Modelling the effect of treatment and behavioral change in HIV transmission dynamics

Jorge X. Velasco-Hernandez[1], Ying-Hen Hsieh[2]

[1] Biometrics Unit 322 Warren Hall, Cornell University Ithaca, NY 14853, USA, and Departamento El Hombre y su Ambiente, Universidad Autonoma Metropolitana-Xochimilco, Calzada del Hueso No. 1100, Col. Villa Quietud, Mexico City, Mexico
[2] Department of Applied Mathematics, National Chung-Hsing University, Taichung, Taiwan, ROC

Abstract. In this paper we analyze a model for the HIV-infection transmission in a male homosexual population. In the model we consider two types of infected individuals. Those that are infected but do not know their serological status and/or are not under any sort of clinical/therapeutical treatment, and those who are. The two groups of infectives differ in their incubation time, contact rate with susceptible individuals, and probability of disease transmission. The aim of this article is to study the roles played by detection and changes in sexual behavior in the incidence and prevalence of HIV. The analytical results show that there exists a unique endemic equilibrium which is globally asymptotically stable under a range of parameter values whenever a detection/treatment rate and an indirect measure of the level of infection risk are sufficiently large. However, any level of detection/treatment rate coupled with a decrease of the transmission probability lowers the incidence rate and prevalence level in the population. In general, only significant reductions in the transmission probability (achieved through, for example, the adoption of safe sexual practices) can contain effectively the spread of the disease.

Key words: Epidemiological models – HIV transmission – Bounded population size – Treatment and behavioral change threshold – Global stability – Nonexistence of periodic solutions

1 Introduction

In this paper we study the dynamics of HIV infection in a closed homosexual population and evaluate the effect that changes in sexual behavior have in the overall incidence rate (number of new cases per unit time) and the prevalence of the disease. Avoidance of risky sexual behavior and the rise of sexual awareness concerning the life-threatening consequences of HIV infection have been very important factors in the decline of incidence rates among white homosexuals in the United States. Changes in sexual behavior involve both avoidance of high risk sexual

practices (e.g., anal intercourse, unprotected sex) and reduction in the number of sexual partners per unit time. Both of them reduce the level of sexual activity and the probability of infection per sexual encounter. There is thus, a direct impact of these behavioral changes on the contact rates and transmission probabilities that infectious persons have with susceptible ones.

Given the long asymptomatic incubation period of HIV it is important to evaluate the role that knowledge of HIV seroconversion and the subsequent treatment program of infected individuals plays in behavioral changes and, consequently, how it relates to the magnitude of incidence rates and prevalence. We assume in this work that a seropositive person is in fact infected and that he will develop full-blown AIDS in a median time of 10 years after exposure to the virus. There are several studies that report the impact of the knowledge of serological status on sexual activity and practices. Hethcote et al. (1991) have included behavioral changes in their modelling of the AIDS epidemic in San Francisco, particularly, they studied the importance of different levels of sexual activity and its associated risk of HIV infection on the incidence rate and prevalence levels in a homosexual population. Other studies have been motivated by the impact that the proportion of cases detected undergoing therapy and medical treatment may have on the decrease in AIDS incidence, and the possible lengthening of HIV-incubation and delayed AIDS related mortality (Gail et al. 1990). Many other authors have explored the problem of associated changes in sexual behavior when control measures are implemented in a population at risk. For example, Anderson et al. (1991) proposed a model for a population with community-wide chemotherapy or immunotherapy for HIV spread to highlight the importance of changing behavior and lowering infectiousness through treatment. Blythe et al. (1991) have studied an S-I model for HIV/AIDS dynamics where behavioral changes depend on the prevalence of the infection and the number of available susceptible individuals. Their model introduces a function F(S, I) that represents the fractional reduction in the effective maximal contact rate as a function of the number of susceptible and infectious individual. Thus behavioral changes, represented by changes in the contact rate and probability of infection, respond to the perception that the susceptible individuals have of the overall prevalence of the disease in the population. In a more recent technical report, Brauer et al. (1992) have considered metapopulation models and the effect that the perceived infection risk, as a function of the number of susceptible and infectious individuals, has on the recruitment rate of specific subgroups.

We consider only a male homosexual population (no drug users or bisexuals) whose infected individuals belong to either of two compartments. The first is composed of those recently infected individuals that have not changed risky sexual behavior. The second compartment is called the compartment of *treated* individuals. Infected individuals enter this compartment after spending some time in the previous one. The speed at which they are recruited depends on the rate at which newly infected individuals are detected and on the effectiveness of the treatment program. We shall call this recruitment rate into the treated compartment the *treatment rate*. We assume lower probability of transmission for these individuals and we will evaluate the impact of the treatment program in reducing prevalence by looking at the magnitude of the treatment rate and of the transmission probability in this compartment. Our assumption that the rate at which one alters sexual behavior is proportional to the HIV prevalence in the untreated population, has been documented by, for example Miller et al. (1990).

