Nsuami and Witbooi *Advances in Difference Equations* (2018) 2018:11
https://doi.org/10.1186/s13662-017-1458-x

Advances in Difference Equations
a SpringerOpen Journal

RESEARCH Open Access

A model of HIV/AIDS population dynamics including ARV treatment and pre-exposure prophylaxis

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Abstract

Antiretroviral treatment (ART) and oral pre-exposure prophylaxis (PrEP) have recently been used efficiently in management of HIV infection. Pre-exposure prophylaxis consists in the use of an antiretroviral medication to prevent the acquisition of HIV infection by uninfected individuals. We propose a new model for the transmission of HIV/AIDS including ART and PrEP. Our model can be used to test the effects of ART and of the uptake of PrEP in a given population, as we demonstrate through simulations. The model can also be used to estimate future projections of HIV prevalence. We prove global stability of the disease-free equilibrium. We also prove global stability of the endemic equilibrium for the most general case of the model, *i.e.*, which allows for PrEP individuals to default. We include insightful simulations based on recently published South-African data.

MSC: 92D30; 34K20

Keywords: HIV/AIDS model; basic reproduction number; pre-exposure prophylaxis; stability

1 Introduction

The HIV/AIDS epidemic continues to be among the most devastating diseases in human history despite the new scientific advances and serious public health interventions. According to UNAIDS data [1], there has been a significant decline and stabilization in the number of new HIV infections since 2012, but Sub-Saharan Africa is still severely affected and more precisely in this region of the world women comprise more than half of all people living with HIV. In particular, in 2016, South Africa had an estimated 7.03 million of people living with HIV [2], and an incidence rate of up to 4 per 100 women-years [3, 4]. The most significant advance in medical management of HIV infection includes two recommendations [5]. First of all, antiretroviral therapy (ART) should be initiated in everyone living with HIV at any CD4 cell count. The HIV treatment reduces viral load to levels below the limits of detection of the most sensitive clinical assays, resulting in a significant reconstitution of the immune system [6]. The Global AIDS Update 2016 of the Joint United Nations Programme on HIV/AIDS, reports that the global coverage of ART therapy reached approximately 46% at the end of 2015. The gains in treatment are largely responsible for a 26% decline in AIDS-related deaths globally since 2010, from an estimated 1.5 million in

2010, to 1.1 million in 2015. Despite this significant achievement, globally there has been 2 million new infections reported in 2015 [7]. Secondly, the use of daily oral pre-exposure prophylaxis (PrEP) is recommended as a prevention choice for people at high risk of HIV infection. Substantial gaps remain in understanding the trade-offs between costs and benefits of choosing alternative HIV prevention strategies, such as the initiation of PrEP by high-risk uninfected individuals [8]. Following WHO, making PrEP drugs available for safe, effective prevention outside the clinical trial setting is the current challenge. However, it is important to recall and highlight that PrEP is not for everyone: only people who are HIV-negative and at very high risk for HIV infection should take PrEP [9]. In 2015, the Medicines Control Council of South Africa issued a full regulatory approval of PrEP, and the country became the first in Sub-Saharan Africa to include PrEP in its national HIV programme. Globally, female sex workers (FSWs) are 13.5 times more likely to be living with HIV than women in the general population [10]. There are many countries with regulatory approval for PrEP. The European Medicines Agency has also granted market authorization for PrEP to be marketed across the European Union's 28 countries [11].

