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Contribution to the study of a pre-exposure prophylaxis HIV model

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Abstract
Pre-Exposure Prophylaxis (PrEP) is a new treatment against HIV spread consisting of taking antiretrovirals to prevent HIV infection. Silva (Discret Contin Dyn Syst Ser S 11:119–141, 2017) introduced a mathematical model of HIV spread including PrEP. Here we propose to complete their work by including the PrEP parameter in the basic reproduction number of the system. To do so, we study stability changes through the influence of this new parameter. We also prove the global stability of the steady states of the system in this new case using Lyapunov functions. Finally, we extend the stability to cases where death induced by AIDS is non-zero using exponential attractors to make the model more applicable to real-life scenarios.

Keywords Mathematical modeling · HIV · PrEPred · Basic reproduction number · Steady state · Lyapunov function · Stability · Exponential attractor

1 Introduction

The objective of this work is to study the qualitative impact of Pre-Exposure Prophylaxis (PrEP) treatment on HIV spread by including PrEP users in a mathematical model of HIV propagation analyzing their behavior and their impact on other individuals. Our analysis is based on the model proposed by Silva and Torres (2017), we here suggest a new Lyapunov function to study the impact of this new treatment on the stability of steady states. We also extend the analysis using exponential attractors

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to prove the stability of steady states when the induced death rate of HIV is non-zero. Beforehand, let us briefly review the background of the HIV epidemic and PrEP treatment.

1.1 The PrEP treatment

PrEP is a recent treatment, first proven to be effective in 2010, that involves the use of antiretrovirals to prevent from being infected with HIV (Arts and Hazuda 2014; WHO 2015). Indeed, the regular intake of these drugs forms a barrier around the T cells CD4 precluding them from bringing and thus letting the HIV proliferate in the body.

Taken as a continuous treatment, the user must take a daily pill to benefit from an optimal protection of 99.9 % efficiency. This protocol appears to be, up to now, one of the most efficient preventing treatment against HIV (Gay and Cohen 2008). When initiated, a week lag is required for full protection. Besides, if the user does not take the medication regularly enough, the protection becomes less effective.

There exists also a non-continuous option of PrEP intake called “PrEP on demand". With this treatment, users do not need to take one pill a day but they have to anticipate their intercourse to take two pills at least two hours before then one pill per day every day until 2 days after the last intercourse. In any case, treatment can be stopped during periods of sexual inactivity.

It is important to note that this treatment is an HIV prevention treatment only (Thigpen et al. 2012), it is softer than Anti Retroviral Therapy (ART) and therefore not used for the treatment of HIV. This is why a person under PrEP needs to get tested every three months with an HIV-negative status. Infection may indeed happen if the treatment is not taken seriously or if the person was already in the incubation period at the start of treatment. If the test is positive, the user stops PrEP and starts ART.

1.2 State of the art of PrEP

According to the annual report of the Joint United Nations Program on HIV/AIDS (UNAIDS), 1.8 million [1.4 million−2.4 million] individuals became newly infected with HIV in 2017 bringing the number of HIV-infected to 77.3 million [59.9 million-100 million] since the pandemic early days. Among them, 35.4 million [25.0 million−49.9 million] already died from AIDS-related illnesses.

It is therefore to stop this epidemic that the use of PrEP has been proposed by the World Health Organization (WHO) since 2015, particularly within high-risk populations such as men-men intercourses, drug injective groups, transgenders, women and serodiscordant couples (one partner is HIV-positive and the other is HIV-negative). The first results seem to be encouraging (WHO 2015).

However, even if the treatment started in 2016, not every country initiated it, and, due to the SARS-CoV-2 pandemic crisis, combined with strict lockdowns, and social distances between individuals, it is hard to guarantee an unbiased statistical study. This is why the results obtained at this time need to be comforted by a longer statistical analysis. For example, in Abbas et al. (2007), it is presumed that the introduction

of PrEP could prevent 2.7 to 3.2 million new cases of HIV in sub-Saharan Africa over 10 years (data before SARS-CoV-2).

In France, before 2017, PrEP had not yet reached the general public and remained largely restricted to clinical use for tests between January 2016 and February 2017 (Madiou 2017). The results of these studies are quite encouraging. However, the treatment is implemented on individuals at high risk and not the entire population.

The difficulty of implementing PrEP in the whole population comes from its high cost (even for the generic drugs) but also because treatment is still not politically accepted in some parts of the world (Spinner et al. 2016). There is therefore an economic dimension to take into account for the use of this treatment but this is not the purpose of our article. A study of the trade-off number of infected/PrEP treatment costs is proposed in section 4 of Silva and Torres (2017) which is based on the theory of optimal control already used for other epidemics (Rodrigues et al. 2017; Denysiuk et al. 2015).

1.3 State of the art of HIV modeling with PrEP

The modeling of PrEP in the context of HIV prevention remains relatively scarce in the scientific literature. Despite its critical importance in controlling the spread of HIV, there are only a limited number of studies that have thoroughly explored the dynamics and impact of PrEP through mathematical models. In this section, we review the current state of the art by examining three key papers that address various aspects of PrEP modeling. We will briefly describe the methodologies, findings, and contributions of each study to provide a comprehensive overview of the existing research landscape.

In Ying et al. (2014), the authors examine the potential impact and cost-effectiveness of universal coverage for both ART and PrEP as preventive measures against HIV. The study uses mathematical modeling to simulate various scenarios of ART and PrEP implementation, aiming to project their effects on HIV incidence and overall public health outcomes. It proves that widespread access to these interventions significantly reduces new HIV infections and improves health outcomes for those at high risk. However, this work does not specifically focus on modeling PrEP and does not conduct a theoretical analysis of numerical simulations to assess the impact of PrEP treatment.

A second approach (Kim et al. 2014) published in 2014 presents a detailed mathematical model of HIV infection through PrEP treatment among men who have sex with men (MSM) in South Korea. This model also incorporates factors such as treatment failure and screening processes. The findings suggest that PrEP is an effective means to reduce the HIV epidemic in this population, although its effectiveness would be further enhanced with regular screening and self-protection measures within these communities. However, the paper relies solely on numerical simulations and does not include a theoretical analysis of the model, such as steady-state or bifurcation analysis.

Another notable model addressing HIV propagation in the context of PrEP was developed in a recent article (Adimy et al. 2022). The paper acknowledges the ongoing HIV/AIDS epidemic and the lack of a definitive cure, highlighting the introduction

of PrEP as a preventive measure based on WHO recommendations from 2014, and its specific application in France since 2016. The authors propose a novel compartmental epidemiological model that accounts for the limited protection time offered by PrEP. They describe the PrEP compartment using an age-structured hyperbolic equation and incorporate a differential equation to govern the PrEP initiation process. This framework results in a nonlinear differential-difference system with discrete delay. Through local stability analysis and proofs of the system's global behavior, the paper provides a comprehensive examination of the model. The study also includes numerical simulations based on data from the French MSM population, demonstrating that the model's logistic time dynamics and Hill-function-like approach yield an excellent fit to the data. These results facilitate forecasting the future trajectory of the HIV epidemic in France, assuming continued PrEP usage.

Finally, Silva and Torres developed a comprehensive mathematical model of the HIV epidemic through PrEP treatment (Silva and Torres 2017), which is the focus of the theoretical analysis in our Sect. 2. Their paper goes beyond modeling by formulating an optimal control problem aimed at addressing the trade-offs between the costs and benefits of implementing PrEP treatment. This is particularly relevant for regions such as Cape Verde, where resource allocation and cost-effectiveness are critical considerations. Their analysis helps to fill the gap in understanding how best to balance these factors to maximize the public health benefits of PrEP while managing the associated costs effectively.

