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ORIGINAL ARTICLE

Basic Reproduction Number for HIV Model Incorporating Commercial Sex and Behavior Change

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Abstract The basic reproduction number is obtained for an HIV epidemic model incorporating direct and indirect commercial sex as well as behavior change by the female commercial sex workers (CSWs) and their male customers in response to the proliferation of the disease in the community. A recent result by van den Driessche P., and Watmough J. (Math. Biosci. 180:29–48, 2002) is utilized to compute the threshold parameters for the local asymptotic stability of the Disease-Free Equilibrium (DFE), by considering the transfers in and out of the infective classes. Numerical examples are used to describe the uniqueness and global properties of the endemic equilibrium when DFE is unstable. Biological interpretation of the results obtained in this work is discussed, as are the implications of our results for the design of public health policies such as targeting strategy to target intervention and control measures toward specific high-risk population groups in order to reduce infections. We show that targeting any one sector of the commercial sex alone for prevention will be difficult to have a decided effect on eradicating the epidemic. However, if the aim of the targeted intervention policy is not eradication of the epidemic but decrease in HIV incidence of a particular high-risk group, then concentrated targeting strategy could be sufficient, if properly implemented. This work also demonstrates the usefulness of the theorem of van den Driessche and Watmough (Math. Biosci. 180:29–48, 2002) in obtaining threshold parameters for complicated infectious diseases models.

Keywords HIV/AIDS · Commercial sex workers · Basic reproduction number · Thailand · Behavior change · Asymptotic stability

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1. Introduction

The basic reproduction number R_0, defined to be the expected number of secondary infections caused by an infective individual upon entering a totally susceptible population, has been used frequently in the past two decades to study the ability of a newly emerging infectious disease to remain endemic in a new environment in the analysis of epidemic models (see, e.g., Diekmann et al., 1990; Anderson and May, 1991; Hethcote, 2000; van den Driessche and Watmough, 2002). R_0 often plays the role of a threshold parameter, where $R_0 > 1$ usually implies that the disease-free state (or DFE for Disease-Free Equilibrium) of the given population is unstable and vulnerable to invasion of the infectious disease in question which might persist for a long time. On the other hand, however, the condition $R_0 < 1$ sometimes but not always imply that the disease can be eradicated quickly, mainly due to the possibility that, in a population of varying size, the infective fraction might approach zero while the actual infective population remains positive for all time (see, e.g., the modeling of the Human Immunodeficiency Syndrome (HIV) epidemic in Thailand studied by Busenberg et al., 1995; Hsieh and Cooke, 2000).

In an extension to Busenberg et al. (1995) and Hsieh and Cooke (2000), a compartmental model was proposed recently (Hsieh and Chen, 2004) which incorporated two levels of commercial sex, namely direct commercial sex taking place in brothels or indirect commercial sex where initial contacts for the business were made in bars, message parlors, nightclubs, etc., but might be conducted elsewhere (see, e.g., Bhassorn et al., 1993; Wathinee and Guest, 1994). Furthermore, the model allows for behavior change of the male customers, switching from brothel visitors to indirect sex patrons and vice versa in reaction to the prevalence of HIV (and other sexual transmitted diseases or STD). Moreover, the model also assumed that the commercial sex workers (CSW) could switch from direct commercial sex to indirect commercial sex due to a decrease in demand of brothel sex, a trend in Thailand since the mid-1990s strongly indicated by government statistics (Venereal Disease Division, Ministry of Public Health of Thailand, 2001), as well observed by several studies (see, e.g., Thai Working Group on HIV/AIDS Projection, 1991; Sittitrai et al., 1996; Nelson et al., 1999; Thailand's Response to AIDS, 2000). (For further discussion on this topic, also see Hsieh, 2002). For the model proposed in Hsieh and Chen (2004), the basic reproduction number was obtained only for several special cases with either restricted mixing of the activity groups or limited behavior change but not both, due to complicated structure of the full model.

Recently, a useful procedure for obtaining the threshold parameter for the local asymptotic stability of DFE in compartmental epidemic models was proposed by van den Driessche and Watmough (2002) with which they consider the transfers into and out of the infectious compartments only in the computation of the Jacobian matrix at the DFE, thus simplifying the complicated matrix one often encounters in local stability analysis. In this work, we will make use of this procedure to obtain the threshold parameter or the basic reproduction number for the general model in Hsieh and Chen (2004). The model is described in Section 2. Section 3 is devoted to obtaining the basic reproduction number. In Section 4, we describe the full dynamics of the model with the aim of numerical simulations.

Finally, in Section 5, we discuss the epidemiological interpretation of the results and its public health implications for targeting strategy of intervention and control measures.

2. The model

The model variables (see Fig. 1 for flow diagram of the model) are given as follows: F_l is the number of susceptible CSWs of sexual activity group l, where $l = 1$ denotes (low activity) indirect CSWs and $l = 2$ denotes (high activity) direct CSWs. f_l is the number of infected CSWs of sexual activity group l where $l = 1, 2$ are the same as above. M_l is the number of susceptible men of sexual activity group l, where $l = 1$ denotes (low activity) single men and $l = 2$ denotes (high activity) single men. m_l is the number of infected men of sexual activity group l where $l = 1, 2$ are the same as above.

The list of model parameters is given as follows: c_{jl} is the contact rate of susceptibles of sex j, activity group l, with $c_{j1} < c_{j2}$. $\bar{c}_{jl}$ is the contact rate of infectives of sex j, activity group l, with $\bar{c}_{j1} < \bar{c}_{j2}$. β_{jlk} is the transmission probability per contact of individual of sex j and activity group l to opposite sex of activity group k, with $\beta_{jlk} > \beta_{jmn}$ if $l + k < m + n$, i.e., the transmission probability is lower if at least one of individuals involved is of higher activity groups. α is the proportionality constant of the number of newly recruited CSWs to the total number of sexual contacts required by males at time t, $N_m(t)$, with $\alpha \in (0, 1)$. θ is the fraction

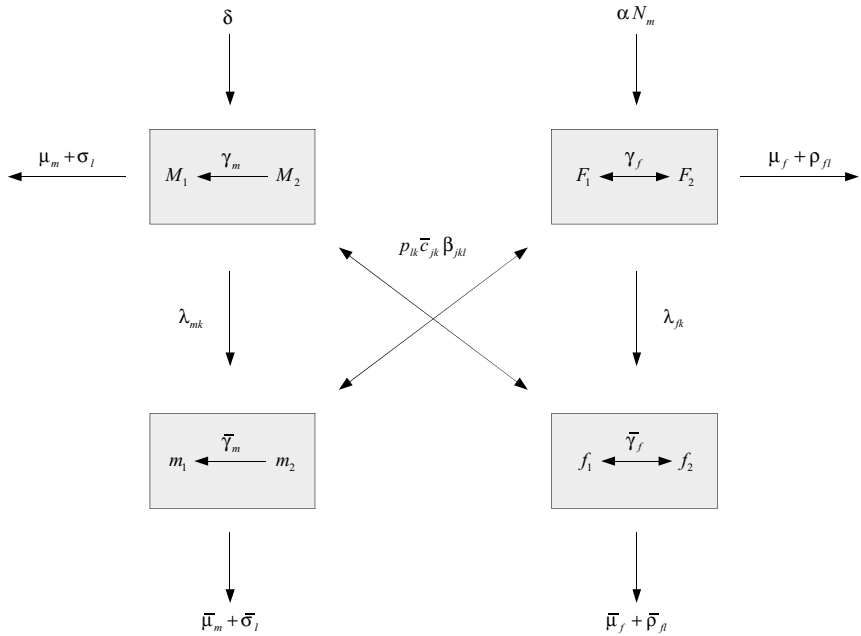

Fig. 1 The model.

