MATHEMATICAL BIOSCIENCES
AND ENGINEERING
Volume **6**, Number **3**, July **2009**

doi:10.3934/mbe.2009.6.427

pp. **427–450**

HIV MODEL INCORPORATING DIFFERENTIAL PROGRESSION FOR TREATMENT-NAIVE AND TREATMENT-EXPERIENCED INFECTIVES

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(Communicated by Christopher Kribs Zaleta)

Abstract. We formulate an HIV/AIDS deterministic model which incorporates differential infectivity and disease progression for treatment-naive and treatment-experienced HIV/AIDS infectives. To illustrate our model, we have applied it to estimate adult HIV prevalence, the HIV population, the number of new infectives and the number of AIDS deaths for Botswana for the period 1984 to 2012. It is found that the prevalence peaked in the year 2000 and the HIV population is now decreasing. We have also found that under the current conditions, the reproduction number is $R_c \approx 1.3$, which is less than the 2004 estimate of $R_c \simeq 4$ by [11] and [13]. The results in this study suggest that the HAART program has yielded positive results for Botswana.

1. **Introduction.** The HIV/AIDS pandemic has continued to be a human catastrophe, inflicting extensive suffering on the global community, with about 25 million deaths from AIDS, thus far, resulting in about 15 million orphans, and an estimated 33 million people living with HIV/AIDS, 95% of whom are in resource-poor developing countries [21] and [25]. In their 2001 declaration of commitment on HIV/AIDS, the United Nations Special Session on AIDS observed that the HIV/AIDS pandemic was a Global Crisis requiring Global Action and recommended an Action Plan which proposed many strategies, including promotion of a rapid uptake of antiretrovirals (ARVs), in order to slow down the epidemic. However, six years later, the pandemic still presents as a global emergency requiring an exceptional and comprehensive global response [23]. Despite provision of resources for prevention, care, support, treatment, and promotion of extensive research, the global response to HIV/AIDS has not yielded satisfactory results as can be seen from the HIV-incidence rates which continue to grow in certain countries or have stabilized at very high endemic levels [24]. While the global HIV/AIDS adult prevalence in

2000 *Mathematics Subject Classification.* Primary: 92D30; Secondary: 92B05; 34D23.
Key words and phrases. HAART, HAART susceptible, infectivity reduction factor, equilibrium, stability, progression reduction factor, relative impact, HIV prevalence.

the period 2004 to 2006 has stabilized at about 1%, it is worth noting that declines in HIV prevalence among young people have been recorded between 2000 and 2005 in some African countries and low stable prevalences have been maintained in East Asia ($< 0.2\%$), the Middle East (0.2% to 0.4%) and North Africa (0.2%) [24]. However, the prevalence in sub-Saharan Africa as a region has stabilized at an unacceptably high level of about 5% [24].

There are initiatives to increase the ARV therapy coverage [21]. As a consequence, treatment coverage in sub-Saharan Africa has increased from 2% in 2003 to 28% in 2006 [22]. However, research into the long-term effect of administering imperfect drugs has just started. Many mathematical models have investigated the potential successes and failures of Highly Active Antiretroviral Therapy (HAART) [1]. One major difference between the various models has been in the number of infection stages incorporated into the models [3], [4], and [10]. The point of initiating HAART has also been an area of variation in the models [3] and [10]. In addition, many models have analyzed HAART in combination with other intervention strategies [7, 27]. While the studies [3] and [27] give composite results that give some insight into the effects of individual strategies, there is a need for further research in this area.

Antiretroviral therapy has nevertheless brought many successes such as: (i) One is reducing HIV-replication in patients taking it, thereby reducing infectiousness and opportunistic infections, resulting in significantly reduced need for treatment of opportunistic infections. The extent of this success, with regard to treatment-induced infectivity reduction factors, is discussed in various studies [3], [5] and [12]. It is obvious from these studies that there is variation in the predictions and conclusions; (ii) HAART has been found to reduce the severity of infectiousness and to slow down HIV progression rates to AIDS and consequently to increase survival time [3] and [4]. These studies have led to different predictions in the magnitude of the factors by which HAART increases survival time with predictions ranging from 1.5 to 3 [3] and 1.5 to 3.7 [4] times that of the none-HAART patients; (iii) HAART has performed well in reducing annual AIDS deaths [2]. Indeed, when HAART is compared with other therapies, its benefits exceed many therapies in other areas of medicine [2]. Despite these benefits, HAART has come at a considerable financial cost to most economies. According to [2], there is a second problem looming if HAART administration is not accompanied by an effective education programme against risky behaviour. The potential for a more severe epidemic exists as partially recovered patients could revert to risky activities that could increase the number of new infections [3, 4].

Although the benefits of HAART are known, the cost of treating large numbers is prohibitive for most sub-Sahara African countries. In order to ensure a sustainable HAART program, most sub-Saharan countries have defined AIDS as a condition whereby an individual's CD4 count is 200 or less. In Botswana, however, this threshold has been revised to 250 or less. As a result, many individuals have managed to access treatment. In most, if not all sub-Sahara Africa, antiretroviral drugs are given to AIDS patients only.

As a sequel to the studies mentioned above, we propose a five-stage HIV/AIDS model with seven active infective classes. We shall consider a simple model that excludes resistant infectives and assume that individuals progress from the susceptible stage through three HIV stages before developing AIDS and upon treatment they progress through two treatment stages before treatment failure. (See Figure 1 for

details.) The analysis is both analytic and numerical, and it explores how treatment affects the spread of the epidemic. Our results are compared with, among others, [3], [10] and [27], who also analyzed models similar to ours in that treatment was used as an intervention strategy against HIV/AIDS.

In sub-Saharan Africa, HIV is transmitted mainly by heterosexual contact. Despite this, we have formulated a one-sex model for two reasons. First, this approach is sufficient to provide a general trend regarding the spread of HIV/AIDS and the effectiveness of the treatment program. Secondly, we want to maintain parsimony and still achieve results that contribute towards understanding the current crisis. We shall find that our results with regard to prevalence and incidence for Botswana agree with the National AIDS Coordination Agency (NACA) predictions.

2. **Model formulation.** Consider a model in which the total population is divided into eight homogeneously mixing sexually active classes. These include a susceptible class, $S(t)$, treatment-naive individuals in the primary HIV stage, I_1, the asymptomatic stage in the chronic HIV stage, I_2, pre-AIDS individuals, I_3, and a class of individuals who have developed AIDS, A_1. After infection, an individual progresses through the classes I_1, I_2, I_3 before entering the AIDS stage, A_1, spending average periods of $\frac{1}{\omega_{12}}$, $\frac{1}{\omega_{23}}$ and $\frac{1}{\omega_{3a_1}}$ years respectively in each of the first three stages. Suppose that individuals in the A_1 class initiate treatment at the rate θ and that a proportion p of these individuals respond to treatment and move into a class of treated AIDS individuals, Y_2. We have assumed differential HIV/AIDS dynamics for treatment-naive individuals in A_1 and those patients from A_1 who progress to A_2 due to treatment failure. This assumption is supported by available literature, [19] for example, which confirms that HAART continues to reduce the severity of HIV/AIDS even after patients have experienced treatment failure. Thus, we assume that those patients from A_1 for whom treatment has failed join the class of treatment failures in A_2 at the rate $(1-p)\theta$. Let the treated AIDS individuals in Y_2 proceed to the pre-treatment failure class, Y_3, at a rate ρ_{23} and suppose that treatment fails at a rate ρ_{3a_2}, (see Figure 1). All individuals are subject to the natural per capita removal rate μ and the infected individuals are assumed to acquire sexual partners at the same constant rate, c per year. In addition to the natural death rate, individuals with full blown AIDS in A_1 and A_2 suffer disease-related removal rates δ_1 and δ_2 respectively.

Let us denote the per capita recruitment rate into the susceptible population by π. Suppose susceptible individuals get infected with HIV by treatment-naive HIV-infected individuals at a rate λ_n and by treated individuals at a rate λ_t. Let β_{nj} for $j = 1, 2, 3, 4$ be composite transmission parameters for normal infectives in the classes I_1, I_2, I_3 and A_1 respectively. Denote by β_{tj}, for $j = 2, 3, 4$, the transmission parameter for infectives who are receiving treatment and are progressing through Y_2, Y_3 and A_2 respectively. The force of infection λ is given by $\lambda = \lambda_n + \lambda_t$ where

$$\begin{cases} \lambda_n = \frac{\beta_{n1}I_1+\beta_{n2}I_2+\beta_{n3}I_3+\beta_{n4}A_1}{N}, \\ \lambda_t = \frac{\beta_{t2}Y_2+\beta_{t3}Y_3+\beta_{t4}A_2}{N} \\ N = S + I_1 + I_2 + I_3 + A_1 + Y_2 + Y_3 + A_2. \end{cases} \tag{1}$$

We assume that treatment reduces the per partnership transmission rate by a factor α [3] and [27]. For simplicity, we assume that if β_i is the per-partnership transmission probability for a treatment-naive class, then the probability of transmission for

the corresponding class on treatment is $\alpha\beta_i$. Figure 1 is a schematic representation of the model.