Mathematical models of the population dynamics of infectious diseases are useful in making forward projections in order to help the public health sector to plan optimally. There is a large literature on mathematical models for communicable diseases. In particular, HIV models that account for the use of PrEP are featured in [12–14]. In [12] for instance, a mathematical model for HIV/AIDS transmission has been proposed, along with a control problem in which the objective was to determine the PrEP strategy that minimizes the number of individuals with pre-AIDS HIV infection, balanced against the costs associated with PrEP. The paper by Mukandavire *et al.* [13] compares the impact of increasing condom use or HIV PrEP use among sex workers. The authors found that condom promotion interventions should remain the mainstay HIV prevention strategy for FSWs, with PrEP only being implemented once condom interventions have been maximized or to fill prevention gaps where condoms cannot be used. In [14], the authors develop a model of HIV risk and compare HIV-risk estimates before and after the introduction of PrEP to determine the maximum tolerated reductions in condom use with regular partners and clients for HIV risk not to change. With a case study of FSWs in South Africa, in [14] it is found that PrEP is likely to be of benefit in reducing HIV risk, even if reductions in condom use do occur. The current paper presents also a significant contribution in this regard. Our aim in this paper is to demonstrate the extent to which PrEP can possibly reduce the prevalence of the HIV in a large population such as South Africa, in the presence of treatment. We introduce a model with two stages of infection and we assume that susceptible individuals have access to PrEP to prevent themselves from HIV. Such individuals become exposed to HIV once they stop taking oral PrEP. The model allows for individuals in the asymptomatic phase to move back to the asymptomatic phase after successful treatment.

The remainder of this paper is set up as follows. In Section 2 we present the model. We calculate the basic reproduction number and prove existence of positive solutions. Section 3 covers both global stability of the disease-free and endemic equilibrium. In Section 4 we provide numerical simulations to illustrate our theoretical results and the utility of the model. In Section 5 we offer some concluding remarks.

2 The model

2.1 Model description

We consider a population with homogeneous mixing of individuals, of size $N(t)$ at time t. The total size $N(t)$ is assumed to be sufficiently large in order to approximate the population as a continuum of points. These are general assumption for modeling with ordinary differential equations; see for instance [15] of Anderson and May. For this model, the population is subdivided into the classes of susceptibles $S(t)$, the asymptomatic phase $I_1(t)$ of HIV, the symptomatic phase $I_2(t)$, the AIDS patients $A(t)$ and the individuals under PrEP $E(t)$, so that

$$N(t) = S(t) + I_1(t) + I_2(t) + A(t) + E(t).$$

The functions $S(t)$, $I_1(t)$, $I_2(t)$, $A(t)$ and $E(t)$ are assumed to be continuous.

We introduce the following parameters that appear in the model equations:

μ	birth and mortality rates by natural causes,
K	the size of the total population when disease-free,
c	the average number of sexual contacts of one individual with others, per unit time,
β_1	the probability of disease transmission in the asymptomatic phase,
β_2	the probability of disease transmission in the symptomatic phase,
ϕ	the proportion of susceptible individuals under PrEP,
θ	the proportion of susceptible individuals who default PrEP,
k_1	progression rate from I_1 to I_2,
k_2	progression rate from the symptomatic phase I_2 to A,
α	the rate of transfer from I_2 to I_1 due to ARV treatment,
δ	disease induced mortality rate.

Our model is then constructed by considering the appropriate in-flow and out-flow rates of each compartment together with parameters in the list above.

$$\begin{aligned}
&\frac{dS}{dt} = \mu K - c(\beta_1 I_1 + \beta_2 I_2)S - (\mu + \phi)S + \theta E,\\
&\frac{dI_1}{dt} = c(\beta_1 I_1 + \beta_2 I_2)S - (\mu + k_1)I_1 + \alpha I_2,\\
&\frac{dI_2}{dt} = k_1 I_1 - (\mu + k_2 + \alpha)I_2,\\
&\frac{dA}{dt} = k_2 I_2 - (\mu + \delta)A,\\
&\frac{dE}{dt} = \phi S - (\mu + \theta)E;\\
&S(0) = S_0 > 0, \qquad I_1(0) = I_{1,0} > 0, \qquad I_2(0) = I_{2,0} > 0,\\
&A(0) = A_0 > 0, \qquad E(0) = E_0 > 0.
\end{aligned} \tag{2.1}$$