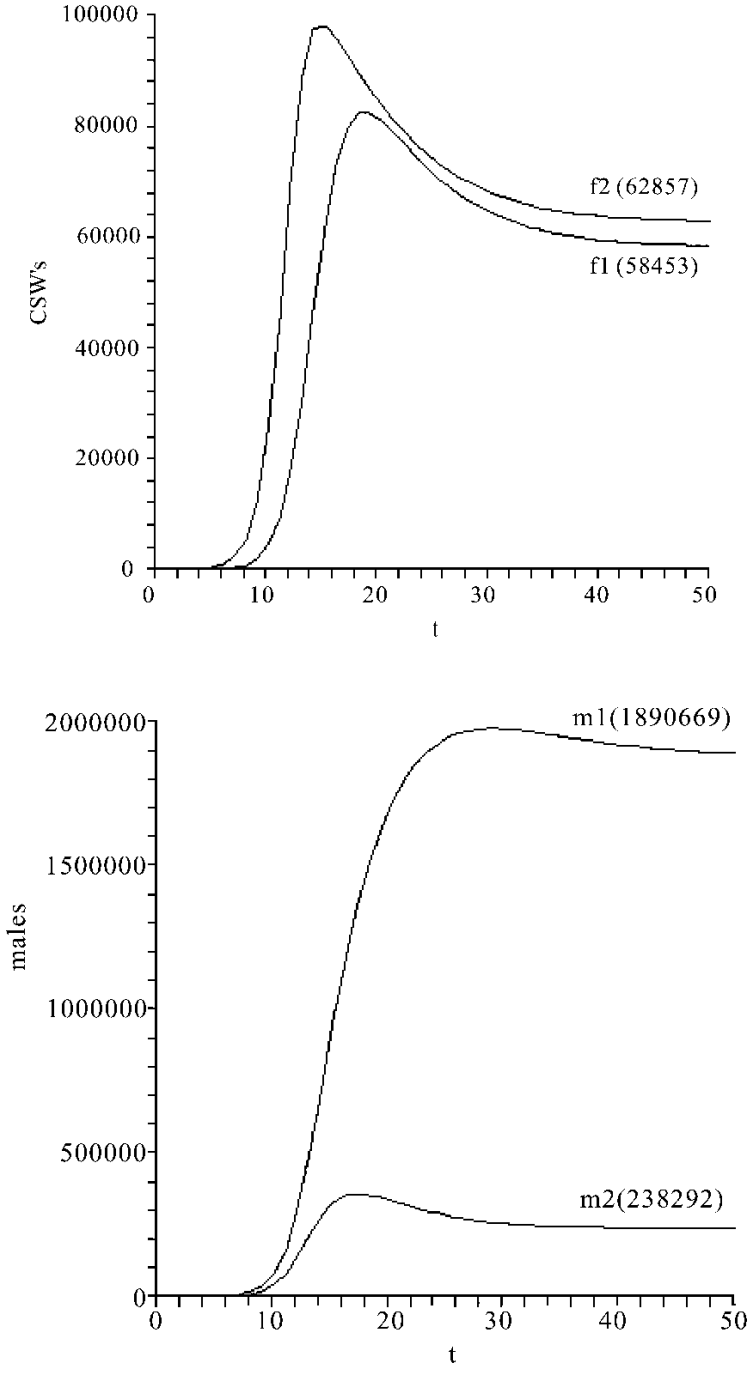

Fig. 2 Simulation for full model with $\theta = 0.5$. The system approaches the endemic equilibrium.

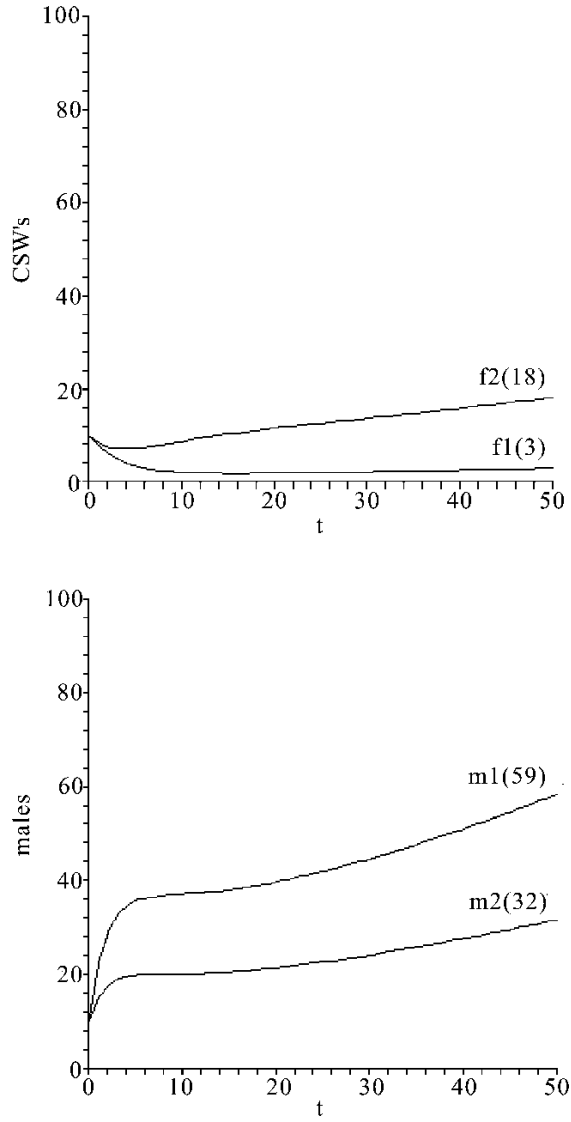

Fig. 3 Simulation for full model with $\theta = 0.5$ and the disease transmission parameters $\beta_{m_{ij}}$ and $\beta_{f_{ij}}$ lowered by 1/5. The system still approaches the endemic equilibrium.

of indirect CSWs needed in order to maintain equilibrium in the fraction of men seeking indirect CSWs. ρ_{fl}, $\bar{\rho}_{fl}$ are the retirement rates of susceptible and infected CSWs, respectively, of activity group l. σ_l, $\bar{\sigma}_l$, $l = 1, 2$ are the pairing rates of susceptible and infected single men, respectively, of group l. μ_l, $\bar{\mu}_l$ are the respective removal (due to death, AIDS, etc.) rates of susceptibles and infected persons of sex l. γ_f, $\bar{\gamma}_f$ are the rates of movement from direct to indirect CSW class (or from

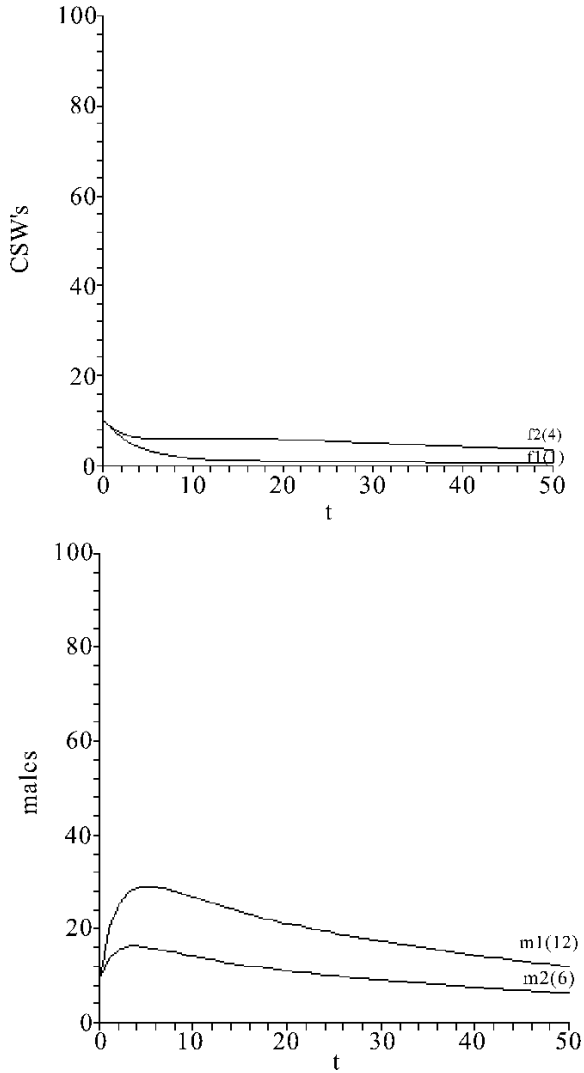

Fig. 4 Simulation for full model with $\theta = 0.5$ and the disease transmission parameters $\beta_{m_{ij}}$ and $\beta_{f_{ij}}$ lowered by 1/6. The system approaches DFE.

indirect to direct depending on the signs of G_1 and G_2) for susceptibles and infected persons, respectively. γ_m, $\bar{\gamma}_m$ are the rates of changed behavior of susceptible and infected single men, respectively, from high to low sexual activity due to the epidemic. δ is the yearly constant recruitment rate of sexually active single men, $\delta \gg 1$. ϕ is the initial fraction of susceptible men who are of low activity group. p_{kl} is the preference probability that a male of group k will have contact with a CSW of group l, with $p_{k1} + p_{k2} \leq 1$ (due to the possibility of contacts with noncommercial partners) and $p_{22} > p_{21}$. Note that no expression is given for the preference of

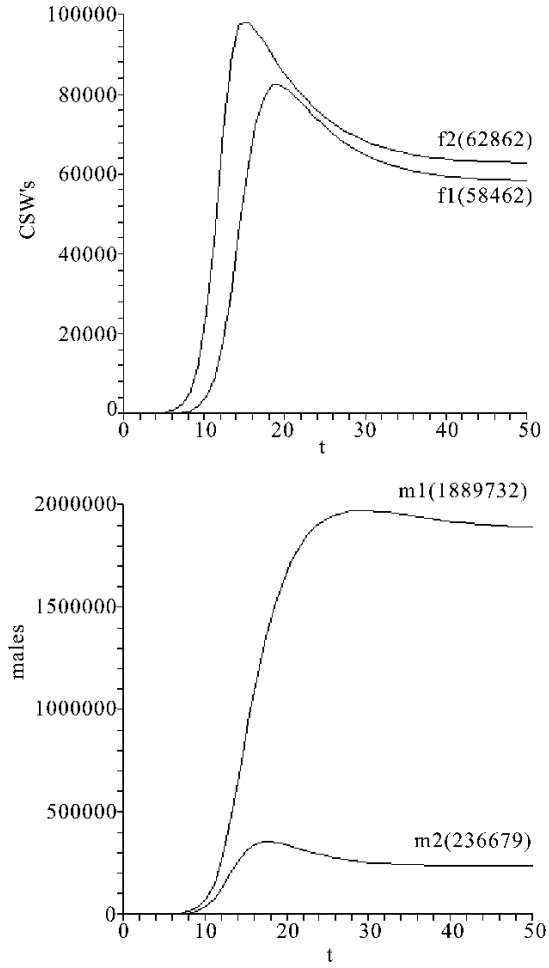

Fig. 5 Simulation for full model with $\theta = 0.5$ and the disease transmission parameters $\beta_{m_{21}}$ and $\beta_{f_{12}}$ lowered by 0.7. The system approaches endemic equilibrium.