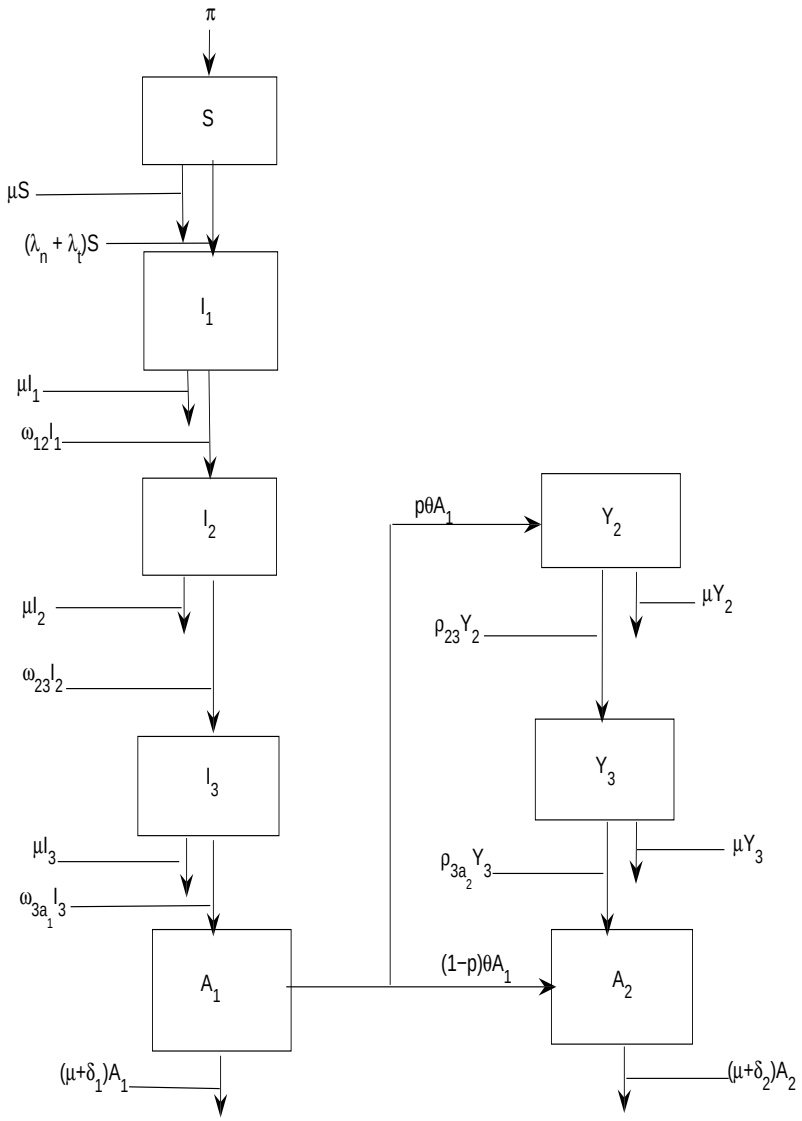

FIGURE 1. HIV/AIDS model with treatment

From Figure 1, we obtain the following system of differential equations:

$$\begin{cases} S' = \pi - \mu S - (\lambda_n + \lambda_t)S \\ I_1' = (\lambda_n + \lambda_t)S - (\mu + \omega_{12})I_1 \\ I_2' = \omega_{12}I_1 - (\mu + \omega_{23})I_2 \\ I_3' = \omega_{23}I_2 - (\mu + \omega_{3a_1})I_3 \\ A_1' = \omega_{3a_1}I_3 - (\mu + \theta + \delta_1)A_1 \\ Y_2' = p\theta A_1 - (\mu + \rho_{23})Y_2 \\ Y_3' = \rho_{23}Y_2 - (\mu + \rho_{3a_2})Y_3 \\ A_2' = \rho_{3a_2}Y_3 + (1-p)\theta A_1 - (\mu + \delta_2)A_2 \\ N' = \pi - \mu N - \delta_1 A_1 - \delta_2 A_2. \end{cases} \tag{2}$$

Suppose that

$$(S(t), I_1(t), I_2(t), I_3(t), A_1(t), Y_2(t), Y_3(t), A_2(t)) \in \Re^8$$

is any solution of the system (2). Then from the system (2), it is easy to show that

$$0 < S^*(t) < \frac{\pi}{\mu + \lambda_n^* + \lambda_t^*} \tag{3}$$

and

$$0 \quad < \quad N^* < \frac{\pi}{\mu + \delta} < \frac{\pi}{\mu}, \quad \text{where} \quad \delta = \min\{\delta_1, \delta_2\} \tag{4}$$

and * indicates equilibrium values of state variables. We conclude that the space

$$\Gamma = \left\{ (S(t), I_1(t), I_2(t), I_3(t), A_1(t), Y_2(t), Y_3(t), A_2(t)) \in \Re^8 \ : \ N^* < \frac{\pi}{\mu} \right\},$$

of biological interest, is positively invariant under the flow induced by the system (2). In order to understand the effects of treatment, we propose to consider the system (2) under two scenarios: (i) when there is no treatment and (ii) when there is treatment.

3. **Analysis of the model.**

3.1. **The model without treatment.**

We begin by considering the model without treatment, obtained by setting $\theta = 0$. The system (2) reduces to

$$S' = \pi - \mu S - \lambda_n S \tag{5}$$
$$I_1' = \lambda_n S - (\mu + \omega_{12})I_1 \tag{6}$$
$$I_2' = \omega_{12}I_1 - (\mu + \omega_{23})I_2 \tag{7}$$
$$I_3' = \omega_{23}I_2 - (\mu + \omega_{3a_1})I_3 \tag{8}$$
$$A_1' = \omega_{3a_1}I_3 - (\mu + \delta_1)A_1. \tag{9}$$

The system (5) to (9) has two equilibrium points, namely the disease-free equilibrium (DFE) point

$$\begin{aligned} E_0 &= (S^*, I_1^*, I_2^*, I_3^*, A_1^*) \\ &= (\frac{\pi}{\mu}, 0, 0, 0, 0), \end{aligned}$$

and the endemic point $E_1^* = (S^*, I_1^*, I_2^*, I_3^*, A_1^*)$ where

$$\begin{cases} S^* = \frac{\pi\Phi}{\mu\Phi+(R_0-1)(\mu+\omega_{12})}, \\ I_1^* = \frac{\pi(R_0-1)}{\mu\Phi+(R_0-1)(\mu+\omega_{12})}, \\ I_2^* = \left(\frac{\omega_{12}}{\mu+\omega_{23}}\right) I_1^*, \\ I_3^* = \left(\frac{\omega_{12}}{\mu+\omega_{3a_1}}\right)\left(\frac{\omega_{23}}{\mu+\omega_{23}}\right) I_1^*, \\ A_1^* = \left(\frac{\omega_{12}}{\mu+\delta_1}\right)\left(\frac{\omega_{23}}{\mu+\omega_{23}}\right)\left(\frac{\omega_{3a_1}}{\mu+\omega_{3a_1}}\right) I_1^*, \end{cases} \tag{10}$$

and where

$$\begin{cases} \Phi = \phi_1 + \phi_2 + \phi_3 + \phi_{a_1} \\ \phi_1 = 1, \quad \phi_2 = \left(\frac{\omega_{12}}{\mu+\omega_{23}}\right), \quad \phi_3 = \left(\frac{\omega_{12}}{\mu+\omega_{3a_1}}\right)\left(\frac{\omega_{23}}{\mu+\omega_{23}}\right), \\ \phi_{a_1} = \left(\frac{\omega_{12}}{\mu+\delta_1}\right)\left(\frac{\omega_{23}}{\mu+\omega_{23}}\right)\left(\frac{\omega_{3a_1}}{\mu+\omega_{3a_1}}\right). \end{cases} \tag{11}$$

The basic reproduction number R_0 for this model determined using the van Driesche and Watmough technique [6] is given by

$$R_0 = \phi_{n1}R_{0n1} + \phi_{n2}R_{0n2} + \phi_{n3}R_{0n3} + \phi_{na_1}R_{0na_1}, \tag{12}$$

where

$$\begin{cases} \phi_{n1} = 1, \quad \phi_{n2} = \left(\frac{\omega_{12}}{\mu+\omega_{12}}\right), \quad \phi_{n3} = \left(\frac{\omega_{12}}{\mu+\omega_{12}}\right)\left(\frac{\omega_{23}}{\mu+\omega_{23}}\right) \\ \phi_{na_1} = \left(\frac{\omega_{12}}{\mu+\omega_{12}}\right)\left(\frac{\omega_{23}}{\mu+\omega_{23}}\right)\left(\frac{\omega_{3a_1}}{\mu+\omega_{3a_1}}\right) \\ R_{0n1} = \frac{\beta_{n1}}{\mu+\omega_{12}}, \quad R_{0n2} = \frac{\beta_{n2}}{\mu+\omega_{23}}, \\ R_{0n3} = \frac{\beta_{n3}}{\mu+\omega_{3a_1}}, \quad \text{and} \quad R_{0na_1} = \frac{\beta_{n4}}{\mu+\delta_1}. \end{cases} \tag{13}$$

R_{0n1}, R_{0n2}, R_{0n3} R_{0na_1} are contributions from the infected classes I_1, I_2, I_3 and A_1 respectively and the coefficients ϕ_{n1}, ϕ_{n2}, ϕ_{n3} and ϕ_{na_1} are the weights.