The model system (2.1) permits a disease-free equilibrium $\Sigma_0 = (\frac{(\mu+\theta)K}{(\mu+\phi+\theta)}, 0, 0, 0, \frac{\phi K}{(\mu+\phi+\theta)})$ and an endemic equilibrium $\Sigma_* = (S^*, I_1^*, I_2^*, A^*, E^*)$ with the coordinates

$$S^* = \frac{\mu K(\mu + \theta)}{(\mu + \theta)(\lambda + \mu) + \mu\phi},$$

$$I_1^* = \frac{\lambda(\mu + k_2 + \alpha)\mu K(\mu + \theta)}{[(\mu + k_2)(\mu + k_1) + \mu\alpha][(\mu + \theta)(\lambda + \mu) + \mu\phi]},$$
$$I_2^* = \frac{k_1\lambda\mu K(\mu + \theta)}{[(\mu + k_2)(\mu + k_1) + \mu\alpha][(\mu + \theta)(\lambda + \mu) + \mu\phi]},$$
$$A^* = \frac{k_1k_2\lambda\mu K(\mu + \theta)}{[(\mu + k_2)(\mu + k_1) + \mu\alpha][(\mu + \theta)(\lambda + \mu) + \mu\phi]},$$
$$E^* = \frac{\mu K\phi}{(\mu + \theta)(\lambda + \mu) + \mu\phi},$$

where

$$\lambda = c\big(\beta_1 I_1^* + \beta_2 I_2^*\big).$$

Following the method expounded in [16] the basic reproduction number of the model is calculated as

$$\mathcal{R}_0 = \frac{c(\mu + \theta)K(\beta_1(\mu + k_2 + \alpha) + \beta_2 k_1)}{(\mu + \phi + \theta)((\mu + k_1)(\mu + k_2) + \alpha\mu)}.$$

2.2 Feasible solutions

Let us introduce the set Ω,

$$\Omega = \big\{x \in \mathbb{R}^5 \mid x_i > 0, i = 1, 2, 3, 4, 5 \text{ and } x_1 + x_2 + x_3 + x_4 + x_5 < K\big\}.$$

Theorem 2.1 *Assume that $X(t)$ is a solution of the system* (2.1) *with $X(0) \in \Omega$. Then $X(t) \in \Omega$ for all $t > 0$.*

Proof The proof is by contradiction. Let $X(t)$ be a solution of the system (2.1) where $X(0) \in \Omega$. Suppose to the contrary that there exists a $t_0 > 0$ such that $X(t_0) \notin \Omega$. Let $T = \inf\{t > 0 : X(t) \notin \Omega\}$. Since Ω is an open set due to continuity of $X(t)$, T is strictly positive.

Choose $a_0 > 0$ sufficiently small in order to have $a_0 c\beta_1 < \mu$ and $a_0 c\beta_2 < \mu$. Consider the function V_1 defined by

$$V_1(t) = \left(S - a_0 \ln\frac{S}{a_0}\right) + (I_1 - \ln I_1) + (I_2 - \ln I_2) + (A - \ln A) + (E - \ln E). \tag{2.2}$$

Note that, for every $T < t$, each of the five bracketed terms on the right hand side of equation (2.2) are positive while $(S, I_1, I_2, A, E) \in \Omega$.

Now we find an upper bound for the set

$$G = \big\{V_1(t) : 0 < t < T\big\}.$$

We note that, for any $0 < t < T$,

$$\dot{V}_1(t) = \left[\left(1 - \frac{a_0}{S}\right)\big(\mu K - c(\beta_1 I_1 + \beta_2 I_2)S - (\mu + \phi)S + \theta E\big)\right] + \left[\left(1 - \frac{1}{I_1}\right)\big(c(\beta_1 I_1 + \beta_2 I_2)S - (\mu + k_1)I_1 + \alpha I_2\big)\right]$$

