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MODELING AND ANALYSIS OF THE SAN FRANCISCO CITY CLINIC COHORT (SFCCC) HIV-EPIDEMIC INCLUDING TREATMENT

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Abstract. We investigate two HIV/AIDS epidemic models. The first model represents the early San Francisco men having sex with men (MSM) epidemic. We use data from the San Francisco City Clinic Cohort Study (SFCCC), documenting the onset of HIV in San Francisco (1978-1984). The second model is a "what-if" scenario model including testing and treatment in the SFCCC epidemic. We use compartmental, population-level models, described by systems of ordinary differential equations. We find the basic reproductive number R_0 for each system, and we prove that if $R_0 < 1$, the system has only the disease-free equilibrium (DFE) which is locally and globally stable, whereas if $R_0 > 1$, the DFE is unstable. In addition, when $R_0 > 1$, both systems have a unique endemic equilibrium (EE). We show that treatment alone would not have stopped the San Francisco MSM epidemic, but would have significantly reduced its impact.

1. **Introduction.** In this paper we develop models for the HIV/AIDS epidemic in a men having sex with men (MSM) population, described by systems of differential equations. The first model is based on the MSM-San Francisco HIV epidemic (1978-1984) [23], which analyzes the longitudinal San Francisco City Clinic Cohort (SFCCC) data set ([7], [15], [27]). This data set is based on blood samples from an earlier Hepatitis B Vaccine Clinical trial that took place during the period in which HIV exploded through the San Francisco MSM population ([7], [8], [15]). The SFCCC study involved 6875 men, 10% of the San Francisco MSM population, in which blood samples and behavioral data were collected. After HIV was identified, stored blood samples were thawed and tested for the presence of HIV antibodies. This is a biological data set; it is not dependent on medical diagnosis or self-reporting [15].

In our second model, we consider how the SFCCC epidemic would have evolved if there had been testing and treatment available. Until recently, guidelines for the

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developed world suggested that, in the absence of an AIDS-defining illness, treatment should start when CD4 levels are between 200 and 350 cells per microliter [9]. A shift in this strategy is to diagnose all HIV-infected people as soon as possible after infection and provide them with antiretrovirals (ART) when their levels of CD4 cells are higher [25]. In May of 2011, a multinational study, led by a University of Carolina-Chapel Hill scientist, gave strong evidence that early treatment dramatically reduces the likelihood of transmitting the virus ([6], [17], [21]). Granich et al. [11] investigated the effect of universal voluntary HIV testing and immediate treatment with ART in a heterosexual epidemic and examined the conditions under which the epidemic could be driven towards elimination. In March of 2012, the United States issued new guidelines for the treatment of HIV-infected patients stating that regardless of CD4 levels, ART is recommended for all HIV-infected individuals [19]; accordingly, we have adjusted the SFCCC model to include treatment. Our data shows a dramatic reduction in the epidemic; combined with a reduction in the sexual behavior of the population due to awareness of the presence of HIV, the epidemic would have been prevented. In a subsequent paper [24] we show more details of this "what-if scenario," namely, the effect testing and treatment would have had on this population.

The assumptions made on the coefficients of the model are sufficiently general, so that our results can be applied to other compartmental models of infectious diseases.

2. **The SFCCC model.**

The SFCCC data splits the population into six groups, reflecting their very different sexual activity levels; the more active half averages more than ten times as many contacts as the lower half. We model interactions among six activity groups, obtained from published SFCCC survey data, as if all sexual contacts were casual and promiscuous, such as was typical in gay bathhouses in San Francisco. SFCCC data gives average contact rates for six different activity levels, and we assume these specify the average frequency with which persons go to the bathhouse, but once inside the mating pattern is random. Thus the bathhouse assumption addresses both the frequency of contacts and the mixing pattern when contacts occur.

For a typical untreated individual who is infected with HIV-1, his or her infectivity varies with the stage of the infection. The disease can be described as passing through three stages, primary, latent, and symptomatic. These are characterized by significantly different blood viral levels and average durations. First comes a period of primary infection (lasting less than a year). Our "primary infectious stage" is defined as the time soon after initial infection when infectiousness first rises and then drops. Seroconversion typically occurs well before the end of our primary stage. One then enters into an asymptomatic period (averaging 7–8 years without treatment), in which infectiousness is very low, followed by a symptomatic stage (averaging three years until death without treatment), where infectiousness rises again. The symptomatic stage begins while individuals are relatively healthy and active though it also includes the more severe AIDS phase. The average times of each stage are based on SFCCC data [1].

The approach in our paper is to divide the population into subgroups with different activity level, from a subgroup with uncommonly high activity, to another with no activity. A different approach, based on age of infection, has been successfully applied by Brauer (see [5] as well as [26], in which treatment is also studied). In

those models, infectivity of an individual is assumed to depend on the time since infection.

In our model, the six groups are ordered according to decreasing sexual activity; here is a schematic representation of the model for the ith group, $i = 1..6$ (see Figure 1).

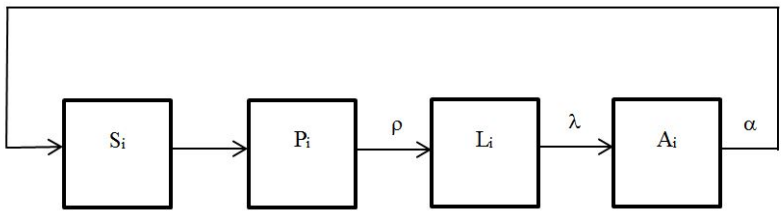

FIGURE 1. The SFCCC model.

The variables are as follows:
- S_i is the percentage of susceptible individuals in the ith group;
- P_i, the percentage of individuals in the primary stage;
- L_i, the percentage of individuals in the latent stage; and
- A_i, the percentage of those who have fully developed AIDS.

Individuals exit the system (they either leave the region, or die) with rate α. We assume the population in each group is kept constant, by either births or immigration, with the same rate α. This is a standing assumption in several infectious diseases models, in particular, HIV (see, for example, [14], p. 38 and p. 46, and [2]). A more realistic approach would be to assume that the population is variable, and consider the factors that affect its rate of change, as done in [4].

All the terms related to the positive transition coefficients indicated at the corresponding arrows are linear; the interactions between S_i and P_i, are not (see system (1) below).

The corresponding system of differential equations is as follows, where a dot means derivative with respect to time, and $i = 1 \dots 6$:

$$\begin{cases} \dot{S}_i = -\left[\sum_{k=1}^{6} N_{ik}(pP_k + \ell L_k + aA_k)\right] S_i + \alpha A_i \,; \\ \dot{P}_i = \left[\sum_{k=1}^{6} N_{ik}(pP_k + \ell L_k + aA_k)\right] S_i - \rho P_i \,; \\ \dot{L}_i = \rho P_i - \lambda L_i \,; \\ \dot{A}_i = \lambda L_i - \alpha A_i \,. \end{cases} \tag{1}$$

The constants p, ℓ, a are the infectivity coefficients of the stages P_i, L_i, and A_i respectively; we assume that they are the same for each group.

System (1) satisfies $\frac{d}{dt}(S_i + P_i + L_i + A_i) = 0$, so that the total population in each group remains constant. We express all the variables P_i, etc. as fractions of the total population in each group, which is assumed to be 1, or 100%.

The coefficient N_{ik} represents the average number of encounters of a person of the ith group having sex with a person of the kth group.