Theorem 3.1. *The endemic equilibrium point E_1^* exists for $R_0 > 1$.*

Note that in (10) as $R_0 \to 1$, $E_1^* \to E_0$. We have a hypothetical model where the two states E_0 and E_1^* communicate as R_0 decreases to one. We can investigate the stability of the two states E_0 and E_1^*.

Theorem 3.2. *For $R_0 < 1$ the disease-free equilibrium point is globally asymptotically stable (g.a.s).*

Proof. We start by assuming that $R_0 < 1$. Now, $I_2 \in [0, \infty)$ since it measures population size. From the boundedness of N in equation (4), we deduce that

$$I_2 < \frac{\pi}{\mu + \delta}.$$

Also from (7), we have

$$I_2'' = \omega_{12} I_1' - (\mu + \omega_{23}) I_2' \leq M\Big(\frac{\pi}{\mu + \delta}\Big),$$

where

$$M = \frac{\omega_{12}\lambda_n(\mu + \delta)}{\mu + \lambda_n} + (\mu + \omega_{23})^2.$$

Hence, I_2'' is bounded and I_2 satisfies all the conditions in Lemma 1 by [20]. Similarly we can show that the other state variables I_3 and A_1 satisfy the conditions of Lemma 1, [20]. Consequently we can choose a sequence $p_n \to \infty$ such that

$$I_2(p_n) \to I_2^\infty, \quad I_2'(p_n) \to 0.$$

From equation (7) and [20], we have

$$I_2^\infty \leq \left(\frac{\omega_{12}}{\mu + \omega_{23}}\right) I_1^\infty. \tag{14}$$

Similarly, by choosing sequences q_n and r_n for I_3 and A_1 respectively, we can show that

$$I_3^\infty \leq \left(\frac{\omega_{12}}{\mu + \omega_{3a_1}}\right)\left(\frac{\omega_{23}}{\mu + \omega_{23}}\right) I_1^\infty, \tag{15}$$

and

$$A_1^\infty \leq \left(\frac{\omega_{12}}{\mu + \delta_1}\right)\left(\frac{\omega_{23}}{\mu + \omega_{23}}\right)\left(\frac{\omega_{3a_1}}{\mu + \omega_{3a_1}}\right) I_1^\infty. \tag{16}$$

Now from (6), we have the inequality

$$I_1^*\Big[R_0 - 1\Big] \geq 0. \tag{17}$$

The assumption $R_0 - 1 < 0$ and the inequality (17) imply that $I_1^\infty \leq 0$. Combining this with the positive invariance condition $I_1^\infty \geq 0$, leads to the conclusion $I_1^\infty = 0$. Applying this in (14), (15), and (16) leads to

$$I_2^\infty(t) \to 0, \quad I_3^\infty(t) \to 0 \quad \text{and} \quad A_1^\infty \to 0 \quad \text{as} \quad t \to \infty.$$

Adding equations (5) to (9) gives

$$\frac{dN}{dt} = \pi - \mu N - \delta_1 A_1 \leq \pi - \mu N.$$

Using the result that $\frac{dN}{dt} < 0$ if $N > \frac{\pi}{\mu}$ and [20] gives

$$N_\infty \geq \frac{\pi}{\mu}. \tag{18}$$

Now, consider solutions with $N(t) \leq \frac{\pi}{\mu}$. Since nonnegative initial data for the model (5) to (9) lead to nonnegative solutions, we deduce that

$$N^\infty \leq \frac{\pi}{\mu}. \tag{19}$$

Hence from (18) and (19), we conclude that

$$N_\infty = N^\infty = \frac{\pi}{\mu}, \tag{20}$$

which is the disease free value for S^*. Hence the DFE point is globally asymptotically stable when $R_0 < 1$. □

Next, we investigate the stability of E_1^* using the technique used by [29].

Theorem 3.3. *The endemic equilibrium point for the model (5) to (9) is locally asymptotically stable for* $R_0 > 1$.

Proof. If we define

$$H = \frac{\beta_{n1}I_1 + \beta_{n2}I_2 + \beta_{n3}I_3 + \beta_{n4}A_1}{N},$$

then the equilibrium state variables can be expressed in terms of H^* as:

$$\begin{aligned} S^* &= \left(\frac{\pi}{\mu + H^*}\right), \quad I_1^* = \psi_{n1}\left(\frac{\pi H^*}{\mu + H^*}\right), \quad I_2^* = \psi_{n2}\left(\frac{\pi H^*}{\mu + H^*}\right) \\ I_3^* &= \psi_{n3}\left(\frac{\pi H^*}{\mu + H^*}\right), \quad A_1^* = \psi_{na_1}\left(\frac{\pi H^*}{\mu + H^*}\right), \quad N^* = \frac{(1 + \Psi H^*)\,\pi}{(\mu + H^*)}, \end{aligned}$$

Hence

$$\begin{cases} H^* &= \frac{R_0 H^*}{1+\Psi H^*} \\ &= \Upsilon\left(H^*\right) \\ \Psi &= \psi_{n1} + \psi_{n2} + \psi_{n3} + \psi_{na_1}. \end{cases} \tag{21}$$

We define

$$\begin{aligned} H &= \frac{R_0 H}{1 + \Psi H} \\ &= \Upsilon\left(H\right). \end{aligned} \tag{22}$$

The full definitions of ψ_{n1}, ψ_{n2}, ψ_{n3} and ψ_{na_1} are given in the appendix. From equation (22) we can see that the equilibrium points are essentially the fixed points of $\Upsilon\left(H\right)$, where the point $\Upsilon(0) = 0$ is the DFE point. (The reader is referred to [15] and [29] for details of this.) We note that the Jacobian of $\Upsilon(H)$ at the endemic equilibrium point is the spectral radius $\rho\Big(D\Big[\Upsilon\Big\{H(E_1)\Big\}\Big]\Big) = \frac{R_0}{(1+\Psi H)^2}$, which is an increasing function of the reproduction number but a decreasing function of the incidence rate H. Clearly, as $H \to \infty$, the spectral radius ρ tends to zero implying that the endemic equilibrium point is asymptotically stable. □

3.2. **The model with treatment.** The model in the presence of a treatment strategy given by equations (2) with $\theta \neq 0$ and $p \neq 0$ has a unique DFE point E_0 and a unique endemic point E_1^* given by

$$\begin{aligned} E_0 &= \left(\frac{\pi}{\mu}, 0, 0, 0, 0, 0, 0, 0\right), \\ E_1^* &= \left(S^*, I_1^*, I_2^*, I_3^*, A_1^*, Y_2^*, Y_3^*, A_2^*\right) \end{aligned}$$

and

$$\begin{cases} S^* &= \frac{\pi\hat{\Phi}}{\mu\hat{\Phi}+\left(\mu+\omega_{12}\right)\left(R_c-1\right)}, \\ I_1^* &= \frac{\pi\left(R_c-1\right)}{\mu\hat{\Phi}+\left(\mu+\omega_{12}\right)\left(R_c-1\right)}, \\ I_2^* &= \left(\frac{\omega_{12}}{\mu+\omega_{23}}\right)I_1^*, \\ I_3^* &= \left(\frac{\omega_{12}}{\mu+\omega_{3a_1}}\right)\left(\frac{\omega_{23}}{\mu+\omega_{23}}\right)I_1^*, \\ A_1^* &= \Psi_{23}\left(\frac{\omega_{12}}{\mu+\theta+\delta_1}\right)I_1^*, \\ Y_2^* &= \Psi_{23}\left(\frac{\omega_{12}}{\mu+\rho_{23}}\right)\left(\frac{p\theta}{\mu+\theta+\delta_1}\right)I_1^*, \\ Y_3^* &= \Psi_{23}\left(\frac{\omega_{12}}{\mu+\rho_{3a_2}}\right)\left(\frac{p\theta}{\mu+\theta+\delta_1}\right)\left(\frac{\rho_{23}}{\mu+\rho_{23}}\right)I_1^* \\ A_2^* &= \Psi_{23}\left(\frac{\omega_{12}}{\mu+\delta_2}\right)\left(\frac{\theta}{\mu+\theta+\delta_1}\right)\left[\left(1-p\right)+p\left(\frac{\rho_{23}}{\mu+\rho_{23}}\right)\left(\frac{\rho_{3a_2}}{\mu+\rho_{3a_2}}\right)\right]I_1^*, \end{cases} \tag{23}$$

where because of the length of the expressions for R_c, Ψ_{23} and $\hat{\Phi}$, ϕ_{t2}, ϕ_{t3} and ϕ_{ta2} and in order to improve the readability of text, we have defined these expressions in the appendix. The existence and stability of the two states are summarized in the following theorems.

Theorem 3.4. *The endemic equilibrium point E_1 of the model (2) exists when $R_c > 1$.*

Remark 1. We note from the expressions for I_i, Y_j and A_k where $i = 1, 2, 3, \quad j = 2, 3$ and $k = 1, 2$ that as $R_c \to 1$, $E_1^* \to E_0$. As in the model without treatment, we investigate the stability of E_0 and E_1^*. We note further that the expression for $I_i, \quad i = 1, \ 2, \ 3$ in the model with treatment have the same structure as those for the model without treatment except that R_0 in (10) is replaced by R_c.

