 have the same form, with p_i and ν_i from the DI model being replaced by q_i and γ_i for the SP model formulas. However, while it could be argued that ν_i and γ_i are both progression rates and thus play similar roles in both models, q_i is quite different from p_i. Not only is q_i a derivative quantity, but also $q_1 = 1$ so that the sum of the q_i is larger than one, while the p_i sum to one. The similarity of formulas can be deceptive in making the models appear more similar than they are.

Table 2.1: Reproductive number R_0, mean duration of infection in group i, $\bar{\tau}_i$, mean duration of infection for the whole population $\bar{\tau}$, mean transmission probability $\bar{\beta}$, equilibrium infection rate λ^*, susceptible population S^*, equilibrium infected group population I_i^*, equilibrium total infected population I_T^*, and equilibrium relative impact ρ_i^* for both models.

Name	DI Model	SP Model	Name	DI Model	SP Model
R_0	$r\bar{\tau}\bar{\beta}$	$r\bar{\tau}\bar{\beta}$	S^*	$\dfrac{\mu S^0}{\mu+\lambda^*}$	$\dfrac{\mu S^0}{\mu+\lambda^*}$
$\bar{\tau}_i$	$\dfrac{1}{\mu+\nu_i}$	$\dfrac{1}{\mu+\gamma_i}$	I_i^*	$p_i\bar{\tau}_i S^*\lambda^*$	$q_i\bar{\tau}_i S^*\lambda^*$
$\bar{\tau}$	$\sum_{i=1}^n p_i\bar{\tau}_i$	$\sum_{i=1}^n q_i\bar{\tau}_i$	I_T^*	$S^*(R_0-1)$	$S^*(R_0-1)$
$\bar{\beta}$	$\sum_{i=1}^n p_i\beta_i\bar{\tau}_i/\bar{\tau}$	$\sum_{i=1}^n q_i\beta_i\bar{\tau}_i/\bar{\tau}$	λ^*	$\dfrac{R_0-1}{\bar{\tau}}$	$\dfrac{R_0-1}{\bar{\tau}}$
q_i	undefined	$\prod_{j=1}^{i-1}\gamma_j\bar{\tau}_j$	ρ_i^*	$\dfrac{p_i\beta_i\bar{\tau}_i}{\bar{\beta}\bar{\tau}}$	$\dfrac{q_i\beta_i\bar{\tau}_i}{\bar{\beta}\bar{\tau}}$

3 Random Screening and Contact Tracing Models

In this section we modify the DI and SP models to account for random sampling and active identification of infected people. The active contact tracing program is modeled on the assumption that when someone has been identified as infected by random sampling this person is asked to identify his/her partners for the past T_M years, and that a fraction f of those past partners are located and tested for HIV infection. In this initial simple model we neglect the snowball effect where someone identified through contact tracing names their partners; that is, we neglect any people who are traced as contacts of contacts. We also assume that all identified infected people subsequently refrain from engaging in activities that would continue to transmit the virus.

We assume the rate, σ, that someone is identified as infected by random sampling is homogeneous in the population. Thus we subtract a term σI_i from the equation for the infected group, I_i, and add it into the equation for a new group, I_{C_i}, the tested and identified infected people.

The rate that the active contact tracing program identifies infected people is the sum of two terms: identification by people who were already infected when they had contact with the identified infected people, and identification by people who were not infected before they had contact with the identified infected people and subsequently became infected. We approximate the last group by people who became infected at the time they were a partner of the identified infected people. We assume that activity levels are high and that people can only identify their past partners and provide contact information (such as phone numbers) for the past T_M years.

We define L_i as the average number of infected people with whom an identified infected person in group I_i had contact in the past T_M years and who were already infected before the contact. Let M_i be the average number of people with whom the identified infected person in group I_i had contact in the past T_M years and who were infected by this identified person. Then $L_i + M_i$ is the total number of infected partners per unit of time in the past T_M years that an identified infected person in group I_i has, and hence $(L_i + M_i)\sigma I_i$ is the total number of infected partners per unit of time in the past T_M years that all identified infected people in group I_i have. If we neglect migration and death, and suppose that the contact tracing program is only able to screen a fraction f of their partners, then we subtract $f\sigma(L_i + M_i)I_i$ from the equation for the infected group I_i, and add it to the tested and counseled group I_{C_i}.

The equations for the DI random screening and contact tracing model illustrated in Fig. 3.1 are

$$\begin{aligned}
\frac{dS}{dt} &= \mu(S^0 - S) - \lambda S, \\
\frac{dI_i}{dt} &= p_i\lambda S - (\mu + \nu_i + \sigma + f\sigma(L_i + M_i))I_i, \qquad i = 1, \cdots, n, \\
\frac{dI_{C_i}}{dt} &= -(\mu + \nu_i)I_{C_i} + (\sigma + f\sigma(L_i + M_i))I_i, \qquad i = 1, \cdots, n, \\
\lambda(t) &= \sum_{i=1}^{n} \lambda_i(t) = \sum_{i=1}^{n} r\beta_i \frac{I_i(t)}{N(t)},
\end{aligned} \tag{3.1}$$

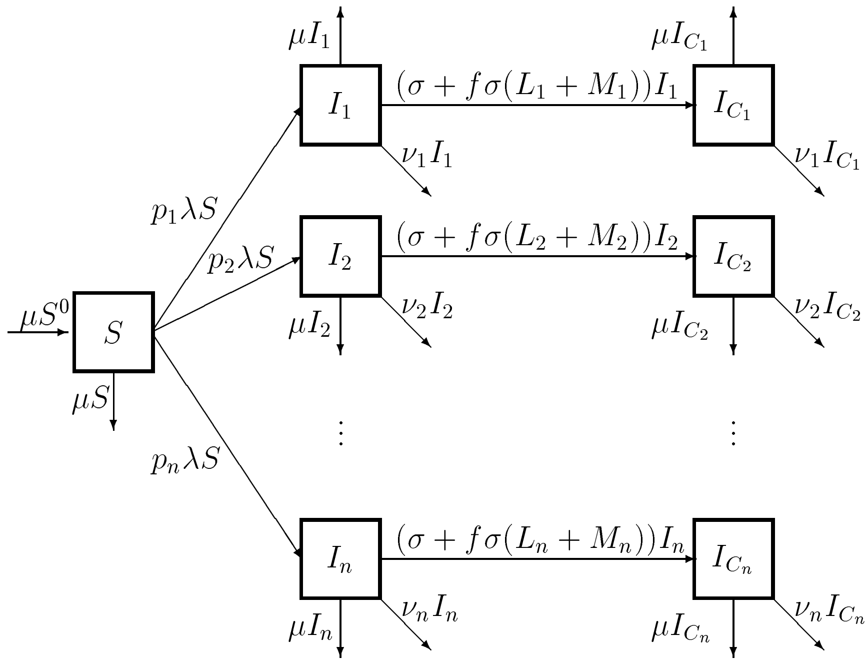

Figure 3.1: The DI model with random screening and contact tracing differs from the original DI model in Fig. 2.1 in that it includes a new category of infected individuals, $I_C i$, who have been identified as infected and are no longer spreading the virus.

where $N(t) = S(t) + I(t)$, and $I(t) = \sum_{i=1}^{n} I_i(t)$ does not include the identified infected people. Here we leave out the equation for the A group since we assume they are no longer active and play no role in the transmission dynamics of HIV in the model.

The equations for the SP random screening and contact tracing model illustrated in Fig. 3.2 are

$$
\begin{aligned}
\frac{dS}{dt} &= \mu(S^0 - S) - \lambda S, \\
\frac{dI_1}{dt} &= \lambda S - (\gamma_1 + \mu + \sigma + f\sigma(L_1 + M_1))I_1, \\
\frac{dI_i}{dt} &= \gamma_{i-1} I_{i-1} - (\gamma_i + \mu + \sigma + f\sigma(L_i + M_i))I_i, \qquad 2 \le i \le n, \\
\frac{dI_{C_1}}{dt} &= -(\gamma_1 + \mu)I_{C_1} + (\sigma + f\sigma(L_1 + M_1))I_1, \\
\frac{dI_{C_i}}{dt} &= \gamma_{i-1} I_{C_{i-1}} - (\gamma_i + \mu)I_{C_i} + (\sigma + f\sigma(L_i + M_i))I_i, \qquad 2 \le i \le n, \\
\lambda(t) &= \sum_{i=1}^{n} \lambda_i(t) = \sum_{i=1}^{n} r\beta_i \frac{I_i(t)}{N(t)},
\end{aligned}
\tag{3.2}
$$

