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Dynamics and optimal control of a non-linear epidemic model with relapse and cure

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HIGHLIGHTS

- The basic reproduction number of a general epidemic model is introduced.
- The necessary and sufficient condition for the exponential stability of the free disease is obtained.
- The global asymptotic stability of the endemic point is shown.
- Two types of control to reduce the number of infectives is considered.
- The optimal control problem is solved numerically.

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ABSTRACT

In this work, we introduce the basic reproduction number $\mathcal{R}_0$ for a general epidemic model with graded cure, relapse and nonlinear incidence rate in a non-constant population size. We established that the disease free-equilibrium state E_f is globally asymptotically exponentially stable if $\mathcal{R}_0 < 1$ and globally asymptotically stable if $\mathcal{R}_0 = 1$. If $\mathcal{R}_0 > 1$, we proved that the system model has at least one endemic state E_e. Then, by means of an appropriate Lyapunov function, we showed that E_e is unique and globally asymptotically stable under some acceptable biological conditions. On the other hand, we use two types of control to reduce the number of infectious individuals. The optimality system is formulated and solved numerically using a Gauss–Seidel-like implicit finite-difference method.

1. Introduction

It is well known that infectious diseases are a major public problem worldwide. Infectious diseases affect not only the health of individuals, but also societies, economies and political systems. It is therefore useful to understand epidemics dynamics and trace the factors that are responsible or contribute to their emergence in order to fight them or at least to bring them under control. Mathematical models are used extensively in the study of epidemiological phenomena. Most models are described by ordinary differential equations with compartments [1–4]. In this type of models, the population is divided into disjoint classes. For instance, the classical Kermack–McKendrick model [5] separated the population into three compartments of susceptible, infective and recovered individuals, with numbers at time t denoted by $S(t)$, $I(t)$ and $R(t)$ respectively. The susceptible class consists of individuals who can incur the disease but are not yet infective. The infective class consists of those who are either infected or able to transmit the disease. The recovered class consists of those who where removed from the susceptible–infective interaction by simple recovery or other reasons [5–9]. Disparate SIR

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epidemic models can be constructed. For example, some models ignore demographics (no births or deaths or immigration are considered). This hypothesis is used if the time-scale of the disease is relatively short or when the birth rate is low compared to the epidemic period [5,10–14]. One of the earliest of these models was the basic SIR epidemic model introduced by Kermack and McKendrick [5]:

$$\begin{cases} \dfrac{dS}{dt} = -\beta SI, \\ \dfrac{dI}{dt} = \beta SI - \lambda I, \\ \dfrac{dR}{dt} = \lambda I, \end{cases} \tag{1}$$

where β is the infection coefficient and λ the recovery rate. Model (1) can be extended to a fluctuating population (with births and deaths). So, if the birth and death rates μ and d respectively, are implemented, system (1) becomes.

$$\begin{cases} \dfrac{dS}{dt} = \mu - dS - \beta SI, \\ \dfrac{dI}{dt} = \beta SI - \lambda I - dI, \\ \dfrac{dR}{dt} = \lambda I - dR. \end{cases} \tag{2}$$

Noting that the total population size $N(t) = S(t) + I(t) + R(t)$ in system (3) verifies the linear equation

$$\frac{dN}{dt} = \mu - dN,$$

and so $N(t)$ converges to $\frac{\mu}{d}$. Therefore, one can suppose that $N(t)$ is constant if we are interested with the asymptotic behavior of the epidemic [15–19]. To ensure a varying population size, some models added a disease induced death rate in the infectious compartment. We find this parameter in deadly infectious diseases like Malaria [20–22]. If the disease is non-fatal, the disease-induced death rate is either very small or null. To generalize, we consider a different death rate for each compartment [23]. Model (2) becomes

$$\begin{cases} \dfrac{dS}{dt} = \mu - \mu_1 S - \beta SI, \\ \dfrac{dI}{dt} = \beta SI - (\mu_2 + \lambda)I, \\ \dfrac{dR}{dt} = \lambda I - \mu_3 R, \end{cases} \tag{3}$$

where μ_1, μ_2 and μ_3 are the death rates of susceptibles, infectives and recovered, respectively. In the previous models, an individual is either susceptible or infected or fully recovered, while, in the present study, we are aiming to analyze the effect of mixing three supplementary parameters in addition to the previous ones: relapse, temporary immunity and cure denoted consecutively σ, ε and γ. In diseases such as herpes and human tuberculosis, recovered individuals may experience relapse and reenter the infective class [24–28]. In addition to tuberculosis and human herpes, Vargas [27] applied two models with relapse to tobacco and alcohol use and studied their stability. Van den Driessche [28] proposed an integro-differential system to model a general relapse phenomenon in infectious diseases including human herpes. In SIRS models, a recovered individual may lose immunity and be susceptible again [29–36]. A famous example is the seasonal influenza. Due to the high mutation of the virus, an influenza vaccine confers immunity for few years [37–39]. Another feature of our model is that we include also a cure rate of infectious individuals. Generally, we use SIS models for this purpose [40–44]. In [45], authors combined SIS and SIR models to marry permanent with temporary immunity. Recently, Muroya [46] posed a general model where all parameters we introduced before are considered. Respecting previous notations the system studied by Muroya can be written as follows:

$$\begin{cases} \dfrac{dS}{dt} = \mu - \mu S - \beta SI + \varepsilon I + \gamma R, \\ \dfrac{dI}{dt} = \beta SI - (\mu + \varepsilon + \lambda)I + \sigma R, \\ \dfrac{dR}{dt} = \lambda I - (\mu + \gamma + \sigma)R. \end{cases} \tag{4}$$

In this model, Muroya considered a constant population and a classical incidence rate βSI. In this paper, we propose the same model with a nonlinear incidence rate and a non-constant population. Many authors used nonlinear incidence rates $\beta Sf(I)$ instead of the standard bilinear βSI. In fact, the bilinear incidence rate is based on the law of mass action and the homogeneous mixing assumption. This contact law is more appropriate for communicable diseases such as influenza, etc.,

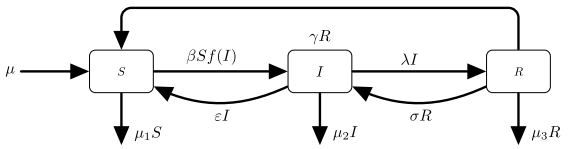

Fig. 1. Transfer diagram for SIRS model with relapse and graded cure rates.

but not for sexually transmitted diseases for example. Furthermore, in reality we found heterogeneous mixing of susceptibles and infective population, this encourages us to consider a non-linear incidence rate [2,47–51] (see Fig. 1).

Considering all the previous assumptions, we write our model as follows:

$$\begin{cases} \dfrac{dS}{dt} = \mu - \mu_1 S - \beta S f(I) + \varepsilon I + \gamma R, \\ \dfrac{dI}{dt} = \beta S f(I) - (\mu_2 + \varepsilon + \lambda) I + \sigma R, \\ \dfrac{dR}{dt} = \lambda I - (\mu_3 + \gamma + \sigma) R. \end{cases} \tag{5}$$

As in [47], we assume that the force of infection $f(I)$ is a function of class $\mathcal{C}^\infty$ on $[0, \infty)$ such that

$$f(0) = 0, \qquad 0 < f(I) < f'(0)I, \qquad \forall I > 0. \tag{6}$$

By a biological meaning, we further assume that the initial condition is given such that

$$S(0) > 0, \quad I(0) > 0, \quad R(0) > 0. \tag{7}$$

It is also biologically meaningful to suppose that $\mu_1 \leq \min(\mu_2, \mu_3)$. That is, epidemics increase the death rate of infective and removed individuals. This paper is organized as follows: in Section 2 we show the well posedness of our model. In Sections 3–5, we give the expression of the basic reproduction number $\mathcal{R}_0$ and discuss the local and global stability of equilibria states. In Section 6, we consider a control problem relative to our model. Using Pontryagin's Maximum Principle, we find the best possible control to reduce the number of infectious individuals. We show the numerical solution of this optimal control problem in Section 7. Finally, the paper ends with concluding remarks in Section 8.

2. Well posedness of the system model

Since the coefficients of system (5) are locally Lipschitz continuous so, thanks to the classical theory of ODE's [52], we can set that system (5) has a unique maximal local solution $(S(t), I(t), R(t))$ defined for all $t \in [0, \tau_e)$ and satisfying the initial condition (7). In the following proposition, we will show that the solution $(S(t), I(t), R(t))$ is positive and global defined (i.e., $\tau_e = \infty$).