Theorem 3.5. *If $R_c < 1$, then the disease-free equilibrium point of the model (2) is g.a.s.*

Proof. In Theorem 3.2, we proved the convergence of I_1^∞, I_2^∞, I_3^∞ and A_1^∞ to zero provided that $I_1^\infty = 0$. Now, it suffices to show that

$$I_1^\infty = 0 \Rightarrow Y_2^\infty = 0, \quad Y_3^\infty = 0 \quad \text{and} \quad A_2^\infty = 0.$$

We can choose sequences τ_n, ϱ_n and υ_n for Y_2, Y_3 and A_2 respectively, and show that

$$Y_2^\infty \leq \left(\frac{\omega_{12}}{\mu+\rho_{23}}\right)\left(\frac{\omega_{23}}{\mu+\omega_{23}}\right)\left(\frac{\omega_{3a_1}}{\mu+\omega_{3a_1}}\right)\left(\frac{p\theta}{\mu+\theta+\delta_1}\right)I_1^\infty \tag{24}$$

$$Y_3^\infty \leq \left(\frac{\omega_{12}}{\mu+\rho_{3a_2}}\right)\left(\frac{\omega_{23}}{\mu+\omega_{23}}\right)\left(\frac{\omega_{3a_1}}{\mu+\omega_{3a_1}}\right)\left(\frac{p\theta}{\mu+\theta+\delta_1}\right)\left(\frac{\rho_{23}}{\mu+\rho_{23}}\right)I_1^\infty \tag{25}$$

$$\begin{aligned} A_2^\infty \leq & \left(\frac{\omega_{12}}{\mu+\delta_2}\right)\left(\frac{\omega_{23}}{\mu+\omega_{23}}\right)\left(\frac{\omega_{3a_1}}{\mu+\omega_{3a_1}}\right)\left[\left(\frac{(1-p)\theta}{\mu+\theta+\delta_1}\right)\right. \\ & \left.+\left(\frac{p\theta}{\mu+\theta+\delta_1}\right)\left(\frac{\rho_{23}}{\mu+\rho_{23}}\right)\left(\frac{\rho_{3a_2}}{\mu+\rho_{3a_2}}\right)\right]I_1^\infty. \end{aligned} \tag{26}$$

Hence using [20] and the equation for I_1' in system (2), we obtain

$$I_1^* \left[R_c - 1\right] \geq 0. \tag{27}$$

Using $I_1^\infty = 0$ in (24), (25) and (26) leads to

$$Y_2^\infty(t) \to 0, \quad Y_3^\infty(t) \to 0 \quad \text{and} \quad A_2^\infty \to 0 \quad \text{as} \quad t \to \infty.$$

Using a similar argument to that in the proof of Theorem 2, we conclude that $N_\infty = N^\infty = \frac{\pi}{\mu}$. This completes the proof. □

To first order, the reproduction number R_c can be expressed as

$$R_c = R_0 - \left(\frac{\theta\phi_{na_1}}{\mu+\delta_1}\right)R_{0na_1} + R_{0t}, \tag{28}$$

where R_{0t} is the average number of secondary infectives generated by an infective on ARV treatment during the infective's period of treatment, and $\left(\frac{\theta\phi_{na_1}}{\mu+\delta_1}\right)R_{0na_1}$ is the average number by which the number of secondary infectives by drug-naive infectives is reduced because some infected individuals with full-blown AIDS in the class A_1 have started treatment.

As $\theta \to 1$ (when everybody is treated)

$$R_c = R_0 - \left(\frac{\phi_{na_1}}{\mu+\delta_1}\right)R_{0na_1} + \hat{R}_{0t} \quad \left(\hat{R}_{0t} > R_{0t}\right). \tag{29}$$

The effect of treatment is to reduce the basic reproduction number (that is, reduce the number of new infectives by treatment-naive infectives) but to increase R_{0t}. In the absence of counseling, treatment could increase the reservoir of treated infectives. As $\theta \to 0$ (when no one is treated) $R_c = R_0$ (as in the earlier model).

Theorem 3.6. *The endemic equilibrium point for the model (2) is asymptotically stable for* $R_c > 1$.

Remark 2. The proof of theorem (3.6) is similar to that of Theorem (3.3).

4. **Numerical simulation.** The model (2) requires several input values of parameters, which can be divided into three sets, namely (i) those that are measured by the statistics office and the national agencies such as μ, δ_1 and δ_2, (ii) those that have been estimated by other researchers such as the disease progression rates ω_{13}, ω_{23} and ω_{3a_1}, probabilities of infection β_{n1}, β_{n2}, β_{n3} and β_{n4}, and (iii) those that are to be estimated using the above parameters, namely the rate of initiating treatment, θ^*, the disease progression reduction factor, g^*, and the infectivity reduction factor, α^*, for which the disease burden may clear from the population.

In this simulation, we shall confine ourselves to the Botswana case for which some input demographic parameters are available and the government has committed itself to offering free ARVs to all those who meet the criteria for the ARV program (CD4 count of 250 cells per mm^{-3} and below). We want to use the estimated parameters to study the following hypothetical problems: (a) What conclusions can we draw regarding the evolution of HIV and AIDS over the next five years if HAART is emphasized as the major intervention strategy? (b) Treatment introduces more HIV sub-populations who progress toward AIDS (treatment failure) at different rates to the normal HIV infectives. We want to investigate the likely impacts of various infected sub-populations on the spread of HIV and AIDS when the progression rates for the normal HIV infectives and for the treated infectives are (i) different (ii) the same. (c) Using the estimated values of the treatment rate, θ^*, the infectivity reduction factor, α^*, and the progression reduction factor, g^*, we want to determine the HIV prevalence over the period 1984 to 2012 and ask the questions: Is the HAART program likely to reduce the HIV/AIDS burden? For HAART to succeed, how many infected individuals should join the HAART programme each year?

In order to reduce the number of parameters in our model we have made the following assumptions: First, we have assumed that the per partnership transmission probabilities for the treated classes Y_2, Y_3 and A_2 are proportional to the per partnership transmission probabilities for the untreated infectives, i.e., $\alpha\beta_{n2}$, $\alpha\beta_{n3}$ and $\alpha\beta_{n4}$ respectively. This assumption is supported by various studies including [3] and [4]. Secondly, [3] and [4] estimated survival time for individuals on ARVs to be about 1.5 to 3 times greater than the survival time for untreated HIV/AIDS individuals. This estimate translates into a reduction in the progression rates from Y_2 to Y_3 and from Y_3 to A_2. However, we have also considered hypothetical scenarios when the treatment rate is large. Table 1 gives the estimated values of θ^*, α^* and g^* for which the reproduction number R_c would eventually be reduced to one. The results in this table show that for a fixed value of θ^*, the infectivity reduction

TABLE 1. Estimated treatment parameters.

θ^*	0.5	0.5	0.5	0.8	0.8	0.8	1	1	1
α^*	0.067	0.0585	0.0546	0.158	0.129	0.12	0.184	0.151	0.135
g^*	0.27	0.47	0.67	0.27	0.47	0.67	0.27	0.47	0.67

factor α^* decreases as the progression reduction factor g^* increases. Furthermore, we note that the threshold values of infectivity reduction factor, α^*, are lower than the corresponding values of the progression reduction factors g^* and this agrees with the conclusion by [27] that a treatment program must at least reduce infectiousness more than the progression rate in order to contain the HIV epidemic.

Using some of the estimated parameters, a sample of which are in Table 1, we have obtained results given in the following figures. Figure 2 compares a plot of the actual antenatal prevalence rates for Botswana and three other plots generated for varying values of α, θ and g. Figure 2 helps us to choose appropriate values of α, θ and g which closely approximate the actual antenatal prevalence rates for Botswana for the period 1999 to 2006. From these plots, we have chosen α, θ and g from Figure 2(iv) for the approximate antenatal prevalence rates.

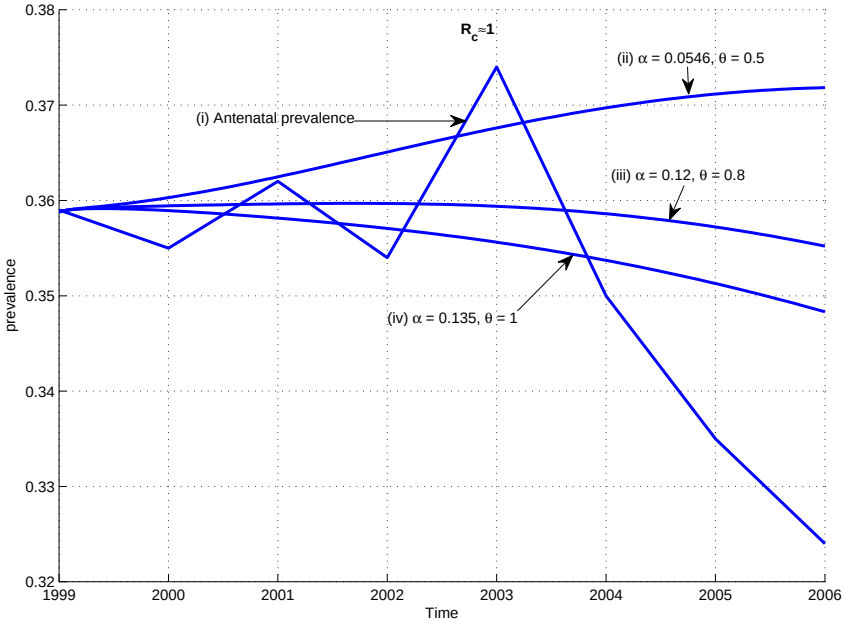

FIGURE 2. Plot (i) prevalence-time plot for Botswana antenatal data. Plots (i), (ii) and (iii) : $R_c \approx 1$, α varies, $(\beta_{n1}, \beta_{n2}, \beta_{n3}, \beta_{n4}) = (0.8, 0.03, 0.04, 0.4)$ and $(\beta_{t2}, \beta_{t3}, \beta_{t4}) = \alpha^* \times (0.03, 0.04, 0.4)$. $g^* = 0.67$ and $(\omega_{12}, \omega_{23}, \omega_{3a_1}, \rho_{23}, \rho_{3a_2}) = (13, 0.2355, 0.2355, 0.1578, 0.1578)$. (i) $\alpha^* = 0.0546$, $\theta^* = 0.5$ (ii) $\alpha^* = 0.12$, $\theta^* = 0.8$ (iii) $\alpha^* = 0.135$, $\theta^* = 1$. The other parameter values are as given in Table 2.