Our work is organized as follows, in Sect. 2, we explore deeper into the dynamics and theoretical analysis of an HIV propagation model, extending the foundational work by Silva and Torres (2017). We expand on their model by incorporating the impact of PreP treatment on the basic reproduction number $\mathcal{R}_0$ and the stability of steady states. This enhancement provides a more comprehensive understanding of how PreP affects the epidemic's potential to spread. In Sect. 3, we perform a rigorous theoretical analysis using exponential attractors. This approach allows us to extend the stability analysis beyond the traditional Lyapunov function method, enabling us to consider a wider range of parameters and thereby enhancing the model's applicability to real-world scenarios. Finally, in Sect. 4, we apply the model to empirical data from a case study in Cape Verde, discussing the practical implications of PreP treatment based on our findings.

2 Deterministic model of HIV spread through PrEP

In this section, we introduce a deterministic model of HIV spread through PrEP proposed in Silva and Torres (2017). We generalize the study proposed in the article by calculating the basic reproduction number taking PrEP into account.

2.1 Introduction of the model

In this approach, five categories of individuals are considered (see Fig. 1). The **Susceptible (S)** are uninfected individuals, they can become HIV **Infected (I)** in contact

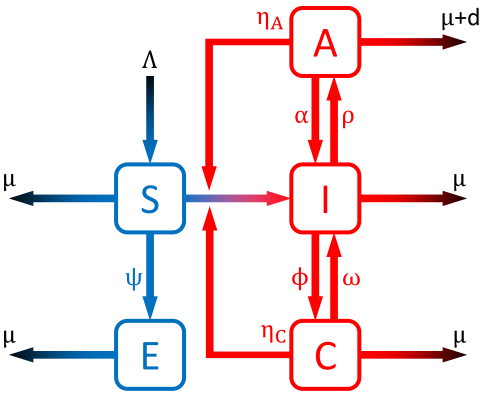

Fig. 1 Diagram of the SEIAC model between each category of individuals. The arrows represent the possible movements between categories with the associated rates. In blue, disease-free individuals S = Susceptible and E = individuals under PrEP. In red, infected individuals, I = Infected, C = Individual under antiretroviral therapy, and A = Individual with AIDS

with other infected or they can take **PrEP (E)**. Infected can take **ART (C)** or develop **AIDS (A)** symptoms, their unit is the number of individuals.

- **Susceptible** denoted $S(t)$ relates to uninfected individuals at time $t \geq 0$. The link between S and the Infected I is given by the term $\frac{\beta(I(t)+\eta_C C(t)+\eta_A A(t))}{N(t)} S(t)$. It describes the probability of contact with each member of the HIV infected where $0 < \beta < 1(\text{ year}^{-1})$ is the effective contact rate for HIV infection. The modification parameter $\eta_A \geq 1(\text{ no unit})$ accounts for the relative infectiousness of individuals with AIDS symptoms who are more infectious than HIV-infected because of their higher viral load in their organism (Wilson et al. 2008). On the other hand, $\eta_C \leq 1(\text{ no unit})$ stands for the partial restoration of immune function of individuals with HIV infection using ART (Deeks et al. 2013).
- **Infected** $I(t)$ represents individuals infected by HIV but not under treatment and without clinical symptoms of AIDS. When taking treatment they move to category (C) at the rate $0 < \Phi < 1(\text{ year}^{-1})$. If not, they may develop AIDS symptoms with a rate $0 < \rho < 1(\text{ year}^{-1})$,
- **Individuals under antiretroviral therapy** $C(t)$ pertains to HIV infected taking an antiretroviral therapy against HIV. They move back to category I if they stop the treatment with a rate $0 \leq \omega < 1(\text{ year}^{-1})$,
- **Individuals with AIDS** $A(t)$ reflects individuals with clinical symptoms of AIDS, they move to category $I(t)$ if they take a treatment with a rate $0 < \alpha < 1(\text{ year}^{-1})$. They also die of AIDS with a rate $0 \leq d \leq 1(\text{ year}^{-1})$,
- **Individuals under PrEP** $E(t)$: this treatment is for non infected in S only. Susceptibles reach E with a rate $0 \leq \psi \leq 1(\text{ year}^{-1})$.

Individuals are all supposed to die with the same rate $\mu > 0$ and the source due to immigration or birth appears in $S(t)$ with a rate $\Lambda > 0$. We note $N(t) = S(t) + I(t) + C(t) + A(t) + E(t)$ the total number of individuals at time $t \geq 0$. Interactions between each category are summarized in Fig.1, and parameters are listed in Table 1.

We assume that antiretroviral therapy is seriously and continuously taken by individuals, in this case, individuals taking ART are considered as not infectious ($\eta_C = 0$). It has been demonstrated that adhering to ART regimens diligently can sig-

Table 1 Parameters of the HIV / AIDS model (1) for Cape Verde. Values from Silva and Torres (2017)

Symbol	Description	Value
$N(0)$	Initial population	323972 ind
Λ	Recruitment rate	13045 ind.year^{-1}
μ	Natural death rate	1 / 69.54 year^{-1}
β	HIV transmission rate	0.752 year^{-1}
η_C	Modification parameter	0.04
η_A	Modification parameter	1.35
Φ	HIV treatment rate for I individuals	1 year^{-1}
ρ	Default treatment rate for I individuals	0.1 year^{-1}
α	AIDS treatment rate	0.33 year^{-1}
ω	Default treatment rate for C individuals	0.09 year^{-1}
d	AIDS induced death rate	1 year^{-1}

nificantly reduce the risk of HIV transmission to levels comparable to those achieved with condom use ($> 99\%$) (Attia et al. 2009). Here, we ideally further assume that individuals undergoing treatment do not discontinue it (it means $(\theta = 0)$ in the model of Silva and Torres (2017)). The random cessation of treatment could be interesting to study and will be addressed in a future publication. This possibility has also been discussed in other studies with delay and time under treatment (Silva 2022; Adimy et al. 2022). The evolution of population in each of these categories as a function of time follows then the system (1) for all $t \geq 0$.

$$\begin{cases} \dot{S}(t) = \Lambda - \frac{\beta(I(t)+\eta_C C(t)+\eta_A A(t))}{N(t)} S(t) - \xi_4 S(t), \\ \dot{I}(t) = \frac{\beta(I(t)+\eta_C C(t)}{+} \eta_A A(t)) N(t) S(t) - \xi_3 I(t) + \alpha A(t) + \omega C(t), \\ \dot{C}(t) = \Phi I(t) - \xi_2 C(t), \\ \dot{A}(t) = \rho I(t) - \xi_1 A(t), \\ \dot{E}(t) = \psi S(t) - \mu E(t). \end{cases} \tag{1}$$

Where $\xi_1 = \alpha + \mu + d$, $\xi_2 = \mu + \omega$, $\xi_3 = \rho + \Phi + \mu$ and $\xi_4 = \mu + \psi$. All the coefficients are non-negative.