First, we define the average number c_i of yearly contacts of an individual in the ith group; we assume that groups are organized in decreasing sexual activity, so that $c_1 > c_2 > \cdots > c_6$; for the San Francisco MSM population we obtained [13]

$$c_1 = 231, \quad c_2 = 81, \quad c_3 = 33, \qquad c_4 = 15, \quad c_5 = 3, \quad c_6 = 0;$$

we thus range from an extremely active first group down to a group that is sexually inactive. Next, we determine the fraction f_i of the total population in the ith group. Again, for the San Francisco model we obtained [13]

$$f_1 = 0.10, \quad f_2 = 0.15, \quad f_3 = 0.25, \qquad f_4 = 0.25, \quad f_5 = 0.15, \quad f_6 = 0.10.$$

The total number of contacts is then calculated as

$$\text{TotalContacts} = C = f_1 c_1 + f_2 c_2 + \ldots + f_6 c_6.$$

The weighted total contacts g_k for the kth group are

$$g_k = \frac{c_k f_k}{C},$$

and finally, we set

$$N_{ik} = c_i g_k. \tag{2}$$

The units of the variables and the parameters are specified in Section 7.

Main assumptions. All results in this paper will be based on the assumption that $c_1 > c_2 > \cdots > c_5 > c_6 = 0$ plus the generic assumption that the coefficient matrix N_{ik} has the expression (2); namely, we assume that N_{ik} is the product $c_i g_k$, a factor depending only on i and a factor depending only on k. This corresponds to the assumption of *proportionate mixing*, using the terminology in [18]. Finally, all infectivities and transition coefficients introduced are assumed positive.

Reduced model. Since we have $S_i + P_i + L_i + A_i = 1$ for all $i = 1, \ldots, 6$, we can find $S_i = 1 - (P_i + L_i + A_i)$ and eliminate the variables S_i. If we introduce the notation

$$Z_i = \sum_{k=1}^{6} N_{ik}(pP_k + \ell L_k + aA_k)$$

to simplify the first equation below, we obtain the following *reduced* system:

$$\begin{cases} \dot{P}_i = Z_i\,[1 - (P_i + L_i + A_i)] - \rho P_i\,; \\ \dot{L}_i = \rho P_i - \lambda L_i\,; \\ \dot{A}_i = \lambda L_i - \alpha A_i\,. \end{cases} \tag{3}$$

Remark. By our assumptions, since $c_6 = 0$, then $N_{6k} = N_{i6} = 0$ for all i and k. Also, the initial conditions for (1) or (3) will be to start with a single infected individual in the primary stage of group 1, never on group 6. It is not hard to see that, in this case, $S_6(t) = 1$ and $P_6(t) = L_6(t) = A_6(t) = 0$ for all t. Hence, it is possible to disregard the last group in our system, and assume that i, k range from 1 to 5. Although we will continue to let i range from 1 to 6, we will use this remark when needed.

3. **Equilibria for the SFCCC model.** To find equilibria for system (1) or, equivalently, for system (3), we need to solve the set of algebraic equations obtained from (3) by setting all rates of change equal to zero:

$$\begin{cases} Z_i\,[1-(P_i+L_i+A_i)]-\rho P_i &= 0\,; \\ \rho P_i-\lambda L_i &= 0\,; \\ \lambda L_i-\alpha A_i &= 0\,; \end{cases} \tag{4}$$

where

$$Z_i=\sum_{k=1}^{6} N_{ik}(pP_k+\ell L_k+aA_k). \tag{5}$$

System (4) always has one clear equilibrium, namely, the *disease-free equilibrium* (DFE). That happens when no infected individuals exist to begin with, so that all the populations in all groups will consist of just susceptibles. This corresponds to $S_i=1$; $P_i=L_i=A_i=0$. Under some circumstances, this is the only equilibrium. In other cases, we will show that the system has a single additional equilibrium, the *endemic equilibrium* (EE). Everything will depend on the *reproduction number* R_0 of the system.

To investigate the equilibria, let us solve the system of the last two linear equations of (4) in terms of P_i. We get

$$L_i=\frac{\rho}{\lambda}P_i; \qquad A_i=\frac{\rho}{\alpha}P_i. \tag{6}$$

Observe that all the coefficients are independent of i.

Equations (6) imply that, if $P_i=0$ for some i, then automatically $A_i=L_i=0$ for that value of i, whereas if $P_i>0$ then both A_i, and L_i are positive as well. Therefore, to investigate the possible existence of a **non-DFE equilibrium**, let us now assume that **at least one of the P_i's is strictly positive**.

If we substitute the values of all the variables in terms of P_i given by (6) into the expression (5) for Z_i, we get

$$Z_i=\sum_{k=1}^{6} N_{ik}\left(p+\frac{\ell\rho}{\lambda}+\frac{a\rho}{\alpha}\right)P_k=\sum_{k=1}^{6} N_{ik}\gamma\,\rho P_k, \tag{7}$$

where we have called

$$\gamma=\frac{p}{\rho}+\frac{\ell}{\lambda}+\frac{a}{\alpha}. \tag{8}$$

Next, to express the first equation of (4) in terms of P_i alone, first observe that, by (6),

$$P_i+L_i+A_i=\left(1+\frac{\rho}{\lambda}+\frac{\rho}{\alpha}\right)P_i=\beta\,\rho P_i, \tag{9}$$

where

$$\beta=\frac{1}{\rho}+\frac{1}{\lambda}+\frac{1}{\alpha}. \tag{10}$$

Substituting (7) and (9) into the first equation of (4), we obtain

$$\sum_{k=1}^{6} N_{ik}\gamma\rho P_k(1-\beta\rho P_i)-\rho P_i=0.$$

Dividing through by the positive coefficient ρ, and bringing P_i to the right-hand side, the equation becomes

$$\sum_{k=1}^{6} N_{ik}\gamma P_k(1-\beta\rho P_i) = P_i. \tag{11}$$

Now, let us use the *proportionate mixing* assumption (2) and substitute $N_{ik} = c_i g_k$ into (11). After dividing through by γ, we get

$$c_i(1-\beta\rho P_i)\left(\sum_{k=1}^{6} g_k P_k\right) = \frac{1}{\gamma}P_i.$$

If we multiply both sides by g_i and make the change of variables

$$g_i P_i = x_i, \quad i = 1,\dots,6, \tag{12}$$

we obtain

$$c_i(g_i-\beta\rho x_i)\left(\sum_{k=1}^{6} x_k\right) = \frac{1}{\gamma}x_i. \tag{13}$$

Let us call for a moment

$$y = \sum_{k=1}^{6} x_k. \tag{14}$$

Then (13) becomes

$$c_i(g_i-\beta\rho x_i)y = \frac{1}{\gamma}x_i. \tag{15}$$

If for some i we had $x_i = \frac{g_i}{\beta\rho}$ (and hence positive), then (15) would imply that $x_i = 0$ for the same i. This contradiction shows that $x_i = \frac{g_i}{\beta\rho}$ is impossible. Also, since the right-hand side of (15) is positive, we must have

$$x_i < \frac{g_i}{\beta\rho}, \quad i = 1,\dots 6. \tag{16}$$

Finally, since we are assuming that at least one P_i is positive, then the corresponding x_i will also be positive and, therefore, y will be strictly positive. It now follows from (15) that $x_i > 0$ if, and only if, $c_i > 0$. We conclude that $x_1, \dots, x_5$ are strictly positive, whereas $x_6 = 0$. For the remainder of this section, since $c_6 = x_6 = 0$, we will consider that i varies from 1 to 5. In particular, in (14), we have $y = \sum_{k=1}^{5} x_k$.

Note. Observe that, by (16) and (12),

$$P_i = \frac{x_i}{g_i} < \frac{1}{\rho\beta}.$$

Hence, by (9),

$$P_i + L_i + A_i = \rho\beta P_i < 1,$$

whence $0 < P_i + L_i + A_i < 1$, and the solution makes sense for our model.