Using the software Estimation and Projection Package (EPP) developed by UNAIDS, we have converted the antenatal prevalence rates for Figure 2 plot (iv) into prevalence rates for the total population in Botswana (Figure 3). Note that in Figure 3 the prevalence reached a peak in the year 2000 and has been declining since then. Using these prevalence rates, we have determined by using the software SPECTRUM, also developed by UNAIDS, the estimated number of individuals infected with HIV for the period 1984 to 2012 (Figure 4). The estimated HIV numbers agree with the NACA estimates [14], [16] and [17].

A study on the global HIV incidence rate by [18] revealed that the HIV incidence rate has peaked for most African countries and, specifically, the number of new infections in Botswana peaked in 1995 and has been declining since then. Our results agree with both the results in [18] and those in the United Nations report [24], which revealed a falling trend in the HIV/AIDS burden in Botswana. Furthermore, using the estimated prevalence rates from our model, we have estimated the number of new HIV infections and the number of AIDS deaths for the age group 15-49 years for the period 1984 to 2012. The results are illustrated in Figure 5(a) and 5(b).

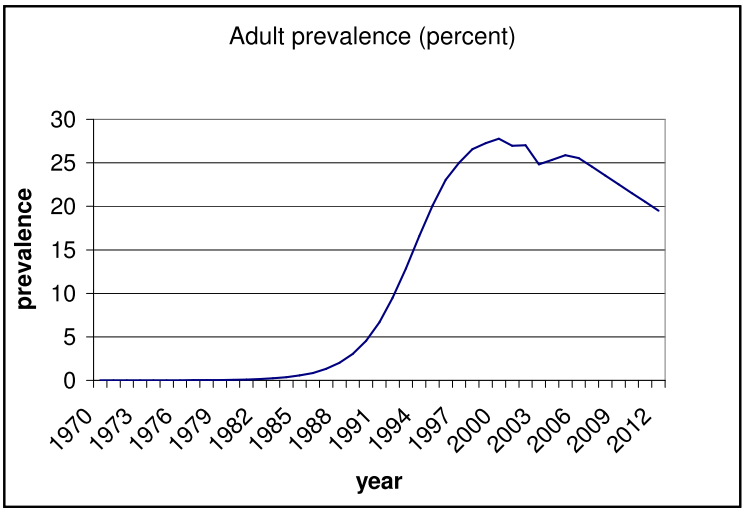

FIGURE 3. Model estimate of HIV prevalence for the 15-49 age group (adult HIV/AIDS prevalence).

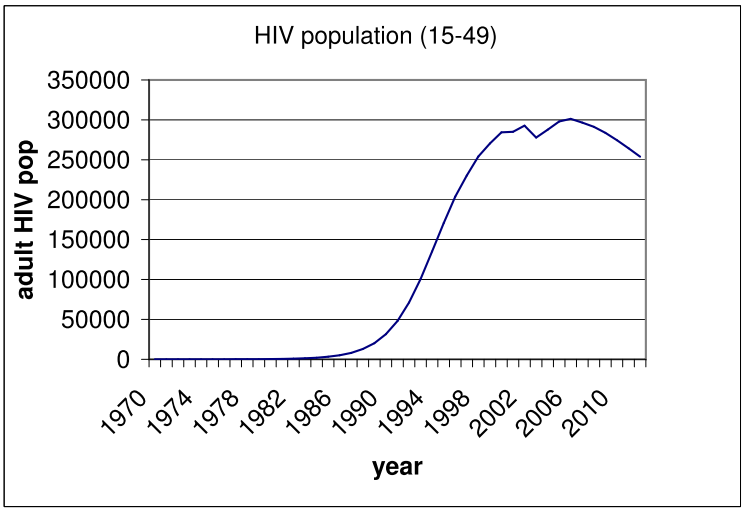

FIGURE 4. Model estimate of the total HIV population among the 15-49 age group.

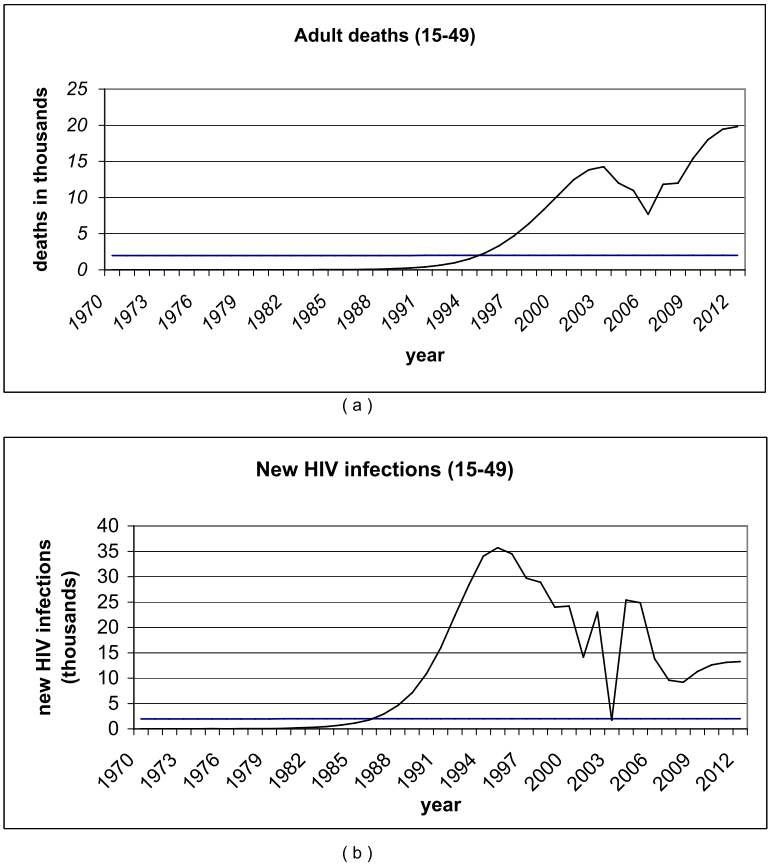

FIGURE 5. (a) Estimated number of annual AIDS-related deaths among the 15-49 year olds. (b) Model estimate of newly HIV infected 15-49 year old individuals.

The number of AIDS deaths peaked in 2001 and has been falling since then because of the HAART programme, which has prevented many deaths. However, our model is predicting that the number of AIDS deaths will rise between 2006 and 2012 as AIDS individuals currently on HAART succumb to AIDS due to treatment failure. The trend of new infections, on the other hand, will keep declining (Figure 5(b)), signifying the success of HAART and other intervention strategies.

Using our estimates of the prevalence rates for the total population, the programme SPECTRUM has estimated the number in need of first line therapy (Figure 6).

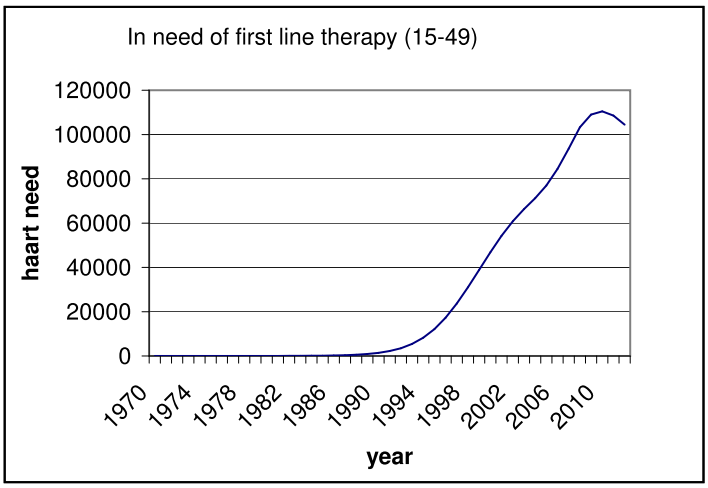

FIGURE 6. Population of 15-49 year old HIV infectives who are in need of first line therapy.

According to our estimates, this number will reach a peak of 110,000 in 2009 and will probably decline thereafter as more individuals on HAART succumb to AIDS. Currently, there are only about 80,000 individuals receiving HAART. Our estimate, according to Figure 6, is that about 105,000 infected individuals should be receiving HAART. There is, therefore an urgent need to enrol more patients if the full benefits of HAART are to be realized.