Proposition 1. *For system (5) the following properties holds:*

(i) *Every solution starting from a positive initial condition exists for all $t \geq 0$ and remains positive.*

(ii) *The set $\Delta = \left\{(x, y, z) \in \mathbb{R}^3;\ x > 0,\ y > 0,\ z > 0,\ x + y + z \leq \frac{\mu}{\mu_1}\right\}$ is positively invariant with respect to system (5).*

Proof. (i) We will proceed by contradiction. Assume that there exists $\tau \in [0, \tau_e)$ such that

$$R(\tau) = 0, \quad \frac{dR(\tau)}{dt} \leq 0 \quad \text{and} \quad R(t) > 0 \quad \text{for all } t \in [0, \tau).$$

Hence, for all $t \in [0, \tau]$

$$\frac{dI}{dt} \geq -(\mu_2 + \lambda + \varepsilon) I + \beta S f(I)$$

which implies, using the comparison principle for ODE's, that $I(t) \geq X(t)$ for all $t \in [0, \tau]$ such that $X(t)$ is the solution of the following ODE:

$$\begin{cases} \dfrac{dX}{dt} = -(\mu_2 + \lambda + \varepsilon) X + \beta S(t) f(X), \\ X(0) = I(0). \end{cases} \tag{8}$$

The axis $x = 0$ is invariant by Eq. (8). Therefore, $X(0) = I(0) > 0$ implies that $X(t) > 0$ and $I(t) > 0$ for all $t \in [0, \tau]$. Thus,

$$0 = \frac{dR}{dt}(\tau) = \lambda I(\tau) > 0.$$

This is a contradiction. So, $R(t) > 0$ and $I(t) > 0$ for all $t \in [0, \tau_e)$. On the other hand , we have

$$\left.\frac{dS}{dt}\right|_{S=0} \geq \mu > 0.$$

Hence, the positivity of $S(t)$ if $S(0) > 0$ is guaranteed. In addition, using the assumption $\mu_1 \leq \min(\mu_2, \mu_3)$ and the positivity of the solution, the total population should verify the equation

$$\frac{dN}{dt} = \frac{d(S+I+R)}{dt} = \mu - \mu_1 S - \mu_2 I - \mu_3 R \leq \mu - \mu_1 N,$$

which gives by integration that

$$N(t) \leq \frac{\mu}{\mu_1} + \left(N(0) - \frac{\mu}{\mu_1}\right) e^{-\mu_1 t}. \tag{9}$$

Therefore, the solution $(S(t), I(t), R(t))$ is bounded. Then, it is defined for all $t \geq 0$.
(ii) It is a direct consequence of the positivity of the solutions and the estimation (9). □

3. The basic reproduction number and the existence of equilibria

To study the existence of equilibria for system (5), we need to introduce the basic reproduction number $\mathcal{R}_0$. It is the number of secondary cases which one case would produce in a completely susceptible population [53]. $\mathcal{R}_0$ is unquestionably the most important quantity to consider when analyzing any epidemic model for an infectious disease. In particular, $\mathcal{R}_0$ determines whether an epidemic can occur or not and summarizes in a simple way the effort required to eliminate an endemic infection from the population [54]. Using the concept of next generation matrix [53], the expression of $\mathcal{R}_0$ is given by

$$\mathcal{R}_0 = \frac{\beta\mu f'(0)}{\mu_1\left(\mu_2 + \varepsilon + \lambda - \frac{\sigma\lambda}{\mu_3+\gamma+\sigma}\right)}.$$

Note that $\frac{1}{\mu_2+\varepsilon+\lambda}$ is the average time that an infectious individual spends in the infective class on the first pass, while $\frac{\lambda}{\mu_2+\varepsilon+\lambda}$ is the probability for an individual to survive the infectious class and to fully recover. Finally the quantity $\frac{\sigma}{\mu_3+\gamma+\sigma}$ represents the probability to lose immunity and enter the infectious class alive. Thus, the total average time in the infectious class on multiple passes is

$$\frac{1}{\mu_2+\varepsilon+\lambda}\sum_{n=0}^{\infty}\left(\frac{\sigma\lambda}{(\mu_3+\varepsilon+\lambda)(\mu_3+\gamma+\sigma)}\right)^n = \frac{1}{\mu_2+\varepsilon+\lambda-\frac{\sigma\lambda}{\mu_3+\gamma+\sigma}}.$$

Multiplying the above expression by $\frac{\beta\mu f'(0)}{\mu_1}$ gives $\mathcal{R}_0$. Once $\mathcal{R}_0$ is found, we can now study the existence of steady state points of system (5). It means that we look for a point (S, I, R) realizing the following system :

$$\begin{cases} \mu - \mu_1 S - \beta S f(I) + \varepsilon I + \gamma R = 0, \\ \beta S f(I) - (\mu_2 + \varepsilon + \lambda) I + \sigma R = 0, \\ \lambda I - (\mu_3 + \gamma + \sigma) R = 0. \end{cases} \tag{10}$$

It is easy to see that $E_f\left(\frac{\mu}{\mu_1}, 0, 0\right)$ is a solution of (10). E_f is called the disease free-equilibrium state. Now, we study the possibility that (10) admits a positive endemic solution (S, I, R). From the third equation of (10), we have

$$R = \frac{\lambda I}{\mu_3 + \gamma + \sigma}. \tag{11}$$

Summing the three equations of (10), we obtain $\mu - \mu_1 S - \mu_2 I - \mu_3 R = 0$, which gives with (11) the following expression of S in terms of I :

$$S = \frac{1}{\mu_1}\left(\mu - (\mu_2 + \frac{\lambda\mu_3}{\mu_3+\gamma+\sigma})I\right). \tag{12}$$

Substituting (11) and (12) in the second equation of (10), then dividing by $I \neq 0$, we obtain

$$F(I) \triangleq \frac{\beta}{\mu_1}\left(\mu - (\mu_2 + \frac{\lambda\mu_3}{\mu_3+\gamma+\sigma})I\right)\frac{f(I)}{I} - (\mu_2+\varepsilon+\lambda) - \frac{\sigma\lambda}{\mu_3+\gamma+\sigma}.$$

- If $\mathcal{R}_0 \leq 1$.
  Since $0 < \frac{f(I)}{I} \leq f'(0)$, we deduce that $F(I) < 0$ for all $I > 0$. So, the model (5) does not have any positive equilibrium state.

- If $\mathcal{R}_0 > 1$.
  We have

$$F(0^+) = \lim_{I\to 0^+} F(I) = \frac{\beta\mu f'(0)}{\mu_1} - (\mu_2+\varepsilon+\lambda) - \frac{\sigma\lambda}{\mu_3+\gamma+\sigma} > 0.$$

  Moreover

$$F\left(\frac{\mu}{\mu_2+\frac{\lambda\mu_3}{\mu_3+\gamma+\sigma}}\right) = -\left((\mu_2+\varepsilon+\lambda) - \frac{\sigma\lambda}{\mu_3+\gamma+\sigma}\right) < 0.$$

  Thanks to the intermediate value theorem , there exists $I_e \in \left(0, \frac{\mu}{\mu_2+\frac{\lambda\mu_3}{\mu_3+\gamma+\sigma}}\right)$ such that

$$F(I_e) = 0.$$

  So

$$R_e = \frac{\lambda I_e}{\mu_3+\gamma+\sigma} > 0,$$

  and

$$S_e = \frac{1}{\mu_1}\left(\mu - \left(\mu_2 + \frac{\lambda\mu_3}{\mu_3+\gamma+\sigma}\right)I_e\right).$$

  Finally, because $\mu_1 \le \min(\mu_2, \mu_3)$, we have

$$\mu - \mu_1(S_e+I_e+R_e) \ge \mu - \mu_1 S_e - \mu_2 I_e - \mu_3 R_e = 0.$$

Thus, $(S_e, I_e, R_e) \in \Delta$. We summarize the above results in the following proposition.

Proposition 2. *Assume conditions (6) on f, then the following statements hold.*

(i) *If $\mathcal{R}_0 \le 1$, the disease-free equilibrium E_f is the unique equilibrium state of model (5).*
(ii) *If $\mathcal{R}_0 > 1$, in addition to E_f, model (5) has at least one positive equilibrium state $E_e(S_e, I_e, R_e)$.*

4. Stability of the disease-free steady state

In the previous section, we have showed that model (5) has at least two steady states. For the local stability analysis of various equilibria, we linearize system (5) in the neighborhood of these equilibrium points. The Jacobian matrix associated with model (5) evaluated at (x, y, z) is given by

$$J(x,y,z) = \begin{pmatrix} -\mu_1 - \beta f(y) & -\beta x f'(y) + \varepsilon & \gamma \\ \beta f(y) & -(\mu_2+\varepsilon+\lambda) + \beta x f'(y) & \sigma \\ 0 & \lambda & -(\mu_3+\gamma+\sigma) \end{pmatrix}.$$

In the following proposition, we characterize the local behavior near the disease-free E_f.