In Sect. 2 we present an S-I model for the population dynamics of HIV in a closed homosexual population. We assume that detection implies treatment that may bring modified sexual practices, i.e., lowered probability of transmission. We then study the evolution of such a population when treatment programs are implemented. Hence, in the model we incorporate a (possible) change in sexual behavior in infected individuals. Without a cure or a vaccine against AIDS, change in sexual behavior is necessary in the prevention of AIDS. Many studies have shown a significant change toward safer sexual behavior among gay men, particularly in large urban areas. (See e.g., Becker and Joseph 1988, Wiktor et al. 1990, and McKusick et al. 1985). On the other hand, reports of unchanged (unsafe) sexual behavior among gay men in low AIDS-prevalence areas are also in abundance. (See p. 83, Miller et al. 1990, for a partial list of such reports from 1988 to 1990). Sexual behavior is difficult to estimate because of a variety of technical and methodological constraints that need to be improved and developed (McQueen 1992). How to measure it and how to quantitatively evaluate its impact in the spread of AIDS are questions yet to be answered. For example, one study on homosexual men in the Netherlands (Griensven et al. 1989) reported that the seropositive individuals were more likely to have high-risk anal intercourse with their nonsteady partners than seronegative and untested men, although they were more likely to use condoms. Hence, not all individuals can be counted on to change their sexual habits and the relationship between AIDS and behavioral change is not altogether clear. However, it is widely known that the most effective way in which the incidence rate in HIV-infection can be lowered is by sexual education and awareness of the risk and life-threatening consequences of AIDS. In many studies of sexual mixing (e.g., Jacquez et al. 1988, Jacquez et al. 1989, Koopman et al. 1989), the level and pattern of sexual contact are assumed to be constant throughout one's (active) lifetime. Recently, Scalia-Tomba (1991) proposed a model which describes the dynamics of change in sexual behavior from a high activity stage to a low activity stage and vice versa. The work of Castillo-Chavez et al. (1989), Castillo-Chavez and Blythe (1989) and Busenberg and Castillo-Chavez (1991), for examples, also address the problem of mixing of subpopulations where mixing may be age or risk dependent and thus introducing, implicitly, behavioral changes.

Section 3 is devoted to the qualitative analysis of the model at the disease-free equilibrium to determine the relative importance of changes in incubation time, probability of transmission, and sexual behavior for an HIV infectious person. We also explore the relationship between the extensiveness of the treatment program and the prevention of the epidemic. Section 4 gives the results on the existence and uniqueness of the endemic equilibrium. In Sect. 5 we provide the stability analysis of the endemic equilibrium point and, finally, we give our conclusions in Sect. 6.

2 Model formulation

Consider a population of homosexual men subdivided into three groups: S (susceptibles), U (the recent infectives not yet in treatment), and I (infectives undergoing treatment) as·described in Sect. 1. The model describing the transmission dynamics of HIV within the population is then given as follows (the symbol ' ' ' indicates derivative with respect to time):

$$S'(t) = \Lambda - B(t) - \mu S + \delta I \tag{2.1}$$

$$U'(t) = B(t) - (\mu + v)U - \sigma U/T \tag{2.2}$$

$$I'(t) = \sigma U/T - (\mu + v' + \delta)I \tag{2.3}$$

with $T(t) = S(t) + U(t) + I(t)$ being the total population. Here Λ is the constant recruitment rate; μ^{-1} average length of the sexually active life of an individual; $B(t)$ is the force of infection term and v and v' are mean removal rates into the AIDS compartment of untreated and treated persons, respectively; σ is the fixed number of individuals tested randomly for HIV per unit time ·with the infectives entering into treatment and δ is the cure rate of the treatment class. Currently δ is equal to zero.

It should be noted that in an AIDS model with screening proposed by Hsieh (1991), σ is the fixed number of individuals screened during each time interval and subsequently, $\sigma U/T$ is the proportion of individuals screened to be HIV-positive and removed from the active population per unit time. The implicit assumption in that model is that all individuals tested positive can be successfully removed from activities likely to be of risk to the susceptible class by means ·of education, changes in behavior, etc. An ongoing program in Cuba which screens the population 15 years and older with those tested positive quarantined in controlled parks run by the government (see Perez-Stable 1991). The major distinction being made in the present model is that those individuals are not removed, but rather are taken into a separate treatment class in the active population where changes in AIDS-related death rates, probability of HIV transmission, and behaviour might occur. As a result, we assume that the number of new cases is proportional to the fraction of untreated infectives in the total population, in which case the recruitment rate into treatment is $\sigma U/T$. Notice that since the total population T now includes the treated class, a more appropriate treatment is $\sigma U/(S + U)$. However, it will be shown in Sect. 3 that this change in treatment term does not alter the results of the analysis and therefore is not important to make such distinction in this article. (Another way to look at the treatment term is to view the number of individuals entering into treatment to be proportional to the prevalence of HIV in the population since changes in behavior might be directly related to the HIV prevalence in the population as reported by Miller et al. (1990). In this case σ is just the constant of proportionality and the treatment term is $\sigma(U + I)/T$. However, we shall not pursue this idea in the present work).

The incidence rate, $B(t)S$, i.e., the number of new infectives in the population per unit time is given by

$$B(t) = S(t) \left(ca \frac{U}{T} + c'a' \frac{I}{T} \right) \tag{2.4}$$

where a is the infectivity rate of a susceptible when in contact with an untreated infective, c is the contact rate (the average number of sexual partners per unit time) of a susceptible individual with individuals in class U; a', c' are the corresponding parameters for the pair formation of a susceptible individual with an infective in the treatment class. We also assume that the average number of contacts of a susceptible with someone under treatment, c', will be less than or equal to the contacts with an untreated infective due to behavioral change. Furthermore, $a' < a$ since treatment does not increase, and may possibly decrease, the transmission rate. Hence we have

$$c'a' < ca. \tag{2.5}$$

The net effect of treatment on the transmission of the disease is assumed to be reflected in relation (2.5). The same assumption cannot be made on the mean removal rates due to AIDS, v and v'. With our earlier assumption of random screening, there is a distributed delay from the time of infection to the time of treatment for the treated infectives. Hence, even if we know for certain that, on average, treatment will retard the progression to full-blown AIDS, v' could still be greater than v if the patients entering treatment are heavily concentrated with individuals already infected for long periods of time – a likely situation. Thus, the relative size of v and v' depends on the magnitude of the delays and the extent to which the treatment prolongs the incubation period. (Unless one assumes that the treatment is applied at the moment of infection, only then can we conclude that $v > v'$!). An improvement of this situation could be introduced by keeping track of the age of infection of individuals. In this model, however, we do not pursue further this possibility.