$$
\begin{aligned}
&+\left[\left(1-\frac{1}{I_2}\right)\left(k_1I_1-(\mu+k_2+\alpha)I_2\right)\right]\\
&+\left[\left(1-\frac{1}{A}\right)\left(k_2I_2-(\mu+\delta)A\right)\right]+\left[\left(1-\frac{1}{E}\right)\left(\phi S-(\mu+\theta)E\right)\right]\\
&=\mu K-\frac{a_0}{S}\mu K-\mu(S+I_1+I_2+A+E)-\frac{a_0}{S}\theta E+a_0(\mu+\phi)+a_0c(\beta_1I_1+\beta_2I_2)\\
&-\frac{1}{I_1}c(\beta_1I_1+\beta_2I_2)S+(\mu+k_1)-\frac{1}{I_1}\alpha I_2+(\mu+k_2+\alpha)-\frac{1}{A}k_2I_2+(\mu+\delta)\\
&-\frac{1}{E}\phi S+(\mu+\theta)\\
&\leq \mu K-\mu(I_1+I_2)+a_0c(\beta_1I_1+\beta_2I_2)+4\mu+a_0(\mu+\phi)+k_1+k_2+\alpha+\delta+\theta.
\end{aligned}
$$

Note that by the choice of a_0 we have

$$a_0c\beta_1I_1-\mu I_1=I_1(a_0c\beta_1-\mu)<0 \quad \text{and} \quad a_0c\beta_2I_2-\mu I_2=I_2(a_0c\beta_2-\mu)<0.$$

Therefore

$$\dot{V}_1(t)\leq C,$$

where $C=\mu K+4\mu+a_0(\mu+\phi)+k_1+k_2+\alpha+\delta+\theta$.

Integrating from 0 to t yields

$$V_1(t)=V_1(0)+\int_0^t \dot{V}_1(s)\,ds\leq V_1(0)+Ct\leq V_1(0)+CT. \tag{2.3}$$

However, we note that, for any positive constant q,

$$\lim_{x\to 0^+}\left(x-q\ln\frac{x}{q}\right)=\infty.$$

Now further, due to positivity of the bracketed terms on the right hand side of equation (2.2), it follows that

$$\lim_{t\to T} V_1(t)=\infty. \tag{2.4}$$

Equation (2.4) is in conflict with the inequality (2.3). Thus we have arrived at a contradiction. □

3 Stability analysis

3.1 Global stability of the disease-free equilibrium

The following positive numbers are useful in the proof of the global stability of disease-free equilibrium:

$$\xi_1=\mu+k_2+\alpha+k_1\frac{\beta_2}{\beta_1},\qquad \xi_2=\alpha+\frac{\beta_2}{\beta_1}(\mu+k_1),\qquad \xi_4=(\mu+k_1)(\mu+k_2)+\alpha\mu.$$

Theorem 3.1 *If $\mathcal{R}_0<1$, then the disease-free equilibrium Σ_0 of system* (2.1) *is globally asymptotically stable.*

Proof We introduce a number Λ by

$$\Lambda = \frac{(\mu + \theta)K}{\mu + \phi + \theta}.$$

Assuming that $\mathcal{R}_0 < 1$, it is possible to find positive numbers ξ_0 and ξ_3 sufficiently small such as to have the following inequality:

$$C_2 = \xi_0 c\beta_2\Lambda + \xi_3 k_2 + \xi_4(\mathcal{R}_0 - 1) < 0.$$

Using such ξ_0 and ξ_3, together with the numbers ξ_i introduced already, we define a function V_2 as follows:

$$V_2(t) = \xi_0\big[K - (S + E)\big] + \xi_1 I_1 + \xi_2 I_2 + \xi_3 A. \tag{3.1}$$

The time derivative of $V_2(t)$ is given by

$$\begin{aligned}\dot{V}_2(t) = {}& \xi_0\big[-\mu\big(K - (S + E)\big) + c(\beta_1 I_1 + \beta_2 I_2)S\big] + \xi_1\big[c(\beta_1 I_1 + \beta_2 I_2)S - (\mu + k_1)I_1 + \alpha I_2\big] \\ & + \xi_2\big[k_1 I_1 - (\mu + k_2 + \alpha)I_2\big] + \xi_3\big[k_2 I_2 - (\mu + \delta)A\big].\end{aligned}$$

