Journal of Mathematical Modeling
Vol. -, No. -, 2021, pp. -

JMM

A stochastic model for HIV with the use of PrEP

Mozart Umba Nsuami* **, Peter Joseph Witbooi**
Department of Mathematics and Applied Mathematics, University of the Western Cape, Private Bag X17, Bellville 7535, Republic of South Africa
Email(s): mnsuami@uwc.ac.za, pwitbooi@uwc.ac.za

Abstract. Pre-exposure prophylaxis (PrEP) has become a promising strategy used by uninfected individuals for the HIV prevention. The risk of infection with HIV after exposure to the virus can be understood through a stochastic framework. In this research we present a stochastic model for HIV/AIDS epidemic with the use of prophylaxis and we show that the model with random perturbation has a unique global positive solution. For a special case, we introduce an analogue, $\mathcal{R}_\sigma$, of the basic reproduction number. This invariant features in a theorem on almost sure exponential stability. Our results show that the disease goes extinct exponentially and almost surely whenever $\mathcal{R}_\sigma$ stays below unity. Simulations serve to illustrate various phenomena.

Keywords: HIV/AIDS stochastic model, basic reproduction number, pre-exposure prophylaxis, almost sure exponential stability, extinction.
AMS Subject Classification 2010: 92D30, 34K20.

1 Introduction

Truvada pre-exposure prophylaxis (PrEP) is an antiretroviral (ARV) pill that combines two ARV drugs, tenofovir disoproxil fumarate (TDF) and emtricitabine (FTC), and has well-established efficacy in reducing the risk of contracting HIV if taken daily [12]. This pre-exposure prophylaxis (PrEP) is used as an antiretroviral medication by uninfected people to prevent them from acquisition of HIV[1]. However, PrEP is different from post-exposure prophylaxis (PEP) which is currently being used as a way to prevent HIV infection after a recent possible exposure to HIV and PEP consists of the in-take of antiretroviral drugs for, usually, 28 days[2]. PrEP is considered to be one of the five pillars by the Joint United Nations Programme on HIV and AIDS (UNAIDS) to drastically reduce HIV transmission. In general, AIDS related death cases have been reduced due to extensive availability of ARV treatment and the use of PrEP. The level of efficacy varied according to differences in adherence within and across the study populations, with Men Who

*Corresponding author.
Received: 20 June 2020 / Revised: 15 December 2021 / Accepted: 1 February 2021
DOI: 10.22124/jmm.2021.16870.1461

[1] https://www.who.int/hiv/topics/prep/en/ [Access date 05 September 2019]
[2] http://aidsmap.com/about-hiv/post-exposure-prophylaxis-pep [Access date 08 July 2019]

Have Sex With Men (MSM) showing higher levels of efficacy than found in the women-only studies [6]. The World Health Organization (WHO) recommended that PrEP should be offered as an additional prevention option for people at substantial risk of HIV infection[3]. In South Africa, sex workers constitute an undeniable risk of HIV infection in everyday reality. According to the South African (SA) Human Sciences Research Council's report women aged 15-25 years are most at risk of contracting HIV [21]. The report informs the Higher Education, the National Department of Health and other training programmes involved with HIV/AIDS on the necessity of rolling out Truvada across universities and colleges because students are also considered as a high-risk section. The roll-out of Truvada aims to offer a better protection against HIV especially to population at high risk of infection if there is a sufficient adherence. In South Africa PrEP was first introduced into sites for female sex workers (FSWs) in June 2016, then into sites for MSM in April 2017, into university sites for young students in October 2017, and most recently in May 2018 into general sites for young people[4].

Epidemics are inevitably affected by environmental random noise, which is an important factor to be taken into account by mathematical models, providing an additional degree of realism in comparison to their deterministic counterparts [20]. A considerable amount of research has been found in the literature which describes the effects of PrEP or PEP on the population dynamics of HIV in the form of modeling with ordinary differential equations or stochastic differential equations. Some of these topics are discussed in [2, 4, 5, 18]. Djomegni et al. [4] propose a mathematical model to understand the transmission dynamics of HIV/AIDS in an environment. Their investigation reveals that when there is both high awareness and high efficacy of PrEP (pre-exposure prophylaxis) use, increasing the efficacy of PrEP use, drastically decreases the basic reproduction number. Djordjevic et al. [5] propose a stochastic epidemic model and prove conditions under which extinction or persistence in mean would hold. Conway et al. [2] present simple theoretical models of HIV dynamics, and apply these models to understand how drug prophylaxis can act to reduce the risk of infection. In this regard, the authors work with stochastic models based on continuous-time branching processes to compute the risk of infection under different scenarios. The paper by Pinto et al. [18] proposes a fractional order model to study the efficacy of the Post-Exposure Prophylaxis (PEP) in human immunodeficiency virus (HIV) within-host dynamics, in the presence of the HIV latent reservoir. In their research the authors focus on the dosage and dosage intervals of antiretroviral therapy (ART) during PEP and in the role of the latent reservoir in HIV infected patients. The papers [3, 7, 19] show that stochastic perturbations can further improve the stability of the disease-free equilibrium for the specific models.

The current paper demonstrates and quantifies how the use of PrEP leads to reducing new infections, and even in the presence of minor stochastic perturbations. The rest of the paper is set up as follows. In Section 2, we describe the model as a system of stochastic differential equations and prove positivity. In Section 3 we present a theorem on almost sure exponential stability for the case of disease-free equilibrium. We provide numerical simulations to in Section 4. In Section 5 we present some concluding remarks.

[3]World Health Organisation. Guideline on When to Start Antiretroviral Therapy and on Pre-Exposure Prophylaxis for HIV. Geneva: World Health Organization, 2015.

[4]Report from the 22nd International AIDS Conference (AIDS 2018), Amsterdam, July 2018.