Proposition 3. *Suppose that $f(I)$ verifies conditions (6). Then, on the neighborhood of E_f, the following statements hold.*

(i) *if $\mathcal{R}_0 < 1$ system (5) is asymptotically stable,*
(ii) *if $\mathcal{R}_0 > 1$ system (5) is unstable.*

Proof. The jacobian matrix at E_f is

$$J(E_f) = \begin{pmatrix} -\mu_1 & -\beta\frac{\mu}{\mu_1}f'(0) + \varepsilon & \gamma \\ 0 & -(\mu_2+\varepsilon+\lambda) + \beta\frac{\mu}{\mu_1}f'(0) & \sigma \\ 0 & \lambda & -(\mu_3+\gamma+\sigma) \end{pmatrix}.$$

So, the characteristic polynomial of $J(E_f)$ is $P(X) = (X+\mu_1)Q(X)$ where

$$Q(X) = X^2 + bX + c$$
$$b = \mu_2+\varepsilon+\lambda - \frac{\beta\mu f'(0)}{\mu_1} + \mu_3 + \gamma + \sigma$$
$$c = (\mu_3+\gamma+\sigma)(\mu_2+\varepsilon+\lambda - \frac{\beta\mu f'(0)}{\mu_1}) - \lambda\sigma = (\mu_3+\gamma+\sigma)(1-\mathcal{R}_0).$$

(i) If $\mathcal{R}_0 < 1$, we have $b, c > 0$. Hence by Descartes rule, $Q(X)$ has two different negative roots, which means that all roots of $P(X)$ are negative and consequently E_f is asymptotically stable.
(ii) If $\mathcal{R}_0 > 1$, we have $c < 0$. So, by Descartes rule again, $Q(X)$ has exactly one positive root, consequently E_f is unstable. □

Note that, if $\mathcal{R}_0 = 1$ then $b > 0$ and $c = 0$, which implies that $J(E_f)$ has 0 as eigenvalue. So, more analysis must be done to conclude if E_f is stable or not. Moreover, the last results are just local. In the following theorem, we study the global stability of E_f when $\mathcal{R}_0 \leq 1$.

Theorem 4.1. *Under the conditions (6) on $f(I)$, let $(S(0), I(0), R(0)) \in \Delta$.*

(i) *If $\mathcal{R}_0 < 1$, then E_f is globally exponentially asymptotically stable.*
(ii) *If $\mathcal{R}_0 = 1$, then E_f is globally asymptotically stable.*

Proof. (*i*) From the last two equations of (5), we have

$$\frac{d}{dt}\left(I(t) + \frac{\sigma}{\mu_3+\gamma+\sigma}R(t)\right) = \beta S(t)f(I(t)) - \left(\mu_2+\varepsilon+\lambda - \frac{\sigma\lambda}{\mu_3+\gamma+\lambda}\right)I(t).$$

Since $(S(0), I(0), R(0)) \in \Delta$ and Δ is positively invariant with respect to system (5), we deduce that $(S(t), I(t), R(t)) \in \Delta$ for all $t \geq 0$. Using property (6), we deduce that

$$\beta S(t)f(I(t)) \leq \beta f'(0)\frac{\mu}{\mu_1}I(t). \tag{13}$$

Hence

$$\frac{d}{dt}\left(I(t) + \frac{\sigma}{\mu_3+\gamma+\sigma}R(t)\right) \leq \frac{-\beta\mu f'(0)}{\mu_1}\left(\frac{1}{\mathcal{R}_0} - 1\right)I(t). \tag{14}$$

On the other hand, from the S-equation and (13), we have

$$\begin{aligned}\frac{d}{dt}\left(\frac{\mu}{\mu_1} - S(t)\right) &= -\mu_1\left(\frac{\mu}{\mu_1} - S(t)\right) + \beta S(t)f(I(t)) - \varepsilon I(t) - \gamma R(t)\\ &\leq -\mu_1\left(\frac{\mu}{\mu_1} - S(t)\right) + \frac{\beta\mu f'(0)}{\mu_1}I(t) - \varepsilon I(t) - \gamma R(t).\end{aligned}$$

which gives with (14) that

$$\begin{aligned}&\frac{d}{dt}\left|\frac{\mu}{\mu_1} - S(t) + \frac{\mathcal{R}_0}{1-\mathcal{R}_0}I(t) + \frac{\mathcal{R}_0}{(1-\mathcal{R}_0)}\frac{\sigma}{(\mu_3+\gamma+\sigma)}R(t)\right|\\ &\leq -\mu_1\left(\frac{\mu}{\mu_1} - S(t)\right) - \varepsilon I(t) - \gamma R(t)\\ &\leq -\min\left(\mu_1, \frac{\varepsilon(1-\mathcal{R}_0)}{\mathcal{R}_0}, \frac{\gamma(1-\mathcal{R}_0)(\mu_3+\gamma+\sigma)}{\sigma\mathcal{R}_0}\right)\\ &\times\left|\frac{\mu}{\mu_1} - S(t) + \frac{\mathcal{R}_0}{1-\mathcal{R}_0}I(t) + \frac{\mathcal{R}_0}{1-\mathcal{R}_0}\frac{\sigma}{\mu_3+\gamma+\sigma}R(t)\right|.\end{aligned}$$

It follows by integration of the above inequality that

$$\begin{aligned}&\left|\frac{\mu}{\mu_1} - S(t) + \frac{\mathcal{R}_0}{1-\mathcal{R}_0}I(t) + \frac{\mathcal{R}_0}{1-\mathcal{R}_0}\frac{\sigma}{\mu_3+\gamma+\sigma}R(t)\right|\\ &\leq \left|\frac{\mu}{\mu_1} - S(0) + \frac{\mathcal{R}_0}{1-\mathcal{R}_0}I(0) + \frac{\mathcal{R}_0}{1-\mathcal{R}_0}\frac{\sigma}{\mu_3+\gamma+\sigma}R(0)\right|\\ &\times\exp\left(-\min\left(\mu_1, \frac{\varepsilon(1-\mathcal{R}_0)}{\mathcal{R}_0}, \frac{\gamma(1-\mathcal{R}_0)(\mu_3+\gamma+\sigma)}{\sigma\mathcal{R}_0}\right)t\right).\end{aligned}$$

That is, E_f is globally exponentially asymptotically stable.
(ii) Let $\mathcal{R}_0 = 1$.
We have

$$\mu_2+\varepsilon+\lambda - \frac{\sigma\lambda}{\mu_3+\gamma+\sigma} = \frac{\beta\mu f'(0)}{\mu_1},$$

and

$$\frac{d}{dt}\left(I(t)+\frac{\sigma}{\mu_3+\gamma+\sigma}R(t)\right) = \beta S(t)f(I(t)) - \left(\mu_2+\varepsilon+\lambda-\frac{\sigma\lambda}{\mu_3+\gamma+\sigma}\right)I(t)$$
$$\leq \beta f'(0)S(t)I(t) - \frac{\beta\mu f'(0)}{\mu_1}I(t)$$
$$= -\beta f'(0)\left(\frac{\mu}{\mu_1}-S(t)\right)I(t). \tag{15}$$

On the other hand

$$\frac{d}{dt}\left(\frac{\mu}{\mu_1}-S(t)\right) = \mu_1\left(\frac{\mu}{\mu_1}-S(t)\right)+\beta f(I)\left(\frac{\mu}{\mu_1}-S(t)\right)-\frac{\beta\mu}{\mu_1}f(I(t))+\varepsilon I(t)+\gamma R(t).$$

Then, using the positivity of $\frac{\mu}{\mu_1}-S(t)$, $I(t)$ and $R(t)$, we get

$$\frac{d}{dt}\left(\frac{\mu}{\mu_1}-S(t)\right)^2 = -2\,\mu_1\left(\frac{\mu}{\mu_1}-S(t)\right)^2 - 2\beta f(I)\left(\frac{\mu}{\mu_1}-S(t)\right)^2$$
$$+\ 2\frac{\beta\mu}{\mu_1}f(I(t))\left(\frac{\mu}{\mu_1}-S(t)\right)-\left(\varepsilon I(t)+\gamma R(t)\right)\left(\frac{\mu}{\mu_1}-S(t)\right)$$
$$\leq -2\,\mu_1\left(\frac{\mu}{\mu_1}-S(t)\right)^2+2\,\frac{\beta f'(0)\mu}{\mu_1}I(t)\left(\frac{\mu}{\mu_1}-S(t)\right). \tag{16}$$

Combining (15) and (16) yields that

$$\frac{d}{dt}\left[\left(\frac{\mu}{\mu_1}-S(t)\right)^2+\frac{2\mu}{\mu_1}\left(I(t)+\frac{\sigma}{\mu_3+\gamma+\sigma}R(t)\right)\right] \leq -2\mu_1\left(\frac{\mu}{\mu_1}-S(t)\right)^2 \leq 0. \tag{17}$$

Then, the function

$$\left(\frac{\mu}{\mu_1}-S(t)\right)^2+\frac{2\mu}{\mu_1}\left(I(t)+\frac{\sigma}{\mu_3+\gamma+\sigma}R(t)\right)$$

is a Lyapunov function for E_f with non-positive derivative along the trajectory of system (5). Thus, E_f is stable. Now, let us show the attractivity of E_f when $\mathcal{R}_0=1$. Integrating (17) gives

$$0 \leq \left(\frac{\mu}{\mu_1}-S(t)\right)^2+\frac{2\mu}{\mu_1}\left(I(t)+\frac{\sigma}{\mu_3+\gamma+\sigma}R(t)\right)$$
$$\leq \left(\frac{\mu}{\mu_1}-S(0)\right)^2+\frac{2\mu}{\mu_1}\left(I(0)+\frac{\sigma}{\mu_3+\gamma+\sigma}R(0)\right)-2\mu_1\int_0^t\left(\frac{\mu}{\mu_1}-S(u)\right)^2du.$$

