BioSystems 103 (2011) 27–37

Contents lists available at ScienceDirect

BioSystems

journal homepage: www.elsevier.com/locate/biosystems

# Modeling gonorrhea and HIV co-interaction

S. Mushayabasa [a,*], J.M. Tchuenche [c], C.P. Bhunu [a,b], E. Ngarakana-Gwasira [d]

[a] Department of Applied Mathematics, Modelling Biomedical Systems Research Group, National University of Science and Technology, P.O. Box 939 Ascot, Bulawayo, Zimbabwe
[b] Department of Veterinary Medicine, University of Cambridge, CB3 OES, UK
[c] Department of Mathematics and Statistics, University of Guelph, Guelph, ON N1G 2W1, Canada
[d] University of Zimbabwe, Department of Mathematics, P.O. Box MP 167, Harare, Zimbabwe

ARTICLE INFO

*Article history:*
Received 27 April 2010
Accepted 14 September 2010

*Keywords:*
HIV/gonorrhea
Co-interaction
Reproductive number
Treatment
Centre Manifold
Stability

ABSTRACT

A mathematical model was designed to explore the co-interaction of gonorrhea and HIV in the presence of antiretroviral therapy and gonorrhea treatment. Qualitative and comprehensive mathematical techniques have been used to analyse the model. The gonorrhea-only and HIV-only sub-models are first considered. Analytic expressions for the threshold parameter in each sub-model and the co-interaction model are derived. Global dynamics of this co-interaction shows that whenever the threshold parameter for the respective sub-models and co-interaction model is less than unity, the epidemics dies out, while the reverse results in persistence of the epidemics in the community. The impact of gonorrhea and its treatment on HIV dynamics is also investigated. Numerical simulations using a set of reasonable parameter values show that the two epidemics co-exists whenever their reproduction numbers exceed unity (with no competitive exclusion). Further, simulations of the full HIV-gonorrhea model also suggests that an increase in the number of individuals infected with gonorrhea (either singly or dually with HIV) in the presence of treatment results in a decrease in gonorrhea-only cases, dual-infection cases but increases the number of HIV-only cases.



## 1. Introduction

By January 2006, AIDS had claimed more than 25 million lives since its recognition in 1981, and nearly 40 million people were living with HIV around the World (UNAIDS/WHO, 2006). Sexually transmitted infections (STIs) other than HIV account for a significant portion of illness globally, with more than 340 million new cases of curable STIs (mainly gonorrhoea, syphilis, chlamydia and trichomoniasis) occurring globally in adults aged 15–49 each year (WHO, 2006). Together, HIV and sexually transmitted infections (STIs) are responsible for the destruction of health on a massive scale globally (Anon., 2010a). We shall focus on gonorrhea mainly which is one of the most common STDs. In the US, CDC estimates that more than 700,000 persons get new gonorrheal infections each year (CDC, 1998). Out of the 40 million people with HIV worldwide, 4.3 million were infected in 2006 alone and 24.7 million live in sub-Saharan Africa, the region of the World currently experiencing the highest concentration of global emergencies (UNAIDS/WHO, 2006). HIV and STIs spread and kill most quickly in populations affected by poverty, social unrest and lack of health infrastructure. These factors are commonly present in humanitarian emergencies (Anon., 2010a), and it is not surprising why these diseases are so rampant in the developing World. In addition, STIs facilitate the transmission of HIV infection (WHO, 2006). Men who are infected with both gonorrhea and HIV are more than twice as likely to shed HIV in their genital secretions than are those who are infected only with HIV and moreover, the median concentration of HIV in semen is as much as 10 times higher in men who are infected with both gonorrhea and HIV than in men infected only with HIV (CDC, 1998). Therefore, understanding the relationship between these two diseases is important as they fuel each other.

Gonorrhea is a sexually transmitted disease caused by a type of germ, a bacteria called *Neisseria gonorrhoeae*. It is passed from one person to another during vaginal, anal, and oral sex. It can be found in the throat, vagina, urethra, and anus. Babies can be infected during birth, causing eye infections. Its symptoms appear within 10 days after a person is exposed to the germ, then disappear (CDC, 1998; Anon., 2010b). Women often have no symptoms at all, but both women and men whose symptoms have disappeared are still infected and infectious. For infection in the throat through oral sex, one may feel like having a sore throat. Gonorrhea is more easily spread to the throat by penis-mouth sex and rarely by mouth-vagina sex (Anon., 2010b). In men, gonorrhea can cause epididymitis, a painful condition of the testicles that can sometimes lead to infertility if left untreated. Without prompt treatment, gonorrhea can also affect the prostate and can lead to scarring inside the urethra, making urination difficult. Gonorrhea can spread to

* Corresponding author.
*E-mail addresses:* steadymushaya@gmail.com, smushayabasa@nust.ac.zw (S. Mushayabasa).

0303-2647/$ – see front matter © 2010 Elsevier Ireland Ltd. All rights reserved.
doi:10.1016/j.biosystems.2010.09.008

the blood or joints (CDC, 1998; Anon., 2010b; Hook and Handsfield, 1999), a condition which can be life-threatening. The predominant transmission mode of both HIV and other STIs is sexual intercourse. Methods for preventing sexual transmission of HIV and STIs are the same, as are the target audiences for interventions. High rates of sexually transmitted infections continue to be experienced in the Southern African States. This is of great concern as the communities are loosing their active force (manpower) (SADC, 2006).

Whereas single disease models have flourished for a long time, co-infection models are now coming to the limelight (Bhunu et al., 2009a; Mtisi et al., 2009; Mukandavire et al., 2009; Roeger et al., 2009; Sharomi et al., 2008). Our model is fundamentally different from previous one in the sense that none of those studies considered treatment of both diseases. Diseases co-dynamics are very complex processes, but in order to keep the model reasonably simple, we make a number of simplifying assumptions, which could be modified in line with relevant (empirical) data (if any!). Nevertheless, the proposed deterministic model (which is not for a specific country or nation) incorporates some basic epidemiological features of the co-dynamics of HIV and gonorrhea and our approach does not preclude the possibility of joint infections. Due to an increase in gonorrhea cases during this HIV era, it is not clear to what extent this (gonorrhea epidemic) may have contributed to the spread of HIV/AIDS. For people living in emergency settings, preventive measures and treatment for HIV and STIs are rarely available. Our objective therefore is to forecast future trends in the incidence of the two diseases using a deterministic mathematical model in the presence of gonorrhea treatment and antiretroviral therapy in a community. For this purpose, we wish to answer the following question: What is the impact of an increase in the number of infected individuals with gonorrhea in a population in which HIV is prevalent? It is our view that this study represents the very first modelling work that provides the in-depth analysis of the qualitative dynamics of HIV-gonorrhea co-interaction.

We begin with a description of the model and derived some of its basic properties in the next section. The sub-models for gonorrhea and HIV are presented and analysed in Sections 3 and 4 respectively. The analysis of the full HIV-gonorrhea model is carried out in Section 5. Numerical simulations of the model are presented in Section 6, while the last section concludes the paper.

## 2. Model description

The total sexually-active population at time $t$, denoted by $N$, is sub-divided into mutually exclusive compartments, namely susceptibles ($S$), newly-and asymptotically-infected individuals with HIV only but displaying no clinical symptoms of AIDS ($I_H$), individuals infected with gonorrhea only $I_G$, individuals dually-infected with HIV and gonorrhea displaying no clinical symptoms of AIDS symptoms ($I_{GH}$), HIV-infected displaying AIDS symptoms of both diseases ($A_H$), AIDS individuals dually-infected with gonorrhea and displaying clinical symptoms ($A_{GH}$), AIDS patients singly infected with HIV and are on antiretroviral therapy ($A_{HT}$) and AIDS patients dually-infected with HIV and gonorrhea who are on both antiretroviral and gonorrhea treatment ($A_{HGT}$), so that

$$N = S + I_H + I_G + I_{GH} + A_H + A_{GH} + A_{HT} + A_{GHT}.$$

The susceptible population is increased by the recruitment of individuals (assumed susceptible) into the population through birth and migration at a rate $\Lambda$. Both singly and dually-infected individuals transmit either gonorrhea or HIV not both. Susceptible individuals acquire infection following contact with HIV-infected individuals at a rate $\lambda_H$, and acquire gonorrhea infection following effective contact with gonorrhea infectives at a rate $\lambda_G$. It is assumed that individuals infected with gonorrhea only recover after treatment and return to the susceptible class at a rate $\phi_1$. Furthermore, natural mortality rate occurs in all classes at a constant rate $\mu$. The force of infection associated with HIV infection, denoted by $\lambda_H$, is given by

$$\lambda_H = \frac{\beta_H[I_H + \eta I_{GH} + \theta_A(A_H + \epsilon_1 A_{GH}) + \vartheta A_{HT} + \varphi A_{GHT}]}{N} \quad (1)$$

where, $\beta_H$ is the effective contact rate for HIV transmission, the modification parameter $\eta > 1$ accounts for the relative infectiousness of individuals dually-infected with gonorrhea and HIV but displaying no clinical symptoms of AIDS in comparison to those with HIV infection alone with no AIDS symptoms. The modification parameter $\theta_A > 1$ captures the fact that individuals in the AIDS class are more infectious than those HIV-infectives not yet displaying AIDS symptoms. This is due to the fact that individuals in AIDS stage have higher viral load compared to other HIV-infected individuals displaying no clinical symptoms of AIDS. Also, the parameter $\epsilon_1 > 1$, models the fact that AIDS individuals dually-infected with gonorrhea are more infectious than those infected with HIV alone and displaying AIDS symptoms. AIDS patients on antiretroviral only ($A_{HT}$) and those on both antiretroviral therapy and gonorrhea treatment ($A_{GHT}$) are assumed to transmit infection at a reduced rate ($0 \le \vartheta \le \varphi \le 1$) due to the fact that treatment reduces the viral load for these individuals. Similarly, susceptibles acquire gonorrhea infection following effective contact with gonorrhea infected individuals at a rate $\lambda_G$, given by,

$$\lambda_G = \frac{\beta_G[I_G + \theta_{GH}(I_{GH} + \epsilon_2 A_{GH}) + \varphi A_{GHT}]}{N}. \quad (2)$$

In (2)$\beta_G$ is the effective contact rate for gonorrhea infection, $\theta_{GH} > 1$ is a modification parameter accounting for the increased likelihood of infection by individuals dually-infected with gonorrhea and HIV compared to those singly infected with gonorrhea. Further, the parameter, $\epsilon_2 > 1$ models the fact that AIDS individuals dually-infected with gonorrhea are more infectious than the corresponding dually-infected individuals displaying no AIDS symptoms.