We consider the biologically feasible region Ω_P defined in (2). Where the population in different categories is obviously positive and where S and E are bounded from above. The feasibility region of this system is bounded by several conditions derived from the system's dynamics. Firstly, $N \leq \frac{\Lambda}{\mu}$, as at this point the derivative of N is negative, indicating that the population decreases. Additionally, $S \leq \frac{\Lambda}{\mu+\psi}$ and $E \leq \frac{\psi\Lambda}{\mu(\mu+\lambda)}$ establish further constraints. These conditions arise when S and E are the only components contributing to N (i.e., $A = I = C = 0$), thus defining the

maximum values for $S + E$. According to the equations for $\dot{S}$ and $\dot{E}$, these values ensure that the population remains within the feasible region defined by the first condition, maintaining system stability.

$$\Omega_P = \left\{ (S, I, C, A, E) \in \mathbb{R}^5_{+0} : S \leq \frac{\Lambda}{\mu + \psi}, E \leq \frac{\psi\Lambda}{\mu(\mu + \psi)}, N \leq \frac{\Lambda}{\mu} \right\}. \quad (2)$$

It is shown in Silva and Torres (2017) that the system (1) is well posed, that the set Ω_P is stable and global population $N(t)$ is uniformly persistent. We refer to Silva and Torres (2017) for the proof of these results and we focus only on the basic reproduction number $\mathcal{R}_0$(dependent in ψ) and the stability of steady states. The basic reproduction number $\mathcal{R}_0$ represents the average number of secondary infections caused by a single infectious individual in a fully susceptible population, serving as a key metric for assessing the potential spread and control of infectious diseases.

2.2 Steady states and basic reproduction number

(a) Disease-free steady state

Let us start with the disease-free steady state (DFSS). The only DFSS is easily given by the expression (3).

$$(DFSS) : (S^0, I^0, C^0, A^0, E^0) = \left(\frac{\Lambda}{(\psi + \mu)}, 0, 0, 0, \frac{\psi\Lambda}{\mu(\psi + \mu)} \right). \quad (3)$$

From this steady state, we compute the basic reproduction number for model (1) $\mathcal{R}_0$ using the next generation method (Van den Driessche and Watmough 2002). Referring to (1) we denote functions F and V as follows :

$$\begin{aligned} F &= \left(\frac{\beta(I(t) + \eta_C C(t) + \eta_A A(t))}{N(t)} S(t), 0, 0\right)^T, \\ V &= (-\xi_3 I(t) + \alpha A(t) + \omega C(t), \Phi I(t) - \xi_2 C(t), \rho I(t) - \xi_1 A(t))^T. \end{aligned} \quad (4)$$

We define matrices $\mathcal{F}$ and $\mathcal{V}$ respectively as the jacobian matrix of F and V evaluated at the disease free steady state (3):

$$\mathcal{F} = \begin{pmatrix} \frac{\beta S^0}{N^0} & \frac{\beta\eta_C S^0}{N^0} & \frac{\beta\eta_A S^0}{N^0} \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix}, \quad \mathcal{V} = \begin{pmatrix} -\xi_3 & \omega & \alpha \\ \Phi & -\xi_2 & 0 \\ \rho & 0 & -\xi_1 \end{pmatrix}.$$

From those two matrices we determine $\mathcal{R}_0$ of this model using the Theorem 2.1 (Van den Driessche and Watmough 2002) that we recall here:

Theorem 2.1 *The matrix $\mathcal{V}$ is invertible and $-\mathcal{F}\mathcal{V}^{-1}$ is a matrix that admits a positive real principal eigenvalue equal to $\rho(-\mathcal{F}\mathcal{V}^{-1})$, and furthermore :*

$$\mathcal{R}_0 = \rho(-\mathcal{F}\mathcal{V}^{-1}).$$

Where ρ is the spectral radius of the matrix.

Here,

$$\mathcal{V}^{-1} = \frac{1}{\det(\mathcal{V})}\begin{pmatrix} \xi_2\xi_1 & \omega\xi_1 & \alpha\xi_2 \\ \Phi\xi_1 & \xi_1\xi_3 - \alpha\rho & \Phi\alpha \\ \xi_2\rho & \omega\rho & \xi_3\xi_2 - \omega\Phi \end{pmatrix}, \tag{5}$$

where,

$$\det(\mathcal{V}) = \mu(\xi_2(\rho + \xi_1) + \Phi\xi_1 + \rho d) + \rho\omega d. \tag{6}$$

To find $\rho(-\mathcal{F}\mathcal{V}^{-1})$, remark that the matrix $\mathcal{F}$ has only non-zero components on its first line, so the matrix $-\mathcal{F}\mathcal{V}^{-1}$ has the same characteristic. The matrix $-\mathcal{F}\mathcal{V}^{-1}$ is an upper triangular matrix with two zeros on its diagonal, so the spectrum of this matrix is the third term of its diagonal.

$$-\mathcal{F}\mathcal{V}^{-1} = \begin{pmatrix} \mathcal{R}_0 & * & * \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix},$$

with

$$\mathcal{R}_0 = \frac{\beta S^0(\omega + mu)(\alpha + \mu + d) + \beta\eta_C\Phi S^0(\alpha + \mu + d) + \beta\eta_A S^0(\omega + \mu)\rho}{N^0\det(\mathcal{V})}.$$

Since $S^0 = \frac{\mu\Lambda}{\mu(\psi+\mu)}$ and $N^0 = \frac{\Lambda}{\mu}$,

$$\mathcal{R}_0 = \frac{\beta\mu(\xi_2(\xi_1 + \rho\eta_A) + \eta_C\Phi\xi_1)}{(\psi + \mu)(\mu(\xi_2(\rho + \xi_1) + \Phi\xi_1 + \rho d) + \rho\omega d)} = \frac{\mu\mathcal{N}}{(\psi + \mu)\mathcal{D}}. \tag{7}$$

Where $\mathcal{N} = \beta(\xi_2(\xi_1 + \rho\eta_A) + \eta_C\Phi\xi_1)$ and $\mathcal{D} = \mu(\xi_2(\rho + \xi_1) + \Phi\xi_1 + \rho d) + \rho\omega d$.

(b) Endemic steady state

Let us follow with the endemic steady state (*ESS*). The system (1) has a unique positive endemic steady state when $\mathcal{R}_0 > 1$(Silva and Torres 2017).

$$(ESS) : (S^*, I^*, C^*, A^*, E^*) = \left(\frac{\Lambda}{\Gamma}, \frac{\Sigma\Lambda\xi_1\xi_2}{\Gamma\mathcal{D}}, \frac{\Sigma\Lambda\xi_1\Phi}{\Gamma\mathcal{D}}, \frac{\Sigma\Lambda\xi_2\rho}{\Gamma\mathcal{D}}, \frac{\psi\Lambda}{\mu\Gamma}\right). \tag{8}$$

Where $\Sigma = \mathcal{N} - \frac{(\mu+\psi)}{\mu}\mathcal{D}$ and $\Gamma = \frac{\Sigma}{(\xi_1\xi_2 + \xi_1\Phi + \xi_2\rho)} + \mu + \psi$.

In the next subsection, we show that (*DFSS*) is globally asymptotically stable whenever $\mathcal{R}_0 < 1$ and (*ESS*) is globally asymptotically stable when $\mathcal{R}_0 > 1$.

2.3 Global stability of the steady states

Assume here that associated AIDS-induced mortality is negligible $(d = 0)$. The extension of stabilities for a non-zero rate d is the subject of Sect. 3.

Furthermore, we assume that the arrival of new individuals Λ compensates for deaths. This way, the global population is constant, for all $t \geq 0$, and is $N(t) = \frac{\Lambda}{\mu}$. These assumptions lead then to the results 2.2 and 2.3.

Theorem 2.2 *The disease-free steady state (DFSS) (3) is globally asymptotically stable for $\mathcal{R}_0 < 1$.*

Remark To prove this result we use a Lyapunov function. For convenience and readability, we do not write dependencies in time (e.g. $S(t)$ is written S).