3 Analysis of the model

Since the disease-free equilibrium of the system (2.1)–(2.3) is $(\Lambda/\mu, 0, 0)$, the well-known basic reproductive number, the number of secondary infections caused by an infective among a population of susceptibles in one infectious period, is

$$R_0 = \frac{\beta}{\mu + v + \sigma\mu/\Lambda} + \frac{\beta'}{\mu + v' + \delta} \frac{\sigma\mu}{\Lambda(\mu + v) + \sigma\mu} \tag{3.1}$$

where we have labeled $\beta = cap$ and $\beta' = c'a'p'$.

In epidemiological studies, the basic reproductive number is closely related to the outcome of an epidemic by the simple criterion that $R_0 > 1$ implies persistence of epidemic while $R_0 < 1$ means the disease will die out.

When $\sigma = 0$, i.e., no one in the population is being treated, we have $I = 0$. In this case the system (2.1)–(2.3) simplifies to

$$S'(t) = \Lambda - \beta S \frac{U}{S + U}, \tag{3.2}$$

$$U'(t) = \beta S \frac{U}{S + U} - (\mu + v)U, \tag{3.3}$$

which are exactly Eqs. (2.5)–(2.6) in Hsieh (1991).

Therefore we have the following result:

Proposition 3.1 *Let $R_0 = \beta/(\mu + v)$. If $R_0 < 1$, the disease-free equilibrium $(\Lambda/\mu, 0)$ is the unique equilibrium for system (2.1)–(2.3) and is globally asymptotically stable. If $R_0 > 1$, there exists a unique endemic equilibrium $(\tilde{S}, \tilde{U})$ which is asymptotically stable for all initial populations except at the disease-free equilibrium.*

For proof of this proposition, see Hsieh (1991).

Our concern then is to know whether a positive value of σ will prevent the convergence of populations toward an endemic population when $R_0 > 1$. Recall that $\sigma > 0$ implies that $\beta > \beta'$ (in other words, the situation $\sigma > 0$ is accompanied by a reduction of transmission probability and/or risky sexual behaviors). At the

disease-free equilibrium $(\Lambda/\mu, 0, 0)$ the characteristic values of the Jacobian matrix are $-\mu$ and the roots of the equation

$$\lambda^2 + \left(\frac{\sigma\mu}{\Lambda} + 2\mu + v + v' - \beta\right)\lambda + (\mu + v')\left(\frac{\sigma\mu}{\Lambda} + \mu + v - \beta\right) - \beta'\frac{\sigma\mu}{\Lambda} = 0 .$$

Performing some elementary computations and using the Routh-Hurwitz criterion, we obtain the following result on the stability of the matrix:

Proposition 3.2 *Let J_0 denote the Jacobian matrix of (2.1)–(2.3). Given $\sigma > 0$ and $\beta > \mu + v$ we have*

(a) *The matrix J_0 is unstable if $\beta' \geqq \mu + v' + \delta$.*

(b) *When $\beta' < \mu + v' + \delta$, then J_0 is unstable if $\sigma < \tilde{\sigma}$, and it is stable if $\tilde{\sigma} \leqq \sigma$; where*

$$\tilde{\sigma} = \frac{\Lambda}{\mu}\frac{\beta - (\mu + v)}{\mu + v' + \delta - \beta'} \quad (\mu + v + \delta) .$$

Proposition 3.2 gives us the local stability result of system (2.1)–(2.3) at the disease-free equilibrium. First we make the observation that $\tilde{\sigma} > \sigma$ is equivalent to $R_0 > 1$. Hence we can state the local stability property of the system (2.1)–(2.3) at disease-free equilibrium in terms of the basic reproduction number:

Proposition 3.3 *Given $\beta > \mu + v$ and $\delta > 0$. If $\beta' > \mu + v' + \delta$, then $R_0 > 1$ for all $\sigma > 0$ and the disease-free equilibrium is unstable. If $\beta' < \mu + v' + \delta$ then the disease-free equilibrium is unstable if $R_0 > 1$ $(\tilde{\sigma} > \sigma)$, and locally asymptotically stable if $R_0 \leqq 1$ $(\tilde{\sigma} \leqq \sigma)$.*

Note that if the treatment term is changed to $\sigma U/(S + U), R_0$ remains the same. The Jacobian matrix J will be different but, at the disease-free equilibrium, J will be the same as in (3.4) and hence Propositions 3.1, 3.2, and 3.3 follow similarly. Therefore having the treatment term proportional to the ratio of the untreated to the total population or the total untreated population does not alter our results. Notice also that when $\beta' = c'a'p'$ is too large, the disease will persist no matter how comprehensive the treatment program is. However, if $\beta' < \mu + v' + \delta$, the convergence of the population will depend on whether the treatment program is comprehensive enough compared to the threshold value for the size of treatment rate.

4 Characterization of the endemic equilibrium

To explore the behavior of the system when the disease-free equilibrium is unstable, we make the assumption that $\delta = 0$ and $v = v' = \hat{v}$. To that end define the new variables

$$t' = \mu t, \quad b = \beta/\mu, \quad b' = \beta'/\mu, \quad \theta = 1 + \hat{v}/\mu, \quad \sigma' = \frac{\sigma}{\Lambda},$$

and

$$\tilde{S} = \frac{\mu S}{\Lambda}, \quad \tilde{U} = \frac{\mu U}{\Lambda}, \quad \tilde{I} = \frac{\mu I}{\Lambda} .$$

With these new variables, system (2.1)–(2.3) is given by

$$\frac{d}{dt'}\tilde{S} = 1 - \tilde{B}(t')\tilde{S} - \tilde{S}\,, \tag{4.1}$$

$$\frac{d}{dt'}\tilde{U} = \tilde{B}(t')\tilde{S} - \theta\tilde{U} - \sigma'\frac{\tilde{U}}{\tilde{T}}\,, \tag{4.2}$$

$$\frac{d}{dt'}\tilde{I} = \sigma'\frac{\tilde{U}}{\tilde{T}} - \theta\tilde{I}\,, \tag{4.3}$$

with $\tilde{T}(t') = \tilde{S}(t') + \tilde{U}(t') + \tilde{I}(t')$ and $\tilde{B} = b\frac{\tilde{U}}{\tilde{T}} + b'\frac{\tilde{I}}{\tilde{T}}$.