The population of individuals infected with HIV only (and displaying no clinical symptoms of AIDS) is generated following infection (at a rate $\lambda_H$) and by the recovery from gonorrhea infection after treatment by individuals dually-infected with HIV and gonorrhea but displaying no AIDS symptoms at a rate $\phi_2$. Individuals in this class acquire gonorrhea infection at a rate $\sigma\lambda_G$, where $\sigma > 1$, accounts for the assumed increase in susceptibility to gonorrhea infection as a result of HIV infection. This population is further decreased following progression to AIDS at a rate $\gamma$.

The population of individuals with AIDS symptoms only is generated following the progression to AIDS by individuals infected with HIV alone but displaying no clinical symptoms of AIDS at a rate $\gamma$ and the recovery from gonorrhea infection after treatment of AIDS individuals dually-infected with gonorrhea at a rate $\phi_3$. Individuals in this class also acquire gonorrhea infection at a rate $\sigma\lambda_G$ and die of AIDS-related illness at a rate $\nu$.

The population of individuals infected with gonorrhea only is generated following infection at the rate $\lambda_G$, and this population decrease following the recovery of infectives after treatment at a rate $\phi_1$. Individuals in this class acquire HIV infection at a rate $\alpha\lambda_H$, where $\alpha > 1$, accounts for the assumed increase in susceptibility to HIV infection as a result of gonorrhea infection.

The population of AIDS individuals dually-infected with gonorrhea is generated by progression to AIDS of individuals dually-infected with HIV and gonorrhea but displaying no AIDS symptoms at a rate $\kappa\gamma$, where $\kappa > 1$ represents the assumption that individuals dually-infected with HIV and gonorrhea but displaying no clinical symptoms of AIDS progress to AIDS at a faster rate compared to those with HIV only and displaying no clinical

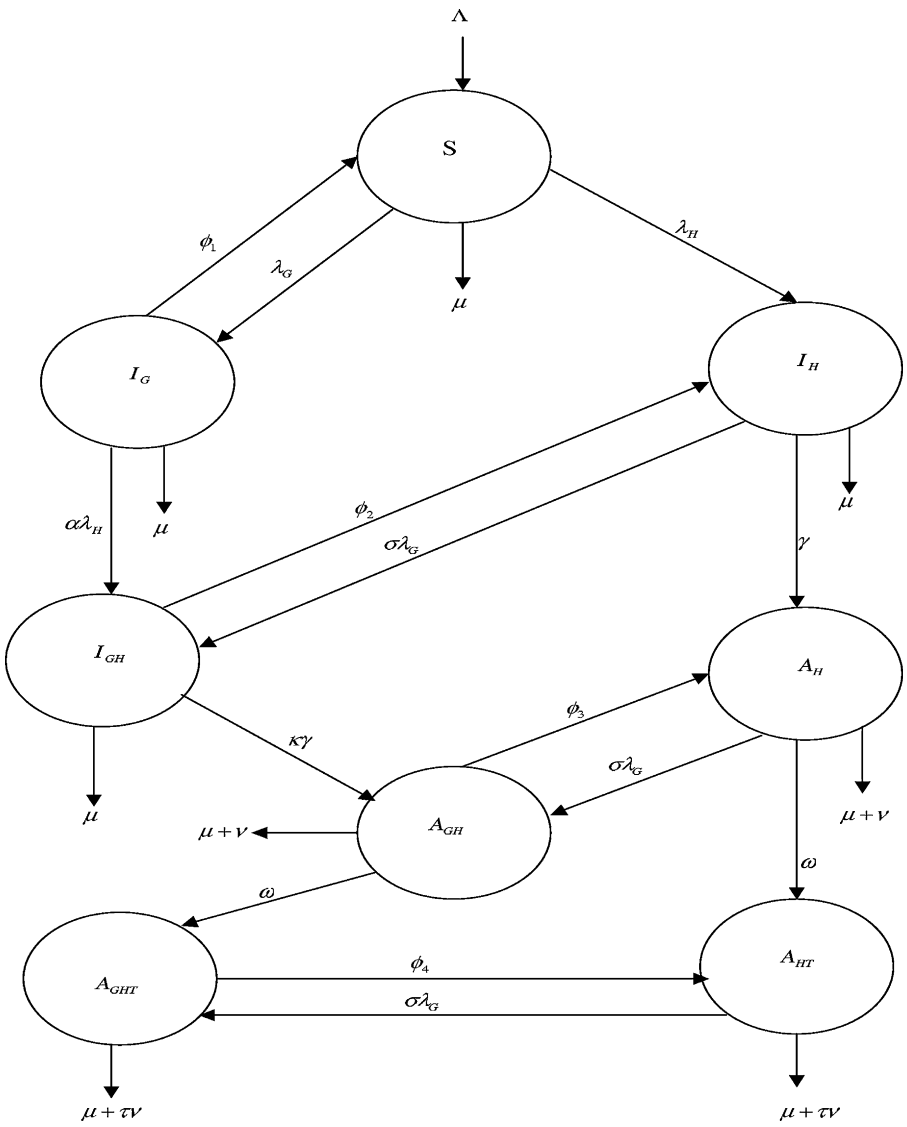


**Fig. 1.** Model flow diagram.

symptoms of AIDS. Individuals in this class suffer an additional disease-induced mortality at a rate $\nu$. AIDS patients are treated at a rate $\omega$, either singly or dually-infected, and dually-infected individuals are assumed to recovery from gonorrhea epidemic at a constant rate $\phi_4$. AIDS patients eventually succumb to HIV mortality as the drug wanes out at a reduced rate ($0 < \tau < 1$). The model flow diagram is depicted in Fig. 1 below.

From the aforementioned description and assumptions together give rise to the following deterministic system of nonlinear differential equations

$$\begin{aligned}
S' &= \Lambda + \phi_1 I_G - \lambda_G S - \lambda_H S - \mu S,\\
I'_G &= \lambda_G S - \alpha\lambda_H I_G - (\phi_1 + \mu) I_G,\\
I'_H &= \lambda_H S + \phi_2 I_{GH} - \sigma\lambda_G I_H - (\gamma + \mu) I_H,\\
I'_{GH} &= \alpha\lambda_H I_G + \sigma\lambda_G I_H - (\kappa\gamma + \phi_2 + \mu) I_{GH},\\
A'_H &= \gamma I_H + \phi_3 A_{GH} - \sigma\lambda_G A_H - (\omega + \mu + \nu) A_H,\\
A'_{GH} &= \kappa\gamma I_{GH} + \sigma\lambda_G A_H - (\omega + \phi_3 + \mu + \nu) A_{GH},\\
A'_{HT} &= \omega A_H + \phi_4 A_{GHT} - \sigma\lambda_G A_{HT} - (\mu + \tau\nu) A_{HT},\\
A'_{GHT} &= \omega A_{GH} + \sigma\lambda_G A_{HT} - (\phi_4 + \nu + \tau\nu) A_{GHT}.
\end{aligned} \tag{3}$$

## 3. Gonorrhea-only sub-model

Before analysing the full model system (3), it is instructive to gain insights into the dynamics of the gonorrhea-only sub-model (obtained by setting $I_H = I_{GH} = A_H = A_{HT} = A_{GH} = A_{GHT} = 0$) in (3) given by

$$\begin{aligned}
S' &= \Lambda - \lambda_G S - \mu S + \phi_1 I_G\\
I'_G &= \lambda_G S - (\phi_1 + \mu) I_G,
\end{aligned} \tag{4}$$

where $\lambda_G = \beta_G I_G / N_G$, and now $N_G = S + I_G$. This is a simple generic *SIS* model without disease-induced death rate. Since death due to gonorrhea is rare and occurs in far less than 1% of cases, it is not accounted herein; this does not alter the dynamical outcome of the analysis. Even though this submodel does not account for some of the features of the disease such as vital dynamics (due to the fact that the complete gonorrhea model cannot cleanly be decouple from the proposed co-dynamic model), its joint dynamics with HIV does, but it is still worth investigating the submodel to set the scene in the sequel. For system (4), it is straightforward to verify that the region

$$\Phi_G = \left\{ (S, I_G) \in \mathbb{R}^2_+ : N_G \leq \frac{\Lambda}{\mu} \right\}$$

is positively invariant and attracting. Thus, the dynamics of gonorrhea-only model will be analysed in $\Phi_G$. The gonorrhea-only model (4) has a disease-free equilibrium point given by,

$$\mathcal{E}_G^0 = (S, I_G) = \left(\frac{\Lambda}{\mu}, 0\right) \tag{5}$$

The linear stability of $\mathcal{E}^0$ is governed by the basic reproductive number $\mathcal{R}_0$ (Anderson and May, 1991; Brauer and Castillo-Chavez, 2001; Castillo-Chavez et al., 2002; Hethcote, 2000). The stability of this equilibrium will be investigated using the *next generation operator* (Diekmann et al., 1990; van den Driessche and Watmough, 2002). Using the notation in van den Driessche and Watmough (2002) on the system (12), the matrices $F$ and $V$, for the new infection terms and the remaining transfer terms are respectively given by

$$F = (\beta_G), \text{and} V = (\mu + \phi_1).$$

It follows that the *basic reproduction number* for model system (4), denoted by $\mathcal{R}_G$ is given by

$$\mathcal{R}_G = \rho(FV^{-1}) = \frac{\beta_G}{\mu + \phi_1} \tag{6}$$

where $\rho$ represents the spectral radius (the dominant eigenvalue in magnitude) of $FV^{-1}$. The reproductive number ($\mathcal{R}_G$) gives the number of secondary gonorrhea infectious cases produced by a gonorrhea infectious individual during his or her infectious period when introduced in a population of mostly gonorrhea susceptibles in the presence of treatment.

