A co-interaction model of HIV and syphilis infection among gay, bisexual and other men who have sex with men

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Abstract

We developed a mathematical model to study the co-interaction of HIV and syphilis infection among gay, bisexual and other men who have sex with men (gbMSM). We qualitatively analysed the model and established necessary conditions under which disease-free and endemic equilibria are asymptotically stable. We gave analytical expressions for the reproduction number, and showed that whenever the reproduction numbers of sub-models and co-interaction model are less than unity, the epidemics die out, while epidemics persist when they are greater than unity. We presented numerical simulations of the full model and showed qualitative changes of the dynamics of the full model to changes in the transmission rates. Our numerical simulations using a set of reasonable parameter values showed that: (a) both diseases die out or co-exist whenever their reproduction number is less than or exceed unity. (b) HIV infection impacts syphilis prevalence negatively and vice versa. (c) one possibility of lowering the co-infection of HIV and syphilis among gbMSM is to increase both testing and treatment rates for syphilis and HIV infection, and decrease the rate at which

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HIV infected individuals go off treatment.

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1. Introduction

HIV is known to be a sexually transmitted and blood-borne infection with a highly variable disease progression in humans [1]. People infected with HIV experience immune suppression as a result of continuous destruction of the $CD4^+T$ lymphocytes, which makes immunosupressed individuals at risk of acquiring other sexually transmitted infections (such as syphilis, gonorrhea [1, 7, 16]). At the end of 2017, approximately 37 million people were living with HIV throughout the world, and over $900,000$ reported deaths were attributed to HIV infection [35]. In 2016, gay, bisexual and other men who have sex with men (gbMSM) accounted for about half of the new HIV infections in Canada [34]. Similarly, gbMSM currently accounts for most new and prevalent cases of HIV in Vancouver [26] and San Francisco [14]. There were about 3320 gbMSM who were newly diagnosed with HIV in the UK in 2015 [19]. The increase of antiretroviral therapy (ART) coverage to reduce and prevent HIV transmission in British Columbia (BC), Canada, made us observe a positive impact of HAART to prevent HIV transmission and decrease HIV diagnosis per year [28].

Syphilis is known to be an infection caused by the *Treponema pallidum bacteria* [16, 33], and progresses from primary $\rightarrow$ secondary $\rightarrow$ latent $\rightarrow$ tertiary stage if left untreated [33]. Infectious syphilis is more frequent in males with an increased rate among gbMSM population in BC and Canada [27, 33]. In 2017, 5% or more of gbMSM in 22 of 34 reporting countries were infected with syphilis [36]. From 2011 to 2015, the rate of reported cases of syphilis per $100,000$ population in the United States rose by 58% (from 14.8 to 23.4), with the highest rate observed in San Francisco, where the rates rose by 77% (from 84.3 to 149.6) [14]. In 2016, gbMSM accounted for about 80.6% of male infectious

syphilis in the United States [25]. Similarly, in BC, the rate of reported cases of infectious syphilis per $100,000$ population in 2016, rose to 16.0 (759 cases) when compared to 4.2 (193 cases) in 2011 [27]. The highest rate in BC was observed in Vancouver and surrounding regions, where the rates rose from 19.6 (131 cases) in 2011 to 63.7 (428 cases) in 2016 [27]. In 2016, gbMSM accounted for about 63.5% of infectious syphilis in Vancouver [27].

Recent increases in sexually transmitted infections (STIs), especially among gbMSM, brought up about the importance for characterising the co-interaction of HIV and syphilis. Increases in the risk of HIV and STI transmission have been attributed to sexual behaviours over the last decade [16, 19, 25]. It is estimated that about 43% of gbMSM in BC with syphilis diagnoses and known HIV status in 2016, were HIV positive [27]. Individuals co-infected with these two diseases are more likely to transmit HIV to their sexual partners, and as well likely to progress to serious disease stages [27, 16]. gbMSM living with HIV are about 2 times more likely to be infected with syphilis compared to those that are HIV negative [25].

This paper considers a single class of infectious syphilis since major stages, such as primary, secondary, early latent and infectious neurosyphilis, are generally classified as infectious syphilis, and is of public health concern [33]. Many mathematical models have been previously used to assess dynamics of the co-infection of HIV and other diseases, such as Hepatitis C virus, gonorrhea, tuberculosis and syphilis [18, 11, 9, 12, 30, 40, 31, 5], but only Nwankwo et al. [31] used a similar approach to study the dynamics of HIV and syphilis. Our study differs from [31] as we consider the gbMSM population in a setting where treatment of both diseases is readily available. We make simplifying assumptions about the natural history of both diseases and incorporate some epidemiological features of the co-dynamics of HIV and syphilis. From our mathematical analyses and using a set of parameter values from published articles, our model aim to answer the following questions: What effect does syphilis infection have on HIV infected individuals and vice versa? What is the impact of change in transmission rate on the dynamics of both diseases? Can we test and treat

mono-infected individuals more to reduce the prevalence of both diseases?

The paper is organised as follows. We develop and describe the model in Section 2, and analyse two sub-models in Sections 3 and 4. We present the analysis of the full co-interaction model and some numerical simulations in Sections 5 and 6 respectively while Section 7 discusses and concludes the paper.

2. Model formulation and description

The total gbMSM population at time t, denoted by $N(t)$ is divided into 8 mutually exclusive compartments stated in Table (1), so that

$$N(t) = S(t) + I_S(t) + U_H(t) + A_H(t) + T_H(t) + U_{SH}(t) + A_{SH}(t) + T_{SH}(t). \quad (1)$$

Table 1: Model Variables and their Descriptions

Variable	Description
S	Susceptible individuals
I_S	Individuals mono-infected with syphilis
U_H	Individuals mono-infected with HIV and unaware
A_H	Individuals mono-infected with HIV and aware
T_H	HIV infected individuals on treatment
U_{SH}	Co-infected individuals unaware of HIV infection
A_{SH}	Co-infected individuals aware of HIV infection
T_{SH}	Co-infected individuals on HIV treatment

We assume that at time t, new recruits enter the population at a constant rate Π. Individuals die in each subclass at a constant natural mortality rate μ. HIV infected individuals $(U_H, A_H, U_{SH}, A_{SH})$ not on treatment have additional HIV induced death rates $d_{UH}, d_{AH}, d_{USH}, d_{ASH}$ respectively. We assume no death from syphilis and that HIV infected individuals on treatment do not transmit HIV infection [22, 37].

Diseases co-dynamics are complicated processes, but for simplicity, we assume that both mono and co-infected individuals can either transmit HIV or

syphilis but not both at the same time. Susceptible individuals may acquire syphilis infection when in contact with individuals in I_S, U_{SH}, A_{SH} and T_{SH} compartments, at a rate λ_S (the force of infection associated with syphilis infection), given by $\lambda_S = \beta_S \frac{(I_S + \phi_1 U_{SH} + \phi_2 A_{SH} + \phi_3 T_{SH})}{N}$, where β_S denotes the transmission rate for syphilis. Parameter β_S is the probability of syphilis transmission from one contact between individuals in S and in other syphilis infected compartments (I_S, U_{SH}, A_{SH}, T_{SH}), times the number of contacts per year per individual. Modification parameters ϕ_1, ϕ_2 and ϕ_3 respectively account for the relative infectiousness of syphilis infected individuals with undiagnosed HIV infection (U_{SH}), coinfected with HIV and aware (A_{SH}), and coinfected with HIV and on HIV treatment (T_{SH}), compared to individuals mono-infected with syphilis. We assume that coinfected individuals are about two times as infectious as mono-infected individuals [25]. Since it is believed that individuals infected with syphilis recover with temporal immunity [38], we then assume that individuals infected with syphilis recover after treatment and return to the susceptible class at a rate σ_1.

Susceptible individuals acquire HIV infection from those in the U_H, A_H, U_{SH} and A_{SH} compartments, at the rate λ_H (the force of infection associated with HIV infection), given by $\lambda_H = \beta_H \frac{(U_H + \kappa_1 A_H + \kappa_2 U_{SH} + \kappa_3 A_{SH})}{N}$, where β_H denotes the transmission rate for HIV. Parameter β_H is the probability of HIV transmission from one contact between individuals in S and in other HIV infectious compartments (U_H, A_H, U_{SH}, A_{SH}), times the number of contacts per year per individual. Modification parameters κ_1, κ_2 and κ_3 respectively account for the relative infectiousness of individuals mono-infected with HIV and aware (A_H), co-infected with HIV and unaware (U_{SH}), co-infected with HIV and aware (A_{SH}), in comparison with individuals mono-infected with HIV.