Equation (15) may be rewritten as

$$c_i g_i y - c_i\rho\beta x_i y = \frac{1}{\gamma}x_i.$$

If we add these equations term-by-term, from $i = 1$ to $i = 5$, we get

$$y\sum_{i=1}^{5} c_i g_i - y\beta\rho\sum_{i=1}^{5} c_i x_i = \frac{1}{\gamma}\sum_{i=1}^{5} x_i$$

Recalling (14), this can be written as

$$y\left[\sum_{i=1}^{5} c_i g_i - \beta\rho \sum_{i=1}^{5} c_i x_i\right] = \frac{1}{\gamma} y. \tag{17}$$

Since we are seeking a non-DFE equilibrium and therefore y is strictly positive, we can divide both sides of (17) by y, and obtain the following equivalent equation for any EE (endemic equilibrium):

$$\rho\beta \sum_{i=1}^{5} c_i x_i = \sum_{i=1}^{5} c_i g_i - \frac{1}{\gamma}. \tag{18}$$

This equation has the advantage that the right-hand side is a *constant*. Moreover, as we will show, this constant is closely related to the reproduction number R_0 of the system.

All possible non-DFE equilibria will be solutions of (18) for which all x_i ($i = 1, \dots, 5$) are strictly positive.

In order to further simplify the study of (18), let us eliminate all variables, except for x_1. To do this, let us re-write (15) as

$$\frac{c_i g_i}{x_i} - \rho\beta c_i = \frac{1}{\gamma y}.$$

The right-hand side is *independent of* i. Hence, so is the left-hand side. This means that

$$\frac{c_1 g_1}{x_1} - \rho\beta c_1 = \frac{c_2 g_2}{x_2} - \rho\beta c_2 = \cdots = \frac{c_5 g_5}{x_5} - \rho\beta c_5 = \frac{1}{\gamma y}. \tag{19}$$

We can use the first four equalities in (19) to find

$$\frac{c_i g_i}{x_i} - \rho\beta c_i = \frac{c_1 g_1}{x_1} - \rho\beta c_1, \quad i = 2, \dots, 5.$$

It follows that

$$\frac{c_i g_i}{x_i} = \frac{c_1 g_1}{x_1} - \rho\beta(c_1 - c_i),$$

whence

$$x_i = \frac{c_i g_i x_1}{c_1 g_1 - \rho\beta(c_1 - c_i) x_1}, \quad i = 2, \dots, 5. \tag{20}$$

Substituting (20) into (18), we get the following non-linear equation for x_1:

$$x_1 \rho\beta \left[c_1 + \sum_{i=2}^{5} \frac{c_i^2 g_i}{c_1 g_1 - \rho\beta(c_1 - c_i) x_1}\right] = \sum_{i=1}^{5} c_i g_i - \frac{1}{\gamma}. \tag{21}$$

Proposition 1. *If the right-hand side of (21) is positive, the equation has a unique positive solution x_1 for which $x_2, \dots x_5$ are also positive. If the right-hand side is negative, or zero, the equation has no such positive solutions.*

Proof. Recall that we assume $c_1 > c_2 > \cdots > c_5 > c_6 = 0$. Therefore,

$$0 < c_1 - c_2 < c_1 - c_3 < c_1 - c_4 < c_1 - c_5.$$

The denominators in (21) vanish when $x_1 = \theta_i$, where

$$\theta_i \stackrel{\text{def}}{=} \frac{c_1 g_1}{\rho\beta(c_1 - c_i)}, \quad i = 2, \dots, 5. \tag{22}$$

The above inequalities imply that $0 < \theta_5 < \theta_4 < \theta_3 < \theta_2$.

Now let us look at the left-hand side of (21) as a function of x_1, namely, consider the function

$$F(x) = \rho\beta x \left[c_1 + \sum_{i=2}^{5} \frac{c_i^2 g_i}{c_1 g_1 - \rho\beta(c_1 - c_i)x} \right],$$

on the interval $[0, \theta_5)$. This function is non-negative and strictly increasing. Indeed, each term in the sum increases with x, so that $F(x)$ is the product of two non-negative increasing functions. Also, $F(x)$ is continuous on $[0, \theta_5)$, with $F(0) = 0$, and $\lim_{x\to\theta_5^-} = +\infty$. Thus, if the right-hand side of (21) is positive, the equation will have exactly one positive solution x_1 on the interval $[0, \theta_5)$, while if the right-hand side is negative, or zero, there will be no positive solutions on that interval. Moreover, if x_1 is such a solution, $0 < x_1 < \theta_5$, then (20) implies that $x_2, \dots, x_5$ will be positive as well. On the other hand, if x_1 is positive, but $x_1 > \theta_5$, then (20) shows that x_5 would be negative, whence also P_5 would be negative, which is not a valid solution. □

4. **Stability for the SFCCC system.** Recall that system (3) always has the *disease-free equilibrium*, or DFE: $P_i = L_i = A_i = 0$ for all $i = 1, \dots, 6$ (and hence all $S_i = 1$). Let us compute the Jacobian matrix of (3) at the DFE. If we name the right-hand sides of (3) as

$$\begin{aligned} f_i &= Z_i\,[1 - (P_i + L_i + A_i)] - \rho P_i\,; \\ g_i &= \rho P_i - \lambda L_i\,; \\ h_i &= \lambda L_i - \alpha A_i\,; \end{aligned}$$

where

$$Z_i = \sum_{k=1}^{6} N_{ik}(pP_k + \ell L_k + aA_k),$$

we find that

$$\frac{\partial f_i}{\partial P_i} = pN_{ii}[1 - (P_i + L_i + A_i)] - \sum_{k=1}^{6} N_{ik}(pP_k + \ell L_k + aA_k) - \rho;$$

and, when $k \neq i$,

$$\frac{\partial f_i}{\partial P_k} = pN_{ik}[1 - (P_i + L_i + A_i)].$$

Hence,

$$\left.\frac{\partial f_i}{\partial P_i}\right|_{DFE} = pN_{ii} - \rho\,; \qquad \left.\frac{\partial f_i}{\partial P_k} = pN_{ik}\right|_{DFE} \quad (k \neq i).$$

Similarly, we find

$$\left.\frac{\partial f_i}{\partial L_i}\right|_{DFE} = \ell N_{ii}\,; \qquad \left.\frac{\partial f_i}{\partial L_k} = \ell N_{ik}\right|_{DFE} \quad (k \neq i);$$

and

$$\left.\frac{\partial f_i}{\partial A_i}\right|_{DFE} = aN_{ii}\,; \qquad \left.\frac{\partial f_i}{\partial A_k} = aN_{ik}\right|_{DFE} \quad (k \neq i).$$

The other equations are linear, so we have, everywhere:

$$\frac{\partial g_i}{\partial P_i} = \rho\,; \qquad \frac{\partial g_i}{\partial L_i} = -\lambda\,;$$

and all other partial derivatives of g_i vanish; and

$$\frac{\partial h_i}{\partial L_i} = \lambda\,; \qquad \frac{\partial h_i}{\partial A_i} = -\alpha\,;$$

and all other partial derivatives of h_i are zero.