### 3.1. Sensitivity analysis of ($\mathcal{R}_G$)

Here, the reproductive number, $\mathcal{R}_G$ is analysed to determine whether or not treatment of gonorrhea patients (modelled by the rate $\phi_1$) can lead to the effective control or elimination of gonorrhea in the community. It follows from (6), that the elasticity (Caswell, 2001) of $\mathcal{R}_G$ with respect to $\phi_1$ can be computed using the approach in (Chitns et al., 2008) as follows:

$$\frac{\phi_1}{\mathcal{R}_G}\frac{\partial \mathcal{R}_G}{\partial \phi_1} = -\frac{\phi_1}{\mu + \phi_1} \tag{7}$$

Eq. (7) suggests that an increase in treatment of gonorrhea infectives have a positive impact in controlling gonorrhea in the community. The sensitivity index of the reproduction numbers is used to assess the impact on the relevant parameters to disease transmission. That is, the elasticity measures the effect a change in $\phi_1$, say has as a proportional change in $\mathcal{R}_G$. We note that the elasticity to $\phi_1$ increases linearly with $\phi_1$, so that the proportional change of $\mathcal{R}_G$ to $\phi_1$ is small for $\phi_1$ near zero, and very large for $\phi_1$ near one. Fig. 2 shows the impact of increase in gonorrhea treatment in the community.

The graphical representation suggests that an increase the number of gonorrhea infectives who receive treatment will have a positive impact in controlling gonorrhea epidemic in the community. Using Theorem 2 in van den Driessche and Watmough (2002), the following result is established.

**Lemma 1.** *The disease-free equilibrium*($\mathcal{E}_G^0$) *of model system (4) is locally asymptotically stable* (LAS) *if* $\mathcal{R}_G < 1$ *and unstable if* $\mathcal{R}_G > 1$.

Lemma 1, implies that gonorrhea can be eliminated from the community (when $\mathcal{R}_G < 1$) if the initial sizes of the sub-populations of the model system (4) are in the basin of attraction of the disease-free equilibrium $\mathcal{E}_G^0$. To ensure that elimination of the virus is independent of the initial sizes of the sub-populations, it is necessary to show that the DFE is globally stable.

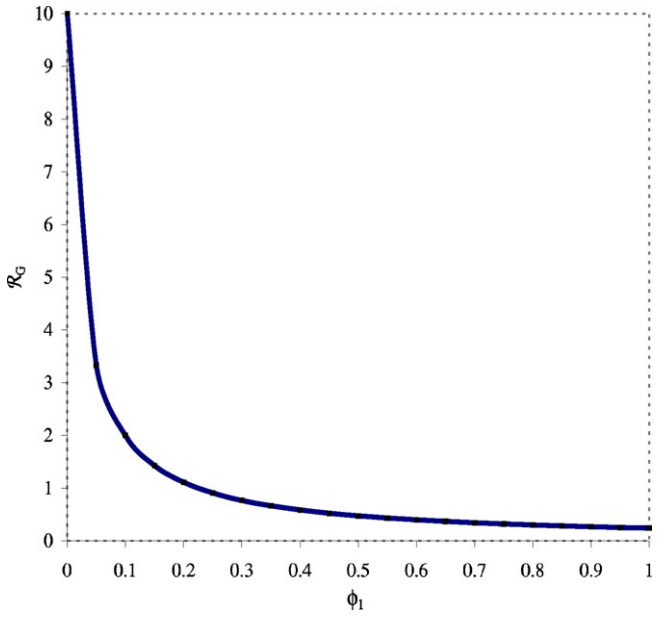


**Fig. 2.** Graphical representation of the relationship between gonorrhea reproductive number $\mathcal{R}_G$ and treatment rate $\phi_1$.

### 3.2. Global stability of the disease-free for gonorrhea-only model

We claim the following result

**Lemma 2.** *For any positive solution*($S(t)$, $I(t)$) *of model system (4), if* $\mathcal{R}_G < 1$, *then, the disease-free* $\mathcal{E}_G^0$ *is a global attractor.*

**Proof.** Let $f_\infty = \liminf_{t\to\infty} f(t)$, $f^\infty = \limsup_{t\to\infty} f(t)$.

From $I_G'(t) = (\beta_G I_G S/N_G) - (\phi + \mu)I_G$, and $(S/N_G) \le 1$, $(I_G/N_G) \le 1$, it follows that

$$\begin{aligned} I_G'(t) &\le \beta_G I_G - (\phi_1 + \mu) I_G \\ &\le \left(\frac{\beta_G}{\mu + \phi_1} - 1\right) I_G \\ &\le (\mathcal{R}_G - 1) I_G. \end{aligned} \tag{8}$$

Choose a sequence $t_n \to \infty$ such that $I(t_n) \to I_G^\infty$, and $I_G'(t_n) \to 0$. (see (Thieme, 1993)), then

$$0 \le (\mathcal{R}_G - 1) I_G^\infty.$$

Since $(\beta_G/\mu + \phi_1) \le 1$, we have $I_G^\infty = 0$, therefore $\lim_{t\to\infty} I_G(t) = 0$.

Finally, We choose the sequences $t_n^1 \to \infty$, such that $S(t_n^1) \to S^\infty$. Then, from the first equation in (4), noticing that $I_G(t) \to 0$ as $t \to \infty$, it follows that

$$0 \le \Lambda - \mu S^\infty, \quad 0 \ge \Lambda - \mu S_\infty. \tag{9}$$

From (9), we obtain

$$S^\infty = S_\infty = \frac{\Lambda}{\mu},$$

and the proof is complete. □

### 3.3. Global stability of the endemic equilibrium for gonorrhea-only sub-model

We claim the following result.

**Lemma 3.** *The endemic equilibrium of the gonorrhea-only sub-model (4) is globally asymptotically stable in* $\Phi_G$ whenever $\mathcal{R}_G > 1$.

**Proof.** It can be shown, as in Lemma 2 above, that the unique endemic equilibrium is globally asymptotically stable for $\mathcal{R}_G > 1$.

Further, $N_G = \Lambda/\mu$ as $t \to \infty$. Thus, using $S = N_G - I_G = \Lambda/\mu - I_G$ and substituting in (4), we obtain

$$I_G' = \lambda_G\left(\frac{\Lambda}{\mu} - I_G\right) - (\phi + \mu)I_G. \tag{10}$$

Using Dulac's multiplier $1/I_G$, it follows that

$$\frac{\partial}{\partial I_G}\left[\frac{\beta_G I_G}{I_G\Lambda/\mu}\left(\frac{\Lambda}{\mu} - I_G\right) - (\phi_1 + \mu)\right] = -\frac{\beta_G\mu}{\Lambda} = -\frac{\beta_G}{N} < 0. \tag{11}$$

Thus, by Dulac's criterion, there ar no periodic orbits in $\Phi_G$. Since $\Phi_G$ is positively invariant, and the endemic equilibrium exists whenever $\mathcal{R}_G > 1$, then it follows from the Poincare–Bendixson Theorem (Perko, 2000) that all solutions of the limiting system originating in $\Phi_G$ remain in $\Phi_G$ for all $t$. Further, the absence of periodic orbits in $\Phi_G$ implies that the endemic equilibrium of gonorrhea-only sub-model is globally asymptotically stable whenever $\mathcal{R}_G > 1$. □

In summary, the gonorrhea-only sub-model (4) has a globally-asymptotically stable infection-free equilibrium whenever $\mathcal{R}_G < 1$, and a unique endemic equilibrium whenever $\mathcal{R}_G > 1$.

## 4. HIV-only sub-model

Consider the HIV only sub-model (obtained by setting $I_G = I_{GH} = A_{GH} = A_{GHT} = 0$) in (3) given by

$$\begin{aligned} S_H' &= \Lambda - \lambda_H S_H - \mu S_H,\\ I_H' &= \lambda_H S_H - (\gamma + \mu)I_H,\\ A_H' &= \gamma I_H - (\omega + \mu + \nu)A_H,\\ A_{HT}' &= \omega A_H - (\mu + \tau\nu)A_{HT}. \end{aligned} \tag{12}$$

where $\lambda_H = (\beta_H(I_H + \theta_A A_H + \vartheta A_{HT})/N_H)$, and now $N = S_H + I_H + A_H$. For system (12) it can be shown that the region

$$\Phi_H = \left\{(S_H, I_H, A_H, A_{HT}) \in \mathbb{R}_+^4 : N_H \le \frac{\Lambda}{\mu}\right\}$$

is positively invariant and attracting. Thus, the dynamics of HIV-only model will be analysed in $\Phi_H$. The HIV-only model (12) has a disease-free equilibrium point given by,

$$\mathcal{E}_H^0 = (S_H, I_H, A_H, A_{HT}) = \left(\frac{\Lambda}{\mu}, 0, 0, 0\right) \tag{13}$$

Following van den Driessche and Watmough (2002) (as in Section 3, on the analysis of the gonorrhea-only model), it can be shown that the *reproduction number* for model system (12), denoted by $\mathcal{R}_H$ is given by

$$\mathcal{R}_H = \frac{\beta_H[\gamma\vartheta\omega + (\mu + \tau\nu)(\gamma\theta_A + \omega + \mu + \nu)]}{(\mu + \gamma)(\mu + \tau\nu)(\mu + \omega + \nu)}. \tag{14}$$

The reproduction number $\mathcal{R}_H$ measures the average number of new infections generated by a single HIV infected individual (but not infected with gonorrhea) during his or her infectious period when introduced in population of HIV susceptibles who have no gonorrhea.

### 4.1. Sensitivity analysis of $(\mathcal{R}_H)$

In this section, the impact of antiretroviral therapy is investigated using the reproductive number, $\mathcal{R}_H$. It follows from (14), that the elasticity (Caswell, 2001) of $\mathcal{R}_G$ with respect to $\omega$ can be computed using the approach in Chitns et al.(2008) as follows:

$$\frac{\omega}{\mathcal{R}_H}\frac{\partial\mathcal{R}_H}{\partial\omega} = -\frac{\gamma\omega[\mu(\theta_A - \vartheta) + \nu(\eta\tau - \vartheta)]}{(\mu+\omega+\nu)[(\mu+\tau\nu)(\mu+\omega+\nu) + \gamma(\theta_A(\mu + \tau\nu + \vartheta\omega))]} \tag{15}$$

Thus, the treatment of AIDS patients will have a positive impact in reducing HIV burden only if $\vartheta \le \tau\eta$. Using Theorem 2 in van den Driessche and Watmough (2002), the following result is established.

**Lemma 4.** *The disease-free equilibrium* $(\mathcal{E}_H^0)$ *of model system* (12) *is locally-asymptotically stable* (LAS) *if* $\mathcal{R}_H < 1$ *and unstable if* $\mathcal{R}_H > 1$.

Lemma 4 implies that HIV can be eliminated from the community (when $\mathcal{R}_H < 1$) if the initial sizes of the sub-populations of the model system (12) are in the basin of attraction of the disease free equilibrium $(\mathcal{E}_H^0)$. To ensure that elimination of the virus is independent of the initial sizes of the sub-populations, it is necessary to show that the DFE is globally stable.