Grouping some terms we have

$$\dot{V}_2(t) \le C_0\big[K - (S + E)\big] + C_1 I_1 + C_2 I_2 + C_3 A,$$

where

$$\begin{aligned}C_0 &= -\mu\xi_0 < 0,\\ C_1 &= \xi_0 c\beta_1\Lambda + \xi_1 c\beta_1\Lambda - (\mu + k_1)\xi_1 + \xi_2 k_1,\\ C_2 &= \xi_0 c\beta_2\Lambda + \xi_1 c\beta_2\Lambda - (\mu + k_2 + \alpha)\xi_2 + \xi_3 k_2 + \xi_1\alpha,\\ C_3 &= -(\mu + \delta)\xi_3 < 0.\end{aligned}$$

Now we show that the coefficients C_1, C_2 are also negative. Firstly, it is easy to see that

$$-(\mu + k_1)\xi_1 + \xi_2 k_1 = -\xi_4 = -\big((\mu + k_1)(\mu + k_2) + \alpha\mu\big).$$

It follows that

$$C_1 = \xi_0 c\beta_1\Lambda + \xi_1 c\beta_1\Lambda - \xi_4 = \xi_0 c\beta_1\Lambda + \xi_4(\mathcal{R}_0 - 1) < 0.$$

Further, notice that

$$-(\mu + k_2 + \alpha)\xi_2 + \xi_1\alpha = -\xi_4\frac{\beta_2}{\beta_1}.$$

Thus, we have

$$\xi_1 c\beta_2\Lambda - \xi_4\frac{\beta_2}{\beta_1} = \xi_4(\mathcal{R}_0 - 1).$$

Therefore,

$$C_2 = \xi_0 c\beta_2 \Lambda + \xi_3 k_2 + \xi_4(\mathcal{R}_0 - 1) < 0,$$

confirming that V_2 is a Lyapunov function. This completes the proof. □

3.2 Global stability of the endemic equilibrium

We investigate global stability of the endemic equilibrium of model (2.1) in the general case, that is, when $\theta \neq 0$ and in particular case, when $\theta = 0$.

Theorem 3.2 *Assume that* $\mathcal{R}_0 > 1$ *and* $\theta E^* < c\beta_1 I_1^* S^*$. *Then the endemic equilibrium* Σ_* *of system* (2.1) *is globally asymptotically stable.*

Proof Consider a function V_3 of the form

$$\begin{aligned} V_3(t) = {} & \left(S - S^* - S^* \ln \frac{S}{S^*}\right) + D_1\left(I_1 - I_1^* - I_1^* \ln \frac{I_1}{I_1^*}\right) \\ & + D_2\left(I_2 - I_2^* - I_2^* \ln \frac{I_2}{I_2^*}\right) + D_3\left(A - A^* - A^* \ln \frac{A}{A^*}\right) \\ & + D_4\left(E - E^* - E^* \ln \frac{E}{E^*}\right), \end{aligned}$$

where D_1, D_2, D_3 and D_4 are positive constants, to be determined at a later stage.

The (endemic) equilibrium values of the system (2.1) satisfy the following equations:

$$\begin{aligned} & \mu K = S^*\left(\beta_1 I_1^* + \beta_2 I_2^*\right)c + (\mu + \phi)S^* - \theta E^*, \\ & (\mu + k_2 + \alpha) = k_1 \frac{I_1^*}{I_2^*}, \\ & (\mu + k_1) = \frac{S^*}{I_1^*}\left(\beta_1 I_1^* + \beta_2 I_2^*\right)c + \alpha \frac{I_2^*}{I_1^*}, \\ & (\mu + \delta) = k_2 \frac{I_2^*}{A^*}, \\ & (\mu + \theta) = \phi \frac{S^*}{E^*}. \end{aligned}$$