Setting the RHS of (4.1)–(4.3) equal to zero we find the expression for the coordinates of the endemic equilibria

$$\hat{S} = \frac{1}{1+\hat{B}}\,, \quad \hat{U} = \frac{\hat{B}\hat{S}}{\theta + \sigma'/\hat{T}}\,, \quad \hat{I} = \frac{\sigma'\hat{U}}{\theta\hat{T}}\,. \tag{4.4}$$

Substituting (4.4) into the expression for $\hat{B}$ and rearranging terms we obtain

$$\hat{B} = \frac{b + \frac{b'\sigma'}{\theta T}}{\theta T + \sigma'} - 1 \quad \text{and} \quad \hat{B} = 0\,. \tag{4.5}$$

Adding together the expressions in (4.4) one obtains, for $\hat{T} > 0$

$$\hat{T} = \frac{1}{1+\hat{B}}\left(1 + \frac{\hat{B}\hat{T}}{\hat{T}\theta + \sigma'} + \frac{\sigma'\hat{B}}{\theta(\hat{T}\theta + \sigma')}\right) \tag{4.6}$$

which together with (4.5) gives a system of non-linear algebraic equations whose solutions correspond to the possible equilibria of system (4.1). Substituting (4.5) into (4.6) we have (to keep the notation simple, we drop the ' ^ ' from the state variables below)

$$T = \frac{T\theta + \sigma'}{T\theta b + \sigma'b'}\left(T\theta - T + \frac{T\theta b + \sigma'b'}{\theta(T\theta + \sigma')}\right)\,. \tag{4.7}$$

Denoting by $F(T)$ the RHS of (4.7), we prove now the existence of a fixed point of F. We look at the fixed points only for values of T in $[0, 1]$ since at the disease-free equilibrium $T = S = 1$. We thus expect that the spread of the virus in the population will produce $T < 1$. Also note that $T(0) = 1/\theta$ for $0 < T < 1$, $F(T)$ is always positive. Evaluating F at $T = 1$ we have

$$F(1) = \frac{b'\sigma' + \theta(b - \sigma') + \theta^2(\sigma' - 1) + \theta^3}{\theta(b'\sigma' + b\theta)}\,.$$

It is clear that $F(1) < 1$ if

$$\theta\sigma' + \theta^2 < b'\sigma' + b\theta \tag{4.8}$$

If the disease-free equilibrium is unstable we have $\theta < b$ (or equivalently, $\beta > \mu + \nu$ under the condition $\theta < b$), then (4.8) is equivalent to $b' \geqq \theta$ or $\sigma' < \frac{\theta(b - \theta)}{\theta - b'}$.

Proposition 4.1 *If $\theta < b$ and condition (4.8) holds, there exists at least one endemic equilibrium point for system (4.1)–(4.3) (and hence the same hold for system (2.1)–(2.3)).*

Proof. Condition (4.8) implies the existence of a value of $\hat{T}$ such that $F(\hat{T}) = \hat{T}$ with $0 < \hat{T} < 1$.   QED

To show uniqueness of the endemic equilibrium, we have the following result:

Proposition 4.2 *Given $\theta < b$, there exists at most one endemic equilibrium for system (4.1)–(4.3).*

Proof. It suffices to show that $G(T) = F(T) - T$ has at most one zero in the interval $[0, 1]$. From (4.7)

$$G(T) = \frac{(T\theta + \sigma')[T\theta(\theta T + \sigma')(\theta - 1) + (T\theta b + \sigma' b'(1 - T\theta)]}{\theta(T\theta + \sigma')(T\theta b + \sigma' b')} . \quad (4.9)$$

Denoting the numerator and denominator of the RHS of (4.9) by $N(T)$ and $D(T)$ respectively, we note that the zeros of $G(T)$ and $N(T)$ coincide. Also

$$N'(T) = a_0 T^2 + a_1 T + a_2$$

with $a_0 = 3\theta^3(\theta - 1 - b), a_1 = 2\theta^2(b + \sigma'(\theta - 1 - b) + \sigma'(\theta - 1 - b)), a_2 = \theta\sigma'[b + b' + \sigma'(\theta - 1 - b')]$. Clearly, $a_0 < 0$. $N(t)$ has two positive zeroes only if $a_2 < 0$ and $a_1 > 0$. But $a_2 < 0$ implies $a_1 < 0$. Hence $N(t)$ and $G(t)$ have at most one zero in $[0, 1]$.   QED

Propositions 4.1 and 4.2 combine to yield the following theorem summarizing the result on existence and uniqueness of the endemic equilibrium for system (4.1)–(4.3).

Theorem 4.3 *Suppose $b > \theta$. System (4.1)–(4.3) has* (i) *a unique endemic equilibrium if either $b' \geqq \theta$ or $\sigma' < \dfrac{\theta(b - \theta)}{\theta - b'}$;* (ii) *no endemic equilibrium if $b' < \theta$ and $\sigma' \geqq \dfrac{\theta(b - \theta)}{\theta - b'}$.*

Proof. For (i), either of the two conditions in the hypothesis implies condition (4.8). The result follows from Propositions 4.1 and 4.2. Conditions in (ii) imply $F(0) > 0$ and $F(1) > 1$, or equivalently, $G(0) > 0$ and $G(1) > 0$. By the proof of Proposition 4.2 and by continuity, a zero of G exists in $[0, 1]$ only if it occurs at a local minimum. Suppose $G(T_0) = 0$ for some T_0 in $(0, 1)$. Subsequently, $N(T_0) = 0$ and, moreover, $N(0) > 0$ and $N(1) > 0$ and T_0 is the unique zero of N in $(0,1)$ from the proof of Proposition 4.2. It follows that $N(T) > 0$ if T is in $[0, 1]-\{T_0\}$. We also know that $N'(T) < 0$ in $[0, T_0]$. But $N'(0) < 0$ implies $a_2 < 0$ thus implying $N'(T) < 0$ for all $T[0,1]$, a contradiction. Hence $G(T)$ has no zero.   QED