In all of the following figures we have used the following parameter values: $(\beta_{n1}, \beta_{n2}, \beta_{n3}, \beta_{n4}) = (0.8, 0.03, 0.04, 0.4)$ and $(\omega_{12}, \omega_{23}, \omega_{3a_1}) = (13, 0.16, 0.5)$. The other parameter values are given in the captions. Figures 7(a) and 8(a) are population time plots for the cases $R_c \leq 1$ for varying values of the parameter θ^*. In both cases the HIV/AIDS burden decreases with time. The relative fraction of new infections generated by an infected group I_i is given by

$$\rho_i = \frac{\beta_i I_i}{\sum_{j=1}^{j=n} \beta_j I_j}$$

and it can be used as a measure of the infected group's contribution towards disease transmission [8, 9]. Consequently, the corresponding relative impacts of I_1, I_2, I_3, A_1, Y_2, Y_3, and A_2 are respectively

$$\begin{aligned} P_1 &= \frac{\beta_{n1} I_1}{P}, \quad P_2 = \frac{\beta_{n2} I_2}{P}, \quad P_3 = \frac{\beta_{n3} I_3}{P}, \quad P_4 = \frac{\beta_{n4} A_1}{P}, \\ P_5 &= \frac{\beta_{t2} Y_2}{P}, \quad P_6 = \frac{\beta_{t3} Y_2}{P}, \quad P_7 = \frac{\beta_{t4} A_2}{P}, \end{aligned}$$

where

$$P = \beta_{n1} I_1 + \beta_{n2} I_2 + \beta_{n3} I_3 + \beta_{n4} A_1 + \beta_{t2} Y_2 + \beta_{t3} Y_3 + \beta_{t4} A_2.$$

Figures 7(b) and 8(b) illustrate the impacts.

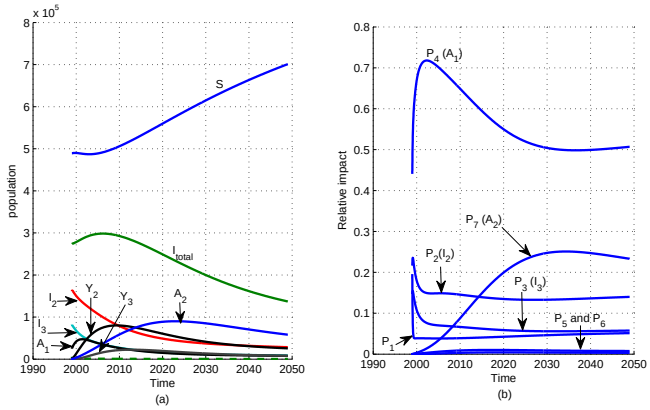

FIGURE 7. (a) Population-time plots (b) relative impact-time plots. $g^* = 0.67$ (fairly good progression rate reduction), $\theta = 0.5$ and $\alpha = 0.055$ (good treatment-induced infectivity reduction). $R_c \approx 1$, $(\beta_{t2}, \beta_{t3}, \beta_{t4}) = (0.00165, 0.0022, 0.022)$ and $(\rho_{23}, \rho_{3a_2}) = (0.1072, 0.335)$. Period : 1999 to 2049.

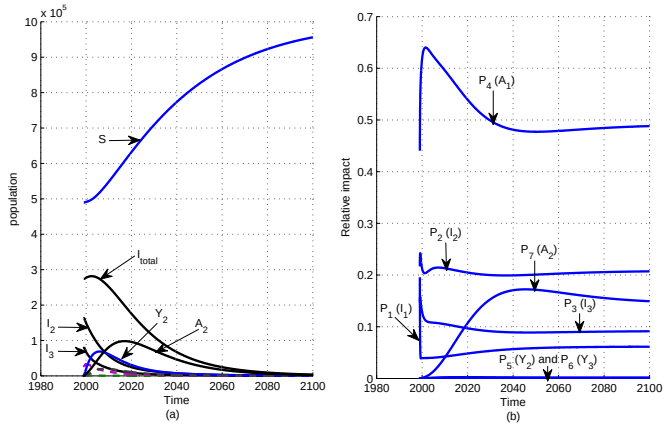

FIGURE 8. (a) Population-time plots (b) relative impact-time plots. $g^* = 1$ (progression rate unchanged by treatment) and $\alpha = 0.01$ (fairly good treatment-induced infectivity reduction). $(\beta_{t2}, \beta_{t3}, \beta_{t4}) = (0.0003, 0.0004, 0.004)$, $(\rho_{23}, \rho_{3a_2}) = (0.16, 0.5)$, $\theta = 0.9$ and $R_c = 0.6376$. Period: 1999 to 2100.

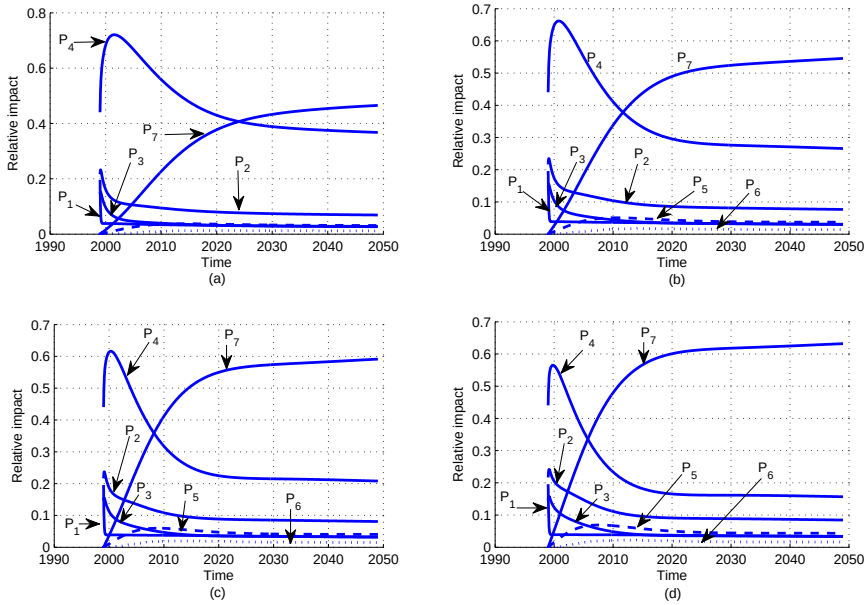

FIGURE 9. Relative impact at $\alpha = 0.5$, and $(\beta_{t2}, \beta_{t3}, \beta_{t4}) = (0.003, 0.004, 0.04)$, $g^* = 0.47$ and $(\rho_{23}, \rho_{3a_2}) = (0.0752, 0.235)$. Treatment levels vary : (a) $\theta = 0.3$, $R_c = 2.3212$ (b) $\theta = 0.5$, $R_c = 2.1443$ (c) $\theta = 0.7$, $R_c = 2.0581$ (d) $\theta = 0.9$, $R_c = 1.9887$.

It is clear from these graphs that in the initial stages of the disease spread, the normal infectives I_1, I_2, I_3 and A_1 are more significant in spreading the disease than the other infectives, namely Y_2, Y_3 and A_2. However, as time increases, most of the infections are caused by the AIDS classes A_1 and A_2. The contribution to the spread of the disease by treated infectives Y_2 and Y_3 remains insignificant for all disease progression rates g. However, Figure 8(b) shows that even if $\theta^* \approx 1$, provided the infectivity reduction factor is low, the contribution to the spread of HIV is dominated by the normal infectives, although the contribution from the treated failure class A_2 may grow with time. Figure 9 reveals a similar pattern for the case $R_c > 1$ for various treatment rates. In this case, however, the dominance of the class A_2 occurs much earlier than for $R_c < 1$.

The relative impacts for our model without treatment and the model with treatments are compared in Figures 10, 11 and 12. From Figures 10(a), 11(a) and 12(a), it is evident that the impact of the individuals with full-blown AIDS in the model without treatment is much greater than that of individuals in the same class in the presence of a treatment strategy. Figures 10(b), 11(b) and 12(b) compare the relative impacts of HAART-naive and HAART-experienced individuals. It is shown that the impact of HAART-naive individuals is greater in the early stages of the treatment programme, but this decreases with time and in the long run the two groups have more or less equal impact if $R_c \approx 1$, the treatment-naive have more impact if $R_c < 1$, and the treatment-experienced have more impact if $R_c > 1$.