The time derivative of $V_3(t)$ is given by

$$\begin{aligned} \dot{V}_3(t) = {} & c\beta_1\left(1 - \frac{S^*}{S}\right)\left(I_1^* S^* - I_1 S\right) + c\beta_2\left(1 - \frac{S^*}{S}\right)\left(I_2^* S^* - I_2 S\right) \\ & + \left(2 - \frac{S}{S^*} - \frac{S^*}{S}\right)S^*(\mu + \phi) + \left(1 - \frac{I_1^*}{I_1}\right)D_1 c\beta_1\left(I_1 S - I_1 S^*\right) \\ & + \left(1 - \frac{I_1^*}{I_1}\right)D_1 c\beta_2\left(I_2 S - I_2^* S^* \frac{I_1}{I_1^*}\right) + \left(E - E^*\right)\theta\left(1 - \frac{S^*}{S}\right) \\ & + D_3\left(1 - \frac{A^*}{A}\right)k_4\left(I_2 - I_2^* \frac{A}{A^*}\right) + D_2\left(I_1 - I_1^* \frac{I_2}{I_2^*}\right)\left(1 - \frac{I_2^*}{I_2}\right)k_3 \\ & + \left(1 - \frac{E^*}{E}\right)D_4\left(S - S^* \frac{E}{E^*}\right)\phi. \end{aligned} \tag{3.2}$$

Let

$$x = \frac{S}{S^*}, \qquad y = \frac{I_1}{I_1^*}, \qquad z = \frac{I_2}{I_2^*}, \qquad v = \frac{A}{A^*}, \qquad w = \frac{E}{E^*}.$$

Then (3.2) becomes

$$\begin{aligned}\dot{V}_3(t) &= S^*(\mu+\phi)\left(2-\frac{1}{x}-x\right) + D_1 c\beta_1 I_1^* S^*\left(1-\frac{1}{y}\right)(xy-y)\\ &\quad + D_1 c\beta_2 I_2^* S^*\left(1-\frac{1}{y}\right)(xz-y)\\ &\quad + D_2 I_1^* k_1\left(1-\frac{1}{z}\right)(y-z) + D_3 I_2^* k_2\left(1-\frac{1}{v}\right)(z-v) + \alpha D_1 I_2^*\left(1-\frac{1}{y}\right)(z-y)\\ &\quad + D_4 k_2\left(1-\frac{1}{w}\right)\phi S^*(x-w) + c\beta_1 I_1^* S^*\left(1-\frac{1}{x}\right)(1-xy)\\ &\quad + \beta_2 I_2^* S^*\left(1-\frac{1}{x}\right)(1-xz) + \left(1-\frac{1}{x}\right)(x-1)\theta E^*. \end{aligned} \tag{3.3}$$

This equation informs a choice of values for the numbers D_i, in order to render V_3 a Lyapunov function. For making our choices, we require the numbers D_i to satisfy the following equations.

$$\begin{aligned}&(D_1-1) = 0,\\ &-D_2 I_1^* k_1 + \alpha D_1 I_2^* + D_3 I_2^* k_2 + c\beta_2 I_2^* S^* = 0,\\ &-D_1 c\beta_1 I_1^* S^* - D_1 c\beta_2 I_2^* S^* + D_2 I_1^* k_1 - \alpha D_1 I_2^* + c\beta_1 I_1^* S^* = 0,\\ &-D_1 c\beta_1 I_1^* S^* + D_4 k_2 \phi S^* + \theta E^* = 0.\end{aligned}$$

This leads us to choose the following D_i-values:

$$D_1 = 1, \qquad D_2 = \frac{c\beta_2 S^* I_2^* + \alpha I_2^*}{k_1 I_1^*}, \qquad D_3 = \frac{D_2 k_1 I_1^* - (c\beta_2 S^* I_2^* + \alpha I_2^*)}{k_2 I_2^*},$$
$$D_4 = \frac{c\beta_1 I_1^* S^* - \theta E^*}{k_2 \phi S^*}.$$

Substituting back the D_i terms in (3.3), we have

$$\begin{aligned}\dot{V}_3(t) &= S^*(\mu+\phi)\left(2-\frac{1}{x}-x\right) + c\beta_2 S^* I_2^*\left(3-\frac{1}{x}-\frac{xz}{y}-\frac{y}{z}\right)\\ &\quad + \alpha I_2^*\left(2-\frac{z}{y}-\frac{y}{z}\right) + \left(c\beta_1 I_1^* S^* - \theta E^*\right)\left(3-w-\frac{1}{x}-\frac{x}{w}\right) \le 0.\end{aligned}$$

This completes the proof. □

In particular, we have the following corollary.