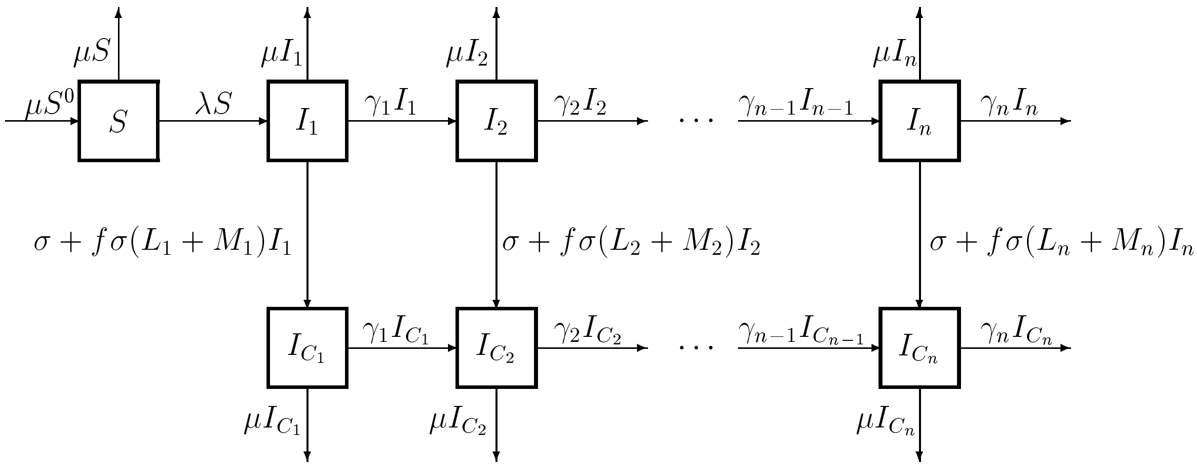

Figure 3.2: The SP model with random screening and contact tracing differs from the original SP model in Fig. 2.2 in that it includes a new category of infected individuals who have been identified as infected and are no longer spreading the virus.

where $N(t) = S(t) + I(t)$, and $I(t) = \sum_{i=1}^{n} I_i(t)$ does not include the identified infected people. We once again leave out the equation for A.

Note that in both models the total number of infected people become the total number of *unidentified* infected people based on our assumption: $I(t) = \sum_{i=1}^{n} I_i(t)$, and that the total active population now is $N(t) = S(t) + I(t)$, with I_{C_i} removed.

3.1 Estimation of L_i

Next we estimate the average number of infected partners of the identified infected individual, L_i. The same procedure works for both models. Suppose that at time t a person has been in the population an average of $T(t)$ years. Let $\hat{T}(t) = \min\{T_M, T(t)\}$. Then the number of infected partners this individual has had is

$$L_i(t) = r \int_{t-\hat{T}(t)}^{t} \frac{I(s)}{N(s)} ds. \tag{3.3}$$

To calculate this quantity exactly requires the mean time that people were susceptible before becoming infected, the mean time that infected people have been infected, and then the evaluation of the integral of I/N over the past. For this preliminary investigation, we approximate L_i by assuming $T_M < T(t)$ such that $\hat{T}(t) = T_M$

and that during this period of time, T_M, $N(s)$ and $I(s)$ have stayed approximately constant at their values of time t. Then, we estimate $L_i(t)$ for both models as

$$L_i(t) = \frac{rT_M I(t)}{N(t)}. \tag{3.4}$$

Note that $L_i(t)$ is independent of i. This approximation greatly simplifies the models and is adequate for the qualitative analysis of the models.

3.2 Estimation of $M_i(t)$

The procedure for estimating the average number of partners infected by the identified infected individual, M_i, is different for the DI and SP models.

3.2.1 $M_i(t)$ for the DI Model

Let $T_i(t)$ be the mean time that an infected person in group I_i has been in that group. It can be approximated as $\bar{\tau}_i = 1/(\mu + \nu_i)$, which, because we are dealing with constant rate flows, is both the mean time that people stay in group i as well as the mean time that people in group i have been in group i when the population is at equilibrium. Let $\tilde{T}_i(t) = \min\{T_M, T_i(t)\}$. Then the average number of people that this infected person has infected is

$$M_i(t) = r\beta_i \int_{t-\tilde{T}_i(t)}^{t} \frac{S(s)}{N(s)} ds.$$

As above, if we make the simplifying assumption that S and N have been constant at their values of time t for the length of time $\tilde{T}_i(t)$, then for the DI model,

$$M_i(t) \approx \frac{r\tilde{T}_i \beta_i S(t)}{N(t)} \tag{3.5}$$

where $\tilde{T}_i = \min\{T_M, \bar{\tau}_i\}$.

3.2.2 $M_i(t)$ for the SP Model

If we continue to approximate the populations by their time t values, then the mean time a person who is in group I_i has been in that group, T_i, is approximately $\bar{\tau}_i = 1/(\mu + \gamma_i)$.

For people in group I_1, the number of people a person has infected is

$$M_1(t) \approx \frac{r\tilde{T}_1 \beta_1 S(t)}{N(t)},$$

where $\tilde{T}_1 = \min\{T_M, \bar{\tau}_1\}$. Because we are assuming that people can identify a fraction of their partners for the past T_M years we can convert this time for people in the infected group I_i to the index $J(i)$ of the earliest infected group that an infected person in I_i was in when they may have infected another person, where $i > 1$ and $J(i) \leq i$. That is, a person in I_i can identify past partners while they were in groups I_j where $j \in [J(i), i]$. For example, if i is 2 and $J(2) = 1$, people in group 2 can identify partners from the time when they were in group I_1, but they cannot identify partners from the times prior to infection.

Define $T_{k,inf}$ to be the average length of time period that people in group I_k have been infected, and T_k^* to be the average length of time period that those people entering group I_{k+1} have been infected. Because these people have survived to the kth group and are still in the active population, we do not include the removal rate (μ) when estimating T_k^*. That is

$$T_k^* = \sum_{l=1}^{k} \frac{1}{\gamma_l},$$

$$T_{k,inf} = \bar{\tau}_k + \sum_{l=1}^{k-1} \frac{1}{\gamma_l}.$$

The index $J(i)$ is determined by T_M and $T_{i,inf}$. That is, $J(i)$ is the index of the group for which

$$T_{i,inf} - T_{J(i)}^* < T_M \leq T_{i,inf} - T_{J(i)-1}^*,$$

or more specifically

$$\bar{\tau}_i + \sum_{k=J(i)+1}^{i-1} \frac{1}{\gamma_k} < T_M \leq \bar{\tau}_i + \sum_{k=J(i)}^{i-1} \frac{1}{\gamma_k}. \tag{3.6}$$

There are three possible cases.

Case 1. $J(i) = i$ and $T_M \leq \bar{\tau}_i$.

In this case, the average infected person arrived in their current infected group so long ago that they cannot identify partners they had while they were in a previous group. For this case we use the estimate

$$M_i(t) \approx \frac{rT_M \beta_i S(t)}{N(t)}. \tag{3.7}$$

Case 2. $1 \leq J(i) < i$.

In this case T_M is longer than the time people have been in group I_i, but shorter than the time they have been infected. The average time they have been in group I_i is $\bar{\tau}_i$, in group $i-1$ is $1/\gamma_{i-1}$, and so on until in group $I_{J(i)}$, where they only recall partners for the amount of time

$$t_{M_{J(i)}} = T_M - \bar{\tau}_i - \sum_{k=J(i)+1}^{i-1} \frac{1}{\gamma_k}.$$

Hence

$$M_i(t) \approx \frac{rS(t)}{N(t)} \left(\beta_J(i) t_{M_{J(i)}} + \sum_{k=J(i)+1}^{i-1} \frac{\beta_k}{\gamma_k} + \beta_i \bar{\tau}_i \right). \tag{3.8}$$

Case 3. $J(i) = 0$.

In this case, T_M is longer than the time the infected people have been infected. The identified infected individuals can identify all of the partners since they have been infected. As a result

$$M_i(t) \approx \frac{rS(t)}{N(t)} \left(\sum_{k=1}^{i-1} \frac{\beta_k}{\gamma_k} + \beta_i \bar{\tau}_i \right). \tag{3.9}$$

4 The Reproductive number and Endemic equilibrium

The results for both the reproductive number and the endemic equilibrium for the DI model and the SP model are summarized here. The details can be found in Appendix

A. In the numerical results section we will use these results to examine the behavior and sensitivity of our two models.

4.1 The Reproductive Number

The reproductive number for the DI model is given by

$$R_0^D = r\sum_{i=1}^{n} \frac{p_i\beta_i}{\mu+\nu_i+\sigma+f\sigma r\tilde{T}_i\beta_i}. \tag{4.1}$$

The reproductive number for the SP model is given by

$$R_0^S = r\sum_{i=1}^{n} \frac{q_i\beta_i}{\mu+\gamma_i+\sigma+f\sigma M_i^0}, \tag{4.2}$$

where we define

$$q_i := \prod_{j=1}^{i-1} \frac{\gamma_j}{\mu+\gamma_j+\sigma+f\sigma M_j^0}, \tag{4.3}$$

and M_i^0 is M_i evaluated at the infection-free equilibrium.