Susceptible individuals infected with HIV at rate λ_H enter the HIV unaware class U_H, where they progress to HIV aware class A_H following testing at a rate α_1, and are then placed on treatment at a rate ρ_2 to enter the class T_H. Individuals in the HIV infected and on treatment classes T_H and T_{SH} can go off treatment at rates ν_1 and ν_2 respectively.

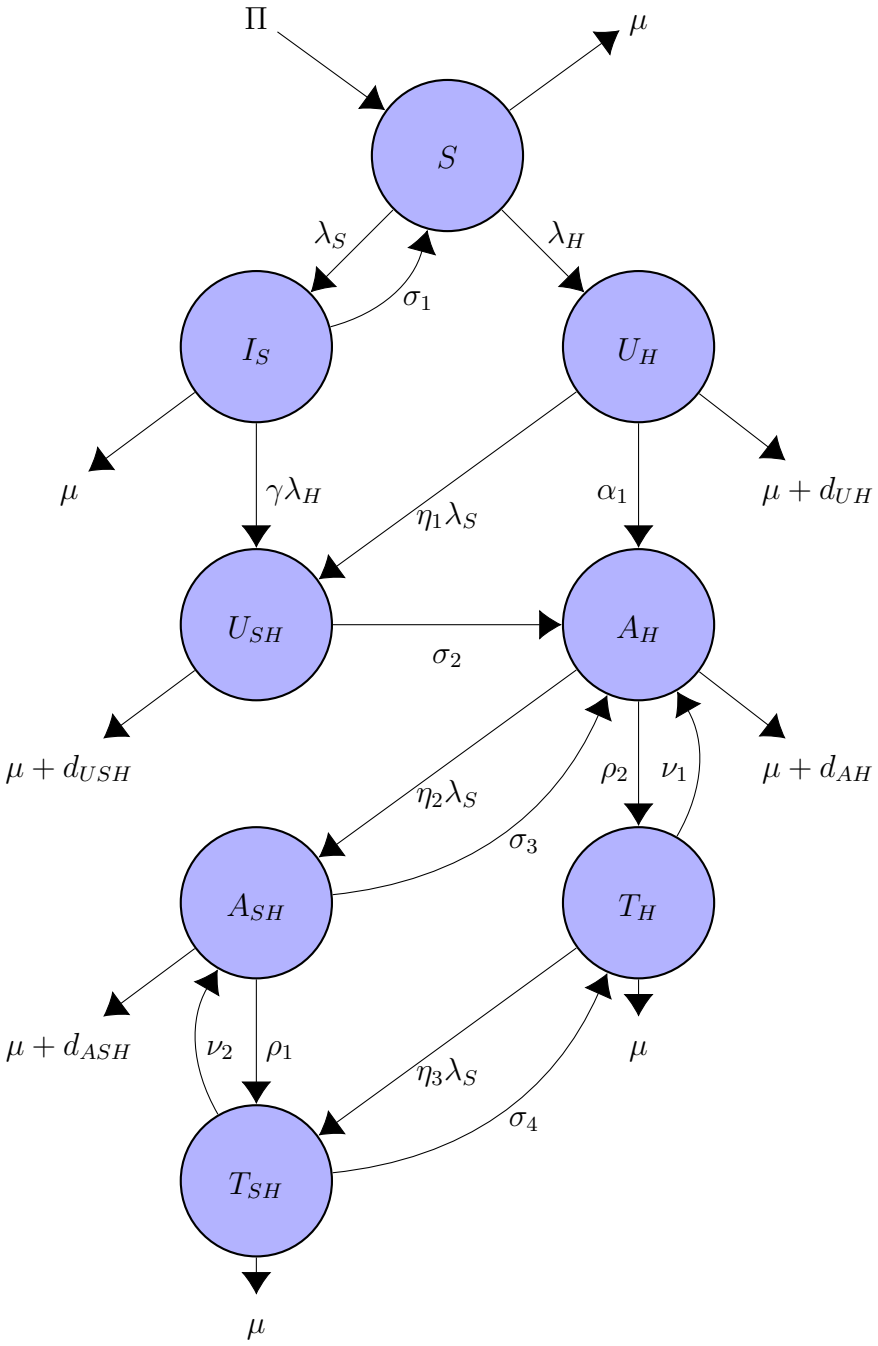


Figure 1: Diagram of the HIV/Syphilis co-interaction model among gbMSM

Individuals mono-infected with HIV (U_H, A_H, T_H) are infected with syphilis at rates $\eta_1\lambda_S,\ \eta_2\lambda_S,\ \eta_3\lambda_S$ to enter classes U_{SH}, A_{SH}, T_{SH} respectively, and modification parameters $\eta_1, \eta_2, \eta_3 > 1$ account for higher risk of syphilis acquisition for people living with HIV.

Individuals mono-infected with syphilis, I_S are infected with HIV at a rate $\gamma\lambda_H$ to enter the class U_{SH}, where the modification parameter $\gamma > 1$ due to higher risk of HIV acquisition for people whose immune system are sabotaged by syphilis infection. Co-infected individuals in the class A_{SH} are placed on treatment at a rate ρ_1 to enter class T_{SH}. Co-infected individuals in the classes U_{SH}, A_{SH}, T_{SH} are tested and treated for syphilis at rates $\sigma_2,\ \sigma_3,\ \sigma_4$ to move back into the classes U_H, A_H, T_H, respectively. This model assumes uniform and homogeneous mixing population. The model diagram presented in Figure 1 is described by the following system of non-linear differential equations.

$$
\begin{aligned}
\frac{\mathrm{d}S}{\mathrm{d}t} &= \Pi + \sigma_1 I_S - (\mu + \lambda_S + \lambda_H)S, \\
\frac{\mathrm{d}I_S}{\mathrm{d}t} &= \lambda_S S - (\mu + \sigma_1 + \gamma\lambda_H)I_S, \\
\frac{\mathrm{d}U_H}{\mathrm{d}t} &= \lambda_H S - (\mu + d_{UH} + \alpha_1 + \eta_1\lambda_S)U_H, \\
\frac{\mathrm{d}A_H}{\mathrm{d}t} &= \alpha_1 U_H + \sigma_2 U_{SH} + \sigma_3 A_{SH} + \nu_1 T_H - (\mu + d_{AH} + \eta_2\lambda_S + \rho_2)A_H, \\
\frac{\mathrm{d}T_H}{\mathrm{d}t} &= \rho_2 A_H + \sigma_4 T_{SH} - (\mu + \eta_3\lambda_S + \nu_1)T_H, \\
\frac{\mathrm{d}U_{SH}}{\mathrm{d}t} &= \gamma\lambda_H I_S + \eta_1\lambda_S U_H - (\mu + d_{USH} + \sigma_2)U_{SH}, \\
\frac{\mathrm{d}A_{SH}}{\mathrm{d}t} &= \eta_2\lambda_S A_H + \nu_2 T_{SH} - (\mu + d_{ASH} + \sigma_3 + \rho_1)A_{SH}, \\
\frac{\mathrm{d}T_{SH}}{\mathrm{d}t} &= \rho_1 A_{SH} + \eta_3\lambda_S T_H - (\mu + \nu_2 + \sigma_4)T_{SH},
\end{aligned}
\tag{2}
$$

We will analyse different diseases separately, and then jointly to understand different components of the general model and as well adapt to different scenarios.

3. Syphilis sub-model

We have the model with syphilis only by setting $U_H = A_H = T_H = U_{SH} = A_{SH} = T_{SH} = 0$ in system (2), and this gives

$$\begin{aligned} \frac{\mathrm{d}S}{\mathrm{d}t} &= \Pi + \sigma_1 I_S - (\mu + \lambda_S)S, \\ \frac{\mathrm{d}I_S}{\mathrm{d}t} &= \lambda_S S - (\mu + \sigma_1)I_S, \end{aligned} \tag{3}$$

where $\lambda_S = \beta_S \dfrac{I_S}{N_S}$, with total population given as $N_S(t) = S(t) + I_S(t)$.

The simple SIS model in (3) ignored syphilis-related death and was extensively discussed in [38] using different stages of syphilis infection to understand the transmission dynamics, and in [4] to track syphilis dynamics in men and women. Hence, the dynamics of system (3) based on biological consideration in the region $\Xi_S = \left\{(S, I_S) \in \mathbb{R}^2_+ : N_S \leq \frac{\Pi}{\mu}\right\}$, is easy to show as being positively invariant with respect to the model. We therefore consider model (3) to be epidemiologically and mathematically well posed with all variables and parameters being positive for all time series as in [9, 11, 20]. Model (3) has a *disease free equilibrium points* given by $E_{0S} = (S_0, I_{0S}) = \left(\dfrac{\Pi}{\mu}, \quad 0\right)$.