Now let us recall that the matrix N splits as $N_{ik} = c_i g_k$, and let us organize the Jacobian at the DFE as

$$J = \left.\frac{\partial(f_1, g_1, h_1, \ldots, f_6, g_6, h_6)}{\partial(P_1, L_1, A_1, \ldots, P_6, L_6, A_6)}\right|_{DFE}. \tag{23}$$

Then we can write $J = F - V$, where V is the block-diagonal matrix

$$V = \begin{pmatrix} V_0 & 0 & \ldots & 0 \\ 0 & V_0 & \ldots & 0 \\ \ldots & \ldots & \ldots & \ldots \\ 0 & 0 & \ldots & V_0 \end{pmatrix}, \tag{24}$$

in which V_0 is defined by:

$$V_0 = \begin{pmatrix} \rho & 0 & 0 \\ -\rho & \lambda & 0 \\ 0 & -\lambda & \alpha \end{pmatrix},$$

and

$$F = \begin{pmatrix} c_1 g_1 p & c_1 g_1 \ell & c_1 g_1 a & c_1 g_2 p & c_1 g_2 \ell & c_1 g_2 a & \ldots \\ 0 & 0 & 0 & 0 & 0 & 0 & \ldots \\ 0 & 0 & 0 & 0 & 0 & 0 & \ldots \\ c_2 g_1 p & c_2 g_1 \ell & c_2 g_1 a & c_2 g_2 p & c_2 g_2 \ell & c_2 g_2 a & \ldots \\ 0 & 0 & 0 & 0 & 0 & 0 & \ldots \\ 0 & 0 & 0 & 0 & 0 & 0 & \ldots \\ \ldots & \ldots & \ldots & \ldots & \ldots & \ldots & \ldots \end{pmatrix}. \tag{25}$$

Observe that V is invertible, and is also block-diagonal, with blocks

$${V_0}^{-1} = \begin{pmatrix} \frac{1}{\rho} & 0 & 0 \\ \frac{1}{\lambda} & \frac{1}{\lambda} & 0 \\ \frac{1}{\alpha} & \frac{1}{\alpha} & \frac{1}{\alpha} \end{pmatrix}.$$

Hence, V^{-1} is non-negative. As in [22] and [10], we now use the results of non-singular M-matrices (see, for example, [3], p. 25) to define the reproduction number R_0 for our system. Namely, let us define the *reproduction number of system* (1), or, equivalently, system (3), as

$$R_0 = \rho(FV^{-1}), \tag{26}$$

where $\rho(FV^{-1})$ means the spectral radius of the product FV^{-1}.

In [10], p. 33, it is explained how the (i,k) entry of FV^{-1} can be regarded as the expected number of new infections in group i produced by one infected individual originally introduced into compartment k. Thus, (26) can be related to the usual interpretation of the reproduction number R_0 of an infectious disease. (R_0 represents the average number of infected individuals created by a single infected person over the entire infection period.)

Connection with the reproduction numbers of each subsystem. We can analogously define the reproduction number R_{0i} for the ith group in the SFCCC system as

$$R_{0i} = \rho(F_i {V_0}^{-1}), \tag{27}$$

where $J_i = F_i - V_0$, and

$$J_i = \left.\frac{\partial(f_i, g_i, h_i)}{\partial(P_i, L_i, A_i)}\right|_{DFE} \qquad i = 1, \dots, 6.$$

Proposition 2. *The reproduction number of system (1) is equal to the sum of the reproduction numbers of each group, that is, $R_0 = \sum_{i=1}^{6} R_{0i}$. Moreover, $R_{0i} = c_i g_i \gamma$, where γ is given by (8), so that $R_0 = (c_1 g_1 + \cdots + c_6 g_6)\gamma$.*

Proof. The matrix F has rank 1. Indeed, it can be written as the product $F = u \cdot v^T$, where u and v are the column vectors

$$u = (c_1, 0, 0, c_2, 0, 0, \dots, c_6, 0, 0); \tag{28}$$

$$v = (g_1 p, g_1 \ell, g_1 a, g_2 p, g_2 \ell, g_2 a, \dots, g_6 p, g_6 \ell, g_6 a). \tag{29}$$

Hence, the product matrix $W = FV^{-1}$ also has rank 1, and can be written as $W = u \cdot w^T$, where w is the column vector $(V^{-1})^T v$. Thus, W has only one nonzero eigenvalue, which is simple, and is equal to $w^T \cdot u$ (see [20]). Now, $w^T \cdot u = v^T V^{-1} u$, and $V^{-1}u$ is the column vector

$$V^{-1}u = \operatorname{col}\left(\frac{c_1}{\rho}, \frac{c_1}{\lambda}, \frac{c_1}{\alpha}, \dots \frac{c_6}{\rho}, \frac{c_6}{\lambda}, \frac{c_6}{\alpha}\right).$$

Hence, the nonzero eigenvalue of W is equal to

$$v^T V^{-1} u = (g_1 c_1 + \cdots + g_6 c_6)\left(\frac{p}{\rho} + \frac{\ell}{\lambda} + \frac{a}{\alpha}\right).$$

Since this eigenvalue is positive, and the rest are zero, this is also the spectral radius of W. Thus,

$$R_0 = \rho(W) = (g_1 c_1 + \cdots + g_6 c_6)\gamma. \tag{30}$$

Finally, a similar argument, or a direct computation using the definition (27), shows that $R_{0i} = \rho(F_i {V_0}^{-1}) = c_i g_i \gamma$. □

Note. As was observed earlier, since we assume $c_6 = 0$, in all computations above one can assume that i ranges from 1 to 5.

Theorem 4.1. *If $R_0 \le 1$, then system (3) has only the disease-free equilibrium (DFE); and if $R_0 < 1$ then the DFE is locally asymptotically stable. If $R_0 > 1$ then, in addition to the DFE, system (3) has a unique equilibrium for which all the variables are strictly positive, the endemic equilibrium (EE). Moreover, if $R_0 > 1$, then the DFE is unstable.*

Proof. First of all, observe that, by (30), the right-hand side of (21) can be written as

$$\sum_{i=1}^{5} c_i g_i - \frac{1}{\gamma} = \frac{1}{\gamma}\left(\gamma \sum_{i=1}^{5} c_i g_i - 1\right) = \frac{R_0 - 1}{\gamma},$$

and (21) can now be re-written as

$$x_1 \rho\beta \left[c_1 + \sum_{i=2}^{5} \frac{c_i^2 g_i}{c_1 g_1 - \rho\beta(c_1 - c_i)x_1}\right] = \frac{R_0 - 1}{\gamma}. \tag{31}$$

Hence, if $R_0 > 1$ then the right-hand side of (21), or equivalently (31), is positive, and therefore, by Proposition 1, system (3) has a unique equilibrium for which all variables are positive (a unique EE). On the other hand, if $R_0 \leq 1$, the right-hand side of (31) is negative, or zero, and the system has no positive equilibria.

As regards the stability of the equilibria, observe that we can write $-J = V - F$, where both V^{-1} and F are non-negative. Observe also that, by the structure of V, the matrix $-J$ is a so-called *Z-matrix*, that is, all its off-diagonal entries are non-positive. Hence [3], the real parts of all eigenvalues of $-J$ have positive real parts if, and only if, the spectral radius of $V^{-1}F$ is strictly less than one. Since the eigenvalues of $V^{-1}F$ are the same as those of FV^{-1}, we conclude that the real parts of all eigenvalues of J have negative real parts if, and only if, the spectral radius R_0 of FV^{-1} is less than one.

This means that when $R_0 < 1$ all eigenvalues of J have negative real parts. Hence, by Hartman's linearization theorem [12], the DFE is locally asymptotically stable.