Note that in order to numerically determine the reproductive number for the SP model we need to first determine M_i^0. Recall that there are three different possible cases for these M_i, so we need to be careful when we evaluate them that we use the appropriate formula for the ith group. In the appendix, we explicitly give R_0^S and q_i for some specific cases of M_i.

The partial derivatives of the reproductive numbers with respect to the rate of random screening, σ, and the fraction of identified partners contact traced, f, are given by

$$\begin{aligned}
\frac{\partial R_0^D}{\partial\sigma} &= -\,r\sum_{i=1}^{n} \frac{p_i\beta_i}{\mu+\nu_i+(1+fr\tilde{T}_i\beta_i)\sigma}\left(\frac{1+fr\tilde{T}_i\beta_i}{\mu+\nu_i+(1+fr\tilde{T}_i\beta_i)\sigma}\right),\\
\frac{\partial R_0^S}{\partial\sigma} &= -\,r\sum_{i=1}^{n} \frac{q_i\beta_i}{\mu+\gamma_i+(1+fM_i^0)\sigma}\left(\sum_{j=1}^{i}\frac{1+fM_j^0}{\mu+\gamma_j+(1+fM_j^0)\sigma}\right),
\end{aligned} \tag{4.4}$$

and

$$\begin{aligned}
\frac{\partial R_0^D}{\partial f} &= -\,r\sum_{i=1}^{n}\frac{p_i\beta_i}{\mu+\nu_i+(1+fr\tilde{T}_i\beta_i)\sigma}\left(\frac{r\tilde{T}_i\beta_i\sigma}{\mu+\nu_i+(1+fr\tilde{T}_i\beta_i)\sigma}\right),\\
\frac{\partial R_0^S}{\partial f} &= -\,r\sum_{i=1}^{n}\frac{q_i\beta_i}{\mu+\gamma_i+(1+fM_i^0)\sigma}\left(\sum_{j=1}^{i}\frac{M_j^0\sigma}{\mu+\gamma_j+(1+fM_j^0)\sigma}\right).
\end{aligned}\tag{4.5}$$

All these derivatives are negative. Hence, both a pure random screening program (with $f=0$) and any contact tracing program will reduce the reproductive number of the epidemic, and thus most likely reduce the severity of the epidemic. The more people are screened (the greater σ is) and the more partners people can recall or more accurate information people give (the greater f is), the more R_0 will be reduced for both models. A large enough screening rate and partner recall will reduce R_0 below the threshold.

Notice that contact tracing has different impact on the reproductive number and hence on the transmission dynamics for the DI and SP models. Contact tracing can reduce R_0 in a clear way for the DI model. However, the contact tracing for the SP model depends on not only the time period that identified infected people can identify their partners back to but also how long they have been infected, which determines how many infected partners they have had.

4.2 The Endemic Equilibrium

For the DI Model, the endemic equilibrium is given by

$$S^* = \frac{\mu G(\hat{x})}{\mu G(\hat{x})+F(\hat{x})-1}S^0, \tag{4.6}$$

$$I_i^* = \frac{\mu p_i(F(\hat{x})-1)}{(a_i+b_i\hat{x})(\mu G(\hat{x})+F(\hat{x})-1)}S^0, \tag{4.7}$$

where

$$G(\hat{x}) := \sum_{i=1}^{n}\frac{p_i}{a_i+b_i\hat{x}}, \quad F(\hat{x}) := r\sum_{i=1}^{n}\frac{\beta_i p_i}{a_i+b_i\hat{x}},$$

and $\hat{x}$ is the (unique) root of the equation $H_D(x)=1$. Here $H_D(x)$ is defined by

$$H_D(x) = r\sum_{i=1}^{n}\frac{\beta_i p_i}{\frac{a_i}{x}+b_i}, \tag{4.8}$$

with

$$a_i = \mu + \nu_i + \sigma + rf\sigma T_M, \quad b_i = f\sigma r(\tilde{T}_i\beta_i - T_M).$$

For the SP model, the endemic equilibrium is given by

$$I_n^* = \frac{\mu S^0}{\left(\mu \dfrac{\sum_{i=1}^{n} \prod_{j=i+1}^{n} (A_j + B_j\tilde{x})}{1/\tilde{x} - 1} + \prod_{j=1}^{n} (A_j + B_j\tilde{x})\right)}, \tag{4.9}$$

$$I_i^* = \prod_{j=i+1}^{n} (A_j + B_j\tilde{x})\, I_n^*, \quad i = 1, \cdots, n-1, \tag{4.10}$$

$$S^* = \frac{\sum_{i=1}^{n} \prod_{j=i+1}^{n} (A_j + B_j\tilde{x})}{1/\tilde{x} - 1} I_n^*, \tag{4.11}$$

where $\tilde{x}$ is the unique root of the algebraic equation

$$H_S(x) = rx \sum_{i=1}^{n} \frac{\beta_i}{\prod_{j=1}^{i} (A_j + B_j x)} - 1, \tag{4.12}$$

$$A_i = (\gamma_i + \mu + \sigma + f\sigma r T_M)/\gamma_{i-1}, \quad B_i = f\sigma r(J_{M_i} - T_M)/\gamma_{i-1},$$

with $\gamma_0 = 1$ and J_{M_i} determined from equations (3.7),(3.8), and (3.9), that is

$$J_{M_i} = \begin{cases} \beta_i T_M, & \text{if } J(i) = i \text{ and } T_M \leq \bar{\tau}_i, \\ \beta_J(i) t_{M_{J(i)}} + \sum_{k=J(i)+1}^{i-1} \dfrac{\beta_k}{\gamma_k} + \beta_i\bar{\tau}_i, & \text{if } 1 \leq J(i) < i, \\ \sum_{k=1}^{i-1} \dfrac{\beta_k}{\gamma_k} + \beta_i\bar{\tau}_i, & \text{if } J(i) = 0. \end{cases} \tag{4.13}$$

The details can be found in Appendix A.

5 Numerical Investigation of the Models

Tables 5.1 and 5.2 gives the parameter values we use for the basic DI and SP models. We estimated these parameters in [8, 9] from the published literature. Here we use the baseline parameters given in [9], which ensure that the two models have the same

Table 5.1: These parameters were chosen based on the studies and calculations cited in the text.

Basic Parameter	**Formula**	**Value**
Sexually active removal rate	α	0.05 yrs^{-1}
Natural death rate	d	0.02 yrs^{-1}
Mean duration of infection (when $\alpha = 0$ in the DI model)	$\bar{\tau}$	12 years
Partner acquisition rate	r	5 partners/yr
Contacts per partner parameter	η	1.0
Initial population size	$N(0)$	S^0
Initial infected population	$I_T(0)$	$0.01S^0$
Normalized infection-free equilibrium	S^0	1
DI parameters		
Distribution of the newly infected	$\boldsymbol{p}$	(0.05, 0.33, 0.5, 0.12)
Progression rates by group	$\boldsymbol{\nu}$	(0.19, 0.096, 0.058, 0.028)yrs^{-1}
Relative per contact transmission	$\boldsymbol{\zeta}$	$(10^3, 10^2, 10, 1)z^D$
Infectivity adjustment factor	z^D	5.1×10^{-5}
SP parameters:		
Progression rates by group	$\boldsymbol{\gamma}$	$(13.0, 0.23553, 0.23553, 0.47)\text{yrs}^{-1}$
Relative per contact transmission	$\boldsymbol{\zeta}$	$(100, 1, 1, 10)z^S$
Infectivity adjustment factor	z^S	9.08×10^{-4}

Table 5.2: Derived Parameters: These parameters are derived from the parameters given in Table 5.1.

Description	**Formula**	**Baseline Value**
Duration of Infection	$\bar{\tau}$	7.3 yrs
Mean probability of transmission per contact	$\bar{\zeta}$	0.003
Number of contacts per partner	$c(r=5)$	21.8 contacts per partner
DI parameters		
Probability of transmission per partner	$\boldsymbol{\beta}$	(0.68, 0.105, 0.011, 0.0011)
Mean probability of transmission per partner	$\bar{\beta}$	0.053
Reproductive number	R_0	1.93
SP parameters:		
Probability of transmission per contact	$\boldsymbol{\beta}$	(0.87, 0.0196, 0.0196, 0.1802)
Mean probability of transmission per contact	$\bar{\beta}$	0.051
Reproductive number	R_0	1.88

value of $\bar{\tau}$, nearly identical values for R_0 and $\bar{\beta}$, and thus nearly identical endemic states, since the sensitivity of the models to the intervention programs can be better compared if these values are the same in the absence of any intervention program ($\sigma = 0$).