It is easy to explain the linear stability of disease free equilibrium by the reproduction number which can be derived using the method of next generation matrix in [20, 42]. Hence, E_{0S} can be explained by $\mathcal{R}_{eS}$, where

$\mathcal{R}_{eS} = \dfrac{\beta_S}{(\mu + \sigma_1)}$ is the reproduction number for syphilis dynamics given by the product of the transmission rate of syphilis infection β_S and the rate that an infective progresses out of syphilis infectious class $\dfrac{1}{(\mu + \sigma_1)}$. The *biological* interpretation of $\mathcal{R}_{eS}$ is the number of syphilis infections produced by one syphilis infective during the period of infectiousness when introduced in a totally syphilis susceptible population in the presence of treatment.

We can establish the local stability of the disease free equilibrium (E_{0S}) using Lemma 1 which follows from [20] and Theorem 2 of [42].

Lemma 1. *The DFE E_{0S} of model* (3) *is locally asymptotically stable (LAS) if $\mathcal{R}_{eS} < 1$ and unstable if $\mathcal{R}_{eS} > 1$.*

The *biological* interpretation of $\mathcal{R}_{eS} < 1$ is that we can eliminate syphilis from the population if the initial sizes of the sub-population of syphilis sub-model are in the attraction region E_{0S}.

To ensure that elimination of syphilis epidemic is independent on the initial sizes of the sub-populations, we establish the *global stability* of the DFE E_{0S} by claiming the result in an easily proved Lemma 2.

Lemma 2. *For any positive solutions* $(S(t), I_S(t))$ *of model system* (3)*, if* $\mathcal{R}_{eS} < 1$*, then, the DFE* E_{0S} *is a global attractor.*

By equating the right-hand side of equation (3) to zero, and solving for S^* and I_S^*, we have the *endemic equilibrium points* given by $E_S^* = (S^*, I_S^*) = \left(\dfrac{\Pi(\mu+\sigma_1)}{\mu(\mu+\sigma_1+\lambda_S^*)}, \quad \dfrac{\lambda_S^* S^*}{(\mu+\sigma_1)}\right)$. The force of infection λ_S^* and the endemic equilibrium points E_S^* can be written in terms of $\mathcal{R}_{eS}$ as $\lambda_S^* = \dfrac{(\mathcal{R}_{eS}-1)}{\Omega}$ and

$$E_S^* = (S^*, I_S^*) = \left(\frac{\Pi}{\mu\mathcal{R}_{eS}}, \quad \frac{\Pi(\mathcal{R}_{eS}-1)}{\mu(\mathcal{R}_{eS})}\right) \tag{4}$$

where $\Omega = \dfrac{1}{(\mu+\sigma_1)}$ denote the mean infective period.

When $\mathcal{R}_{eS} > 1$, E_S^* is positive and the epidemic of syphilis persists in the community. We can summarize the uniqueness of the endemic equilibrium in an easily proved Lemma 3.

Lemma 3. *The endemic equilibrium* E_S^* *exists and is unique if and only if* $\mathcal{R}_{eS} > 1$.

Proof. It is enough to show that the components of E_S^* are positive only if $\mathcal{R}_{eS} > 1$. We have I_S^* in equation (4) to be non-zero and positive only when $\mathcal{R}_{eS} > 1$. The same follows for S^*. QED.

The global stability of the endemic equilibrium for syphilis-only model can be easily shown from Chapter 2 in [2, 10], three basic epidemiological models in [20] and by claiming the result in an easily proved Lemma 4

Lemma 4. *The endemic equilibrium of syphilis-only model 3 is globally asymptotically stable in* Ξ_S *whenever* $\mathcal{R}_{eS} > 1$.

In summary, the syphilis-only model (3) has a globally asymptotically stable disease-free equilibrium whenever $\mathcal{R}_{eS} < 1$, and a unique endemic equilibrium whenever $\mathcal{R}_{eS} > 1$.

3.1. Sensitivity analysis of $\mathcal{R}_{eS}$

In this section, we investigate the effect of testing and treating syphilis on the dynamics of syphilis by the elasticity of $\mathcal{R}_{eS}$ with respect to σ_1. From $\mathcal{R}_{eS} = \dfrac{\beta_S}{\mu + \sigma_1}$, we use the approach in [11, 9, 15] to compute the elasticity ([13]) of $\mathcal{R}_{eS}$ with respect to σ_1 as:

$$\frac{\sigma_1}{\mathcal{R}_{eS}} \frac{\partial \mathcal{R}_{eS}}{\partial \sigma_1} = -\frac{\sigma_1}{\mu + \sigma_1}. \tag{5}$$

Equation (5) is used to measure the impact of a change in σ_1 on a proportional change in $\mathcal{R}_{eS}$. Equation (5) suggests that an increase in the testing and treatment rate of syphilis always leads to decrease of $\mathcal{R}_{eS}$, indicating a positive impact on the control of syphilis in the community.

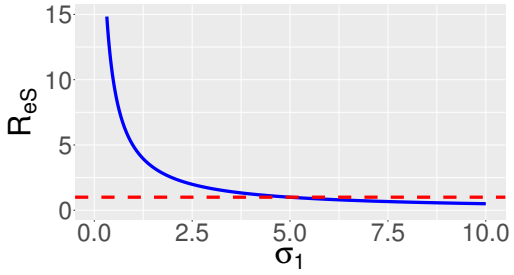


Figure 2: *Syphilis reproduction number $\mathcal{R}_{eS}$ as a function of testing and treatment rate σ_1, with all parameters as in Table 2 except $\beta_S = 5.0$. The red dash line indicates the reproduction number $\mathcal{R}_{eS} = 1$*

Figure 2 shows the effect of increasing treatment of syphilis in the community. For the set of parameters used, the figure shows that, by increasing the testing and treatment rate to 5 or more ($\mathcal{R}_{eS} \leq 0.99$) (i.e., test and treat all susceptible males for syphilis every 2.4 months or less), the reproduction number would be below unity, which indicates syphilis eradication in the community.

4. HIV sub-model

We have the model with HIV only by setting $I_S = U_{SH} = A_{SH} = T_{SH} = 0$ in (2) given by

$$\begin{aligned} \frac{\mathrm{d}S}{\mathrm{d}t} &= \Pi - (\mu + \lambda_H)S, \\ \frac{\mathrm{d}U_H}{\mathrm{d}t} &= \lambda_H S - (\mu + d_{UH} + \alpha_1)U_H, \\ \frac{\mathrm{d}A_H}{\mathrm{d}t} &= \alpha_1 U_H + \nu_1 T_H - (\mu + d_{AH} + \rho_2)A_H, \\ \frac{\mathrm{d}T_H}{\mathrm{d}t} &= \rho_2 A_H - (\mu + \nu_1)T_H, \end{aligned} \tag{6}$$

$$\lambda_H = \beta_H \frac{(U_H + \kappa_1 A_H)}{N_H}, \tag{7}$$

with the total population given as $N_H(t) = S(t) + U_H(t) + A_H(t) + T_H(t)$.

Please note that the population is not constant and the equation of N_H that denotes the total sub-population of HIV-only model follows that

$$\frac{\mathrm{d}N_H}{\mathrm{d}t} = \Pi - \mu N - d_{UH}U_H - d_{AH}A_H \leq \Pi - \mu N, \tag{8}$$

and (8) implies that $\lim_{t\to\infty} \sup N_H(t) \leq \dfrac{\Pi}{\mu}$. Therefore the dynamics of system (6) will be studied based on biological consideration in the region $\Xi_H = \left\{(S, U_H, A_H, T_H) \in \mathbb{R}^4_+ : N_H \leq \frac{\Pi}{\mu}\right\}$, which is easy to show as being positively invariant with respect to the model. We can similarly consider model (6) to be epidemiologically and mathematically well posed with all variables and parameters being positive for all time series as in [20].

4.1. Disease free equilibrium point

We have the disease free equilibrium when $U_H = A_H = T_H = 0$ in model system (6) . This gives $E_{0H} = \Big(\frac{\Pi}{\mu}, \quad 0, \quad 0, \quad 0\Big)$.