### 4.2. Global stability of the disease-free for HIV-only sub-model

We shall use the following Theorem of Castillo-Chavez et al. (2002) in the sequel (herein stated for elucidation)

**Theroem 1.** (Castillo-Chavez et al., 2002) *If system* (12) *can be written in the form*

$$\begin{aligned} \frac{dX}{dt} &= F(\mathbf{x}, Z),\\ \frac{dZ}{dt} &= G(X, Z),\ G(\mathbf{x}, 0) = 0, \end{aligned} \tag{16}$$

*where* $X \in \mathbb{R}^m$ *denotes* (*its components*) *the number of uninfected individuals and* $Z \in \mathbb{R}^n$ *denotes* (*its components*) *the number of infected individuals including latent, infectious, etc.* $\mathcal{E}_H^0 = (\mathbf{x}^*, 0)$ *denotes the disease-free equilibrium of the system. And assume that* (*i*) *For* $(dX/dt) = F(X, 0)$, $X^*$ *is globally asymptotically stable* (GAS), (ii) $G(X, Z) = AZ - \hat{G}(X, Z)$, $\hat{G}(X, Z) \ge 0$ for $(X, Z) \in \Phi_H$, where $A = D_Z G(X*, 0)$ *is an M-matrix* (*the off diagonal elements of A are nonnegative*) *and* $\Phi_H$ *is the region where the model makes biological sense. Then the fixed point* $\mathcal{E}_H^0 = (\mathbf{x}*, 0)$ *is a globally asymptotic stable equilibrium of model system* (12) *provided that* $\mathcal{R}_H < 1$.

Applying Theorem 1 to model system (12) gives

$$\hat{G}(X, Z) = \begin{bmatrix} \beta_H(I_H + \theta_A A_H + \vartheta A_{HT})\left(1 - \dfrac{S_H}{S_H + I_H + A_H + A_{HT}}\right)\\ 0\\ 0 \end{bmatrix}, \tag{17}$$

Since, $S_H \le N_H(S_H + I_H + A_H + A_{HT})$ thus $\hat{G}(X, Z) \ge 0$, and by Theorem 1, $\mathcal{E}_H^0$ is GAS. We summarise the result in Lemma 5.

**Lemma 5.** *The disease-free equilibrium* $(\mathcal{E}_H^0)$ *of model system* (12) *is GAS if* $\mathcal{R}_H < 1$ *and unstable if* $\mathcal{R}_H > 1$.

### 4.3. Local stability of the endemic equilibrium for HIV-only model

We now employ the Centre Manifold theory (Carr, 1981) as described in Theorem 4.1 by Castillo-Chavez and Song (Carr, 1981), to establish the local asymptotic stability of the endemic equilibrium. Let us make the following change of variables in order to apply the Center Manifold theory: $S_H = x_1$, $I_H = x_2$, $A_H = x_3$, $A_{HT} = x_4$, so that $N_H = x_1 + x_2 + x_3 + x_4$. We now use the vector notation $X = (x_1, x_2, x_3, x_4)^T$. Then, model system (12) can be written in the form

$(dX/dt) = F = (f_1, f_2, f_3, f_4)^T$, where

$$\begin{aligned} x_1'(t) &= f_1 = \Lambda - \frac{\beta_H(x_2 + \theta_A x_3 + \vartheta x_4)}{\sum_{n=1}^{4} x_n} x_1 - \mu x_1, \\ x_2'(t) &= f_2 = \frac{\beta_H(x_2 + \theta_A x_3 + \vartheta x_4)}{\sum_{n=1}^{4} x_n} x_1 - (\gamma + \mu) x_2, \\ x_3'(t) &= f_3 = \gamma x_2 - (\mu + \omega + \nu) x_3, \\ x_4'(t) &= f_4 = \omega x_3 - (\mu + \tau\nu) x_4, \end{aligned} \tag{18}$$

The Jacobian matrix of system (18) at $\mathcal{E}_H^0$ is given by

$$J(\mathcal{E}_H^0) = \begin{bmatrix} -\mu & -\beta_H & -\theta_A\beta_H & -\vartheta\beta_H \\ 0 & \beta_H - \gamma - \mu & \theta_A\beta_H & \vartheta\beta_H \\ 0 & \gamma & -\mu - \omega - \nu & 0 \\ 0 & 0 & \omega & -\mu - \tau\nu \end{bmatrix}, \tag{19}$$

from which it can be shown that the HIV/AIDS induced reproduction number is

$$\mathcal{R}_H = \frac{\beta_H[\vartheta\gamma\omega + (\mu + \tau\nu)(\theta\gamma + \omega + \mu + \nu)]}{(\mu + \gamma)(\mu + \nu)(\mu + \omega + \nu)} \tag{20}$$

If $\beta_H$ is taken as a bifurcation parameter and if we consider the case $\mathcal{R}_A = 1$ and solve for $\beta_H$ gives

$$\beta_H = \beta_H^* = \frac{(\mu + \gamma)(\mu + \nu)(\mu + \omega + \nu)}{[\vartheta\gamma\omega + (\mu + \tau\nu)(\theta\gamma + \omega + \mu + \nu)]}. \tag{21}$$

Note that the linearised system of the transformed Eq. (18) with $\beta_H = \beta_H^*$, has a simple zero eigenvalue. Hence, the Centre Manifold theory can be used to analyze the dynamics of (18) near $\beta_H = \beta_H^*$. For convenience, the Centre Manifold theory is reproduced below.

**Theorem 2.** *Consider the following general system of ordinary differential equations with a parameter* $\phi$,

$$\frac{dx}{dt} = f(x, \phi), f : \mathbb{R}^n \times \mathbb{R} \to \mathbb{R} \text{ and } f \in \mathbb{C}^2(\mathbb{R}^n \times \mathbb{R}), \tag{22}$$

*where* 0 *is an equilibrium of the system that is* $f(0, \phi) = 0$ *for all* $\phi$ *and assume*

A1: $A = D_x f(0, 0) = ((\partial f_i/\partial x_j)(0, 0))$ *is linearisation of system (22) around the equilibrium* 0 *with* $\phi$ *evaluated at* 0. *Zero is a simple eigenvalue of A and other eigenvalues of A have negative real parts*;

A2: *Matrix A has a right eigenvector u and a left eigenvector v corresponding to the zero eigeinvalue.*

*Let* $f_k$ *be the* $K^{th}$ *component of f and*

$$\begin{aligned} a &= \sum_{k,i,j=1}^{n} v_k w_i w_j \frac{\partial^2 f_k}{\partial x_i \partial x_j}(0, 0), \\ b &= \sum_{k,i=1}^{n} v_k w_i \frac{\partial^2 f_k}{\partial x_i \partial \phi}(0, 0). \end{aligned} \tag{23}$$

*The local dynamics of (22) around* 0 *are totally governed by a and b.*

i. $a > 0, b > 0$, *When* $\phi < 0$ *with* $|\phi| \ll 1$, 0 *is locally asymptotically stable, and there exists a positive unstable equilibrium*; *when* $0 < \phi << 1$, 0 *is unstable and there exists a negative and locally asymptotically stable equilibrium*;

ii. $a < 0, b < 0$. *When* $\phi < 0$ *with* $|\phi| \ll 1$, 0 *is unstable*; *when* $0 < \phi << 1$, *asymptotically stable, and there exists a positive unstable equilibrium*;

iii. $a > 0, b < 0$. *When* $\phi < 0$ *with* $|\phi| \ll 1$, 0 *is unstable, and there exists a locally asymptotically stable negative equilibrium*; *when* $0 < \phi << 1$, , 0 *is stable, and a positive unstable equilibrium appears*;

iv. $a < 0, b > 0$. *When* $\phi$ *changes from negative to positive*, 0 *changes its stability from stable to unstable. Correspondingly a negative equilibrium becomes positive and locally asymptotically stable.*

It can be shown that the Jacobian of (18) at $\beta_H = \beta_H^*$ has a right eigenvector associated with the zero eigenvalue given by $w = [w_1, w_2, w_3, w_4]^T$, where

$$\begin{aligned} w_1 &= \frac{-\beta_H^*(w_2 + \theta_A w_3 + \vartheta w_4)}{\mu}, \quad w_2 = w_2 > 0, \quad w_3 = \frac{\gamma w_2}{\omega + \nu + \mu}, \\ w_4 &= \frac{\omega w_3}{\mu + \tau\nu}. \end{aligned} \tag{24}$$

The left eigenvector of $J(\mathcal{E}_H^0)$ associated with the zero eigenvalue at $\beta_H = \beta_H^*$ is given by $v = [v_1, v_2, v_3, v_4]^T$, where

$$v_1 = 0, \quad v_2 = \frac{\gamma v_3}{\mu + \gamma - \beta_H^*}, \quad v_3 = v_3 > 0, \quad v_4 = \frac{\vartheta\beta_H^* v_2}{\mu + \tau\nu}. \tag{25}$$

**Computations of** $a$ **and** $b$:

For system (18), the associated non-zero partial derivatives of $F$ associated with $a$ at the disease-free equilibrium are given by

$$\begin{aligned} &\frac{\partial^2 f_2}{\partial x_2^2} = -\frac{2\beta_H^*\mu}{\Lambda}, \frac{\partial^2 f_2}{\partial x_2 \partial x_3} = \frac{\partial^2 f_2}{\partial x_3 \partial x_2} = -\frac{\beta_H^*(1 + \theta_A)\mu}{\Lambda}, \frac{\partial^2 f_2}{\partial x_3^2} = -\frac{2\beta_H^*\theta_A\mu}{\Lambda}, \\ &\frac{\partial^2 f_2}{\partial x_2 \partial x_4} = \frac{\partial^2 f_2}{\partial x_4 \partial x_2} = -\frac{\beta_H^* c(1 + \vartheta)\mu}{\Lambda}, \frac{\partial^2 f_2}{\partial x_3 \partial x_4} = \frac{\partial^2 f_2}{\partial x_4 \partial x_3} = -\frac{\beta_H^*(\theta_A + \vartheta)\mu}{\Lambda}, \\ &\frac{\partial^2 f_2}{\partial x_4^2} = -\frac{2\vartheta\beta_H^*\mu}{\Lambda}. \end{aligned} \tag{26}$$

From (26), it follows that

$$a = -\frac{2\beta_H^*\mu}{\Lambda}(w_2 + w_3 + w_4)(w_2 + \theta_A w_3 + \vartheta w_4)v_2 < 0. \tag{27}$$

For the sign of $b$, it is associated with the following non-vanishing partial derivatives of $F$,

$$\frac{\partial^2 f_2}{\partial x_2 \partial \beta_H^*} = 1, \quad \frac{\partial^2 f_2}{\partial x_3 \partial \beta_H^*} = \theta_A, \quad \frac{\partial^2 f_2}{\partial x_4 \partial \beta_H^*} = \vartheta, \tag{28}$$

from which it

$$b = (w_2 + \theta w_3 + \vartheta w_4)v_2 > 0. \tag{29}$$

Thus, $a < 0$ and $b > 0$ and Theorem 4.1 item $(iv)$ above, the following result is established: the endemic equilibrium $\mathcal{E}_H^*$ is locally asymptotically stable for $\mathcal{R}_H > 1$, but close to 1.