Proof Consider the following Lyapunov function:

$$\begin{aligned}\mathcal{L} =&(\xi_1\xi_2 + \xi_1\Phi\eta_C + \xi_2\rho\eta_A)(S - S^0\ln(S)) + (S^0 - S^0\ln(S^0))\\ &+ (\xi_1\xi_2 + \xi_1\Phi\eta_C + \xi_2\rho\eta_A)I\\ &+ (\xi_1\omega + \xi_1\xi_3\eta_C + \rho\eta_A\omega - \eta_C\rho\alpha)C\\ &+ (\alpha\xi_2 + \xi_2\xi_3\eta_A + \Phi\eta_C\alpha - \Phi\eta_A\omega)A.\end{aligned} \tag{9}$$

This function is non-negative only when $(S, I, C, A) = (DFSS)$. The time derivative of $\mathcal{L}$ computed along the trajectories of (1) is given by :

$$\begin{aligned}\dot{\mathcal{L}} =&(\xi_1\xi_2 + \xi_1\Phi\eta_C + \xi_2\rho\eta_A)\left(1 - \frac{S^0}{S}\right)\dot{S} + (\xi_1\xi_2 + \xi_1\Phi\eta_C + \xi_2\rho\eta_A)\dot{I}\\ &+ (\xi_1\omega + \xi_1\xi_3\eta_C + \rho\eta_A\omega - \eta_C\rho\alpha)\dot{C} + (\alpha\xi_2 + \xi_2\xi_3\eta_A + \Phi\eta_C\alpha - \Phi\eta_A\omega)\dot{A},\\ =&(\xi_1\xi_2 + \xi_1\Phi\eta_C + \xi_2\rho\eta_A)\left(1 - \frac{S^0}{S}\right)(\Lambda - \frac{\beta}{N}(I + \eta_C C + \eta_A A)S - \mu S - \psi S)\\ &+ (\xi_1\xi_2 + \xi_1\Phi\eta_C + \xi_2\rho\eta_A)(\frac{\beta}{N}(I + \eta_C C + \eta_A A)S - \xi_3 + \omega C + \alpha A)\\ &+ (\xi_1\omega + \xi_1\xi_3\eta_C + \rho\eta_A\omega - \eta_C\rho\alpha)(\Phi I - \xi_2 C)\\ &+ (\alpha\xi_2 + \xi_2\xi_3\eta_A + \Phi\eta_C\alpha - \Phi\eta_A\omega)(\rho I - \xi_1 A).\end{aligned} \tag{10}$$

We use the relation at the steady state $\Lambda = \mu S^0 + \psi S^0$. After some simplifications, we obtain :

$$\begin{aligned}\dot{\mathcal{L}} = &\left(1-\frac{S^0}{S}\right)(S^0-S)(\mu+\psi)\\ &+ \ [(\xi_1\xi 2+\xi_1\Phi\eta_C+\xi_2\rho\eta_A)\frac{\beta S^0}{N}+(-\xi_1\xi_2\xi_3+\xi_1\omega\Phi+\alpha\xi_2\rho)]I\\ &+ \ [\eta_C(\xi_1\xi 2+\xi_1\Phi\eta_C+\xi_2\rho\eta_A)\frac{\beta S^0}{N}+\eta_C(-\xi_1\xi_2\xi_3+\xi_1\omega\Phi+\alpha\xi_2\rho)]C\\ &+ \ [\eta_A(\xi_1\xi 2+\xi_1\Phi\eta_C+\xi_2\rho\eta_A)\frac{\beta S^0}{N}+\eta_A(-\xi_1\xi_2\xi_3+\xi_1\omega\Phi+\alpha\xi_2\rho)]A.\end{aligned} \tag{11}$$

The first line is negative because $\frac{S^0}{S} \geq 1$ when $S^0 \geq S$ so $(S^0 - S)$ is positive.

$$\begin{aligned}\dot{\mathcal{L}} = &\left(1-\frac{S^0}{S}\right)(S^0-S)(\mu+\psi)+\mathcal{D}\left(\mathcal{R}_0\frac{S^0}{N}-1\right)I\\ &+ \ \eta_C\mathcal{D}\left(\mathcal{R}_0\frac{S^0}{N}-1\right)C+\eta_A\mathcal{D}\left(\mathcal{R}_0\frac{S^0}{N}-1\right)A.\end{aligned} \tag{12}$$

However, with our hypothesis $\frac{S^0}{N} = \frac{\mu}{\psi+\mu}$ which gives

$$\begin{aligned}\dot{\mathcal{L}} \leq &\left(1-\frac{S^0}{S}\right)(S^0-S)(\mu+\psi)+\mathcal{D}(\mathcal{R}_0-1)I\\ &+ \ \eta_C\mathcal{D}(\mathcal{R}_0-1)C+\eta_A\mathcal{D}(\mathcal{R}_0-1)A \leq 0 \text{ for } \mathcal{R}_0<1.\end{aligned} \tag{13}$$

This function is zero only when (S, I, C, A) is the (*DFSS*). This proves, by Lyapunov Theorem, that the disease-free steady state (*DFSS*) is globally asymptotically stable for $\mathcal{R}_0 < 1$. □

The endemic steady state (*ESS*) exists only when the basic reproduction number is greater than 1 (Silva and Torres 2017). In this case, we have the results 2.3 :

Theorem 2.3 *The endemic steady state (8) of the system (1) is globally asymptotically stable whenever $\mathcal{R}_0 > 1$ with nonzero initial conditions.*

Proof Consider the following Lyapunov function :

$$\mathcal{L} = (S - S^*\ln(S)) + (I - I^*\ln(I)) + \frac{\omega}{\xi_2}(C - C^*\ln(C)) + \frac{\alpha}{\xi_1}(A - A^*\ln(A)). \tag{14}$$

The time derivative of $\mathcal{L}$ computed along the solutions of (1) is given by

$$\begin{aligned}\dot{\mathcal{L}} &= \left(1-\frac{S^*}{S}\right)\dot{S} + \left(1-\frac{I^*}{I}\right)\dot{I} + \frac{\omega}{\xi_2}\left(1-\frac{C^*}{C}\right)\dot{C} + \frac{\alpha}{\xi_1}\left(1-\frac{A^*}{A}\right)\dot{A},\\ &= \left(1-\frac{S^*}{S}\right)[\Lambda - \frac{\beta}{N}(I+\eta_C C+\eta_A A)S - \mu S - \psi S]\\ &+ \left(1-\frac{I^*}{I}\right)[\frac{\beta}{N}(I+\eta_C C+\eta_A)S - \xi_3 I + \alpha A + \omega C]\\ &+ \frac{\omega}{\xi_2}\left(1-\frac{C^*}{C}\right)[\Phi I - \xi_2 C] + \frac{\alpha}{\xi_1}\left(1-\frac{A^*}{A}\right)[\rho I - \xi_1 A].\end{aligned} \tag{15}$$

Using relation $\Lambda = \frac{\beta}{N}(I^* + \eta_C C^* + \eta_A A^*)S^* + \mu S^* + \psi S^*$ at the steady state in the Eq. (1) we write

$$\begin{aligned}\dot{\mathcal{L}} &= \left(1-\frac{S^*}{S}\right)\left[\frac{\beta}{N}(I^*+\eta_C C^*+\eta_A A^*)S^* + \mu S^* + \psi S^*\right.\\ &\left. - \frac{\beta}{N}(I+\eta_C C+\eta_A A)S - \mu S - \psi S\right]\\ &+ \left(1-\frac{I^*}{I}\right)[\frac{\beta}{N}(I+\eta_C C+\eta_A)S - \xi_3 I + \alpha A + \omega C]\\ &+ \frac{\omega}{\xi_2}\left(1-\frac{C^*}{C}\right)[\Phi I - \xi_2 C] + \frac{\alpha}{\xi_1}\left(1-\frac{A^*}{A}\right)[\rho I - \xi_1 A].\end{aligned} \tag{16}$$