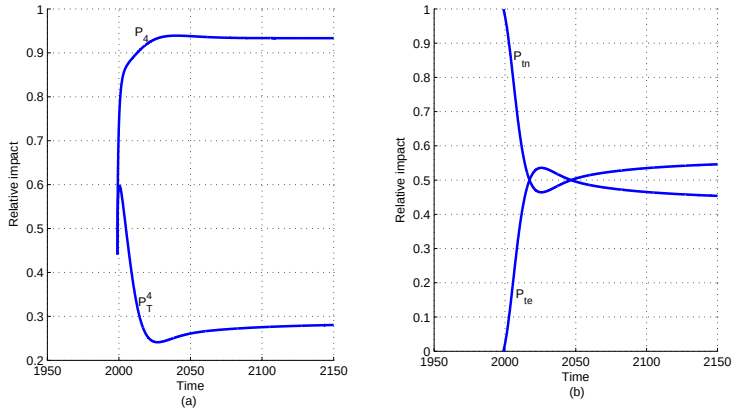

FIGURE 10. Comparing relative impacts. Parameter values : $\alpha = 0.135$, $g^* = 0.67$, $\theta = 1$, $(\beta_{t2}, \beta_{t3}, \beta_{t4}) = (0.00405, 0.0054, 0.054)$, $(\rho_{23}, \rho_{3a_2}) = (0.1072, 0.335)$, $R_c \approx 1$ and $R_0 = 4.2454$. (a) Time plots of the relative impact of A_1 in the presence of treatment(P_4^T) and the relative impact of A_1 in the absence of treatment (P_4). (b) Time plots of the relative impact of treatment-experienced infectives (P_{te}) and treatment-naive infectives (P_{tn}).

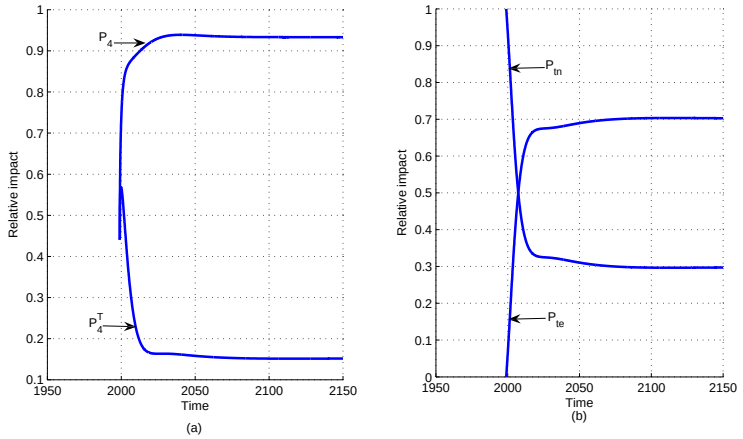

FIGURE 11. Comparing relative impacts. Parameter values : $\alpha = 0.45$, $g^* = 0.67$, $\theta = 1$, $(\beta_{t2}, \beta_{t3}, \beta_{t4}) = (0.00405, 0.0054, 0.054)$, $(\rho_{23}, \rho_{3a_2}) = (0.0432, 0.135)$, $R_c = 1.9339$ and $R_0 = 4.2454$. The relative impact-time plots in (a) and (b) are as described in Figure 10.

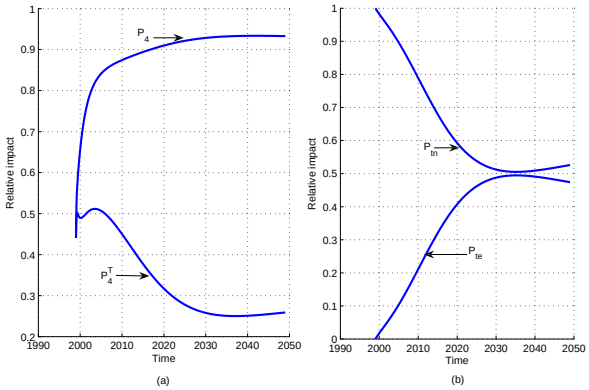

FIGURE 12. Comparing relative impacts. Parameter values : $\alpha = 0.45$, $g^* = 0.67$, $\theta = 1$, $(\beta_{t2}, \beta_{t3}, \beta_{t4}) = (0.00405, 0.0054, 0.054)$, $(\rho_{23}, \rho_{3a_2}) = (0.0432, 0.135)$, $R_c = 0.8777$ and $R_0 = 4.2454$. The relative impact-time plots in (a) and (b) are as described in Figure 10.

Changes in the total susceptible $(S(t))$ and total infected $(I(t))$ populations at time t as fractions of their initial values $(S(0))$ and $(I(0))$ respectively may depict how the HIV-susceptible and -infected populations vary relative to each other. We can also deduce how these populations vary relative to their initial values. Figures 13 and 14 show these trends for the cases $R_c < 1$ and $R_c > 1$ respectively.

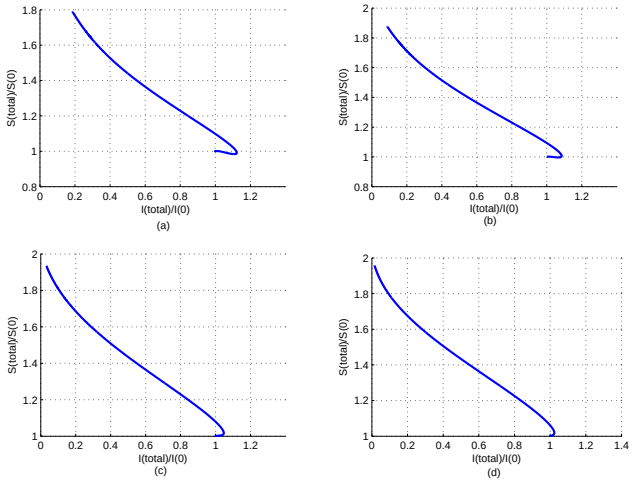

FIGURE 13. Dynamics of susceptible fraction in relation to total infected fraction for $(\beta_{t2}, \beta_{t3}, \beta_{t4}) = \alpha \times (0.03, 0.04, 0.4)$, $g^* = 0.47$, $(\rho_{23}, \rho_{3a_2}) = (0.1578, 0.1578)$ and $R_c < 1$. Period : 1999 to 2150 (a) $\theta = 0.4$, $\alpha = 0.01$, $R_c = 0.9683$ (b) $\theta = 0.5$, $\alpha = 0.01$, $R_c = 0.8553$ (c) $\theta = 0.7$, $\alpha = 0.01$, $R_c = 0.7162$ (d) $\theta = 1$, $\alpha = 0.01$, $R_c = 0.6042$.

It is shown that for $R_c < 1$ the proportion of infectives decreases while the proportion of susceptibles increases, while for $R_c > 1$ the proportion of infectives grows while the proportion of susceptibles decreases.

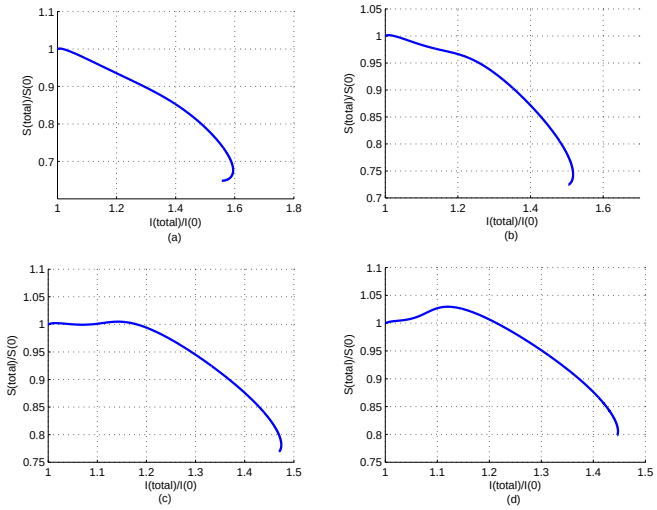

FIGURE 14. Dynamics of susceptible fraction in relation to total infected fraction for $(\beta_{t2}, \beta_{t3}, \beta_{t4}) = \alpha \times (0.03, 0.04, 0.4)$, $g^* = 0.47$, $(\rho_{23}, \rho_{3a_2}) = (0.0432, 0.135)$ and $R_c > 1$. Period : 1999 to 2099. (a) $\theta = 0.3$, $\alpha = 0.5$, $R_c = 2.3212$ (b) $\theta = 0.5$, $\alpha = 0.5$, $R_c = 2.1443$ (c) $\theta = 0.7$, $\alpha = 0.5$, $R_c = 2.0581$ (d) $\theta = 0.9$, $\alpha = 0.5$, $R_c = 2.0071$.

Figure 15 is a prevalence versus time plot for various values of the reproduction number R_c.

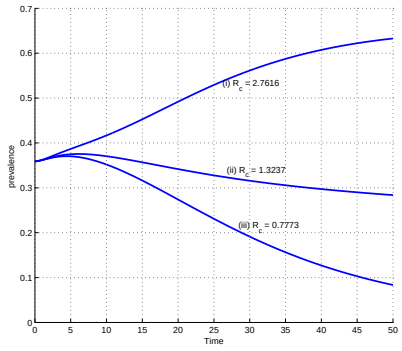

FIGURE 15. Prevalence-time graphs for $(\beta_{t2}, \beta_{t3}, \beta_{t4}) = \alpha \times (0.015, 0.02, 0.2)$, $g^* = 0.67$ and $(\rho_{23}, \rho_{3a_2}) = (0.1072, 0.335)$ and $\theta = 0.6$ and (i) $\alpha = 0.7$, $R_c = 2.7616$, (ii) $\alpha = 0.2$, $R_c = 1.3237$, (iii) $\alpha = 0.01$, $R_c = 0.7773$. Other parameter values are as given in the appendix.