4.2. Effective reproduction Number $\mathcal{R}_{eH}$

Similarly, using the method of next generation matrix and the approach in [20, 42], as in $\mathcal{R}_{eH} = \rho(FV^{-1})$, we have the reproduction number of HIV infections produced by HIV positive cases to be $\mathcal{R}_{eH}$, which is given as .

$$\mathcal{R}_{eH} = \rho(FV^{-1}) = \frac{\beta_H\left((\mu+\nu_1)(\mu+\alpha_1\kappa_1+d_{AH})+\mu\rho_2\right)}{(\mu+d_{UH}+\alpha_1)\left((\mu+\nu_1)(\mu+d_{AH})+\mu\rho_2\right)}, \tag{9}$$

and we can write $\mathcal{R}_{eH} = B_U + B_A$, where

$$\begin{aligned} B_U &= \frac{\beta_H}{(\mu+d_{UH}+\alpha_1)}, \\ B_A &= \frac{\beta_H\alpha_1\kappa_1(\mu+\nu_1)}{(\mu+d_{UH}+\alpha_1)\left((\mu+\nu_1)(\mu+d_{AH})+\mu\rho_2\right)}. \end{aligned} \tag{10}$$

$\mathcal{R}_{eH}$ denotes the effective reproduction number for HIV dynamics (the number of HIV infection produced by one HIV case).

Remark 1. We can *epidemiologically* interpret the terms for the expression of $\mathcal{R}_{eH}$ in Equation (10). We have denoted B_U as the average number of new cases of HIV generated by individuals in the class U_H, and B_A as the average number of new cases of HIV generated by individuals in the class A_H.

B_U is interpreted as the product of the transmission rate of HIV infected individuals in the U_H class (β_H) and the average duration spent in the U_H class $\left(\frac{1}{\mu+d_{UH}+\alpha_1}\right)$.

Similarly, we can interpret B_A as the product of the transmission rate of HIV infected individuals in the A_H class ($\beta_H\kappa_1$), the fraction that survives the U_H class $\left(\frac{\alpha_1}{\mu+d_{UH}+\alpha_1}\right)$ and the average duration spent in the A_H class, which include the duration of the fraction that goes off treatment from class $T_H\left(\frac{1}{\mu+d_{AH}+\frac{\rho_2\mu}{\mu+\nu_1}}\right)$. Then the reproduction number $\mathcal{R}_{eH}$ is the sum of the expressions for B_U and B_A, which is the number of HIV infections produced by one HIV infective during the period of infectiousness when introduced in a totally HIV susceptible population in the presence of treatment.

We can establish the local stability of the disease free equilibrium (E_{0H}) using Lemma 5 which follows from [20] and Theorem 2 of [42].

Lemma 5. *The DFE E_{0H} of model* (6) *is locally asymptotically stable (LAS) if $\mathcal{R}_{eH} < 1$ and unstable otherwise.*

The *biological* interpretation of $\mathcal{R}_{eH} < 1$ means that we can eliminate HIV from the population if the initial sizes of the sub-population of HIV sub-model are in the attraction region E_{0H}. To be sure that eradication of HIV epidemic is independent of the initial sizes of the sub-populations, It makes sense to show that the disease free equilibrium E_{0H} is globally asymptotically stable.

4.3. Global stability of the disease-free for HIV-only model

We can rewrite model (6) as,

$$\begin{aligned} \frac{dU}{dt} &= F(U,V), \\ \frac{dV}{dt} &= G(U,V), \quad G(U,0)=0, \end{aligned} \tag{11}$$

where $U = S$ and $V = (U_H, A_H, T_H)$, with $U \in \mathcal{R}^1_+$ denoting the number of susceptible individuals and $V \in \mathcal{R}^3_+$ denoting the number of infected individuals.

We now denote the disease free equilibrium by,

$$E_{0H} = (U^*, 0), \quad \text{where} \quad U^* = \left(\frac{\Pi}{\mu}\right). \tag{12}$$

Conditions $S1$ and $S2$ in equation (13) must be satisfied to guarantee local asymptotic stability.

$$\begin{aligned} S1 : \frac{dU}{dt} &= F(U,0), \quad U^* \quad \text{is globally asymptotic stable (g.a.s)} \\ S2 : G(U,V) &= AV - \widehat{G}(U,V), \quad \widehat{G}(U,V) \geq 0 \quad \text{for} \quad (U,V) \in \Xi_H, \end{aligned} \tag{13}$$

where $A = D_V G(U^*, 0)$ denotes the M-matrix (the off diagonal elements of A are non-negative) and Ξ_H denotes the region where the model makes biological sense. Lemma 6 holds if system (11) satisfies the conditions in (13).

Lemma 6. *The disease free equilibrium point E_{0H} of HIV-only model is globally asymptotically stable if $\mathcal{R}_{eH} < 1$ and conditions in* (13) *are satisfied.*

PROOF. We have from Lemma 5 that E_{0H} is locally asymptotically stable if $\mathcal{R}_{eH} < 1$. Now consider

$$F(U,0) = \{\Pi - \mu S\},$$

$$G(U,V) = AV - \widehat{G}(U,V),$$

$$A = \begin{pmatrix} \beta_H - (\mu + d_{UH} + \alpha_1) & \kappa_1\beta_H & 0 \\ \alpha_1 & -(\mu + d_{AH} + \rho_2) & \nu_1 \\ 0 & \rho_2 & -(\mu + \nu_1) \end{pmatrix}. \tag{14}$$

$$\widehat{G}(U,V) = \begin{pmatrix} \widehat{G_1}(U,V) \\ \widehat{G_2}(U,V) \\ \widehat{G_3}(U,V) \end{pmatrix} = \begin{pmatrix} \beta_H \left(1 - \frac{S}{N_H}\right)(U_H + \kappa_1 A_H) \\ 0 \\ 0 \end{pmatrix}. \tag{15}$$

We have the conditions in 13 satisfied since $\widehat{G_1}(U,V) \geq 0$ and $\widehat{G_2}(U,V) = \widehat{G_3}(U,V) = 0 \Rightarrow \widehat{G}(U,V) \geq 0$. And therefore we can conclude that E_{0H} is globally asymptotically stable for $\mathcal{R}_{eH} < 1$. QED.

4.4. Endemic equilibrium points

We can solve equation (6) in terms of the force of infection $\lambda_H = \beta_H \dfrac{(U_H + \kappa_1 A_H)}{N_H}$ to find the conditions for the existence of an equilibrium, and for which HIV is endemic in a population.

Equating the right-hand side of equations (6) to zero, solving, substituting and writing in terms of the basic reproduction number $\mathcal{R}_{eH}$ gives the endemic

equilibrium point in terms of $\mathcal{R}_{eH}$ as $E_H^* = (S^*, \quad U_H^*, \quad A_H^*, \quad T_H^*)$, where

$$S^* = \frac{\Pi\Sigma}{\mu\Sigma + (\mathcal{R}_{eH} - 1)}, \tag{16}$$

$$U_H^* = \frac{\Pi(\mathcal{R}_{eH} - 1)}{(\mu + d_{UH} + \alpha_1)(\mu\Sigma + (\mathcal{R}_{eH} - 1))}, \tag{17}$$

$$A_H^* = \frac{\alpha_1\Pi(\mu + \nu_1)(\mathcal{R}_{eH} - 1)}{(\mu + d_{UH} + \alpha_1)(\mu(\mu + d_{AH} + \rho_2) + \nu_1(\mu + d_{AH}))(\mu\Sigma + (\mathcal{R}_{eH} - 1))}, \tag{18}$$

$$T_H^* = \frac{\alpha_1\rho_2\Pi(\mathcal{R}_{eH} - 1)}{(\mu + d_{UH} + \alpha_1)(\mu(\mu + d_{AH} + \rho_2) + \nu_1(\mu + d_{AH}))(\mu\Sigma + (\mathcal{R}_{eH} - 1))}, \tag{19}$$

$\lambda_H^* = \dfrac{(\mathcal{R}_{eH} - 1)}{\Sigma}$, and Σ denotes the mean infective period given by

$$\Sigma = \frac{1}{(\mu + d_{UH} + \alpha_1)}\left(1 + \frac{\alpha_1(\mu + \nu_1)}{((\mu + \nu_1)(\mu + d_{AH}) + \mu\rho_2)} + \frac{\alpha_1\rho_2}{((\mu + \nu_1)(\mu + d_{AH}) + \mu\rho_2)}\right).$$

The endemic equilibrium point E_H^* must be positive since the model in (6) also keeps track of human population. We have from Equations (16) - (19) that when $\mathcal{R}_{eH} > 1$, E_H^* is positive and HIV is able to attack the population. That is $\mathcal{R}_{eH} > 1$ shows the possibility of HIV to prevail in the community where there is no syphilis infection.

We can summarize the uniqueness of the endemic equilibrium in Lemma 7.