We use the relations at the steady state in (1), $\xi_3 I^* = \frac{\beta}{N}(I^* + \eta_C C^* + \eta_A A^*)S^* + \alpha A^* + \omega C^*$, $\xi_2 C^* = \Phi I^*$ and $\xi_1 A^* = \rho I^*$.

$$\begin{aligned}\dot{\mathcal{L}} =& (\frac{\beta}{N}I^*S^* + \mu S^* + \psi S^*)\left(2 - \frac{S}{S^*} - \frac{S^*}{S}\right) + \frac{\beta}{N}S^*(\eta_C C^* + \eta_A A^*)\left(1-\frac{S^*}{S}\right)\\ &+ \frac{\beta}{N}S^*(\eta_C C^* + \eta_A A^*)\left(1-\frac{I}{I^*}\right) + \frac{\beta}{N}S^*(\eta_C C + \eta_A A)\left(1-\frac{I^*}{I}\frac{S}{S^*}\right)\\ &+ \alpha A^*\left(2 - \frac{A}{A^*}\frac{I^*}{I} - \frac{I}{I^*}\frac{A^*}{A}\right) + \omega C^*\left(2 - \frac{C}{C^*}\frac{I^*}{I} - \frac{I}{I^*}\frac{C^*}{C}\right).\end{aligned} \tag{17}$$

The first and the last two terms are of the form of $2 - x - 1/x$ multiplied by a positive term so they are negative and equal to zero only when $(S, I, C, A) = (ESS)$. Finally, we have to prove that the remaining three terms are negative.

For each t we choose in the finite set $\{(C^*, A^*), (C^*, A), (C, A^*), (C, A)\}$ the couple $(\tilde{C}, \tilde{A})$ that maximizes the sum of those three terms. Thus, for each $t \geq 0$:

$$
\begin{aligned}
&\frac{\beta}{N}S^*(\eta_C C^* + \eta_A A^*)\left(1 - \frac{S^*}{S}\right) + \frac{\beta}{N}S^*(\eta_C C^* + \eta_A A^*)\left(1 - \frac{I}{I^*}\right) \\
&\quad + \frac{\beta}{N}S^*(\eta_C C + \eta_A A)\left(1 - \frac{I^*}{I}\frac{S}{S^*}\right), \\
&\leq \frac{\beta}{N}S^*(\eta_C \tilde{C} + \eta_A \tilde{A})\left(1 - \frac{S^*}{S}\right) + \frac{\beta}{N}S^*(\eta_C \tilde{C} + \eta_A \tilde{A})\left(1 - \frac{I}{I^*}\right) \\
&\quad + \frac{\beta}{N}S^*(\eta_C \tilde{C} + \eta_A \tilde{A})\left(1 - \frac{I^*}{I}\frac{S}{S^*}\right), \\
&\leq \frac{\beta}{N}S^*(\eta_C \tilde{C} + \eta_A \tilde{A})\left(3 - \frac{S^*}{S} - \frac{I}{I^*} - \frac{I^*}{I}\frac{S}{S^*}\right).
\end{aligned}
\tag{18}
$$

The term between the brackets in the right-hand side of the inequality is of the form $3 - 1/x - 1/y - xy$ and it is negative when x and y are positive and is zero only when $x = y = 1$ so when $S = S^*$ and $I = I^*$. For the details of the function analysis, see Appendix B. The function $\mathcal{L}$ is thus a Lyapunov function so the endemic steady state (*ESS*) is globally asymptotically stable for nonzero initial conditions using Lyapunov Theorem. □

This proof of stability is different from the one in Silva and Torres (2017) because $\mathcal{R}_0$ is not the same. In fact, $\mathcal{R}_0$ in Silva and Torres (2017) is incorrectly the same for both SIAC and SEAIC models. It means the number of individuals taking PrEP (ψ) does not impact the basic reproduction number. In this study, we computed this basic reproduction number again (7). Therefore, it was necessary to prove the stability of both steady states according to this new value of $\mathcal{R}_0$.

Note that an erratum was published in 2020 by the author (Silva and Torres 2020). In this paper, the basic reproduction number is corrected and is the same as the one in this paper. However, the Lyanupov function linked to the endemic steady state is the same as previously and it does not work. In fact, in the derivation, $\mathcal{N}_0/\mathcal{D}_0$ is replaced by $\mathcal{R}_0$ and this is only true for the basic reproduction number without PrEP, not the one including it. Also note that authors published another paper on the model adding a delay in the PrEP treatment (Silva 2022). In this paper, the basic reproduction number is indeed consistent with that presented in the 2020 erratum (when delay is 0) and is therefore correct for analyzing the disease-free steady state. However, we acknowledge that no stability analysis using a Lyapunov function was conducted for the endemic steady state in the study.

To enrich our analysis, we extend the stability investigation to include the case where $d \neq 0$. This extension introduces additional complexity, as the assumption of a constant global population no longer holds. When $d \neq 0$, the dynamic behavior of the population changes significantly, requiring a more sophisticated approach to ensure accurate stability analysis. To tackle this challenge and extend stability beyond the limitations of previous assumptions, we utilize a result proposed by Efendiev and Yagi (2005). This approach allows us to rigorously analyze the stability of the system using the concept of exponential attractors, thereby providing a more comprehensive understanding of the model's behavior under a wider range of parameters. This advancement is crucial for making our model more applicable to real-life scenarios where population dynamics are inherently variable.

3 Exponential attractor and stability for a non-zero induced death rate *d*

As stated in the first part, the infectivity of an individual infected with HIV but under ART is a controversial subject (Deeks et al. 2013). In this part, to simplify the calculations, we assume that individuals under treatment are not infectious ($\eta_C = 0$) which is close to reality (Granich et al. 2012). In addition, we suppose that treatments are taken seriously and are not interrupted ($\omega = 0$) which could be true for a subclass of population at risk. It is possible to change this hypothesis later because the result can be extended to that case. The significance of this work on exponential attractors lies in addressing the realistic scenario where the induced death rate of AIDS d cannot be set to zero because the death rate of people with AIDS is higher than other individuals of the model (Eyawo et al. 2017; Sabin 2013). The presence of the term $-dA(t)$ in the derivative of N complicates the use of Lyapunov functions for stability analysis, making it a less feasible approach. By leveraging exponential attractors, we overcome these challenges and provide a robust framework for analyzing the stability of the system under more realistic conditions. This advancement is essential for enhancing the applicability and accuracy of HIV propagation models in real-world contexts.

3.1 Exponential attractor and main theorem

For all $t \geq 0$, we denote $X(t) = (S(t), I(t), C(t), A(t), E(t)) \in \mathbb{R}_+^* \times \mathbb{R}_+^4$ such that (1) is written $\dot{X} = f(X)$ with $f \in \mathcal{C}^\infty(\mathbb{R}_+^* \times \mathbb{R}_+^4, \mathbb{R}_+^* \times \mathbb{R}_+^4)$.