CSW to contacts with male of a particular group, since CSWs do not choose their male customers. Hence, there is no conservation of contacts for this model. This is an underlying property of the "demand and supply" assumption, where the total number of contacts is predicated on the behavior of male customers. A detailed discussion of the key model assumptions was given in Hsieh and Chen (2004).

The model equations for the model in question, with "$\prime$" denoting derivative with respect to time:

$$F_1'(t) = \theta\alpha N_m(t) - [\mu_f + \rho_{f_1} + \lambda_{f_1}(t)]F_1(t) + \gamma_f G_1(t) \times \left[\frac{c_{m_1} M_1(t) + \bar{c}_{m_1} m_1(t)}{N_m(t)} - \theta\right]^2, \quad (1)$$

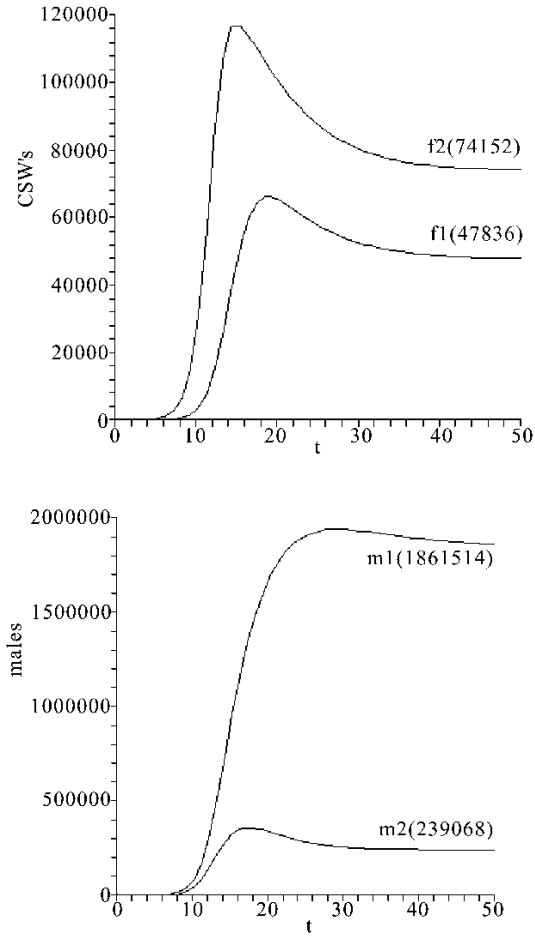

Fig. 6 Simulation for full model with $\theta = 0.4$. The system approaches the endemic equilibrium.

$$F_2'(t) = (1-\theta)\alpha N_m(t) - [\mu_f + \rho_{f_2} + \lambda_{f_2}(t)]F_2(t) - \gamma_f G_1(t) \times \left[\frac{c_{m_1} M_1(t) + \bar{c}_{m_1} m_1(t)}{N_m(t)} - \theta\right]^2, \tag{2}$$

$$M_1'(t) = \phi\delta - [\mu_m + \sigma_1 + \lambda_{m_1}(t)]M_1(t) + \gamma_m M_2(t)\frac{\sum_{l=1}^{2} f_l(t)}{\sum_{l=1}^{2}[F_l(t) + f_l(t)]}, \tag{3}$$

$$M_2'(t) = (1-\phi)\delta - [\mu_m + \sigma_2 + \lambda_{m_2}(t)]M_2(t) - \gamma_m M_2(t)\frac{\sum_{l=1}^{2} f_l(t)}{\sum_{l=1}^{2}[F_l(t) + f_l(t)]}, \tag{4}$$

$$f_1'(t) = -[\bar{\mu}_f + \bar{\rho}_{f_1}]f_1(t) + \lambda_{f_1}(t)F_1(t) + \bar{\gamma}_f G_2(t)\left[\frac{c_{m_1} M_1(t) + \bar{c}_{m_1} m_1(t)}{N_m(t)} - \theta\right]^2, \tag{5}$$

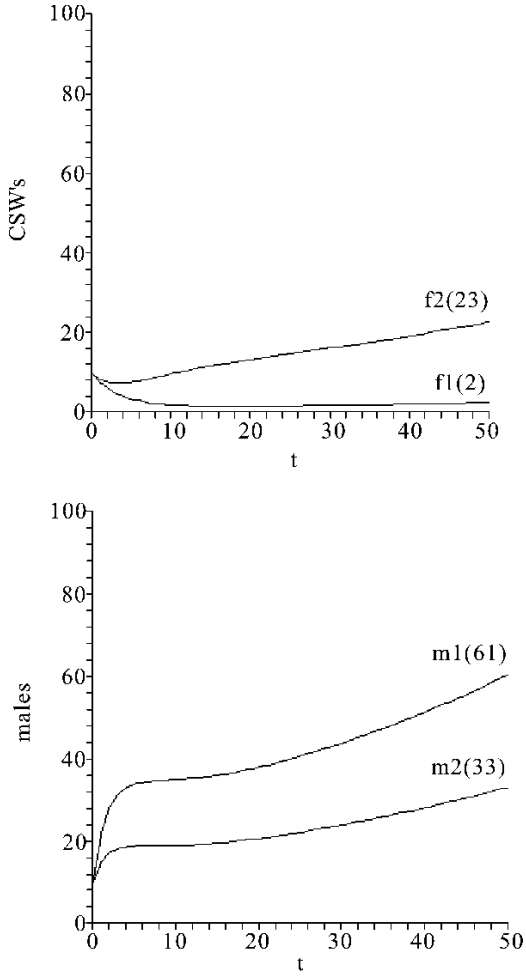

Fig. 7 Simulation for full model with $\theta = 0.4$ and the disease transmission parameters $\beta_{m_{ij}}$ and $\beta_{f_{ij}}$ lowered by 1/5. The system still approaches the endemic equilibrium.

$$f_2'(t) = -[\bar{\mu}_f + \bar{\rho}_{f_2}] f_2(t) + \lambda_{f_2}(t) F_2(t) - \bar{\gamma}_f G_2(t) \left[\frac{c_{m_1} M_1(t) + \bar{c}_{m_1} m_1(t)}{N_m(t)} - \theta \right]^2, \quad (6)$$

$$m_1'(t) = \lambda_{m_1}(t) M_1(t) - [\bar{\mu}_m + \bar{\sigma}_1] m_1(t) + \bar{\gamma}_m m_2(t) \frac{\sum_{l=1}^{2} f_l(t)}{\sum_{l=1}^{2} [F_l(t) + f_l(t)]}, \quad (7)$$

$$m_2'(t) = \lambda_{m_2}(t) M_2(t) - [\bar{\mu}_m + \bar{\sigma}_2] m_2(t) - \bar{\gamma}_m m_2(t) \frac{\sum_{l=1}^{2} f_l(t)}{\sum_{l=1}^{2} [F_l(t) + f_l(t)]}, \quad (8)$$

where

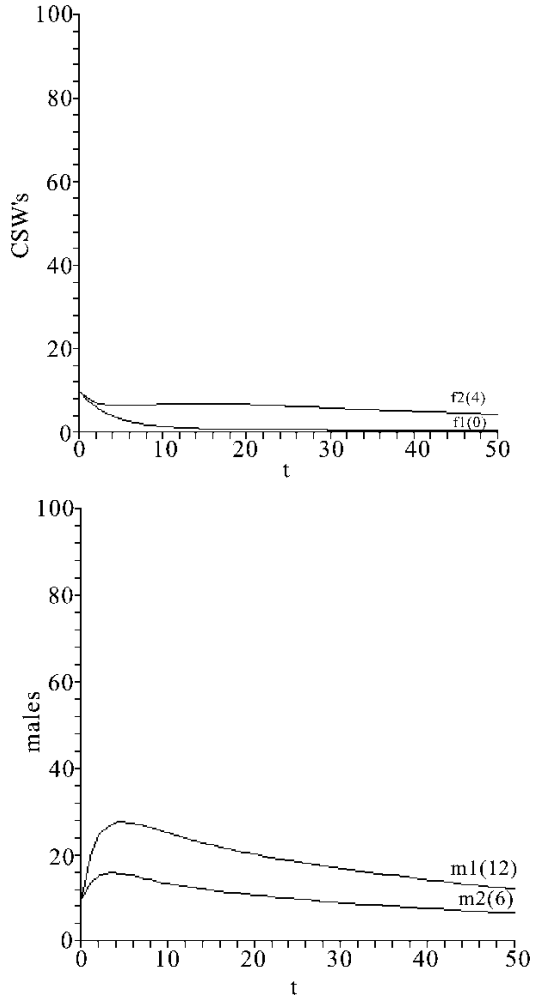

Fig. 8 Simulation for full model with $\theta = 0.4$ and the disease transmission parameters $\beta_{m_{ij}}$ and $\beta_{f_{ij}}$ lowered by 1/6. The system approaches DFE.

$$G_1(t) = \begin{cases} F_2(t), & \text{if } \frac{c_{m_1} M_1(t) + \bar{c}_{m_1} m_1(t)}{N_m(t)} \geq \theta, \\ -F_1(t), & \text{otherwise,} \end{cases}$$

$$G_2(t) = \begin{cases} f_2(t), & \text{if } \frac{c_{m_1} M_1(t) + \bar{c}_{m_1} m_1(t)}{N_m(t)} \geq \theta, \\ -f_1(t), & \text{otherwise.} \end{cases}$$

The incidence rates of new infections, λ_{fk} and λ_{mk} , where the subscript f denotes females and m denotes males, are given by

Table 1 Summary table for spectral radius and reproduction numbers of simulation examples.