Assume now that $R_0 = \rho(FV^{-1}) = \rho(V^{-1}F) > 1$. This implies that at least one eigenvalue of $-J = V - F$ has negative, or zero, real part. Arguing by contradiction, assume that no eigenvalue of $-J$ has negative real part. Then the smallest one will have zero real part. But then, for small positive ε, all eigenvalues of $-J + \varepsilon I = (V + \varepsilon I) - F$ would be positive. This implies [3] that $\rho(F(V + \varepsilon I)^{-1}) < 1$. By continuity of eigenvalues, we conclude that $\rho(FV^{-1}) \leq 1$, which contradicts the assumption that $R_0 = \rho(FV^{-1}) > 1$.

This contradiction proves that some eigenvalue of $-J$ must have strictly negative real part. Since J is the Jacobian of system (3) at the DFE, it follows by linearization that the DFE is unstable. □

Global stability of the disease-free equilibrium. We have shown that when $R_0 < 1$, system (3) has only the disease free equilibrium, DFE, which is locally asymptotically stable. We now show this equilibrium is also globally stable.

Theorem 4.2. *If $R_0 < 1$, then the DFE is globally stable.*

Proof. As in [14], p. 51, or in [16], we will prove global stability using a suitable Lyapunov function. To this end, let us call $X = (P_1, L_1, A_1, \ldots, P_5, L_5, A_5)$ the column vector of all variables of affected individuals, except those of the inactive Group 6, for which $P_6 = L_6 = A_6 = 0$ all the time. Then system (4) for the first five groups (that is, $i = 1, \ldots 5$) can be rewritten as $\dot{X} = JX - Q(X)$, where J is the Jacobian (23) of the system at the DFE, restricted to the first five groups, and $Q(X)$ is the column vector $Q(X) = (Q_1(X), 0, 0, \ldots Q_5(X), 0, 0)$, with $Q_i(X)$ being the non-negative quadratic form

$$Q_i(X) = \sum_{k=1}^{5} N_{ik}(pP_k + \ell L_k + aA_k)(P_i + L_i + A_i), \qquad i = 1, \ldots, 5.$$

Then we can write $J = F - V$, where F and V are the restrictions of (25) and (24) to the first five groups. Finally $F = u \cdot v^T$, where u and v are the corresponding restrictions of the column vectors (28) and (29), that is,

$$u = (c_1, 0, 0, c_2, 0, 0, \ldots, c_5, 0, 0);$$

and

$$v = (g_1 p, g_1 \ell, g_1 a, g_2 p, g_2 \ell, g_2 a, \ldots, g_5 p, g_5 \ell, g_5 a).$$

Let us define the Lyapunov function

$$\mathcal{V}(X) = v^T V^{-1} X.$$

Then, since all entries of v are positive, we conclude that on the non-negative orthant $X \geq 0$, the function $\mathcal{V}(X)$ vanishes if, and only if, $X = 0$.

The derivative $\dot{\mathcal{V}}$ of $\mathcal{V}$ along the trajectories of (3) is

$$\dot{\mathcal{V}}(X) = v^T V^{-1} \dot{X} = v^T V^{-1} \left[JX - Q(X)\right] = v^T V^{-1} \left[(F - V)X - Q(X)\right],$$

or

$$\dot{\mathcal{V}}(X) = v^T V^{-1} F X - v^T X - v^T V^{-1} Q(X).$$

Here $V^{-1}F = (V^{-1}u)\cdot v^T$, so that the nonzero eigenvalue is $v^T \cdot V^{-1}u$. This nonzero eigenvalue is also the spectral radius $\rho(V^{-1}F) = \rho(FV^{-1}) = R_0$; recall definition (26). Moreover, v^T is a left eigenvector for this eigenvalue; hence, $v^T(V^{-1}F) = R_0 v^T$. Thus,

$$\dot{\mathcal{V}}(X) = R_0 v^T X - v^T X - v^T V^{-1} Q(X) = (R_0 - 1)X - v^T V^{-1} Q(X).$$

If $R_0 < 1$, $\dot{\mathcal{V}}$ is strictly negative for $X \geq 0$, $X \neq 0$. Notice, finally, that the convex set determined by $X \geq 0$, $P_i + L_i + A_i \leq 1$ for $i = 1, \ldots 5$, is invariant for the trajectories of system (3). Indeed, on the boundary, say $P_i = 0$, the velocity vector points inward, and the same happens on all other boundaries.

We conclude that all solutions that start on this set tend to the origin. □

5. **The SFCCC model with testing and treatment.** We modified the original SFCCC model to study the effect that testing and treatment would have had on the San Francisco HIV epidemic. A schematic representation of our model is given in Fig. 2.

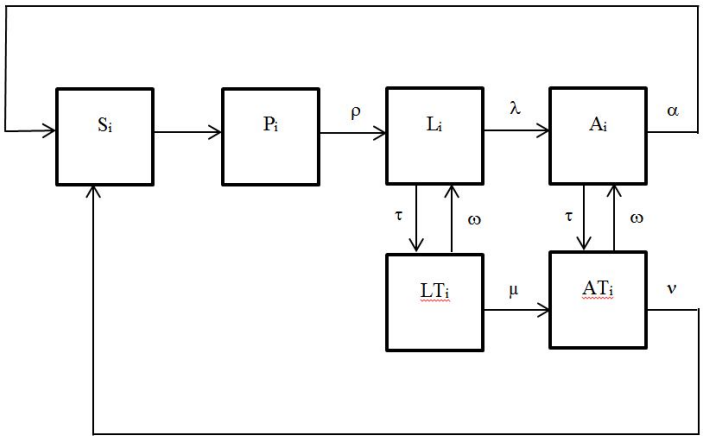

FIGURE 2. The SFCCC model with testing and treatment.

We have added new population groups LT_i and AT_i; those are the individuals from groups L_i and A_i respectively, who have decided to undergo treatment, after having tested HIV positive.

Individuals exit the system (they either leave the region, or die) with rates α (for the HIV-AIDS group) and μ (for the treated HIV-AIDS group). As in the first

model, we add balancing population input, to keep the total population in each group constant.

Again, all equations, except those for $\dot{S}_i$, are linear. Individuals opt into testing and treatment with rate τ; we also consider the case of individuals opting out of treatment (with rate ω), and re-entering the corresponding non-treated populations groups.

Here is the corresponding system of differential equations, which includes individuals undergoing treatment; again $i = 1, \ldots, 6$:

$$\begin{cases} \dot{S}_i &= -\left[\sum_{k=1}^{6} N_{ik}(pP_k + \ell L_k + \ell_T LT_k + aA_k + a_T AT_k\right] S_i + \alpha A_i + \mu AT_i\,; \\ \dot{P}_i &= \left[\sum_{k=1}^{6} N_{ik}(pP_k + \ell L_k + \ell_T LT_k + aA_k + a_T AT_k\right] S_i - \rho P_i\,; \\ \dot{L}_i &= \rho P_i - \lambda L_i - \tau L_i + \omega LT_i\,; \\ \dot{A}_i &= \lambda L_i - \alpha A_i - \tau A_i + \omega AT_i\,; \\ \dot{LT}_i &= \tau L_i - \omega LT_i - \nu LT_i\,; \\ \dot{AT}_i &= \tau A_i - \omega AT_i + \nu LT_i - \mu AT_i\,. \end{cases} \tag{32}$$

We have added infectivity coefficients ℓ_T, a_T for the groups undergoing treatment, which are assumed to be the same for all groups.

Again, for system (32) we have $\frac{d}{dt}(S_i + P_i + L_i + A_i + LT_i + AT_i) = 0$, so that the total population in each group remains constant (and equal to 1). The transition matrix $N = (N_{ik})$ is defined as in the SFCCC system (1).