Then

$$\int_0^t\left(\frac{\mu}{\mu_1}-S(u)\right)^2du \leq \frac{\left(\frac{\mu}{\mu_1}-S(0)\right)^2+\frac{2\mu}{\mu_1}\left(I(0)+\frac{\sigma}{\mu_3+\gamma+\sigma}R(0)\right)}{2\mu_1}$$

which implies

$$\int_0^\infty\left(\frac{\mu}{\mu_1}-S(t)\right)^2du<\infty.$$

Since $\frac{dS}{dt}$ is bounded then, by Barbalat's lemma we have

$$\lim_{t\to\infty}\left(\frac{\mu}{\mu_1}-S(t)\right)^2=0,$$

that is $\lim_{t\to\infty}S(t)=\frac{\mu}{\mu_1}$. Furthermore, it is easy to see that $\frac{d^2S}{dt^2}$ is bounded. Then, $\frac{dS}{dt}$ is uniformly continuous. Hence, according to Barbalat's lemma again we also have $\lim_{t\to\infty}\frac{dS}{dt}=0$. Using the equation of $S(t)$, we get

$$\lim_{t\to\infty}\left[-\beta S(t)f(I(t))+\varepsilon I(t)+\gamma R(t)\right]=0. \tag{18}$$

In addition, from (17) we have

$$\lim_{t\to\infty}\left(I(t)+\frac{\sigma}{\mu_3+\gamma+\sigma}R(t)\right)<\infty.$$

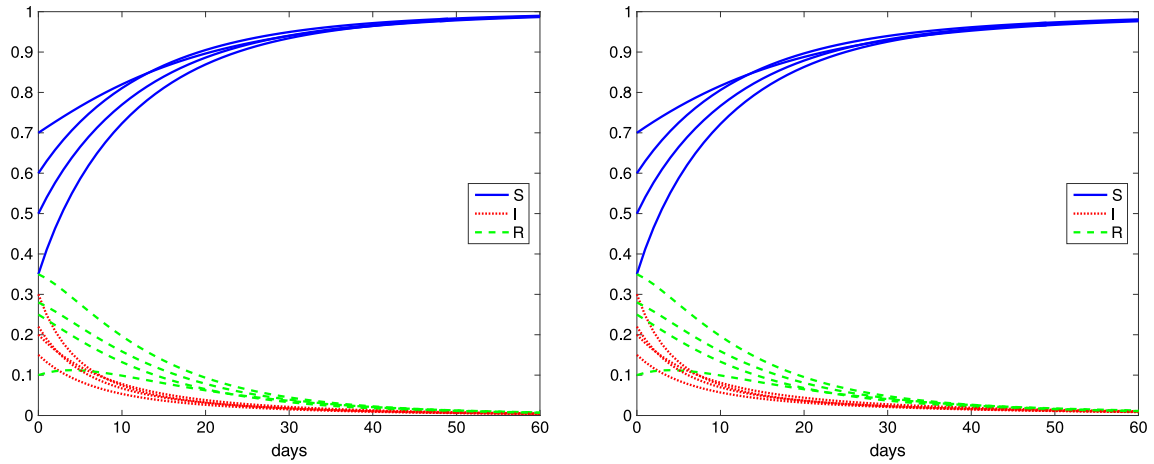

Fig. 2. For the left subfigure, we use the function $f(I) = \frac{I}{1+0.001I}$. For the right one, we take $f(I) = 1 - e^{-1.01}I$. We see that the solutions converge to E_f. In this example $\mathcal{R}_0 = 0.82$.

Table 1
Table of parameter values used in the numerical simulation.

μ	μ_1	μ_2	μ_3	β	γ	λ	σ	ε
0.09	0.09	0.092	0.092	0.2	0.007	0.08	0.001	0.07

And by virtue of Barbalat's theorem

$$\lim_{t\to\infty} \frac{d}{dt}\left(I(t) + \frac{\sigma}{\mu_3+\gamma+\sigma}R(t)\right) = 0.$$

That is,

$$\lim_{t\to\infty} \beta S(t)f(I(t)) - \left(\mu_2 + \varepsilon + \lambda - \frac{\sigma\lambda}{\mu_3+\gamma+\sigma}\right) I(t) = 0. \tag{19}$$

Adding (18) and (19) we obtain that

$$\lim_{t\to\infty} \left[\left(\mu_2 + \lambda - \frac{\sigma\lambda}{\mu_3+\gamma+\sigma}\right) I(t) + \gamma R(t)\right] = 0.$$

Thus, $\lim_{t\to\infty} I(t) = \lim_{t\to\infty} R(t) = 0$. □

Example 1. In Fig. 2, we show an example of four solutions of system (5) simulated using the classical Euler scheme in MATLAB with a time step $dt = 1$ (day) and a final time $T = 60$ (days) for two different incidence rate functions. The model parameter values are shown in Table 1. Remark that $\mu = \mu_1$, so the total population size verifies $S(t) + I(t) + R(t) \leq 1$. The numerical result supports the analytical results proven in Theorem 4.2. That is, E_f is globally asymptotically stable.

5. Stability of the endemic steady state

Before studying the global behavior of the endemic equilibrium state E_e, we give in the following some sufficient conditions for the local stability of E_e

Proposition 4. *Suppose that $f(I)$ verify conditions (6), and $\mathcal{R}_0 > 1$. Moreover, if*

$$(\mu_3+\gamma+\sigma)\left[(\mu_2+\varepsilon+\lambda) - \beta S_e f'(I_e)\right] \geq \sigma\lambda. \tag{20}$$

Then, E_e is asymptotically stable.

Proof. The jacobian matrix at E_e is

$$J(E_e) = (J_{ik})_{1\leq i,k\leq 3} \begin{pmatrix} -\mu_1 - \beta f(I_e) & -\beta S_e f'(I_e) + \varepsilon & \gamma \\ \beta f(I_e) & -(\mu_2 + \varepsilon + \lambda) + \beta S_e f'(I_e) & \sigma \\ 0 & \lambda & -(\mu_3 + \gamma + \sigma) \end{pmatrix}.$$

Then, the characteristic equation associated to $J(E_e)$ is given by

$$X^3 + a_1X^2 + a_2X + a_3 = 0,$$

where

$$\begin{aligned} a_1 &= -\text{Trace}(J(E_e)), \\ a_2 &= (J_{11}J_{22} + J_{11}J_{33} + J_{22}J_{33}) - (J_{21}J_{12} + J_{31}J_{13} + J_{32}J_{23}), \\ a_3 &= -\det(J(E_e)). \end{aligned}$$

Hence, using condition (20), we have

$$a_1 = \mu_1 + \beta f(I_e) + \underbrace{(\mu_2 + \varepsilon + \lambda) - \beta S_e f'(I_e)}_{>0} + (\mu_3 + \gamma + \sigma) > 0.$$

For the sign of a_2, we compute

$$\begin{aligned} a_2 &= \big(\mu_1 + \beta f(I_e)\big)\big(\mu_2 + \varepsilon + \lambda - \beta S_e f'(I_e)\big) + \big(\mu_1 + \beta f(I_e)\big)\big(\mu_3 + \gamma + \sigma\big) \\ &\quad + \big(\mu_3 + \gamma + \sigma\big)\big(\mu_2 + \varepsilon + \lambda - \beta S_e f'(I_e)\big) - \beta f(I_e)\big(\varepsilon - \beta S_e f'(I_e)\big) - \sigma\lambda. \end{aligned}$$

After simplification, we get according to (20) that

$$\begin{aligned} a_2 &= \mu_1 \underbrace{\big(\mu_2 + \varepsilon + \lambda - \beta S_e f'(I_e)\big)}_{>0} + \underbrace{\Big((\mu_3 + \gamma + \sigma)(\mu_2 + \varepsilon + \lambda - \beta S_e f'(I_e)) - \sigma\lambda\Big)}_{>0} \\ &\quad + \big(\mu_1 + \beta f(I_e)\big)(\mu_3 + \gamma + \sigma) + (\mu_2 + \lambda)\beta f(I_e) > 0. \end{aligned}$$

Using again assumption (20), we obtain

$$\begin{aligned} a_3 &= (\mu_1 + \beta f(I_e)) \underbrace{\big[(\mu_3 + \gamma + \sigma)(\mu_2 + \varepsilon + \lambda - \beta S_e f'(I_e)) - \sigma\lambda\big]}_{>0} \\ &\quad + \beta f(I_e)\big[(\mu_3 + \gamma + \sigma)(\beta S_e f'(I_e) - \varepsilon) - \gamma\lambda\big] \\ &= \mu_1 \underbrace{\big[(\mu_3 + \gamma + \sigma)(\mu_2 + \varepsilon + \lambda - \beta S_e f'(I_e)) - \sigma\lambda\big]}_{>0} \\ &\quad + \beta f(I_e) \underbrace{[(\mu_3 + \gamma + \sigma)(\mu_2 + \lambda) - (\gamma + \sigma)\lambda]}_{>0} > 0. \end{aligned}$$