Parameter values	$\rho(FV^{-1})$	R_1	R_2	Stability of DFE
$\theta = 0.5$				
Original $\beta_{m_{ij}}$ and $\beta_{f_{ij}}$ (Fig. 2)	5.403	1.721	—	Unstable
$\beta_{m_{ij}}, \beta_{f_{ij}}$ lowered by 1/5 (Fig. 3)	1.081	1.078	—	Unstable
$\beta_{m_{ij}}, \beta_{f_{ij}}$ lowered by 1/6 (Fig. 4)	0.900	0.903	0.647	Asymptotically stable
$\beta_{m_{21}}, \beta_{f_{12}}$ lowered by 0.7 (Fig. 5)	5.335	0.738	3.840	Unstable
$\theta = 0.4$				
Original $\beta_{m_{ij}}$ and $\beta_{f_{ij}}$ (Fig. 6)	5.473	3.349	—	Unstable
$\beta_{m_{ij}}, \beta_{f_{ij}}$ lowered by 1/5 (Fig. 7)	1.095	1.092	—	Unstable
$\beta_{m_{ij}}, \beta_{f_{ij}}$ lowered by 1/6 (Fig. 8)	0.912	0.914	0.652	Asymptotically stable

$$\lambda_{fk}(t) = c_{fk} \sum_{l=1}^{2} \frac{p_{lk} \bar{c}_{ml} \beta_{mlk} m_l(t)}{N_m(t)}, \quad k = 1, 2,$$

$$\lambda_{mk}(t) = c_{mk} \sum_{l=1}^{2} \frac{p_{kl} \bar{c}_{fl} \beta_{flk} f_l(t)}{N_f(t)}, \quad k = 1, 2.$$

The total numbers of sexual contacts for males and females, N_m and N_f, where f denotes females and m denotes males, are

$$N_m(t) = \sum_{l=1}^{2} [c_{ml} M_l(t) + \bar{c}_{ml} m_l(t)],$$

$$N_f(t) = \sum_{l=1}^{2} [c_{fl} F_l(t) + \bar{c}_{fl} f_l(t)].$$

Again, see Hsieh and Chen (2004) for detailed discussion on the choice of functions $G_i(t)$, $i = 1, 2$.

3. The basic reproduction number

Before analyzing the full model, we first note that by applying Theorem 2 in van den Driessche and Watmough (2002) to the two subcases of the model for which the basic reproduction number was obtained in Sections 4 and 5 of Hsieh and Chen (2004) (namely, the case with preferred mixing and no behavior change and the case with restricted mixing and behavior change), we can more easily obtain the same expressions for basic reproduction number as derived in Hsieh and Chen (2004). Moreover, the determination of DFE and the expressions for the disease-free population groups $\hat{M}_i$ and $\hat{N}_i$ at DFE are the same as the results in Section 3 of the 2004 paper, and hence are not repeated here for the sake of brevity. To consider the full model for which no local stability was done in Hsieh and Chen (2004), we will discuss two cases separately:

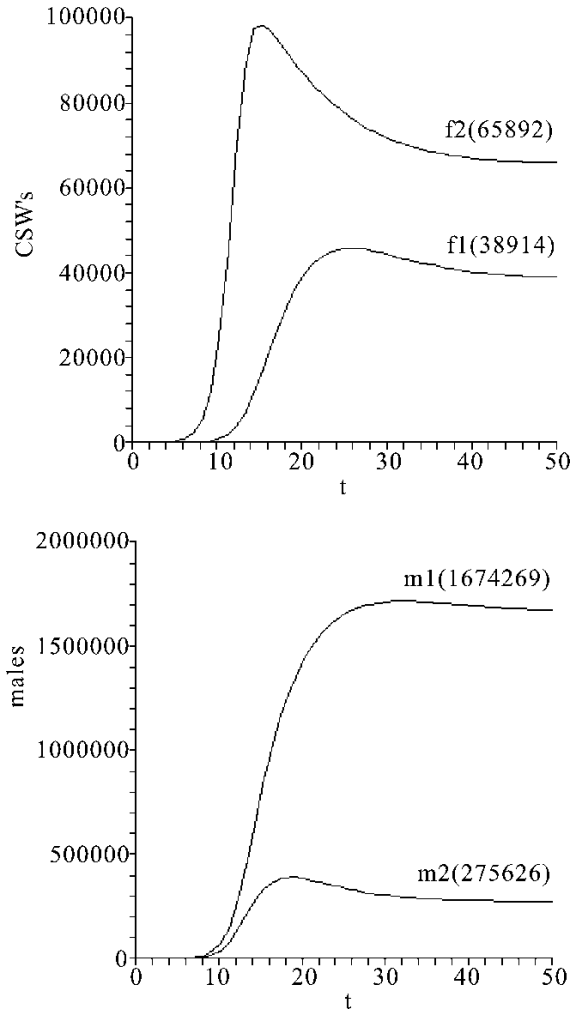

Fig. 9 Simulation for full model with $\theta = 0.5$ and the disease transmission parameters $\beta_{m_{11}}$ and $\beta_{f_{11}}$ lowered by 1/5. The system approaches endemic equilibrium.

3.1. Case (i)

When $\frac{c_{m_1} M_1(t) + \bar{c}_{m_1} m_1(t)}{N_m(t)} \geq \theta$, and $G_2(t) = f_2(t)$, the model equations for the infective classes are

$$f_1'(t) = -\bar{\mu}_f f_1(t) + \lambda_{f_1}(t) F_1(t) + \bar{\gamma}_f f_2(t) \left[\frac{c_{m_1} M_1(t) + \bar{c}_{m_1} m_1(t)}{N_m(t)} - \theta \right]^2,$$

$$f_2'(t) = -\bar{\mu}_f f_2(t) + \lambda_{f_2}(t) F_2(t) - \bar{\gamma}_f f_2(t) \left[\frac{c_{m_1} M_1(t) + \bar{c}_{m_1} m_1(t)}{N_m(t)} - \theta \right]^2,$$

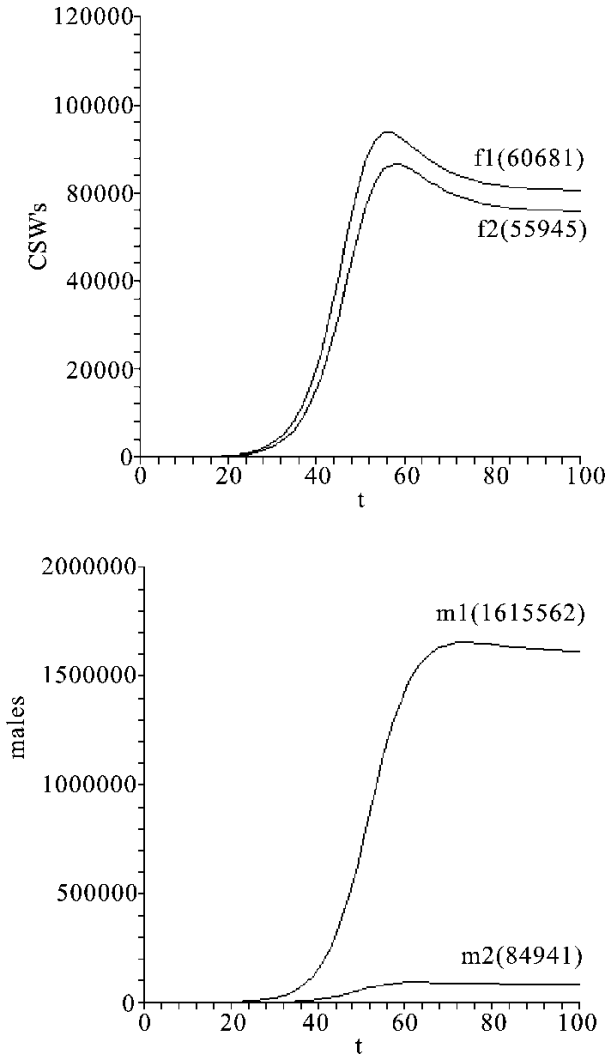

Fig. 10 Simulation for full model with $\theta = 0.5$ and the disease transmission parameters $\beta_{m_{22}}$ and $\beta_{f_{22}}$ lowered by 1/5. The system approaches endemic equilibrium.

$$m_1'(t) = \lambda_{m_1}(t)M_1(t) - \bar{\mu}_m m_1(t) + \bar{\gamma}_m m_2(t)\frac{\sum_{l=1}^{2} f_l(t)}{\sum_{l=1}^{2}\left[F_l(t) + f_l(t)\right]},$$

$$m_2'(t) = \lambda_{m_2}(t)M_2(t) - \bar{\mu}_m m_2(t) - \bar{\gamma}_m m_2(t)\frac{\sum_{l=1}^{2} f_l(t)}{\sum_{l=1}^{2}\left[F_l(t) + f_l(t)\right]}.$$

