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An epidemiological model for the HIV-AIDS epidemics including the PrEP treatment through delay difference-differential equations

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1 Introduction

Since its onset in the homosexual population in California during the early eighties and its clear identification by a French team of researchers in 1983, Human Immunodeficiency Virus (HIV) and then Acquired Immune Deficiency Syndrome (AIDS) has still been one of the most deadly active worldwide epidemics. In the last UNAIDS study released in 2019, about 38 million of individuals lived with HIV, 1.7 million got infected and 690000 died of /AIDS-related diseases in the world[1].

We briefly remind that HIV is part of the retrovirus family, attacks directly the TCD4-cells in charge of the immune responses, and eventually destroys as many as possible. This infection proceeds in 3 phases. Phase 1 : the Acute HIV infection. Few weeks after being infected, an individual may show flu-like symptoms. Known as the Chronic HIV infection, phase 2 : can last up to $10 - 15$ years without any symptoms and the virus keeps on reproducing at a very low level. Phase 3 : AIDS stage : if no treatment is taken, HIV destroys enough TCD4 up to the immune system failure[2]. One can notice that a fondamental problem in this infection is its latency. Indeed, the chronic HIV infection lasting many years without any symptoms, this complicates and delays HIV/AIDS-diagnosis (See Figure 1 in [1]). The main reason of the global spread of this epidemic is the different ways of transmission. There are 3 main ways to transmit HIV : during sexual intercourses, blood exchanges or from a mother to child via breastfeeding. Sharing syringes or any material used for drug injection may also transmit HIV[3].

Despite extensive investigations, there is still neither drugs nor therapy that totally cure HIV. However, since 1996, there exists a therapy, called ART, that consists in a combination of 3 (or more) antiretroviral drugs taken daily. It is important to understand that this treatment does not cure HIV but reduces significantly the presence of the virus in the body. An impressive benefit of ART is that individuals under ART do not transmit HIV if ART is taken conscientiously. In 2019, 25.4 million of HIV-infected individuals accessed antiretroviral therapy[1] [4].

Recently, in addition to the use of condom, a big step appeared with the Pre-Exposure Prophylaxy (PrEP). This treatment addresses individuals that are not HIV-infected but are at high risk of contamination. PrEP consists in taking a combination of 2 antiretrovirals in two different ways : either on a daily basis or on demand that is just 1 day before and 2 days after sexual intercouses. Every 3 months, patients under PrEP must take a global screening and decide whether they continue PrEP treatment or not[4] [5]. It is important to remind that PrEP is a preventive treatment and it does not cure HIV, but effectively reduces HIV transmission[4]. Our study focuses on the French population, where PrEP is completely effective since 2016, and followed by about 20000 individuals [2].

Many epidemiological models have been used in modelling HIV epidemics. A classical SICA (Susceptible - Infected - Infected under ART with low viral charge - Infected with AIDS symptom) compartmental model on HIV/AIDS epidemic has been studied and confronted to data from Cape-Verde in order to fit the epidemic dynamic [3]. In another paper [4], the authors suggested a SIRCA compartmental model in which R is a kind of recovered compartment, where individuals recovered adopted a behaviour such that we assume that they are completely protected from HIV. They studied the global stability and made some numerical simulations but did not use specific data. Some other compartmental models with ordinary differential equations underline the role of screening individuals and stress the importancy of individuals' awareness and preventing policy of HIV/AIDS epidemic [5, 6, 7, 8, 9]. Numerous numerical simulations in these models show that the screening of unaware individuals enables to reduce the transmission of HIV and may have financial benefits. In [10], the authors used a model with delay, *i.e* an age structure that models the incubation between infection and declaration of AIDS symptoms. They proceed through a stability analysis and shown the persistence of the model. In [11], the authors introduced a model including the screening of individuals and a delay that represents time between exposition to HIV and the onset of the infection. They investigated a complete stability analysis and showed that periodic solutions can arise. In [12], they endowed each compartment with an age structure that represents the time since an individuals is in the compartment. In a second part they took into account the ART and the possibility of treatment drop out. Lots of simulations show that intervention methods enables to reduce the number of AIDS cases. Also, in [13], authors built a model that contains two different delays : one represents the time between the beginning of the treatment and the first effects of the treatment and the other the latency period.

But recently, some papers took into account a new compartment : the PrEP. In a previous paper [14], autors suggested vaccination approach. Numerical simulations showed that the spread of the epidemic

[1]UNAIDS; Global HIV & AIDS statistics - 2020 fact sheet. `https://www.unaids.org/en/resources/fact-sheet`

[2]HIV.gov; HIV BASICS : Overview : About HIV & AIDS : Symptoms of HIV ; `https://www.hiv.gov/hiv-basics/overview/about-hiv-and-aids/symptoms-of-hiv`

[3]Centers for Disease Control and Prevention (CDC); HIV Basics: HIV Transmission ; `https://www.cdc.gov/hiv/basics/transmission.html`

[4] World Health Organization (WHO) - HIV/AIDS ; `https://www.who.int/news-room/fact-sheets/detail/hiv-aids`

[5]AIDES - La PrEP ; https://www.aides.org/prep

can be controlled thanks to the vaccination, even if the basic reproduction number is greater than 1. Nowadays, we may see this preventing method as the use of PrEP. In [15, 16], a compartment for individuals under PrEP is included into classical SICA epidemiological models. Parameters of model in [16] are adjusted with clinical data and the effectivness of PrEP is mathematically proven. In [17], the autors divided the compartment of PrEP users according to the adherence of users to the treatment. They shown that with at least 70% of PrEP users it the male homosexual population, the HIV epidemic can be effectively controlled. And finally, in [18], they have combined the use of PrEP and the screening of individuals and confronted their model to Portuguese data. The authors underlined that screening of individuals and the use of PrEP are necessary to fight against the HIV epidemic.

In our paper, we present a compartmental model SIP (susceptible - infected - protected), inspired from [16], with an age structure on the compartment of the PrEP users (protected). In our model, age represents the time since an individuals started a new 3 month period of PrEP. Furthermore, it takes into account the fact that an individual may stop the treatment every three month, when the global screening is proposed to renew the treatment, which was not considered in [16]. This three-months period is represented by a parameter τ. Two choices are then offered at the end of this three-months period : to continue the treatment and so remain in the PrEP compartment, or to stop the treatment and thus become susceptible again. This choice is quantified by a parameter $\theta \in [0, 1]$. Moreover, each month, some individuals may begin the treatment and then enter in the PrEP compartment. It is measured by a parameter ψ.

The construction of this model comes from [19] where the authors suggest a SIR (Susceptible - Infected - Recovered) compartmental model with an age-structured phase of protection with limited duration. Our goal is to improve this model by considering a nonlinear function of the susceptibles. Moreover, we decide to endow the parameter ψ with a temporal dynamic. Those modifications are done in order to fit real data and to be able to correspond exactly to the real situation of the use of PrEP. All this construction leads us to a linear and a nonlinear difference-differential model with discrete delay. We make a complete mathematical study of the model, analysis stability and investigate some precise subcases of our model. Then, we compare our model to official clinical French data in order to understand the role that the PrEP have in the dynamic of the HIV/AIDS epidemic. With some numerical simulations, we see that if we choose a logisitc equation for the parameter ψ and a Hill function for the dynamic of S, we perfectly fit our data. Then, we can also claim that the use of PrEP in a certain small proportion of a precise population enables to reduce the spread of the HIV significantly on the long term.

2 A SI model with age-structured compartment of PrEP protection

In the next section, we study an HIV/AIDS infection model, inspired from [16] , with an age-structure in the PrEP compartment. Then, we give existence, uniqueness and positivity of the solutions. We compute the basic reproduction number $\mathcal{R}_0$ and study the equilibria and invstigate their stability.

2.1 Construction and reduction of our model

As previously done in [16], we divide our total population N into five compartments : susceptibles (S), infected (I), infected under ART (tritherapy) (C), infected at AIDS stage (A) and individuals under PrEP (P).

First of all, we make the following assumption : we suppose that individuals in (C) and (A) cannot be contaminated (they already are) and cannot contaminated. Indeed, individuals in (C) cannot contaminate thanks to the effectiveness of the antiretroviral therapy and individuals in (A) do not contaminate as they behave with caution due to their stage of infection. Thus, we do not take into account equations for (C) and (A).

Now, we give an age structure to the class (P) of individuals following the PrEP program, inspired from [19]. We consider that the PrEP is taken by an individual within a limited duration τ. We know that each 3 months, an individual under PrEP has a global screening. We then assume that, after a period of τ unity, an individual might decide to stop or continue his treatment. We will then fix $\tau = 3$ months.

We define $(t, a) \longmapsto p(t, a)$ as the age distribution of the population under PrEP, in other words, the number of individual under PrEP since $a \leqslant \tau$ unity at time t. Here, the age represents the time since an indivudual is under PrEP. The total number of individual under PrEP at time t is then :

$$P(t) = \int_0^\tau p(t, a)da,$$

Then, we get the following model :

$$\begin{cases} S'(t) = \sigma - \beta I(t)S(t) - (\mu + \psi)S(t) + (1-\theta)p(t,\tau), \\ I'(t) = \beta I(t)S(t) - \mu I(t), \end{cases} \qquad \text{with } t \in \mathbb{R}^+. \tag{1}$$

with nonnegative inital conditions :

$$S(0) = S_0, \quad I(0) = I_0 \quad \text{and} \quad p(0,a) = p_0(a),\ 0 < a < \tau$$

It is a classical model SI with an additional term in the first equation. This term represents individuals who come from the (P) compartment when they decided to stop their treatment.
This is summarized in Figure 2 bellow :

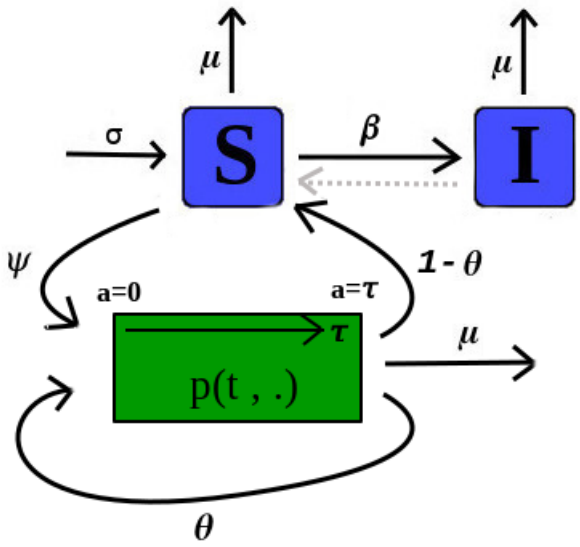

Figure 2: Representation of interactions within our population of susceptibles(S), Infected(I) and PrEp users (P). Continuous arrows represent movements between compartments. Dashed arrow represents the way infection is transmitted.

The description of the parameters is in the next Table 1 :

Symbols	Signification	Unity
ψ	Rate that a susceptible begins PrEP treatment	
θ	Probability that an individual remains under PrEP	
σ	Recruitment	individuals
μ	Natural death rate	individual.month^{-1}
β	HIV transmission rate per infective individual	
τ	Duration of the period of PrEP taking	month

Table 1: Table of parameters used in the system (1)

Remark 1. *We then have* $\theta \in]0,1[$.

We know that the distribution $(t,a) \longmapsto p(t,a)$ follows the next PDE with the corresponding boundary condition :

$$\begin{cases} \dfrac{\partial p}{\partial t}(t,a) + \dfrac{\partial p}{\partial a}(t,a) = -\mu p(t,a), \qquad 0 < a < \tau, \\ p(t,0) = \psi S(t) + \theta p(t,\tau). \end{cases} \tag{2}$$

Indeed, let us consider a group of individuals of age included in a small interval of age Δa. The number of individuals in this group is $p(t,a)\Delta a$. During a small interval of time Δt, then the individuals at time $t + \Delta t$ are $a + \Delta t$ time-old. Thus, the number of these individuals is $p(t + \Delta t, a + \Delta t)\Delta a$. Both groups are the same, but some individuals died. Here, μ represents rate of natural death. The number

of individuals that dies between a and $a+\Delta a$ at time t is $\mu p(t,a)\Delta a$. During the entire interval of time Δt, this number is $\mu p(t,a)\Delta a\Delta t$. Thus, we can write a conservation law as :

$$p(t+\Delta t, a+\Delta t)\Delta a - p(t,a)\Delta a = -\mu p(t,a)\Delta a\Delta t \iff \frac{p(t+\Delta t, a+\Delta t)-p(t,a)}{\Delta t} = -\mu p(t,a)$$

If we suppose at least p differentiable, at the limit we get :

$$\lim_{\Delta t\longrightarrow 0}\frac{p(t+\Delta t,a+\Delta t)-p(t+\Delta t,a)}{\Delta t} = \frac{\partial p(t,a)}{\partial a} \qquad \text{and} \qquad \lim_{\Delta t\longrightarrow 0}\frac{p(t+\Delta t,a)-p(t,a)}{\Delta t} = \frac{\partial p(t,a)}{\partial t}$$

And thus, we get :

$$\begin{aligned}\lim_{\Delta t\longrightarrow 0}\frac{p(t+\Delta t,a+\Delta t)-p(t,a)}{\Delta t} &= \lim_{\Delta t\longrightarrow 0}\frac{p(t+\Delta t,a+\Delta t)-p(t+\Delta t,a)}{\Delta t}\\ &+ \lim_{\Delta t\longrightarrow 0}\frac{p(t+\Delta t,a)-p(t,a)}{\Delta t}\\ &= \frac{\partial p(t,a)}{\partial a}+\frac{\partial p(t,a)}{\partial t} = -\mu p(t,a)\end{aligned}$$

We can solve this equation using the characteristics method (we can use [20]) and we obtain, for $t>0$ and $a\in[0,\tau]$,

$$p(t,a) = \begin{cases} e^{-\mu t}p(0,a-t) = e^{-\mu t}p_0(a-t), & 0\le t\le a,\\ e^{-\mu\tau}p(t-a,0), & t>a.\end{cases}$$

We then define :

$$u(t) := p(t,0), \qquad t\ge\tau.$$

We now rewrite the age-structured equation of the (P) class :

$$P(t) = e^{-\mu t}\int_{t-\tau}^{t} e^{\mu a}u(a)da, \qquad t\ge\tau. \tag{3}$$

Thus, we get the complete model, with the same initial condition :

$$\begin{cases} S'(t) = \sigma-\beta I(t)S(t)-(\mu+\psi)S(t)+(1-\theta)e^{-\mu\tau}u(t-\tau),\\ I'(t) = \beta I(t)S(t)-\mu I(t),\\ P(t) = e^{-\mu t}\displaystyle\int_{t-\tau}^{t} e^{\mu a}u(a)da, \qquad \text{with } t>\tau.\\ u(t) = \psi S(t)+\theta e^{-\mu\tau}u(t-\tau),\end{cases} \tag{4}$$

$$S(0)=S_0, \quad I(0)=I_0, \quad \text{and} \quad u(t)=\varphi(t), \quad -\tau\leqslant t\leqslant 0,$$

Remark that the third equation of (2) depends only on u. The other equations of (2) are independent of P. Then, we get our final complete model with the corresponding initial conditions :

$$\begin{cases} S'(t) = \sigma-\beta I(t)S(t)-(\mu+\psi)S(t)+(1-\theta)e^{-\mu\tau}u(t-\tau),\\ I'(t) = \beta I(t)S(t)-\mu I(t), \qquad \text{with } t>\tau.\\ u(t) = \psi S(t)+\theta e^{-\mu\tau}u(t-\tau),\end{cases} \tag{5}$$

$$S(0)=S_0, \qquad I(0)=I_0, \qquad \text{and} \qquad u(t)=\varphi(t), \qquad -\tau\leqslant t\leqslant 0, \tag{6}$$

The problem which consists in equation (5) with initial conditions (6) is a coupled system of differential and difference equations with discrete delay.

Remark 2. *Knowing that* $P(t) = e^{-\mu t}\displaystyle\int_{t-\tau}^{t} e^{\mu a}u(a)da$, *we get the formula :*

$$P'(t) = -\mu e^{-\mu t}\int_{t-\tau}^{t} e^{\mu a}u(a)da + e^{-\mu t}\left(e^{\mu t}u(t)-e^{\mu(t-\tau)}u(t-\tau)\right).$$

Then, substituting $u(t)$ *by its expression , we get :*

$$P'(t) = -\mu P(t)+\psi S(t)+(\theta-1)e^{-\mu\tau}u(t-\tau). \tag{7}$$

Also, we define the total population as

$$N(t) = S(t)+P(t)+I(t), \tag{8}$$

we then have

$$N'(t) = S'(t) + I'(t) + P'(t) = \sigma - \mu N(t).$$

We easily get that $N(t) = \left(N_0 - \frac{\sigma}{\mu}\right) e^{-\mu t} + \frac{\sigma}{\mu}$. *And thus,*

$$\lim_{t \longrightarrow +\infty} N(t) = \frac{\sigma}{\mu} \tag{9}$$

2.2 Well-posedness of the problem

This subsection is dedicated to existence, uniqueness, positivity and boundedness of solutions of our model (5).

2.2.1 Existence and uniqueness

In that aim, we could rewrite our system (5) as a neutral diferential equation as in [21]. But, we prefer using the step method.

Theorem 2.1. *For each nonnegative initial value* (S_0, I_0, φ)*, with* $\varphi \in \mathcal{C}^0([-\tau, 0])$*, the model (5) has a unique solution defined on* $[-\tau; +\infty[$.

Proof. We first solve the system (5) on $[-\tau, 0]$. In this cas, we have the following system :

$$\begin{cases} S'(t) = \sigma - \beta I(t)S(t) - (\mu + \psi)S(t) + (1-\theta)e^{-\mu\tau}\varphi(t), \\ I'(t) = \beta I(t)S(t) - \mu I(t), \\ u(t) = \psi S(t) + \theta e^{-\mu\tau}\varphi(t), \end{cases} \qquad \text{with } t \in [-\tau; 0].$$

We have a system of ODE on (S, I) and u is completely defined. As S and I are at least supposed continuous, by the theorem of Cauchy-Lipschitz, this system has a unique solution on $[-\tau; 0]$. Then, we repeat this method on each interval of type $[k\tau, (k+1)\tau]$ with $k \in \mathbb{N}$. This system has a unique solution by Cauchy-Lipschitz as we know the solution on $[-\tau, k\tau]$. Thus, we get a unique solution on $[-\tau; +\infty]$ of (5). □

2.2.2 Positivity

Now, we investigate the nonnegatvity of solutions of (5).