2 Model description

2.1 Overview of the underlying deterministic model

Our stochastic model is based on the deterministic model in [13]. We first divide the force of infection of the model in [13] by the total population N and we introduce a function Γ which denotes the drug efficacy. The refined underlying deterministic model has been constructed by considering the appropriate in-flow and out-flow rates of each compartment together with parameters listed in the diagram below:

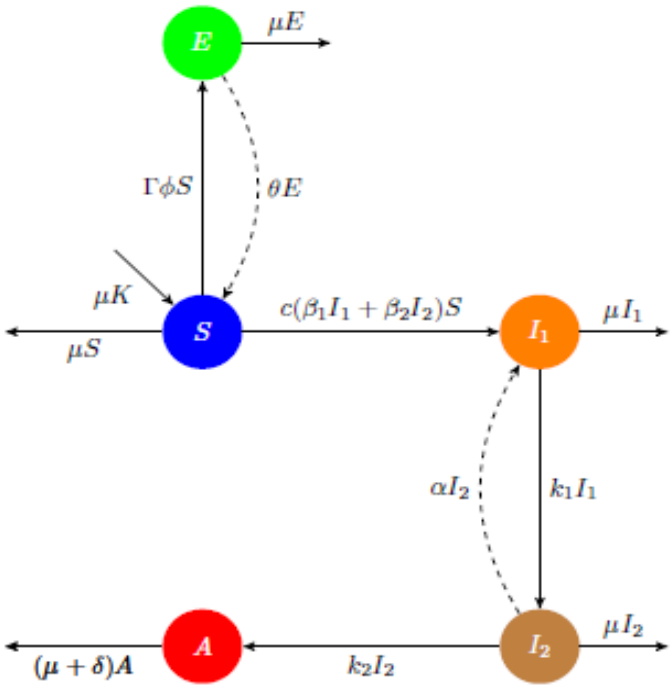

Figure 1: Flow diagram of HIV/AIDS model with PrEP

$$\begin{aligned}
\frac{dS}{dt} &= \mu K - c(\beta_1 I_1 + \beta_2 I_2)S - (\mu + \Gamma\phi)S + \theta E,\\
\frac{dI_1}{dt} &= c(\beta_1 I_1 + \beta_2 I_2)S - (\mu + k_1)I_1 + \alpha I_2,\\
\frac{dI_2}{dt} &= k_1 I_1 - (\mu + k_2 + \alpha)I_2,\\
\frac{dA}{dt} &= k_2 I_2 - (\mu + \delta)A,\\
\frac{dE}{dt} &= \Gamma\phi S - (\mu + \theta)E,
\end{aligned} \tag{1}$$

with $S(0) = S_0 > 0$, $I_1(0) = I_{1,0} > 0$, $I_2(0) = I_{2,0} > 0$, $A(0) = A_0 > 0$, $E(0) = E_0 > 0$.

For the mathematical formulation of the model, we use the following notations:

μ : Birth and mortality rates by natural causes,
K : Size of the total population,
c : An individual's average number of sexual contacts with others per unit time,
β_1 : Probability of disease transmission in the asymptomatic phase,
β_2 : Probability of disease transmission in the symptomatic phase,
ϕ : Proportion of susceptible individuals under PrEP,
θ : 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 : Rate of transfer from I_2 to I_1 due to ARV treatment,
δ : Disease induced mortality rate,
Γ : The drug efficacy,

The basic reproduction number of the deterministic model (1) is computed as

$$\mathcal{R}_0 = \frac{c(\mu+\theta)K\beta_1 b_1}{(\mu+\Gamma\phi+\theta)b_4}, \tag{2}$$

where $b_1 = \mu + k_2 + \alpha + k_1\frac{\beta_2}{\beta_1}$ and $b_4 = (\mu+k_1)(\mu+k_2) + \alpha\mu)$.

The function Γ provides the information on how susceptible individuals at high-risk section respond or default to PrEP programme. We assume that the drug has the ability to produce the desired result (efficacy) after a certain clinical trial. In fact, the PrEP effectiveness is also directly linked to an individual's proper adherence to the programme. Thus, a complete adherence to the PrEP programme indicates a big change in infection risk. However, in real life, a minor default rate to the PrEP programme is inevitable. The default can result by the necessity for daily drug intake, which often makes it difficult for individual to comply with the PrEP programme and the cost of PrEP to adhere to the once-daily regimen. The default rate θ takes this form: $\theta = f^{-1}[\Gamma]$. In fact, Γ serves the basis for the calculation of θ and vice versa. Therefore, in our sample simulations, we choose the default rate to be $\theta = -0.01\Gamma + 0.0101$ for Γ highly effective (100%). An increase in the default rate does not necessary mean the drug did not produce its effect, but rather the medication was not used effectively.

2.2 HIV stochastic model

Throughout this paper we assume to have a complete probability space $(\Omega, \mathcal{F}, \mathbb{P})$ with a filtration, $\{\mathcal{F}_t\}_{t\geq 0}$, that is right continuous and with $\mathcal{F}_0$ containing all the subsets having measure zero.

Consider an equation of the form (3) below, for an k-dimensional Brownian motion $B(t)$ on Ω.

$$dx(t) = f(t,x)dt + g(t,x)dB(t) \;\; t \geq 0. \tag{3}$$

A solution with initial value $x(0) = x_0$ is denoted by $x(t, x_0)$. Assume that $f(t,0) = g(t,0) = 0$ for all $t \geq 0$, so the origin point is an equilibrium of (3).

By $\mathcal{L}$ we denote the infinitesimal generator of an equation of the form (3), see [17] of Øksendal, defined for a function $V(t,x) \in C^{1,2}(\mathbb{R}_+ \times \mathbb{R}^k)$.

We introduce white noise type stochastic perturbations directly proportional to the classes S, I_1, I_2, A and E into the model system (1). Let $B(t) = (B_0(t), B_1(t), B_2(t), B_3(t), B_4(t))$ be a 5-dimensional Brownian motion $B(t)$ defined on the given probability space. The components of the 5-dimensional Brownian motion B_i are assumed to be mutually independent. The non-negative constants $\sigma_0, \sigma_1, \sigma_2$, σ_3 and σ_4 symbolize the intensities of the stochastic perturbations. We have the following stochastic model:

$$\begin{aligned} dS(t) &= [\mu K - \lambda S(t) - (\mu + \Gamma\phi)S + \theta E]dt + \sigma_0 S(t)dB_0(t), \\ dI_1(t) &= [\lambda S(t) - (\mu + k_1)I_1(t) + \alpha I_2(t)]dt + \sigma_1 I_1(t)dB_1(t), \\ dI_2(t) &= [k_1 I_1(t) - (\mu + k_2 + \alpha)I_2(t)]dt + \sigma_2 I_2(t)dB_2(t), \\ dA(t) &= [k_2 I_2 - (\mu + \delta)A]dt + \sigma_3 A(t)dB_3(t), \\ dE(t) &= [\Gamma\phi S - (\mu + \theta)E]dt + \sigma_4 E(t)dB_4(t), \end{aligned} \tag{4}$$

where $\lambda = c(\beta_1 I_1(t) + \beta_2 I_2(t))$.