**Lemma 6.** *The endemic equilibrium of the HIV-only sub-model (12) is globally asymptotically stable in* $\Phi_H$ *whenever* $\mathcal{R}_H > 1$.

## 5. Analysis of the HIV-gonorrhea model

Having analysed the dynamics of the two sub-models, the full HIV-gonorrhea model (3) is now considered. Its disease-free equilibrium is given by,

$$\mathcal{E}_{GH}^0 = (S, I_G, I_H, I_{GH}, A_H, A_{GH}, A_{HT}, A_{GHT}) = \left(\frac{\Lambda}{\mu}, 0, 0, 0, 0, 0, 0, 0\right) \tag{30}$$

Using the next generation method (van den Driessche and Watmough, 2002), it can be shown that the reproductive number

for the full HIV-gonorrhea model (3) denoted by $\mathcal{R}_{GH}$ is given by

$$\mathcal{R}_{GH} = \max\left\{\frac{\beta_G}{\mu+\phi_1}, \frac{\beta_H[\gamma\vartheta\omega + (\mu+\tau\nu)(\gamma\theta_A+\omega+\mu+\nu)]}{(\mu+\gamma)(\mu+\tau\nu)(\mu+\omega+\nu)}\right\}, \tag{31}$$

so that the following results follows from Theorem 2 in van den Driessche and Watmough (2002).

**Lemma 7.** *The disease-free equilibrium*($\mathcal{E}^0_{GH}$) *of model system* (3) *is locally asymptotically stable* (LAS) *if* $\mathcal{R}_{GH} < 1$ *and unstable if* $\mathcal{R}_{GH} > 1$.

### 5.1. Global stability of the disease-free of the full HIV-gonorrhea model

We claim the following result from Lemmas 2 and 5 above.

**Lemma 8.** *The disease-free equilibrium*($\mathcal{E}^0_{GH}$) *of model system* (3) *is GAS if* $\mathcal{R}_{GH} < 1$ *and unstable if* $\mathcal{R}_{GH} > 1$.

**Proof.** The proof is based on using a Comparison Theorem (Lakshmikantham et al., 2010) (by closely following the approach in Gumel et al., 2006; Mtisi et al., 2009; Sharomi and Gumel, 2007). Note that the equations of the infected components in system (12) can be written as

$$\begin{pmatrix} \frac{dI_G}{dt} \\ \frac{dI_H}{dt} \\ \frac{dI_{GH}}{dt} \\ \frac{dA_H}{dt} \\ \frac{dA_{GH}}{dt} \\ \frac{dA_{HT}}{dt} \\ \frac{dA_{GHT}}{dt} \end{pmatrix} = (F-V)\begin{pmatrix} I_G \\ I_H \\ I_{GH} \\ A_H \\ A_{GH} \\ A_{HT} \\ A_{GHT} \end{pmatrix} - \left(1-\frac{S}{N}\right)$$

$$\times \begin{pmatrix} \beta_G & 0 & \theta_{GH}\beta_G & 0 & \theta_{GH}\beta_{GH}\epsilon_2 & 0 & \varphi\beta_G \\ 0 & \beta_H & \eta\beta_H & \theta_A\beta_H & \theta_A\beta_H\epsilon_1 & \vartheta\beta_H & \varphi\beta_H \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \end{pmatrix} \begin{pmatrix} I_G \\ I_H \\ I_{GH} \\ A_H \\ A_{GH} \\ A_{HT} \\ A_{GHT} \end{pmatrix}$$

where $F$ and $V$ are given by

$$F = \begin{pmatrix} \beta_G & 0 & \theta_{GH}\beta_G & 0 & \theta_{GH}\beta_{GH}\epsilon_2 & 0 & \varphi\beta_G \\ 0 & \beta_H & \eta\beta_H & \theta_A\beta_H & \theta_A\beta_H\epsilon_1 & \vartheta\beta_H & \varphi\beta_H \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \end{pmatrix}$$

and

$$V = \begin{pmatrix} \mu+\phi_1 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & \gamma+\mu & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & \kappa\gamma+\mu+\phi_2 & 0 & 0 & 0 & 0 \\ 0 & -\gamma & 0 & \omega+\mu+\nu & -\phi_3 & 0 & 0 \\ 0 & 0 & -\kappa\gamma & 0 & \omega+\mu+\nu+\phi_3 & 0 & 0 \\ 0 & 0 & 0 & -\omega & 0 & \mu+\tau\nu & -\phi_4 \\ 0 & 0 & 0 & 0 & -\omega & 0 & \phi_4+\mu+\tau\nu \end{pmatrix}$$

Since $S \le N$, (for all $t \ge 0$) in $\Phi_{GH}$, it follows that

$$\begin{pmatrix} \frac{dI_G}{dt} \\ \frac{dI_H}{dt} \\ \frac{dI_{GH}}{dt} \\ \frac{dA_H}{dt} \\ \frac{dA_{GH}}{dt} \\ \frac{dA_{HT}}{dt} \\ \frac{dA_{GHT}}{dt} \end{pmatrix} \le (F-V)\begin{pmatrix} I_G \\ I_H \\ I_{GH} \\ A_H \\ A_{GH} \\ A_{HT} \\ A_{GHT} \end{pmatrix} \tag{32}$$

Using the fact that the eigenvalues of the matrix $F-V$ all have negative real parts, it follows that the linearized differential inequality system (32) is stable whenever $\mathcal{R}_{GH} < 1$. Consequently, $(I_G, I_H, I_{GH}, A_H, A_{GH}, A_{HT}A_{GHT}) \to (0,0,0,0,0,0,0)$ as $t \to \infty$. It follows by a Comparison Theorem (Lakshmikantham et al., 2010) that $(I_G, I_H, I_{GH}, A_H, A_{GH}, A_{HT}A_{GHT}) \to (0,0,0,0,0,0,0)$ as $t \to \infty$ and evaluating system (3) at, $I_G = I_H = I_{GH} = A_H = A_{GH} = A_{HT} = A_{GHT} = 0$ gives, $S \to S^0$ for $\mathcal{R}_H < 1$. Hence, the DFE ($\mathcal{E}^0_{GH}$) is GAS for $\mathcal{R}_{GH} < 1$. □

### 5.2. Endemic equilibrium of the full HIV-gonorrhea model

We establish the stability of the endemic equilibrium of the HIV-gonorrhea model (3), using the Centre Manifold theory. To apply this theory, the following simplification and change of variables are made first. Let $S = x_1, I_G = x_2, I_H = x_3, I_{GH} = x_4, A_H = x_5, A_{GH} = x_6, A_{HT} = x_7$ and $A_{GHT} = x_8$, so that $N = x_1 + x_2 + x_3 + x_4 + x_5 + x_6 + x_7 + x_8$. Further, by using the vector notation $\mathbf{x} = (x_1, x_2, x_3, x_4, x_5, x_6, x_7, x_8)^T$, the HIV-gonorrhea model system (3) can be written in the form $(d\mathbf{x}/dt) = F(\mathbf{x})$, with $\mathbf{F} = (f_1, f_2, f_3, f_4, f_5, f_6, f_7, f_8)^T$

$$\begin{aligned}
\frac{dx_1}{dt} &= f_1 = \Lambda + \phi_1 x_2 - \lambda_G x_1 - \lambda_H x_1 - \mu x_1 \\
\frac{dx_2}{dt} &= f_2 = \lambda_G x_1 - \alpha\lambda_H x_2 - (\phi_1+\mu)x_2, \\
\frac{dx_3}{dt} &= f_3 = \lambda_H x_1 + \phi_2 x_4 - \sigma\lambda_G x_3 - (\gamma+\mu)x_3, \\
\frac{dx_4}{dt} &= f_4 = \alpha\lambda_H x_2 + \sigma\lambda_G x_3 - (\kappa\gamma+\phi_2+\mu)x_4, \\
\frac{dx_5}{dt} &= f_5 = \gamma x_3 + \phi_3 x_6 - \sigma\lambda_G x_5 - (\omega+\mu+\nu)x_5, \\
\frac{dx_6}{dt} &= f_6 = \kappa\gamma x_4 + \sigma\lambda_G x_5 - (\omega+\phi_3+\mu+\nu)x_6, \\
\frac{dx_7}{dt} &= f_7 = \omega x_5 + \phi_4 x_8 - \sigma\lambda_G x_7 - (\mu+\tau\nu)x_7, \\
\frac{dx_8}{dt} &= f_8 = \omega x_6 + \sigma\lambda_G x_7 - (\phi_4+\mu+\tau\nu)x_8,
\end{aligned} \tag{33}$$

with

$$\lambda_H = \frac{\beta_H[x_3 + \eta x_4 + \theta_A(x_5 + \epsilon_1 x_6) + \vartheta x_7 + \varphi x_8]}{\sum_{n=1}^{8} x_n},$$

and

$$\lambda_G = \frac{\beta_G[x_2 + \theta_{GH}(x_4 + \epsilon_2 x_6) + \varphi x_8]}{\sum_{n=1}^{8} x_n},$$

The method entails evaluating the Jacobian of the system (33) at the disease-free ($\mathcal{E}^0_{GH}$) denoted $J(\mathcal{E}^0_{GH})$. This gives

$$J(\mathcal{E}_H) = \begin{bmatrix} -\mu & -\beta_H + \phi_1 & -\beta_H & -\eta\beta_H - \theta_{GH}\beta_G & -\theta_A\beta_H & -k_1 & -\vartheta\beta_H & -k_2 \\ 0 & \beta_G - \mu - \phi_1 & 0 & \theta_{GH}\beta_G & 0 & \theta_{GH}\beta_{GH}\epsilon_2 & 0 & \varphi\beta_G \\ 0 & 0 & \beta_H - \gamma - \mu & \eta\beta_H + \phi_2 & \theta_A\beta_H & \theta_A\beta_H\epsilon_1 & \vartheta\beta_H & \varphi\beta_H \\ 0 & 0 & 0 & -k_3 & 0 & 0 & 0 & 0 \\ 0 & 0 & \gamma & 0 & -k_4 & \phi_3 & 0 & 0 \\ 0 & 0 & 0 & \kappa\gamma & 0 & -k_5 & 0 & 0 \\ 0 & 0 & 0 & 0 & \omega & 0 & -k_6 & \phi_4 \\ 0 & 0 & 0 & 0 & 0 & \omega & 0 & -k_7 \end{bmatrix}, \quad (34)$$

where

$k_1 = \theta_A\beta_H\epsilon_1 - \theta_{GH}\beta_G\epsilon_2$, $k_2 = \varphi(\beta_H + \beta_G)$, $k_3 = \kappa\gamma + \mu + \phi_2$, $k_4 = \omega + \mu + \nu$, $k_5 = \omega + \mu + \nu + \phi_3$, $k_6 = \mu + \tau\nu$, $k_7 = \phi_4 + \mu + \tau\nu$.