Proposition 2.2. *For any nonnegative initial conditions* $(S_0, I_0, \varphi) \in \mathbb{R}^+ \times \mathbb{R}^+ \times \mathcal{C}^0([-\tau, 0], \mathbb{R}^+)$*, the corresponding solution* (S, I, u) *of system (5) is nonnegative.*

Proof. We first proove the nonnegativity on the interval $[0, \tau]$ and then we repeat our result on intervals $[k\tau, (k+1)\tau]$, for $k \in \mathbb{N}^*$. Let us consider a solution of (5) (S, I, u) associated to the initial condition $(S_0, I_0, \varphi) \in \mathbb{R}^+ \times \mathbb{R}^+ \times \mathcal{C}^0([-\tau, 0], \mathbb{R}^+)$. Since $t \in [0, \tau]$, we have $t - \tau \in [-\tau, 0]$. We rewrite our system (5) on $[-\tau, 0]$ as :

$$\begin{cases} S'(t) = \sigma - \beta I(t)S(t) - (\mu + \psi)S(t) + (1-\theta)e^{-\mu\tau}\varphi(t), \\ I'(t) = \beta I(t)S(t) - \mu I(t), \\ u(t) = \psi S(t) + \theta e^{-\mu\tau}\varphi(t), \end{cases}$$

Thus

$$S(t) = 0 \text{ gives } S'(t) = \sigma + (1-\theta)e^{-\mu\tau}\varphi(t) \geqslant 0$$

$$I(t) = 0 \text{ gives } I'(t) = 0 \geqslant 0$$

Then applying Theorem 3.4 of [22], we get that $S(t), I(t) \geqslant 0$ on $[0, \tau]$. Looking at the last equation, we easily get that $u(t) = \psi S(t) + \theta e^{\mu\tau}\varphi(t - \tau) \geqslant 0$ on $[0, \tau]$.

□

2.2.3 Boundedness

And finally, we study the boundedness of solutions of (5).

Proposition 2.3. *Solutions of our system (5) are uniformly bounded.*

Proof. Let (S, I, u) be solutions of (5) associated to the initial conditions $(S_0, I_0, \varphi) \in \mathbb{R}^+ \times \mathbb{R}^+ \times \mathcal{C}^0([-\tau, 0], \mathbb{R}^+)$. Equation (8) gives us that for all $t \geqslant 0$, $0 \leqslant I(t), S(t) \leqslant N(t)$. Then equation (9) gives :

$$0 \leqslant \limsup_{t \longrightarrow +\infty} S(t) \leqslant \frac{\sigma}{\mu} \qquad \text{and} \qquad 0 \leqslant \limsup_{t \longrightarrow +\infty} I(t) \leqslant \frac{\sigma}{\mu}.$$

We can deduce that S and I are uniformly bounded.
To obtain that u is uniformly bounded, we use section 9.3 of [21]. We rewrite the equation on u of (5) as :

$$u(t) = \psi S(t) + \theta e^{-\mu\tau} u(t-\tau) \iff Du_t = h(t),$$

where $u_t(\alpha) := u(t+\alpha)$, $h(t) := \psi S(t)$ and $Dy := -\theta e^{-\mu\tau} y(-\tau) + u(0)$ for $t \geqslant 0$.
We observe that $||D|| := \sup_{||\varphi|| \leqslant 1} |D\varphi| = \theta e^{-\mu\tau} < 1$. This implies that the zero solution of the homogeneous linear difference equation $Du_t = 0$ is globally asymptotically stable. Thus, D is a stable operator and we can use Theorem 3.5 of [21] and get constants $C > 0$, $\gamma > 0$ such that for $t > 0$:

$$|u(t)| \leqslant C \left[|\varphi| e^{-\gamma t} + \psi \sup_{0 \leqslant s \leqslant t} |S(s)| \right],$$

Thus u is bounded. Now, since $t \longmapsto S(t)$ is uniformly bounded, there exists $K > 0$ such that for every $t \geqslant 0$, we have $|S(t)| < K$, *i.e.* $\sup_{t>0} |S(t)| < K$. We have :

$$|u(t)| \leqslant C \left(|\varphi| + \psi K \right), \qquad \text{for all } t > 0.$$

And finally, we get that u is uniformly bounded and :

$$\sup_{t>0} |u| < \tilde{K}, \qquad \text{for all } t > 0.$$

□

2.3 Characterization and study of steady-states

Here, we investigate the existence of steady-states for the system (5). Let us consider such an equilibrium (S^*, I^*, u^*) of (5). Then :

$$\begin{cases} 0 = \sigma - \beta I^* S^* - (\mu + \psi) S^* + (1-\theta) e^{-\mu\tau} u^*, \\ 0 = \beta I^* S^* - \mu I^*, \\ u^* = \psi S^* + \theta e^{-\mu\tau} u^*. \end{cases} \tag{10}$$

Last equation of (10) gives us the solution for u^* :

$$u^* = \frac{\psi S^*}{1 - \theta e^{-\mu\tau}}. \qquad (*)$$

The second equation of (10) gives us a condition :

$$I^* \left(\beta S^* - \mu \right) = 0 \iff I^* = 0 \ \text{ or } \ S^* = \frac{\mu}{\beta}.$$

Consider each case.

2.3.1 The disease-free steady-state (S^0, I^0, u^0)

If $I^* = 0$.
The first equation of (10) and $(*)$ give :

$$0 = \sigma - (\mu + \psi) S^* + (1-\theta) e^{-\mu\tau} u^* \iff S^* = \frac{\sigma(1 - \theta e^{-\mu\tau})}{\mu + \psi - (\mu\theta + \psi) e^{-\mu\tau}}.$$

Then using the expression of S^* in $(*)$, we get :

$$u^* = \frac{\psi\sigma}{\mu + \psi - (\mu\theta + \psi)e^{-\mu\tau}}.$$

Those two formulas have a biological meanning if and only if $\mu+\psi-(\mu\theta+\psi)e^{-\mu\tau} > 0$, which is provided if $\mu + \psi > 0$. Thus, under the condition $\mu + \psi > 0$, we have existence of a disease-free equilibrium (as $I^* = 0$) given by :

$$(S^0, I^0, u^0) := \left(\frac{\sigma(1 - \theta e^{-\mu\tau})}{\mu + \psi - (\mu\theta + \psi)e^{-\mu\tau}} \ , \ 0 \ , \ \frac{\psi\sigma}{\mu + \psi - (\mu\theta + \psi)e^{-\mu\tau}} \right). \tag{11}$$

2.3.2 The endemic steady-state $(\overline{S}, \overline{I}, \overline{u})$

Let us now consider $S^* = \dfrac{\mu}{\beta}$.
We directly get the form of u^* :

$$u^* = \frac{\mu\psi}{\beta(1 - \theta e^{-\mu\tau})}.$$

We check first if the denominator is non zero :

$$1 - \theta e^{-\mu\tau} = 0 \iff \theta = e^{\mu\tau}.$$

However $e^{\mu\tau} > 1$. Thus, Remark 1 gives a contradiction. The denominator never vanishes. Then, using the first equation of (10), we get :

$$I^* = \frac{\sigma}{\mu} - \frac{\mu + \psi - (\psi + \mu\theta)e^{-\mu\tau}}{\beta(1 - \theta e^{-\mu\tau})}.$$

This last result gives us a condition on the existence of this equilibrium through the biological feasibility :

$$I^* > 0 \iff \frac{\sigma}{\mu} > \frac{\mu + \psi - (\psi + \mu\theta)e^{-\mu\tau}}{\beta(1 - \theta e^{-\mu\tau})}.$$

Thus, under this previous condition, we obtain the existence of one endemic equilibrium defined by the following expressions :

$$(\overline{S}, \overline{I}, \overline{u}) := \left(\frac{\mu}{\beta} \ , \ \frac{\sigma}{\mu} - \frac{\mu + \psi - (\psi + \mu\theta)e^{-\mu\tau}}{\beta(1 - \theta e^{-\mu\tau})} \ , \ \frac{\mu\psi}{\beta(1 - \theta e^{-\mu\tau})} \right). \tag{12}$$

Remark 3. *Using equation (7), we get the explicit value of the equilibrium on P :*

$$P^* = \frac{1}{\mu} \left[\psi S^* + (\theta - 1) \exp^{-\tau\mu} u^* \right].$$

We sum up the previous calculations in the following theorem :

Theorem 2.4. *Suppose that the following condition holds :*

$$\frac{\sigma}{\mu} > \frac{\mu + \psi - (\psi + \mu\theta)e^{-\mu\tau}}{\beta(1 - \theta e^{-\mu\tau})} \qquad (H)$$

Then, system (5) has two steady-states : one disease-free equilibrium defined by equation (11) and one endemic equilibrium defined by relation (12). If the previous condition (H) does not hold, then only the disease-free equilibrium exists.

2.4 The basic reproduction number $\mathcal{R}_0$

We compute here the basic reproduction number $\mathcal{R}_0$, which definition is given in [23]. Since we are not in presence of an ODE system, we cannot use the next generation matrix method, explained in [24], in order to compute $\mathcal{R}_0$.

Rewrite the second equation of (5) as :

$$I'(t) = I(t)\left[\beta S(t) - \mu\right] \iff \frac{I'(t)}{\mu I(t)} = \frac{\beta S(t)}{\mu} - 1.$$

As the product $\mu I(t) > 0$, if the left member in the previous equation is negative, it means that $I'(t)$ is negative and that the infection vanishes. Else, the left-hand side is nonnegative, then $I'(t)$ is nonnegative and the infection continues. In other words, the infection triggers if and only if

$$\frac{\beta S(t)}{\mu} - 1 > 0 \iff \frac{\beta S(t)}{\mu} > 1.$$

Then, the basic reproduction number $\mathcal{R}_0$ of our system (5) is given by :

$$\mathcal{R}_0 := \frac{\beta S^0}{\mu} = \frac{\beta\sigma(1-\theta e^{-\mu\tau})}{\mu(\mu+\psi-(\mu\theta+\psi)e^{-\mu\tau})}. \tag{13}$$

Remark 4. *We see that condition (H) in Theorem 1.4 is equivalent to $\mathcal{R}_0 > 1$. Then the existence of the endemic equilibrium is equivalent to $\mathcal{R}_0 > 1$.*

We get easily the following proposition about the behaviour of $\mathcal{R}_0$.

Proposition 2.5. *The number $\mathcal{R}_0$ is a decreasing function as a function of τ, ψ and θ. Also, we have*

$$\sup_{\tau\in[0,+\infty[} \mathcal{R}_0(\tau) = \mathcal{R}_0(\tau=0) = \frac{\beta\sigma}{\mu^2} \qquad \textit{and} \qquad \inf_{\tau\in[0,+\infty[} \mathcal{R}_0(\tau) = \lim_{\tau\longrightarrow+\infty} \mathcal{R}_0(\tau) = \frac{\beta\sigma}{\mu(\mu+\psi)}$$

$$\sup_{\psi\in[0,+\infty[} \mathcal{R}_0(\psi) = \mathcal{R}_0(\psi=0) = \frac{\beta\sigma}{\mu^2} \qquad \textit{and} \qquad \inf_{\psi\in[0,+\infty[} \mathcal{R}_0(\psi) = \lim_{\psi\longrightarrow+\infty} \mathcal{R}_0(\psi) = 0$$

$$\sup_{\theta\in[0,1]} \mathcal{R}_0(\theta) = \mathcal{R}_0(\theta=0) = \frac{\beta\sigma}{\mu(\mu+\psi(1-e^{-\mu\tau}))} \qquad \textit{and} \qquad \inf_{\theta\in[0,1]} \mathcal{R}_0(\theta) = \frac{\beta\sigma}{\mu(\mu+\psi)}$$

Proof. We show this result for τ. The techniques are the same for the other variables.

The derivative of the function $\tau \longmapsto \mathcal{R}_0(\tau)$ is

$$\mathcal{R}_0'(\tau) = \frac{\mu^2\psi\beta\sigma e^{-\mu\tau}(\theta-1)}{\left[\mu(\mu+\psi-(\mu\theta+\psi)e^{-\mu\tau})\right]^2}$$

As the denominator is positive, the sign is given by the numerator. Since $\theta \in [0,\theta]$, we get that $\theta - 1 \leqslant 0$, thus $\mathcal{R}_0'(\tau) \leqslant 0$ for every τ. Then the function $\tau \longmapsto \mathcal{R}_0(\tau)$ is nonincreasing. As $\tau \longmapsto \mathcal{R}_0(\tau)$ is continuous, we get that the maximum is reached at $\tau = 0$ and the minimum, which is actually an infimum, is reached when $\tau \longrightarrow +\infty$. □

This proposition shows that there is at least three ways to reduce the $\mathcal{R}_0$. We will have to find the perfect combination of those three paramaters in order to make the $\mathcal{R}_0$ as small as possible, at least less than 1. Moreover, those parameters describe the way the PrEP is used. Thus, the PrEP treatment has a non-negligible role in the behaviour of the HIV/AIDS epidemic and may be powerfull to reduce it.

2.5 Local asymptotic stability of the steady-states

In this section, we aim at studying the local stability of the equilibria considering both cases of $\mathcal{R}_0 > 1$ and $\mathcal{R}_0 < 1$. Let us first linearize our system (5) about an equilibrium (S^*, I^*, u^*). The last row is already linear. We write the Jacobian of the two first rows evaluated in a steady-state and get the next matrix :

$$J = \begin{pmatrix} -\beta I^* - (\mu+\psi) & -\beta S^* \\ \beta I^* & \beta S^* - \mu \end{pmatrix}.$$

Then, our linearized system is :

$$\begin{cases} S'(t) = -\beta I^* S(t) - \beta S^* I(t) - (\mu+\psi)S(t) + (1-\theta)e^{-\mu\tau}u(t-\tau), \\ I'(t) = \beta I^* S(t) + \beta I(t) S^* - \mu I(t), \\ u(t) = \psi S(t) + \theta e^{-\mu\tau}u(t-\tau). \end{cases} \qquad t \geqslant \tau \tag{14}$$

We now look for solutions of the form $S(t) = e^{\lambda t}S_0$, $I(t) = e^{\lambda t}I_0$ and $u(t) = e^{\lambda t}u_0$, with $(S_0, I_0, u_0) \neq 0$. After simplifying by $e^{\lambda t}$, we obtain the algebraic system

$$\begin{cases} \lambda S_0 = -\beta I^* S_0 - \beta S^* I_0 - (\mu + \psi)S_0 + (1-\theta)e^{-\mu\tau}e^{-\tau\lambda}u_0, \\ \lambda I_0 = \beta I^* S_0 + \beta I_0 S^* - \mu I_0, \\ u_0 = \psi S_0 + \theta e^{-\mu\tau}e^{-\tau\lambda}u_0. \end{cases}$$

Then, we rewrite this previous system as a matrix system :

$$\begin{pmatrix} \lambda + \beta I^* + \mu + \psi & \beta S^* & -(1-\theta)e^{-\mu\tau}e^{-\tau\lambda} \\ -\beta I^* & \lambda - \beta S^* + \mu & 0 \\ -\psi & 0 & 1 - \theta e^{-\mu\tau}e^{-\tau\lambda} \end{pmatrix} \begin{pmatrix} S_0 \\ I_0 \\ u_0 \end{pmatrix} = \begin{pmatrix} 0 \\ 0 \\ 0 \end{pmatrix}.$$

The characteristic equation is given by

$$\begin{vmatrix} \lambda + \beta I^* + \mu + \psi & \beta S^* & -(1-\theta)e^{-\mu\tau}e^{-\tau\lambda} \\ -\beta I^* & \lambda - \beta S^* + \mu & 0 \\ -\psi & 0 & 1 - \theta e^{-\mu\tau}e^{-\tau\lambda} \end{vmatrix} = 0. \tag{15}$$

Then, computing this determinant, our characteristic equation becomes :

$$\Delta(\lambda, \tau) = 0, \tag{16}$$

where $\Delta(\lambda, \tau)$ is given by :

$$\begin{aligned} \Delta(\lambda, \tau) := \lambda^2 &+ (2\mu + \beta(I^* - S^*) + \psi)\lambda + \mu(\beta(I^* - S^*) + \psi) - \psi\beta S^* \\ &- e^{-\mu\tau}e^{-\tau\lambda}\left[\theta(\lambda^2 + (\mu + \beta(I^* - S^*))\lambda + \mu(\mu + \beta(I^* - S^*)) + \psi\lambda + \psi(\mu - \beta S^*)\right]. \end{aligned}$$

Remark 5. *We notice that the function $\Delta(\lambda, \tau)$ defined in (16) is an entire function of λ. Thus, this function must have at most countably many zeros. And by the principle of isolated zeros, the set of those zeros cannot have an accumulation point. So, if we take a sequence of roots $(\lambda_n)_n \in \mathbb{C}^{\mathbb{N}}$ of (16), this one verfies $\lim_{n \longrightarrow +\infty} |\lambda_n| = +\infty$.*
Moreover, we rewrite our equation (16) as it follows :

$$\begin{aligned} &1 + \frac{2\mu + \beta(I^* - S^*) + \psi)}{\lambda} + \frac{\mu(\beta(I^* - S^*) + \psi) - \psi\beta S^*}{\lambda^2} \\ &- e^{-\mu\tau}e^{-\mu\lambda}\left[\theta(1 + \frac{\mu + \beta(I^* - S^*)}{\lambda} + \frac{\mu(\mu + \beta(I^* - S^*)}{\lambda^2} + \frac{\psi}{\lambda} + \frac{\psi(\mu - \beta S^*)}{\lambda^2}\right] = 0 \end{aligned}$$

subtituting by such a sequence and taking the modulus in the previous equation, we have that, as $n \longrightarrow +\infty$, the sequence $(\lambda_n)_n$ approaches one root of the roots of the equation :

$$e^{\lambda\tau} - \theta e^{-\mu\tau} = 0$$

which are

$$\tilde{\lambda}_k = \frac{\ln(\theta) - \mu\tau}{\tau} + \frac{2k\pi i}{\tau} \qquad \text{with } k \in \mathbb{Z}$$

As $\theta \in]0, 1[$, we see that each root that appears from infinity has a negative real part.

2.5.1 Local stability without delay, *ie* $\tau = 0$

We study here the stability of our system with no delay. The determinant given by (15) becomes

$$\begin{vmatrix} \lambda + \beta I^* + \mu + \psi & \beta S^* & \theta - 1 \\ -\beta I^* & \lambda - \beta S^* + \mu & 0 \\ -\psi & 0 & 1 - \theta \end{vmatrix}$$

Summing the second and third rows to the first one, and computing the determinant, the characteristic equation for $\tau = 0$ is given by :

$$(1 - \theta)(\lambda + \mu)(\lambda + \mu + \beta(I^* - S^*)) = 0 \tag{17}$$

Now, let us check the stability of our steady-states. We get the two following results.

Proposition 2.6. *For $\tau = 0$, we get the following stability : if $\mathcal{R}_0 < 1$ the disease-free equilibrium, given by (11), is the unique steady-state and is locally asymptotically stable. Else, $\mathcal{R}_0 > 1$, both of the steady-states coexist and the disease-free is unstable and the endemic one, given by (12) is locally asymptotically stable.*

Proof. Let us consider the disease-free equilibrium (S^0, I^0, u^0) given by (11). The equation (17) applied to the disease-free is :

$$(1-\theta)(\lambda+\mu)(\lambda+\mu-\beta S^0) = 0 \iff (1-\theta)(\lambda+\mu)(\lambda+\mu(1-\mathcal{R}_0)) = 0.$$

This equation gives us that

$$\lambda + \mu = 0 \quad \text{or} \quad \lambda + \mu(1-\mathcal{R}_0) = 0,$$
$$\lambda = -\mu \quad \text{or} \quad \lambda = \mu(\mathcal{R}_0 - 1)$$

Thus, we see that if $\mathcal{R}_0 < 1$ then $\lambda = \mu(\mathcal{R}_0 - 1) < 0$ and we have both of the roots that are negative, we conclude that the disease-free equilibrium is locally asymptotically stable.

But, if $\mathcal{R}_0 > 1$, then $\lambda = \mu(\mathcal{R}_0 - 1) > 0$ and the disease-free equilibrium is unstable as one of the eigenvalues is positive.