Now, we prove that $a_1a_2 - a_3$ is positive, so,

$$\begin{aligned} a_1a_2 - a_3 &= \Big[(\mu_1 + \beta f(I_e) + (\mu_2 + \varepsilon + \lambda) - \beta S_e f'(I_e) + (\mu_3 + \gamma + \sigma)\Big] \times \Big[\mu_1\big(\mu_2 + \varepsilon + \lambda - \beta S_e f'(I_e)\big) \\ &\quad + (\mu_3 + \gamma + \sigma)(\mu_2 + \varepsilon + \lambda - \beta S_e f'(I_e)) - \sigma\lambda) + (\mu_1 + \beta f(I_e))(\mu_3 + \gamma + \sigma) + (\mu_2 + \lambda)\beta f(I_e)\Big] \\ &\quad - \mu_1\left[(\mu_3 + \gamma + \sigma)(\mu_2 + \varepsilon + \lambda - \beta S_e f(I_e)) - \sigma\lambda\right] \\ &\quad - \beta f(I_e)(\mu_3 + \gamma + \sigma)(\mu_2 + \lambda) + \beta f(I^*)(\gamma + \sigma)\lambda. \\ &= \mu_1\left[\mu_1(\mu_2 + \varepsilon + \lambda - \beta S_e f'(Ie)) + (\mu_1 + \beta f(I_e))(\mu_3 + \gamma + \sigma)(\mu_2 + \lambda)\beta f(I_e)\right] \\ &\quad + \left[(\mu_2 + \varepsilon + \lambda) - \beta S_e f'(I_e)\right][\mu_1(\mu_2 + \varepsilon + \lambda - \beta S_e f'(I_e)) + (\mu_3 + \gamma + \sigma)(\mu_2 + \lambda - \beta S_e f'(I_e)) - \sigma\lambda \\ &\quad + (\mu_1 + \beta f(I_e))(\mu_3 + \gamma + \sigma) + (\mu_2 + \lambda)\beta f(I_e)] + \beta f(I_e)(\gamma + \sigma)\lambda > 0. \end{aligned}$$

Hence, by Routh–Hurwitz criteria we may conclude that all the eigenvalues of $J(E_e)$ have negative real part. Therefore for $\mathcal{R}_0 > 1$ the endemic equilibrium E_e exists and locally asymptotically stable. □

Now, we try to get a sufficient and practical conditions on the force of infection $f(I)$ to insure the asymptotic stability of E_e. From the equations verified by (S_e, I_e, R_e), one can see that

$$\begin{aligned}(\mu_3+\gamma+\sigma)\left[(\mu_2+\varepsilon+\lambda)-\beta S_e f'(I_e)\right] &= \frac{\lambda I_e}{R_e}\left[(\mu_2+\varepsilon+\lambda)-\beta S_e f'(I_e)\right]\\ &= \frac{\lambda}{R_e}\left[\beta S_e f(Ie)+\sigma R_e-\beta S_e I_e f'(I_e)\right]\\ &= \sigma\lambda+\frac{\lambda\beta S_e}{R_e}\left[f(I_e)-I_e f'(I_e)\right].\end{aligned}$$

Therefore, if $f(I_e)-I_e f'(I_e)\geq 0$, then the condition (20) is satisfied and E_e is asymptotically stable under the condition $\mathcal{R}_0>1$. Note that

$$\begin{aligned}\frac{I_e f'(I_e)-f(I_e)}{I_e^2} &= \frac{d}{dI}\frac{f(I)}{I}\Big|_{I=I_e}\\ &= \lim_{I\to I_e}(I-I_e)^{-1}\left(\frac{f(I)}{I}-\frac{f(I_e)}{I_e}\right).\end{aligned}$$

Then, if $(I-I_e)\left(\frac{f(I)}{I}-\frac{f(I_e)}{I_e}\right)\leq 0$ for all I, we have $f(I_e)-I_e f'(I_e)\geq 0$. Therefore, E_e is asymptotically stable. We summarize the above result in the following corollary.

Corollary 1. *Let $\mathcal{R}_0>1$ and $(S(0),I(0),R(0))\in\Delta$.*

(i) *If $f(I_e)-I_e f'(I_e)\geq 0$, then E_e is asymptotically stable.*
(ii) *Assume that the condition*

$$(I-I_e)\left(\frac{f(I)}{I}-\frac{f(I_e)}{I_e}\right)\leq 0 \qquad \text{for all } I, \tag{21}$$

holds. Then E_e is asymptotically stable.

In the following theorem, we prove that E_e is globally asymptotically stable under the condition (21).

Theorem 5.1. *Let $\mathcal{R}_0>1$ and $(S(0),I(0),R(0))\in\Delta$. Under the conditions (6) and (21) imposed on $f(I)$, the steady state E_e is unique and globally asymptotically stable.*

Proof. Put

$$N_m(t)=S(t)+I(t)+mR(t),$$

where m is a positive real number to be determined in the sequel. A direct computation leads to

$$\frac{dN_m}{dt}=\mu-\mu_1 S-(\mu_2+(1-m)\lambda)I-[m(\mu_3+\gamma+\sigma)-(\gamma+\sigma)]R,$$

we choose m such that $m(\mu_3+\gamma+\sigma)-(\gamma+\sigma)=\mu_1 m$, which is equivalent to

$$m=\frac{\gamma+\sigma}{\mu_3-\mu_1+\gamma+\sigma}.$$

So, $m\in(0,1]$ due to the assumption $\mu_1\leq\min(\mu_2,\mu_3)$.

Hence

$$\begin{aligned}\frac{dN_m}{dt} &= \mu-\mu_1 S-(\mu_2+(1-m)\lambda)I-\mu_1 mR\\ &= \mu-\mu_1 S-\mu_1 I-\mu_1 mR-(\mu_2-\mu_1+(1-m)\lambda)I\\ &= \mu-\mu_1 N_m-\alpha I\end{aligned}$$

where

$$\alpha=\mu_2-\mu_1+(1-m)\lambda=\mu_2-\mu_1+\frac{(\mu_3-\mu_1)\lambda}{\mu_3-\mu_1+\gamma+\sigma}\geq 0.$$

Let $N_m^e=S_e+I_e+mR_e$. Then (22) can be rewritten as follows:

$$\frac{dN_m}{dt}=-\mu_1(N_m-N_m^e)-\alpha(I-I_e).$$

Hence

$$\frac{d}{dt}(N_m-N_m^e)^2=2(N_m-N_m^e)\frac{dN_m}{dt}=-2\mu_1(N_m-N_m^e)^2-2\alpha(I-I_e)(N_m-N_m^e). \tag{22}$$

On the other hand, we have

$$\begin{aligned}\frac{d}{dt}\left(I-I_e-I_e\ln\frac{I}{I_e}\right) &= \frac{I-I_e}{I}\frac{dI}{dt}\\ &= (I-I_e)\left(-(\mu_2+\varepsilon+\lambda)+\beta S\frac{f(I)}{I}+\frac{\sigma R}{I}\right).\end{aligned}$$

At the equilibrium state E_e we have

$$(\mu_2+\varepsilon+\lambda)=\beta S_e\frac{f(I_e)}{I_e}+\frac{\sigma R_e}{I_e}.$$

Thereby

$$\begin{aligned}\frac{d}{dt}\left(I-I_e-I_e\ln\frac{I}{I_e}\right) &= (I-I_e)\left(\beta\left(\frac{Sf(I)}{I}-\frac{S_ef(I_e)}{I_e}\right)+\sigma\left(\frac{R}{I}-\frac{R_e}{I_e}\right)\right)\\ &= (I-I_e)\left(\beta S\left(\frac{f(I)}{I}-\frac{f(I_e)}{I_e}\right)+\beta\frac{f(I_e)}{I_e}(S-S_e)+\frac{\sigma R_e}{I_e}\left(\frac{I_eR}{IR_e}-1\right)\right)\\ &= \beta S\left(\frac{f(I)}{I}-\frac{f(I_e)}{I_e}\right)(I-I_e)+\beta\frac{f(I_e)}{I_e}(S-S_e)(I-I_e)+\sigma R_e\left(\frac{I_eR}{IR_e}-1\right)\left(\frac{I}{I_e}-1\right).\end{aligned}$$

Thus, by the assumption (21), we get

$$\frac{d}{dt}\left(I-I_e-I_e\ln\frac{I}{I_e}\right)\le\beta\frac{f(I_e)}{I_e}(S-S_e)(I-I_e)+\sigma R_e\left(\frac{I_eR}{IR_e}-1\right)\left(\frac{I}{I_e}-1\right). \tag{23}$$

Substituting $S-S_e=-(I-I_e)-m(R-R_e)+(N_m-N_m^e)$, yields

$$\begin{aligned}\frac{d}{dt}\left(I-I_e-I_e\ln\frac{I}{I_e}\right) &\le -\beta\frac{f(I_e)}{I_e}(I-I_e)^2-m\beta\frac{f(I_e)}{I_e}(I-I_e)(R-R_e)\\ &+\beta\frac{f(I_e)}{I_e}(I-I_e)(N_m-N_m^e)+\sigma R_e\left(\frac{I_eR}{IR_e}-1\right)\left(\frac{I}{I_e}-1\right).\end{aligned} \tag{24}$$

To eliminate the last term in the right side of (24), we calculate

$$\begin{aligned}\frac{d}{dt}\left(R-R_e-R_e\ln\frac{R}{R_e}\right) &= (R-R_e)\left(-(\mu_3+\sigma+\gamma)+\lambda\frac{I}{R}\right)\\ &= \lambda(R-R_e)\left(\frac{I}{R}-\frac{I_e}{R_e}\right)\\ &= \lambda I_e\left(\frac{IR_e}{I_eR}-1\right)\left(\frac{R}{R_e}-1\right).\end{aligned} \tag{25}$$

To eliminate the product $(R-R_e)(I-I_e)$ from the right side of (24) we consider

$$\begin{aligned}\frac{d}{dt}(R-R_e)^2 &= 2\,(R-R_e)\,(-\,(\mu_3+\sigma+\gamma)\,R+\lambda I)\\ &= 2(R-R_e)\,(-(\mu_3+\sigma+\gamma)(R-R_e)+\lambda(I-I_e))\\ &= -2(\mu_3+\sigma+\gamma)(R-R_e)^2+2\lambda(I-I_e)(R-R_e).\end{aligned} \tag{26}$$

Now, we discuss two cases.