Consider, the case when $\mathcal{R}_{GH} = 1$ (that is, $\mathcal{R}_G < \mathcal{R}_H = 1$). Suppose, further, that $\beta_H = \beta^*_H$ is chosen as a bifurcation parameter. Solving for $\beta_H$ from $\mathcal{R}_H = 1$, gives

$$\beta_H = \beta^*_H = \frac{(\mu + \gamma)(\mu + \tau\nu)(\mu + \omega + \nu)}{[\gamma\vartheta\omega + (\mu + \tau\nu)(\gamma\eta + \omega + \mu + \nu)]}.$$

It follows that $J_{\beta^*_H}$, the Jacobian of system (33) at the disease-free with $\beta_H = \beta^*_H$ has a simple zero eigenvalues (with all other eigenvalues having negative real part). Hence, the Centre Manifold theory (Carr, 1981) can be used to analyze the dynamics of system (33).

**Eigenvectors of $J_{\beta^*}$:**

For the case when $\mathcal{R}_H = 1$, it can be shown that $J_{\beta^*_H}$ has a right eigenvector (corresponding to the zero eigenvalue) given by $\mathbf{w} = (w_1, w_2, w_3, w_4, w_5, w_6, w_7, w_8)^T$, where

$$w_1 = \frac{-\beta^*_H w_3 - \theta_A\beta^*_H w_5 - \vartheta\beta^*_H w_7}{\mu}, \quad w_2 = 0,$$
$$w_3 = w_3 > 0, w_4 = 0, w_5 = \frac{\gamma w_3}{\mu + \nu}, \quad w_6 = 0,$$
$$w_7 = \frac{\omega w_5}{\mu + \tau\nu}, \quad w_8 = 0.$$

Further, the Jacobian $J_{\beta^*_H}$ has a left eigenvector (associated with the zero eigenvalue) given by $\mathbf{v} = (v_1, v_2, v_3, v_4, v_5, v_6, v_7, v_8)^T$, where

$$v_1 = v_2 = 0, \quad v_3 = v_3 > 0, \quad v_4 = \frac{(\eta\beta^*_H + \phi_2)v_3 + \kappa\gamma v_6}{\kappa\gamma + \mu + \phi_2},$$
$$v_5 = \frac{\theta_A\beta^*_H v_3 + \omega v_7}{\omega + \mu + \nu}, \quad v_6 = \frac{\theta_A\beta^*_H\epsilon_1 v_3 + \phi_3 v_5 + \omega v_8}{\omega + \mu + \nu + \phi_3},$$
$$v_7 = \frac{\vartheta\beta^*_H v_3}{\mu + \tau\nu}, \quad v_8 = \frac{\vartheta\beta^*_H v_3 + \phi_4 v_7}{\phi_4 + \mu + \tau\nu}.$$

**Computations of $a$ and $b$:**

It can be shown, after some algebraic manipulations (involving the associated partial non-zero partial derivative of $F$ (at the DFE) to be used in the expression for ($a$) in Theorem 2), that

$$a = -\frac{2\mu\beta^*_H v_3(w_3 + w_5 + w_7)(w_3 + \theta_A w_5 + \vartheta w_7)}{\Lambda} < 0$$

and

$$b = v_3(w_3 + \theta_A w_5 + \vartheta w_7) > 0,$$

so that the following results follows from Theorem 2 item ($iv$) above.

**Lemma 9.** *The full HIV-gonorrhea model (3) has a unique endemic equilibrium state which is locally-asymptotically stable* (LAS) *if* $\mathcal{R}_{GH} < 1$ *and unstable if* $\mathcal{R}_{GH} > 1$.

### 5.3. Impact of Gonorrhea on HIV dynamics

Trends in the incidence of a communicable disease are related to the number of new cases caused by each infective (the infectee number, analogous to the net reproductive rate in population dynamics) (Nold, 1979). The sensitivity indices of the reproduction numbers which measures initial disease transmission (Chitns et al., 2008) with respect to the relevant drivers (of the disease) are key in quantifying their impact on the disease dynamics. That is, the reproduction numbers for gonorrhea and HIV, $\mathcal{R}_G$ and $\mathcal{R}_H$ are directly related to the infection levels of the respective diseases (in the absence of the other disease) (Roeger et al., 2009). Thus, we consider the theoretical impact of gonorrhea on HIV by first examining the effect of $\mathcal{R}_G$ on the prevalence of HIV. Rewriting $\mathcal{R}_H$ in terms of $\mathcal{R}_G$, we have

$$\mathcal{R}_H(\mathcal{R}_G) = \frac{\beta_H[(\mathcal{R}_G(\tau\nu - \phi) + \beta_H)(\mathcal{R}_G(\nu - \phi + \omega) + \beta_H) + \eta\gamma(\mathcal{R}_G(\tau\nu - \phi + \theta\omega) + \beta_H)]}{(\mathcal{R}_G(\gamma - \phi) + \beta_H)(\mathcal{R}_G(\tau\nu - \phi) + \beta_H)(\mathcal{R}_G(\nu - \phi + \omega) + \beta_H)} \quad (35)$$

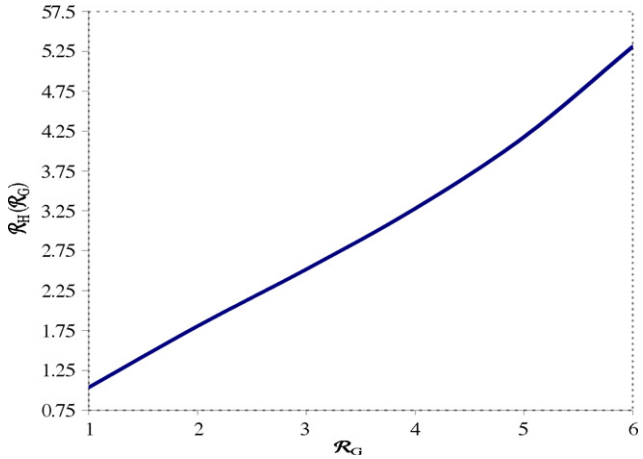


**Fig. 3.** Effect of increasing secondary gonorrhea infection on the transmission dynamics of HIV.

**Table 1**
Model parameters and their interpretations.

| Parameter | Symbol | Value | Source |
|---|---|---|---|
| Recruitment rate for humans | $\Lambda$ | 100 000 $yr^{-1}$ | Malunguza et al. (2010) |
| Natural mortality rate for humans | $\mu$ | 0.025 $yr^{-1}$ | Castillo-Chavez et al. (1997) |
| AIDS-induced mortality rate | $\nu$ | 0.333 $yr^{-1}$ | Malunguza et al. (2010) |
| Rate of progression to AIDS stage | $\gamma$ | 0.125 $yr^{-1}$ | Malunguza et al. (2010) |
| Transmission probability for HIV infection | $\beta_H$ | 0.011–0.95 | Bhunu et al. (2009b) and Hyman et al. (1999) |
| Transmission probability for gonorrhea infection | $\beta_G$ | 0.05 | Castillo-Chavez et al. (1997) |
| Modification parameters | $\vartheta, \varphi\epsilon_1, \epsilon_2$ | 0.4, 0.5, 1.19, 1.2 | Assume |
| Modification parameter | $\kappa, \sigma, \alpha$ | 1.02, 1.21, 1.22 | Assume |
| Modification parameters | $\eta, \theta_A, \theta_{GH}$ | 0.4, 1.15, 1.25, 1.3 | Assume |
| Rate of recovery from gonorrhea after treatment | $\phi_1, \phi_2, \phi_3, \phi_4$ | 0.2, 0.025, 0.003, 0.0031 | Assume |

Graphical representation of (35) is shown in Fig. 3 with parameter values as in Table 1 and Fig. 3 suggests that an increase in gonorrhea prevalence may have a significant impact on the infection level of HIV. It is worth noting that other factors may also play an important role such as the rate of progression to AIDS of individuals already infected with gonorrhea, nevertheless, gonorrhea infection has a negative effect on the health of the population, irrespective of their HIV status and possibly other infections as well, and as such, control of gonorrhea should be reinforced in resource limited settings. The good news is that the immune changes caused by gonorrhea infection do revert to normal after its successful treatment. Therefore, reducing the burden caused by gonorrhea infection is attainable.