Lemma 7. *The endemic equilibrium E_H^* of model* (6) *exists and is unique if and only if $\mathcal{R}_{eH} > 1$.*

Proof. It is enough to show that the components of E_H^* are positive only if $\mathcal{R}_{eH} > 1$. We have the numerator and denominator of U_H^* in Equation (17) to be positive only when $\mathcal{R}_{eH} > 1$. Therefore, both the numerator and denominator of U_H^* are non-zero and positive when $\mathcal{R}_{eH} > 1$. The same follows for S^*, A_H^* and T_H^* . QED.

4.5. Global stability of the endemic equilibrium for HIV-only model

For the special case of when there is no HIV-related death (i.e $d_{UH} = d_{AH} = 0$), the model in (6) becomes

$$\begin{aligned} \frac{\mathrm{d}S}{\mathrm{d}t} &= \Pi - (\mu + \lambda_H)S, \\ \frac{\mathrm{d}U_H}{\mathrm{d}t} &= \lambda_H S - (\mu + \alpha_1)U_H, \\ \frac{\mathrm{d}A_H}{\mathrm{d}t} &= \alpha_1 U_H + \nu_1 T_H - (\mu + \rho_2)A_H, \\ \frac{\mathrm{d}T_H}{\mathrm{d}t} &= \rho_2 A_H - (\mu + \nu_1)T_H. \end{aligned} \tag{20}$$

The new model (20) has a similar unique endemic equilibrium as model (6), but with $d_{UH} = d_{AH} = 0$.

Let $\Xi_{H0} = \left\{(S, U_H, A_H, T_H) \in \Xi_h : U_H = A_H = T_H = 0\right\}$ and $\mathcal{R}_{eH0} = \mathcal{R}_{eH}|_{d_{UH}=d_{AH}=0}$.

We claim Lemma 8.

Lemma 8. *The endemic equilibrium of HIV-only model 20 is globally asymptotically stable in $\Xi_H \setminus \Xi_{H0}$ whenever $\mathcal{R}_{eH0} > 1$.*

Using a regular perturbation argument together with Liapunov function theory as was done in [8], it is easy to show the proof of (8) for the case of when $d_{UH} \geq 0, d_{AH} \geq 0$ but small.

In summary, the HIV-only model in (3) has a globally asymptotically stable disease-free equilibrium whenever $\mathcal{R}_{eH} < 1$, and a unique endemic equilibrium whenever $\mathcal{R}_{eH} > 1$. This unique endemic equilibrium is globally asymptotically stable whenever $\mathcal{R}_{eH0} > 1$ (the case of $d_{UH} = d_{AH} = 0$).

4.6. Sensitivity analysis of $\mathcal{R}_{eH}$

Firstly, we investigate the effect of treating HIV on the dynamics of HIV by the elasticity of $\mathcal{R}_{eH}$ with respect to ρ_2. From Equation (9), we use the approach in [11, 9, 15] to compute the elasticity ([13]) of $\mathcal{R}_{eH}$ with respect to ρ_2 as:

$$\frac{\rho_2}{\mathcal{R}_{eH}}\frac{\partial \mathcal{R}_{eH}}{\partial \rho_2} = -\frac{\alpha_1\kappa_1\mu\rho_2(\mu+\nu_1)}{\Big((\mu+\nu_1)(\mu+d_{AH})+\mu\rho_2\Big)\Big((\mu+\nu_1)(\mu+\alpha_1\kappa_1+d_{AH})+\mu\rho_2\Big)}. \tag{21}$$

Equation (21) is used to measure the impact of a change in ρ_2 on a proportional change in $\mathcal{R}_{eH}$. Equation 21 suggests that an increase in the rate of treatment of HIV always lead to decrease of $\mathcal{R}_{eH}$, indicating a positive impact on the control of HIV infection in the community.

Figure 3a shows the effect of increasing treatment of HIV in the community. The figure predicts that even though increasing the number of cases treated can positively impact HIV epidemics by reducing the reproduction number, but elimination may only be achieved with aggressive treatment (i.e $\rho_2 = 50$ means treat all diagnosed cases every week). Note that based on Equation (10), no matter how high we increase ρ_2, B_U will not be affected, which indicates that elimination of HIV requires more than increasing the number of cases treated, and may never be achieved by increasing ρ_2 if $B_U > 1$.

Secondly, we investigate the effect of testing HIV on the dynamics of HIV by the elasticity of $\mathcal{R}_{eH}$ with respect to α_1. From Equation (9), we use the approach in [11, 9, 15] to compute the elasticity ([13]) of $\mathcal{R}_{eH}$ with respect to α_1 as:

$$\frac{\alpha_1}{\mathcal{R}_{eH}}\frac{\partial \mathcal{R}_{eH}}{\partial \alpha_1} = \frac{\alpha_1\kappa_1(\mu+\nu_1)(\mu+d_{UH}) - \alpha_1\Big((\mu+\nu_1)(\mu+d_{AH})+\mu\rho_2\Big)}{(\mu+d_{UH}+\alpha_1)\Big((\mu+\nu_1)(\mu+\alpha_1\kappa_1+d_{AH})+\mu\rho_2\Big)}. \quad (22)$$

Equation (22) is used to measure the impact of a change in α_1 on a proportional change in $\mathcal{R}_{eH}$. Equation (22) suggests that an increase in the rate of testing HIV will have a positive impact in decreasing $\mathcal{R}_{eH}$ and reducing HIV burden only if the numerator of Equation (22) is negative, i.e. if

$$\kappa_1(\mu+\nu_1)(\mu+d_{UH}) - \Big((\mu+\nu_1)(\mu+d_{AH})+\mu\rho_2\Big) < 0$$

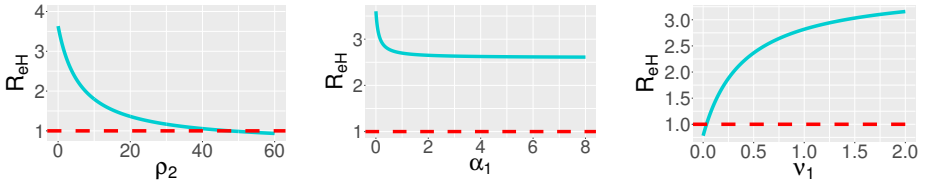
Figure 3b shows the effect of increasing testing of HIV in the community. The figure predicts that increasing the number of cases tested could positively impact HIV epidemic by reducing the reproduction number, but elimination will never be achieved with testing alone. Note that based on Equation (10), no matter how high we increase α_1, there will always be an asymptote of B_A for $\alpha_1 \to \infty$. This indicates that elimination of HIV requires more than increasing the number

of cases tested, and may never be achieved by increasing α_1 if the asymptote of $B_A > 1$.

Thirdly, we investigate the effect of the rate of treatment failure on the dynamics of HIV by the elasticity of $\mathcal{R}_{eH}$ with respect to ν_1. We compute the elasticity ([13]) of $\mathcal{R}_{eH}$ with respect to ν_1 as:

$$\frac{\nu_1}{\mathcal{R}_{eH}}\frac{\partial \mathcal{R}_{eH}}{\partial \nu_1} = \frac{\alpha_1\kappa_1\nu_1\mu\rho_2}{\Big((\mu+\nu_1)(\mu+\alpha_1\kappa_1+d_{AH})+\mu\rho_2\Big)\Big((\mu+\nu_1)(\mu+d_{AH})+\mu\rho_2\Big)} \tag{23}$$

Equation (23) is used to measure the impact of a change in ν_1 on a proportional change in $\mathcal{R}_{eH}$. Equation (23) suggests that a decrease in the rate of treatment failure always lead to a decrease of $\mathcal{R}_{eH}$, indicating a positive impact on the control of HIV in the community.



(a) HIV reproduction number $\mathcal{R}_{eH}$ as a function of treatment rate ρ_2

(b) HIV reproduction number $\mathcal{R}_{eH}$ as a function of testing rate α_1

(c) HIV reproduction number $\mathcal{R}_{eH}$ as a function of rate of treatment failure ν_1

Figure 3: *Impact of increasing testing rate α_1, treatment rate ρ_2 and rate of treatment failure ν_1 on HIV reproduction number $\mathcal{R}_{eH}$, with all parameters as in Table 2 except for $\beta_H = 0.4$. The red line shows when $\mathcal{R}_{eH} = 1$.*

Figure 3c shows the effect of treatment failure on the dynamics of HIV in the community. This Figure predicts that increasing the rate of treatment failure (time retained on treatment) could negatively impact HIV epidemics by increasing the reproduction number and possibly increasing HIV epidemics.