We now discuss some of the properties of the endemic equilibrium of system (4.1)–(4.3). Define the first term on the RHS of (4.5) as

$$\phi(\sigma', \hat{T}) = \frac{b + \dfrac{b'}{\theta\hat{T}}\sigma'}{\hat{T}\theta + \sigma'} . \quad (4.11)$$

Using (4.4) and (4.5), we have

$$S = \frac{1}{\phi}, \quad U = \frac{\phi - 1}{\phi(T\theta + \sigma')}, \quad I = \frac{\sigma'(\phi - 1)}{(T\theta + \sigma')\theta\phi} \tag{4.12}$$

where $\phi = \phi(\sigma', T)$. Notice that $\phi = 1$ results in the disease equilibrium and $\phi > 1$ yields the endemic equilibrium. Actually, it is easy to see that $\phi(\sigma', 0) = R_0$.

The system (4.1)–(4.3) yields the equation for the total population

$$\frac{dT}{dt'} = 1 - \theta T - (1 - \theta)S.$$

At the endemic equilibrium, $\hat{S} = \frac{\theta\hat{T} - 1}{\theta - 1}$. Hence from (4.1) and (4.2),

$$\hat{\phi} = \phi(\sigma', \hat{T}) = \frac{\theta\hat{T}b + b'\sigma'}{\theta\hat{T}(\theta\hat{T} + \sigma')} = \frac{\theta - 1}{\theta\hat{T} - 1}.$$

Solving for the unique positive root $\hat{T}$, we obtain an explicit expression for $\hat{T}$,

$$\hat{T} = \frac{b + \sigma'(\theta - 1 - b') + [(b + \sigma'(\theta - 1 - b')^2 + 4b'\sigma'(b - \theta - 1)]^{1/2}}{2\theta(b - \theta + 1)} \tag{4.13}$$

which is valid ($0 < \hat{T} < 1$) if and only if $b' \geq \theta$ or $\sigma' < \tilde{\sigma}/\Lambda$.

The magnitude of the populations at equilibrium depends on the properties of ϕ. Of interest in this work is the nature of the relationship between ϕ, σ' and T, the total population. Specifically we have

$$\frac{\partial\phi}{\partial\sigma'} = \frac{b' - b}{(\sigma' + T\theta)^2} < 0$$

if and only if $b' < b$.

This means that in order for treatment to be effective in bringing down the incidence rate of HIV, it is necessary to enforce behavior which will effectively reduce the transmission rate b', otherwise, no matter how large σ' is, the incidence rate will always be positive.

Notice that ϕ depends on the size of the total population. It can be easily verified that, as a function of T,

$$\frac{\partial\phi}{\partial T} < 0$$

due to the fact that in a larger population the contacts of infective individuals in either class is diluted among all the members (this is a consequence of assuming a homogeneous population and proportional mixing).

5 Stability analysis

Next we look at the local stability property of the endemic equilibrium of the system (4.1–4.3). We consider the equivalent system for (T, S, I):

$$T' = 1 - \theta T - (1 - \theta)S, \tag{5.1}$$

$$S' = 1 - (1 + b)S - \frac{b'I - b(S + I)}{T}S, \tag{5.2}$$

$$I' = \sigma' - \theta I - \frac{\sigma'}{T}(S + I). \tag{5.3}$$

The characteristic values of the Jacobian matrix of (5.1)–(5.3) at $(\hat{T}, \hat{S}, \hat{I})$ are negative when $b > b'$. Therefore the endemic equilibrium is locally asymptotically stable.

For global result, let $D = \{(S, U, I) : S, U, I \geq 0, S + U + I \leq 1\}$. In the equivalent system for (5.1)–(5.3) $D = \{(T, S, I) : S, I \geq 0, S + I \leq T \leq 1\}$. We consider the 2-dimensional simplex $\Sigma = \{(S, U, I) \in D : S + \theta(U + I) = 1\}$, or equivalently,

$$\Sigma = \left\{ (T, S, I) \in D : T = \frac{1 + (\theta - 1)S}{\theta} \right\}.$$

From (5.1), it is obvious that $T = 0$ in Σ. Moreover, $T' < 0$ if $T > \frac{1 + (\theta - 1)S}{\theta}$ and $T' > 0$ if $T < \frac{1 + (\theta - 1)S}{\theta}$. It follows that Σ is an attracting invariant set in D and all flows in D obeying (5.1)–(5.3) tend toward Σ monotonically, or equivalently,

Lemma 5.2 *Let D and Σ be defined as above. Then, all flows in D obeying (4.1)–(4.3) tend toward Σ as t goes to infinity.*

Therefore, all ω-limit sets of (4.1)–(4.3) are contained in Σ. Next we want to show the nonexistence of periodic solutions in Σ.

Lemma 5.3 *The system (4.1)–(4.3) has no periodic solutions (closed orbits, homoclinic loops, or oriented phase polygons) in Σ.*

Proof. We make use of Corollary 4.2 in Busenberg and van der Driessche (1990) to prove the nonexistence of periodic solutions. Let $f_i, i = 1, 2, 3$ be the RHS of (4.1), (4.2) and (4.3) respectively. Also let $g = g_1 + g_2 + g_3$ be defined in Σ with

$$g_1 = \left(0, \frac{-f_3(U, I)}{UI}, \frac{f_2(U, I)}{UI} \right),$$

$$g_2 = \left(\frac{f_3(S, I)}{SI}, 0, \frac{-f_1(S, I)}{SI} \right),$$

$$g_3 = \left(\frac{-f_2(S, U)}{SU}, \frac{f_1(S, U)}{SU}, 0 \right),$$

where the functions f_i are obtained by applying the relation $S + \theta(U + I) = 1$.