Let us define the following notation:

$$\mathbb{R}^n_{++} = \{x \in \mathbb{R}^n | x_i > 0 \text{ for all } i = 1, 2, .., n\}. \tag{5}$$

In what follows we now show that solutions of (4) exist globally and are (a.s) positive and (a.s) bounded over compact intervals. We follow a methodology that has been popularly used, [11, 14, 15] for instance.

Theorem 1. *For any initial value $(S(0), I_1(0), I_2(0), A(0), E(0)) \in \mathbb{R}^5_{++}$ of model (4), there is (a.s) a unique positive solution $(S(t), I_1(t), I_2(t), A(t), E(t))$ on the interval $t \in [0, \infty)$.*

Proof. All the coefficients of the system (4) are locally Lipschitz continuous. Thus there exists a unique local solution on $t \in [0, \tau_e)$, where τ_e is the explosion time. We show the solution is global almost surely, that is, we prove that $\tau_e = \infty$ a.s.

Let $n_0 > 0$ be sufficiently large such that $S(0), I_1(0), I_2(0), A(0)$ and $E(0)$ sit in the interval $[1/n_0, n_0]$. A sequence of stopping times is defined as follows:

$$\begin{aligned} \tau_n = \inf \Big\{ & t \in [0, \tau_e) : \min\{S(t), I_1(t), I_2(t), A(t), E(t)\} \leq \frac{1}{n} \\ & \text{or } \max\{S(t), I_1(t), I_2(t), A(t), E(t)\} \geq n \Big\}, \end{aligned}$$

and with our conventional notation $\inf\emptyset = \infty$. It is obvious that τ_n increases. We write $\tau_\infty = \lim_{n\to\infty} \tau_n$, and we note that $\tau_\infty \leq \tau_e$ (a.s.). It suffices to show that

$$\tau_\infty = \infty \text{ a.s.}, \tag{6}$$

and then $\tau_e = \infty$ a.s., so $(S(t), I_1(t), I_2(t), A(t), E(t)) \in \mathbb{R}^5_{++}$ for all $t \geq 0$ almost surely (a.s.). Now suppose that (6) is not true. Then, there exists $T > 0$ and $\epsilon \in (0, 1)$ such that

$$\mathbb{P}\{\tau_\infty \leq T\} > \epsilon. \tag{7}$$

Thus, there is an integer $n_1 \geq n_0$ such that

$$\mathbb{P}\{\tau_n \leq T\} \geq \epsilon \quad \forall n \geq n_1.$$

Consider the function V_1 defined by

$$V_1(S, I_1, I_2, A, E) = \Big(S - a_0 - a_0 \ln \frac{S}{a_0}\Big) + \Big(I_1 - 1 - \ln I_1\Big) + \Big(I_2 - 1 - \ln I_2\Big) + \Big(A - 1 - \ln A\Big) + \Big(E - 1 - \ln E\Big).$$

Note that each of the five bracketed terms are non-negative while $(S, I_1, I_2, A, E) \in \mathbb{R}^5_{++}$. Choose $a_0 > 0$ sufficiently small in order to have $a_0 c\beta_1 < \mu$ and $a_0 c\beta_2 < \mu$. By applying the Itô's formula we have,

$$\begin{aligned} dV_1(S, I_1, I_2, A, E) &= \mathcal{L}V_1 dt + (S - a_0)\sigma_0 dB_0(t) + (I_1 - 1)\sigma_1 dB_1(t) \\ &\quad + (I_2 - 1)\sigma_2 dB_2(t) + (A - 1)\sigma_3 dB_3(t) \\ &\quad + (E - 1)\sigma_4 dB_4(t), \end{aligned} \tag{8}$$

where

$$\begin{aligned} \mathcal{L}V_1 &= \Big[\big(1 - \frac{a_0}{S}\big)\big(\mu K - \lambda S(t) - (\mu + \Gamma\phi)S + \theta E\big)\Big] + \Big[\big(1 - \frac{1}{I_1}\big) \times \\ &\quad \big(c(\beta_1 I_1 + \beta_2 I_2)S - (\mu + k_1)I_1 + \alpha I_2\big)\Big] + \Big[(1 - \frac{1}{I_2})(k_1 I_1 - (\mu + k_2 + \alpha)I_2)\Big] \\ &\quad + \Big[(1 - \frac{1}{A})(k_2 J - (\mu + \delta)A)\Big] + \Big[(1 - \frac{1}{E})(\Gamma\phi S - (\mu + \theta)E)\Big] \\ &\quad + \frac{1}{2}\left(a_0\sigma_0^2 + \sigma_1^2 + \sigma_2^2 + \sigma_3^2 + \sigma_4^2\right) \\ &= \mu K - \frac{a_0}{S}\mu K - \mu(S + I_1 + I_2 + A + E) - \frac{a_0}{S}\theta E + a_0(\mu + \Gamma\phi) \\ &\quad + a_0 c(\beta_1 I_1 + \beta_2 I_2) - \frac{1}{I_1}c(\beta_1 I_1 + \beta_2 I_2)S + (\mu + k_1) - \frac{1}{I_1}\alpha I_2 \\ &\quad + (\mu + k_2 + \alpha) - \frac{1}{A}k_2 J + (\mu + \delta) - \frac{1}{E}\Gamma\phi S + (\mu + \theta) \\ &\quad + \frac{1}{2}\left(a_0\sigma_0^2 + \sigma_1^2 + \sigma_2^2 + \sigma_3^2 + \sigma_4^2\right), \\ \mathcal{L}V_1 &\leq \mu K - \mu(I_1 + I_2) + a_0 c(\beta_1 I_1 + \beta_2 I_2) + 4\mu + a_0(\mu + \Gamma\phi) + k_1 + k_2 \\ &\quad + \alpha + \delta + \theta + \frac{1}{2}\left(a_0\sigma_0^2 + \sigma_1^2 + \sigma_2^2 + \sigma_3^2 + \sigma_4^2\right). \end{aligned}$$

By the choice of a_0 we have:

$$a_0 c\beta_1 I_1 - \mu I_1 = I_1\left(a_0 c\beta_1 - \mu\right) < 0 \text{ and } a_0 c\beta_2 I_2 - \mu I_2 = I_2\left(a_0 c\beta_2 - \mu\right) < 0.$$

Therefore

$$\mathcal{L}V_1 \leq C,$$

where

$$\begin{aligned} C &= \mu K + 4\mu + a_0(\mu + \Gamma\phi) + k_1 + k_2 + \alpha + \delta + \theta \\ &\quad + \frac{1}{2}\left(a_0\sigma_0^2 + \sigma_1^2 + \sigma_2^2 + \sigma_3^2 + \sigma_4^2\right) \end{aligned}$$

is a constant.