5. Analysis of the HIV-syphilis model

Having analyzed the two sub-models, we have the full HIV-syphilis model as in (2). From the equation of N that denotes the total population as in Equation (1), it follows that

$$\frac{\mathrm{d}N}{\mathrm{d}t} = \Pi - \mu N - d_{UH}U_H - d_{AH}A_H - d_{USH}U_{SH} - d_{ASH}A_{SH} \leq \Pi - \mu N, \quad (24)$$

and (24) implies that $\lim_{t\to\infty} \sup N(t) \leq \frac{\Pi}{\mu}$. Therefore the dynamics of system (2) will be studied based on biological consideration in the region $\Xi = \left\{(S, I_S, U_H, A_H, T_H, U_{SH}, A_{SH}, T_{SH}) \in \mathbb{R}^8_+ : N \leq \frac{\Pi}{\mu}\right\}$, which is easy to show as being positively invariant with respect to the model. Similarly, we can consider model (2) to be epidemiologically and mathematically well posed with all variables and parameters being positive for all time series as in [20].

5.1. Disease free equilibrium point (DFE) of the full HIV-syphilis model

We have the disease free equilibrium when $I_S = U_H = A_H = T_H = U_{SH} = A_{SH} = T_{SH} = 0$ in model (2). This gives

$$E_0 = (S_0, I_{0S}, U_{0H}, A_{0H}, T_{0H}, U_{0SH}, A_{0SH}, T_{0SH}) = \left(\frac{\Pi}{\mu}, \quad 0, \quad 0, \quad 0, \quad 0, \quad 0, \quad 0, \quad 0\right).$$

5.2. Effective reproduction Number $\mathcal{R}_e$

We have the effective reproduction number for the full model to be $\mathcal{R}_e$. Using the next generation method in [20, 42], we can show that the effective reproduction number for the full HIV-syphilis model (2) is given by

$$\mathcal{R}_e = \max\left\{\frac{\beta_S}{(\mu+\sigma_1)}, \frac{\beta_H\left((\mu+\nu_1)(\mu+\alpha_1\kappa_1+d_{AH})+\mu\rho_2\right)}{(\mu+d_{UH}+\alpha_1)\left((\mu+\nu_1)(\mu+d_{AH})+\mu\rho_2\right)}\right\}, \quad (25)$$

We can establish the local stability of the disease free equilibrium (E_0) using Lemma 9 which follows from [20] and Theorem 2 of [42].

Lemma 9. *The DFE E_0 of model* (2) *is locally asymptotically stable (LAS) if $\mathcal{R}_e < 1$ and unstable otherwise.*

Biological interpretation of $\mathcal{R}_e < 1 (\mathcal{R}_{eS} < 1 \quad \& \quad \mathcal{R}_{eH} < 1)$ means that we can eliminate both diseases from the population if the initial sizes of the population are in the attraction region Ξ.

In the section below, we show that the elimination of HIV and syphilis epidemics is independent on the initial sizes of the populations by showing the global stability of the DFE E_0.

5.3. Global stability of the disease-free of the full HIV-syphilis model

We claim the result in Lemma 10 from Lemmas 2 and 6.

Lemma 10. *The DFE E_0 of model (2) is globally asymptotically stable if $\mathcal{R}_e < 1$ and unstable otherwise.*

5.4. Endemic equilibrium point of the full HIV-syphilis model

The computation of the endemic equilibrium of the full HIV-syphilis model is analytically complicated, and therefore the endemic equilibria of model (2) corresponds to;

1. $E_1 = (S1, I_{S1}, 0, 0, 0, 0, 0, 0)$, the HIV free equilibrium, where

$$E_1 = \left(\frac{\Pi}{\mu \mathcal{R}_{eS}}, \frac{\Pi(\mathcal{R}_{eS} - 1)}{\mu \mathcal{R}_{eS}}, 0, 0, 0, 0, 0, 0 \right), \tag{26}$$

   This exists when $\mathcal{R}_{eS} > 1$. The analysis of the equilibria E_1 is similar to the endemic equilibria E_S^* in equation (4).

2. $E_2 = (S2, 0, U_{H2}, A_{H2}, T_{H2}, 0, 0, 0)$, the syphilis free equilibrium, where

$$\begin{aligned} S_2 &= \frac{\Pi\Sigma}{\mu\Sigma + (\mathcal{R}_{eH} - 1)}, \\ U_{H2} &= \frac{\Pi(\mathcal{R}_{eH} - 1)}{(\mu + d_{UH} + \alpha_1)(\mu\Sigma + (\mathcal{R}_{eH} - 1))}, \\ A_{H2} &= \frac{\alpha_1 \Pi(\mu + \nu_1)(\mathcal{R}_{eH} - 1)}{(\mu + d_{UH} + \alpha_1)(\mu(\mu + d_{AH} + \rho_2) + \nu_1(\mu + d_{AH}))(\mu\Sigma + (\mathcal{R}_{eH} - 1))}, \\ T_{H2} &= \frac{\alpha_1 \rho_2 \Pi(\mathcal{R}_{eH} - 1)}{(\mu + d_{UH} + \alpha_1)(\mu(\mu + d_{AH} + \rho_2) + \nu_1(\mu + d_{AH}))(\mu\Sigma + (\mathcal{R}_{eH} - 1))}, \end{aligned} \tag{27}$$

   This exists when $\mathcal{R}_{eH} > 1$. The analysis of the equilibria E_2 is similar to the endemic equilibria E_H^* in equations (16), (17), (18) and (19).

3. $E_3 = (S3, I_{S3}, U_{H3}, A_{H3}, T_{H3}, U_{SH3}, A_{SH3}, T_{SH3})$, the HIV-syphilis co-interaction equilibrium.

We summarize the existence of the disease free equilibrium points in the following theorem:

Theorem 11. *The system of equations* (2) *has the following disease free equilibrium points:*

1. E_{0S} *which exist when* $\mathcal{R}_{eS} < 1$.
2. E_{0H} *which exist when* $\mathcal{R}_{eH} < 1$.
3. E_0 *which exists when* $\mathcal{R}_{eS} < 1$ *and* $\mathcal{R}_{eH} < 1$, *i.e.* $\mathcal{R}_e < 1$.

We similarly summarize the existence of the endemic equilibrium points in the following theorem:

Theorem 12. *The system of equations in* (2) *has the following endemic equilibrium points:*

1. E_S^* *or* E_1 *which exist when* $\mathcal{R}_{eS} > 1$.
2. E_H^* *or* E_2 *which exist when* $\mathcal{R}_{eH} > 1$.
3. E_3 *which exists when* $\mathcal{R}_{eS} > 1$ *and* $\mathcal{R}_{eH} > 1$, *i.e.* $\mathcal{R}_e > 1$. *A detailed explanation of* E_3 *will be given in our numerical simulations. These endemic equilibria will be explored and justified using numerical simulations. Our numerical simulations will also explore epidemiological scenarios when*
   (a) $\mathcal{R}_{eH} > 1$ *and* $\mathcal{R}_{eS} < 1$,
   (b) $\mathcal{R}_{eH} < 1$ *and* $\mathcal{R}_{eS} > 1$.

6. Numerical simulations of the full model

In order to illustrate the results of the preceding analysis, the full HIV-syphilis model (2) is numerically simulated using R programming language and ggplot2 [43, 45]. Unfortunately, we are unable to calibrate the model to data as a result of the complexity of our model and unavailability of data on HIV-syphilis co-interaction, but we make assumptions of parameters for illustrative

purposes. Hence the shape of the figures or time of epidemic take-off in our simulations may change if the model is fitted or calibrated to the data of a particular region. We suggest that this theoretical study be seen as a guide for future research and data collection.

Initial conditions used are:

$$(S(0),\, I_S(0),\, U_H(0), A_H(0),\, T_H(0),\, U_{SH}(0),\, A_{SH}(0),\, T_{SH}(0)) = (5500, 6, 7, 5, 3, 4, 3, 2) \tag{28}$$

which indicate the presence of both diseases in the community,

$$(S(0),\, I_S(0),\, U_H(0), A_H(0),\, T_H(0),\, U_{SH}(0),\, A_{SH}(0),\, T_{SH}(0)) = (5500,\, 0,\, 7,\, 5,\, 3,\, 0,\, 0,\, 0) \tag{29}$$

which indicate the presence of only HIV infection in the community, and

$$(S(0),\, I_S(0),\, U_H(0), A_H(0),\, T_H(0),\, U_{SH}(0),\, A_{SH}(0),\, T_{SH}(0)) = (5500,\, 6,\, 0,\, 0,\, 0,\, 0,\, 0,\, 0), \tag{30}$$

which indicate the presence of only syphilis infection in the community. Parameters in Table (2) are also used, except otherwise stated.