Fig. 3 suggests that an increase in secondary gonorrhea cases may result in increased HIV prevalence when the two epidemics co-exists in the community (with no competitive exclusion). Further, sensitivity analysis on the impact of gonorrhea treatment is carried out by computing the partial derivatives of $\mathcal{R}_H(\mathcal{R}_G)$ with respect to gonorrhea treatment $\phi_1$. It follows from Eq. (7) on the analysis of the reproductive number $(\mathcal{R}_G)$ on the impact of gonorrhea treatment whenever the gonorrhea epidemic exists in the community, that gonorrhea treatment has an impact, and also it

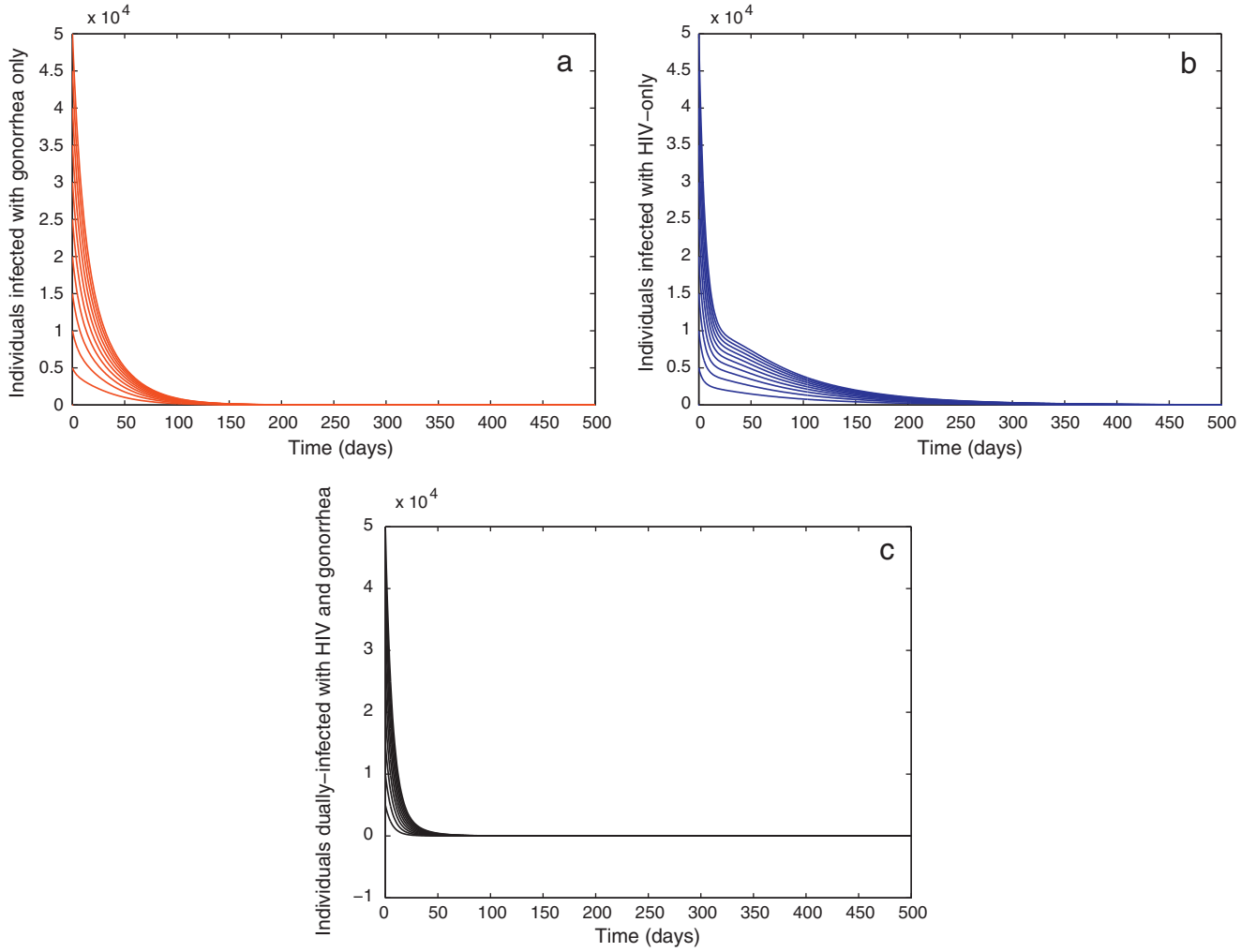


**Fig. 4.** Simulations of model (3) showing plots of individuals infected with gonorrhea only ($I_G$), individuals with HIV only but no AIDS symptoms ($I_H$) and individuals dually-infected with HIV and gonorrhea but displaying no clinical symptoms of AIDS ($I_{GH}$) for the case $\mathcal{R}_{GH} < 1$, using various initial conditions. Parameter values used are as in Table 1 with $\beta_H = 0.015$ and $\beta_G = 0.051$ (so that $\mathcal{R}_G = \mathcal{R}_H = \mathcal{R}_{GH} = 0.22$).

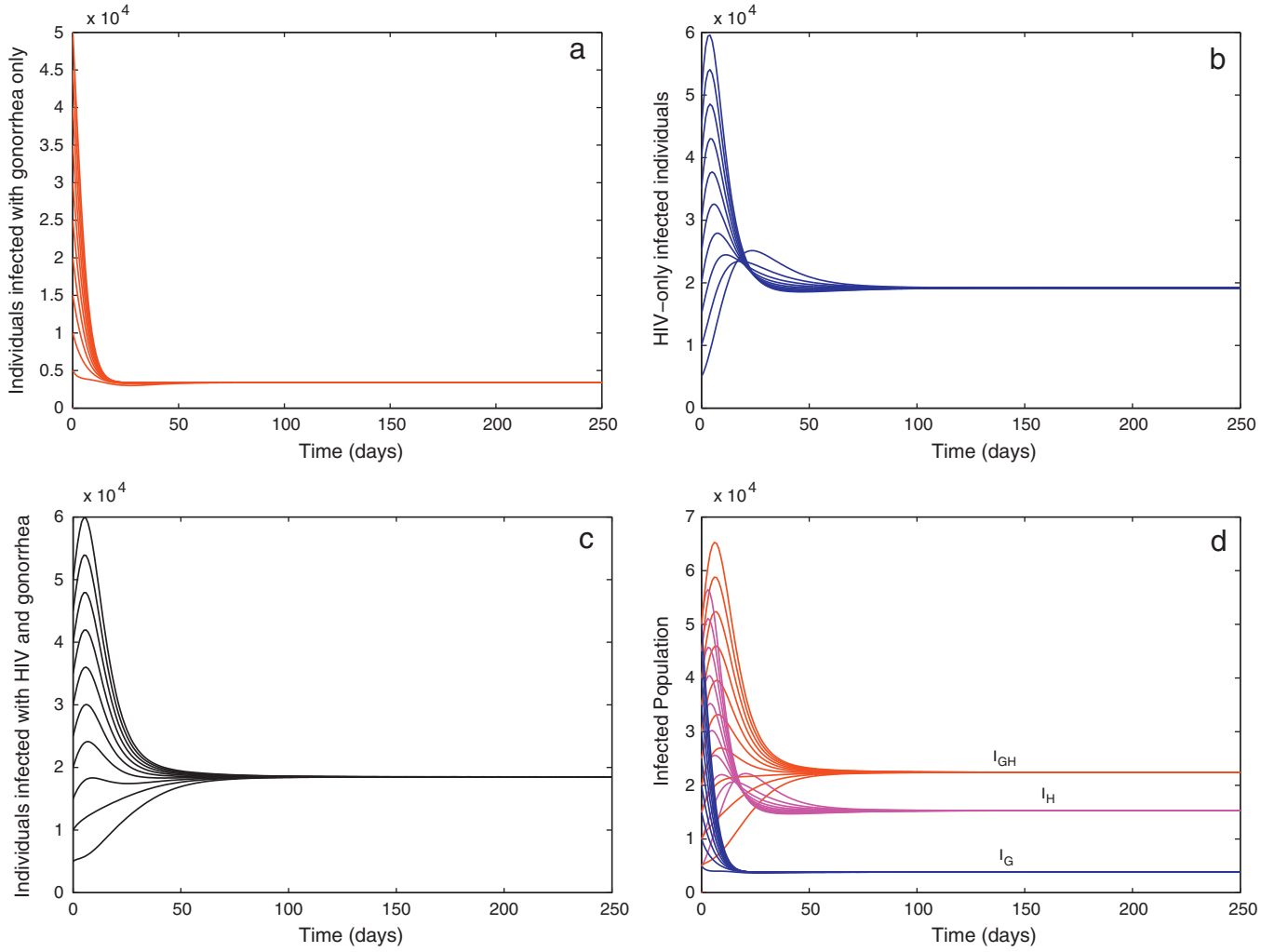


**Fig. 5.** Simulations of model (3) showing plots of individuals infected with gonorrhea only ($I_G$), individuals with HIV only but no AIDS symptoms ($I_H$) and individuals dually-infected with HIV and gonorrhea but displaying no clinical symptoms of AIDS ($I_{GH}$) for the case $\mathcal{R}_{GH} < 1$, using various initial conditions. Parameter values used are as in Table 1 with $\beta_H = 0.15$ and $\beta_G = 0.51$ (so that $\mathcal{R}_G = \mathcal{R}_H = \mathcal{R}_{GH} = 2.285$).

is worth noting that from the graphical representation of Eq. (35) an increase in gonorrhea epidemic may result in an increase in HIV in the community implying that $(\mathcal{R}_G/\mathcal{R}_H(\mathcal{R}_G))(\partial\mathcal{R}_H(\mathcal{R}_G)/\partial\mathcal{R}_G) > 0$. Thus, the elasticity (Caswell, 2001) of $\mathcal{R}_H(\mathcal{R}_G)$ with respect to $\phi_1$ can be computed using the approach in (Chitns et al., 2008) as follows:

$$\frac{\phi_1}{\mathcal{R}_H(\mathcal{R}_G)}\frac{\partial\mathcal{R}_H(\mathcal{R}_G)}{\partial\phi_1} = \frac{\phi_1}{\mathcal{R}_H(\mathcal{R}_G)}\left[\frac{\partial\mathcal{R}_H(\mathcal{R}_G)}{\partial\mathcal{R}_G}\times\frac{\partial\mathcal{R}_G}{\partial\phi_1}\right] < 0. \tag{36}$$

Biologically and economically speaking, Eq. (36) suggests that gonorrehea treatment may have a positive impact in controlling the two epidemics whenever they co-exists and their reproduction numbers exceeds a unity (with no competitive exclusion) and this further suggests that when two epidemics co-exists in poor communities of sub-Saharan Africa, gonorrhea treatment which is usually available and is less expensive compared to antiretroviral therapy may have a positive impact in controlling the two epidemics.

## 6. Numerical simulations

In order to illustrate the results of the foregoing analysis, numerical simulations of the full HIV-gonorrhea model is carried out, using a set of plausible parameter values given in Table 1. Unfortunately, the scarcity of data on HIV-gonorrhea co-dynamics limits our ability to calibrate, but nevertheless, we assume some of the parameters in their realistic ranges for illustrative purpose. These parsimonious assumptions reflect the lack of information currently available on the co-infection of the two diseases. Since this theoretical study is seemingly the first of its kind, it should be seen as a template for future research, especially in data collection.