Because we are considering a high risk population, we assume that individuals realize they are at risk and are more likely to come in for testing than in the general population. We use a 5% average screening rate per year ($\sigma = 0.05$) in our numerical simulations, and study the sensitivity of the model to screening rates between 0 and 20%. For the contact tracing program for an active population with an average of 5 partners a year we take $T_M = 2$ years and study the sensitivity of the model to variations between 0 and 4 years. In active populations, the fraction of partners named, located, and screened varies widely. Some programs seem to have no difficulty locating partners, but find a great reluctance to be tested, while other programs have more difficulty locating partners, and less difficulty getting them to be tested [18]. We also include in our factor f an estimated 10% of the infected people who are located and tested, but do not change behaviors. For most simulations we assume that half of all named partners will be tested and change behaviors, ($f = 0.5$), and study the sensitivity of the models to variations in f. Some studies cited in [18] seem to have done better than this, and some have done worse, but in none of these studies is there a way to evaluate the fraction of partners that individuals were able to identify.

Estimates of the mean probability per contact, $\bar{\zeta}$, range from 0.0003 (lowest value estimated for female-to-male transmission) to 0.08 (highest value estimated for male-to-male transmission) [27]. Here we use $\bar{\zeta} = 0.003$ at baseline.

In this section, we first use numerical simulations of the time-varying dynamics to investigate the effectiveness of these simple random screening and contact tracing programs for three levels of interventions: none, random screening only, and random screening plus contact tracing. Next, we use the analytical formulas for R_0 to analyze the sensitivity of the early epidemic to different levels of intervention programs, varying σ, f, and T_M. We then examine the sensitivity of the long-term epidemic to these three parameters. Finally, we investigate the impact of our approximations for the SP contact tracing model on the smoothness of R_0 and the endemic equilibrium.

The impact of these interventions on the DI and SP epidemics shows how the effectiveness of the intervention strategy depends on the underlying etiology of the disease transmission. These simulations confirm that contact tracing is more effective when there are core groups which are transmitting the majority of the infections (as in the DI model) than when most of the infections are spread by those who have just been infected (as in the SP model). In particular, we illustrate that contact tracing is an effective approach to identifying the superspreaders in the DI model. We conclude that if the impact of the intervention program depends on the underlying etiology of the infection, this etiology must be understood in order to design the cost-effective intervention programs.

The timing of a multigroup model epidemic is extremely sensitive to the initial distribution of the infected population. We defined the initial distribution of the 1% infected population using the *Numerical Preinitialization Procedure* described in [9]. This distribution is defined to simulate the behavior of a naturally occurring epidemic, and to minimize the initial transients created by artificial initial conditions. First a tiny fraction (0.01%) of the population is distributed among the infected groups based on the relative fraction of time an individual is in a particular group. That is, the I_i is initialized with $0.0001 S^0 \bar{\tau}_i / \bar{\tau}$, where $\bar{\tau}_i$ is the duration of infection of infected individuals in group i. The model is then run forward in time until 1% of the population has become infected. At that time, the population is renormalized to equal S^0 and the time is renormalized for this point to be $t = 0$. The $I_i(0)$ are given the same relative distribution as they had when the simulation is stopped, and their sum is set to $0.01 S^0$. This approach is an approximation of the natural initial conditions that would occur if a very small number of infected people were initially introduced into the population.

5.1 Transient Dynamics of the Models

The impact of random screening and contact tracing on the transient dynamics can be seen in Figure 5.1. In the first simulation (solid lines), there is no intervention, and all parameters are at the baseline values in Table 5.1. In the second simulation (dash–dot lines), there is screening of 5% of the active population and no contact-tracing. In the third simulation (dash lines), contact tracing is added to the 5% screening program, with $T_M = 2$ and $f = 0.5$.

In the DI model there is a small, not insignificant, impact from screening alone. However, a modest amount of contact tracing added to this screening program leads to a large reduction in the epidemic. The lower plots show the relative impact, ρ_i, defined as the fraction of infections caused by group i. In the DI model, with just a modest amount of screening and contact tracing, members of the most infectious groups are quickly identified and removed from the infectious population. Surprisingly, in the DI model contact tracing has only a slight shift in the relative impact of the different

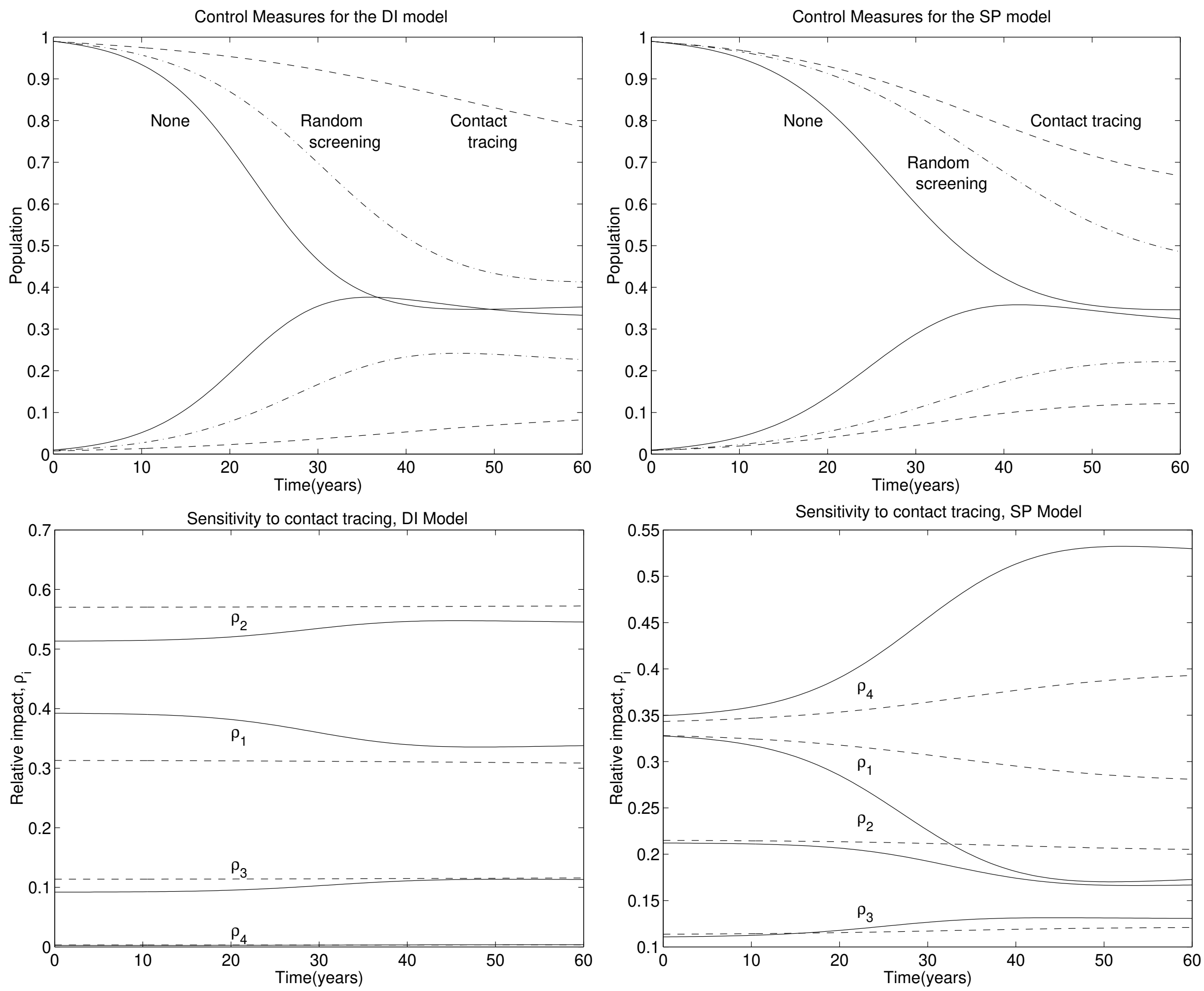

Figure 5.1: The solid lines plot the epidemic when there is no screening or contact tracing, the dash-dot lines are when 5% of the population is screened, and there is no contact tracing, and the dashed lines show what happens when contact tracing is added to the the random screening model with $T_M = 2$ years and $f = 0.5$. The upper figures show the overall model dynamics for these three cases for each of the two models. In the upper left hand figure we see that random screening has a modest impact in slowing the DI model epidemic when compared to the dramatic impact of contact tracing. On the upper right we see that random screening alone has slightly more impact on the SP model than the DI model. However, random screening plus contact tracing has less impact on the SP model epidemic. The lower two figures show the relative impact, ρ_i, (see Equation 2.6), for each of the two models, for the baseline and contact tracing cases. We see that contact tracing changes the relative importance of the most infectious groups more in the SP model than in the DI model.

groups on spreading the epidemic even though there is a huge reduction in the infected population.

The 5% random screening program has slight more impact on the SP model than on the DI model. In simulations (not shown here) we found that screening 10% of the population in the SP model has almost the same effect as 5% screening with contact tracing. The relative impact plots illustrate that the contact tracing changes the underlying dynamics of the SP epidemic. With no intervention program, the one third of infections early in the epidemic are caused by group 1, and most of infections late in the epidemic by group 4. Contact tracing identifies people before they enter group 4 and therefore with contact tracing, group 1 has more relative impact on the epidemic throughout the epidemic.