Corollary 3.3 *If $\theta = 0$, then the endemic equilibrium Σ_* of system* (2.1) *is globally asymptotically stable for $\mathcal{R}_0 > 1$.*

Table 1 The following parameters values are fixed

Parameters	Value	Source
α	0.33	[17]
k_1	0.125	[18]
k_2	0.1	[17]
c	3	*cf.* [19, 20]
δ	0.279	[2]
μ	$\frac{1}{62.4}$	[2]
ϕ	0.01	Nominal
θ	0.001	Nominal

4 Numerical simulation

The model can be used to test the efficiency of a given intervention. In particular, authorities may want to see the effect of, for example, expanding the use of PrEP. Thus, simulations in this context will also be shown.

We illustrate the analytical results by way of numerical simulations with the parameters applicable to South Africa as in Table 1.

4.1 Details on estimation of parameters

In [19, 20] for instance, the average number of sexual partners per given time denoted by c is determined; values ranging from 1 to 2 for a specific case. In our case we find it convenient to take $c = 3$. We expect the inequality $\beta_1 < \beta_2$ to hold since the intensity of disease transmission in the symptomatic phase exceeds that of the asymptomatic phase. In the year 2016, the life expectancy in South Africa was estimated at 62.4 years; see for instance [2]. The mortality rate μ is simply the inverse of the life expectancy, and thus $\mu = \frac{1}{62.4}\text{year}^{-1}$. The parameter K is the size of the population when it is free from HIV. According to [2], in 2016 South Africa had an estimated total population 55.91 million. Thus we consider it reasonable to choose $K = 56$ million. We assume that 1% of the susceptible individuals take PrEP, that is, $\phi = 0.01$ and the default rate takes the value $\theta = 0.001$.

4.2 Initial conditions

For initial conditions, we first refer to the South African statistical release [2] of 2016 in order to do some projections.

Let us denote the time 25 August 2016 by t_0. We note that

$$N(t_0) = S(t_0) + I_1(t_0) + I_2(t_0) + A(t_0) + E(t_0).$$

An estimated 7.03 million of the total population were infected with HIV/AIDS in 2016. This number can be split between the classes of $I_1(t_0)$, $I_2(t_0)$ and $A(t_0)$. We shall then use the parameters listed in Table 1 below to find a suitable equilibrium point to split the numbers between the classes of $I_1(t_0)$, $I_2(t_0)$ and $A(t_0)$. In this process we keep varying the value of β_1 and β_2 in order to vary the value of the basic reproduction number. This method leads to the following initial values for our simulations:

$$I_{1,0} = 5.11, \qquad I_{2,0} = 1.43, \qquad A_0 = 0.48.$$

We note that in endemic equilibrium,

$$E^* = \frac{\phi}{\mu + \theta} S^*.$$

Therefore, we consider it reasonable to use the initial value

$$E(t_0) = \frac{1}{50}\frac{\phi}{\mu+\theta}S(t_0).$$

This consideration leads us to assign initial values to S_0 and E_0, and thus our initial state for these two variables are taken as:

$$S_0 = 46.18, \qquad E_0 = 1.12.$$

4.3 Simulations on the effect of PrEP

In the following we show the trajectories of $I_1(t)$, $I_2(t)$, $A(t)$ of the model for $\phi = 0.01$ in Figure 1, and in Figure 2 the trajectories of $I_2(t)$ for different values of ϕ, $\phi = 0.01, 0.02, 0.03$. For the different values of ϕ, the corresponding value of $\mathcal{R}_0$ will be denoted by $\mathcal{R}_0(\phi)$.