The system has two steady states which are globally asymptotically stable according to the values of $\mathcal{R}_0$, we say that the set $\mathbb{E} = \{(DFSS), (ESS)\}$ is a global attractor in the sense that regardless the initial conditions chosen, the trajectories converge on this set. This means that : for all initial conditions $X(0) = (S(0), I(0), C(0), A(0), E(0)) \in \mathbb{R}_+^* \times \mathbb{R}_+^4$ $X(t) \underset{t \to +\infty}{\longrightarrow} \mathbb{E}$

However, in order to study the robustness of these steady states and their sensitivity to parameters (for example d) we need more than convergence. we need information on the order of this convergence.

Definition 3.1 A set of steady state for a system $\dot{X} = f(X)$ is called an **exponential attractor** if both following conditions are respected :

- for all initial conditions $X(0) = (S(0), I(0), C(0), A(0), E(0)) \in \mathbb{R}_+^* \times \mathbb{R}_+^4$ $X(t) \underset{t \to +\infty}{\longrightarrow} \mathbb{E}$,
- with C and γ non negative constants such as for all t in $[0, t_f]$, $\text{dist}(X(t), \mathbb{E}) \leq C.e^{-\gamma.t}$.

In other words, it is possible to control the distance of the system's trajectories with respect to the set of steady states by an exponential. The following results give a characterization of exponential attractors.

Theorem 3.2 *Let $\dot{X(t)} = f(X(t))$ be a dynamical system with $X(t) \in \mathbb{R}^5$ for all t in $[0, t_f]$ and $f : \mathbb{R}^5 \mapsto \mathbb{R}^5$ and assume :*

- $\mathbb{E}$ is the set of the steady states,
- there exists F such as $f = \nabla F$,
- all steady states are hyperbolic, that is :

$$\mathcal{R}e\left(\lambda_j\left(\frac{\partial f}{\partial X}(X^*)\right)\right) < 0,$$

where λ_j are the eigenvalues of the jacobian of f and for all $X^* \in \mathbb{E}$. Then, $\mathbb{E}$ is an ***exponential attractor*** for the system $\dot{X} = f(X)$.

The presence of an exponential attractor offers robustness to the steady states, it allows to maintain the overall stability in case of a small disturbance of one of the parameters of the system.

This result is the subject of Efendiev and Yagi (2005) where the following Theorem 3.3 is taken from.

Theorem 3.3 *(Efendiev and Yagi 2005) Consider a dynamical system $\dot{X} = f_\lambda(X)$ depending on a parameter λ:*

- Assume that $(\lambda, X) \mapsto f_\lambda(X)$ is continuous.
- for $\lambda = 0$, the system has an exponential attractor.

Then, there exists λ_* such as for all $|\lambda| < \lambda_*$ the system has an exponential attractor called $\mathcal{M}_\lambda$. Furthermore, $\mathcal{M}_\lambda \to \mathcal{M}_0$ and $\text{dist}(\mathcal{M}_\lambda, \mathcal{M}_0) \leq C.\lambda^\gamma$ with $C > 0$ and $\gamma > 0$ constant.

To apply this result and thus extend the overall stability of the set $\mathbb{E}$ of steady states for $d > 0$, we must show that the system (1) has an exponential attractor.

Remark We note that the parameter λ in Theorem 3.3 can be a couple. It means we can extend the overall stability for a couple (ω, d) of non-zero values.

3.2 Application to the system of HIV spread through PrEP

To apply the result in our problem to extend the steady state stability to cases where $\omega \neq 0$ and $d \neq 0$, we check the hypotheses of the Theorem 3.3, namely that the system has an exponential attractor in the case $(\omega, d) = (0, 0)$.

To show the existence of an exponential attractor with Theorem 3.2, we show that the system is a gradient and steady states are hyperbolic. The existence of a Lyapunov function tells us already that the system is a gradient, so we only need to show that steady states are hyperbolic.

Steady states are hyperbolic if and only if the eigenvalues of the Jacobian system applied in this steady state all have a non-positive real part. The Jacobian of the system is the following matrix:

$$\begin{pmatrix} \frac{-\beta\Theta(t)(N(t)-S(t))}{N(t)^2} - \xi_4 & \frac{-\beta S(t)(N(t)-\Theta(t))}{N(t)^2} & 0 & \frac{-\beta\eta_A S(t)(N(t)-\Theta(t))}{N(t)^2} & 0 \\ \frac{\beta\Theta(t)(N(t)-S(t))}{N(t)^2} & \frac{\beta S(t)(N(t)-\Theta(t))}{N(t)^2} - \xi_3 & 0 & \frac{\beta\eta_A S(t)(N(t)-\Theta(t))}{N(t)^2} + \alpha & 0 \\ 0 & \Phi & -\mu & 0 & 0 \\ 0 & \rho & 0 & -\xi_1 & 0 \\ \psi & 0 & 0 & 0 & -\mu \end{pmatrix},$$

with $\Theta(t) = (I(t) + \eta_A A(t))$. We study the eigenvalues of this matrix for the two steady states of the system.

3.2.1 The disease-free steady state

We apply the Jacobian matrix of f to the disease free steady state (*DFSS*) :

$$(DFSS) : (S^0, I^0, C^0, A^0, E^0) = \left(\frac{\Lambda}{(\psi+\mu)}0, 0, 0, \frac{\psi\Lambda}{\mu(\theta+\psi+\mu)}\right).$$

Investigate the eigenvalues of the Jacobian matrix at the (*DFSS*). Three negative obvious eigenvalues are given by $v_{p1} = -\xi_4$ and $v_{p2} = v_{p3} = -\mu$. For the last two, we need to find the roots of :

$$\mathcal{P}(X) = X^2 + (\xi_1 - \beta + \xi_3)X - (\beta\xi_1 - \xi_1\xi_3 + \rho\beta\eta_A + \rho\alpha).$$

Denote, $\Delta = (\xi_1 - \beta + \xi_3)^2 + 4(\beta\xi_1 + \rho\beta\eta_A + \rho\alpha - \xi_1\xi_3)$.

If $\Delta \leq 0$: the real part of the roots is $\frac{-(\xi_1-\beta+\xi_3)}{2}$. It is negative if and only if $(\xi_1 + \xi_3 - \beta) > 0$.

If $\Delta > 0$: the largest root is $\frac{-(\xi_1-\beta+\xi_3)+\sqrt{\Delta}}{2}$. However,

$$-(\xi_1 - \beta + \xi_3) + \sqrt{\Delta} < 0 \text{ when } (\xi_1 - \beta + \xi_3) > 0 \text{ and } (\xi_1 - \beta + \xi_3) > \sqrt{\Delta}.$$

So $-(\xi_1 - \beta + \xi_3) + \sqrt{\Delta} < 0$ when $(\xi_1 - \beta + \xi_3) > 0$ and $(\beta\xi_1 + \rho\beta\eta_A + \rho\alpha - \xi_1\xi_3) < 0$.

In cases where Δ is negative or zero, condition $(\xi_1 + \xi_3 - \beta) > 0$ must be satisfied. When Δ is positive, both conditions $(\xi_1 + \xi_3 - \beta) > 0$ and $(\beta\xi_1 + \rho\beta\eta_A + \rho\alpha - \xi_1\xi_3) < 0$ must be fulfilled. However, condition $(\beta\xi_1 + \rho\beta\eta_A + \rho\alpha - \xi_1\xi_3) < 0$ is less restrictive than the condition for Δ being negative or zero (as a negative Δ automatically satisfies $(\beta\xi_1 + \rho\beta\eta_A + \rho\alpha - \xi_1\xi_3) < 0$). Thus, the conditions to be met can be expressed as $(\xi_1 + \xi_3 - \beta) > 0$ and $(\beta\xi_1 + \rho\beta\eta_A + \rho\alpha - \xi_1\xi_3) < 0$, which encompass both scenarios for the sign of Δ.