The group causing the most infections can impact which control methods will work best. Because in the SP model people stay in group 1 for such a short time, they are hard to detect. However, by the time they reach group 4, there is a reasonable chance that they know about their infection. This implies that contact tracing used in conjunction with an early identification program, such as a concerted effort to screen people who have early symptoms of infection may be an effective intervention program for an SP epidemic.

5.2 Sensitivity of R_0

In Section 4, we determined that R_0 decreases for both models as either σ or f decreases. Thus the more screening or partner contact tracing there is, the slower the initial epidemic will grow. To measure the sensitivity of the initial epidemic to the intervention programs, we evaluate R_0 using the baseline parameters given in Table 5.1, and varying the random screening rate, σ, the fraction of partners traced, f, and the time window for remembering past partners, T_M. These results are shown in Figure 5.2. The upper figures show R_0 as a function of σ for 5 values of T_M, (0,1,2,3,4 years), and $f = 0.5$. The lower figures show R_0 as a function of f for 5 values of σ, (0.0 , 0.05, 0.1, 0.15, 0.2), and $T_M = 2$ years.

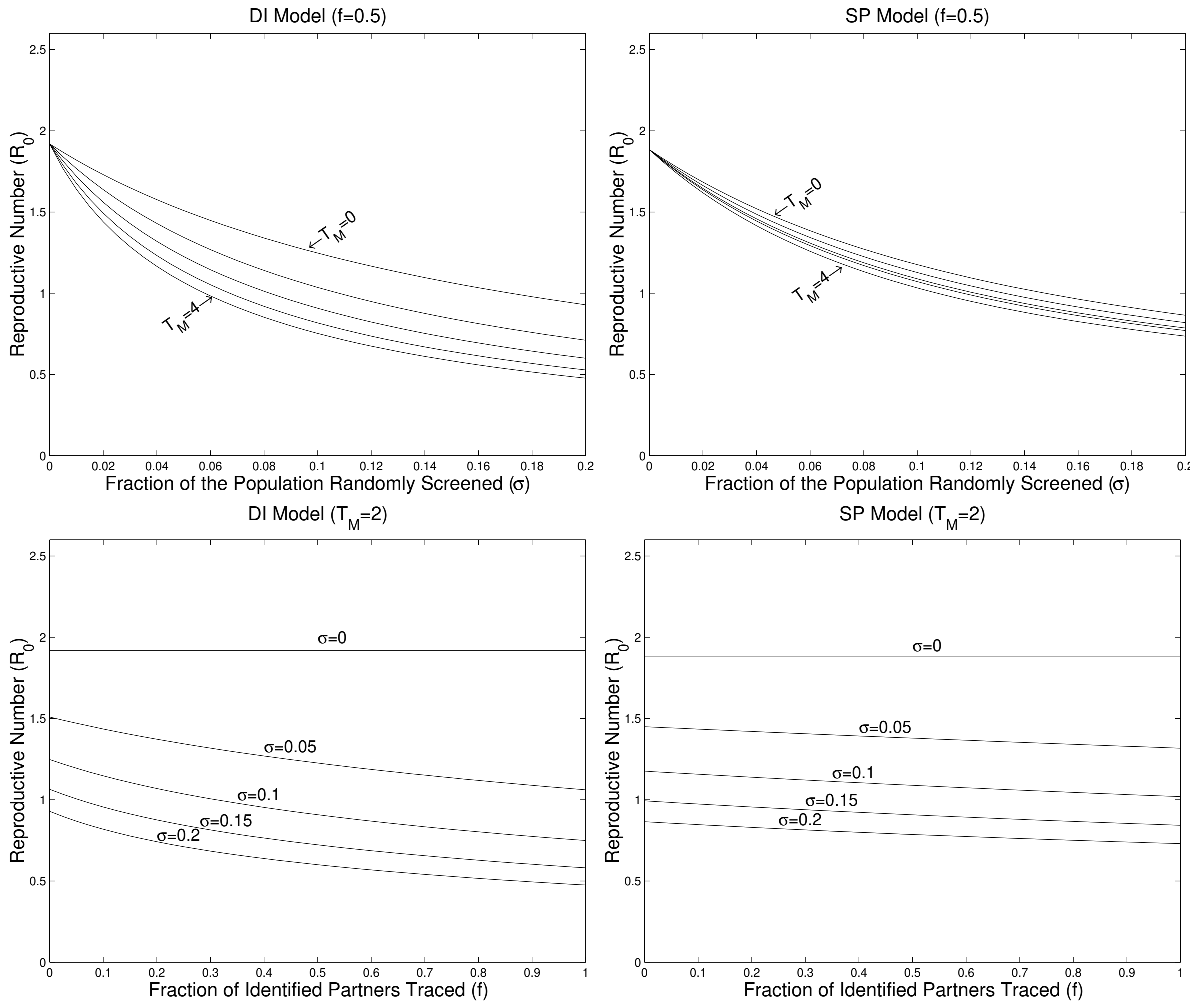

Figure 5.2: In the top figures, R_0 is plotted as a function of the fraction of the population that is randomly screened for infection. The different curves illustrate how much greater the impact of contact tracing ($f = 0.5$) is for the DI model than the SP model for $T_M = 0, 1, 2, 3, 4$. To illustrate the sensitivity of the models to f in the lower figures, we fix $T_M = 2$ years and plot R_0 as a function of the fraction of partners traced, f. The multiple curves illustrate the impact when the fraction of the population randomly screened is varied, $\sigma = 0$, 0.05, 0.1, 0.15, 0.2. R_0 is reduced more in the DI model than in the SP model as the fraction of partners traced increases.

These figures show that R_0 is more sensitive to changes in σ than to variations in either f or T_M over their range. As random screening increases, R_0 for the DI model decreases much more rapidly than R_0 for the SP model for the same level of contact tracing. The upper plots show that the SP model is much less sensitive to T_M than the DI model. For the DI model, at a 10% screening rate, R_0 rapidly drops as T_M increases crossing threshold conditions ($R_0 = 1$) before $T_M = 2$ years, and decreasing less rapidly as T_M increases for the DI model. Thus, if identified infected people can identify their partners for just one year, and half of their partners can be traced, then the DI model goes below threshold when 12.5% of at risk people are randomly tested. Furthermore, if the identified infected people can identify their partners for the past four years, only 6.5% of the population needs to be randomly tested in order to bring the DI epidemic below the threshold. However, the epidemic is always above the threshold for the SP model for these conditions.

The lower graphs show that R_0 is less sensitive to the fraction of partners traced than to the random screening rate, but is still more sensitive in the DI than in the SP model. Note that R_0 drops below threshold on the 10% random screening curve at f slightly less than 0.5, so that if half of the past partners are traced and 10% population randomly screened, the epidemic is below threshold for the DI model, while $R_0 > 1.4$ with the same parameters for the SP model.

Finally, we remark that additional studies have shown that in the SP model, R_0 remains in the range [1.5, 1.9]) for $\sigma = 0.05$, $f \in (0, 1)$, and $T_M \in (0, 4)$. In the DI model, R_0 decreases more rapidly, falling quickly at small values of f and T_M, and drops below threshold at larger values of f and T_M.

5.3 Sensitivity of the Endemic Equilibrium

We show in Appendix A that when $R_0 > 1$ there exists a unique endemic equilibrium for both models. We solve for the endemic equilibrium by numerically finding the roots of the algebraic equilibrium equations defined in Section 4. This is easily accomplished because $\hat{x}$ in (4.8) and (4.12) is an increasing function of σ, f, and T_M. However, the dependence of the endemic equilibrium on σ, f, and T_M is complex