- **Case 1 :** if $\alpha>0$. In this case, we consider the positive definite function

$$\begin{aligned}L_\alpha(S,I,R) = &\frac{\beta f(I_e)}{I_e}(N_m-N_m^e)^2+2\alpha\left(I-I_e-I_e\ln\frac{I}{I_e}\right)\\ &+\frac{2\alpha\sigma R_e}{\lambda I_e}\left(R-R_e-R_e\ln\frac{R}{R_e}\right)+\frac{\alpha m\beta f(I_e)}{\lambda I_e}(R-R_e)^2.\end{aligned} \tag{27}$$

Combining (22)–(26) and multiplying appropriately by coefficients determined by (27), the derivative of L_α along the trajectory of system (5) can be estimated as follows:

$$\begin{aligned}\frac{dL_\alpha}{dt} \leq\ & \frac{-2\mu_1\beta f(I_e)}{I_e}(N_m - N_m^e)^2 \\ & - \frac{2\alpha\beta f(I_e)}{I_e}(I-I_e)^2 - \frac{2\alpha m\beta f(I_e)(\mu_3+\sigma+\gamma)}{\lambda I_e}(R-R_e)^2 \\ & + 2\alpha\sigma R_e\left(\left(\frac{I_eR}{IR_e}-1\right)\left(\frac{I}{I_e}-1\right)+\left(\frac{IR_e}{I_eR}-1\right)\left(\frac{R}{R_e}-1\right)\right).\end{aligned} \tag{28}$$

To complete, noting that

$$\begin{aligned}\left(\frac{I_eR}{IR_e}-1\right)\left(\frac{I}{I_e}-1\right)+\left(\frac{IR_e}{I_eR}-1\right)\left(\frac{R}{R_e}-1\right) &= 2-\frac{I_eR}{IR_e}-\frac{IR_e}{I_eR} \\ &= -\left(\sqrt{\frac{I_eR}{IR_e}}-\sqrt{\frac{IR_e}{I_eR}}\right)^2.\end{aligned} \tag{29}$$

Thus, $\frac{dL_\alpha}{dt}$ is negative definite. Consequently it follows from Lyapunov–LaSalle theorem that E_e is globally asymptotically stable. Since the derivative of a Lyapunov function must be equal to zero at an equilibrium state, and $\frac{dL_\alpha}{dt} = 0$ holds only for E_e, we deduce that system (5) has no steady state apart E_e and that proves its uniqueness.

- **Case 2 :** if $\alpha = 0$.

Then $\mu_1 = \mu_2 = \mu_3$ and $m = 1$. So

$$\frac{d}{dt}(N-N_e)^2 = \frac{d}{dt}(N-N_e)^2 = -2\mu_1(N-N_e). \tag{30}$$

In (24), we estimate $(I-I_e)(N-N_e)$ using the elementary inequality

$$(I-I_e)(N-N_e) \leq \frac{1}{2}(I-I_e)^2 + \frac{1}{2}(N-N_e)^2.$$

Injecting the above inequality in (24) gives

$$\begin{aligned}\frac{d}{dt}\left(I-I_e-I_e\ln\frac{I}{I_e}\right) \leq & -\frac{\beta f(I_e)}{I_e}(I-I_e)(R-R_e)+\frac{\beta f(I_e)}{2I_e}(N-N_e)(I-I_e) \\ & +\sigma R_e\left(\frac{I_eR}{IR_e}-1\right)\left(\frac{I}{I_e}-1\right)-\frac{\beta f(I_e)}{2I_e}(I-I_e)^2.\end{aligned} \tag{31}$$

Finally, considering the Lyapunov function

$$\begin{aligned}L_0(S,I,R) = & \frac{\beta f(I_e)}{4\mu_1 I_e}(N-N_e)^2+\left(I-I_e-I_e\ln\frac{I}{I_e}\right) \\ & +\frac{\beta f(I_e)}{2\lambda I_e}(R-R_e)^2+\frac{\sigma R_e}{\lambda I_e}\left(R-R_e-R_e\ln\frac{R}{R_e}\right).\end{aligned}$$

Using (25), (26), (29), (30) and (31) it is easy to obtain that

$$\begin{aligned}\frac{dL_0}{dt} \leq & -\frac{\beta f(I_e)}{4\mu_1 I_e}(N-N^*)^2-\frac{\beta f(I_e)}{2I_e}(I-I_e)^2 \\ & -\frac{\beta f(I_e)(\mu_3+\gamma+\sigma)}{\lambda I_e}(R-R_e)^2 \\ & -\sigma R_e\left(\sqrt{\frac{I_eR}{IR_e}}-\sqrt{\frac{IR_e}{I_eR}}\right)^2.\end{aligned}$$

Hence, $\frac{dL_0}{dt} \leq 0$ and we one can see that $\frac{dL_0}{dt} = 0$ if and only if $(S,I,R) = (S_e,I_e,R_e)$. Thus, we have the same conclusion as the first case, and the proof of Theorem 5.1 is completed. □

Example 2. In Fig. 3, we show an example of four solutions converging to the endemic equilibrium point when $\mathcal{R}_0$ is greater than 1. The same numerical technique and software were used as previously explained. The values of parameters used for this simulation are shown in Table 1 (except $\beta = 0.4$). The initial conditions for the four solutions are the same as in Example 1. The numerical result is consistent with the analytical study we have made.

6. Optimal control of the model

It is easy to see from the expression of $\mathcal{R}_0$ that is a decreasing function of ε and increasing as a function of σ. Moreover, from Sections 3 and 4 we deduce that to control the spread of the epidemic, it is imperative to reduce the basic reproduction number $\mathcal{R}_0$. Thereby, we can minimize the number of infective individuals by increasing the cure rate ε and enlarging the period time before relapse which corresponds to $\frac{1}{\sigma}$. A successful intervention strategy reduces the number of infective individuals with minimum costs. An effectual way of procuring the best strategy for achieving this goal is using optimal control theory. Therefore in this section, we consider that the public health policy maker aim to minimize the total number of infective individuals while keeping the cost associated with therapeutic treatment and implementation of awareness campaigns minimum; for example, we seek the minimum sufficient number of television ads to aware drug and alcohol users, the minimum budget dedicated to give psychological support by specialists to drug users in order to avoid relapse [18]. For some references on different control strategies, we refer the reader to [55,56]. Before stating the optimal control problem for system (5), we introduce a general form of the ordinary differential system we study here and the general formulation of an optimization problem. System (5) can be written as the following:

$$\begin{cases} x'(t) = \psi(x(t), u(t)), \\ x(0) = x_0. \end{cases} \tag{32}$$

where $x \in \mathbb{R}^3$ and u is a real function on a convex set K. The function ψ is a real valued function defined on $\mathbb{R}^3 \times K$. We consider that x_u is a solution of system (32). So, a general optimization problem can be obtained as the following

$$\min_{u\in K} \mathcal{J}(u) = \min_{u\in K} \int_0^T G(t, x_u(t), u(t))dt + \varphi(x_u(T)). \tag{33}$$

The function $\mathcal{J}(u)$ is called the objective or cost function, $\varphi(x_u(T))$ the reward term if we end at time T with value $x_u(T)$. The set K represents the control set. In our case, we apply a control on cure and relapse. So, model (5) becomes

$$\begin{cases} \dfrac{dS}{dt} = \mu - \mu_1 S - \beta S f(I) + \big(1 + u_1(t)\big)\varepsilon I + \gamma R, \\ \dfrac{dI}{dt} = \beta S f(I) - \big(\mu_2 + (1 + u_1(t)\big)\varepsilon + \lambda)I + \big(1 - u_2(t)\big)\sigma R, \\ \dfrac{dR}{dt} = \lambda I - \Big(\mu_3 + \big(1 - u_2(t)\big)\sigma + \gamma\Big)R, \end{cases} \tag{34}$$

with initial conditions (7). The control functions $u_1(t)$ and $u_2(t)$ are bounded and Lebesgue integrable on a finite interval $[0, T]$. The control $u_1(t)$ represents the effort on therapeutic treatment of infected individuals to increase the number of susceptible individuals. While the control $u_2(t)$ is the effort (e.g., awareness campaigns) that prevents the relapse of recovered individuals so as to reduce the number of individuals partially recovered. Hence, we consider an optimal control problem to minimize the objective functional

$$\begin{cases} \mathcal{J}(u) = \displaystyle\int_0^T \Big(aI(t) + bu_1^2(t) + cu_2^2(t)\Big)dt, \\ u = (u_1, u_2) \in K, \end{cases} \tag{35}$$

subject to system (34), where a, b, c are positive weight factors in relation with the costs of infection and controls. The control set K is defined by

$$K = \big\{u(t) = \big(u_1(t), u_2(t)\big)/\ 0 \le u_1(t) \le u_1^m;\ 0 \le u_2(t) \le u_2^m, \quad \forall t \in [0, T]\big\}. \tag{36}$$

In the following theorem, we establish the existence of an optimal control which minimizes the objective function (35) subject to the system of differential equation (34).