Let us consider the endemic equilibrium $(\overline{S}, \overline{I}, \overline{u})$ given by (12). The equation (17) applied to the endemic steady-state is :

$$(1-\theta)(\lambda+\mu)(\lambda+\mu+\beta(\overline{I}-\overline{S})) = 0 \iff (1-\theta)(\lambda+\mu)(\lambda+\beta\overline{I}) = 0.$$

And then, we see that the two roots are

$$\lambda = -\mu \quad \text{and} \quad \lambda = -\beta\overline{I}$$

As $\overline{I} > 0$, we get that all the roots are negative. Then, for $\mathcal{R}_0 > 1$, the endemic steady-state is locally asymptotically stable.

□

2.5.2 Local stability of the disease-free equilibrium

The linearized system (14) evaluated in the disease-free equilibrium (S^0, I^0, u^0) (11) is :

$$\begin{cases} S'(t) = -\beta S^0 I(t) - (\mu+\psi)S(t) + (1-\theta)e^{-\mu\tau}u(t-\tau), \\ I'(t) = \beta I(t) S^0 - \mu I(t), \\ u(t) = \psi S(t) + \theta e^{-\mu\tau}u(t-\tau). \end{cases}$$

As previously, we compute the caracteristic equation around the disease-free equilibrium and we get :

$$\Delta(\lambda,\tau) := (\lambda+\mu-\beta S^0)(\lambda+\mu+\psi-(\theta(\lambda+\mu)+\psi)e^{-\mu\tau}e^{-\lambda\tau}) = 0 \tag{18}$$

From now on, let us set $\mathcal{R}_0 < 1$. The eigenvalue given by $\lambda = \mu(-1+\mathcal{R}_0)$ is then negative. We must now assure that the roots λ (*i.e.* the eigenvalues of the linearized system around the disease-free equilibrium) of the equation :

$$\lambda+\mu+\psi-(\theta(\lambda+\mu)+\psi)e^{-\mu\tau}e^{-\lambda\tau} = 0 \tag{19}$$

have a negative real part. We get the following theorem :

Theorem 2.7. *Suppose that $\mathcal{R}_0 < 1$. The disease-free equilibrium given by (11) is locally asymptotically stable.*

Proof. In order to get this demonstration, we must show that all the roots of the previous characteristic equation (19) have a negative real part. Indeed, we already shown in remark 4 that all the roots that come from the infinity have a negative real part. Thus, we consider the roots that appears in a bounded set. Let us consider the disease-free equilibrium $(S^0, 0, u^0)$.

First, we notice that $f : (\lambda,\tau) \in \mathbb{C} \times [0,+\infty[\longmapsto \lambda+\mu+\psi-(\theta(\lambda+\mu)+\psi)e^{-\mu\tau}e^{-\lambda\tau}$ is $\mathcal{C}^1$ in both of variables. We notice that the partial derivate on the second variable is not zero. We can then use the implicit functions theorem and study the roots λ as a $\mathcal{C}^1$ function of τ. We also consider $\mathcal{R}_0$ as a function in τ, $\tau \longmapsto \mathcal{R}_0(\tau)$, with $\tau \in \mathbb{R}^+$.
For $\tau = 0$, we have already shown that the equilibrium is stable thanks to proposition 1.6.
Let us now chose a fixed $\tau \in]0,+\infty[$ and let us seek a pure imaginary root $\pm i\omega$, with $\omega \in \mathbb{R}$. Indeed, if there exists such a root of (19), then, by the continuity of $\tau \longmapsto \lambda(\tau)$ and the remark 5, we can assure that there exists roots with positive real part.

Substituting λ in (19) and defining :

$$\eta := \theta e^{-\mu\tau} \qquad \text{and} \qquad \rho := (\theta\mu + \psi)e^{-\mu\tau},$$

and thus we get :

$$i\omega + \mu + \psi - (\eta\lambda + \rho)e^{-i\omega\tau} = 0.$$

And then, separating the real and the imaginary part, we get the following system :

$$\begin{cases} \eta\omega\cos(\omega\tau) - \rho\sin(\omega\tau) = \omega, \\ \eta\omega\sin(\omega\tau) + \rho\cos(\omega\tau) = \mu + \psi. \end{cases}$$

Solving this system, we get :

$$\begin{cases} \cos(\omega\tau) = \dfrac{1}{(\eta\omega)^2 + \rho^2}\left[\eta\omega^2 + \rho(\mu + \psi)\right], \\ \sin(\omega\tau) = \dfrac{1}{(\eta\omega)^2 + \rho^2}\left[-\rho\omega + \eta\omega(\mu + \psi)\right] \end{cases}$$

Using the well-known formula $\cos(\omega\tau)^2 + \sin(\omega\tau)^2 = 1$, we get :

$$1 = \frac{1}{((\eta\omega)^2 + \rho^2)^2}\left[(\eta\omega^2 + \rho(\mu + \psi))^2 + (-\rho\omega + \eta\omega(\mu + \psi))^2\right]^2$$

Expanding this expression and factoring in ω, we have :

$$\begin{aligned} &\eta^2(\eta^2 - 1)\omega^4 + (2\rho^2\eta^2 - \rho^2 - \eta^2\mu^2 - \eta^2\psi^2 - 2\eta^2)\omega^2 + \rho^2(\rho^2 - \mu^2 - 2\mu\psi - \psi^2) = 0 \\ \iff &\eta^2(\eta^2 - 1)\omega^4 + \left[\rho^2(\eta^2 - 1) + \eta^2(\rho - (\mu + \psi))(\rho + \mu + \psi)\right]\omega^2 + \rho^2(\rho - (\mu + \psi))(\rho + \mu + \psi) = 0 \\ \iff &aX^2 + bX + c = 0 \end{aligned}$$

with $X := \omega^2$ as a change of variables and

$$a := \eta^2(\eta^2 - 1) \quad ; \quad b := \rho^2(\eta^2 - 1) + \eta^2(\rho - (\mu + \psi))(\rho + \mu + \psi) \quad \text{and} \quad c := \rho^2(\rho - (\mu + \psi))(\rho + \mu + \psi)$$

We can notice the following facts : as $\eta \leqslant 1$, we have that $a < 0$. Then, c is also negative since we have $\rho < \mu + \psi$. And finally, b is negative thanks to the same reasons.
As the three coefficients are negative, the Routh-Hurwitz criterion tells us that all roots of our equation have a negative real part. In other words, there exists $\alpha < 0$ and $\beta \in \mathbb{R}$ such as $X = \alpha \pm i\beta$. Then we have :

$$X = \alpha + i\beta \iff \omega^2 = \alpha + i\beta \implies \omega^2 = \alpha$$

the last equality is absurd since $\omega^2 > 0$ and $\alpha < 0$.
Thus, for every $\tau > 0$, it does not exist $\omega > 0$ such as $\lambda = \pm i\omega$.

And for $\mathcal{R}_0(\tau) < 1$, oth $\tau \geqslant 0$ all roots of (19) have negative real part. Thus, $(S^0, 0, u^0)$ is locally asymptotically stable.

□

2.5.3 Local asymptotic stability of the endemic equilibrium

Now we are interested in the study of the stability of the endemic stead-state given by (12) for a $\tau > 0$. First, we suppose in this subsection that $\mathcal{R}_0 > 1$.

Taking the determinant (15) applied to the endemic equilibrium, we get :

$$\begin{vmatrix} \lambda + \beta\overline{I} + \mu + \psi & \beta\overline{S} & -(1-\theta)e^{-\mu\tau}e^{-\tau\lambda} \\ -\beta\overline{I} & \lambda - \beta\overline{S} + \mu & 0 \\ -\psi & 0 & 1 - \theta e^{-\mu\tau}e^{-\tau\lambda} \end{vmatrix} = 0. \tag{20}$$

Summing the second and third row to the first one and computing it, we get the characteristic equation :

$$\Delta(\lambda, \tau) = 0 \tag{21}$$

where $\Delta(\lambda, \tau)$ is given by :

$$\Delta(\lambda, \tau) := \lambda^2 + (\psi + \mu + \beta\overline{I})\lambda + \mu\beta\overline{I} - \left[\theta(\lambda^2 + (\mu + \beta\overline{I}) + \lambda\mu\beta\overline{I}) + \psi\lambda\right]e^{-\mu\tau}e^{-\tau\lambda} = 0 \tag{22}$$

Then, in order to study the stability, we follow the same steps as the proof of theorem 1.8. We still consider $\mathcal{R}_0$ and λ as function of the variable τ .
Thanks to the proposition 1.7, we have already shown that the endemic equilibrium is locally asymptotically stable for $\tau = 0$ with $\mathcal{R}_0(\tau) > 1$. We then show the result for any $\tau > 0$ following the same steps as in Theorem 1.8.

Theorem 2.8. *Let us take $\tau > 0$ and assume that $\mathcal{R}_0(\tau) > 1$. Then, all the roots of (21) have negative real part and thus the endemic equilibrium is locally asymptotically stable.*

Proof. We follow the same steps as in the proof of theorem 1.8. We show that there is no purely imaginary roots $\lambda = \pm i\omega$ and we can assume $\omega > 0$. Separating real and imaginary parts in equation (18), we get the system :

$$\begin{cases} \rho_\omega \cos(\omega\tau) - \eta\omega \sin(\omega\tau) = \omega^2 - b, \\ \eta\omega \cos(\omega\tau) - \rho_\omega \sin(\omega\tau) = (\psi + a)\omega. \end{cases}$$

with

$$a := \mu + \beta\bar{I} \quad ; \quad c := e^{-\mu\tau} \quad ; \quad b := \mu\beta\bar{I}$$
$$\eta := c(\theta a + \psi) \qquad \text{and} \qquad \rho_\omega := c\theta(\omega^2 - b)$$

Then, solving this system and using the same formula as in the proof of Theorem 1.8, we get

$$\rho_\omega^2 + (\eta\omega)^2 = \omega^2(\psi + a)^2 + (\omega^2 - b)^2.$$

Expanding this expression, we have that $X := \omega^2$ satisfies the equation :

$$X^2 + DX + b^2 = 0, \tag{23}$$

with

$$D := \frac{(\psi + a)^2 + 2b((\theta c)^2 - 1) - \eta^2}{1 - (\theta c)^2}.$$

Let us show that D is nonnegative. By absurd, let us suppose that $D < 0$. Then, the discriminant of the equation (19) is

$$\Delta = D^2 - 4b^2 = (D - 2b)(D + 2b)$$

We clearly see that $D - 2b < 0$. Moreover, let us compute :

$$(1 - (\theta c)^2)(D + 2b) = (\psi + a)^2 - \eta^2 = (\psi + a + \eta)(\psi + a - \eta)$$

But

$$\psi + a + \eta = \psi + a - c\theta a - c\psi = \psi(1 - c) + a(1 - c\theta) > 0$$

Then necessarily, as $1-(\theta c)^2 > 0$ and $(\psi+a+\eta)(\psi+a-\eta) > 0$, we have $D+2b > 0$. Thus, $\Delta < 0$ and the equation has complexe roots, in other words, there exists $u, v \in \mathbb{R}$, with $v \neq 0$, such as $x = \omega^2 = u + iv$, which is absurd.
So, D is positive. The Routh-Hurwitz criterion gives us that equation (19) has roots with negative real part, ie there exists $\tilde{u} < 0$ and $v \in \mathbb{R}$ such as $x = \omega^2 = u + iv$, which implies $\omega^2 = u$, but it is impossible. Thus, there does not exists ω such as $\lambda = \pm i\omega$. And then, we cannot have a change of stability and all λ has negative real part. So, the endemic equilibrium is locally asymptotically stable.

□

2.6 Uniform persistence of the disease

In this section, we study the persistence of the disease. First, we assume that $\mathcal{R}_0 > 1$.
The persistence of the disease is defined in [25] and [26] by

$$\exists\ \varepsilon > 0,\ I_0 > 0 \implies \liminf_{t \longrightarrow +\infty} I(t) > \varepsilon.$$

Indeed, the assumption $\mathcal{R}_0 > 1$ is not incompatible with the disappearance of the disease. But, in this section, we show that, even if $\mathcal{R}_0 > 1$, the disease persists.

2.6.1 Study and stability of an auxiliary system

In this subsection, we are interested in the study of the following system :

$$\begin{cases} x'(t) = \sigma - (\mu + \psi)x(t) + (1 - \theta)e^{-\mu\tau}v(t - \tau), \\ v(t) = \psi x(t) + \theta e^{-\mu\tau}v(t - \tau), \\ x(0) = x_0, \quad v(z) = \varphi(z), \text{ for } -\tau \leqslant z \leqslant 0 \end{cases} \qquad \text{with } t > 0. \tag{24}$$

We easily compute that this system has a unique equilibrium (x^0, v^0) given by

$$x^0 := \frac{\sigma(1 - \theta e^{-\mu\tau})}{\mu + \psi - (\theta\mu + \psi)e^{-\mu\tau}} \quad ; \quad v^0 := \frac{\psi}{1 - \theta e^{-\mu\tau}} x^0 \tag{25}$$

And then, the main theorem we have is the following :

Theorem 2.9. *For any initial condition $(x_0, \varphi) \in \mathbb{R}^+ \times \mathcal{C}^0([-\tau; 0], \mathbb{R}^+)$, we have that the solution $(x(t), v(t))$ of (24) satisfies*

$$(x(t), v(t)) \xrightarrow[t \longrightarrow +\infty]{} (x^0, v^0)$$

In other words, the steady-state (x^0, v^0) given by (25) is globally asymptotically stable.

Proof. We first set :

$$\begin{cases} \hat{x}(t) := x(t) - x^0, \\ \hat{v}(t) := v(t) - v^0. \end{cases} \tag{26}$$

Then, those variables satisfy the following linear differential-difference system :

$$\begin{cases} x'(t) = -(\mu + \psi)x(t) + (1 - \theta)e^{-\mu\tau}v(t - \tau), \\ v(t) = \psi x(t) + \theta e^{-\mu\tau}v(t - \tau). \end{cases} \qquad \text{with } t > 0. \tag{27}$$

Our system (26) is a difference-differential system. We show that it is also an input-to-state system. The definition can be found in [27]. This implies that the trivial steady-state is globally asymptotically stable. In order to proove it, we use the Theorem 3 in [27].
Let us define the following function $V : \mathbb{R} \times \mathcal{C}^0([-\tau, 0], \mathbb{R}) \longrightarrow \mathbb{R}$ given by

$$V(x_0, \varphi) = \frac{x_0^2}{2} + \xi \int_{-\tau}^{0} \varphi^2(s)ds,$$

with $\xi > 0$ a constant that we determine later.
First, we have the following functional inequality :

$$u(x_0) \leqslant V(x_0, \varphi) \leqslant v(||(x_0, \varphi)||)$$

with $u(x) := \frac{x^2}{2}$ and $v(x) := (1 + \tau)x^2$. Those functions are clearly continuous, nondecreasing, positive, satisfy $u(0) = v(0) = 0$ and $\lim\limits_{a \longrightarrow +\infty} u(a) = +\infty$.
As shown in section 2.1, $t \longmapsto \hat{x}$ and $t \longmapsto \hat{v}(t)$, solution of (24) are uniformly bounded.
Now, we want to show that our system is input-to-state (See[27]). This shows that our equilibrium is globally asymptotically stable. .
Then, we differentiate the fonction $t \longmapsto V(\hat{x}(t), \hat{v}_t)$ along the solution $(\hat{x}, \hat{v})$ of (24), we get for $t > 0$:

$$\begin{aligned} \frac{dV}{dt}(\hat{x}, \hat{v}_t) &= \hat{x}'(t)\hat{x} + \xi\hat{v}^2(t) - \xi\hat{v}^2(t - \tau) \\ &= -(\mu + \psi - \xi\psi^2)\hat{x}^2(t) + \left[(1 - \theta)e^{-\mu\tau} + 2\psi\theta e^{-\mu\tau}\right]\hat{x}(t)\hat{v}^2(t - \tau) - \xi\hat{v}^2(t - \tau)\left[1 - \theta^2(e^{-\tau\mu})^2\right]. \end{aligned}$$

To use Theorem 3 of [27], we want to find $\varepsilon > 0$ such as

$$\frac{d}{dt}V(\hat{x}, \hat{v}_t) \leqslant -\varepsilon\hat{x}^2(t).$$

Let us consider the function $\frac{d}{dt}V(\hat{x}, \hat{v}_t) + \varepsilon\hat{x}^2(t)$ as a second order polynomial function of $\hat{x}$. We compute the discriminant of that polynom $\hat{\Delta}$:

$$\hat{\Delta} = \hat{v}^2(t - \tau)\left[((1 - \theta)e^{-\mu\tau} + 2\psi\theta e^{-\mu\tau})^2 - 4\xi(\mu + \psi - \xi\psi^2 - \varepsilon)(1 - \theta^2(e^{-\tau\mu})^2)\right]$$

To find such a ε, we must have the leading coefficient of this polynom and the discriminant negative. In other words :

$$\hat{\Delta} < 0 \qquad \text{and} \qquad \mu + \psi - \xi\psi^2 - \varepsilon > 0$$

Let us consider this discriminant as a function of $\varepsilon, \varepsilon \longmapsto \hat{\Delta}(\varepsilon)$. We easily see that this function is continuous and has a positive derivative. As $\varepsilon \in]0; +\infty[$, if $\hat{\Delta}(0)$ is negative, then by the continuity and the monotonicity of $\varepsilon \longmapsto \hat{\Delta}(\varepsilon)$, we can find a $\varepsilon > 0$ such as $\hat{\Delta} < 0$. As the term $\hat{v}^2(t - \tau)$ is positive, it will not change the sign and we can "forget" it. Then we have

$$\hat{\Delta}(0) = 4\xi^2\psi^2 + 4\xi(-\psi - \mu + \mu\alpha^2e^{-2\tau\mu}) + (1 - \theta)^2e^{-2\tau\mu} = a\xi^2 + b\xi + c := f(\xi),$$

with $a := 4\psi^2$, $b := 4(-\psi - \mu + \mu\alpha^2e^{-2\tau\mu})$ and $c := (1 - \theta)^2e^{-2\tau\mu}$.
The discriminant of this polynom is

$$\Delta_f = b^2 - 4ac = 16(-\psi + \mu(\alpha^2e^{-2\tau\mu} - 1)^2 - 16\psi^2(1 - \theta)^2e^{-2\tau\mu} > 0.$$

The leading coefficient of f and its discriminant are positive, then f has a negative minimum reached at

$$\xi^* := \frac{-b}{2a} = \frac{\psi + \mu(1-(\alpha e^{-\mu\tau})^2)}{2\psi^2}.$$

Thus $f(\xi^*) < 0$. Then, if we choose the constant $\xi := \xi^*$, we have that $\hat{\Delta}(0) < 0$ and we can find an $\varepsilon > 0$ such as $\hat{\Delta} < 0$.
Now, it is clear that we also can find a $\varepsilon > 0$ satisfying $\mu + \psi - \xi\psi^2 - \varepsilon > 0$ as

$$\mu + \psi - \xi\psi^2 - \varepsilon = \frac{1}{2}(\psi + \mu(1-(\alpha e^{-\mu\tau})^2) - \varepsilon.$$

Thus, we can apply Theorem 3 of [27] and we get that (25) is globally asymptotically stable. □

2.6.2 A weak form of uniform persistence

We begin with a weak form of persistence (See [25]).