Fig. 4 illustrates the solution profiles of the population of individuals infected with gonorrhea only ($I_G$), individuals with HIV only but no AIDS symptoms ($I_H$) and individuals dually-infected with HIV and gonorrhea but displaying no clinical symptoms of AIDS ($I_{GH}$) for the case $\mathcal{R}_{GH} < 1$, using various initial conditions. Parameter values used are as in Table 1 with $\beta_H = 0.015$ and $\beta_G = 0.051$ (so that $\mathcal{R}_G = \mathcal{R}_H = \mathcal{R}_{GH} = 0.23$) shows convergence to the disease-free equilibrium in line with Lemma 7.

Fig. 5 illustrates time series plots of individuals infected with gonorrhea only ($I_G$), individuals with HIV only but no AIDS symptoms ($I_H$) and individuals dually-infected with HIV and gonorrhea but displaying no clinical symptoms of AIDS ($I_{GH}$) for the case $\mathcal{R}_{GH} < 1$, using various initial conditions. Simulating the model (3) using parameter values given in Table 1 with $\beta_H = 0.15$ and $\beta_G = 0.51$ (so that $\mathcal{R}_G = \mathcal{R}_H = \mathcal{R}_{GH} = 2.285$) shows convergence to the endemic equilibrium in line with Lemma 9. Fig. 5(*d*) illustrates that for $\mathcal{R}_{GH} > 1$, ($\mathcal{R}_H = \mathcal{R}_G = 2.285$) the population of dually-infected individuals always has a higher steady-state value followed by HIV-only infected population and lastly gonorrhea infected individuals. Fur-

ther, these simulations show that whenever $\mathcal{R}_{GH} > 1$, there is always co-existence of the two diseases no matter which reproduction number is greater. Consequently, there is no competitive exclusion of the two diseases.

## 7. Conclusion

The study of the joint dynamics of gonorrhea and HIV present some mathematical challenges even though the modes of transmission are quite similar. Although there is overlap in the populations at risk of gonorrhea and HIV, the magnitude of the proportion of individuals at risk for both diseases is not known. Herein, we considered a simplified deterministic model that incorporates their joint dynamics (gonorrhea and HIV infections). A deterministic mathematical model for investigating the co-interaction of HIV and gonorrhea in a community in the presence of treatment is presented and rigorously analysed. We began with with a comprehensive qualitative analysis of the two sub-models, namely the gonorrhea-only model and HIV-only model. The epidemic thresholds parameters which are closely related to disease transmission (it also determines the outcome of the disease) in each model (two sub-models and the co-interaction model) is computed and used to assess the dynamics of the disease(s) in the community. Analytical result reveal that the two sub-models studied separately are globally stable whenever their respective threshold parameter is less than unity and unstable otherwise. The Centre Manifold theory is used to prove the local asymptitoc stability of the endemic equilibrium for the HIV-only model and the full model when the associated reproduction number is greater than unity. Thus, there is no competitive exclusion occurring. The impact of Gonorrhea on HIV dynamics is investigated numerically. A question was posed at the beginning of this study. To determine the effect an increase in the number of infected individuals with gonorrhea in a population in which HIV is prevalent has on the HIV dynamics. Numerical results suggest that an increase in the number of infected individuals with gonorrhea (singly and dually infected with HIV) in the presence of treatment results in a decrease in gonorrhea-only cases, dual-infection cases but with an increase in HIV-only cases and this may suggests that gonorrhea treatment only is a bright approach in curtailing the epidemic in the community but its not enough. Consequently, apart from malaria and TB, one other factor that fuels the high incidence of HIV in sub-Saharan Africa is the dual infection with gonorrhea. This negative impact of the synergistic interactions between HIV and gonorrhea have not been given prominence worldwide, and there is almost no existing statistical or mathematical models that explore the consequences of their joint dynamics at the population level. Nevertheless, our approach is closely related to those found in the literature as we focus on the joint dynamics of the two infections with therapeutic measures (gonorrhea treatment and antiretroviral therapy for HIV/AIDS) in a pseudo-competitive environment at the population level, with a fundamental difference that none of those studies considered treatment of both diseases. The model assumes that invasions are bad news for each single host and that joint invasions are worse. This was also the conclusion in a recent study on TB and HIV co-infections (Roeger et al., 2009).

This in-depth study of the co-interaction of the above mentioned diseases in a community can be extended in various ways: by (1) investigating their dynamics in the presence of HIV intervention strategies (preventive and therapeutic) such such as the use of condom use, voluntary HIV testing and screening as well as branding; (2) considering the possible consequences of HIV-gonorrhea co-infection in vertical transmission (mother-to-child) of HIV. Some diseases maintain unacceptable levels even if much of the population at risk receives adequate medical care, and gonorrhea is an example (Nold, 1980). The dynamic behavior of a family of disease models for a heterogeneous population is important as it was shown in Nold (1980) that the effects of particularly infectious subgroups within a population should be given prominence as relatively small numbers of infectives having numerous contacts during their infectious periods fuels the epidemic.

## References


Anderson, R.M., May, R.M., 1991. Infectious diseases of humans. Oxford University Press, London/New York.

Anon., 2010a. http://www.raiseinitiative.org.

Anon., 2010b. http://www.cdc.gov/nchstp/dstd/Fact-Sheets/FactsGonorrhea.htm.

Bhunu, C.P., Garira, W., Mukandavire, Z., 2009a. Modelling HIV/AIDS and tuberculosis coinfection. Bull. Math. Biol.

Bhunu, C.P., Garira, W., Magombedze, G., 2009b. Mathematical analysis of a two strain HIV/AIDS model with antiretroviral treatment. doi:10.1007/s10441-009-9080-2.

Brauer, F., Castillo-Chavez, C., 2001. Mathematical models in population biology and epidemiology. In: Texts in Applied Mathematics Series, 40. Springer-Verlag, New York.

Carr, J., 1981. Applications of Centre Manifold Theory. Springer-Verlag, New York.

Castillo-Chavez, C., Huang, W., Jia, L., 1997. The effects of females' susceptibility on the coexistence of multiple pathogen strains of sexually transmitted diseases J. Math. Biol. 35, 503–522.

Castillo-Chavez, C., Feng, Z., Huang, W., 2002. On the computation of $\mathcal{R}_0$ and its role on global stability. (math.la.asu.edu/chavez/2002/JB276.pdf).

Caswell, H., 2001. Matrix Population Models: Construction, Analysis and Interpretation. Sinauer Associates, Sunderland, MA.

CDC, 1998. Guidelines for treatment of sexually transmitted diseases. Morbidity and Mortality Weekly Report, 47 (RR-1).

Chitns, N., Hyman, J.M., Cushing, J.M., 2008. Determining important parameters in the spread of malaria through the sensitivity analysis of a mathematical model. Bull. Math. Biol., 70 (5), 1272–1296.

Diekmann, O., Heesterbeek, J.A.P., Metz, J.A.P., 1990. On the definition and computation of the basic reproduction ratio $\mathcal{R}_0$ in models for infectious diseases in heterogeneous populations. J. Math. Biol., 365–382.

Gumel, A., McCluskey, B.C., van den Driessche, C.P., 2006. Mathematical study of a staged-progression HIV model with imperfect vaccine. Bull. Math. Biol. 68, 2105–2128.

Hethcote, H.W., 2000. The mathematics of infectious diseases. SIAM Rev. 42 (4), 599–653.

Hook, E.W., Handsfield III, H.H., 1999. In: Holmes, K., Markh, P., Sparling, P., et al. (Eds.), Sexually Transmitted Diseases, 3rd edition. McGraw-Hill, New York, pp. 451–466.

Hyman, J., Li, M.J., Stanley, E.A., 1999. The differential infectivity and staged progression models for the transmission of HIV. Math. Biosci. 155, 77–109.

Lakshmikantham, V., Leela, S., Martynyuk, A.A., 2010. Stability Analysis of Nonlinear Systems. Marcel Dekker, Incl.

Malunguza, N., Mushayabas, S., Chiyaka C., Mukandavire, Z., 2010. Modelling the effects of condom use and antiretroviral therapy in controlling HIV/AIDS among heterosexuals, homosexuals and bisexuals. doi:10.1080/17486700903325167.

Mtisi, E., Rwezaura, H., Tchuenche, J.M., 2009. A mathematical analysis of malaria and tuberculosis co-dynamics. Discrete Cont. Dyn. Syst. B 12 (4), 827–864.

Mukandavire, Z., Gumel, A.B., Garira, W., Tchuenche, J.M., 2009. Mathematical analysis of a model for HIV-malaria co-infection. Math. Biosci. Eng. 6, 333–362.

Nold, A., 1979. The infectee number at equilibrium for a communicable disease. Math. Biosci. 46, 131–138.

Nold, A., 1980. Heterogeneity in disease-transmission modeling. Math. Biosci. 52, 227–240.

Perko, L., 2000. Differential Equations and Dynamical Systems. Text in Applied Mathematics vol. 7. Springer, Berlin.

Roeger, L-I., Feng, Z., Castillo-Chavez, C., 2009. Modeling TB and HIV co-infections. Math. Biosci. Eng. 6 (4), 815–837.

SADC HIV RESPONSE UPDATE, 2006.

Sharomi, O., Gumel, A.B., 2007. Curtailing smoking dynamics: A mathematical modeling approach. Appl. Math. Comput. 195, 475–499.

Sharomi, O., Podder, C.N., Gumel, A.B., Song, B., 2008. Mathematical analysis of the transmission dynamics of HIV/TB co-infection in the presence of treatment. Math. Biosci. Eng. 5, 145–174.

Thieme, H.R., 1993. Persistence under relaxed point-dissipativity (with applications to an endemic model). SIAM J. Math. Anal. 24, 407.

UNAIDS/WHO, 2006. 2006 Report on the global AIDS epidemic: Executive summary. UNAIDS and WHO, Geneva, http://data.unaids.org/pub/GlobalReport/2006/2006-GR-ExecutiveSummary-en.pdf.

van den Driessche, P., Watmough, J., 2002. Reproduction numbers and sub-threshold endemic equilibria for compartmental models of disease transmission. Math. Biosci., 29–48.

WHO, 2006. Prevention and Control of Sexually Transmitted Infections: Draft Global Strategy. Report by the Secretariat. WHO, Geneva, http://www.who.int/reproductivehealth/docs/stisstrategy.pdf.