Since we have $S_i + P_i + L_i + A_i + LT_i + AT_i = 1$ for all $i = 1, \ldots, 6$, as in the SFCCC system we can find $S_i = 1 - (P_i + L_i + A_i + LT_i + AT_i)$ and eliminate the variable S_i. If we now call

$$Z_i = \sum_{k=1}^{6} N_{ik}(pP_k + \ell L_k + \ell_T LT_k + aA_k + a_T AT_k)$$

we obtain the following reduced system with treatment:

$$\begin{cases} \dot{P}_i &= Z_i\,[1 - (P_i + L_i + A_i + LT_i + AT_i)] - \rho P_i\,; \\ \dot{L}_i &= \rho P_i - \lambda L_i - \tau L_i + \omega LT_i\,; \\ \dot{A}_i &= \lambda L_i - \alpha A_i - \tau A_i + \omega AT_i\,; \\ \dot{LT}_i &= \tau L_i - \omega LT_i - \nu LT_i\,; \\ \dot{AT}_i &= \tau A_i - \omega AT_i + \nu LT_i - \mu AT_i\,. \end{cases} \tag{33}$$

6. **Equilibria and stability for the SFCCC system with treatment.** The equilibria for system (32), or (33), are the solutions of the following algebraic system:

$$\begin{cases} Z_i\,[1 - (P_i + L_i + A_i + LT_i + AT_i)] - \rho P_i &= 0\,; \\ \rho P_i - \lambda L_i - \tau L_i + \omega LT_i &= 0\,; \\ \lambda L_i - \alpha A_i - \tau A_i + \omega AT_i &= 0\,; \\ \tau L_i - \omega LT_i - \nu LT_i &= 0\,; \\ \tau A_i - \omega AT_i + \nu LT_i - \mu AT_i &= 0\,; \end{cases} \tag{34}$$

where

$$Z_i = \sum_{k=1}^{6} N_{ik}(pP_k + \ell L_k + \ell_T LT_k + aA_k + a_T AT_k). \tag{35}$$

System (34) has always the DFE (disease-free equilibrium), for which $S_i = 1$; $P_i = L_i = A_i = LT_i = AT_i = 0$, for all $i = 1, \ldots, 6$. As for the regular SFCCC

model, depending on the reproduction number R_0, system (34) will either only have the DFE, or an additional equilibrium with all positive variables, the EE (endemic equilibrium).

Proceeding as for the SFCCC case, let us solve the system of the last four equations of (34), which are linear, with respect to P_i. This system can be re-written as

$$\begin{cases} (\lambda+\tau)L_i - \omega LT_i &= \rho P_i\,; \\ \lambda L_i - (\alpha+\tau)A_i + \omega AT_i &= 0\,; \\ \tau L_i - (\omega+\nu)LT_i &= 0\,; \\ \tau A_i + \nu LT_i - (\omega+\mu)AT_i &= 0\,. \end{cases} \tag{36}$$

If we call

$$\begin{cases} m &= \lambda\omega + \lambda\nu + \tau\nu; \\ n &= \alpha\omega + \alpha\mu + \tau\mu; \\ r &= \lambda\omega^2 + \lambda\omega\mu + \tau\omega\nu + \lambda\omega\nu + \lambda\mu\nu \\ &= \omega m + \mu\lambda(\omega+\nu); \\ s &= \nu\alpha + \nu\tau + \lambda\omega + \lambda\nu = \nu\alpha + m; \end{cases} \tag{37}$$

then the solution is

$$A_i = \frac{\rho r}{mn}P_i; \qquad AT_i = \frac{\tau\rho s}{mn}P_i; \qquad L_i = \frac{\rho(\omega+\nu)}{m}P_i; \qquad LT_i = \frac{\tau\rho}{m}P_i, \tag{38}$$

where all the coefficients are independent of i.

As before, observe that if $P_i = 0$ then all other variables will be 0 as well, and we get the DFE for that i. On the other hand, if $P_i > 0$, then all other variables will be positive as well, and we get the EE.

Substituting (38) into (35), we obtain

$$Z_i = \sum_{k=1}^{6} N_{ik}\left[p + \frac{\ell\rho(\omega+\nu)}{m} + \frac{a\rho r}{mn} + \frac{\ell_T\tau\rho}{m} + \frac{a_T\tau\rho s}{mn}\right]P_k. \tag{39}$$

Let us call

$$\gamma = \frac{p}{\rho} + \ell\,\frac{\omega+\nu}{m} + a\,\frac{r}{mn} + \ell_T\,\frac{\tau}{m} + a_T\,\frac{\tau s}{mn}. \tag{40}$$

Then Z_i can be rewritten as

$$Z_i = \sum_{k=1}^{6} N_{ik}\rho\gamma P_k. \tag{41}$$

Next, using (38),

$$P_i + L_i + A_i + LT_i + AT_i = \left[1 + \frac{\rho(\omega+\nu)}{m} + \frac{\rho r}{mn} + \frac{\tau\rho}{m} + \frac{\tau\rho s}{mn}\right]P_i.$$

If we call

$$\beta = \frac{1}{\rho} + \frac{\omega+\nu}{m} + \frac{r}{mn} + \frac{\tau}{m} + \frac{\tau s}{mn}, \tag{42}$$

then we can write

$$P_i + L_i + A_i + LT_i + AT_i = \rho\beta P_i. \tag{43}$$

Substituting (41) and (43) into the first equation of (3), we obtain

$$\sum_{k=1}^{6} N_{ik}\rho\gamma P_k(1-\rho\beta P_i) - \rho P_i = 0,$$

or

$$\sum_{k=1}^{6} N_{ik}\gamma P_k(1-\rho\beta P_i) = P_i. \tag{44}$$

This equation is formally identical to (11), although the positive constants γ and β are now significantly more involved. This motivates the following definition.

Definition 6.1. The reproduction number R_{0i} for the ith group of the SFCCC system with treatment is $R_{0i} = c_i g_i \gamma$, where

$$\gamma = \frac{p}{\rho} + \ell\,\frac{\omega+\nu}{m} + a\,\frac{r}{mn} + \ell_T\,\frac{\tau}{m} + a_T\,\frac{\tau s}{mn},$$

and m, n, r, s are given by (37). The reproduction number R_0 for system (32), or (33), is $R_0 = \sum_{i=1}^{6} R_{0i} = \gamma\left(\sum_{i=1}^{6} c_i g_i\right)$.

We now prove the following result.

Theorem 6.2. *If $R_0 \le 1$, then system (33) has only the disease-free equilibrium (DFE); if $R_0 < 1$, then the DFE is locally asymptotically stable, and it is also globally stable. If $R_0 > 1$ then, in addition to the DFE, system (33) has a unique equilibrium for which all the variables are strictly positive, the endemic equilibrium (EE). Moreover, if $R_0 > 1$, then the DFE is unstable.*

Proof. After introducing new coefficients γ and β given by (40) and (42) respectively, equation (44) coincides with (11). The same algebraic manipulations done for the previous case will then lead to equation (21), which can be rewritten as (31), for R_0 given by Definition 6.1. Hence, by Proposition 1, we conclude that if $R_0 \le 1$ then (33) has only one equilibrium, the DFE, and if $R_0 > 1$, in addition to the DFE, the system has a unique equilibrium for which all variables are positive, the EE.