Condition $(\mathcal{DF})$:

- $(\xi_1 + \xi_3 - \beta) > 0$,
- $(\beta\xi_1 + \rho\beta\eta_A + \rho\alpha - \xi_1\xi_3) < 0$.

Thus, if the condition on the parameters ($\mathcal{DF}$) is satisfied, the disease-free steady state is an exponential attractor for the system. However, both steady states need to be such attractors to apply Theorem 3.3.

3.2.2 The endemic steady state

We apply the Jacobian matrix of f to the endemic steady state (*ESS*) :

$$(ESS) : (S^*, I^*, C^*, A^*, E^*)$$

Denote $\mathcal{B} = \frac{\beta(I^*+\eta_A A^*)(N^*-S^*)}{N^{*2}}$ and $\mathcal{C} = \frac{\beta S^*(N^*-(I^*+\eta_A A^*))}{N^{*2}}$.

As for the (*DFSS*), we compute the eigenvalues of the Jacobian matrix applied at the endemic steady states. Two negative obvious eigenvalues are $v_{p1} = v_{p2} = -\mu < 0$. The last three eigenvalues are the roots of the next polynomial of degree three :

$$\begin{aligned}\mathcal{P}(X) =& X^3 + (\xi_1 + \xi_3 + \xi_4 + \mathcal{B} - \mathcal{C})X^2 + (\xi_1\xi_3 + \xi_1\xi_4 + \xi_3\xi_4 + \xi_3\mathcal{B} \\ &- (\xi_1 + \xi_4 + \rho\eta_A)\mathcal{C} - \rho\alpha)X \\ &+ \xi_1\xi_3\xi_4 + \xi_1\xi_3\mathcal{B} - \rho\alpha\mathcal{B} - \rho\alpha\xi_4 - (\rho\eta_A + \xi_1)\mathcal{C}\xi_4.\end{aligned}$$

For this second steady state, we deal with the study of a unitary polynomial of degree 3. So we have to find conditions on the coefficients of these polynomials to get roots with non-positive real parts.

$$\mathcal{P}(X) = X^3 + aX^2 + bX + c$$

A simple computation leads to two independent conditions depending if the roots are real or complex.

Condition ($\mathcal{E}_A$) :

- $c > 0$,
- $0 < 3b < a^2$,
- $a > 0$,
- $\mathcal{P}'(\alpha_1) \geq 0$ and $\mathcal{P}'(\alpha_2) < 0$(or $\mathcal{P}'(\alpha_1) > 0$ and $\mathcal{P}'(\alpha_2) \leq 0$).

Condition ($\mathcal{E}_B$) :

- $3b \geq a^2$ or $\mathcal{P}'(\alpha_1) < 0$ or $\mathcal{P}'(\alpha_2) > 0$,
- $-a < r_1 < 0$.

To be an exponential attractor, the endemic steady states need to satisfy at least one of those two conditions. If we combine this result with the previous one about the disease-free steady state, we have all conditions to make the set of steady states $\mathbb{E}$ an exponential attractor.

3.2.3 Main result

From this study of the eigenvalues and the conditions found, one can deduce from the Theorems 3.2 and 3.3 the following result :

Theorem 3.4 *Consider the dynamical system* $\dot{X} = f_{(d,\omega)}(X)$ *from (1) with the set of steady states* $\mathbb{E}((d,\omega))$ *and assume that* $(\mathcal{DF})$ *and* $((\mathcal{E}_A)$ *or* $(\mathcal{E}_B))$ *are satisfied then there exist* $d^* > 0$ *and* $\omega^* > 0$ *such as for all* $|d| < d^*$ *and* $|\omega| < \omega^*$*:*

- $\mathbb{E}((d,\omega))$ is an exponential attractor
- $\mathbb{E}((d,\omega)) \underset{(d,\omega)\to(0,0)}{\longrightarrow} \mathbb{E}((0,0))$ and $\text{dist}(\mathbb{E}((d,\omega)), \mathbb{E}((0,0))) \leq C|(d,\omega)|^\gamma$ for C and γ non negative constants.

Proof The proof of this result comes from the previous section. Conditions $(\mathcal{DF})$ and ($(\mathcal{E}_A)$ or $(\mathcal{E}_B)$) give the set of steady states to be an exponential attractor because they ensure the negativity of the eigenvalues of the Jacobian. Moreover, the existence of a Lyapunov function is sufficient to apply the theorem 3.3 and then concludes the proof. □

It is therefore possible with this result to extend the stabilities studied in Sect. 2.3 beyond the null hypothesis of the AIDS-induced death parameter d. This stability is very difficult to obtain using the Lyapunov functions because hypothesis $d = 0$ greatly simplifies the computations. Indeed the hypothesis $d = 0$ induces that $\dot{N} = \Lambda - \mu N$, it is therefore very easy to obtain a constant population N (by posing $N = \frac{\Lambda}{\mu}$).

On the other hand, if $d \neq 0$, $\dot{N} = \Lambda - \mu N - dA$. It is therefore much more complicated to obtain a constant global population N and, without this latter hypothesis, finding a Lyapunov function remains an open problem.

The main point of our study is to compute the basic reproduction number $\mathcal{R}_0$ of the SEIAC model, taking into account the PrEP treatment parameter ψ. This work gives the possibility to numerically see the impact of this treatment on the overall stability of steady states and therefore the evolution of the epidemic.

We discuss below the variations of the basic reproduction number according to the parameter ψ applied to data from Cape Verde (Silva and Torres 2017) using numerical simulations.

4 Numerical simulations and discussions

In this part, we study numerically the impact of the PrEP parameter ψ on the basic reproduction number $\mathcal{R}_0$. Furthermore, as seen in Sect. 2 the disease-free steady state (*DFSS*) is globally asymptotically stable when $\mathcal{R}_0 < 1$ and the endemic steady state (*ESS*) when $\mathcal{R}_0 > 1$.

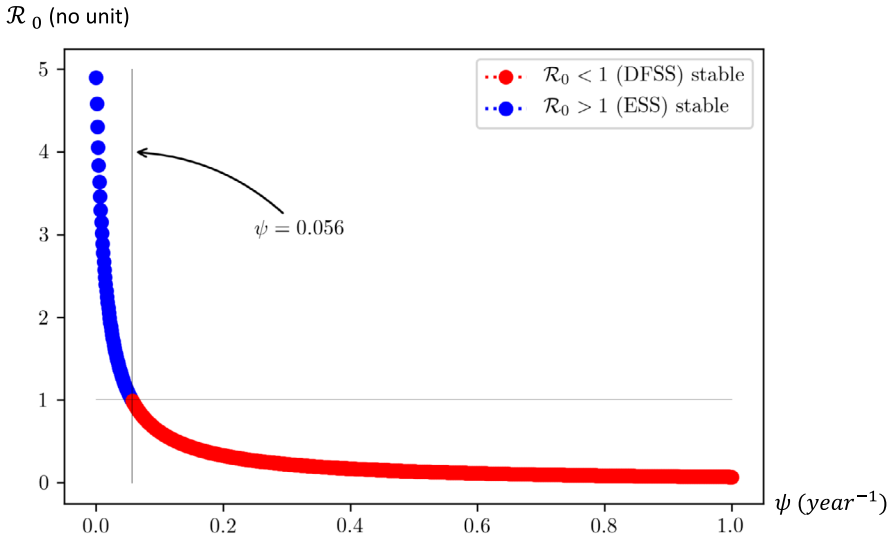

Fig. 2 Stability of steady states according to the values of ψ. In blue, $\mathcal{R}_0$ is greater than 1 so the endemic steady state (*ESS*) is globally asymptotically stable. In red, $\mathcal{R}_0$ is smaller than 1 so the disease-free steady state (*DFSS*) is globally asymptotically stable. The change of stability happens for a value $\psi \approx 0.056$. $\mathcal{R}_0$ is computed using the formula (7)

Our numerical study is applied to the Cape Verde data given in Silva and Torres (2017) (see Table 1). The parameter ψ describes the number of individuals taking the PrEP treatment. It is therefore interesting to see how this number impacts the epidemic's evolution. We compute the basic reproduction number $\mathcal{R}_0$ for each value of ψ in [0, 1]. This calculus gives an idea of the number of people necessary to contain the spread. Results of this simulation appear in Fig. 2.