We have

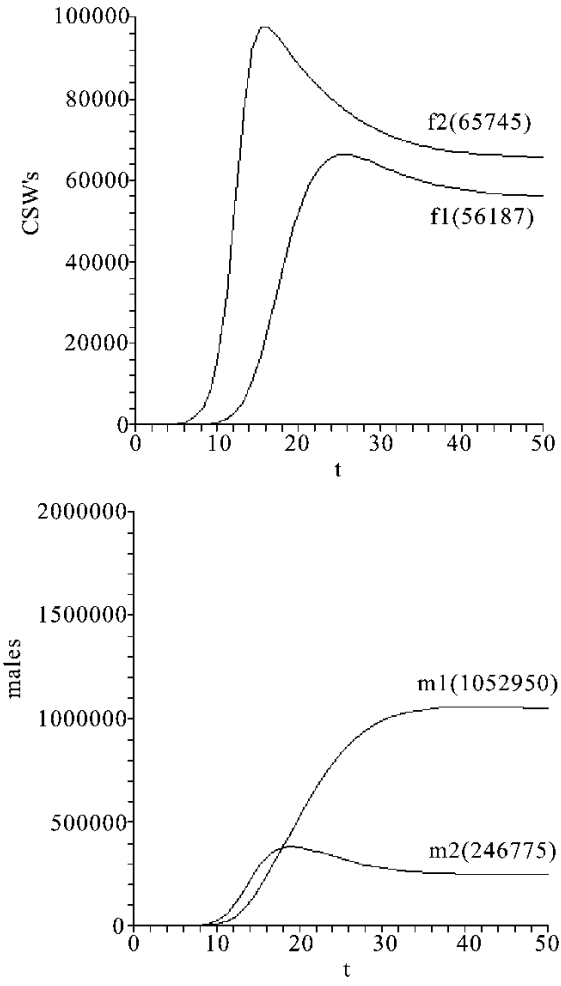

Fig. 11 Simulation for full model with $\theta = 0.5$ and the disease transmission parameters $\beta_{m_{12}}$ and $\beta_{f_{21}}$ lowered by 1/5. The system approaches endemic equilibrium.

$$\tilde{F} = \begin{pmatrix} \lambda_{f_1}(t)F_1(t) \\ \lambda_{f_2}(t)F_2(t) \\ \lambda_{m_1}(t)M_1(t) \\ \lambda_{m_2}(t)M_2(t) \end{pmatrix} \quad \text{and} \quad \tilde{V} = \begin{pmatrix} \bar{\mu}_f f_1(t) - \bar{\gamma}_f f_2(t)\left[\frac{c_{m_1}M_1(t)+\bar{c}_{m_1}m_1(t)}{N_m(t)} - \theta\right]^2 \\ \bar{\mu}_f f_2(t) + \bar{\gamma}_f f_2(t)\left[\frac{c_{m_1}M_1(t)+\bar{c}_{m_1}m_1(t)}{N_m(t)} - \theta\right]^2 \\ \bar{\mu}_m m_1(t) - \bar{\gamma}_m m_2(t)\frac{\sum_{l=1}^{2} f_l(t)}{\sum_{l=1}^{2}\left[F_l(t)+f_l(t)\right]} \\ \bar{\mu}_m m_2(t) + \bar{\gamma}_m m_2(t)\frac{\sum_{l=1}^{2} f_l(t)}{\sum_{l=1}^{2}\left[F_l(t)+f_l(t)\right]} \end{pmatrix}.$$

Consequently,

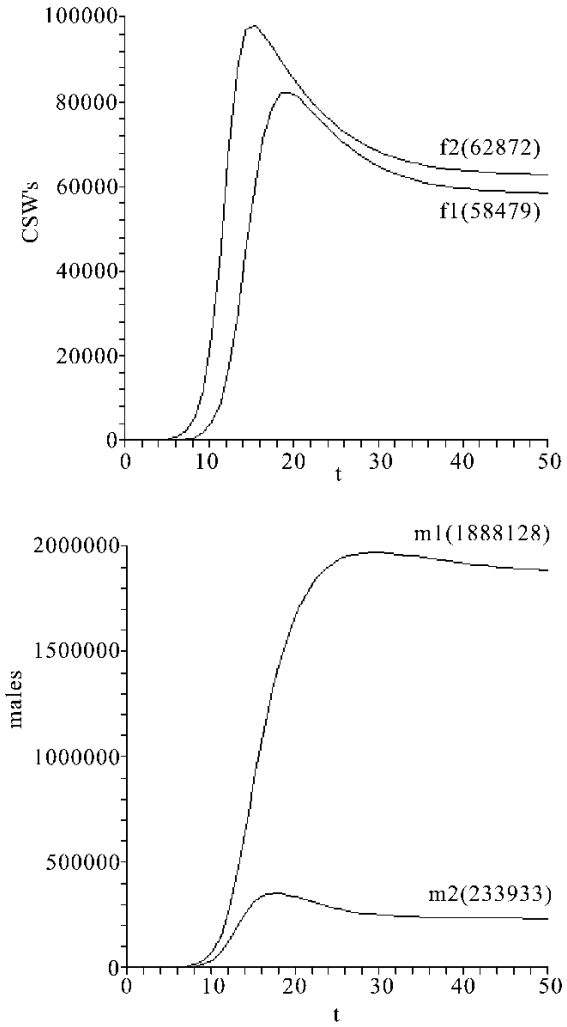

Fig. 12 Simulation for full model with $\theta = 0.5$ and the disease transmission parameters $\beta_{m_{21}}$ and $\beta_{f_{12}}$ lowered by 1/5. The system approaches endemic equilibrium.

$$F = \begin{pmatrix} 0 & 0 & \frac{c_{f_1} F_1 p_{11} \bar{c}_{m_1} \beta_{m_{11}}}{N_m} & \frac{c_{f_1} F_1 p_{21} \bar{c}_{m_2} \beta_{m_{21}}}{N_m} \\ 0 & 0 & \frac{c_{f_2} F_2 p_{12} \bar{c}_{m_1} \beta_{m_{12}}}{N_m} & \frac{c_{f_2} F_2 p_{22} \bar{c}_{m_2} \beta_{m_{22}}}{N_m} \\ \frac{c_{m_1} M_1 p_{11} \bar{c}_{f_1} \beta_{f_{11}}}{N_f} & \frac{c_{m1} M_1 p_{12} \bar{c}_{f_2} \beta_{f_{21}}}{N_f} & 0 & 0 \\ \frac{c_{m_2} M_2 p_{21} \bar{c}_{f_1} \beta_{f_{12}}}{N_f} & \frac{c_{m_2} M_2 p_{22} \bar{c}_{f_2} \beta_{f_{22}}}{N_f} & 0 & 0 \end{pmatrix}$$

and

Table 2 Comparison of spectral radius, approximate total infective population, and percentage decrease of the targeted risk group at endemic equilibrium N_∞ for targeting specific activity groups for transmission rates $\beta_{m_{ij}}$ and $\beta_{f_{ij}}$ lowered by 1/5 (with $\theta = 0.5$).

Parameters decreased by 1/5	$\rho(FV^{-1})$	Stability of DFE	N_∞	Target group (% decrease)
None (Fig. 2)	5.403	Unstable	2,250,908	—
$\beta_{m_{11}}, \beta_{f_{11}}$ (Fig. 9)	5.378	Unstable	2,054,701	f_1 (−33.4)
$\beta_{m_{22}}, \beta_{f_{22}}$ (Fig. 10)	2.098	Unstable	1,883,405	m_2 (−64.4)
$\beta_{m_{12}}, \beta_{f_{21}}$ (Fig. 11)	5.221	Unstable	1,421,657	m_1 (−44.3)
$\beta_{m_{21}}, \beta_{f_{12}}$ (Fig. 12)	5.220	Unstable	2,243,412	m_1 (−0.1)

$$V = \begin{pmatrix} \bar{\mu}_f & -\bar{\gamma}_f\left[\frac{c_{m_1} M_1}{N_m} - \theta\right]^2 & 0 & 0 \\ 0 & \bar{\mu}_f + \bar{\gamma}_f\left[\frac{c_{m_1} M_1}{N_m} - \theta\right]^2 & 0 & 0 \\ 0 & 0 & \bar{\mu}_m & 0 \\ 0 & 0 & 0 & \bar{\mu}_m \end{pmatrix}.$$

It follows that

$$V^{-1} = \begin{pmatrix} \frac{1}{\bar{\mu}_f} & \frac{1}{\bar{\mu}_f}\frac{\bar{\gamma}_f\left(c_{m_1} M_1 - \theta N_m\right)^2}{\bar{\mu}_f N_m^2 + \bar{\gamma}_f\left(c_{m_1} M_1 - \theta N_m\right)^2} & 0 & 0 \\ 0 & \frac{N_m^2}{\bar{\mu}_f N_m^2 + \bar{\gamma}_f\left(c_{m_1} M_1 - \theta N_m\right)^2} & 0 & 0 \\ 0 & 0 & \frac{1}{\bar{\mu}_m} & 0 \\ 0 & 0 & 0 & \frac{1}{\bar{\mu}_m} \end{pmatrix}$$

and

$$FV^{-1} = \begin{pmatrix} 0 & 0 & R_{m_{11}}^2 \frac{N_f}{N_m} & R_{m_{21}}^2 \frac{N_f}{N_m} \\ 0 & 0 & R_{m_{12}}^2 \frac{N_f}{N_m} & R_{m_{22}}^2 \frac{N_f}{N_m} \\ R_{f_{11}}^2 \frac{N_m}{N_f} & \frac{N_m}{N_f}\left[\frac{R_{f_{11}}^2 \bar{\gamma}_f\left(c_{m_1} M_1 - \theta N_m\right)^2 + R_{f_{12}}^2 \bar{\mu}_f N_m^2}{\bar{\mu}_f N_m^2 + \bar{\gamma}_f\left(c_{m_1} M_1 - \theta N_m\right)^2}\right] & 0 & 0 \\ R_{f_{21}}^2 \frac{N_m}{N_f} & \frac{N_m}{N_f}\left[\frac{R_{f_{21}}^2 \bar{\gamma}_f\left(c_{m_1} M_1 - \theta N_m\right)^2 + R_{f_{22}}^2 \bar{\mu}_f N_m^2}{\bar{\mu}_f N_m^2 + \bar{\gamma}_f\left(c_{m_1} M_1 - \theta N_m\right)^2}\right] & 0 & 0 \end{pmatrix}.$$