Theorem 6.1. *There exists an optimal solution u^* to problem (34) such that*

$$\mathcal{J}(u^*) = \min_u \mathcal{J}(u).$$

Proof. First, using Theorem 9.2.1 and Theorem 9.2.3 in [57], the non-autonomous system (34) admits has a unique local solution $(S(t), I(t), R(t))$ for any initial value $(S(0), I(0), R(0)) \in \Delta$ and any admissible control $u(t)$. Then, using the same arguments as in the proof of Proposition 1, one can show that the solution $(S(t), I(t), R(t))$ is global, positive and remains in Δ for all $t \ge 0$. So, The set of control and corresponding state variables is non-empty. By definition, the control set K is convex and closed. Hence, using the boundedness of solutions, one can easily show that the right-hand side of the state system is bounded by a linear function in the state and control variables. Furthermore, the integrand $\big(a \cdot I(t) + b \cdot u_1^2(t) + c \cdot u_2^2(t)\big)$ in the cost functional $\mathcal{J}$ is convex on control set K. Finally, using the positivity of the state variable, we have

$$a \cdot I + b \cdot u_1^2 + c \cdot u_2^2 \ge \omega_1 \|u\|^\rho - \omega_2,$$

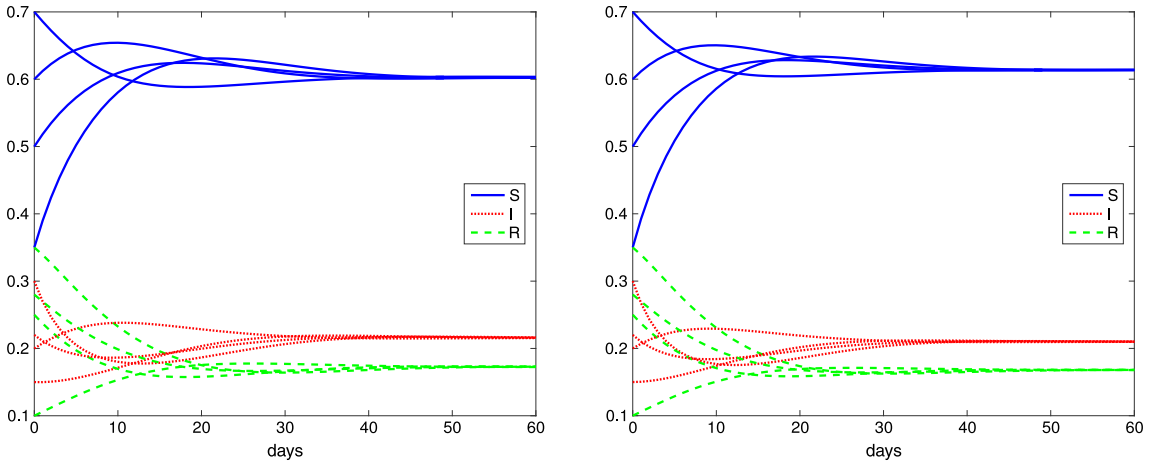

Fig. 3. In the left subfigure , we use the function $f(I) = \frac{I}{1+0.001I}$. For the right one, we take $f(I) = 1 - e^{-1.1I}$ in Fig. 3(b). It is clear that the solutions converge to the endemic equilibrium E_e. Here $\mathcal{R}_0 = 1.64$.

where $\omega_1 = \min(b, c)$, $\rho = 2 > 1$ and $\omega_2 > 0$. Hence, according to the Corollary 4.1 in [58], the problem (34) admits an optimal control solution u^*. □

In order to find an optimal solution pair, first we find the Hamiltonian for the optimal control problem (35). It can be expressed as follows:

$$\mathbb{H}(S, I, R, u_1, u_2, \lambda_1, \lambda_2, \lambda_3, t) = a \cdot I(t) + b \cdot u_1^2(t) + c \cdot u_2^2(t) + \sum_{i=1}^{3} \lambda_i \phi_i,$$

where (ϕ_1, ϕ_2, ϕ_3) is the right-hand side of model (34) and λ_i are the adjoint variables given by the following equations:

$$\begin{cases} \frac{d\lambda_1}{dt} = -\frac{\partial \mathbb{H}}{\partial S} = \lambda_1(\mu_1 + \beta f(I)) - \lambda_2 \beta f(I), \\ \frac{d\lambda_2}{dt} = -\frac{\partial \mathbb{H}}{\partial I} = \lambda_1(\beta S f'(I) - (1+u_1)\varepsilon) + \lambda_2((\mu_2 + (1+u_1)\varepsilon + \lambda) - \beta S f(I)) - \lambda_3 \lambda - a, \\ \frac{d\lambda_3}{dt} = -\frac{\partial \mathbb{H}}{\partial R} = -\lambda_1 \gamma - \lambda_2(1-u_2)\sigma + \lambda_3(\mu_3 + \gamma + (1-u_2)\sigma). \end{cases}$$

With transversality conditions $\lambda_i(T) = 0$, for $i = 1, 2, 3$. According to Pontryagin's Maximum Principle, the optimal control conditions are

$$\frac{\partial \mathbb{H}}{\partial u_1} = \frac{\partial \mathbb{H}}{\partial u_2} = 0. \tag{37}$$

At optimal point (u_1^*, u_2^*) in the set K we get

$$u_1^* = \frac{\lambda_2 - \lambda_1}{2b} \varepsilon I^* \quad \text{and} \quad u_2^* = \frac{\lambda_3 - \lambda_2}{2c} \sigma R^* \tag{38}$$

and taking into accounts the bounds on u_1^* and u_2^*, the characterizations are

$$u_1^* = \begin{cases} 0 & \text{if } (\lambda_2 - \lambda_1) I^* < 0, \\ \frac{\lambda_2 - \lambda_1}{2b} \varepsilon I^* & \text{if } 0 \le (\lambda_2 - \lambda_1) I^* \le 2\, \frac{b\, u_1^m}{\varepsilon}, \\ u_1^m & \text{if } (\lambda_2 - \lambda_1) I^* > \frac{2\, b\, u_1^m}{\varepsilon} \end{cases} \tag{39}$$