Comparing the results in Figure 15 with the actual antenatal prevalence rates for Botswana, it is clear that the plot which best describes the Botswana prevalence is that corresponding to the reproduction number $R_c = 1.3237$. A declining trend in the reproduction number was also found by [7] in their stochastic simulation of the Uganda HIV incidence. Furthermore, [7] concluded that any treatment program which does not treat all HIV-infected individuals can not reduce the reproduction number below 1.0 unless it is coupled with other intervention strategies like vaccination and/or counseling. The studies by [11] and [13] which used the Botswana HIV/AIDS data up to the year 2004 found $R_c = 4$ for the period 1989 to 2002 which was the period of rising antenatal prevalence (which reached a peak value of 0.374 in 2003). The result in this study shows that intervention strategies, particularly the HAART program, which was made accessible by all those who met the criteria in 2002 are bearing fruit.

5. **Discussion.** Our work makes a contribution to one of the questions that has been raised on whether large-scale HAART programmes would significantly reduce the HIV/AIDS burden. In developing countries which lack the capacity to provide and sustain the required infrastructure, the answer to this question will remain elusive. However, in the case of Botswana, which has kept good demographic data on HIV and AIDS, our study shows that there will be a slow decline in the prevalence rate even though the reproduction number remains above one, but that it will decline to below 20% by 2012. However, what is notable is that the reproduction number has declined significantly from $R_c = 4$ to $R_c \approx 1.3237$ during the period 2003 to 2007. The decline of course cannot be attributed to HAART alone but to a combination of education on prevention of HIV combined with HAART. What is clear from our results is that the sharp decline in the reproduction number occurred when the government embraced the HAART programme. Many mathematical models which have been analyzed before confirm that HAART reduces the severity of the HIV/AIDS epidemic by reducing the reproduction number, prevalence or incidence. See [3, 5, 7, 10] for more details.

Our results on the relative impacts of various infected subgroups show that for high treatment rates the infected group that is responsible for most of the infections is the group A_2 (treatment failure AIDS individuals). Individuals in this group will have undergone counseling. Hence, if the effects of education were included in the model, there would be further reduction in the reproduction number.

Figure (9) illustrates the dangers of low rates of treatment and the low rates of reduction in infectivity which include among other things (i) a significantly high reproduction number and (ii), analyzing Figure (9)(c) and (d), dominance of untreated infectives in the spread of HIV. These are groups that have not accessed counseling. We could not get data on other southern African countries, where HIV/AIDS is still a problem, to illustrate what is happening in those countries. However, the gap in the knowledge about the comparative risks of getting HIV between males and females and between urban and rural communities in Southern Africa is the same in the region [26]. We are confident that the results in this study apply to other southern African states.

6. **Appendix.**

Lemma 6.1. *(Thieme's lemma) Let*

$$f : [0, \infty) \to \mathbf{R}$$

be bounded and twice differentiable with bounded second order derivative. Let $t \to \infty$ and $f(t_n)$ converge to f^∞ or f_∞ for $n \to \infty$. Then

$$f'(t_n) \to 0, \quad n \to \infty.$$

Definitions of ψ_{n1}, ψ_{n2}, ψ_{n3} and ψ_{na} as used in system (21).

$$\begin{cases} \Psi' & = & \left(\frac{\omega_{12}}{\mu+\omega_{12}}\right)\left(\frac{\omega_{23}}{\mu+\omega_{23}}\right)\left(\frac{\omega_{3a_1}}{\mu+\omega_{3a_1}}\right), \ \psi_{n1} = \frac{1}{\mu+\omega_{12}}, \\ \psi_{n2} & = & \left(\frac{\omega_{12}}{\mu+\omega_{12}}\right)\left(\frac{1}{\mu+\omega_{23}}\right), \ \psi_{na} = \Psi'\left(\frac{1}{\mu+\delta_1}\right), \\ \text{and } \psi_{n3} & = & \left(\frac{\omega_{12}}{\mu+\omega_{12}}\right)\left(\frac{\omega_{23}}{\mu+\omega_{23}}\right)\left(\frac{1}{\mu+\omega_{3a_1}}\right). \end{cases}$$

Parameters used in (23):

$$\begin{aligned} R_c &= \phi_{n1}R_{0n1} + \phi_{n2}R_{0n2} + \phi_{n3}R_{0n3} + \phi_{na_1}R_{0na} + \phi_{t2}R_{0t2} \\ &\quad + \phi_{t3}R_{0t3} + \phi_{ta_2}R_{0ta}, \\ \hat{\Phi} &= \phi_1 + \phi_2 + \phi_3 + \phi_{a_1} + \phi_{22} + \phi_{23} + \phi_{2a}, \end{aligned}$$

where ϕ_1, ϕ_2, ϕ_3 and ϕ_{a_1} are given in (11) and

$$\begin{aligned} \phi_{22} &= \Psi_{23}\left(\frac{\omega_{12}}{\mu+\rho_{23}}\right)\left(\frac{p\theta}{\mu+\theta+\delta_1}\right), \\ \Psi_{23} &= \left(\frac{\omega_{23}}{\mu+\omega_{23}}\right)\left(\frac{\omega_{3a_1}}{\mu+\omega_{3a_1}}\right), \\ \phi_{23} &= \left(\frac{\Psi_{23}\omega_{12}}{\mu+\rho_{3a_2}}\right)\left(\frac{p\theta}{\mu+\theta+\delta_1}\right)\left(\frac{\rho_{23}}{\mu+\rho_{23}}\right), \\ \phi_{2a} &= \frac{\Psi_{23}\omega_{12}\theta}{(\mu+\delta_2)(\mu+\theta+\delta_1)}\left[(1-p) + p\left(\frac{\rho_{23}}{\mu+\rho_{23}}\right)\left(\frac{\rho_{3a_2}}{\mu+\rho_{3a_2}}\right)\right], \\ \phi_{n1} &= 1, \ \phi_{n2} = \left(\frac{\omega_{12}}{\mu+\omega_{12}}\right), \ \phi_{n3} = \left(\frac{\omega_{12}}{\mu+\omega_{12}}\right)\left(\frac{\omega_{23}}{\mu+\omega_{23}}\right), \\ \phi_{na_1} &= \Psi', \ \phi_{t2} = \Psi'\left(\frac{p\theta}{\mu+\theta+\delta_1}\right), \\ \phi_{t3} &= \Psi'\left(\frac{p\theta}{\mu+\theta+\delta_1}\right)\left(\frac{\rho_{23}}{\mu+\rho_{23}}\right), \\ \phi_{ta_2} &= \Psi'\left(\frac{\theta}{\mu+\theta+\delta_1}\right)\left[p\left(\frac{\rho_{23}}{\mu+\rho_{23}}\right)\left(\frac{\rho_{3a_2}}{\mu+\rho_{3a_2}}\right) + (1-p)\right]. \end{aligned}$$

R_{0t} and $\hat{R}_{0t}$ as used in (28):

$$\begin{aligned} R_{0t} &= \Psi'\left(\frac{p\theta}{\mu+\theta+\delta_1}\right)R_{0t2} + \Psi'\left(\frac{p\theta}{\mu+\theta+\delta_1}\right)\left(\frac{\rho_{23}}{\mu+\rho_{23}}\right)R_{0t3} \\ &\quad +\Psi'\left(\frac{\theta}{\mu+\theta+\delta_1}\right)\left[p\left(\frac{\rho_{23}}{\mu+\rho_{23}}\right)\left(\frac{\rho_{3a_2}}{\mu+\rho_{3a_2}}\right)+(1-p)\right]R_{0ta} \\ \hat{R}_{0t} &= \Psi'\left(\frac{p}{\mu+\delta_1}\right)R_{0t2} + \Psi'\left(\frac{p}{\mu+\delta_1}\right)\left(\frac{\rho_{23}}{\mu+\rho_{23}}\right)R_{0t3} \\ &\quad +\Psi'\left[\left(\frac{p}{\mu+\delta_1}\right)\left(\frac{\rho_{23}}{\mu+\rho_{23}}\right)\left(\frac{\rho_{3a_2}}{\mu+\rho_{3a_2}}\right)+\left(\frac{1-p}{\mu+\delta_1}\right)\right]R_{0ta}. \end{aligned}$$

TABLE 2. Parameter values common for all the simulations.

Parameter and symbol	Value	Source
Susceptible recruitment rate (π)	$30000yr^{-1}$	Estimate
Natural removal rate (μ)	0.03	Estimate
AIDS removal rate (δ_1, δ_2)	0.05	[8] and [9]
Progression rates (ω_{12}, ω_{23} and ω_{3a_1})	(13, 0.16 and 0.5) respectively	[8] and [9]
Progression rates : ρ_{23} and ρ_{3a_2} respectively	$g \times (0.16, 0.5)$ $g \in (0,1)$	[8]
Per-partnership probabilities ($\beta_{n1}, \beta_{n2}, \beta_{n3}, \beta_{n4}$)	$(0.4, 0.015, 0.02, 0.2)$ respectively	estimated using [9]
Per-partnership probabilities ($\beta_{t2}, \beta_{t3}, \beta_{t4}$)	$\alpha \times (0.015, 0.02, 0.2)$	$\alpha \in (0,1)$ (estimate)
Partner acquisition rate (c)	2	[28].

Acknowledgments. We would like to thank the University of Botswana, SACEMA and Midlands State University for their support. We are also grateful for the very useful comments from the referees.

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Received February 14, 2008; Accepted November 5, 2008.

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