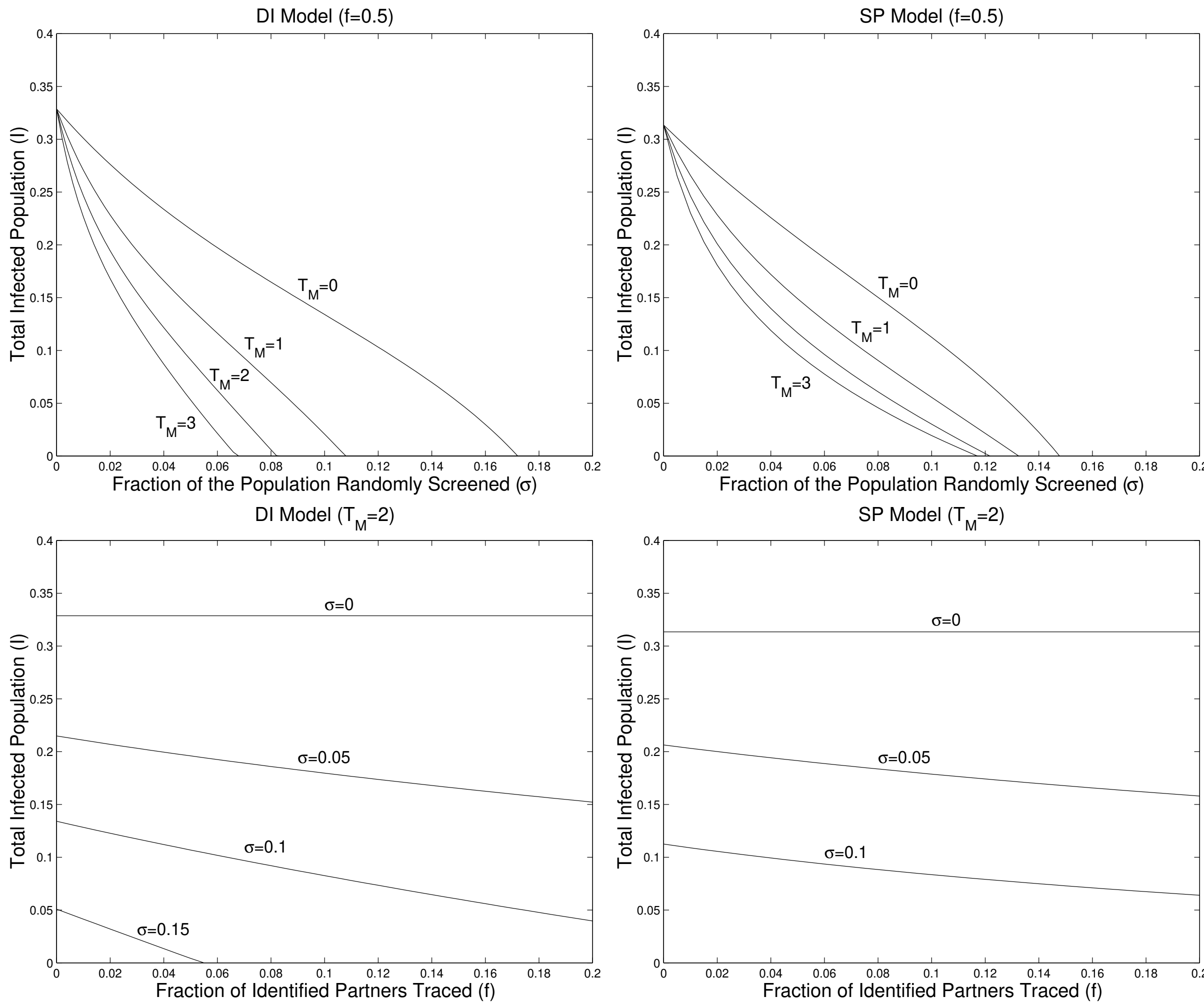

Figure 5.3: To examine the sensitivity of the endemic equilibria, we plot the total infected population of the DI and SP models at the endemic equilibrium as we vary the fraction of the population randomly screened (σ) for 4 values of T_M and $f = 0.5$, and the fraction of the population traced (f) for 3-4 values of σ and $T_M = 2$ years. Notice that in all of these sensitivity studies, contact tracing has a more impact on the endemic equilibrium for the DI model.

because changes in σ, f, or T_M affect not only the endemic equilibrium I_i^* given in (4.7) or in (4.9) and (4.10), as functions of $\hat{x}$ but also the values of a_i and b_i for the DI model, or the values of A_i and B_i for the SP model. Because of these complex interrelationships, we investigate the sensitivity of the endemic equilibrium numerically and illustrate our results in Figure 5.3.

In Figure 5.3 we see that I^* is a decreasing function of all three parameters in the models. Whenever R_0 crosses the threshold values $R_0 = 1$, the total number of infected people at the endemic equilibrium vanishes and the lines on the graph intersect the x-axis. As in our studies of R_0, we find that the contact tracing program has more impact on the DI model epidemic than the SP model epidemic. For example, when $f = 0.5$ and $T_M = 1, 2, 3$ years, there is a more rapid decrease of I^* in the DI model than in the SP model. Surprisingly, if there is no contact tracing, ($T_M = 0$), then screening alone has a bigger impact at slowing the epidemic in the SP model than in the ID model. As T_M is increased, the critical value of σ for stopping the epidemic decreases almost twice for the DI model than for the SP model. There is a similar response to increasing f and σ, at fixed T_M. If the screening rate is small and the DI model holds, a good contact tracing program can bring the epidemic under control.

5.4 Impact of the Discrete Approximations in the SP Model

In developing the contact tracing SP model we estimated how far back people can recall their partners. We made the approximation that the mean time an individual has been in a group can be approximated by the mean time an individual stays in a group, $\bar{\tau}_i = 1/(\mu + \gamma_i)$. We also assumed that we can use the mean time people stayed in previous groups to estimate how many past groups a person in group i can recall their partners from. The first of these approximations ignores variability in population sizes over time and is exact when the population is at equilibrium. The second assumption about how to compute averages leads to a possible discontinuity in the SP model as the parameter T_M changes and the index $J(i)$ jumps.

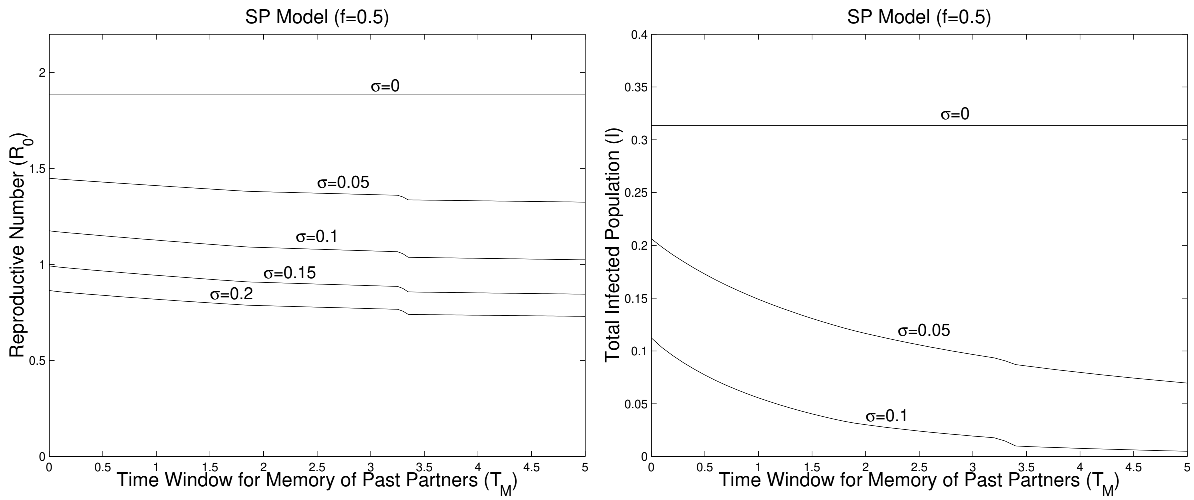

Figure 5.4: To examine the impact of the discontinuity in the parameter T_M that are introduced into the SP model by the model approximations and the structure of the SP model, we plotted R_0 and the total number of infecteds at equilibrium as a function of T_M for different values of σ. We see that in fact these quantities are continuous in T_M. There is a discontinuity in their slope at about $T_M = 3.3$ years, but the changes are fairly small.

In Figure 5.4, we investigate the nature of these jumps and show that they are small and lead to kinks, but not to discontinuities, in R_0 and the endemic equilibrium. Both plots exhibit a rapid drop at about $T_M = 3.3$ years, but this shift is short-lived, due to the discontinuous change in slope.

Because of our approximations, as T_M passes critical values, the index $J(i)$ changes discretely from group to group. This causes the slope in R_0 and I^* to jump as a function of T_M at a value of T_M between 2 and 3 years. The effect of this jump can also be seen in Figure 5.2 as a rapid change in R_0 in the top right SP model graph. Note that the $T_M = 2$ and 3 years lines are much closer together than the $T_M = 1$ and 2 lines are or the $T_M = 3$ and 4 lines are.

6 Summary and Conclusions

We have investigated how mathematical models can help predict the effectiveness of control measures on the spread of HIV and other sexually transmitted diseases. We studied the impact of random screening and contact tracing within the context of two HIV transmission models. In the DI model the infected population is divided into groups according to their infectiousness, and HIV is primarily spread by a small highly infectious group of superspreaders. Random screening alone reduces the impact of the epidemic a small amount for this model, while contact tracing slows the epidemic significantly by identifying the superspreaders. In the SP model an infected individual goes through a series of infection stages and the virus is primarily spread by individuals in an initial highly infectious stage or in the late stages of the infection. In the SP model, we find that contact tracing is only slightly more effective than random screening, because it cannot identify very many of the people in the very short, initial, most infectious period. Thus the effectiveness of the intervention strategy strongly depends on the underlying etiology of the disease transmission.