To determine stability, we will look at the Jacobian J of the system at the DFE. The computations will follow those that were done for the SFCCC system without treatment, only now the algebraic computations will be significantly more involved. The Jacobian of system (33) at the DFE can now be written as $J = F - V$, where V is the block diagonal matrix

$$V = \begin{pmatrix} V_0 & 0 & \dots & 0 \\ 0 & V_0 & \dots & 0 \\ \dots & \dots & \dots & \dots \\ 0 & 0 & \dots & V_0 \end{pmatrix}, \tag{45}$$

with

$$V_0 = \begin{pmatrix} \rho & 0 & 0 & 0 & 0 \\ -\rho & \lambda+\tau & 0 & -\omega & 0 \\ 0 & -\lambda & \alpha+\tau & 0 & -\omega \\ 0 & -\tau & 0 & \omega+\nu & 0 \\ 0 & 0 & -\tau & -\nu & \omega+\mu \end{pmatrix}, \tag{46}$$

and

$$F = \begin{pmatrix} c_1g_1p & c_1g_1\ell & c_1g_1a & c_1g_1\ell_T & c_1g_1a_T & c_1g_2p & c_1g_2\ell & \dots \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & \dots \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & \dots \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & \dots \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & \dots \\ c_2g_1p & c_2g_1\ell & c_2g_1a & c_2g_1\ell_T & c_2g_1a_T & c_2g_2p & c_2g_2\ell & \dots \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & \dots \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & \dots \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & \dots \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & \dots \\ \dots & \dots & \dots & \dots & \dots & \dots & \dots & \dots \end{pmatrix}.$$

Then V is invertible and block-diagonal, with blocks

$${V_0}^{-1} = \begin{pmatrix} \frac{1}{\rho} & 0 & 0 & 0 & 0 \\ \frac{\omega+\nu}{m} & \frac{\omega+\nu}{m} & 0 & \frac{\omega}{m} & 0 \\ \frac{r}{mn} & \frac{r}{mn} & \frac{\omega+\mu}{n} & \frac{\omega(m+\lambda\mu)}{mn} & \frac{\omega}{n} \\ \frac{\tau}{m} & \frac{\tau}{m} & 0 & \frac{\tau+\lambda}{m} & 0 \\ \frac{s\tau}{mn} & \frac{s\tau}{mn} & \frac{\tau}{n} & \frac{\alpha\nu(\tau+\lambda)+\tau m}{mn} & \frac{\alpha+\tau}{n} \end{pmatrix},$$

so that V^{-1} is non-negative. Here m, n, r, s are given by (37).

We write the rank-1 matrix F as $F = u \cdot v^T$, where u and v are the column vectors

$$u = (c_1, 0, 0, 0, 0, \dots, c_6, 0, 0, 0, 0);$$

$$v = (g_1p, g_1\ell, g_1a, g_1\ell_T, g_1a_T, \dots, g_6p, g_6\ell, g_6a, g_6\ell_T, g_6a_T). \tag{47}$$

Then the product matrix $W = FV^{-1}$ is $W = u \cdot w^T$, where w^T is the row vector v^TV^{-1}. It follows that the (only) nonzero eigenvalue of W is $w^T \cdot u$. But $w^T \cdot u = v^TV^{-1}u$, and

$$V^{-1}u = \operatorname{col}\left(\frac{c_1}{\rho}, \frac{c_1(\omega+\nu)}{m}, \frac{c_1r}{mn}, \frac{c_1\tau}{m}, \frac{c_1s\tau}{mn}, \dots \frac{c_6}{\rho}, \frac{c_6(\omega+\nu)}{m}, \frac{c_6r}{mn}, \frac{c_6\tau}{m}, \frac{c_6s\tau}{mn}\right).$$

Thus the nonzero eigenvalue of W is positive, and equal to

$$v^TV^{-1}u = (g_1c_1 + \dots + g_6c_6)\left(\frac{p}{\rho} + \frac{\ell(\omega+\nu)}{m} + \frac{ar}{mn} + \frac{\ell_T\tau}{m} + \frac{a_Ts\tau}{mn}\right).$$

But the second factor in the last expression is precisely our γ, defined in (40), so that the spectral radius of $W = FV^{-1}$ is equal to $\rho(FV^{-1}) = (g_1c_1 + \dots + g_6c_6)\gamma$. An analogous (and simpler) computation shows that $\rho(F_i{V_0}^{-1}) = c_ig_i\gamma$, where J_i is the Jacobian for the ith group, split as $J_i = V_0 - F_i$. Since the values of these spectral radii agree with the ones in Definition 6.1, we have established that $R_0 = R_{01} + \dots + R_{06}$ also holds true when the reproduction numbers are regarded as spectral radii of the corresponding matrices FV^{-1} and $F_i{V_0}^{-1}$.

The local stability of the DFE for $R_0 < 1$ and its unstability when $R_0 > 1$ follow now from the properties of M-matrices, repeating the arguments for the SFCCC system with no treatment.

The global stability of the DFE, when $R_0 < 1$, is established using the same arguments as for the case withouth treatment, with the Lyapunov function

$$\mathcal{V}(X) = v^T V^{-1} X,$$

where now $X = (P_1, L_1, A_1, LT_1, AT_1, \ldots, P_5, L_5, A_5, LT_5, AT_5)$;
$Q(X) = (Q_1(X), 0, 0, 0, 0, \ldots, Q_5(X), 0, 0, 0, 0)$, with

$$Q_i(X) = \sum_{k=1}^{5} N_{ik}(pP_k + \ell L_k + aA_k + \ell_T LT_k + a_t AT_k)(P_i + L_i + A_i + LT_i + AT_i);$$

v is given by

$$v = (g_1 p, g_1 \ell, g_1 a, g_1 \ell_T, g_1 a_T, \ldots, g_5 p, g_5 \ell, g_5 a, g_5 \ell_T, g_5 a_T), \tag{48}$$

and V is the matrix (45)-(46), except that now V consists of five diagonal blocks V_0, instead of six. □

7. **Numerical results.** For the SFCCC system without testing and treatment, the following values were adopted for the coefficients [7], [23], [13]:

$$\rho = 6, \quad \lambda = \frac{1}{7}, \quad \alpha = 0.5;$$

$$c_1 = 231, \quad c_2 = 81, \quad c_3 = 33, \quad c_4 = 15, \quad c_5 = 3, \quad c_6 = 0;$$

$$f_1 = 0.10, \quad f_2 = 0.15, \quad f_3 = 0.25, \quad f_4 = 0.25, \quad f_5 = 0.15, \quad f_6 = 0.10.$$

The units of the variables, and the coefficients, are as follows. The variables S_i, P_i, L_i, and A_i represent fractions of the total population in the ith group, and are therefore dimensionless. Time is measured in years, and the units of ρ, λ, α are $\frac{1}{\text{year}}$. The c_i are measured in $\frac{\text{encounters}}{\text{year}}$; consequently, the g_k are dimensionless, and the N_{ik} have dimension $\frac{\text{encounters}}{\text{year}}$.

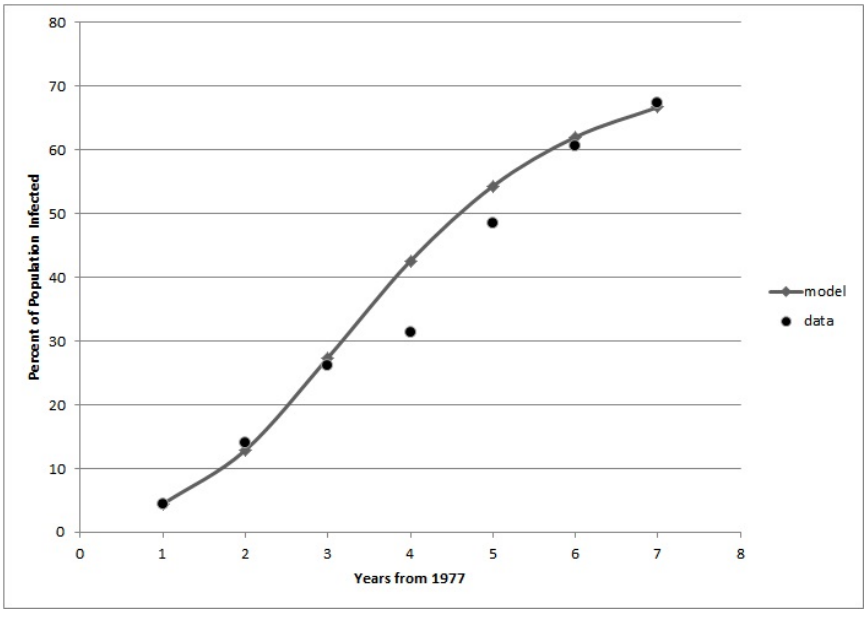

FIGURE 3. Comparing the model output with the SFCCC data.