From the construction of g, clearly we have $gf = 0$ on Σ, where $f = (f_1, f_2, f_3)$. Since the normal vector to Σ is $n = (1, 0, 0)$, we also have, after some elementary computations:

$$\text{curl } g \cdot n = (\text{curl } g)(1, \theta, \theta) = -\frac{\theta}{S^2}\left[\frac{1}{I} + \frac{1}{U}\right] - \frac{\sigma}{SI^2T} - \frac{b}{TI} - \frac{b'}{TU^2} < 0 \text{ in } \Sigma.$$

By Corollary 4.2 of Busenberg and van den Driessche (1990) there is no periodic solution of (4.1)–(4.3) in Σ.   QED

We now give the main global result:

Theorem 5.4 *Suppose $b > \theta$.*

(i) *If $b' < \theta$ and $\sigma' \geqq \dfrac{\theta(b - \theta)}{\theta - b'}$, the disease-free equilibrium of system (4.1)–(4.3) is globally asymptotically stable in D.*

(ii) *If $b' \geqq \theta$ or $\sigma' \leqq \dfrac{\theta(b - \theta)}{\theta - b'}$, the unique endemic equilibrium in (4.4) is globally asymptotically stable in $D^* = D - \{(S, U, I) \in D : U = I = 0\}$, and all solutions in $\{(S, U, I) \in D : U = I = 0\}$ tend toward the disease-free equilibrium.*

Proof. (i) From Lemma 5.2, all solutions in D tend toward Σ for t sufficiently large and Σ has no periodic solutions by Lemma 5.3. Hence all solutions in D tend toward the only equilibrium of the system, the disease-free equilibrium. Since this equilibrium is locally stable, it is also attracting for all solutions $(S(t), U(t), I(t))$ in D.

(ii) Clearly, when $U(t) = I(t) = 0$, the system (4.1)–(4.3) becomes $U'(t) = I'(t) = 0$ and $S'(t) = 1 - S(t)$, so the disease-free equilibrium $(1, 0, 0)$ is the attractor in $\{(S, U, I) \in D : U = I = 0\}$.

Now we consider solutions in D^*. We know Σ is an attracting invariant set. We also know that when $b' \geqq \theta$ or $\sigma' \leqq \dfrac{\theta(b - \theta)}{\theta - b'}$, the disease-free equilibrium is unstable and there is a unique endemic equilibrium $(\hat{S}, \hat{U}, \hat{I})$ contained in Σ and it is locally asymptotically stable by Proposition 3.1. Since the disease-free equilibrium is unstable and there is no periodic solution in Σ, every solution in any neighborhood of the disease-free equilibrium in D^* will leave that neighborhood for t sufficiently large; because otherwise, there would have to be homoclinic orbit containing the disease-free equilibrium in Σ.

Once we know the disease-free equilibrium does not attract anything in D^*, by Lemmas 5.2 and 5.3, and the local asymptotic stability of the unique endemic equilibrium, this equilibrium must be the global attractor in D^*.   QED

We now proceed with a few words on the stability of the equilibrium points of system (2.1)–(2.3) which represents the case when $v = v'$ and $\delta = 0$. Equation (3.1) can be rewritten as

$$R_0(\beta', \sigma) = \frac{1}{\mu + v + \sigma\mu/\Lambda}\left(\beta + \beta'\frac{\sigma\mu}{(\mu + v)\Lambda}\right).$$

Since the parameters are all positive, R_0 is a continuous function in the variable β' and σ. When $\beta = \beta'$ and $\beta > \mu + v$ hold, $R_0(\beta', \sigma) > 1$ and the disease-free equilibrium is unstable. Furthermore, in this case there exists a unique endemic equilibrium $(\hat{S}, \hat{U}, \hat{I})$ as shown in the preceeding section.

Using a continuity argument, together with Proposition 3.3, and Theorem 5.4, we have the following result for the system (2.1)–(2.3) in a small neighborhood of $|v - v'| = 0$ and $\delta = 0$.

Proposition 5.5 *Given $|v - v'|$ small, δ small and positive, and $\beta > \mu + v$, if $\beta' \geqq \mu + v + \delta$, then the disease-free equilibrium for system (2.1)–(2.3) is unstable and there exists a unique endemic equilibrium which is globally asymptotically stable in D^*. If, however, $\beta' < \mu + v + \delta$, then the disease-free equilibrium is globally asymptotically stable provided $\sigma \geqq \tilde{\sigma}$ and there is no endemic equilibrium. If $\sigma < \hat{\sigma}$ then the disease-free equilibrium is unstable and there exists a globally asymptotically stable unique equilibrium point.*

6 Conclusions

The life-threatening consequences of exposure to HIV-infection have already had a very important impact in the sexual practices and sexual behavior of the population at large, not only of the white homosexual populations in which the virus first appear. It is well known, among those in charge of coping with the control of the virus, that the most effective way of reducing the incidence rate and lowering prevalence levels, is to educate the general population and to make it aware of the consequences of engaging in unprotected sex or other types of risky sexual behavior. In this work, we have centered our attention in two of the factors that, from the epidemiological point of view, are more directly affected by these sexual education programs. One is the rate at which new cases are detected and subjected to treatment and surveilliance of some type, and the other is the probability that a given infectious individual has of transmitting the disease given that it has engaged in sex with a susceptible person (for studies that report results of the impact of HIV-infection awareness, see McKusick et al. 1985, Wiktor et al. 1990). A successful program in the prevention of HIV-infection must, on one hand, have a relatively effective method of detecting and putting into treatment new cases in a short period of time, and also, it must decrease the magnitude of the probability of transmission of infected individuals either by reducing the susceptible contact rate with infectious individuals, by reducing the infectivity of the infectious sexual contacts or by reducing the mixing probability of individuals with opposite HIV-status. The results in earlier sections highlight the importance of the net transmission rate β' of those under treatment. On the population level, lowering of the transmission rate β' is necessary in achieving lower prevalence. To eradicate the disease, however, we also need to have a high turnover rate of infectious individuals into treatment. In other words, small values of β' and large σ are necessary and sufficient to eliminate the disease in the population. To illustrate the previous comment we present in Fig. 1 the case when there is no treatment available for the infected population. The convergence to the endemic equilibrium is fast. In this example we have taken the initial population $S(0) = 30\,000$, $U(0) = 100$, $I(0) = 0$.