The rest of the proof is similar and we omit. At the end we deduce that $\tau_\infty = \infty$. This completes the proof. □

Proposition 1. *If $\sigma_0 = 0$ and $\sigma_4 = 0$, then (a.s.), $S(t) + E(t) \leq K$ for all $t > 0$.*

Proof. If $\sigma_0 = \sigma_4 = 0$, then

$$\begin{aligned} d(K - S(t) - E(t)) &= -\mu K + \lambda S(t) + \mu(S(t) + E(t)) \\ &\geq -\mu(K - S(t) - E(t)) \ (a.s.), \end{aligned}$$

since by Theorem 1, $\lambda S(t) > 0$ for all t $(a.s.)$. Therefore, since $K - S(0) - E(0) \geq 0$, it follows that $K - S(t) - E(t) \geq 0$ for all $t > 0$ $(a.s.)$. This implies also that $S \leq K$. □

3 Almost sure exponential stability

The following subset Φ of sample paths will be of interest:

$$\Phi = \left\{\omega \in \Omega | \, (S(t,\omega), I_1(t,\omega), I_2(t,\omega), A(t,\omega), E(t,\omega)) \in \mathbb{R}^5_{++} \text{ for all } t \geq 0\right\}.$$

From Theorem 1 it follows that $\mathbb{P}(\Omega \backslash \Phi) = 0$. In the remainder of this section we assume that sample paths are restricted to Φ.

Definition 1. *(see [11]). The equilibrium $x = 0$ of the system (3) is said to be almost surely exponentially stable if for all $x_0 \in \mathbb{R}^n$,*

$$\limsup_{t\to\infty} \frac{1}{t} \ln |x(t, x_0)| < 0 \text{ a.s.}$$

In the following, we introduce some more concepts leading to our main theorem on almost sure exponential stability. Assuming that $\sigma_0 = \sigma_4 = 0$, then the model system (4) exhibits a disease-free equilibrium

$$E_0 = (\frac{(\mu+\theta)K}{(\mu+\Gamma\phi+\theta)}, 0, 0, 0, \frac{\Gamma\phi K}{(\mu+\Gamma\phi+\theta)}).$$

Remark 1. *We introduce the new invariant $\mathcal{R}_\sigma$ for the model, that will serve as an indicator of stability. To this end we require a function $h : (0, 1] \to \mathbb{R}_+$, and we fix two numbers b_1 and b_2:*

$$b_1 = \left(\mu + k_2 + \alpha + k_1 \frac{\beta_2}{\beta_1}\right), \quad b_2 = \left(\alpha + \frac{\beta_2}{\beta_1}(\mu + k_1)\right).$$

Now let h be given by the formula

$$h(x) = \frac{(\sigma_1 x)^2 + (\sigma_2(1-x))^2}{x/b_1 + \frac{\beta_2}{\beta_1}(x-1)/b_2}. \tag{9}$$

Note that for $x \in (0,1]$, the denominator of this expression will always be positive. We also note that $\lim_{x\to 0^+} h(x) \neq 0$. Therefore, h has a least value, h_*, which is positive. The positivity of h_* is important and we define:

$$\mathcal{R}_\sigma = \frac{c(\mu+\theta)K\beta_1(\mu+k_2+\alpha+k_1\frac{\beta_2}{\beta_1})}{(\mu+\Gamma\phi+\theta)(b_4+h_*/2)}$$

We define, for any b_0, b_1, b_2, b_3

$$Z(t) = b_0(K-(S(t)+E(t)) + b_1I_1(t) + b_2I_2(t) + b_3A(t), \tag{10}$$

and let $V_2(t) = \ln Z(t)$. For a stochastic process $x(t)$ we write

$$\langle x\rangle_t = \frac{1}{t}\int_0^t x(s)ds.$$

Proposition 2. *Consider the model system (4) in the special case that $\sigma_0 = \sigma_4 = 0$. The disease-free equilibrium is almost surely exponentially stable if*

$$\limsup_{t\to\infty} \langle \mathcal{L}V_2(X)\rangle_t < 0 \quad \text{(a.s.)}.$$

Proof. We start off by noting that

$$V_2(X(t)) = V_2(X(0)) + \int_0^t \mathcal{L}V_2(X(u))du + M_t,$$

where

$$\begin{aligned} M_t = \int_0^t \Bigg(& -b_0\sigma_0\frac{S(u)}{Z(X(u))}dB_0(u) + b_1\sigma_1\frac{I_1(u)}{Z(X(u))}dB_1(u) + b_2\sigma_2\frac{I_2(u)}{Z(X(u))}dB_2(u) \\ & + b_3\sigma_3\frac{A(u)}{Z(X(u))}dB_3(u) - b_0\sigma_4\frac{E(u)}{Z(X(u))}dB_4(u)\Bigg) \end{aligned}$$

The strong law of large numbers for local martingales, see [11, p12] for instance, implies that

$$\lim_{t\to\infty}\frac{1}{t}M_t = 0 \text{ (a.s.)}.$$

Also, we observe that

$$\lim_{t\to\infty}\frac{1}{t}V_2(X(0)) = 0.$$

Therefore

$$\limsup_{t\to\infty}\frac{1}{t}V_2(X(t)) = \limsup_{t\to\infty}\frac{1}{t}\int_0^t \mathcal{L}V_2(X(u))du = \limsup_{t\to\infty}\langle \mathcal{L}V_2(X)\rangle_t \quad \text{(a.s.)}.$$

This completes the proof. □

We now calculate $\mathcal{L}V_2$ for the special case that $\sigma_0 = \sigma_4 = 0$. .

$$\begin{aligned}\mathcal{L}V_2 = & -\mu b_0\frac{[K-(S+E)]}{Z} + \frac{I_1}{Z}[(b_0+b_1)c\beta_1 S - b_1(\mu+k_1)+b_2k_1] \\ & +\frac{I_2}{Z}[(b_0+b_1)c\beta_1 S + b_1\alpha - b_2(\mu+k_2+\alpha)+b_3k_2] \\ & -b_3(\mu+\delta)\frac{A}{Z} - \frac{1}{2Z^2}\left(b_1^2\sigma_1^2I_1^2 + b_2^2\sigma_2^2I_2^2 + b_3^2\sigma_3^2A^2\right). \end{aligned} \tag{11}$$