The spectral radius is then

$$\rho(FV^{-1}) = \left[\frac{x + y + z + w + \sqrt{(x + y + z + w)^2 - 4xy - 4zw + 4m + 4n}}{2}\right]^{1/2}, \qquad (9)$$

Table 3 Comparison of spectral radius and approximate total infective population at endemic equilibrium N_∞ for targeting specific activity groups for decreased transmission.

Target group	Parameters (with $\theta = 0.5$)	$\rho(FV^{-1})$	Stability of DFE	N_∞
—	Original $\beta_{m_{ij}}$ and $\beta_{f_{ij}}$ (Fig. 2)	5.403	Unstable	2,250,908
m_1	$\beta_{m_{11}}, \beta_{f_{11}}, \beta_{m_{12}}, \beta_{f_{21}}$ lowered by 1/5	5.215	Unstable	1,015,028
m_2	$\beta_{m_{21}}, \beta_{f_{12}}, \beta_{m_{22}}, \beta_{f_{22}}$ lowered by 1/5	1.500	Unstable	1,791,484
f_1	$\beta_{m_{11}}, \beta_{f_{11}}, \beta_{m_{21}}, \beta_{f_{12}}$ lowered by 1/5	5.215	Unstable	2,048,994
f_2	$\beta_{m_{12}}, \beta_{f_{21}}, \beta_{m_{22}}, \beta_{f_{22}}$ lowered by 1/5	1.502	Unstable	587,380

where $x = R_{m_{11}}^2 R_{f_{11}}^2$, $y = R_{m_{22}}^2 \left[\frac{R_{f_{21}}^2 \bar{\gamma}_f \left(c_{m_1} M_1 - \theta N_m\right)^2 + R_{f_{22}}^2 \bar{\mu}_f N_m^2}{\bar{\mu}_f N_m^2 + \bar{\gamma}_f \left(c_{m_1} M_1 - \theta N_m\right)^2} \right]$,

$$z = R_{m_{12}}^2 \left[\frac{R_{f_{11}}^2 \bar{\gamma}_f \left(c_{m_1} M_1 - \theta N_m\right)^2 + R_{f_{12}}^2 \bar{\mu}_f N_m^2}{\bar{\mu}_f N_m^2 + \bar{\gamma}_f \left(c_{m_1} M_1 - \theta N_m\right)^2} \right], \quad w = R_{m_{21}}^2 R_{f_{21}}^2,$$

$$m = R_{m_{11}}^2 \left[\frac{R_{f_{11}}^2 \bar{\gamma}_f \left(c_{m_1} M_1 - \theta N_m\right)^2 + R_{f_{12}}^2 \bar{\mu}_f N_m^2}{\bar{\mu}_f N_m^2 + \bar{\gamma}_f \left(c_{m_1} M_1 - \theta N_m\right)^2} \right] R_{m_{22}}^2 R_{f_{21}}^2,$$

$$n = R_{m_{21}}^2 R_{f_{11}}^2 R_{m_{12}}^2 \left[\frac{R_{f_{21}}^2 \bar{\gamma}_f \left(c_{m_1} M_1 - \theta N_m\right)^2 + R_{f_{22}}^2 \bar{\mu}_f N_m^2}{\bar{\mu}_f N_m^2 + \bar{\gamma}_f \left(c_{m_1} M_1 - \theta N_m\right)^2} \right].$$

We have the following theorem for the local stability of DFE:

Theorem 3.1. *For the system in Eqs. (1)–(8), if* $x + y + z + w + m + n - xy - zw < 0$, *then the DFE is always unstable. On the other hand, if* $x + y + z + w + m + n - xy - zw \geq 0$ *and let* $R_1^2 = x + y + z + w + m + n - xy - zw$, $R_2^2 = \frac{x+y+z+w}{2}$, *the following holds:*

(1) If $R_1 > 1$, *then DFE is unstable.*
(2) If $R_1 < 1$ *and* $R_2 < 1$, *then DFE is locally asymptotically stable.*
(3) If $R_1 < 1$ *and* $R_2 > 1$, *then DFE is unstable.*

Proof The first result follows from the expression for the spectral radius. For the remaining results, there are two cases which we need to consider:

(a) If $x + y + z + w + \sqrt{(x + y + z + w)^2 - 4xy - 4zw + 4m + 4n} < 2$ (which implies $R_2 < 1$), then

$$\begin{aligned}
[\rho(FV^{-1})]^2 &= \frac{x + y + z + w + \sqrt{(x + y + z + w)^2 - 4xy - 4zw + 4m + 4n}}{2} < 1 \\
&\iff (x + y + z + w)^2 - 4xy - 4zw + 4m + 4n < (2 - x - y - z - w)^2 \\
&\iff x + y + z + w + m + n - xy - zw < 1.
\end{aligned}$$

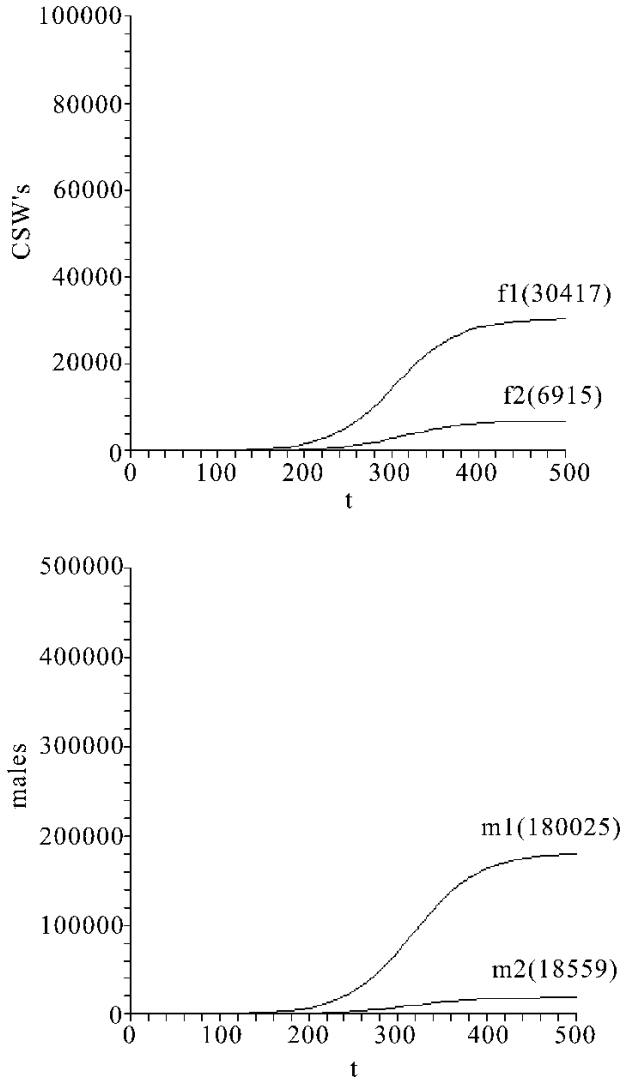

Fig. 13 Simulation for full model with $\theta = 0.5$ and targeting the highly active infective brothel CSW(f_2) for intervention by lowering the disease transmission parameters $\beta_{m_{12}}$, $\beta_{f_{21}}$, $\beta_{m_{22}}$ and $\beta_{f_{22}}$ by 1/10. The system approaches an endemic equilibrium.

We note that the left-hand side of the last inequality is R_1^2.