Theorem 2.10. *Suppose that $\mathcal{R}_0 > 1$. Then, there exists a real $\varepsilon > 0$ such that for any initial condition $(S_0, I_0, \varphi) \in \mathbb{R}^+ \times \mathbb{R}_+^* \times \mathcal{C}^0([-\tau, 0], \mathbb{R}^+)$, we have*

$$\limsup_{t \longrightarrow +\infty} I(t) \geqslant \varepsilon.$$

Proof. We have $\mathcal{R}_0 > 1$, ie $\dfrac{\beta S^0}{\mu} > 1$ with S^0 given in (11) by $S^0 = \dfrac{\sigma(1-\theta e^{-\mu\tau})}{\mu + \psi - (\mu\theta + \psi)e^{-\mu\tau}}$.
Then, we can choose $\varepsilon > 0$ small enough in order to have

$$\mathcal{R}_0^\varepsilon := \frac{\beta S_\varepsilon^0}{\mu} > 1 \quad \text{with} \quad S_\varepsilon^0 := \frac{\sigma(1-\theta e^{-\mu\tau})}{\mu + \psi - (\mu\theta + \psi)e^{-\mu\tau} + \beta\varepsilon(1-\theta e^{-\mu\tau})} \tag{28}$$

since $\lim\limits_{\varepsilon \longrightarrow 0} \beta\varepsilon(1-\theta e^{-\mu\tau}) = 0$.
Notice that for any choice of $\varepsilon > 0$, we have $S^0 > S_\varepsilon^0 > 0$. With the precise choice of ε satisfying (28), we show that we get the result of our theorem.
Let us suppose that we have

$$\limsup_{t \longrightarrow +\infty} I(t) \leqslant \varepsilon. \tag{29}$$

It means that there exists $T_\varepsilon > 0$ such that, for all $t \geqslant T_\varepsilon$, we have $\sup\limits_{x \geqslant t} I(x) \leqslant \varepsilon$. In particular, there exists $T_\varepsilon > 0$ such that for all $t \geqslant T_\varepsilon$, we have $I(t) \leqslant \varepsilon$. Using the majoration in our initial system, we get that $\forall\ t \geqslant T_\varepsilon$,

$$\begin{cases} S'(t) \geqslant \sigma - \beta\varepsilon S(t) - (\mu + \psi)S(t) + (1-\theta)e^{-\mu\tau}u(t-\tau), \\ u(t) = \psi S(t) + \theta e^{-\mu\tau}u(t-\tau). \end{cases}$$

Now, we consider the system (24). Adding the term $-\beta\varepsilon S(t)$ to the first equation of system (24) and we can easily adapt our results. We have already computed the corresponding steady-state (25). We are going to use a comparison principle on this system.
Then, we can choose a $\tilde{\varepsilon} > 0$ small enough such as

$$\mathcal{R}_0^{\varepsilon,\tilde{\varepsilon}} := \frac{\beta(S_\varepsilon^0 - \tilde{\varepsilon})}{\mu} > 1 \tag{30}$$

In the same time, using Theorem 2.9, we get a constant $T'_{\tilde{\varepsilon}}$, that we can choose satisfying $T'_{\tilde{\varepsilon}} > T_\varepsilon > 0$, such as $\tilde{S}_\varepsilon(t) > S_\varepsilon^0 - \tilde{\varepsilon}$, for all $t \geqslant T'_{\tilde{\varepsilon}}$, where $\tilde{S}_\varepsilon(t)$ is the solution of (24). Using a comparison principle (see [28], Lemma 3.4) , we then have that $S(t) \geqslant \tilde{S}_\varepsilon(t) > S_\varepsilon^0 - \tilde{\varepsilon}$ for all $t \geqslant T'_{\tilde{\varepsilon}}$.
Finally, let us choose a constant $\xi > 0$ such as $\dfrac{\beta(S_\varepsilon^0 - \tilde{\varepsilon})}{\xi + \mu} > 1$. And then, using the equation on I, we have

$$\int_{T'_{\tilde{\varepsilon}}}^{+\infty} e^{-\xi t} I'(t)dt = \int_{T'_{\tilde{\varepsilon}}}^{+\infty} e^{-\xi t} I(t)(\beta S(t) - \mu)dt.$$

Thanks to an integration by part, we have

$$-e^{\xi T'_{\tilde{\varepsilon}}} I(T'_{\tilde{\varepsilon}}) = \int_{T'_{\tilde{\varepsilon}}}^{+\infty} e^{-\xi t} I(t)(\beta S(t) - \mu - \xi)dt.$$

And then, by the choice of ξ, we get the following inequality

$$0 > -e^{\xi T'_{\tilde{\varepsilon}}} I(T'_{\tilde{\varepsilon}}) > \left[\beta(S_\varepsilon^0 - \tilde{\varepsilon}) - \mu - \xi\right] \int_{T'_{\tilde{\varepsilon}}}^{+\infty} e^{-\xi t} I(t)dt > 0.$$

Thus, we have a contradiction with (29) and our theorem is demonstrated. □

2.6.3 Uniform persistence

In this subsection, we are going to show that the disease is uniformly persistent (See [25]).

Theorem 2.11. *Assume $\mathcal{R}_0 > 1$. There exists a constant $0 < \varepsilon' < \varepsilon$, where $\varepsilon > 0$ is given by Theorem 2.10, such that for any initial condition $(S_0, I_0, \varphi) \in \mathbb{R}^+ \times \mathbb{R}_+^* \times \mathcal{C}^0([-\tau, 0], \mathbb{R}^+)$, we have*

$$\liminf_{t \longrightarrow +\infty} I(t) > \varepsilon'.$$

Proof. First, from Theorem 2.10, we have that $\limsup_{t \longrightarrow +\infty} I(t) > \varepsilon$. Then, there exists a positive sequence $(u_n)_n$ such as $u_n \longrightarrow +\infty$ and $I(u_n) > \varepsilon$. Indeed, as the function $x \longmapsto \sup\{I(t)\ ;\ t \geqslant x\}$ is decreasing, we have that $\limsup_{t \longrightarrow +\infty} I(t) > \varepsilon$ gives $\sup\{I(t)\ ;\ t \geqslant x\} > \varepsilon,\ \forall x$. Also, by definition of supremum, for each x, there exists a positive sequence $u_n^x \geqslant x$ such as $I(u_n^x) \longrightarrow \sup\{I(t)\ ;\ t \geqslant x\}$. By definition of the limit, we can choose an index n'_x such as $I(u^x_{n'_x}) > \varepsilon$. Then, we can construct an increasing positive sequence (u_n), choosing those previous indexes since $x \longrightarrow +\infty$, such as $I(u_n) > \varepsilon$ and $u_n \longrightarrow +\infty$.

Now, we are going to prove our theorem by contradiction. We suppose that for every $\varepsilon' \in]0, \varepsilon]$, there exists an initial condition $(S_0, I_0, \varphi) \in \mathbb{R}^+ \times \mathbb{R}_+^* \times \mathcal{C}^0([-\tau, 0], \mathbb{R}^+)$ such as

$$\liminf_{t \longrightarrow +\infty} I(t) \leqslant \varepsilon'. \tag{31}$$

Then, there exists two sequences, one positive and increasing $(v_n)_{n\in\mathbb{N}}$ and one positive and decreasing $(\beta_n)_{n\in\mathbb{N}}$ such as

$$v_n > u_n, \quad \lim_{n \longrightarrow +\infty} \beta_n = 0 \qquad \text{and} \qquad I(v_n) < \beta_n < \varepsilon'. \tag{32}$$

Indeed, let us fix one ε'. Then we can chose another $\tilde{\varepsilon} \in]0, \varepsilon'[$ such as $\liminf_{t \longrightarrow +\infty} I(t) \leqslant \tilde{\varepsilon} < \varepsilon'$. Thus, we have, for all $x \geqslant 0$, $\inf\{I(t)\ ;\ t \geqslant x\} \leqslant \tilde{\varepsilon}$. By definition of the infinimum, we get a sequence $(v_n^x)_n$ that we can chose greater than (u_n) such as $I(v_n^x) \longrightarrow \inf\{I(t)\ ;\ t \geqslant x\}$ and we can chose an index $\tilde{N}$ such as $I(v_{\tilde{N}}) < \tilde{\varepsilon} < \varepsilon'$. And finally, we get both sequences needed as previously.
We get that $I(v_n) < \beta_n < \varepsilon'$.
By continuity of $t \longrightarrow I(t)$, there exists another sequence $(\alpha_n)_n$, $\alpha_n\ ]v_n; u_n[$ for all n, such as

$$I(\alpha_n) = \varepsilon \qquad \text{and} \qquad I(t) < \varepsilon, \quad \text{for all } t \in]\alpha_n; u_n[. \tag{33}$$

Now, let us define two sequences $(I_n)_n$ and $(S_n)_n$ by $I_n := \varepsilon$ and $S_n := S(\alpha_n)$ for all $n \in \mathbb{N}$. Both sequences are bounded, we can extract a convergent subsequence that we denote also by $(I_n)_n$ and $(S_n)_n$ and we have $I_n = \varepsilon$ and $\lim_{n \longrightarrow +\infty} S_n = \rho$, with $\rho \in \mathbb{R}^+$.
We now consider the following problem :

$$w(t) = \begin{cases} \psi\rho + \theta e^{-\tau\mu} w(t-\tau), & t > 0, \\ \varphi(t), & t \in [-\tau, 0]. \end{cases}$$

For each initial condition $\varphi \in \mathcal{C}^0([-\tau, 0], \mathbb{R})$ of the previous difference equation, we have a unique continuous solution w on $]0, +\infty[$ (by the step method). Let $(f_n)_{n\in\mathbb{N}} \subset \mathcal{C}^0([-\tau, 0], \mathbb{R})$ the functional sequence defined by $f_n(x) = w(\alpha_n + x),\ x \in [-\tau, 0]$, with $\alpha_n > \tau$, for n large enough ; then we make a translation in n to get $\alpha_n > \tau$ for all $n \in \mathbb{N}$. Then, by definition we have

$$f_n(x) = \psi\rho + \theta e^{-\mu\tau} f_n(x-\tau), \qquad \text{for all } n \in \mathbb{N},\ x \in [-\tau, 0].$$

From the proposition 2.3, we get that the sequence $(f_n)_n$ is uniformly bounded, then ponctually bounded on $[-\tau, 0]$. Moreover, for $n \in \mathbb{N}$ and $x_1, x_2 \in [-\tau, 0]$, we get

$$\begin{aligned} |f_n(x_1) - f_n(x_2)| &= \theta e^{-\tau\mu} |f_n(x_1 - \tau) - f_n(x_2 - \tau)|, \\ &\leqslant (\theta e^{-\tau\mu})^{\tilde{N}_n + 1} |\varphi(\alpha_n + x_1 - (\tilde{N}_n + 1)\tau) - \varphi(\alpha_n + x_2 - (\tilde{N}_n + 1)\tau)|, \\ &\leqslant |\varphi(\alpha_n + x_1 - (\tilde{N} + 1)\tau) - \varphi(\alpha_n + x_2 - (\tilde{N}_n + 1)\tau)|. \end{aligned}$$

with $\tilde{N}_n := \lfloor \alpha_n / \tau \rfloor$.
Since φ is continuous on a compact set $[-\tau, 0]$, the Heine theorem gives us that φ is uniformly continuous on $[-\tau, 0]$. Thus, previous inequality and using the definition on the uniform continuity, we get that the family $(f_n)_{n\in\mathbb{N}}$ is equicontinuous and uniformly equicontiunous as it is defined on a compact set. Hence, the Arzela-Ascoli Theorem (see [29]) gives us that there exists a convergent subsequence of (f_n), that denote also by (f_n) such as $\lim_{n \longrightarrow +\infty} f_n = f^*$.

Now, let us consider the solution of (5) corresponding to the following initatil conditions $S_0 = \rho,\ I_0 = \varepsilon$ and $u_0 = f^* \in \mathcal{C}^0([-\tau, 0], \mathbb{R}^+)$. We denote this solution by $(S^\infty, I^\infty, u^\infty)$. From Theorem 2.10, there exists a $\sigma > 0$ and we can find a $0 < m < \sigma$, such that

$$I^\infty(\sigma) > \varepsilon \quad \text{and} \quad I^\infty(t) > m \ \text{ for all } t \in]0, \sigma[.$$

Next, we get the contradiction. For each $n \in \mathbb{N}$, we define $\tilde{I}_n(t) := I(\alpha_n + t),\ t > 0$. From the two previous inequalities, the continuity and the fact that

$$\tilde{I}_n(0) = I_n = \varepsilon, \qquad \lim_{n \longrightarrow +\infty} S_n = \rho, \qquad \lim_{n \longrightarrow +\infty} f_n = f^*,$$

we have, recalling that $\lim_{n \longrightarrow +\infty} \beta_n = 0$, for n large enough,

$$\tilde{I}_n(\sigma) > \varepsilon \quad \text{and} \quad \tilde{I}_n(t) > m > \beta_n \ \text{ for all } t \in]0, \sigma[. \tag{34}$$

On the other hand, for $\tilde{v_n} := v_n - \alpha_n$, we have from (31) and (32) that

$$\tilde{I}_n(\tilde{v}_n) = I(v_n) < \beta_n < \varepsilon \qquad \text{and} \qquad \tilde{I}_n(t) = I(\alpha + t) < \varepsilon \quad \text{for all } t \in]0, \tilde{v}_n[. \tag{35}$$

Thus, we distinguish three different cases :

- $\sigma < \tilde{v}_n$: The second inequality in (34) gives us that $\tilde{I}_n(\sigma) < \varepsilon$, which contradicts the first inequality of (33).
- $\sigma = \tilde{v}_n$: Then the first inequality of (33) contradicts the first of (34).
- $\sigma > \tilde{v}_n$: The second inequality of (33) gives us that $\tilde{I}_n(\tilde{v}_n) > \beta_n$, which contradicts the first of (34).

Thus, there exists $\varepsilon' \in]0, \varepsilon]$, such that for any initial condition $(S_0, I_0, \varphi) \in \mathbb{R}^+ \times \mathbb{R}_+^* \times \mathcal{C}^0([-\tau, 0], \mathbb{R}^+)$, we have $\liminf_{t \longrightarrow +\infty} I(t) > \varepsilon'$. □

2.7 Global asymptotic stability

In this section, we study the global asymptotic stability of the equilibria of (5) defined by (11) and (12). In order to get these results, we use Lyapunov technics and functions.

2.7.1 Global asymptotic stability of the disease-free steady-state

In this section, we show that the disease-free equilibrium defined by (11) of (5) is globally asymptotically stable. In order to demonstrate this stability, we use an auxiliary difference-differential system. We show that its equilibrium is globally asymptotically stable thanks to the Lyapunov theorem. And finally, we apply a comparison theorem.
First, we assume that $\mathcal{R}_0 < 1$. We consider our model given by

$$\begin{cases} S'(t) = \sigma - \beta I(t)S(t) - (\mu + \psi)S(t) + (1-\theta)e^{-\mu\tau}u(t-\tau), \\ I'(t) = \beta I(t)S(t) - \mu I(t), \\ u(t) = \psi S(t) + \theta e^{-\mu\tau}u(t-\tau), \\ S(0) = S_0, \quad I(0) = I_0, \quad \text{and} \quad u(t) = \varphi(t), \ \ -\tau \leqslant t \leqslant 0 \end{cases} \qquad \text{with } t > \tau.$$

and the corresponding disease-free equilibrium

$$(S^0, I^0, u^0) := \left(\frac{\sigma(1 - \theta e^{-\mu\tau})}{\mu + \psi - (\mu\theta + \psi)e^{-\mu\tau}} \ , \ 0 \ , \ \frac{\psi\sigma}{\mu + \psi - (\mu\theta + \psi)e^{-\mu\tau}} \right).$$

The solution of the previous system satisfies also the following system

$$\begin{cases} S'(t) \leqslant \sigma - (\mu + \psi)S(t) + (1-\theta)e^{-\mu\tau}u(t-\tau), \\ u(t) = \psi S(t) + \theta e^{-\mu\tau}u(t-\tau), \\ S(0) = S_0, \quad \text{and} \quad u(t) = \varphi(t), \ \ -\tau \leqslant t \leqslant 0 \end{cases} \qquad \text{with } t > 0.$$

Using a comparison principle (See [28]), we get that $S(t) \leqslant S^+(t)$ and $u(t) \leqslant u^+(t)$ for all $t > 0$, where (S^+, u^+) is the solution of

$$\begin{cases} \dfrac{dS^+}{dt}(t) = \sigma - (\mu+\psi)S^+(t) + (1-\theta)e^{-\mu\tau}u^+(t-\tau), \\ u^+(t) = \psi S^+(t) + \theta e^{-\mu\tau}u^+(t-\tau), \\ S^+(0) = x_0, \quad u^+(z) = \varphi(z), \text{ for } -\tau \leqslant z \leqslant 0 \end{cases} \qquad \text{with } t > 0. \tag{36}$$

As developped in the subsection 2.6.1, the system (35) has a unique equilibrium given by (25) that we denote by (S^0, u^0), since they are the same as (11).
Theorem 2.9 of subsection 2.6.1 gives us that this equilibrium is globally asymptotically stable, ie $S^+(t) \xrightarrow[t\longrightarrow+\infty]{} S^0$ and $u^+(t) \xrightarrow[t\longrightarrow+\infty]{} u^0$.
Now, let us chose $\varepsilon > 0$ and define the following region :

$$\Omega_\varepsilon := \left\{ (S, I, u) \in \mathbb{R}^+ \times \mathbb{R}^+ \times \mathcal{C}^0([-\tau, 0], \mathbb{R}^+) \ ; \ 0 \leqslant S \leqslant S^0 + \varepsilon \text{ and } 0 \leqslant u(s) \leqslant u^0 + \varepsilon, \ s \in [-\tau, 0] \right\} \tag{37}$$

Thus, we just have shown the following :

Lemma 2.12. *For any $\varepsilon > 0$ small enough, the subset $\Omega_\varepsilon \subset \mathbb{R}^+ \times \mathbb{R}^+ \times \mathcal{C}^0([-\tau, 0], \mathbb{R}^+)$ is a global attractor for the system (5).*

Then, thanks to the Lemme 2.12, we can restrict the study of the global asymptotic stability of the disease-free of (5) to the region Ω_ε. We get then

Theorem 2.13. *Suppose that $\mathcal{R}_0 < 1$. Then, the disease-free steady-state $S^0, 0, u^0)$ given by (12) of our model (5) is globally asymptotically stable.*

Proof. As given by the previous lemme, it suffices to study the stability for solutions in Ω_ε, for any $\varepsilon > 0$. Then, forall $t > 0$, we have

$$I'(t) \leqslant -\mu I(t) + \beta(S^0 + \varepsilon)I(t) = -\mu\left(1 - \frac{\beta(S^0+\varepsilon)}{\mu}\right) I(t)$$

Since $\mathcal{R}_0 = \frac{\beta S^0}{\mu} < 1$, we can find an $\varepsilon > 0$ such as the right-hand side of the previous inequality is negative. This implies that $t \longrightarrow I(t)$ is decreasing as its derivative is negative for al $t > 0$, thus $\lim\limits_{t\longrightarrow+\infty} I(t) = 0$, as I is positive.
By the definition of the limit, we see that for any $\varepsilon > 0$, there exists a $T_\varepsilon > 0$, such that $I(t) \leqslant \varepsilon$, for $t \geqslant T_\varepsilon$. We then have for $t \geqslant T_\varepsilon$:

$$\begin{cases} S'(t) \geqslant \sigma - (\mu+\psi)S(t) - \varepsilon\beta S(t) + (1-\theta)e^{-\mu\tau}u(t-\tau), \\ u(t) = \psi S(t) + \theta e^{-\mu\tau}u(t-\tau). \end{cases}$$