By [19, Lemma 2.3], for every sample path w of the Wiener process $W(t)$, there exists an unbounded increasing sequence t_n of positive time values for which

$$\limsup_{t\to\infty}\mathcal{L}V_2(t,w) = \lim_{n\to\infty}\mathcal{L}V_2(t_n,w),$$

and for which we can define the following limits:

$$s = \lim_{n\to\infty}\langle S\rangle_{t_n}, \quad i_1 = \lim_{n\to\infty}\left\langle\frac{I_1}{Z}\right\rangle_{t_n}, \quad i_2 = \lim_{n\to\infty}\left\langle\frac{I_2}{Z}\right\rangle_{t_n}, \quad a = \lim_{n\to\infty}\left\langle\frac{A}{Z}\right\rangle_{t_n},$$

and

$$q = \lim_{n\to\infty}\left\langle\frac{K-(S+E)}{Z}\right\rangle_{t_n}.$$

In particular we note the identity

$$b_0q + b_1i_1 + b_2i_2 + b_3a = 1, \tag{12}$$

and the fact:

$$b_0q, b_1i_1, b_2i_2, b_3a \in [0,1].$$

We define $F(b)$ as:

$$F(b) = F(b_0,b_1,b_2,b_3) = \limsup_{t\to\infty}\mathcal{L}V_2(t).$$

Then $F(b)$ takes the form:

$$\begin{aligned}F(b) = & -\mu b_0q + [(b_0+b_1)c\beta_1 s - b_1(\mu+k_1)+b_2k_1]i_1 \\ & +[(b_0+b_1)c\beta_1 s + b_1\alpha - b_2(\mu+k_2+\alpha)+b_3k_2]i_2 \\ & -b_3(\mu+\delta)a - \frac{1}{2}\left(b_1^2\sigma_1^2i_1^2 + b_2^2\sigma_2^2i_2^2 + b_3^2\sigma_3^2a^2\right) \end{aligned} \tag{13}$$

Noting that $s < K$. We drop the last term in (13) $-\frac{1}{2}b_3^2\sigma_3^2a^2$, then we obtain the inequality

$$\begin{aligned}F(b) \le & -\mu b_0q + [(b_0+b_1)c\beta_1 K - b_1(\mu+k_1)+b_2k_1]i_1 \\ & +[(b_0+b_1)c\beta_1 K + b_1\alpha - b_2(\mu+k_2+\alpha)+b_3k_2]i_2 \\ & -b_3(\mu+\delta)a - \frac{1}{2}\left(b_1^2\sigma_1^2i_1^2 + b_2^2\sigma_2^2i_2^2\right) \end{aligned} \tag{14}$$

Theorem 2. *Consider the model system (4) in the special case that $\sigma_0 = \sigma_4 = 0$. If*

$$\mathcal{R}_\sigma < \frac{\mu+\theta}{\mu+\Gamma\phi+\theta},$$

then $(I_1(t), I_2(t))$ converges exponentially to $(0,0)$ (a.s.)

Proof. Consider $b = (0, b_1, b_2, 0)$ from V_2. Then equation (13) yields

$$\begin{aligned} F(b) \leq\ & b_1 cK(\beta_1 i_1 + \beta_2 i_2) + [-b_1(\mu+k_1) + b_2 k_1] i_1 \\ & + [b_1\alpha - b_2(\mu + k_2 + \alpha)] i_2 \\ & - \frac{1}{2}\left(b_1^2\sigma_1^2 i_1^2 + b_2^2\sigma_2^2 i_2^2\right), \end{aligned} \tag{15}$$

Now we observe that if we write $x = b_1 i_1$ and note that $b_2 i_2 = 1 - x$, then

$$\begin{aligned} (b_1\sigma_1 i_1)^2 + (b_2\sigma_2 i_2)^2 &= (i_1 + i_2\frac{\beta_2}{\beta_1})\left[\frac{(\sigma_1 x)^2 + (\sigma_2(1-x))^2}{x/b_1 + \frac{\beta_2}{\beta_1}(1-x)/b_2}\right] \\ &= (i_1 + i_2\frac{\beta_2}{\beta_1})(h(x)) \\ &= (i_1 + i_2\frac{\beta_2}{\beta_1})h_*. \end{aligned}$$

Therefore, $F(b) \leq i_1 C_1 + i_2 C_2$, where

$$\begin{aligned} C_1 &= b_1 c\beta_1 K - b_1(\mu + k_1) + b_2 k_1 - \frac{h_*}{2} \\ C_2 &= b_1 c\beta_2 K - b_2(\mu + k_2 + \alpha) + b_1\alpha - \frac{\beta_2}{\beta_1}\frac{h_*}{2}, \end{aligned}$$

Simplifying gives

$$C_1 = b_1 c\beta_1 K - b_4 - \frac{h_*}{2}.$$

Since

$$\mathcal{R}_\sigma < \frac{\mu+\theta}{\mu+\Gamma\phi+\theta},$$

it follows that $C_1 < 0$. Also $C_2 = \frac{\beta_2}{\beta_1} C_1 < 0$. This completes the proof. □

Theorem 3. *If $\sigma_0 = \sigma_4 = 0$ and $\mathcal{R}_\sigma < \frac{\mu+\theta}{\mu+\Gamma\phi+\theta}$, then the disease-free equilibrium is almost surely exponentially stable.*

Proof. The proof is by contradiction. From Theorem 2 we know that $\lim_{t\to\infty} I_1(t) = 0$ (a.s) and $\lim_{t\to\infty} I_2(t) = 0$ (a.s). Let us now suppose, contrary to the claim of this theorem, that for some subset Θ of Φ with $\mathbb{P}(\Theta) > 0$, on Θ we have:

$$\lim_{t\to\infty}[(K - (S(t) + E(t)) + A(t)] \neq 0. \tag{16}$$

Now let Z be as in (10) and $F(b)$ as in (13). In particular we choose $b_0 = b_1 = b_2 = b_3 = 1$. Then in view of (16) and by the definition of i_1 and i_2 , on Φ we have $i_1 = 0$ and $i_2 = 0$ (a.s). Thus, from (13) it follows that

$$F(b) \leq -\mu q - (\mu + \delta)a - \frac{1}{2}(\sigma_3 a)^2 \quad \text{(a.s)}.$$