(b) If $x + y + z + w + \sqrt{(x + y + z + w)^2 - 4xy - 4zw + 4m + 4n} > 2$, then

$$\left[\rho(FV^{-1})\right]^2 = \frac{x + y + z + w + \sqrt{(x + y + z + w)^2 - 4xy - 4zw + 4m + 4n}}{2} > 1$$

$$\Longleftrightarrow \sqrt{(x + y + z + w)^2 - 4xy - 4zw + 4m + 4n} > (2 - x - y - z - w).....(*).$$

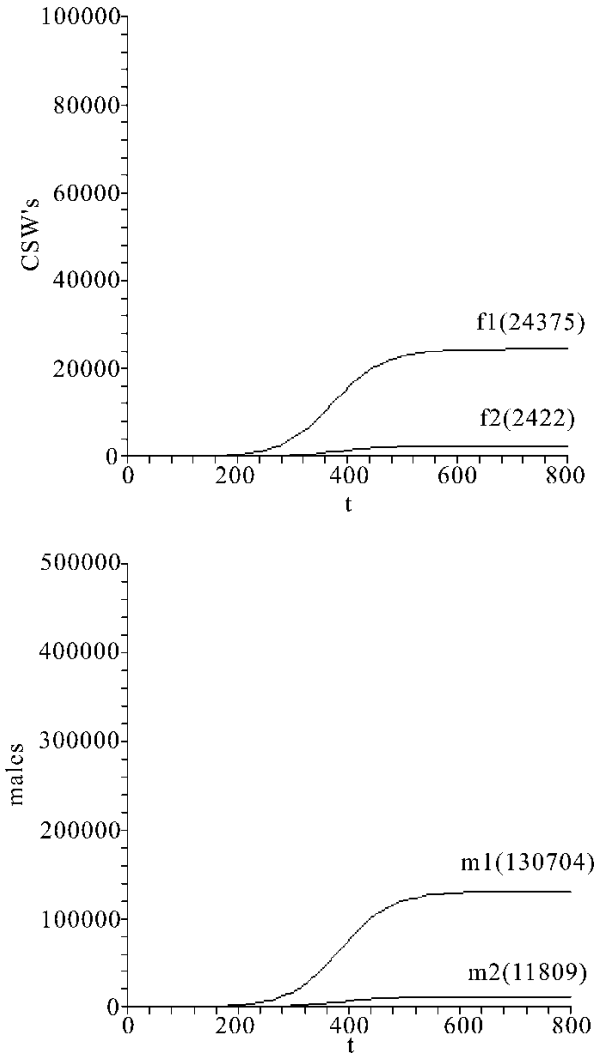

Fig. 14 Simulation for full model with $\theta = 0.5$ and targeting the highly active infective brothel CSW(f_2) for intervention by lowering the disease transmission parameters $\beta_{m_{12}}$, $\beta_{f_{21}}$, $\beta_{m_{22}}$ and $\beta_{f_{22}}$ by 1/20. The system approaches an endemic equilibrium.

This is the case where DFE is unstable, but R_1 could be either greater or less than 1. First, we consider the case where $\sqrt{(x+y+z+w)^2 - 4xy - 4zw + 4m + 4n} > x + y + z + w - 2$. We then have

$$(*) \iff (x+y+z+w)^2 - 4xy - 4zw + 4m + 4n > (2 - x - y - z - w)^2$$
$$\iff x + y + z + w + m + n - xy - zw > 1.$$

On the other hand, if $\sqrt{(x+y+z+w)^2-4xy-4zw+4m+4n} < x+y+z+w-2$, then

$$\begin{aligned}(*) &\Longleftrightarrow (x+y+z+w)^2-4xy-4zw+4m+4n < (2-x-y-z-w)^2\\ &\Longleftrightarrow x+y+z+w+m+n-xy-zw<1\\ &\Longleftrightarrow 2-(x+y+z+w+m+n-xy-zw)>1.\end{aligned}$$

Subsequently, in both of these two instances where DFE is unstable, there is a secondary condition, in addition to the usual condition on the reproduction number R_1. Consequently, for both cases (a) and (b), we have the theorem.

Remark 1. Alternatively, we could restate Theorem 3.1 in the following manner.

Corollary 3.2. For the system in Eqs. (1)–(8), DFE is locally asymptotically stable if and only if $x+y+z+w+m+n-xy-zw \geq 0$, $R_1<1$ and $R_2<1$.
Biological interpretation of this result will be given later in Section 5.

3.2 Case (ii)

When $\frac{c_{m_1}M_1(t)+\bar{c}_{m_1}m_1(t)}{N_m(t)} < \theta$ and $G_2(t) = -f_2(t)$.

Similarly to the case (i), we obtain

$$\rho(FV^{-1}) = \left[\frac{x+y+z+w+\sqrt{(x+y+z+w)^2-4xy-4zw+4m+4n}}{2}\right]^{1/2},$$

where

$$x = R_{m_{11}}^2\left[\frac{R_{f_{12}}^2\bar{\gamma}_f\left(c_{m_1}M_1-\theta N_m\right)^2+R_{f_{11}}^2\bar{\mu}_f N_m^2}{\bar{\mu}_f N_m^2+\bar{\gamma}_f\left(c_{m_1}M_1-\theta N_m\right)^2}\right],\ y = R_{m_{22}}^2R_{f_{22}}^2,$$

$$z = R_{m_{12}}^2R_{f_{12}}^2,\ w = R_{m_{21}}^2\left[\frac{R_{f_{22}}^2\bar{\gamma}_f\left(c_{m_1}M_1-\theta N_m\right)^2+R_{f_{21}}^2\bar{\mu}_f N_m^2}{\bar{\mu}_f N_m^2+\bar{\gamma}_f\left(c_{m_1}M_1-\theta N_m\right)^2}\right],$$

$$m = R_{m_{11}}^2R_{f_{12}}^2R_{m_{22}}^2\left[\frac{R_{f_{22}}^2\bar{\gamma}_f\left(c_{m_1}M_1-\theta N_m\right)^2+R_{f_{21}}^2\bar{\mu}_f N_m^2}{\bar{\mu}_f N_m^2+\bar{\gamma}_f\left(c_{m_1}M_1-\theta N_m\right)^2}\right],$$

$$n = R_{m_{21}}^2\left[\frac{R_{f_{12}}^2\bar{\gamma}_f\left(c_{m_1}M_1-\theta N_m\right)^2+R_{f_{11}}^2\bar{\mu}_f N_m^2}{\bar{\mu}_f N_m^2+\bar{\gamma}_f\left(c_{m_1}M_1-\theta N_m\right)^2}\right]R_{m_{12}}^2R_{f_{22}}^2.$$

Note that while the expression for the spectral radius is the same as Case (i), the definitions for the parameters x, y, z, w, m, and n are different.

Again, we discuss the following two cases separately:

(a) If $x + y + z + w + \sqrt{(x + y + z + w)^2 - 4xy - 4zw + 4m + 4n} < 2$, then

$$\frac{x + y + z + w + \sqrt{(x + y + z + w)^2 - 4xy - 4zw + 4m + 4n}}{2} < 1$$
$$\Longleftrightarrow x + y + z + w + m + n - xy - zw < 1.$$

(b) If $x + y + z + w + \sqrt{(x + y + z + w)^2 - 4xy - 4zw + 4m + 4n} > 2$, then

$$\frac{x + y + z + w + \sqrt{(x + y + z + w)^2 - 4xy - 4zw + 4m + 4n}}{2} > 1.$$

It follows similarly that if $\sqrt{(x + y + z + w)^2 - 4xy - 4zw + 4m + 4n} > x + y + z + w - 2$
then $x + y + z + w + m + n - xy - zw > 1$.

But when $\sqrt{(x + y + z + w)^2 - 4xy - 4zw + 4m + 4n} < x + y + z + w - 2$
we have $2 - (x + y + z + w + m + n - xy - zw) > 1$.

Subsequently, by letting $R_1^2 = x + y + z + w + m + n - xy - zw$, $R_2^2 = \frac{x+y+z+w}{2}$, we know that Theorem 3.1 for Case (i) holds here also, albeit with different definition for the parameters x, y, z, w, m and n as mentioned before.

Remark 2. Since DFE is on the boundary of the positive region in the eight-dimensional space $D_8 = \{F_i, M_i > 0 \text{ and } f_i, m_i \geq 0, i = 1, 2\}$, when it is unstable we have obviously the existence of endemic equilibrium. We further conjecture that the endemic equilibrium is unique and globally asymptotically stable, but the proof is difficult to obtain. Therefore, we will make use of numerical simulations to describe the global properties of the system in question.

4. Numerical examples

We first illustrate our results using some simulated examples. The following parameter values were used for the example in Fig. 10 of Hsieh and Chen (2004): $c_{f_1} = 100$, $c_{f_2} = 1000$, $c_{m_1} = 10$, $c_{m_2} = 50$, $\mu_f = 0.16$, $\mu_m = 0.09$, $\bar{c}_{f_1} = 100$, $\bar{c}_{f_2} = 850$, $\bar{c}_{m_1} = 10$, $\bar{c}_{m_2} = 50$, $\bar{\mu}_f = 0.25$, $\bar{\mu}_m = 0.13$, $\beta_{f_{11}} = 0.05$, $\beta_{f_{12}} = 0.02$, $\beta_{f_{21}} = 0.02$, $\beta_{f_{22}} = 0.005$, $\beta_{m_{11}} = 0.08$, $\beta_{m_{12}} = 0.004$, $\beta_{m_{21}} = 0.004$, $\beta_{m_{22}} = 0.01$, $\alpha = 0.0005$, $\delta = 500000$, $\theta = 0.5$, $\phi = 0.8$, $\gamma_f = 0.1$, $\bar{\gamma}_f = 0.1$, $\gamma_m = 0.1$, $\bar{\gamma}_m = 0.1$. However, we use preferred mixing where $p_{11} = 0.5$, $p_{12} = 0.5$, $p_{21} = 0.1$, $p_{22} = 0.9$.