While the term that accounts for random screening is easy to add to a mathematical model of disease transmission, it is not obvious how to account for contact tracing. At first glance it would appear that, since contact tracing involves identifying events that occurred in the past, a model that includes it would contain nested integrals over the past. These integrals would be analytically intractable. In order to properly study contact tracing, it thus might appear that one would have to abandon continuous differential equation models in favor of individual agent-based models. However, individual agent-based models would be highly nonlinear, and thus could only be studied using large numbers of simulations at any given set of parameter values. Rather than doing this, we derived a differential equation model directly from the physics of the situation, by coming up with several simplifying, but reasonable, assumptions which allow us to add contact-tracing terms to our previous differential equation models. These terms have the advantage that we are able to determine analytical formulas for the reproductive number and endemic equilibrium, and use those formulas to quickly study how effective contact tracing would be as part of an intervention program.

Using our results on the reproductive number and endemic equilibrium, we analyzed the impact of various levels of intervention programs on the early epidemic and the endemic equilibrium. We also simulated numerically the time evolution of several scenarios, and examined the effectiveness of contact tracing in identifying the most infectious group transmitting the infection. These studies led us to the following conclusions:

- Random screening and contact tracing can be included in simple STD differential equation transmission models.
- Contact tracing is most effective when there are core groups of individuals remaining in for long periods of time that are transmitting the majority of the infections (as in the DI model).
- Contact tracing is only slightly more effective than random screening when a large fraction of the infections are transmitted by individuals in a short, highly infectious early stage within the disease progression (as in the SP model).
- When using models to guide intervention strategies, the underlying eitiology of the disease transmission must be captured by the model before it can be used to estimate the impact of the intervention on the epidemic.

We have described how mathematical models based on the transmission mechanisms of HIV can help the scientific community evaluate the potential effectiveness of different approaches for bringing an epidemic under control. It would be possible for public health officials or economists to add dollar amounts to various levels of screening and contact tracing in a particular population, and estimate the cost of reducing the epidemic to certain levels using these two models. However, we caution that the real epidemic is more complex that the models we have studied here, in part because of the complexities of sexual partner selection.

Although we have separated the DI and SP mechanisms in order to understand each of their roles, it appears from the data that HIV infected people both go through stages and have different individual levels of virus during the chronic infection stage. The real model should be a combined DI and SP model, which we will study in a future paper. Thus these insights are just one step in improving our understanding of the essential relationships between the social and biological mechanisms that influence the spread of the disease and can help set priorities in research, saving time, resources, and lives.

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A Appendix

We derive explicit formulas for R_0 for the contact tracing DI (3.1) and SP (3.2) models, show the existence of the unique endemic equilibrium, and reduce the formulas for the endemic equilibria to a single equation for each model.

A.1 The Reproductive Number

We define the reproductive number R_0 such that the infection-free equilibrium is asymptotically stable if $R_0 < 1$ and is unstable if $R_0 > 1$.

A.1.1 R_0 for the DI Model

The Jacobian of the contact tracing DI model (3.1) at the infection-free equilibrium can be written in the form

$$\begin{pmatrix} -\mu & \cdot & 0 \\ 0 & J_{DI} & 0 \\ 0 & \cdot & D_1 \end{pmatrix}, \tag{A.1}$$

where

$$D_1 = \mathrm{diag}\left(-(\mu+\nu_1), \cdots, -(\mu+\nu_n)\right),$$

and

$$J_{DI} = \begin{pmatrix} p_1 r\beta_1 - \delta_1 & p_1 r\beta_2 & \cdots & p_1 r\beta_n \\ p_2 r\beta_1 & p_2 r\beta_2 - \delta_2 & \cdots & p_2 r\beta_n \\ \vdots & \vdots & \ddots & \vdots \\ p_n r\beta_1 & p_n r\beta_2 & \cdots & p_n r\beta_n - \delta_n \end{pmatrix}, \tag{A.2}$$

with $\delta_i = \mu + \nu_i + \sigma + f\sigma M_i^0$. Here $M_i^0 = r\tilde{T}_i\beta_i$ is M_i in (3.5) evaluated at the infection-free equilibrium. Because all of the entries of the diagonal submatrix D_1 are negative, the stability of (A.1) is determined by J_{DI}.

Using the same approach as in [8] to analyze the matrix J_{DI}, it is a straightforward calculation to obtain the reproductive number

$$R_0^D = r\sum_{i=1}^{n} \frac{p_i\beta_i}{\delta_i} = r\sum_{i=1}^{n} \frac{p_i\beta_i}{\mu + \nu_i + \sigma + f\sigma r\tilde{T}_i\beta_i} \tag{A.3}$$

for the DI model.

A.1.2 R_0 for the SP Model

The Jacobian at the infection-free equilibrium for the contact tracing SP model (3.2) can also be written in the form

$$\begin{pmatrix} -\mu & \cdot & 0 \\ 0 & J_{SP} & 0 \\ 0 & \cdot & D_2 \end{pmatrix}, \tag{A.4}$$

where

$$D_2 = \mathrm{diag}\left(-(\mu+\gamma_1), \cdots, -(\mu+\gamma_n)\right),$$

and

$$J_{SP} = \begin{pmatrix} r\beta_1 - \delta_1 & r\beta_2 & r\beta_3 & \cdots & r\beta_{n-1} & r\beta_n \\ \gamma_1 & -\delta_2 & 0 & \cdots & 0 & 0 \\ 0 & \gamma_2 & -\delta_3 & \cdots & 0 & 0 \\ \vdots & \vdots & \vdots & \ddots & \vdots & \vdots \\ 0 & 0 & 0 & \cdots & \gamma_{n-1} & -\delta_n \end{pmatrix}, \tag{A.5}$$

with $\delta_i = \mu + \gamma_i + \sigma + f\sigma M_i^0$ and M_i^0 being M_i for the SP model evaluated at the infection-free equilibrium. Again, the stability of (A.4) is determined by that of matrix J_{SP} in (A.5).

Using a similar approach as in the derivation of R_0 for the SP model in [8] we can express the reproductive number for (3.2) as

$$R_0^S = r\sum_{i=1}^{n} \frac{\beta_i q_i}{\delta_i} = r\sum_{i=1}^{n} \frac{q_i\beta_i}{\mu+\gamma_i+\sigma+f\sigma M_i^0}, \tag{A.6}$$

where

$$q_i := \prod_{j=1}^{i-1} \frac{\gamma_j}{\mu+\gamma_j+\sigma+f\sigma M_j^0}. \tag{A.7}$$

Note that M_i^0 depends on how far back people can identify their partners. If T_M is small and a typical infected person can only identify partners from their current infection stage ($J(i) = i$) and $T_M < 1/(\mu+\gamma_i)$, then $M_i^0 = rT_M\beta_i$ and

$$R_0^S = r\sum_{i=1}^{n} \frac{q_i\beta_i}{\mu+\gamma_i+\sigma+f\sigma rT_M\beta_i},$$

where

$$q_i := \prod_{j=1}^{i-1} \frac{\gamma_j}{\mu+\gamma_j+\sigma+f\sigma rT_M\beta_j}.$$

At the other extreme if T_M is large and a typical infected person can identify all their partners, then

$$M_i^0 = r\left(\sum_{k=1}^{i-1}\frac{\beta_k}{\gamma_k} + \frac{\beta_i}{\mu+\gamma_i}\right),$$

and

$$R_0^S = r\sum_{i=1}^{n}\frac{q_i\beta_i}{\mu+\gamma_i+\sigma+f\sigma r\left(\sum_{k=1}^{i-1}\frac{\beta_k}{\gamma_k}+\frac{\beta_i}{\mu+\gamma_i}\right)},$$

where

$$q_i = \prod_{j=1}^{i-1}\frac{\gamma_j}{\mu+\gamma_j+\sigma+f\sigma r\left(\sum_{k=1}^{i-1}\frac{\beta_k}{\gamma_k}+\frac{\beta_i}{\mu+\gamma_i}\right)}.$$

A.2 The Endemic Equilibrium

We now show that when $R_0 > 1$ both the models have a unique nonzero endemic equilibrium and derive a single equation for the equilibrium of each model that can be easily solved numerically.