Then, we have, by a comparison principle (See [28]), $S(t) \geqslant S_\varepsilon(t)$ and $u(t) \geqslant u_\varepsilon(t)$ for all $t \geqslant T_\varepsilon$, where $(S_\varepsilon, u_\varepsilon)$ are the solutions of the following system :

$$\begin{cases} S'_\varepsilon(t) = \sigma - (\mu+\psi)S_\varepsilon(t) - \varepsilon\beta S_\varepsilon(t) + (1-\theta)e^{-\mu\tau}u_\varepsilon(t-\tau), \\ u_\varepsilon(t) = \psi S_\varepsilon(t) + \theta e^{-\mu\tau}u_\varepsilon(t-\tau), \\ S_\varepsilon(0) = S_0, \ u_\varepsilon(z) = \varphi(z), \quad \text{for } -\tau \leqslant z \leqslant 0. \end{cases} \tag{38}$$

Adapting easily the section 2.6.1 and 2.6.2 , we can show that $S_\varepsilon(t) \xrightarrow[t\longrightarrow+\infty]{} S^0_\varepsilon$ and $u_\varepsilon(t) \xrightarrow[t\longrightarrow+\infty]{} u^0_\varepsilon$, where $(S^0_\varepsilon, u^0_\varepsilon)$ is the steady-state of the system (36) given by (25).
Then, there exists a $\tilde{T}_\varepsilon > T_\varepsilon > 0$, such that for all $t > \tilde{T}_\varepsilon$ we have

$$S^0_\varepsilon - \varepsilon \leqslant S(t) \leqslant S^0 + \varepsilon \qquad \text{and} \qquad u^0_\varepsilon - \varepsilon \leqslant u(t) \leqslant u^0 + \varepsilon$$

Then, since $\varepsilon > 0$ is arbitrary and $S^0_\varepsilon \xrightarrow[\varepsilon\longrightarrow0]{} S^0$ and $u^0_\varepsilon \xrightarrow[\varepsilon\longrightarrow0]{} u^0$, we get, with the previous inequalities, that

$$\lim_{t\longrightarrow+\infty} S(t) = S^0 \qquad \text{and} \qquad \lim_{t\longrightarrow+\infty} u(t) = u^0$$

From Theorem 2.7, we have that the disease-free equilibrium $(S^0, 0, u^0)$ is locally asymptotically stable. Then, we shown that $(S^0, 0, u^0)$ is globally asymptotically stable. □

2.7.2 Global asymptotic stability of the endemic equilibrium

In this section, we show the global asymptotic stability of the endemic equilibrium $(\overline{S}, \overline{I}, \overline{u})$ of (5) given by (12).
First, let us assume that $\mathcal{R}_0 > 1$.
This equilibrium satisfies $\overline{S} > 0, \overline{I} > 0$ and $\overline{u} > 0$. Let us define $\tilde{S}(t) := S(t) - \overline{S}$ and $\tilde{u}(t) := u(t) - \overline{u}$. Then, the system (5) becomes, with $\beta\overline{S} = \mu$,

$$\begin{cases} \tilde{S}'(t) = -(\mu+\psi)\tilde{S}(t) - \beta\tilde{S}(t)I(t) - \beta\overline{S}I(t) + \beta\overline{S}\ \overline{I} + (1-\theta)e^{-\mu\tau}\tilde{u}(t-\tau), \\ I'(t) = -\mu I(t) + \beta\tilde{S}(t)I(t) + \beta\overline{S}I(t) = \beta\tilde{S}(t)I(t), \\ \tilde{u}(t) = \psi\tilde{S}(t) + \theta e^{-\mu\tau}\tilde{u}(t-\tau). \end{cases} \tag{39}$$

We then get the following result :

Theorem 2.14. *Let us suppose that $\mathcal{R}_0 > 1$. Then, the endemic steady-state given by (12) of our model (5) is globally asymptotically stable.*

Proof. In order to proove this result, we use a Lyapunov-like theorem in [30] (also see Lemma 8.2 in [28]). We define the following function $V : \mathbb{R}^+ \times \mathbb{R}^+ \times \mathcal{C}^0([-\tau; 0], \mathbb{R}^+) \longrightarrow +\infty$ given by

$$V(S_0, I_0, \varphi) = \frac{S_0^2}{2} + \xi \int_{-\tau}^{0} \varphi^2(s)ds + \overline{S}\left(I_0 - \overline{I} - \overline{I}\ln\frac{I_0}{\overline{I}}\right)$$

with $\xi = \dfrac{\psi + \mu(1-(\alpha e^{-\mu\tau})^2)}{2\psi^2}$.

Notice that the following function $f : I_0 \longmapsto I_0 - \overline{I} - \overline{I}\ln\dfrac{I_0}{\overline{I}}$, for $I_0 > 0$, is nonnegative. Indeed, it suffices to study the function $x \longmapsto x\ln(x) - x + 1$ and to evaluate this function at $x = \frac{\overline{I}}{I_0}$. Moreover, $f(I_0) = 0$ if and only if $I_0 = \overline{I}$, this gives us that $V(S_0, I_0, \varphi) = 0$ if and only if $(S_0, I_0, \varphi) = (0, \overline{I}, 0)$.
Let us compute now the derivative of $t \longmapsto V(\tilde{S}(t), I(t), \tilde{u}_t)$ along the solution trajectory. We get

$$\begin{aligned} \frac{dV}{dt}(\tilde{S}(t), I(t), \tilde{u}_t) &= -(\mu+\psi-\xi\psi^2)\tilde{S}^2(t) + \left[(1-\theta)e^{-\mu\tau} + 2\psi\theta e^{-\mu\tau}\right]\tilde{S}(t)\tilde{u}^2(t-\tau), \\ &\quad - \xi\tilde{u}^2(t-\tau)\left[1-\theta^2(e^{-\tau\mu})^2\right] - \beta I(t)\tilde{S}^2(t), \\ &= -a\tilde{S}^2(t) + b\tilde{S}(t)\tilde{u}^2(t-\tau) - c\tilde{u}^2(t-\tau) - \beta I(t)\tilde{S}^2(t), \\ &\leqslant -a\tilde{S}^2(t) + b\tilde{S}(t)\tilde{u}^2(t-\tau) - c\tilde{u}^2(t-\tau), \\ &\leqslant -c\left[\left(\tilde{u}(t-\tau) - \frac{b}{2c}\tilde{S}(t)\right)^2 + \frac{4ac-b^2}{4c^2}\right]. \end{aligned}$$

with $a = \mu + \psi - \xi\psi^2 > 0$, $b = (1-\theta)e^{-\mu\tau} + 2\psi\theta e^{-\mu\tau} > 0$ and $c = \xi\left[1-\theta^2(e^{-\tau\mu})^2\right] > 0$.
Since $c > 0$, we get

$$\frac{dV}{dt}(\tilde{S}(t), I(t), \tilde{u}_t) \leqslant \frac{b^2-4ac}{4c} = -\omega\tilde{S}^2(t), \tag{40}$$

with $\omega := \dfrac{4ac-b^2}{4c}$ which is positive since $b^2 - 4ac < 0$ (see proof of Theorem 2.9). The function $t \longmapsto V(\tilde{S}(t), I(t), \tilde{u}_t)$ is nonincreasing and we get, as V is lower bounded by 0, that

$$V(\tilde{S}(t), I(t), \tilde{u}_t) \xrightarrow[t\longrightarrow+\infty]{} \inf_{t\geqslant 0}\left\{V(\tilde{S}(t), I(t), \tilde{u}_t)\right\} := V^*.$$

Thus, V is a lower bounded function (bounded by its infimum) and such as

$$-\frac{dV}{dt}(\tilde{S}(t), I(t), \tilde{u}_t) \geqslant M(\tilde{S}(t)),$$

with $M : x \longmapsto \omega x^2$. This function M is clearly continuous, positive definite and radially unbounded since $\lim\limits_{t\longrightarrow+\infty} M(x) = +\infty$.

Moreover, $t \longmapsto \tilde{S}'(t)$ is uniformly unbounded since $t \longmapsto S(t)$, $t \longmapsto I(t)$ and $t \longmapsto u(t)$ are uniformly unbounded (see Proposition 2.3.). Thus $t \longmapsto \tilde{S}(t)$ is Lipschitzian and then uniformly continuous. We can now apply Corollary 2 of [30] and we get

$$\lim_{t\longrightarrow+\infty}\tilde{S}(t) = 0 \iff \lim_{t\longrightarrow+\infty} S(t) = \overline{S}.$$

After, we write the equation of $\tilde{u}$ in (39) like in the demonstration of Proposition 2.3 :

$$\tilde{u}(t) = \psi\tilde{S}(t) + \theta e^{-\mu\tau}\tilde{u}(t-\tau) \iff D\tilde{u}_t = h(t),$$

where $h(t) := \psi\tilde{S}(t)$ and $Dy := \theta e^{-\mu\tau}y(-\tau)$ for $t \geqslant 0$. As D is uniformly stable and $\tilde{S}(t) \underset{t\longrightarrow+\infty}{\longrightarrow} 0$, we can use the Lemma 3.5 of [31] and get

$$\lim_{t\longrightarrow+\infty}\tilde{u}_t = 0 \iff \lim_{t\longrightarrow+\infty}u_t = \overline{u}$$

Furthermore, using the expression of V, we get

$$\lim_{t\longrightarrow+\infty}f(I(t)) = \frac{V^*}{\overline{S}}.$$

Then, since the function $t \longmapsto \tilde{S}(t)$ is bounded and continuously differentiable, the fluctuation lemma (see Lemma 2.8 in [32]) gives us that there exists a sequence $(s_n)_n$ such as

$$s_n \underset{n\longrightarrow+\infty}{\longrightarrow} +\infty \qquad \text{and} \qquad \lim_{n\longrightarrow+\infty}\tilde{S}'(s_n) = 0.$$

And, the first equation of (39) gives us $\lim_{n\longrightarrow+\infty} I(s_n) = \overline{I}$. The continuity of f gives

$$\lim_{n\longrightarrow+\infty}f(I(s_n)) = f(\overline{I}) = 0.$$

More precisely, we get $V^* = 0$ and then $\lim_{t\longrightarrow+\infty}f(I(t)) = 0$.
Using the properties of f, we get that $\lim_{t\longrightarrow+\infty} I(t) = \overline{I}$.
This concludes our proof and $(\overline{S}, \overline{I}, \overline{u})$ is globally asymptotically stable.

□

3 Numerical simulations and analysis

In this section, we test our model on real datasets of HIV/AIDS epidemic in France in male homosexual population.

3.1 Detected Vs infected

Before we introduce our concrete datasets, we discuss about the distinction between detected and infected individuals at a time t. We know that if we are detected, we then are infected. The problem is that all infected individuals are not detected. For the HIV-AIDS epidemic this problem is major. Indeed, the HIV infection is divided in three parts[6] : the primo-infection/acute stage, in which individuals may have some weak symptoms such as flu-like symptoms and lasts more or less one month ; the chronic infection in which individuals may have no symptoms and can lead to AIDS stage in about 8-10 years ; the AIDS stage in which individuals get infected by any disease and without a treatment, this stage lasts at most 3 years.
Thus, between infection and detection of an HIV-infected individual, years may have passed. In [1] Figure 1, we can have an idea of the time between seroconversion, *i.e.* HIV-infection, and the HIV/AIDS-detection. We can have a better estimation of this delay with our dataset.
Because of a lack of considerable datas to clearly distinguish infected from detected individuals, we will assume that both of these populations are the same.

3.2 Datasets

In this section, I introduce the datasets I used to test on the model.

3.2.1 HIV population

In order to estimate some parameter of the model, we need datas on the situation of HIV-AIDS epidemic in France, more precisely in the MSM (Men who have sexual intercourses with men) population, such as the number of infected individuals. We remind that for our purpose and with the data we own, we assimilate the detected and the infected individuals.

[6] `https://aidsinfo.nih.gov/understanding-hiv-aids/fact-sheets/19/46/the-stages-of-hiv-infection`

We mainly use the following two papers [33] and [34] to extract our datasets. We summarize those datasets in the following Table 2 :

Year	Number of HIV-detected in the French population	Number of HIV-detected in the French MSM population
2003	7647	###
2004	7823	###
2005	7583	###
2006	7096	###
2007	6510	###
2008	6309	###
2009	6303	###
2010	6240	2040
2011	6085	1980
2012	6372	2160
2013	6688	2145
2014	6480	2080
2015	6380	2005
2016	6330	1910
2017	6583	1970
2018	6155	1700

Table 2: Table of detected HIV cases in the French population (second column) and in the French MSM population (third column). # represents datas that could not be found with a sufficient precision. See Figure 1 in [33], Figure 1 in [34] and Figure 3 in [35].

Furthermore, as discussed in the previous section, in [35], we can extract the time repartition between the detection and the infection of an individual in the French MSM population. Indeed, in Figure 4 of [35], we get that an average of $42,5\%$ of the individuals was detected in the acute stage, 38.5% was detected in the chronic infection phase and 19% was detected in the AIDS stage .

3.2.2 PrEP users

In the model, we include the PrEP treatment. This treatment is quite recent, thus we have few data. Each 3 month, the patient decides if he/she wants to give up the treatment or to continue. That is why in our model, we need the probability that an individual continues his treatment and the proportion of individuals that begin the PrEP treatment.
We found those datas in [2]. As said in this rapport, the main PrEP users in the considered population (French population) may be MSM (See section 5 in [2]). Thus we assume that 60% of the individuals of the population considered in the dataset of [2] is MSM. We transcribe here the main dataset in [2] in the following Table 3 :

Semester	Initiation of PrEP	Renewal of the treatment	Total of PrEP users
S1 - 2016	1166	###	1166
S2 - 2016	1826	911	2737
S1 - 2017	2193	2273	4666
S2 - 2017	2564	3807	6371
S1 - 2018	3138	5413	8551
S2 - 2018	4488	7647	12135
S1 - 2019	5103	10398	15501

Table 3: Total number of PrEP users in France since 2016, given by semester (See [2], Table 3).

3.3 Time dependent basic reproduction number $\mathcal{R}_0(t)$

One important data we need to estimate is the current basic reproduction number of the HIV-AIDS epidemic. We want to have a tendency of the current $\mathcal{R}_0$ to be able to assume a future $\mathcal{R}_0$. In order to

get it, we use the package in R language untitled R0[7]. We precisely use the function *est.R0.SB* which estimates the $\mathcal{R}_0$ using a Bayesian approach following the idea developped in [36].
First, we compute this one in the global French population using the datas of Table 2. We get the following tendency ploted in Figure 2 (See below).

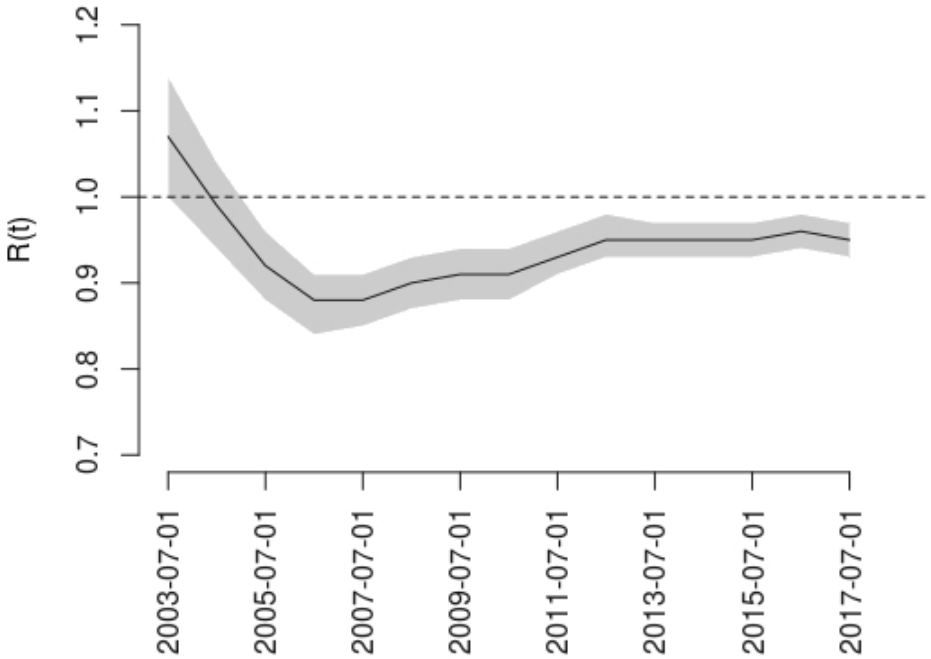

Figure 3: Plot of the time dependent basic reproduction number $\mathcal{R}_0(t)$ of HIV-AIDS epidemic in the French population. The grey zone represents the confidence interval of the estimation.

We see in Figure 2 that the tendancy is globally constant since 2012 and $\mathcal{R}_0(t)$ equals 0.95.

Now, we focus on the MSM French population. Using the datas in Table 2, we also compute the time dependent basic reproduction number $\mathcal{R}_0(t)$ in our precise population (See Figure 3 below).

[7]See : `https://www.rdocumentation.org/packages/R0/versions/1.2-6`

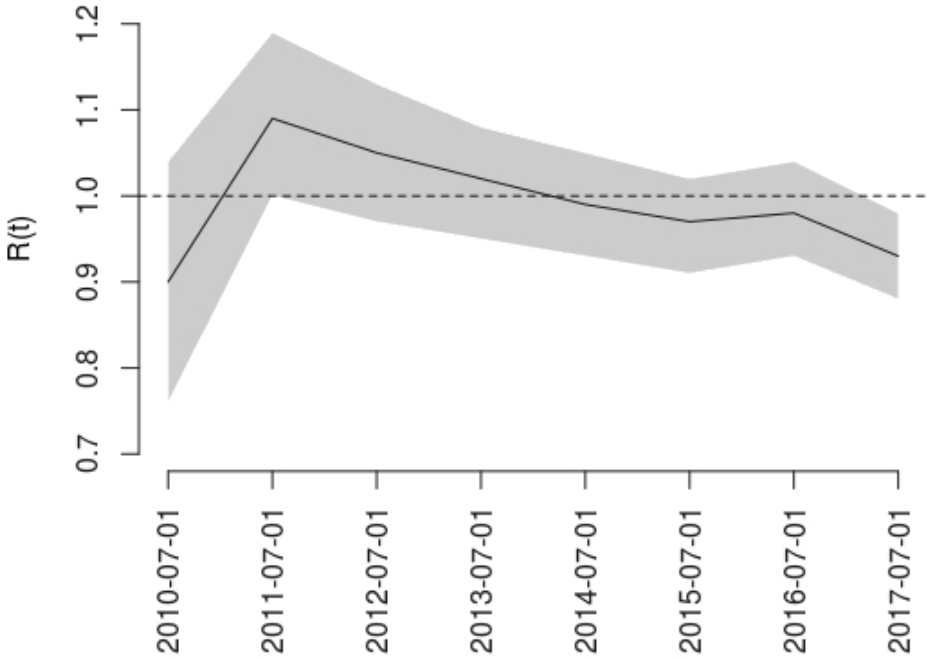

Figure 4: Plot of the time dependent basic reproduction number $\mathcal{R}_0(t)$ of HIV-AIDS epidemic in the French MSM population. The grey zone represents the confidence interval of the estimation.