In both Figure 1 and Figure 2 we have chosen the values: $\beta_1 = 0.000481$, $\beta_2 = 0.000581$. In Figure 1 we compute the basic reproduction number, $\mathcal{R}_0(0.01) = 1.401 > 1$. The trajectories show that the disease is prevailing at the endemic level. We also compute the endemic equilibrium values $I_1^* = 5.28$, $I_2^* = 1.48$ and $A^* = 0.50$ (in millions). In Figure 2, we show the graph of $I_2(t)$ with different values of ϕ. In the case $\phi = 0.02$, the basic reproduction number reduces to $\mathcal{R}_0(0.02) = 1.021$. This is due to increasing uptake of PrEP from 0.01 to 0.02, and we observe that the increase in the uptake of PrEP has decreased the basic reproduction number and the class of $I_2(t)$. The equilibrium value is computed as $I_2^* = 0.12$. The same scenario is also very well observed in the simulation for the case where

Figure 1 Population dynamics of the model for the case $\phi = 0.01$.

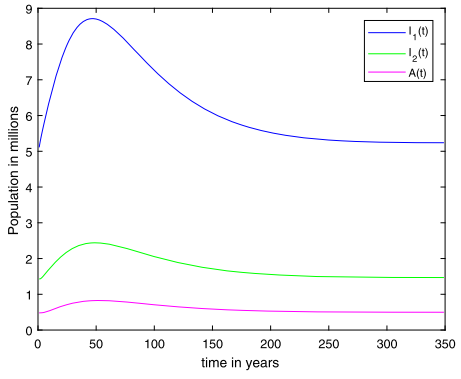
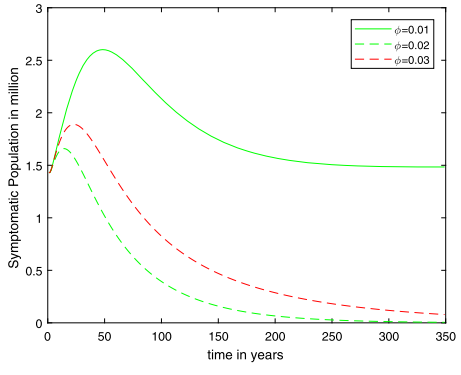


Figure 2 Comparing the class of symptomatic infectives, I_2, for different values of ϕ.



$\phi = 0.03$. In this case, the basic reproduction number is found to be below unity, that is, $\mathcal{R}_0(0.02) = 0.8039$. The class of $I_2(t)$ converges to zero. We note I_2^* is a decreasing function of ϕ. We note that also the long term (or asymptotic) values of I_1 and A are decreasing functions of ϕ.

5 Concluding remarks

In this paper, we have investigated a model describing the population dynamics of HIV/AIDS including treatment and pre-exposure prophylaxis (PrEP) in the context of South Africa. We proved global stability of disease-free and endemic equilibria, Theorem 2.1 and Theorem 3.2, respectively. Our analytical results and our sample simulations are quite meaningful as we work with the current HIV trend in South Africa. We showed the substantial impact that treatment has on the incidence, prevalence and mortality due to AIDS. Managing HIV with early treatment can decrease transmission and possibly decrease the number of AIDS-related deaths. Our model quantifies how the use of PrEP potentially reduces the number of new HIV infections, and this has been well observed in the sample simulations. South Africa has a wide range of its population being exposed to HIV. Its high-risk sections of the population include adolescent girls and young women, sex workers, men who have sex with men (MSM), discordant couples and truckers, all of whom face various barriers to access including stigma, criminalization and lack of supportive service delivery infrastructure [21]. If they are to be the focal point for PrEP, it will be imperative to assess how best to introduce PrEP into programmes where these high-risk sections of the population can be supported [22].

Competing interests
The authors declare that there is no conflict of interest regarding the publication of this paper.

Authors' contributions
The main idea of this paper was proposed by MUN. MUN did most of the proofs of results, in consultation with PJW, and prepared the first draft. The final form of the paper was a joint effort. Both authors read and approved the final manuscript.

Publisher's Note

Received: 15 October 2017 Accepted: 27 December 2017 Published online: 11 January 2018

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