A.2.1 The Endemic Equilibrium for the DI Model

We now show there exists a unique endemic equilibrium when the infection-free equilibrium is unstable ($R_0 > 1$). The endemic equilibrium for (3.1) satisfies the equation:

$$\begin{aligned}
p_i\lambda S^* &= (\mu+\nu_i+\sigma+f\sigma(L_i+M_i))I_i^* \\
&= \left(\mu+\nu_i+\sigma+f\sigma\left(\frac{rT_M I^*}{N^*}+\frac{r\tilde{T}_i\beta_i S^*}{N^*}\right)\right)I_i^* \\
&= \left(\mu+\nu_i+\sigma+f\sigma\left(rT_M\left(1-\frac{S^*}{N^*}\right)+r\tilde{T}_i\beta_i\frac{S^*}{N^*}\right)\right)I_i^* \\
&:= \left(a_i+b_i\frac{S^*}{N^*}\right)I_i^*,
\end{aligned} \tag{A.8}$$

where $a_i = \mu+\nu_i+\sigma+rf\sigma T_M$, $b_i = f\sigma r(\tilde{T}_i\beta_i - T_M)$. Hence,

$$I_i^* = \frac{p_i\lambda S^*}{a_i+b_i\dfrac{S^*}{N^*}},$$

which gives

$$\lambda^* = r \sum_{i=1}^{n} \frac{\beta_i I_i^*}{N^*} = r \sum_{i=1}^{n} \frac{\beta_i p_i \lambda^* S^*}{N^* \left(a_i + b_i \dfrac{S^*}{N^*} \right)}.$$

That is:

$$1 = r \frac{S^*}{N^*} \sum_{i=1}^{n} \frac{\beta_i p_i}{a_i + b_i \dfrac{S^*}{N^*}}. \tag{A.9}$$

The fraction of the population that is susceptible at the equilibrium as $x := S^*/N^* \in (0,1)$ is used as a variable to define the function

$$H_D(x) := r \sum_{i=1}^{n} \frac{\beta_i p_i}{\dfrac{a_i}{x} + b_i} - 1, \tag{A.10}$$

where $H_D(x) = 0$ at the equilibrium. Because $H_D(x)$ is an increasing function, $\lim_{x \to 0} H_D(x) = -1$, and

$$\lim_{x \to 1} H_D(x) = r \sum_{i=1}^{n} \frac{\beta_i p_i}{a_i + b_i} = r \sum_{i=1}^{n} \frac{\beta_i p_i}{\mu + \nu_i + \sigma + f \sigma r \tilde{T}_i \beta_i} = R_0 - 1,$$

there exists a unique solution of $H_D(\hat{x}) = 0$ for $\hat{x} \in (0,1)$, if and only if $R_0 > 1$.

Combining the equilibrium equation for (3.1), $\mu(S^0 - S^*) = \lambda^* S^*$, and (A.8) we have

$$I_i^* = \frac{p_i}{a_i + b_i \hat{x}} \mu(S^0 - S^*). \tag{A.11}$$

Hence,

$$\sum_{i=1}^{n} I_i^* = \mu(S^0 - S^*) \sum_{i=1}^{n} \frac{p_i}{a_i + b_i \hat{x}} = \mu(S^0 - S^*) G(\hat{x}),$$

where $G(\hat{x}) := \sum_{i=1}^{n} \dfrac{p_i}{a_i + b_i \hat{x}}$.

Define the function $F(\hat{x}) := r \sum_{i=1}^{n} \dfrac{\beta_i p_i}{a_i + b_i \hat{x}}$ of the equilibrium solution $\hat{x}$ and note that $N^* = S^* F(\hat{x})$. Therefore,

$$S^* + \mu(S^0 - S^*) G(\hat{x}) = S^* F(\hat{x}), \tag{A.12}$$

or

$$S^* = \frac{\mu G(\hat{x})}{\mu G(\hat{x}) + F(\hat{x}) - 1} S^0. \tag{A.13}$$

From (A.12) it also follows that

$$\mu(S^0 - S^*) = \frac{F(\hat{x}) - 1}{G(\hat{x})} S^*. \tag{A.14}$$

Substituting (A.14) into (A.11) gives

$$I_i^* = \frac{p_i(F(\hat{x}) - 1)}{(a_i + b_i\hat{x})G(\hat{x})} S^* = \frac{\mu p_i(F(\hat{x}) - 1)}{(a_i + b_i\hat{x})(\mu G(\hat{x}) + F(\hat{x}) - 1)} S^0. \tag{A.15}$$

Because $F(\hat{x}) = 1/\hat{x} > 1$ and (A.12) we can conclude that $S^* > 0$ and $I_i^* > 0$.

A.2.2 The Endemic Equilibrium for the SP Model

The equilibrium equations for the SP model (3.2),

$$\begin{aligned} \lambda S^* =& (\gamma_1 + \mu + \sigma + f\sigma(L_1 + M_1)) I_1^* \\ \gamma_{i-1} I_{i-1}^* =& (\gamma_i + \mu + \sigma + f\sigma(L_i + M_i)) I_i^*, \qquad 2 \le i \le n, \end{aligned}$$

can be combined to give the conditions

$$\lambda S^* = \left(A_1 + B_1 \frac{S^*}{N^*} \right) I_1^*, \tag{A.16}$$

and

$$I_{i-1}^* = \left(A_i + B_i \frac{S^*}{N^*} \right) I_i^*. \quad i = 1, \cdots, n-1. \tag{A.17}$$

That is,

$$I_i^* = \prod_{j=i+1}^{n} \left(A_j + B_j \frac{S^*}{N^*} \right) I_n^*, \quad i = 1, \cdots, n-1, \tag{A.18}$$

where $A_i = (\gamma_i + \mu + \sigma + f\sigma r T_M)/\gamma_{i-1}$, $B_i = f\sigma r(J_{M_i} - T_M)/\gamma_{i-1}$, with $\gamma_0 = 1$ and J_{M_i} are given by (4.13)

Substituting λ and (A.18) into (A.16) then leads to

$$r\frac{S^*}{N^*} \left(\sum_{i=1}^{n} \beta_i \prod_{j=i+1}^{n} \left(A_j + B_j \frac{S^*}{N^*} \right) \right) = \prod_{j=1}^{n} \left(A_j + B_j \frac{S^*}{N^*} \right). \tag{A.19}$$

Defining $x := S^*/N^*$ and dividing (A.19) by the right hand side, we obtain

$$H_S(x) := rx \sum_{i=1}^{n} \frac{\beta_i}{\prod_{j=1}^{i} (A_j + B_j x)} - 1 = 0. \tag{A.20}$$

The two end limits are $\lim_{x\to 0} H_S(x) = -1$ and

$$\lim_{x\to 1} H_S(x) = r \sum_{i=1}^{n} \frac{\beta_i}{\prod_{j=1}^{i} (A_j + B_j)} - 1 = R_0 - 1.$$

Therefore, if $R_0 > 1$, there exists a solution $\tilde{x} \in (0, 1)$ of (A.20) and the solution is unique if the derivative of $H_S(x)$ is positive.

The derivative of $H_S(x)$ is given by

$$\begin{aligned} H_S'(x) =& r \left(\sum_{i=1}^{n} \frac{\beta_i}{\prod_{j=1}^{i} (A_j + B_j x)} - x \sum_{i=1}^{n} \frac{\beta_i}{\prod_{j=1}^{i} (A_j + B_j x)} \sum_{j=1}^{i} \frac{B_j}{A_j + B_j x} \right) \\ =& r \sum_{i=1}^{n} \frac{\beta_i}{\prod_{j=1}^{i} (A_j + B_j x)} \left(1 - \sum_{j=1}^{i} \frac{B_j x}{A_j + B_j x} \right). \end{aligned} \tag{A.21}$$

It follows from (3.6)-(3.9) that $J_{M_i} \le T_M$ for all three cases of $J(i)$. Then, $B_j \le 0$ for all j, and $A_j + B_j x > 0$ for $x \in (0, 1)$. Hence $H_S'(x) > 0$, which ensures the uniqueness of the endemic equilibrium.

To solve for I^*, note that substituting $\tilde{x}$ into (A.18) yields

$$I_i^* = \prod_{j=i+1}^{n} (A_j + B_j x)\, I_n^*, \quad i = 1, \cdots, n-1. \tag{A.22}$$

It follows from $S^* = xN^* = x(S^* + \sum_{i=1}^{n} I_i^*)$ that

$$S^* = \frac{\sum_{i=1}^{n} I_i^*}{1/\tilde{x} - 1} = \frac{\sum_{i=1}^{n} \prod_{j=i+1}^{n} (A_j + B_j \tilde{x})}{1/\tilde{x} - 1} I_n^*. \tag{A.23}$$

Combining the equilibrium equation (3.2) for S with (A.16) and (A.22) yields

$$\mu(S^0 - S^*) = \lambda S^* = (A_1 + B_1\tilde{x})I_1^* = \prod_{j=1}^{n} (A_j + B_j\tilde{x})\, I_n^*,$$

which when combined with (A.23) gives

$$\mu S^0 = \left(\mu \frac{\sum_{i=1}^{n} \prod_{j=i+1}^{n} (A_j + B_j\tilde{x})}{1/\tilde{x} - 1} + \prod_{j=1}^{n} (A_j + B_j\tilde{x}) \right) I_n^*.$$

Solving this equation for I_n^* gives

$$I_n^* = \frac{\mu S^0}{\left(\mu \frac{\sum_{i=1}^{n} \prod_{j=i+1}^{n} (A_j + B_j\tilde{x})}{1/\tilde{x} - 1} + \prod_{j=1}^{n} (A_j + B_j\tilde{x}) \right)}. \tag{A.24}$$

and substituting this into (A.18) and (A.23) then completely solves for S^* and I_i^*, $i = 1, \cdots, n$.