In Figure 3, we see that the time dependent basic reproduction number in the MSM French population is clearly decreasing and the last value, in 2017, is around $\mathcal{R}_0(2017) \simeq 0.93$, and we assume that the future tendency of this $\mathcal{R}_0(t)$ is still decreasing.
Thus, in our numerical simulations, we choose $\mathcal{R}_0 = 0.93$.

3.4 Choices of parameters

In this section, I explain how I chose the parameters used in our numerical simulations.
In the previous section (See 3.3), we already chose $\mathcal{R}_0$ equals to 0.93.
Also, since the beginning, we chose $\tau = 3$ months.
With official French datas[8], we get the rate of death per year for 1000 inhabitants in France in 2019 is 9.1.
Thus, as we need the rate for one individual per month, we get that $\mu = 0.75 \times 10^{-3}$ individuals.month^{-1}.
Thanks to Table 3, we get values of parameters θ and ψ. Indeed, each semester, we get a different θ by using the following formula coming from its definition :

$$\theta(\text{semester}) = \frac{(\text{Number of renewal treatment of the current semester}) \times 0.6}{\text{Total of PrEP users of the previous semester}}.$$

And then we choose ψ, per semester, as it follows :

$$\psi(\text{semester}) = \frac{\text{Number of individuals who begins the treatment}}{S(0)},$$

where $S(0)$ is the initial condition for the compartment S.

In the folowing Table 4, we summarize all those parameters :

[8]See : `https://www.insee.fr/fr/statistiques/2383440#tableau-figure1`.

Semester	Values of ψ	Values of θ
S1 - 2016	0.00027	###
S2 - 2016	0.00043	0.7813
S1 - 2017	0.00052	0.8305
S2 - 2017	0.00061	0.8159
S1 - 2018	0.0007	0.8496
S2 - 2018	0.0011	0.8943
S1 - 2019	0.0012	0.8569

Table 4: Values of parameters ψ and θ per semester, computed according to datasets.

Remark 6. *The values of ψ in Table 4 are given per semester. In our simulations, we need ψ per month. We use the following formula to get the required ψ :*

$$\psi(month) = \frac{(Number\ of\ individuals\ who\ begins\ the\ treatment) \div 6}{S(0)},$$

Dividing each value of ψ in Table 4 by 6, we get the required values of ψ (see Table 5 below) :

Semester	Values of ψ
S1 - 2016	0.0000466
S2 - 2016	0.000073
S1 - 2017	0.0000876
S2 - 2017	0.00010
S1 - 2018	0.000125
S2 - 2018	0.000179
S1 - 2019	0.000204

Table 5: Values of parameter ψ per month accordingly to each semester, computed according to datasets.

Thus, for our simulation we choose $\psi = 0.000204$, the last value of the previous ψ since it is increasing, and $\theta = 0.83$ as the average value of all the previous θ. This choice will be discussed in sections 4.
Now, we have to choose the initial condition for the function $t \longmapsto S(t)$, $t \longmapsto I(t)$ and $t \longmapsto u(t)$. In deed, we choose for $t = 0$ the date January, the 1^{st} of 2016.

Thus, for the initial condition we chose the function $u_{\text{init}} : [-\tau = -3, 0] \longrightarrow \mathbb{R}^+,\ t \longmapsto u_{\text{init}}(t)$ as the cubic spline interpolation of 60% of each total number of the last column in Table 3.

A French institute of statistics made a study that deals with sexual orientation in France[9]. We can find that 4% of the French population declare to be homosexual. Assuming that French population is around 65000000 of inhabitants, we can choose that $S(0) = 2600000$.

Then, on the official website of UNAIDS[10], we get that 170000 individuals are infected by HIV in France in 2016. We assume that most of them is homosexual. Thus, we assume that $I(0) = 90000$.

Now, it remains 2 parameters to be chosen : β and σ. We choose them in order to make $\mathcal{R}_0$ be equal to 0.93. We can choose $\sigma = 3000$, in other words, each month, 3000 individuals might have been in contact with an infected one and then become susceptible. Thus, we play on the value of β in order to get $\mathcal{R}_0 = 0.93$.

3.5 Simulations

3.5.1 Simulations

In this section, we show the results we get using the parameters obtained in the previous section. We summarize them in the following table 5 :

[9]See `https://www.ifop.com/wp-content/uploads/2018/03/2669-1-study_file.pdf`, on page 14.
[10]See `https://www.unaids.org/en/regionscountries/countries/france`.

Parameter	Value
ψ	*See Table* 5
θ	*See Table* 4
σ	3000
μ	0.75×10^{-3}
β	1.821×10^{-10}
τ	3
S(0)	2500000
I(0)	90000

Table 6: Values of the parameters used in the numerical simulations.

We plot then 2 simulations. The first simulations is over 400 years (see Figure 4 below) and the second one is over 15 years (see Figure 5 below).

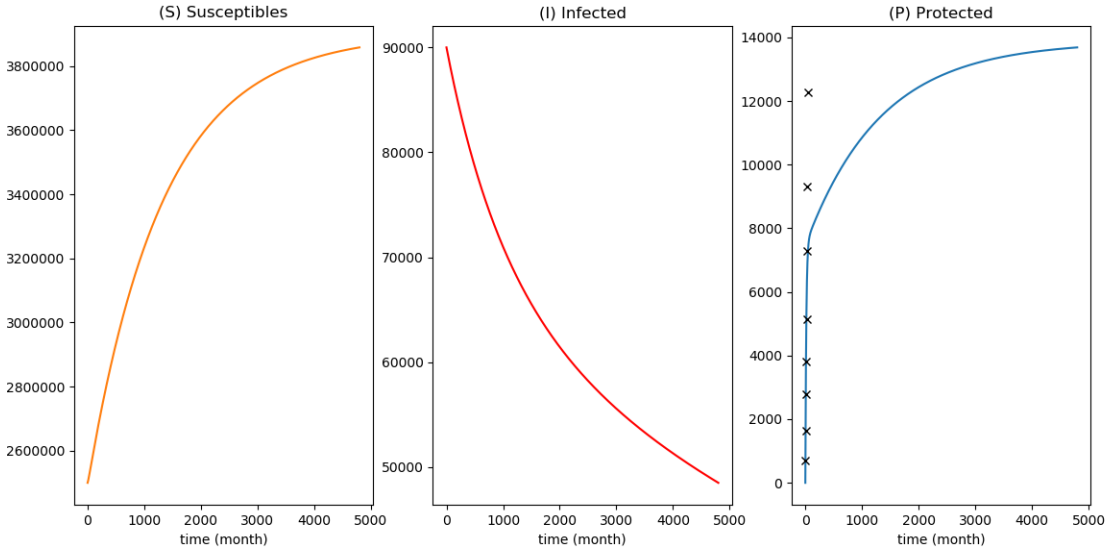

Figure 5: Plot of the evolution of the different compartments along the time (over 400 years). The crosses in the last plot represent the real values of the number of PrEP users got in the Table 3.

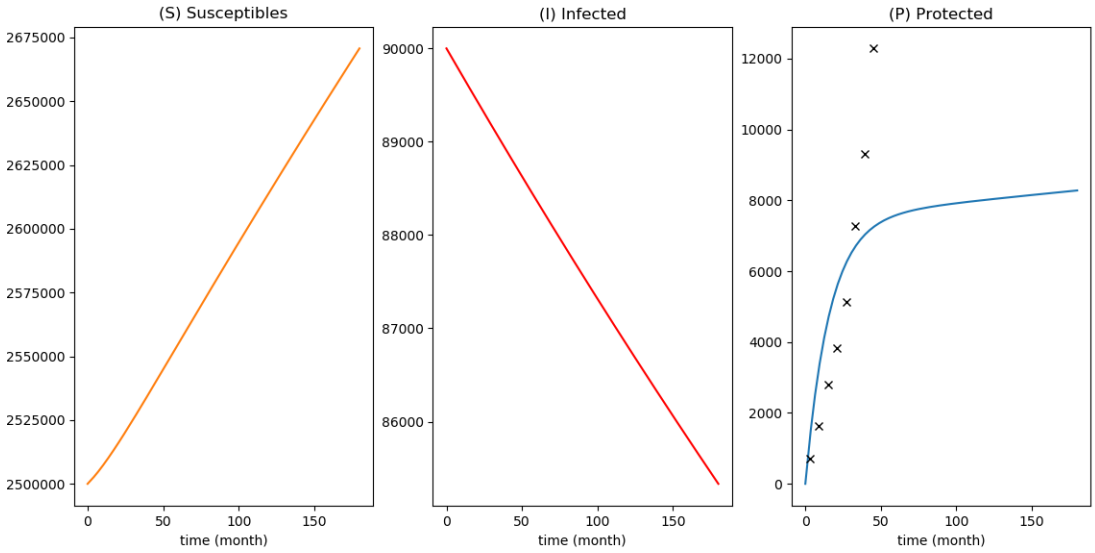

Figure 6: Plot of the evolution of the different compartments along the time (over 15 years). The crosses in the last plot represent the real values of the number of PrEP users got in the Table 3.

With our parameters, we get that $\mathcal{R}_0 = 0.9305$. Thus, the disease-free equilibrium is globally asymptotically stable and the respective values are :

$$S^0 = 3942026.075 \quad ; \quad I^0 = 0 \quad ; \quad P^0 = 14019.62$$

3.5.2 Discussion

Let us discuss the previous simulations. On Figure 4, we see after 400 years, the number of protected individuals slowly reaches 14000 wheres the true datas has already reached 1200 in 3 years. Thus, too few individuals goes in the compartment of protected individuals in the long term.

On Figure 5, we clearly see a difference in the way the real datas of protected individuals (crosses) and our simulation of protected individuals (green curve) grow. Indeed, the first one is clearly convexe whereas the second one is concave. It means that we have too much protected individuals in our simulation at the beginning, in other words, too much suscpetibles are sent in the compartment of the protected ones.

Thus, the parameter ψ may be too high at the beginnig but too much small in the long term. According to Table 4, the value of ψ is clearly time dependent and is clearly less than 0.000204 during the first semesters (around ten times inferior). This remark leads us to the next section in which we focus on the choice of ψ and its time-dependence.

4 Hill function and a new model

In this section, we deal with some modifications in model (5). We first modify intial condition of the PDE (2), which is satisfied by the distribution p. This leads us to a new non-linear model. We study its properties and its stability. Then, we make some numerical simulations.

4.1 Hill function

In this subsection, we remind some facts about the function of Hill.
We call **Hill function** the following function $H : \mathbb{R}^+ \longrightarrow \mathbb{R}$ defined by

$$\forall x \in \mathbb{R}^+, \quad H(x) = x_{\text{sat}} \frac{x^n}{K^n + x^n}.$$

We easily notice that H is increasing and

$$\lim_{x \longrightarrow +\infty} H(x) = x_{\text{sat}} \quad ; \quad \lim_{x \longrightarrow 0} H(x) = 0.$$

In the definition of H, $n \in \mathbb{N}$, $x_{\text{sat}}, K \in \mathbb{R}$ are constants to be chosen. They have precise role.

- x_{sat} : This constant represents the saturation of the Hill function, in other words, it is the threshold that cannot be passed.
- K : This constant satisfies $H(K) = \dfrac{x_{\text{sat}}}{2}$. And more precisely, it is the abscisse of the inflexion point.
- n : This integer gives the intensity of the slope of H. The bigger n, the more inclined the slope.

4.2 Hill function as initial conditions

4.2.1 New model

In this subsection, we modify model (5). In the previous one, the initial condition of the PDE (2), which is satisfied by the distribution p, is linear. This choice may be debatable. Indeed, it supposes that, at any time t, any quantity of susceptible individuals might begin the PrEP treament, which seems unreal. That is why, we assume the this quantity of new PrEP users is bounded and follow a precise dynamic within the time.

We assume that the time evolution of susceptibles who is allowed to begin the PrEP treatment behave as a Hill function.

This modification makes the initial condition of the PDE not to be linear any more. We are going to see how this modification modifies the system (5). Let us rewrite the PDE satisfied by the distribution p. We get

$$\begin{cases} \dfrac{\partial p}{\partial t}(t,a) + \dfrac{\partial p}{\partial a}(t,a) = -\mu p(t,a), \qquad 0 < a < \tau, \\ p(t,0) = \psi H(S(t)) + \theta p(t,\tau). \end{cases} \tag{41}$$

with H the Hill function whose parameters are $n = 2$, $x_{\text{sat}} = 5000000$ and $K = 120$(months). this gives us that

$$H(t) = 5000000 \frac{t^2}{120^2 + t^2} \tag{42}$$

Those parameters are totally assumed by the autor. Indeed, we can choose the speed of reaching the saturation of susceptible individuals who may begin the PrEP, by choosing n, the maximal number of them that may begin the PrEP treatment, by fixing x_{sat}, and the time when the number of susceptible individuals is big enough in order to diminish the slope of H, by choosing K. Indeed, we suppose that the growth is quite slow ($n = 2$). Also, our initial condition of susceptibles is $S(0) = 2500000$, thus taking $x_{\text{sat}} = 5000000$ seems reasonable assuming that the MSM French population may grow. And, according to Table 3, we see that the number of PrEP users grows quicker within the time, thus we may assume that in 10 years, we reach a sufficient number of susceptibles who problably may be interested in taking the PrEP.

Following the same steps as in subsection 2.1, we get a new model given by

$$\begin{cases} S'(t) = \sigma - \beta I(t)S(t) - \mu S(t) - \psi H(S(t)) + (1-\theta)e^{-\mu\tau}u(t-\tau), \\ I'(t) = \beta I(t)S(t) - \mu I(t), \qquad \text{with } t > \tau. \\ u(t) = \psi H(S(t)) + \theta e^{-\mu\tau}u(t-\tau), \end{cases} \tag{43}$$

$$S(0) = S_0, \quad I(0) = I_0, \quad \text{and} \quad u(t) = \varphi(t), \quad -\tau \leqslant t \leqslant 0, \tag{44}$$

Remark 7. *The differential equation on P is also modified and satisfies*

$$P'(t) = -\mu P(t) + \psi H(S(t)) + (\theta - 1)e^{-\mu\tau}u(t-\tau). \tag{45}$$

4.2.2 Well-posedness of the new model

As we did in section 2.2, we give a theorem that sum up the fondamental properties of model (43).

Theorem 4.1. *For each nonnegative initial value (S_0, I_0, φ), with $\varphi \in \mathcal{C}^0([-\tau, 0])$, the model (43) has a unique solution defined on $[-\tau; +\infty[$.*
Moreover, the solution is positive on $\mathbb{R}^+$ for any positive initial conditions and they are uniformly bounded.

Proof. The proof of this theorem follows the same steps as for model (5) since $t \longmapsto H(t)$ is positive. □

4.2.3 Existence and characterization of the steady states

In this subsection, we are interested in the existence and the characterization of the equilibria of system (43). Let us consider (S^*, I^*, u^*) a potential equilibrium. This one satisfies :

$$\begin{cases} 0 = \sigma - \beta I^* S^* - \mu S^* - \psi H(S^*) + (1-\theta)e^{-\mu\tau}u^*, \\ 0 = \beta I^* S^* - \mu I^*, \\ u^* = \psi H(S^*) + \theta e^{-\mu\tau}u^*. \end{cases} \tag{46}$$

Last equation of (46) gives directly the expression for u^* :

$$u^* = \frac{\psi H(S^*)}{1-\theta e^{-\mu\theta}} \qquad (\oplus)$$

The second equation of (46) gives two cases to be considered :

$$0 = \beta I^* S^* - \mu I^* \iff I^* = 0 \text{ or } S^* = \frac{\mu}{\beta}.$$

Endemic steady-state $(\overline{S}^H, \overline{I}^H, \overline{u}^H)$

We consider here $S^* = \frac{\mu}{\beta} = \overline{S}^H$. This gives us the expression of $\overline{u}^H$ using $(\oplus)$:

$$\overline{u}^H = \frac{\psi H(\overline{S}^H)}{1-\theta e^{-\mu\tau}} = \frac{\psi H(\frac{\mu}{\beta})}{1-\theta e^{-\mu\tau}}.$$

And finally the first equation of (46) gives the expression of $\overline{I}^H$:

$$\overline{I}^H = \frac{1}{\mu}\left[\sigma - \frac{\mu^2}{\beta} - \psi H(\overline{S}^H) + (1-\theta)e^{-\mu\tau}\right] = \frac{\sigma}{\mu} - \frac{\mu^2 + \psi\beta H(\frac{\mu}{\beta}) - (\mu^2\theta + \psi\beta H(\frac{\mu}{\beta}))e^{-\mu\tau}}{\beta\mu(1-\theta e^{-\mu\tau})}.$$

And as previously, this equilibrium exists by definition if and only if $\overline{I}^H > 0$ and in other words if and only if $\frac{\sigma}{\mu} > \frac{\mu^2+\psi\beta H(\frac{\mu}{\beta})-(\mu^2\theta+\psi\beta H(\frac{\mu}{\beta}))e^{-\mu\tau}}{\beta\mu(1-\theta e^{-\mu\tau})}$.
We can summarize that the system (43) has a unique endemic equilibrium $(\overline{S}^H, \overline{I}^H, \overline{u}^H)$ if and only if

$$\frac{\sigma}{\mu} > \frac{\mu^2 + \psi\beta H(\frac{\mu}{\beta}) - (\mu^2\theta + \psi\beta H(\frac{\mu}{\beta}))e^{-\mu\tau}}{\beta\mu(1-\theta e^{-\mu\tau})}$$

which is given

$$(\overline{S}^H, \overline{I}^H, \overline{u}^H) := \left(\frac{\mu}{\beta} \; ; \; \frac{\sigma}{\mu} - \frac{\mu^2 + \psi\beta H(\frac{\mu}{\beta}) - (\mu^2\theta + \psi\beta H(\frac{\mu}{\beta}))e^{-\mu\tau}}{\beta\mu(1-\theta e^{-\mu\tau})} \; ; \; \frac{\psi H(\frac{\mu}{\beta})}{1-\theta e^{-\mu\tau}}\right) \tag{47}$$

Disease free steady-state (S_0^H, I_0^H, u_0^H)
Now we consider the second case : $I^* = 0 = I_0^H$.
Thank to $(\oplus)$, we get that

$$u_0^H = \frac{\psi H(S_0^H)}{1-\theta e^{-\mu\tau}}.$$

Then, the first equation of (46) becomes

$$0 = \sigma - \mu S^* + \psi H(S^*)\left(\frac{(1-\theta)e^{-\tau\mu}}{1-\theta e^{-\tau\mu}} - 1\right) = F(S^*),$$

where $F : x \longmapsto \sigma - \mu x + \psi H(x)\left(\frac{(1-\theta)e^{-\tau\mu}}{1-\theta e^{-\tau\mu}} - 1\right)$ and is continuous. We now have to show if such a S^* does exist. We first have

$$\begin{aligned} e^{-\mu\tau} - 1 < 0 &\iff e^{-\mu\tau} + \theta e^{-\mu\tau} - \theta e^{-\mu\tau} - 1 < 0 \\ &\iff e^{-\mu\tau}(1-\theta) < 1 - \theta e^{-\mu\tau} \\ &\iff \frac{e^{-\mu\tau}(1-\theta)}{1-\theta e^{-\mu\tau}} - 1 < 0 \end{aligned}$$

Thus, F is decreasing since $x \longmapsto H$ is increasing.
Moreover, $F(0) = \sigma > 0$ and $F(\frac{\sigma}{\mu}) = \psi H(\frac{\sigma}{\mu}) \left(\frac{(1-\theta)e^{-\tau\mu}}{1-\theta e^{-\tau\mu}} - 1 \right) < 0$. Then, using the continuity and the Intermediate Value Theorem, we get that there exists a unique $S_0^H > 0$ such that $F(S_0^H) = 0$. This gives us existence of a unique disease-free equilibrium given by

$$(S_0^H, I_0^H, u_0^H) := \left(S_0^H \ ; \ 0 \ ; \ \frac{\psi H(S_0^H)}{1 - \theta e^{-\mu\tau}} \right). \tag{48}$$

We can then sum up the characterization of the equilibria by the following theorem :

Theorem 4.2. *Suppose that the following condition holds :*

$$\frac{\sigma}{\mu} > \frac{\mu^2 + \psi\beta H(\frac{\mu}{\beta}) - (\mu^2\theta + \psi\beta H(\frac{\mu}{\beta}))e^{-\mu\tau}}{\beta\mu(1 - \theta e^{-\mu\tau})} \qquad (\tilde{H})$$

Then system (43) has two steady-states : a disease free steady-state given by (48) and an endemic steady-state defined by relation (47). If the condition $(\tilde{H})$ does not hold any more, then system (43) has only the disease-free equilibrium.