Table 2: **Model parameters and their interpretations.**

Symbol	**Parameter**	**Value**(yr^{-1})	**Source**
Π	Recruitment rate estimated from $N \leq \Pi/\mu$	100	
μ	Natural mortality rate 0.017 corresponds to the life expectancy of 58.8 years	0.017	[17]
d_{UH}	death rate due to unaware HIV infection in mono-infected individuals	0.094	[39]
d_{AH}	death rate due to aware HIV infection in mono-infected individuals	0.094	[39]
d_{USH}	death rate due to unaware HIV infection in co-infected individuals	0.094	[39]
d_{ASH}	death rate due to aware HIV infection in co-infected individuals	0.094	[39]

β_S	Transmission rate for syphilis infection. This is the product of the probability of syphilis transmission from one contact between individuals in S and in other syphilis infected compartments (I_S, U_{SH}, A_{SH}, T_{SH}), and the number of contacts per year per individual	Variable	
β_H	Transmission rate for HIV infection. This is the product of the probability of HIV transmission from one contact between individuals in S and in other HIV infectious compartments (U_H, U_{SH}, A_H, A_{SH}), and the number of contacts per year per individual	Variable	
σ_1	Testing and treatment rate of syphilis among mono-infected males in the class I_S. The value 4year^{-1} means the average time for diagnosis and treatment is $1/\sigma_1 = 1/4$ year $= 3$ months.	4	[31]
$\sigma_2, \sigma_3, \sigma_4$	Testing and treatment rate of syphilis among HIV infected males in classes U_{SH}, A_{SH}, T_{SH} respectively. The value 4year^{-1} means the average time for diagnosis and treatment is $1/\sigma_4 = 1/4$ year $= 3$ months.	$4, 4, 4$	[31]
ρ_2	Treatment initiation rate of HIV. The value 2.5year^{-1} means the time from HIV diagnosis to treatment initiation among mono-infected males in the class A_H is $1/\rho_2 = 1/2.5$ year $= 4.8$ months.	2.5	Assumed
ρ_1	Treatment initiation rate of HIV. The value 2.5year^{-1} means the time from HIV diagnosis to treatment initiation among co-infected males in the class A_{SH} is $1/\rho_1 = 1/2.5$ year $= 4.8$ months.	2.5	Assumed

ν_1, ν_2	Rate of treatment failure for mono and coinfected individuals in classes T_H and T_{SH} respectively. The value 0.9375year^{-1} means the time retained on HIV treatment for mono-infected and coinfected males is $1/\nu_i = 1/0.9375$ year $= 12.8$ months for $i = 1, 2$. That is, HIV infected males on treatment spend at least 12.8 months before going off treatment	$0.9375, 0.9375$	[44]
η_1, η_2, η_3	Modification parameters accounting for the higher risk of syphilis acquisition for people living with HIV in classes U_H, A_H, T_H respectively	$2.237, 2.237, 2.237$	[25]
γ	Modification parameters accounting for the higher risk of HIV acquisition for people living with syphilis in the class I_S	2.5	[6, 21, 23, 24, 32]
ϕ_1, ϕ_2, ϕ_3	Modification parameters accounting for the higher risk of syphilis transmission for coinfected individuals in classes U_{SH}, A_{SH}, T_{SH} respectively, compared with individuals monoinfected with syphilis in the class I_S	$2.867, 2.867, 2.867$	[29]
κ_1	Modification parameter accounting for the risk of HIV transmission for individuals mono-infected with HIV and aware (A_H), compared with individuals mono-infected with HIV and unaware (U_H). We assume that the risk of transmitting HIV among U_H is not significantly different from A_H	1.0	Assumed
κ_2, κ_3	Modification parameters accounting for the higher risk of HIV transmission for individuals coinfected with HIV (U_{SH}, A_{SH}), compared with individuals monoinfected with HIV (U_H)	$2, 2$	[3, 32]

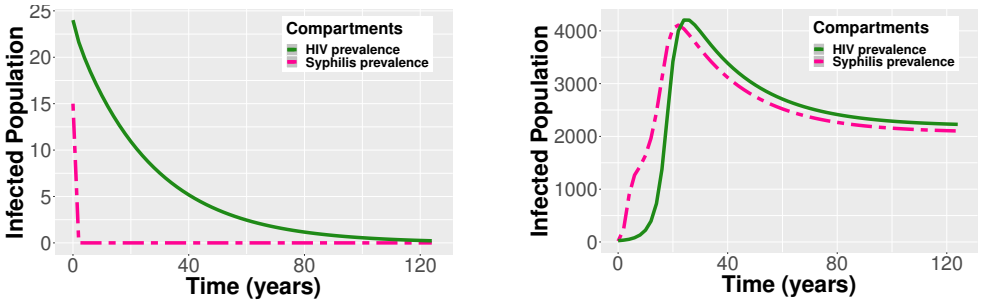
α_1	Progression (testing) rate for individuals mono infected with HIV in the class U_H. The value 0.5year^{-1} means the time from HIV infection to diagnosis is $1/\alpha_1 = 1/0.5$ year $= 2$ years.	0.5	[41]

Figure 4 shows the HIV and syphilis epidemics with initial condition (28) and parameters in Table (2). If the reproduction number is less than unity ($\mathcal{R}_{eH} = 0.139 < 1, \mathcal{R}_{eS} = 0.025 < 1, \mathcal{R}_e = 0.139 < 1$) due to smaller transmission rates of HIV and syphilis ($\beta_H = 0.02$, $\beta_S = 0.1$), the number of individuals living with HIV and/or syphilis decreases and converges to the asymptotically stable disease-free equilibrium (Figure 4a). Biologically, both diseases go to extinction and the epidemics of HIV and syphilis die out in the community. In contrast, if the transmission rates are larger ($\beta_H = 0.4$, $\beta_S = 5.0$) and $\mathcal{R}_e > 1$ ($\mathcal{R}_{eH} = 2.780 > 1, \mathcal{R}_{eS} = 1.245 > 1, \mathcal{R}_e = 2.780 > 1$), the number of infected individuals converges to the HIV-syphilis endemic equilibrium (Figure 4b). This biologically means that the epidemics of both HIV and syphilis persist in the community. The simulations are consistent with Lemma 9 and Theorem 12.

Furthermore, Figure 5 shows the HIV and syphilis epidemics with initial condition (28). If the reproduction number of syphilis is greater than unity ($\mathcal{R}_{eH} = 0.139 < 1, \mathcal{R}_{eS} = 1.245 > 1, \mathcal{R}_e = 1.245 > 1$) due to a larger transmission rate of syphilis ($\beta_H = 0.02$, $\beta_S = 0.5$), then the reproduction number of the co-infection system is greater than unity. The number of individuals mono-infected and co-infected with HIV persists for a long time and then decreases slowly to zero because of the long life time of people living with HIV (Figures 5A and 5B). The number of individuals mono-infected with syphilis increases (Figure 5C) and then becomes stable after about 6 years (the zoomed-in plot of I_S in Figure 5C) to converge to the asymptotically stable syphilis endemic equilibrium showing one possibility of Theorem 12, (3*b*). This biologically means that with our choice of parameters and over a long period of time, a community with smaller transmission rate of HIV and larger transmission rate of syphilis will experience syphilis epidemics, while the epidemic of HIV will die out. In

this case, the maximum reproduction number of the HIV-syphilis full model will be the reproduction number of the syphilis sub-model.

Figure 6 similarly shows the HIV and syphilis epidemics with initial condition (28). If the reproduction number of HIV is greater than unity ($\mathcal{R}_{eH} = 2.780 > 1, \mathcal{R}_{eS} = 0.025 < 1, \mathcal{R}_e = 2.780 > 1$) due to a larger transmission rate of HIV ($\beta_H = 0.4$, $\beta_S = 0.1$), then the reproduction number of the co-infection system is greater than unity . The number of individuals mono-infected and co-infected with syphilis decrease to zero (Figures 6B and 6C) in less than 2 years (the zoomed-in plot of I_S in Figure 6C) since syphilis is curable. The number of individuals mono-infected with HIV infection first increase to a maximum value and then decrease to converge to the asymptotically HIV endemic equilibrium (Figures 6A) showing one possibility of Theorem 12, $(3a)$. This biologically means that with our choice of parameters, a community with larger transmission rate of HIV and smaller transmission rate of syphilis will experience the HIV epidemic, while the syphilis epidemic will die out. In this case, the maximum reproduction number of the HIV-syphilis full model will be the reproduction number of HIV sub-model.