In Fig.2 the parameter ψ influence on $\mathcal{R}_0$ is shown. When ψ grows, $\mathcal{R}_0$ drops and the outbreak (when $\mathcal{R}_0$ goes below 1) happens when ψ goes over $\psi_{lim} \approx 0.056$.

This outbreak has direct consequences on the stability of steady states because the endemic steady state (*ESS*) loses its stability to the disease-free steady state (*DFSS*), which shows classically a transcritical bifurcation according to the parameter ψ.

This study completes previous work (Silva and Torres 2017) about the trade-off between the number of infected and the cost of treatment. Actually, PrEP treatment is expensive and therefore hard to implement on a large scale, especially in developing countries. In Silva and Torres (2017), the authors showed that the best value to manage this trade-off as well as possible is $\psi = 0.6$. This tenfold change with our value can be explained by the fact that their study focuses on the number of people infected over 25 years whereas the $\mathcal{R}_0$ only gives hints on the theoretical asymptotic behavior of the epidemic, it can be on the very long term.

The ψ value of 0.056 is therefore not a very good indicator to set up an effective short-term defense against HIV because even if it ensures the death of the epidemic in the long term, it does not give information on the number of individuals infected before the end of the propagation. However, this number is crucial in the long term and needs to be added to the previous study of Silva and Torres (2017). In fact, if the

value $\psi = 0.6$ is the best way to deal with the trade-off control of the epidemic and logistic means. It is important to ensure that this value also allows for fighting the epidemic in the long term ($0.6 > 0.056$).

Furthermore, the ψ_{lim} found in our study is the minimal value of the individual to put under PrEP treatment even after having controlled the epidemic to avoid a second wave. This ψ value is not optimal for fighting the epidemic because it does not avoid a lot of individuals from being infected before it ends. However, it gives us minimal value to prevent an outbreak and uncontrolled growth of the epidemic.

Declarations

Conflict of interest The authors do not have any conflict of interest.

References

Abbas UL, Anderson R, Mellors J (2007) Potential impact of antiretroviral chemoprophylaxis on hiv-1 transmission in resource-limited settings. PLoS ONE 2(9):1–11

Adimy M, Molina J, Pujo-Menjouet L, Ranson G, Wu J (2022) Forecasting the effect of pre-exposure prophylaxis (prep) on hiv propagation with a system of differential-difference equations with delay. Mathematics 10(21):4093

Arts EJ, Hazuda DJ (2014) Antiretroviral drug therapy. Cold Spring Harb Perspect Med 2(4):1–23

Attia S, Egger M, Müller M, Zwahlen M, Low N (2009) Sexual transmission of hiv according to viral load and antiretroviral therapy: systematic review and meta-analysis. AIDS 23(11):1397–1404

Deeks S, Lewin S, Havlir D (2013) The end of aids: Hiv infection as a chronic disease. The Lancet 382(9903):1525–1533

Denysiuk R, Silva C, Torres D (2015) Multiobjective approach to optimal control for a tuberculosis model. Optim Methods Softw 30(5):893–910

Van den Driessche P, Watmough J (2002) Reproduction numbers and sub-threshold endemic equilibria for compartmental models of disease transmission. Math Biosci 180:p.29–48

Efendiev MA, Yagi A (2005) Continuous dependence on a parameter of exponential attractors for chemotaxis-growth system. J Math Soc Japan 57(1):167–181

Eyawo O, Franco-Villalobos C, Hull MW, Nohpal A, Samji H, Sereda P, Lima VD, Shoveller J, Moore D, Montaner JSG et al (2017) Changes in mortality rates and causes of death in a population-based cohort of persons living with and without hiv from 1996 to 2012. BMC Infect Dis 17:1–15

Gay CL, Cohen MS (2008) Antiretrovirals to prevent hiv infection: Pre- and postexposure prophylaxis. Curr Infect Dis Rep 10(4):323–331

Granich R, Kahn JG, Bennett R, Holmes CB, Garg N, Serenata C, Sabin ML, Makhlouf-Obermeyer C, De Filippo Mack C, Williams P et al (2012) Expanding art for treatment and prevention of hiv in south africa: estimated cost and cost-effectiveness 2011–2050. PLoS ONE 7(2):e30216

Kim SB, Yoon M, Ku NS, Kim MH, Song JE, Ahn JY, Jeong SJ, Kim C, Kwon HD, Lee J et al (2014) Mathematical modeling of hiv prevention measures including pre-exposure prophylaxis on hiv incidence in south korea. PLoS ONE 9(3):e90080

Madiou J (2017) Implementation de la prep par tdf/ftc en france : bilan à 1 an. IAS Conference

Rodrigues F, Silva C, Torres D (2017) Optimal control of a delayed hiv model. Discrete and Continuous Dynamical Systems - Series B 23(1), https://doi.org/10.3934/dcdsb.2018030

Sabin CA (2013) Do people with hiv infection have a normal life expectancy in the era of combination antiretroviral therapy? BMC Med 11:1–7

Silva CJ (2022) Stability and optimal control of a delayed hiv/aids-prep model. Discrete & Continuous Dynamical Systems-Series S 15(3)

Silva CJ, Torres DFM (2017) Modeling and optimal control of hiv/aids prevention through prep. Discrete and Continuous Dynamical Systems - Series S 11 (1):p.119–141

Silva CJ, Torres DFM (2020) Errata to "modeling and optimal control of hiv/aids prevention through prep, discrete contin. dyn. syst. ser. s 11 (2018), no. 1,119–141". Discrete & Continuous Dynamical Systems-S 13(5):1619

Spinner C, Boesecke C, Zink A, Jessen H, Stellbrink H, Rockstroh J, Esser S (2016) Hiv pre exposure prophylaxis (prep): a review of current knowledge of oral systemic hiv prep in humans. Infection 44:151–158

Thigpen M, Kebaabetswe P, Lt Paxton (2012) Antiretroviral preexposure prophylaxis for heterosexual hiv transmission in botswana. N Engl J Med 367(5):423–434

WHO (2015) Policy brief on oral pre-exposure prophylaxis of HIV infection (PrEP). Geneva

Wilson D, Law M, Grulich AE, Cooper D, Kaldor J (2008) Relation between hiv viral load and infectiousness: A model-based analysis. The Lancet 372(9635):314–320

Ying R, Barnabas RV, Williams BG (2014) Modeling the implementation of universal coverage for hiv treatment as prevention and its impact on the hiv epidemic. Curr HIV/AIDS Rep 11:459–467