Therefore, $F < 0$ (a.s). Then by Proposition 2 it follows that on Θ, we have that $\lim_{t\to\infty}(K - (S(t) + E(t)) = 0$ (a.s) and $\lim_{t\to\infty} A(t) = 0$ (a.s). This a contradiction, and it completes the proof. □

Remark 2. *For the next stability theorem we consider the special case of model (4) in which we assume the following conditions:*

$$\sigma_0 = 0, \quad \sigma_4 = 0, \quad \theta = 0.$$

In this case we define a stochastic process $\{Y(t)\}$ *as follows:*

$$Y(t) = \lambda b_1 g\left(\frac{S(t)}{\Lambda}\right) + b_1 I_1(t) + b_2 I_2(t),$$

with $g(x) := x - 1 - \ln(x)$, $\Lambda = \frac{(\mu+\theta)K}{(\mu+\Gamma\phi+\theta)}$ *and with* b_1, b_2 *as before. Let* $V_3(t) = \ln Y(t)$.

Theorem 4. *Consider the special case of model (4) under assumptions as in Remark 2. If* $\mathcal{R}_0 < 1$ *then the 3-tuple* $(S(t), I_1(t), I_2(t))$ *converges exponentially to* $(\Lambda, 0, 0)$ *(a.s).*

Proof. Let $Y(t)$ and $V_3(t)$ be as above. It suffices to prove that

$$\lim_{t\to\infty} \sup V_3(Y(t)) < 0.$$

Following similar arguments as earlier in this section, it suffices to prove that

$$\lim_{t\to\infty} \sup \langle \mathcal{L}V_3(Y)\rangle < 0.$$

Now we calculate $\mathcal{L}V_3(Y(t))$.

$$\begin{aligned}
\mathcal{L}V_3(Y(t)) &= \frac{b_1}{Y}\left(1 - \frac{\Lambda}{S}\right)[\Lambda - c(\beta_1 I_1 + \beta_2 I_2)S - (\mu + \Gamma\phi)S] \\
&\quad + \frac{b_1}{Y}[c(\beta_1 I_1 + \beta_2 I_2)S - (\mu + k_1)I_1 + \alpha I_2] \\
&\quad + \frac{b_2}{Y}[k_1 I_1 - (\mu + k_2 + \alpha)I_2] - \frac{1}{2}\left[(b_1\sigma_1 I_1)^2 + (b_2\sigma_2 I_2)\right] \\
&\leq \frac{b_1}{Y}\left(1 - \frac{\Lambda}{S}\right)[(\mu + \Gamma\phi)(\lambda - S)] - \frac{b_1}{Y}\lambda S + \frac{b_1}{Y}\lambda\Lambda \\
&\quad + \frac{b_1}{Y}[c(\beta_1 I_1 + \beta_2 I_2)S - (\mu + k_1)I_1 + \alpha I_2] \\
&\quad + \frac{b_2}{Y}[k_1 I_1 - (\mu + k_2 + \alpha)I_2] - \frac{1}{2}\left[(b_1\sigma_1 I_1)^2 + (b_2\sigma_2 I_2)\right].
\end{aligned}$$

Therefore we obtain

$$\mathcal{L}V_3(Y) < -\frac{(b_1\mu + \Gamma\phi)}{S}\frac{(\Lambda - S)^2}{Y} + D_1\frac{I_1}{Y} + D_2\frac{I_2}{Y},$$

where, similarly as in the proof of Theorem 2 we have:

$$\begin{aligned} D_1 &= b_1 c\beta_1\Lambda - b_1(\mu + k_1) + b_2 k_1, \\ D_2 &= \frac{\beta_2}{\beta_1}D_1. \end{aligned}$$

Since $\mathcal{R}_0 < 1$, it follows that $D_1 < 0$. Consequently also $D_2 < 0$. Therefore, $\mathcal{L}V_3(Y(t)) < 0$. □

4 Numerical simulation

We use the Euler-Maruyama scheme for our simulations. It is more or less the standard way of working on applications of $SDEs$, in view of all the complications that come with higher order simulations, see [8]. In our sample simulations, we perform a projection by using the South African HIV trend since 2018. Some of the parameters values are summarized in Table (1) below:

Table 1: The following parameters values are fixed:

Parameters	Value	Source
α	0.25	Estimate, cf. [5]
k_1	0.125	[10]
k_2	0.1	[1]
c	3	Estimate, cf. [9, 16]
δ, μ	resp. 0.2206, $\frac{1}{64.2}$	Estimate,cf. [6]

4.1 Details on estimation of parameters

In 2018 the total population of South Africa was estimated at 57.73 million[7]. Thus, our total population size is taken to be 58 million. The prevalence of HIV/AIDS and incidence rates were both estimated at 13.06% (7.53 million) and 1.2% (692760 new infections) in 2018 respectively. In 2018, an estimated 3.4 million individuals diagnosed with HIV have been on ART treatment. The number of AIDS death related cases is estimated at 115167 (22.06%) in 2018. The current estimated number of people with PrEP varies between 13,500-14,500[8] and the country has a target to have many people enrolled with PrEP by the end of 2019 or 2020. The papers [9, 16]

[5] https://www.tbfacts.org/hiv-statistics-south-africa/ [Access date 01 July 2019].
[6] StatsSA. Mid-year population estimates 2018; statistical release P0302.
[7] StatsSA. Mid-year population estimates 2018; statistical release P0302.
[8] https://www.prepwatch.org/country/south-africa/ [Access date 29 June 2019]

estimate the average number of sexual partners per given time denoted by c; values ranging from 1 to 2 for a specific case. In our case we find it convenient to take $c = 3$. The values of β_1 and β_2 are not easily obtainable, but in our sample simulations the following inequality $\beta_1 < \beta_2$ holds, because in real life the intensity of disease transmission in the symptomatic phase should exceed that of the asymptomatic phase.

4.2 Initial conditions

We denote by t_0 the time 23 July 2018 and we also note that

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

Thus, from an estimated 7.53 million of the total population infected with HIV/AIDS in 2018, our aim is to split this number between the classes of $I_1(t_0)$, $I_2(t_0)$ and $A(t_0)$, see for instance [13]. Together with the Γ already introduced, we assign the following initial values:

$$S_0 = 50.19, \quad E_0 = 0.00155, \quad I_{1,0} = 5.42, \quad I_{2,0} = 1.43, \quad A_0 = 0.68$$

In the following we only show the trajectories of infectious class $I_2(t)$. We use the parameter values as in Table 1. For a certain value of ϕ, we write $\mathcal{R}_0(\phi)$ for the underlying deterministic model and $\mathcal{R}_\sigma(\phi)$ for the stochastic model.