The initial susceptible populations sizes are the same as the DFE population sizes, i.e., $\hat{M}_1 = 4,444,444$, $\hat{M}_2 = 1,111,111$, $N_m = 100,000,000$, $\hat{F}_1 = 155,948$, $\hat{F}_2 = 156,552$ and $N_f = 172,146,800$. Assuming we have infectives entering a susceptible community at $t = 0$, the initial infective population sizes are given by

$m_1 = m_2 = f_1 = f_2 = 10$. The simulation result is given in Fig. 2. The system satisfies Case (ii) described in Section 3.3 with $\frac{c_{m_1} M_1(t) + \bar{c}_{m_1} m_1(t)}{N_m(t)} < \theta$. Consequently, we have $R_1 = 1.721$ and the system approaches an endemic equilibrium with the approximate asymptotic infective population sizes given for f_1, f_2, m_1 and m_2. If we lower the disease transmission parameters $\beta_{m_{ij}}$ and $\beta_{f_{ij}}$ by 1/5, we obtain the value of $R_1 = 1.078$ and the system still goes to the endemic equilibrium (Fig. 3). Clearly, the numbers of infective populations at the endemic equilibrium is much smaller than those of Fig. 2, hence showing the benefit of reduced disease transmission via safe behavior resulting in reduction in contact rate or per contact transmission probability. If we further reduce the disease transmission parameters $\beta_{m_{ij}}$ and $\beta_{f_{ij}}$ just slightly more, i.e., by 1/6, we get $R_1 = 0.903$, and $R_2 = 0.647$, hence by Theorem 3.1 the system goes to DFE (Fig. 4). Furthermore, to illustrate the possibility of subcase 3 in Theorem 3.1 where $R_1 < 1$ and $R_2 > 1$, and DFE is unstable, we let only $\beta_{m_{21}}$ and $\beta_{f_{12}}$ be lowered by 0.7 to obtain $R_1 = 0.738$ and $R_2 = 3.840$, and hence DFE is unstable even though we have $R_1 < 1$ (Fig. 5).

If we let $\theta = 0.4$ and $\hat{F}_1 = 125,234$, $\hat{F}_2 = 187,266$, $N_f = 199,789,400$ due to the change in θ, with all other parameters remain the same, we then have Case (i) in Section 3.3 with $\frac{c_{m_1} M_1(t) + \bar{c}_{m_1} m_1(t)}{N_m(t)} \geq \theta$ instead. Hence we have Fig. 6 where $R_1 = 3.349$ and the system approaches an endemic equilibrium. Again, lowering the disease transmission parameters $\beta_{m_{ij}}$ and $\beta_{f_{ij}}$ by 1/5 results in $R_1 = 1.092$ and the system still goes to the endemic equilibrium (Fig. 7) with smaller asymptotic infective population sizes, and reducing the disease transmission parameters $\beta_{m_{ij}}$ and $\beta_{f_{ij}}$ by 1/6, we get $R_1 = 0.914$, $R_2 = 0.652$, hence by Theorem 3.1 the system goes to DFE (Fig. 8).

To summarize the simulation results clearly, we give the values of $\rho(FV^{-1})$, R_1, and R_2 when applicable, as well as the local stability of DFE for the above simulation examples in Table 1.

5. Discussions

We first note that the very useful theorem proposed by van den Driessche and Watmough (2002), which depends on the simple condition of whether the spectral radius $\rho(FV^{-1})$ is greater or less than 1, is the most straight forward and simple criterion for the local stability of DFE for a general class of infectious disease models. However, for more complicated models such as our current model, it lacks simple epidemiological interpretation. Subsequently, we derive the equivalent conditions for local stability of DFE using the parameters R_1 and R_2, the meaning of which we shall explain later in this section. We also ran various simulations with a wide range of initial infective populations under the condition that the DFE is unstable, all of which approaching the same endemic equilibrium. Hence, we conjecture that the endemic equilibrium, when exists, is unique and the asymptotic stability is global.

To consider the possibility of targeting certain populations for intervention and control of the epidemic, we further simulate the results where only the transmission rates of each of the four possible paths of transmission (see Fig. 1) are lowered.

The lowered transmission rates can be accomplished by government campaign to reduce risk of transmission by, for example, advocating safe sex or abstinence. Figures 9–12 give the result of simulations by lowering the transmission rates of each of the four paths of transmission by 1/5. Table 2 shows that all values of the spectral radius are still well above 1. In fact, unlike the previous examples in Figs. 4 and 8 where sufficient reduction in all transmission rates would result in eradication of the epidemic, further simulations with smaller transmission rates show that if only one of the four paths is lowered, no matter by how much, the DFE is always unstable. Hence, targeting any one type of sex commerce will not have a decided effect on eradicating the epidemic. On the other hand, we note that targeting any particular path of transmission for prevention has decidedly different effect, and the most efficient way to reduce the spectral radius is by lowering $\beta_{m_{22}}$ and $\beta_{f_{22}}$ (see Table 2). However, the goal of any intervention measure is decreasing the number of infections, if not total eradication. To this end, we also compute the approximate total infective population at endemic equilibrium $N_\infty = f_1 + f_2 + m_1 + m_2$ for targeting specific activity groups for decreased transmission, where f_1, f_2, m_1, and m_2 are the approximate asymptotic infective population sizes given in Figs. 9–12. The results show that the reduction in total infections vary significantly, ranging from trivial reduction in targeting the transmission route between highly active males and indirect CSWs (Fig. 12 and last row in Table 2) to reduction almost by half in targeting the transmission route between lowly active males and direct brothel CSW's (Fig. 11 and next to last row in Table 2). Moreover, the last column in Table 2 gives the largest percentage decrease in any group at the endemic equilibrium. Note that there is no significant decrease in any group in Fig. 12 even if $\beta_{m_{21}}$, $\beta_{f_{12}}$ lowered by 1/5 (last entry of last row in Table 2). Therefore, if the aim of the policy-makers is not eradication of the epidemic but decrease in HIV incidence of specific high-risk groups, then concentrated targeting strategy could be sufficient, if the targeted group is correctly chosen. One should note, however, that the use of asymptotic results for our interpretation place emphasis on the long-term effect, hence prevention measures targeted toward the susceptibles among the lowly active males, which is most numerous of the four susceptible population groups considered and most vulnerable to long-term infections, is intuitively most crucial.

To complete the examination of all feasible targeting strategies and to provide further insight into the epidemiological consequence of this modeling study, we further consider the effectiveness of targeted intervention measures aimed at one particular high-risk group by performing simulations where the transmission rates of one of high-risk groups is lowered. That is, we lower two of the four paths of transmission belonging to the infective activity group we wish to target our intervention. For example, to target the lowly active infective males (m_1), we would lower the transmission paths $\beta_{m_{11}}$, $\beta_{f_{11}}$, $\beta_{m_{12}}$ and $\beta_{f_{21}}$, to account for the reduction in transmission for this infective group's contact with both indirect and direct CSWs (f_1 and f_2, respectively). Table 3 shows that all values of the spectral radius are still well above 1. However, for reduction of infections, the most crucial activity group to target is the direct brothel CSW group (f_2, see last row of Table 3). This is intuitively obvious, as the direct brothel CSW group has the highest contact rate of any group considered.

We note that, similar to our simulations for targeting one transmission route (see Table 2), further lowering transmission rates of a single infective group does not change the stability of the endemic equilibrium. Figure 13 gives the simulation with $\theta = 0.5$ and targeting the highly active infective brothel CSW(f_2) for intervention by lowering the disease transmission parameters $\beta_{m_{12}}$, $\beta_{f_{21}}$, $\beta_{m_{22}}$ and $\beta_{f_{22}}$ by 1/10, with the system approaches an endemic equilibrium. Figure 14 is the simulation with $\theta = 0.5$ and targeting the same group for intervention by lowering the disease transmission parameters $\beta_{m_{12}}$, $\beta_{f_{21}}$, $\beta_{m_{22}}$ and $\beta_{f_{22}}$ by 1/20, and the system also approaches an endemic equilibrium with lower infective population size. Further lowering the transmission rates will further lower the infective population size, but the endemic equilibrium remains asymptotically stable. Hence, total eradication of the disease requires full-scale intervention across all possible routes of transmission.

Finally, the use of the spectral radius of FV^{-1}, $\rho(FV^{-1})$, as proposed by van den Driessche and Watmough (2002), yields a simple and straightforward criterion for the stability of DFE. However, at least in this model, the resulting expression lacks clear epidemiological meaning. Therefore, we restated the criterion in terms of the reproduction numbers R_1 and R_2. As stated in Corollary 3.2, DFE is locally asymptotically stable if and only if $x + y + z + w + m + n - xy - zw \geq 0$, $R_1 < 1$, and $R_2 < 1$. Using the terminology of Hsieh and Chen (2004), x, y, z, and w account for the numbers of secondary infections due to infection cycles of length 2 (see Fig. 6 in Hsieh and Chen, 2004), while m and n represent the corresponding numbers due to infection cycles of length 4 (Fig. 7 in Hsieh and Chen, 2004). xy and zw are the redundant number due to nonexistent infection cycles of length 4 (Fig. 8 in Hsieh and Chen, 2004). Since the total sum of squares of the numbers of secondary infections must be nonnegative for it to be meaningful. Furthermore, it must be less than 1. The last condition ($R_2 < 1$) that the sum of squares of numbers of secondary infections due to the infection cycles of length 2 must be less than 2, or alternatively the arithmetic mean of the sum of squares of number of secondary infections due to the four infection cycles of length 2 is less than 1/2, is less intuitive. But it seems to be a necessary additional constraint on the amount of restricted mixing between like activity groups in order for DFE to be asymptotically stable.

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