If we assume now that HIV-infected persons are detected and perhaps medically treated, but the sexual education program, for example, is unable to change sexual practices of high risk we still have a high prevalence of HIV in the population. This case is illustrated by Fig. 2 where we take $\sigma = 1,000$ but $\beta = \beta' = 1.0$. Moreover, even if β' is sufficiently low (so that $b' < \theta$), but not enough infected individuals
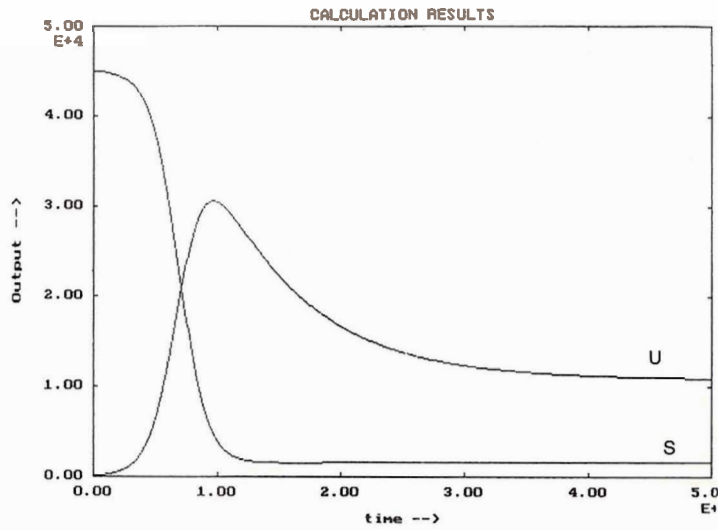
Fig. 1. Simulation of model (2.1)–(2.3) covering a time lapse of 50 yr. Parameter values are $\Lambda = 1500, \beta = 1.0, \mu = 1/30, \nu = 1/10$ and $\sigma = 0$
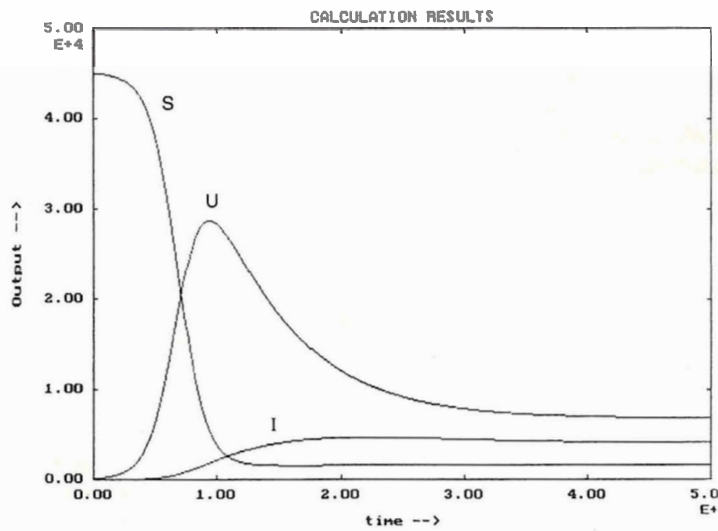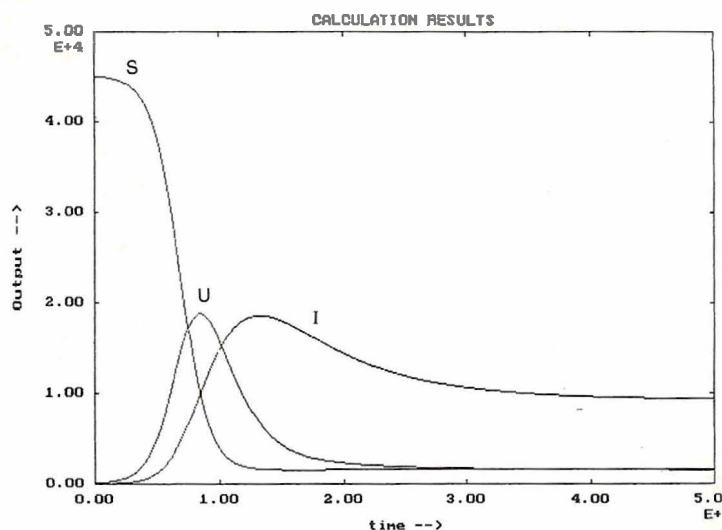

Fig. 2. Simulation of model (2.1)–(2.3) covering a time lapse of 50 yr. Parameter values are $\Lambda = 1500, \beta = 1.0, \beta' = 1.0, \mu = 1/30, \nu = \nu' = 1/10$ and $\sigma = 1000$

change sexual practices or are detected, i.e., σ is not large enough, the population still tends toward the endemic equilibrium (see Fig. 3).

Note, however, that in Fig. 3, most of the infected individuals belong to the treated compartment and thus the incidence rate is reduced. Contrary to screening models (Hsieh 1991), where programs do not lower HIV incidence unless they are comprehensive enough to eradicate the disease eventually, a good treatment program

Fig. 3. Simulation of model (2.1)–(2.3) covering a time lapse of 50 yr. Parameter values are $\Lambda = 1500, \beta = 1.0, \beta' = 0.1, \mu = 1/30, \nu = \nu' = 1/10$ and $\sigma = 10000$. Initial conditions same as in Fig. 1

which successfully alters the risky sexual practices or lower the infectiousness of the treated infectives will be sufficient to lower HIV incidence. Figure 3 also shows that treatment does not only have the potential to prolong the patient's survival time, but also slows done the spread of HIV in population regardless of the scale of the program, as long as one can ensure its effectiveness is lowering the net transmission rate β'.