4.2.4 Basic reproduction number $\mathcal{R}_0^H$

In this subsection, we compute the basic reproduction number of system (43). As in section 2.4, let us have a look at the second equation of (43) and rewrite it :

$$I'(t) = I(t)\left[\beta S(t) - \mu\right] \iff \frac{I'(t)}{\mu I(t)} = \frac{\beta S(t)}{\mu} - 1.$$

By the same reasons as in section 2.4, we have that the infection triggers if and only if $\frac{\beta S(t)}{\mu} - 1 > 0$. Thus, we define the basic reproduction number of (43) by

$$\mathcal{R}_0^H := \frac{\beta S_0^H}{\mu}. \tag{49}$$

4.2.5 Stability of the equilibria

In this section, we study the local stability of the equilibria. First, we linearize our system (43) around an equilibrium (S^*, I^*, u^*). Aftercomputing the Jacobian of the system evaluated in (S^*, I^*, u^*), we get the linearized system

$$\begin{cases} S'(t) = -\beta I^* S(t) - \beta S^* I(t) - \mu S(t) - \psi S(t) H'(S^*) + (1-\theta)e^{-\mu\tau}u(t-\tau), \\ I'(t) = \beta I^* S(t) + \beta I(t) S^* - \mu I(t), \\ u(t) = \psi S(t) H'(S^*) + \theta e^{-\mu\tau}u(t-\tau). \end{cases} \qquad t \geqslant \tau \tag{50}$$

Looking for solution of the form $S(t) = S_0 e^{\lambda t}, I(t) = I_0 e^{\lambda t}$ and $u_0 = u_0 e^{-\lambda t}$, we get the following linear system :

$$\begin{pmatrix} \lambda + \beta I^* + \mu + \psi H'(S^*) & \beta S^* & -(1-\theta)e^{-\mu\tau}e^{-\tau\lambda} \\ -\beta I^* & \lambda - \beta S^* + \mu & 0 \\ -\psi H'(S^*) & 0 & 1 - \theta e^{-\mu\tau}e^{-\tau\lambda} \end{pmatrix} \begin{pmatrix} S_0 \\ I_0 \\ u_0 \end{pmatrix} = \begin{pmatrix} 0 \\ 0 \\ 0 \end{pmatrix}.$$

Then, the characteristic equation $\Delta^H(\lambda) = 0$ of (43) is the determinant of the previous matrix equals to zero.
In order to demonstrate the local stability of both of the steady-states of (43), we are going to follow the same steps as we did in section 2.5.

Local stability without delay
Let us consider any equilibrium (S^*, I^*, u^*) of (43). In this no-delay case, *ie* $\tau = 0$, the characteristic equation is given by

$$\Delta^H(\lambda) = (\lambda + \mu)(1-\theta)(\lambda - \beta S^* + \mu + \beta I^*) = 0.$$

We get then the following theorem

Theorem 4.3. *For $\tau = 0$, we get the following local stability : if $\mathcal{R}_0^H < 1$, the disease-free equilibrium, given by (48), is the unique steady-state and is locally asymptotically stable. Else, if $\mathcal{R}_0^H > 1$, both of the steady-states coexist, the disease-free is unstable and the endemic one, given by (47), is locally asymptotically stable.*

Proof. Exactly the same as Theorem 2.6. □

Local stability of the disease-free equilibrium

Let us consider the disease-free equilibrium (S_0^H, I_0^H, u_0^H) given by (48). The characteristic equation around this disease-free steady-state is given by

$$\Delta^H(\lambda,\tau) = (\lambda+\mu+\beta S_0^H)\left[\lambda+\mu+\psi H'(S_0^H) - (\theta(\lambda+\mu)+\psi H'(S_0^H))e^{\mu\tau}e^{\lambda\tau}\right] = 0.$$

We then get the following theorem :

Theorem 4.4. *Suppose that $\mathcal{R}_0^H < 1$. The disease-free given by (48) is locally asymptotically stable.*

Proof. Since $t \longmapsto H(t)$ is increasing for every $t \in \mathbb{R}^+$, we get that $H'(S_0^H) > 0$. Now let us define $\xi := \psi H'(S_0^H) > 0$. We rewrite our characteristic equation :

$$\Delta^H(\lambda,\tau) = (\lambda+\mu+\beta S_0^H)\left[\lambda+\mu+\xi - (\theta(\lambda+\mu)+\xi)e^{\mu\tau}e^{\lambda\tau}\right] = 0.$$

This equation is the same as in section 2.5.1. Thus, the rest of the proof follows the same steps as Theorem 2.7. □

Local stability of the endemic equilibrium

Here ,let us focus on the endemic equilibrium $(\overline{S}^H, \overline{I}^H, \overline{u}^H)$ given by (47). The characteristic equation around this steady-state is

$$\Delta(\lambda,\tau) = \lambda^2+(\psi H'(\overline{S}^H)+\mu+\beta\overline{I}^H)\lambda+\mu\beta\overline{I}^H - \left[\theta(\lambda^2+(\mu+\beta\overline{I}^H)+\lambda\mu\beta\overline{I}^H)+\psi H'(\overline{S}^H)\lambda\right]e^{-\mu\tau}e^{-\tau\lambda} = 0$$

We then get the following theorem :

Theorem 4.5. *Let us take $\tau > 0$ and assume that $\mathcal{R}_0^H(\tau) > 1$. Then, all the roots of the previous characteristic equation have a negative real part and thus, the endemic equilibrium of (43) is locally asymptotically stable.*

Proof. We can easily adapt the proof of Theorem 2.8. □

4.3 Numerical simulations

4.3.1 Simulations

Then, using the same parameters as before (see Table 6), in section 4, we make two numerical simulations of model (43). One simulation over 400 years (see Figure 6) and one over 15 years (see Figure 7).

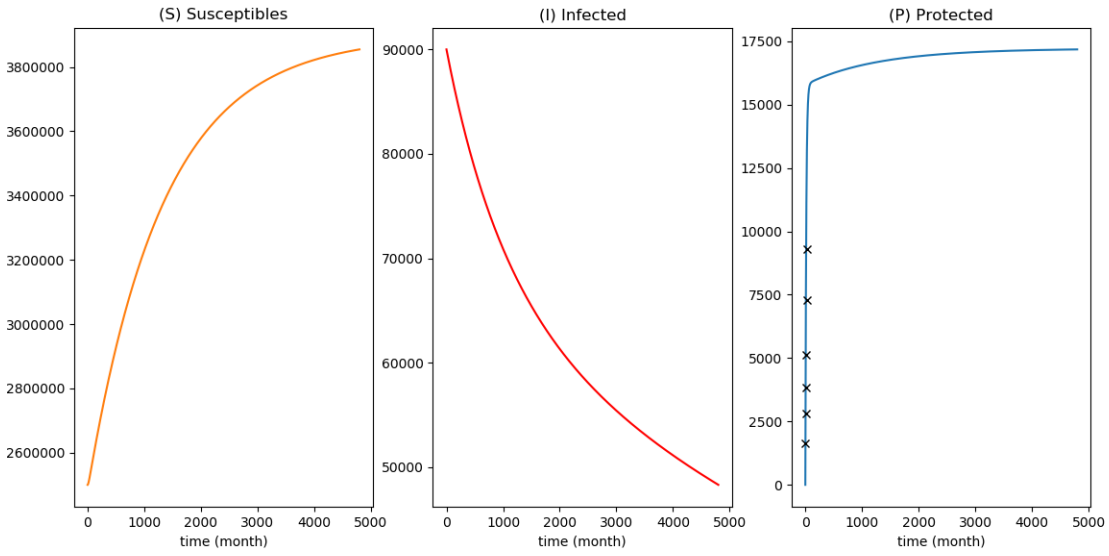

Figure 7: Plot of the evolution of the different compartments of the model (43) along the time (over 400 years). The crosses in the last plot represent the real values of the number of PrEP users got in the Table 3.

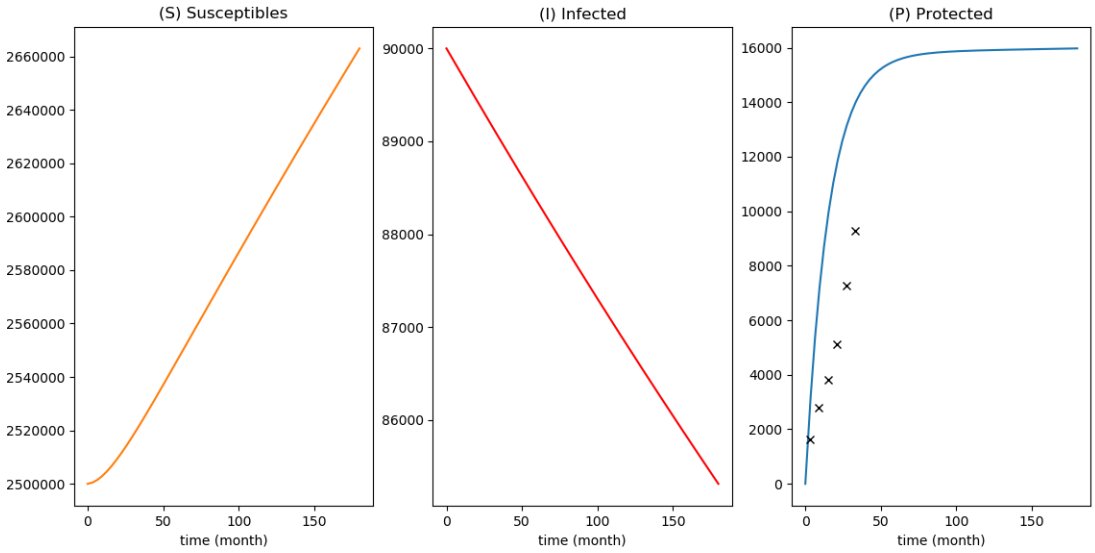

Figure 8: Plot of the evolution of the different compartments of model (43) along the time (over 15 years). The crosses in the last plot represent the real values of the number of PrEP users got in the Table 3.

4.3.2 Discussion

Let us comment on these figures. We see that within the configuration of parameters of Table 6, we have $\mathcal{R}_0 < 1$. We can guess that $S^0 \simeq 3900000$ and $P^0 \simeq 175000$. In comparison to the first simulation in section 3.5, we observe that the number of protected passes the current data. But we can notice that the equilibrium of the protected might be under-estimated, according the dynamic of the dataset (black crosses on Figures 6 and 7). Indeed, the main issue still lies in the dynamics of the protected. We remark that the data of Protected has convex growth whereas the blue curve of the simulation is concave. This convexity expresses that there are too much protected individuals in a small interval of time. Thus, the choice of ψ is still surestimated in the first months. This leads us to rethink the time dependence of ψ.

5 Hill function to fit the evolution of ψ

In this section, we come back to our first model (5) but we considered the parameter ψ as time-dependent. this leads us to a non-autonomous model. We do not study its mathematical propoperties because of the complexity of the non-autonomy, but we make some numerical simulations and discuss the results.

5.1 Parameter ψ is time-dependent

In this section, we are going to investigate the choice of ψ. We clearly saw that ψ is time-dependent (See Table 4). This time-dependence makes our system not be an autonomous system any more. Thus, all the study made in Section 1 must be remade. That is why, in this section, we only focus on numerical aspect and forget the mathematical dimension.

We assume ψ is time-dependent and follows a Hill function-like growth (according to data in Table 5). Indeed, this parameter cannot grow indefinitely, thus it reaches a saturation (x_{sat} in section 4.1).

So, we now fit the dynamic of the dataset of ψ (Table 5) with a Hill function.
We set $x_{\text{sat}} = 0.0007$. Indeed, if we consider that the susceptible population is around 4000000 after some decades, then we have $x_{\text{sat}} \times 4000000 = 2800$ susceptibles per month that begin the PrEP, which seems reasonable on the long term.

Then, taking $n = 2$ and $K = 146000$ (which represents 146 months for some computational reasons), we obtain the following plot (see Figure 8 bellow) :

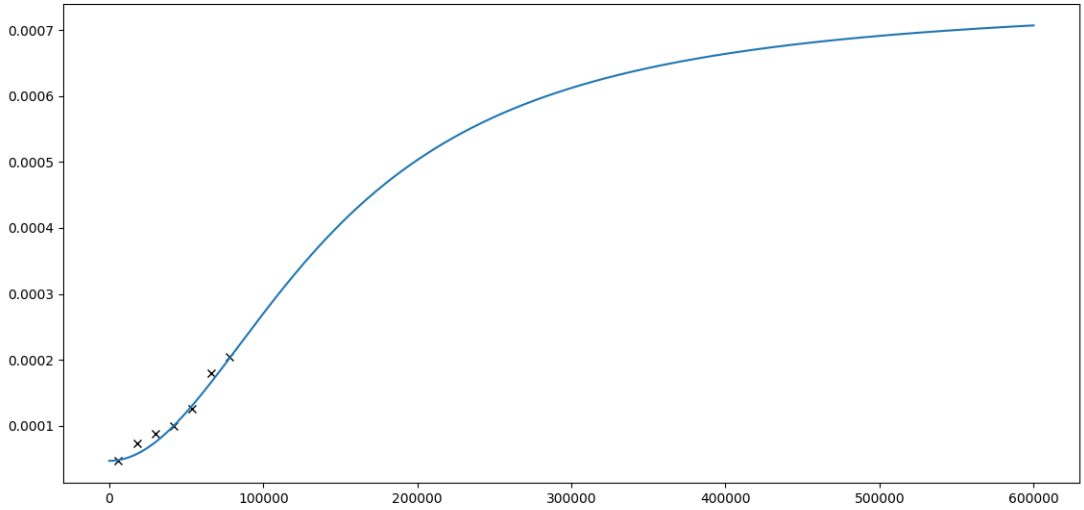

Figure 9: Fitting of the dataset given in Table 5 with a Hill function. Black crosses represent the data and the blue curve is the Hill function fit. *The scale of the abscisse is adapted to the numerical simulations.*

More precisely, the equation of the Hill function for ψ is

$$\psi(t) = 0.0007\frac{t^2}{146000^2 + t^2} + 0.0000466. \tag{51}$$

We forget temporarly what we did in the previous subsection 4.2 and write a new non-autonomous model by :

$$\begin{cases} S'(t) = \sigma - \beta I(t)S(t) - (\mu + \psi(t))S(t) + (1-\theta)e^{-\mu\tau}u(t-\tau), \\ I'(t) = \beta I(t)S(t) - \mu I(t), \qquad \text{with } t > \tau. \\ u(t) = \psi(t)S(t) + \theta e^{-\mu\tau}u(t-\tau), \end{cases} \tag{52}$$

$$S(0) = S_0, \quad I(0) = I_0, \quad \text{and} \quad u(t) = \varphi(t), \quad -\tau \leqslant t \leqslant 0, \tag{53}$$

Then, we make two numerical simulations of this new model (52) (See figures 9 and 10 below).

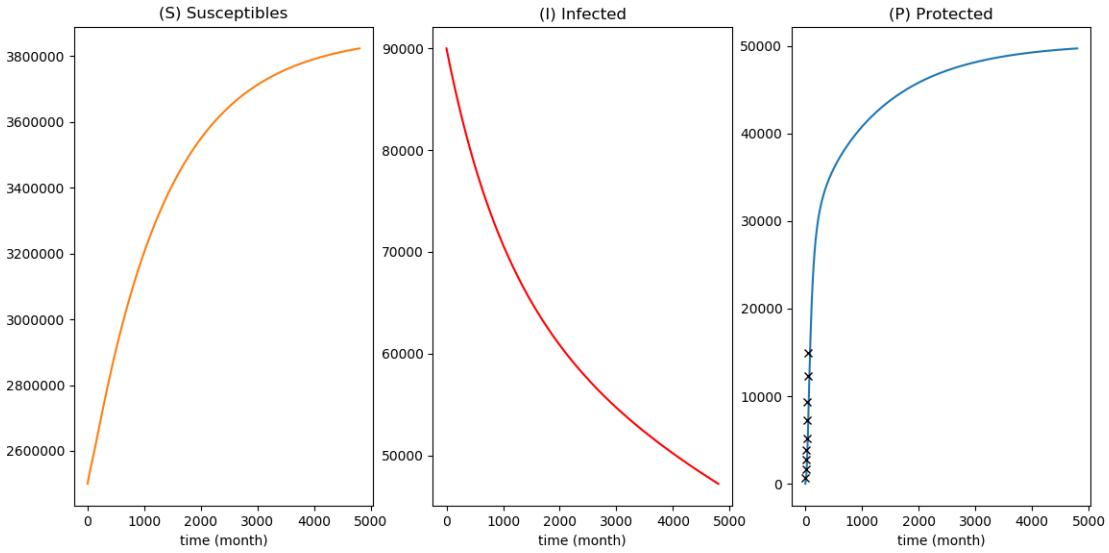

Figure 10: Plot of the evolution of the different compartments of model (52) along the time (over 400 years). The crosses in the last plot represent the real values of the number of PrEP users got in the Table 3.