Estimates of average infectiousness for each of the three stages are obtained using the Figure 1 model based on Figure 3 data as done in [23]. The model can be run for any choice of the three infectivities, and an epidemic is produced. We have seven data points (for each of the seven years 1978 − 1984). We use the most reliable data points ([27], [7], [15]). These points correspond to the years 1978, 1979, 1980 and 1984. We compute the square of the difference between this model epidemic and the actual SFCCC epidemic at these four data points. Let RMS (root mean square) denote the square root of the average of those four numbers. We use a minimization technique (Newton's Method applied to the gradients of $E = RMS$ errors in SFCCC fit to data for the four years) to select the choice of infectivities for which the RMS is minimized. The minimum is obtained for stage infectivity rates

$$p = 0.00198, \quad \ell = 0.0000456; \quad a = 0.15449588$$

with an RMS of 0.00034. We call these infectivity estimates the best fit infectivities. The model solution displayed in Figure 3 reproduces the cumulative SFCCC epidemic using these best fit infectivities. We take the output closest to 4.5% to be the year 1978. Working backwards we can determine the starting year of the epidemic (when one person was infected).

The corresponding numerical value for the coefficient γ given by (8) is $\gamma = 0.301918$. The rounded-off reproduction numbers $R_{0i} = \gamma c_i g_i$ for each subsystem are

$$R_{01} = 33.7745, \quad R_{02} = 6.2292, \quad R_{03} = 1.7232,$$
$$R_{04} = 0.3560, \quad R_{05} = 0.0085, \quad R_{06} = 0.$$

The reproduction number R_0 for the entire system is the sum of these, which yields $R_0 = 42.0919$. Since $R_0 > 1$, our results imply that the system has precisely two equilibria: the disease-free equilibrium (DFE), which is unstable, and an endemic equilibrium (EE).

Although so far we haven't succeeded in proving, for the general case, that the EE is stable when $R_0 > 1$, a numerical analysis of the 18×18-Jacobian of system (3) at the EE shows that all its eigenvalues have negative real parts, and is hence (at least locally) stable. The total infected population at the EE is 74.018%. On the other hand, the numerical solution of the total infected population for system (3) at $t = 25$ is about 74%, and at $t = 100$ practically coincides with the value at the EE.

We have explored several treatment options for the model with treatment. For all of them we picked the same parameter values as for the untreated model, plus $\mu = 0.2$, $\nu = 0.05$,

$$\ell_T = 0.04 \cdot \ell = 0.00000912; \quad a_T = 0.04 \cdot a = 0.00599984.$$

For $\tau = 0.5$ (50% of the population being tested and, if tested positive, immediately put on antiretroviral treatment), $\omega = 0.03$ (the rate of withdrawal from treatment), the total infected population approaches its EE value of 56.18%. For $\tau = 1.0$ and $\omega = 0$, the asymptotic value for the total infected is 40.79%. If we assume that the number of contacts was drastically reduced—by a factor of ten—around 1986, when the San Francisco MSM population became aware of the HIV threat, then for the untreated model the total infected will still approach 33.37%, whereas for the model with treatment, for $\omega = 0.03$ and $\tau = 0.75$ or larger, this limit value will be zero, that is, the infection will be totally eradicated.

For more details, see our upcoming paper [24].

Sensitivity and genericity. The stability of the disease-free equilibrium DFE when $R_0 < 1$, and its instability when $R_0 > 1$, were proved under very general assumptions on the parameters—namely, that they are all positive, and the c_i are strictly decreasing ($i = 1, \dots 6$), with $c_6 = 0$. Therefore, they are generic, and a small change in the data will not influence their long-term behavior. The only result that is pending for now is the stability of the endemic equilibrium EE for the case when $R_0 > 1$. To investigate the stability of the EE under small perturbations, as well as to measure the effect produced in the data by a variation in the parameters, we conducted sensitivity analysis. Due to the lengthy computations required for each run, we used the OFAT (one factor at a time) method. The parameters investigated were the three chosen infectivities p, ℓ, and a, which, as we have explained in this section, were chosen to minimize the difference between the model output and most reliable available data. We sampled 10 variations for each parameter.

We found that up to a 50% variation in the infectivity p produced insignificant change in the total infected population (less than 0.001%), and a very small change in the reproduction number R_0 (about 0.005%). The same variation in the infectivity ℓ produced a change of less than 0.008% in the total infected, and about 0.05% in R_0. For the infectivity a, which is larger than either p or ℓ by a thousandfold, we computed a variation of up to 5%. The result was a change of less than 0.8% in the total infected, and less than 5% in R_0 (always from its original value of about 43.12).

Finally, we found that the largest real part of the eigenvalues of the Jacobian matrix at the EE was always the same, namely, $-\frac{1}{7}$, which corresponds to $-\rho$. This implies that in all the runs, the EE is in fact stable. Incidentally, it is not hard to show that $-\rho$, $-\alpha$, and $-\lambda$ are always eigenvalues for the Jacobian at the EE, for any values of the infectivities a, ℓ, p (this is due to the fact that $c_6 = 0$).

8. **Discussion.** We offer two models for the development of the HIV-AIDS epidemic in a MSM population, described by systems of differential equations. The first model is based on data obtained for the MSM-San Francisco HIV epidemic (1978-1984), the longitudinal San Francisco City Clinic Cohort (SFCCC) data set [7], [15],([27]); we have shown that this model agrees quite well with the data.

The second model represents a "what if" scenario: how the SFCCC epidemic would have evolved if there had been testing and treatment available. We show how treatment would have dramatically reduced the likelihood of transmitting the virus, in agreement with the conclusions of recent studies ([6], [17], [21]). More details are in our upcoming paper [24].

Each system assumes that the population is divided into six groups, with decreasing sexual activity levels c_i. In each group, the population consists of susceptible individuals S_i, and sick individuals which, in turn, are either in the primary stage P_i, latent stage L_i, or AIDS stage A_i, for $i = 1, \dots 6$.

We analyze the properties of the two SFCCC systems, under fairly general assumptions; namely, that the average encounter matrix N_{ik} splits as $N_{ik} = c_i g_k$ (*proportionate mixing*).

For a dynamical system describing an infection, a crucial role is played by the *reproduction number* R_0, which represents the number of individuals infected by a single sick individual during his/her lifetime. We deduce the expression of the reproduction number R_0 for each system and prove that, for each one, if $R_0 < 1$, then the system has only the disease-free equilibrium (DFE), for which there are no

sick individuals; and if $R_0 > 1$ then, in addition to the DFE, the system has a single endemic equilibrium (EE), with a positive number of sick individuals. Moreover, we show that when $R_0 < 1$, the DFE is locally, as well as globally, stable, while if $R_0 > 1$, the DFE is unstable. Numerical evidence shows that in this case the EE is stable, but for the moment this remains to be proved for the general case.

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