In Fig. 3, the threshold value $\tilde{\sigma}$ given in Proposition 3.2 is set equal to 156,000. In this example it can be seen that lowering the net transmission rate ten-fold, from $\beta' = 1.0$ to $\beta' = 0.1$, will not effectively eradicate the disease unless the screening rate per year is, initially, significantly larger than Λ/μ per year (45,000/year in this example). On the other hand, since the threshold value $\tilde{\sigma}$ is an increasing function of β', we can lower the threshold $\tilde{\sigma}$ to some extent, by lowering β'. In Fig. 4 we let $\beta' = 0.01$, i.e., the net transmission rate is lowered 100-fold! Then the threshold value $\tilde{\sigma}$ is approximately 42,162/unit time. In this example we have set $S(0) = 45,000$ and $U(0) = 100$. If $\sigma = 42,500$/year (around 95% of the population per year), the population tends to the disease-free equilibrium. However if $\sigma = 42,000$/year, for example, and all other parameters are the same, the population tends to the (globally) stable endemic state (see Fig. 5).

The simulations illustrate that, in general, it would be too much to expect of a treatment program to eliminate the disease altogether. But, as long as it effectively lowers the net transmission rate of the treated infectives, it will reduce the incidence rate and the prevalence of the virus.

Buehler et al. (1992) reported that in the US, AIDS surveillance identifies between 70–90% of cases of men in the age group of 25–44 years old. The effect of surveillance and notification is important in altering sexual behaviors of high risk. Giesecke et al. (1992) reported that seropositive individuals diagnosed in 1989 or later engaged in less high risk sexual practices than those individuals diagnosed
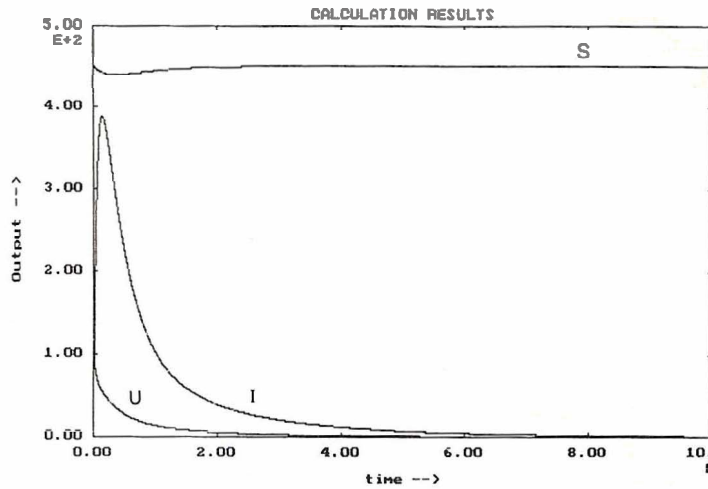
Fig. 4. Simulation of the long term behavior of model (2.1)–(2.3). Parameter values are same as in Fig. 3 except $\beta' = 0.01$, and $\sigma = 42500$. $S(0) = 45000, U(0) = 100, I(0) = 0$. $S(t)$ has been rescaled and $S(t)/100$ is the quantity shown.
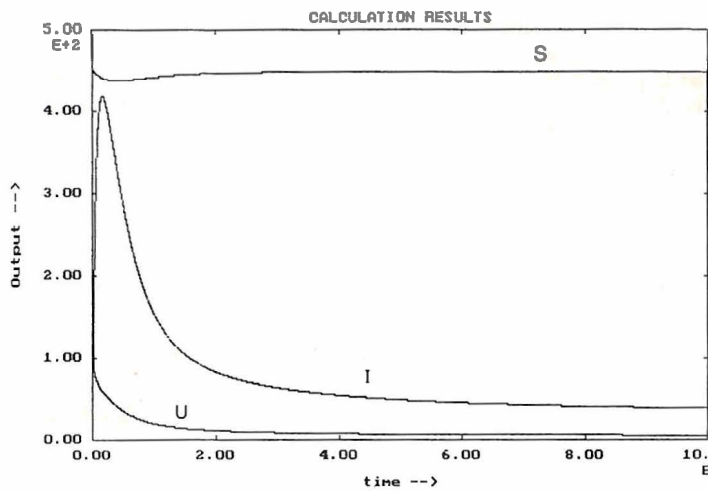

Fig. 5. Simulation of the long term behavior of model (2.1)–(2.3). Parameter values and initial conditions the same as Fig. 4 except $\sigma = 42000$. $S(t)$ has been rescaled and $S(t)/100$ is the quantity shown

earlier. The effect of surveillance, included in our model by 'treatment', has an impact in the magnitude of p' (transmission probability) since the information obtained through surveys is used to monitor the spread of the disease, to optimize the allocation of resources, and to help in the assessment of control measures (Gertig et al. 1991). There are, however, problems. The understanding of behaviors that

put at risk susceptible individuals is far from clear (McQueen 1992) because of the methodological and technical problems associated with surveys and data collection. What is clear, though, is that only through the adoption of prophylactic measures to prevent infection, one can expect to temper the spread of the epidemic to the general population.

This model also can be used to assess the relative effect on disease spread of chemotherapeutic and other forms of medical treatment (e.g., drug administration). These factors apparently can alter either the level of defenses in the body and/or lengthen the duration of the incubation period to the onset of full-blown AIDS. Both have an impact on the magnitude of the parameters of the basic reproductive number in (3.1), specifically β, β' and ν and ν'.

Finally, a few words, about ν' and δ. From Proposition 3.3, a necessary condition for eradication of the disease is $\beta' < \mu + \nu' + \delta$. Hence even if the cure rate δ is very high, we still need β' relatively small to have an impact on the population level. Otherwise people would simply be cured and then re-infected. As for ν', prolonging the survival time to full-blown AIDS implies decreasing ν', which would have an adverse effect if β' is fixed. In other words, given β' is unaltered, prolonging the incubation time only prolongs the time a susceptible can be exposed to these infective individuals.

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