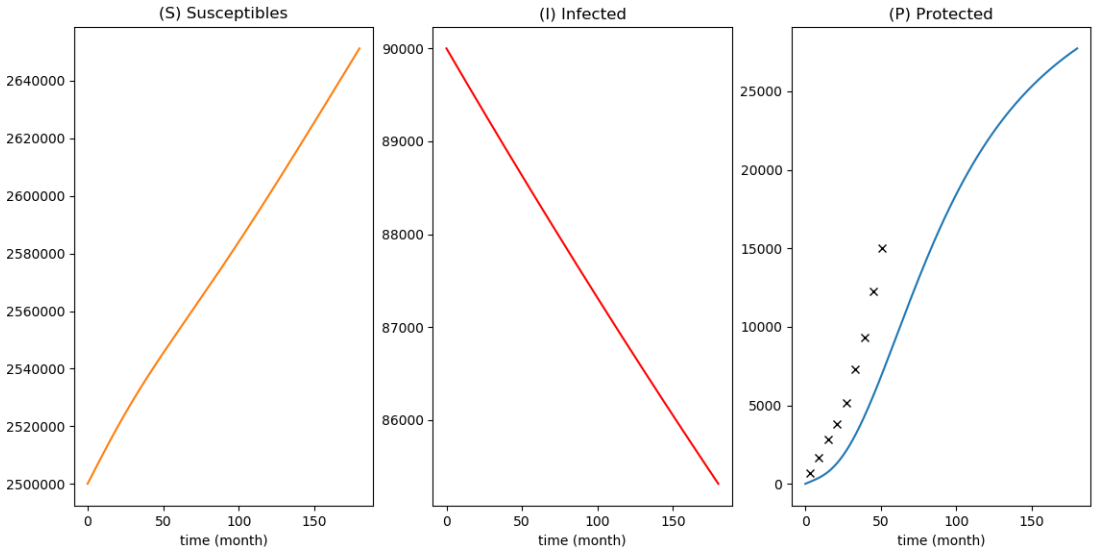

Figure 11: Plot of the evolution of the different compartments of model (52) along the time (over 15 years). The crosses in the last plot represent the real values of the number of PrEP users got in the Table 3.

5.2 Discussion

In figures 9 and 10, with the same parameters and thefunction $t \longmapsto \psi(t)$, we see that we still have $\mathcal{R}_0 < 1$. Precisely, we get that $S^0 \simeq 3900000$ and $P^0 \simeq 50000$. The modification made in model (52) presents two advantages : on the on hand, we reach a important number of susceptibles in few decades, and on the other hand the dynamics of the data and curve of the simulation are quite the same, we got the same dynamicin terms of convexity.

The unique difference lies in the growth of our simulation that is still a little too slow in comparison to the data. This fact leads us to the next subsection.

6 Complete Hill function-like model

6.1 Hill function and simulations

In this subsection, we finally combine both of the modifications made in subsections 4.2 and 4.3. We get the following non-autonomous difference-differential model with discrete delay

$$\begin{cases} S'(t) = \sigma - \beta I(t)S(t) - \mu S(t) - \psi(t)H(S(t)) + (1-\theta)e^{-\mu\tau}u(t-\tau), \\ I'(t) = \beta I(t)S(t) - \mu I(t), \\ u(t) = \psi(t)H(S(t)) + \theta e^{-\mu\tau}u(t-\tau), \end{cases} \quad \text{with } t > \tau. \tag{54}$$

$$S(0) = S_0, \quad I(0) = I_0, \quad \text{and} \quad u(t) = \varphi(t), \quad -\tau \leqslant t \leqslant 0, \tag{55}$$

with $t \longmapsto \psi(t)$ given by equation (51) and $t \longmapsto H(t)$ given by equation (42). Other parameters are taken in Table 6.

As previously, we make two numerical simulations of this model that we compare to our data of Table 3.

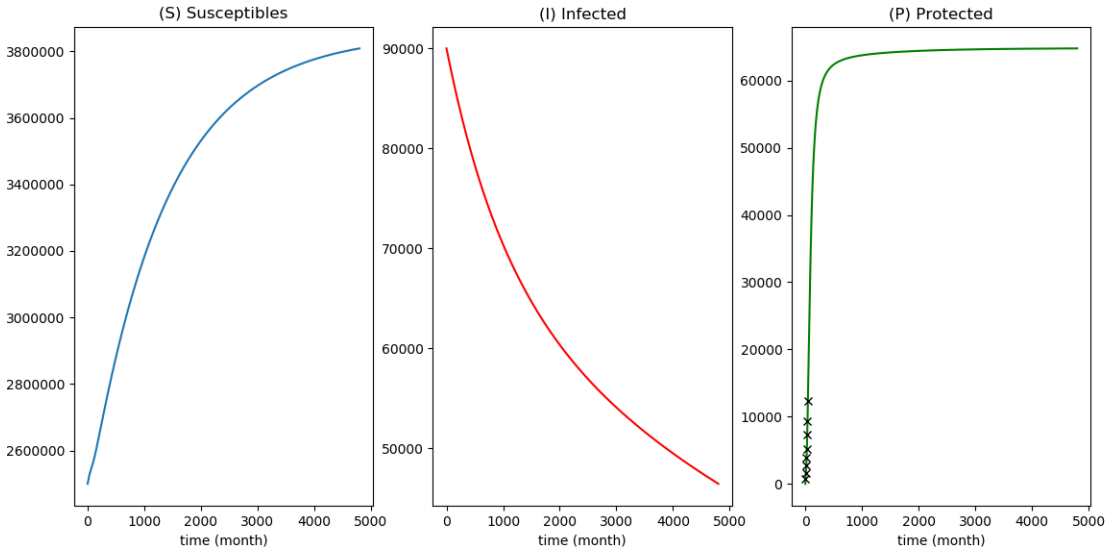

Figure 12: Plot of the evolution of the different compartments of model (54) along the time (over 400 years). The crosses in the last plot represent the real values of the number of PrEP users got in the Table 3.

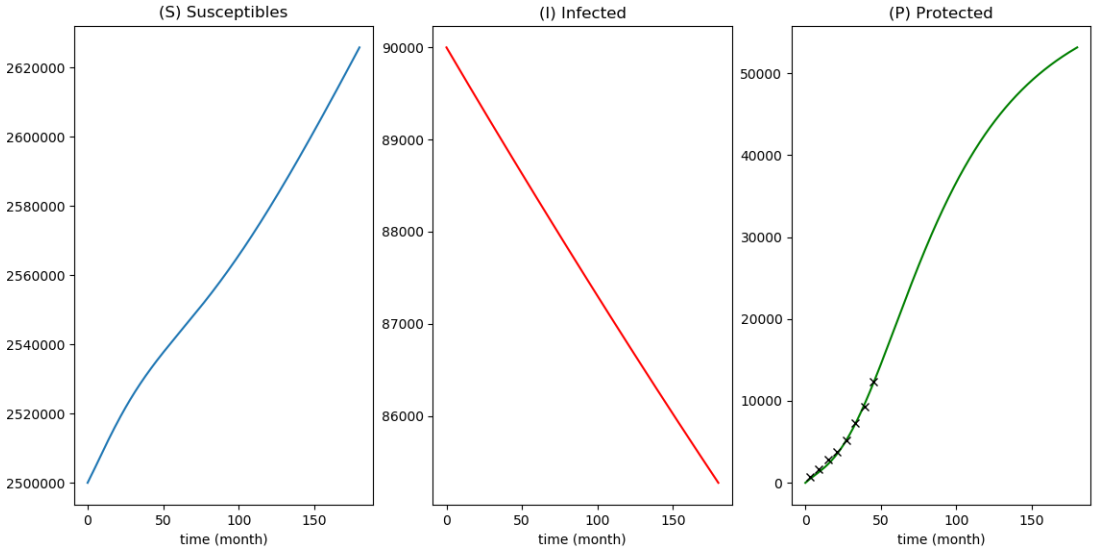

Figure 13: Plot of the evolution of the different compartments of model (54) along the time (over 15 years). The crosses in the last plot represent the real values of the number of PrEP users got in the Table 3.

Within this combination of parameters, we still have $\mathcal{R}_0 < 1$ and we can estimate that $S^0 \simeq 3900000$ and $P^0 \simeq 65000$. We observe also that the time-dependence of ψ and the control of $S(t)$ with a Hill function-like behaviour fit perfectly the data of the protected.

7 PrEP global effectiveness

In this section, we explain how the use of PrEP can help to fight against the HIV epidemics. We see that a well control of the PrEP enables to reduce the $\mathcal{R}_0$ and, in the long term, to earn money in terms of public health.

7.1 Effectiveness in terms of public health

As expected, the use of PrEP enables clearly to reduces the number of infected individuals. The more protected individuals there are, the less infected individuals there are along the time. Figure 13 shows this evolution.

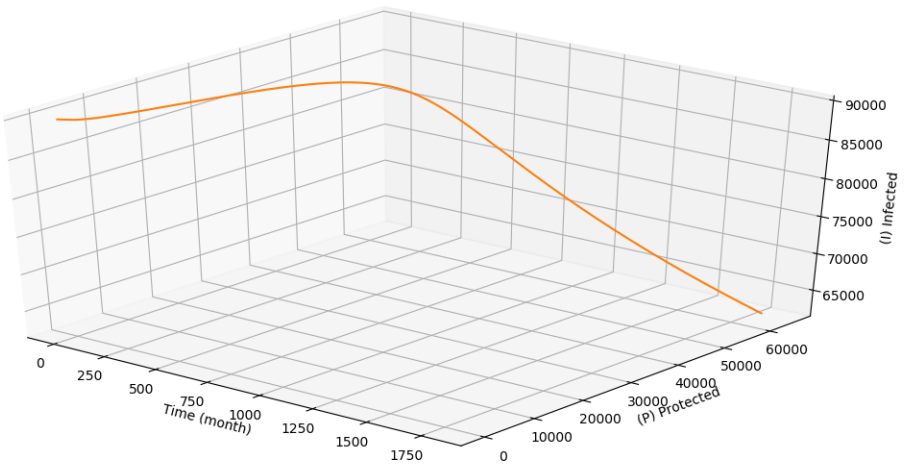

Figure 14: Evolution of the number of protected and infected individuals along the time.

More precisely, in terms of epidemiology, we succed to reduce the $\mathcal{R}_0$ thanks to the parameters linked to the use of PrEP. We have three parameters to rely on : θ, ψ and τ. In the following figures 14 and 15, we plot the evolution of $\mathcal{R}_0$ in function of two of these parameters.
Proposition 2.5. tells us that $\mathcal{R}_0$ is a decreasing function of ψ, τ and θ. In figure 14, we see that for $\theta > 0.90$, the $\mathcal{R}_0$ decreases very quickly for ψ as big as possible. It means that, for a certain rate of ψ fixed, the more protected individuals remain under PrEP after one period, the more the $\mathcal{R}_0$ keeps decreasing. In other words, we do not need to make the whole population take the PrEP but we must focus on those who are under PrEP and make them continue under PrEP.
In figure 15, we plot the evolution of $\mathcal{R}_0$ in fonction of θ and τ. We see that the longer the period under PrEP, in other words, the bigger τ, the less $\mathcal{R}_0$. Indeed, as we assumed that an individual under PrEP will not stop it till the end of the τ-period, we ensure that we keep individuals under PrEP for a longer time. And thus, we do not need a lot of new individuals to begin the PrEP treatment.

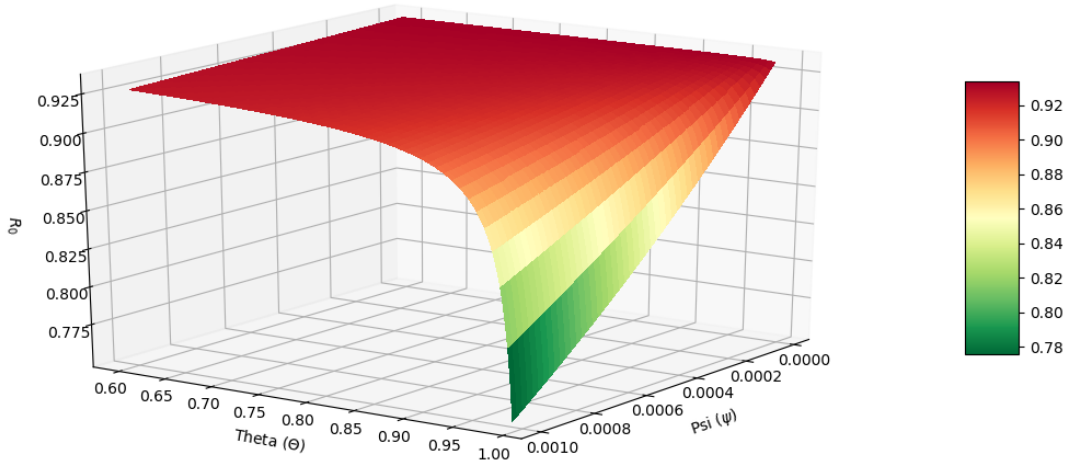

Figure 15: The basic reproduction number $\mathcal{R}_0$ in function of the parameters θ and ψ.

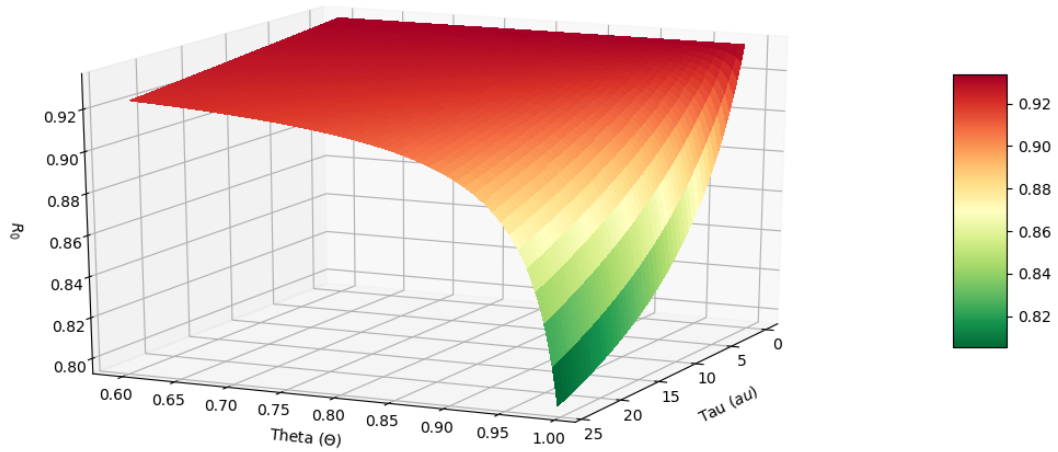

Figure 16: The basic reproduction number $\mathcal{R}_0$ in function of the parameters θ and τ.

7.2 Saving money in comparison to the Tritherapy

An important point to study about the use of PrEP is its costs in order to know how expensive could be an awareness campaign about the PrEP.
In figure 16, we plot the cost of some combinations of treatment along the time to see how expensive it is. In France, we assume that the tritherapy is aroung 1000 €[11]. Then, we know thatthe cost of the PrEP

[11] https://www.latribune.fr/actualites/economie/france/20130405trib000757841/1.000-a-1.500-euros-le-cout-mensuel-de-la-tritherapie-d-un-malade-du-sida.html#:~:text=Ces%20traitements%20ont%20évidemment%20un,et%20des%20analyses%20sanguines%20régulières.

drug (TRUVADA) is around 300€ for a month[12] and the generic drug for the PrEP is around 100€. In Figure 16, we see that the global tendency of the costs (green and yellow curves) is decreasing. Obviously, the coexistence of PrEP and Tritherapy is more expensive than the tritherapy only. But, for a fixed number of individual under PrEP, we know that along the time, there will be less individual under Tritherapy and thus the cost will keep diminishing. Thus, it is worth investing in the PrEP as within some years, the combination of PrEP and tritherapy will be cheaper than the use of tritherapy only.

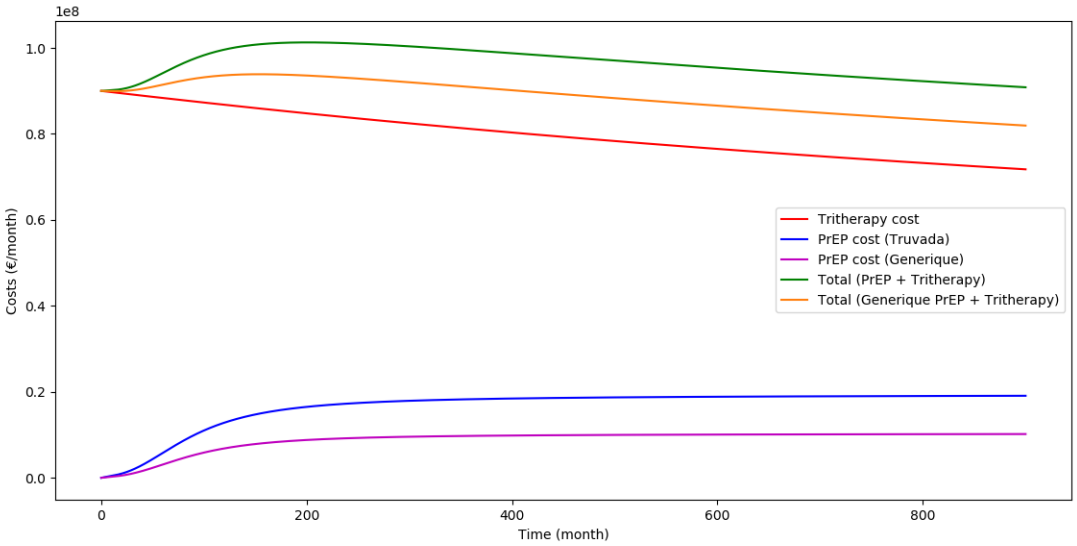

Figure 17: Cost evolution of different combinations of treatment along the time.

8 Conclusion and discussion

In this dissertation, we presented a new mathematical compartmental model of the HIV-AIDS epidemics. This model is a coupled system of difference-differential equations. We make a complete study. This model has two steady-states, a disease-free one and an endemic one. We demonstrated that the disease-free equilibrium is globally asymptotically stable if the basic reproduction number $\mathcal{R}_0$ is less than 1, and the endemic equilibrium is globally asymptotically stable if $\mathcal{R}_0 > 1$. Moreover, in order to fit our dataset, we improve our model. We thus consider a nonlinear initial condition using a Hill function. Also, we make our system of equations non-autonomous. Indeed, we choose one parameter and fit its time evolution with a hill function. Then, we make some numerical simulations and we claim that the best simulation is the one with the use of the Hill function in the two cases. We see that the use of PrEP enables to cleary reduce the number of infected individuals and thus to maintain the intensity of the HIV epidemics along the time. That is why the PrEP treatment should be and must be more spread and introduced in the population.

However, some points of our model are questionable. The most important problem with the HIV epidemics is about the data. As we already discussed, it is really difficult to estimate the true number of infected individual since there is a very long incubation period before AIDS symptoms and susceptible individuals since there is no ways to know exactly every interourses between individuals. Thus, we should find a way to estimate better those populations. Moreover, we assumed that during the three month period, an individual under PrEP will not stop the treatment. Obviously, we know that some individuals will not respect the treatment (forget it, stop it...). Thus we may consider it in a future model by adding an arrow going outside from the compartment of the protected. Furthermore, about the parameter μ. We consider it as being the natural dead rate. But to be more precise, this parameter contains also the rate of sexual life end. However, we clearly assume that the rate of sexual life end is less than the natural dead rate. Finally, our model takes into account only the PrEP as a preventing method. That is why the $\mathcal{R}_0$ cannot decrease a lot. But we must remind that the use of condom is a widely used and helps reduce the $\mathcal{R}_0$ and contain the epidemics. Finally, in a future work, we must make a complete study of the non-autonomous model in order to have a better of comprehension of the stability of this model.

[12] `https://www.vidal.fr/Medicament/truvada-69657-prescription_delivrance_prise_en_charge.htm`

To end with this work, a recent other way to use the PrEP was discovered. An injection of another combination of drugs every two month is made[13]. This way of treatment has shown a better accuracy in the protection against HIV transmission than the oral way of treatment. Thus, we should adapt our work to this new injection and see through numerical simulations which PrEP treatment is the most accurate.

[13] https://www.aidsmap.com/news/jul-2020/injectable-prep-offers-superior-efficacy-oral-prep-clinical-trial

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