(a) Disease free equilibrium

(b) Endemic equilibrium

Figure 4: *Number of HIV infected individuals (green) and syphilis infected individuals (red) based on initial condition* (28) *and parameters in Table 2, with different transmission rates and reproduction number:* $\beta_H = 0.02, \beta_S = 0.1, \mathcal{R}_e = 0.139$ *(left);* $\beta_H = 0.4, \beta_S = 5.0, \mathcal{R}_e = 2.780$ *(right).*

Figure 7 shows the impact of the presence of one disease on the other in

a community where either one or both diseases persist at the initial stage of the epidemic. Figure 7a shows the number of individuals living with HIV using initial conditions (28) (blue line) and (29)) (red line). It is worth noting that the steady state in blue line is about 5% higher than the one in red line, which indicates that, for the same community, the presence of syphilis infection is likely to enhance the HIV prevalence in comparison to no syphilis infection and efforts towards eradicating syphilis infection may in turn decrease HIV prevalence.

Figure 7b shows the number of individuals living with syphilis using initial conditions (28) (blue line) and (30)) (red line). Similarly, it is worth noting that the steady state in blue line is about 30% higher than the one in red line, which indicates that, for the same community, the presence of HIV infection is likely to enhance the syphilis prevalence in comparison to no HIV infection and efforts aim at decreasing or eradicating HIV infection will in turn decrease syphilis prevalence.

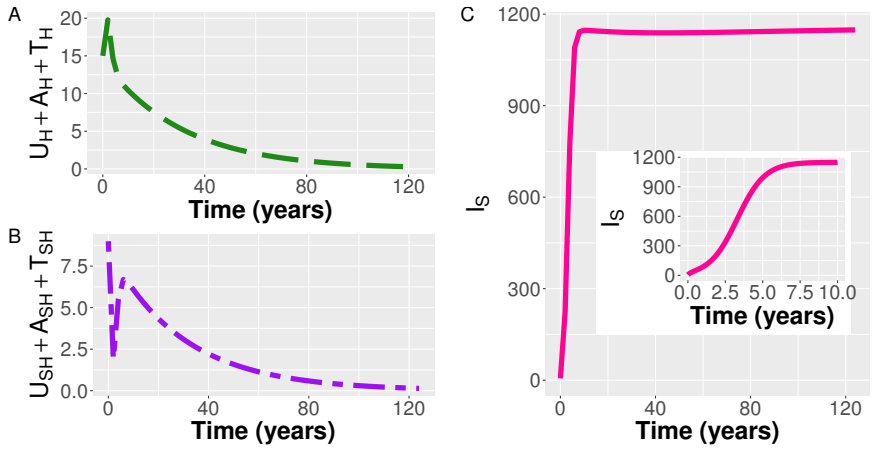


Figure 5: *Using the initial condition in* (28) *with* $\beta_H = 0.02$ *and* $\beta_S = 5.0$*, the figure shows dynamics of HIV mono-infected individuals* $(U_H + A_H + T_H)$ *(A), co-infected individuals* $(U_{SH} + A_{SH} + T_{SH})$ *(B), and syphilis mono-infected individuals* (I_S) *(C).*

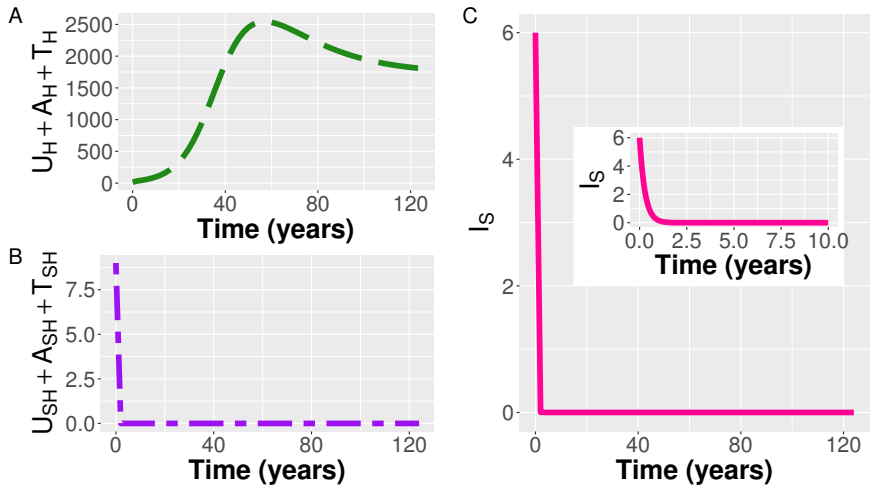
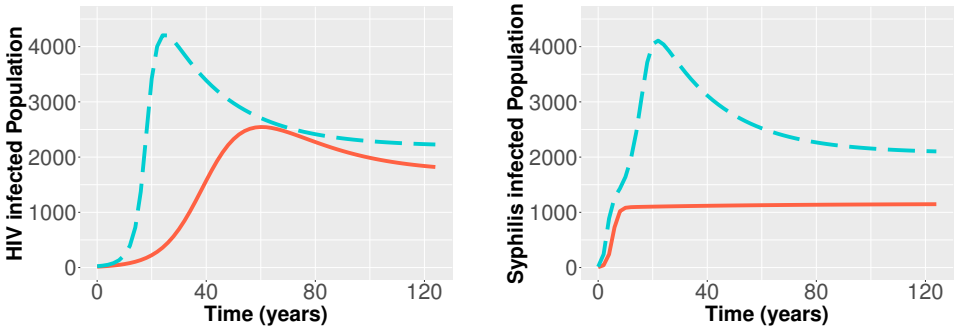


Figure 6: *Using the initial condition in* (28) *with* $\beta_H = 0.4$ *and* $\beta_S = 0.1$*, the figure shows dynamics of HIV mono-infected individuals* $(U_H + A_H + T_H)$ *(A), co-infected individuals* $(U_{SH} + A_{SH} + T_{SH})$ *(B), and syphilis mono-infected individuals* (I_S) *(C).*



(a) Population of HIV positive individuals

(b) Population of syphilis positive individuals

Figure 7: *Prevalence of HIV and syphilis with* $\beta_H = 0.4$ *and* $\beta_S = 5.0$ *(*$\mathcal{R}_{eH} = 2.780 > 1, \mathcal{R}_{eS} = 1.245 > 1, \mathcal{R}_e = 2.780 > 1$*). (a) Figure 7a shows the prevalence of HIV with syphilis at the initial stage of the epidemic (initial condition* (28)*, blue dashed line) and without syphilis (initial condition* (29)*, red solid line). (b) Figure 7b shows the prevalence of syphilis infection with HIV at the initial stage of the epidemic (initial condition* (28)*, blue dashed line) and without HIV (initial condition* (30)*, red solid line).*

7. Discussion and conclusion

We presented a mathematical model that rigorously analysed the co-interaction of HIV and syphilis infections in the presence of treatment of both diseases. We carried out the stability analysis of disease-free and endemic equilibra, and showed that

(a) disease-free equilibra for sub-models and the full model were locally and asymptotically stable whenever their respective reproduction numbers are less than unity.

(b) endemic equilibra for sub-models and the full model were locally and asymptotically stable whenever their respective reproduction numbers are greater than unity.

(c) increasing testing and treatment rate of mono-infected individuals with syphilis may bring the reproduction number of syphilis below unity, and thereby eradicating the disease among mono-infected individuals in the community.

(d) increasing the testing rate, treatment rate and reducing the rate of treatment failure for mono-infected individuals impact HIV epidemic by lowering the reproduction number of HIV, but may not be able to eradicate the disease in the community.

Despite the limitations of assuming homogeneous mixing populations and using parameter values from published articles, our results and analyses of the reproduction number indicated that

(a) HIV infection increases syphilis prevalence and vice versa.

(b) we could bring the reproduction number of syphilis below unity if syphilis is tested and treated more, but testing and treating cases of HIV alone may not be sufficient to bring down the prevalence of HIV as this may depend on some other factors, for example, some parameters in Equation (10) (lower HIV-related death, increase time retained on treatment and so on).

Great attention have not been given to the negative effect of the co-interaction of HIV and syphilis globally, and there are not many mathematical models that considered synergistic interactions with treatment of both diseases among gbMSM population. Even though our approach is similar to those considered in the literature [18, 11, 9, 12, 30, 40, 31, 5] in terms of the joint dynamics of both diseases, but treatment of both HIV and syphilis infections among gbMSM population is an essential difference that none of those studies examined. Our model can be extended to include general population, and can also be stratified into different age group or risk level.

8. Declaration of Competing Interest

None to declare.

9. Acknowledgements

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