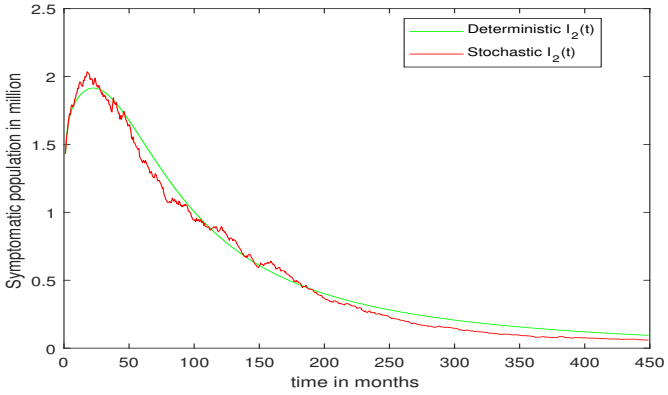

Figure 2: No convergence to the disease-free equilibrium.
Chosen values: $\beta_1 = 0.0155, \beta_2 = 0.049, \sigma_1 = 0.015, \sigma_2 = 0.02$. Calculated values: $\mathcal{R}_0(0.01) = 1.021, \mathcal{R}_\sigma(0.01) = 1.002$.

In Figure 2, for $\phi = 0.01$, $\sigma_1 = 0.015$ and $\sigma_2 = 0.02$, $\mathcal{R}_0(0.01) = 1.021$ while $\mathcal{R}_\sigma(0.01) = 1.002 > 1$. In this case, Theorem 2 does not guarantee almost sure exponential stability and indeed there does not seem to have convergence to the disease-free equilibrium. In Figure 4, decreasing the value of β_2 while increasing σ_1 results in decreasing the basic reproduction number to $\mathcal{R}_0(0.01) = 1.002 > 1$ while $\mathcal{R}_\sigma(0.01) = 0.9714 < 1$. The disease-free equilibrium is almost sure exponentially stable. In this case, we have expected the disease to converge to zero according to Theorem 3. In most of the figures not illustrated here, it is found that a substantial

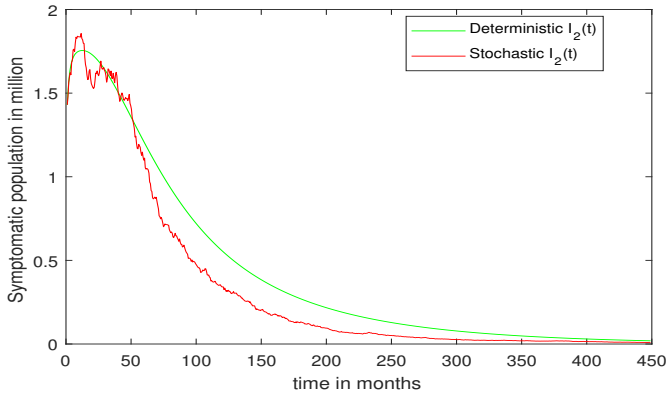

Figure 3: Convergence to the disease-free equilibrium $\mathcal{R}_0(\phi) < 1$.
Chosen values: $\beta_1 = 0.0155, \beta_2 = 0.048, \sigma_1 = 0.0225, \sigma_2 = 0.0132$. Calculated values: $\mathcal{R}_0(0.01) = 1.002, \mathcal{R}_\sigma(0.01) = 0.9714$.

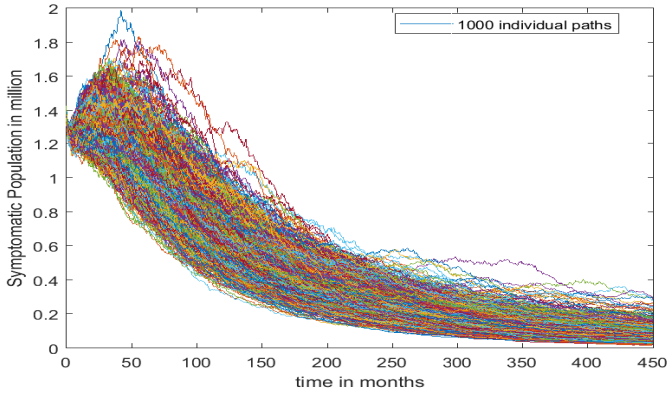

Figure 4: Mean of 1000 discretized Brownian paths.

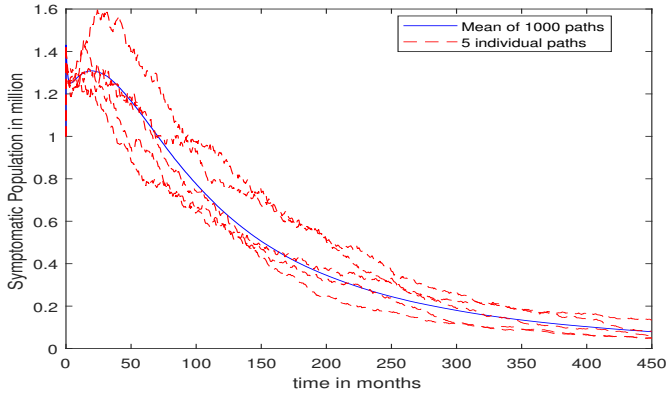

Figure 5: Mean of 1000 discretized Brownian paths and along 5 individual paths.

change in the value of the basic reproduction number was due to both increasing uptake of PrEP and the stochastic perturbations, which led to decreasing the value of the the class of I_2. It was also seen that the function Γ has established a good relationship between both $\mathcal{R}_0(\phi)$ and $\mathcal{R}_\sigma(\phi)$. Thus, decreasing Γ by 5% leads to increasing $\mathcal{R}_0(\phi)$ from 1.021 to 1.033 and $\mathcal{R}_\sigma(\phi)$ from 1.002 to 1.014. It is also noticed that every 5% decrease in the Γ will result in an increase of both $\mathcal{R}_0(\phi)$ and $\mathcal{R}_\sigma(\phi)$ by 1.175% (0.012 unit increase). For instance, if Γ decreases by 0.90, then both $\mathcal{R}_0(\phi)$ and $\mathcal{R}_\sigma(\phi)$ will be respectively 1.045 and 1.026. Thus, for Γ equal to 0.85, then both $\mathcal{R}_0(\phi)$ and $\mathcal{R}_\sigma(\phi)$ will be respectively 1.057 and 1.038. Therefore, Γ is an inverse function of both the default rate and basic reproduction number. Figures 4 and 5 display the maximum discrepancy between the sample average and the exact expected value over all points. For a sample size of 1000 paths, the average is found to be 0.0768. Decreasing the number of sample for instance by 800 paths, the average decreases by 0.0772. Increasing the number of samples to 2000 increases the average to 0.0779.

5 Concluding remarks

This paper investigated a stochastic model describing the population dynamics of HIV with pre-exposure prophylaxis (PrEP). We proved existence of solutions which are almost surely global and positive by using Lyapunov techniques. We also proved a theorem on almost sure exponential stability of the disease-free equilibrium (Theorem 3). From Theorem 3, we found that the disease-free equilibrium is almost surely exponentially stable whenever the requirement is fulfilled. The simulations show that minor stochastic perturbations on the model has a stabilizing effect. The range of the indicating invariant $\mathcal{R}_0$ specified in Theorem 4 can be improved, seeing that it does not mention the perturbation parameters. Nevertheless, the upper bound becomes closer to maximal as σ_1 and σ_2 approach 0. Likewise the range of $\mathcal{R}_\sigma$ as specified in Theorem 2 becomes closer to maximal as $\Gamma\phi$ approaches 0. Our model has showed that if PrEP is being used efficiently, then the number of infectious can potentially be reduced, and even when minor stochastic perturbations are taken into account. We also showed that stochastic framework with PrEP predicts extinction rather than persistence of the disease. Furthermore, we have observed that decreasing the value of Γ leads to increasing both the basic reproduction and the default rate. In fact, the effectiveness of PrEP is closely linked to an individual proper adherence to the programme. For instance, people who adhere to PrEP programme are advised to take medication on a daily basis and not to default. They have also been advised to combine use of PrEP with condoms and other safer sex practices. The risk of HIV infection may increase substantially if the default rate keeps increasing. It can be ideal to investigate the impact of opportunistic infections such as flu or COVID-19 on the population dynamics of HIV.

References

[1] C.P. Bhunu, *Assessing the impact of homelessness on HIV/AIDS transmission dynamics*, Cogent Math. Stat. **2** (2015) 1021602.

[2] J.M. Conway, B.P. Konrad, D. Coombs, *Stochastic analysis of pre-and postexposure prophylaxis against HIV infection*, SIAM J. Appl. Math. **73** (2013) 904–928.

[3] N. Dalal, D. Greenhalgh, X. Mao, *A stochastic model of AIDS and condom use*, J. Math. Anal. Appl. **325** (2007) 36–53 .

[4] P.M.T. Djomegni, A. Tekle, M.Y. Dawed, *Pre-exposure prophylaxis HIV/AIDS mathematical model with non classical isolation*, Japan J. Indust. Appl. Math. **37** (2020) 781-801.

[5] J. Djordjevic, C.J. Silva, D.F. Torres, *A stochastic SICA epidemic model for HIV transmission*, Appl. Math. Lett. **84** (2018) 168–175.

[6] V.A. Fonner, S.L. Dalglish, C.E. Kennedy, R. Baggaley K.R. O'Reilly, F.M. Koechlin, M. Rodolph, I. Hodges-Mameletzis, R.M. Grant, *Effectiveness and safety of oral HIV preexposure prophylaxis for all populations*, AIDS (London, England) **30** (2016) 1973.

[7] A. Gray, D. Greenhalgh, L. Hu, X. Mao, J. Pan, *A stochastic differential equation SIS epidemic model*, SIAM J. Appl. Math. **71** (2011) 876–902.

[8] D.J. Higham, *Stochastic ordinary differential equations in applied and computational mathematics*, IMA J. Appl. Math. **76** (2011) 449-474.

[9] S.D. Hove-Musekwa, F. Nyabadza, *The dynamics of an HIV/AIDS model with screened disease carriers*, Comput. Math. Model. Med. **10** (2009) 287–305.

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

[11] X. Mao, *Stochastic Differential Equations and Applications*, Horwood, Chichester, 1997.

[12] K. Montjane, S. Dlamini, C. Dandara, *Truvada (emtricitabine/tenofovir) pre-exposure prophylaxis roll-out among South African university students: Lots of positives, but let us keep an eye on possible surprises*, South African Med. J. **108** (2018) 79–81.

[13] M.U. Nsuami, P.J. Witbooi, *A model of HIV/AIDS population dynamics including ARV treatment and pre-exposure prophylaxis*, Adv. Difference Equ. **2018** (2018) 1–12.

[14] M.U. Nsuami, P.J. Witbooi, *Stochastic dynamics of an HIV/AIDS epidemic model with treatment*, Quaest. Math. **42** (2019) 605–621.

[15] M.U. Nsuami, P.J. Witbooi, *A stochastic model for HIV epidemic with treatment and inflow of infectives*, Int. J. Appl. Math. **31** (2018) 545–568.

[16] F. Nyabadza, Z. Mukandavire, *Modelling HIV/AIDS in the presence of an HIV testing and screening campaign*, J. Theoret. Biol. **280** (2011) 167–179.

[17] B. Øksendal, *Stochastic Differential Equations: An Introduction with Applications*, 4th Edition, Springer, Berlin, 1995.

[18] C. Pinto, A.R. Carvalho, D. Baleanu, H.M. Srivastava, *Efficacy of the post-exposure prophylaxis and of the HIV latent reservoir in HIV infection*, Math. **7** (2019) 515.

[19] P.J. Witbooi, *An SEIRS epidemic model with stochastic transmission*, Adv. Difference Equ. **2017** (2017) 1–16.

[20] Y. Zhao, D. Jiang, *The threshold of a stochastic SIRS epidemic model with saturated incidence*, Appl. Math. Lett. **34** (2014) 90–93.

[21] K. Zuma, O. Shisana, T.M. Rehle, L.C. Simbayi, S. Jooste, N. Zungu, D. Labadarios, D. Onoya, M. Evans, S. Moyo, F. Abdullah, *New insights into HIV epidemic in South Africa: key findings from the National HIV Prevalence, Incidence and Behaviour Survey*, 2012, Afr. J. AIDS Res. **15** (2016) 67–75.