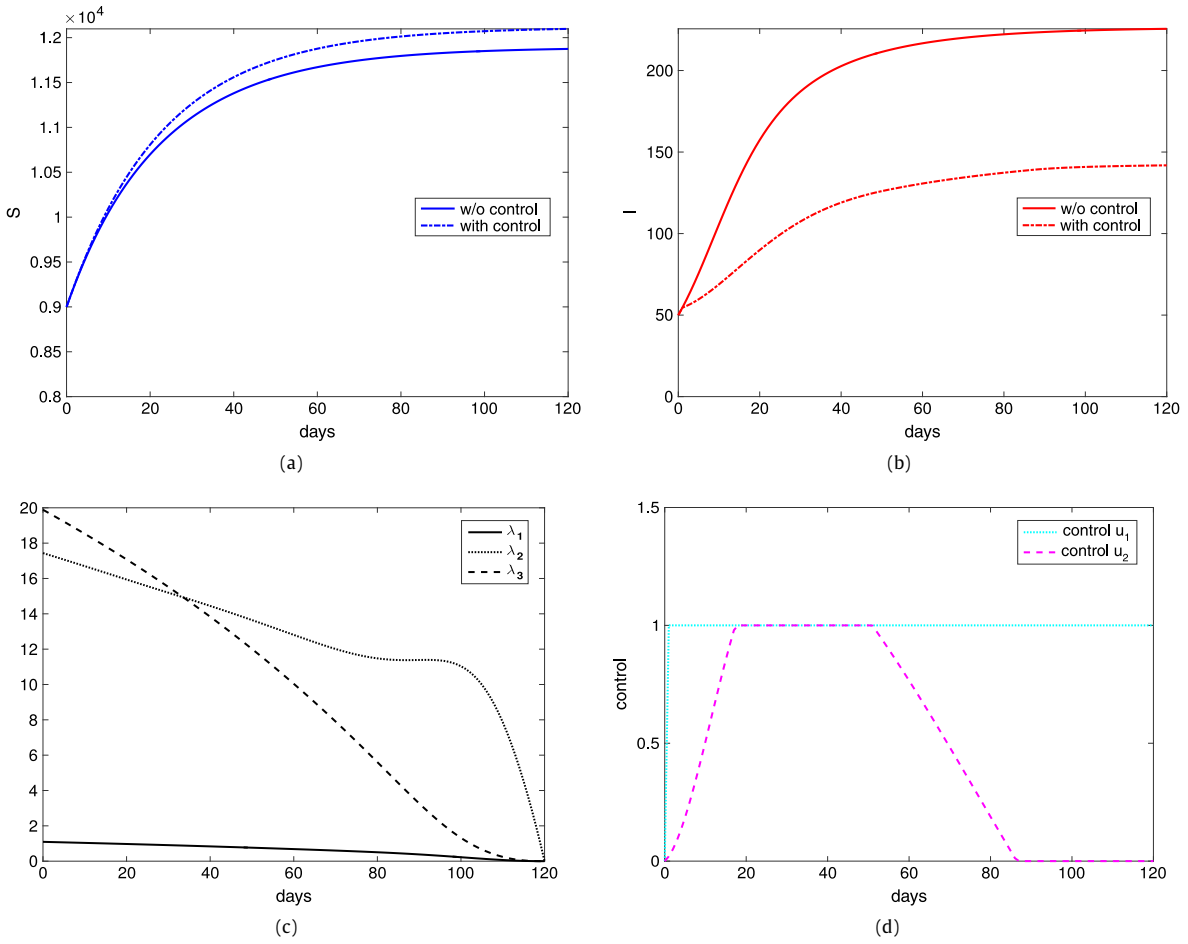

Fig. 4. The first scenario. The values of parameters are given in Table 2. Weight factors: $b = c = 1$.

and

$$u_2^* = \begin{cases} 0 & \text{if } (\lambda_3 - \lambda_2)R^* < 0, \\ \dfrac{\lambda_3 - \lambda_2}{2c} R^* & \text{if } 0 \le (\lambda_3 - \lambda_2)\sigma R^* \le \dfrac{2\,c\,{u_2}^m}{\sigma}, \\ {u_2}^m & \text{if } (\lambda_3 - \lambda_2)R^* > \dfrac{2\,c\,{u_2}^m}{\sigma}. \end{cases} \tag{40}$$

7. Simulation and numerical results

In this section we used the Gauss–Seidel-like implicit finite-difference method (GSS1) developed by Gumel et al. in [59]. For more details about the algorithm, we refer the reader also to [60]. We first discretize uniformly the interval $[0, T]$, where T is a period of 120 days and $t_k = k * dt$ for all $k \in [\![0, n]\!]$. We define $S(t)$, $I(t)$, $R(t)$, $\lambda_1(t)$, $\lambda_2(t)$, $\lambda_3(t)$, $\varepsilon(t)$ and $u_2(t)$ in terms of nodal points S^k, I^k, R^k, λ_1^k, λ_2^k, λ_3^k, ε^k and u_2^k. Using a first-order forward difference to approximate the time derivative of the variables $S(t)$, $I(t)$ and $R(t)$, we obtain the following scheme:

$$\begin{cases} \dfrac{S^{k+1} - S^k}{dt} &= \mu - \mu_1 S^k - \beta S^k f(I^k) + \varepsilon I^k + \gamma R^k, \\ \dfrac{I^{k+1} - I^k}{dt} &= \beta S^k f(I^k) - (\mu_2 + \varepsilon + \lambda) I^k + \sigma R^k, \\ \dfrac{R^{k+1} - R^k}{dt} &= \lambda I^k - (\mu_3 + \gamma + \sigma) R^k. \end{cases}$$

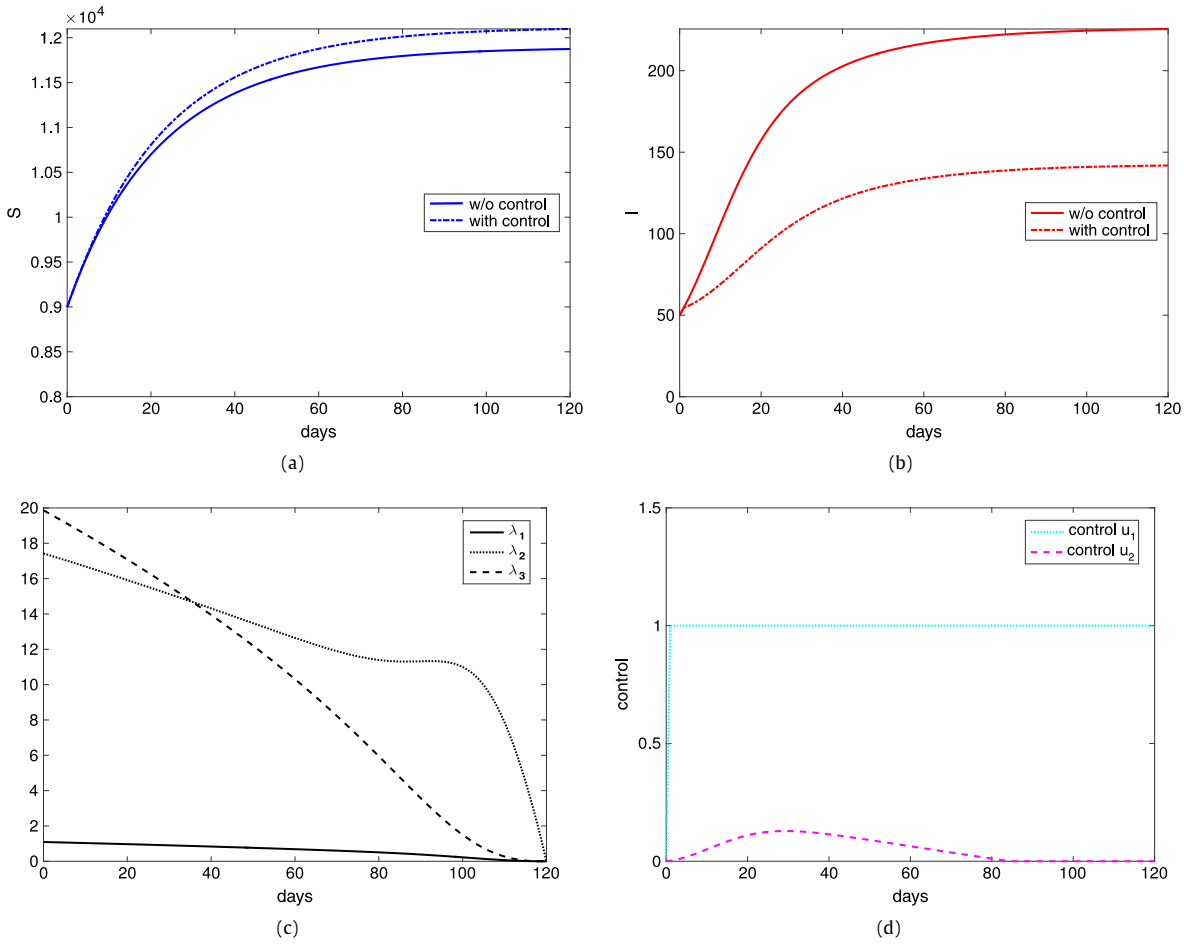

Fig. 5. The second scenario. The values of parameters are given in Table 2. Weight factors: $b = 0.01$ and $c = 10$.

Table 2
Table of parameter values used in the numerical simulation to solve the optimal control problem.

μ	μ_1	μ_2	μ_3	β	γ	λ	σ	ε	θ	${u_1}^m$	${u_2}^m$
500	0.04	0.043	0.041	0.004	0.007	0.08	0.003	0.07	0.01	1	1

For the adjoint variables, we apply a first-order backward difference approximation. The scheme is given as follows:

$$\begin{cases} \dfrac{\lambda_1^{n-k} - \lambda_1^{n-k-1}}{dt} = \lambda_1^{n-k}\big(\mu_1 + \beta f(I^k)\big) - \lambda_2^{n-k}\beta f(I^k), \\ \dfrac{\lambda_2^{n-k} - \lambda_2^{n-k-1}}{dt} = \lambda_1^{n-k}\big(\beta S^k f'(I^k) - (1+u_1^k)\varepsilon\big) + \lambda_2^{n-k}\big(-\beta S^k f'(I^k) + \mu_2 + (1+u_1^k)\varepsilon + \lambda\big) - \lambda_3^{n-k}\lambda - a, \\ \dfrac{\lambda_3^{n-k} - \lambda_3^{n-k-1}}{dt} = -\lambda_1^{n-k} - \lambda_2^{n-k-1}(1-u_2^k)\sigma + \lambda_3^{n-k}\big(\mu_3 + \gamma + (1-u_2^k)\sigma\big). \end{cases}$$

Then, the values of u_1^k and u_2^k are deduced using (39) and (40). We built MATLAB code to run the simulations. Table 2 shows the parameter values used for these numerical simulations. We choose the following nonlinear incidence rate function:

$$f(I) = \frac{I}{1+\theta I}.$$

We consider a 120 days period with a time step of 1 day. We expressed parameters of Table 2 per day. The initial values are: $S_0 = 9000$, $I_0 = 50$ and $R_0 = 10$.

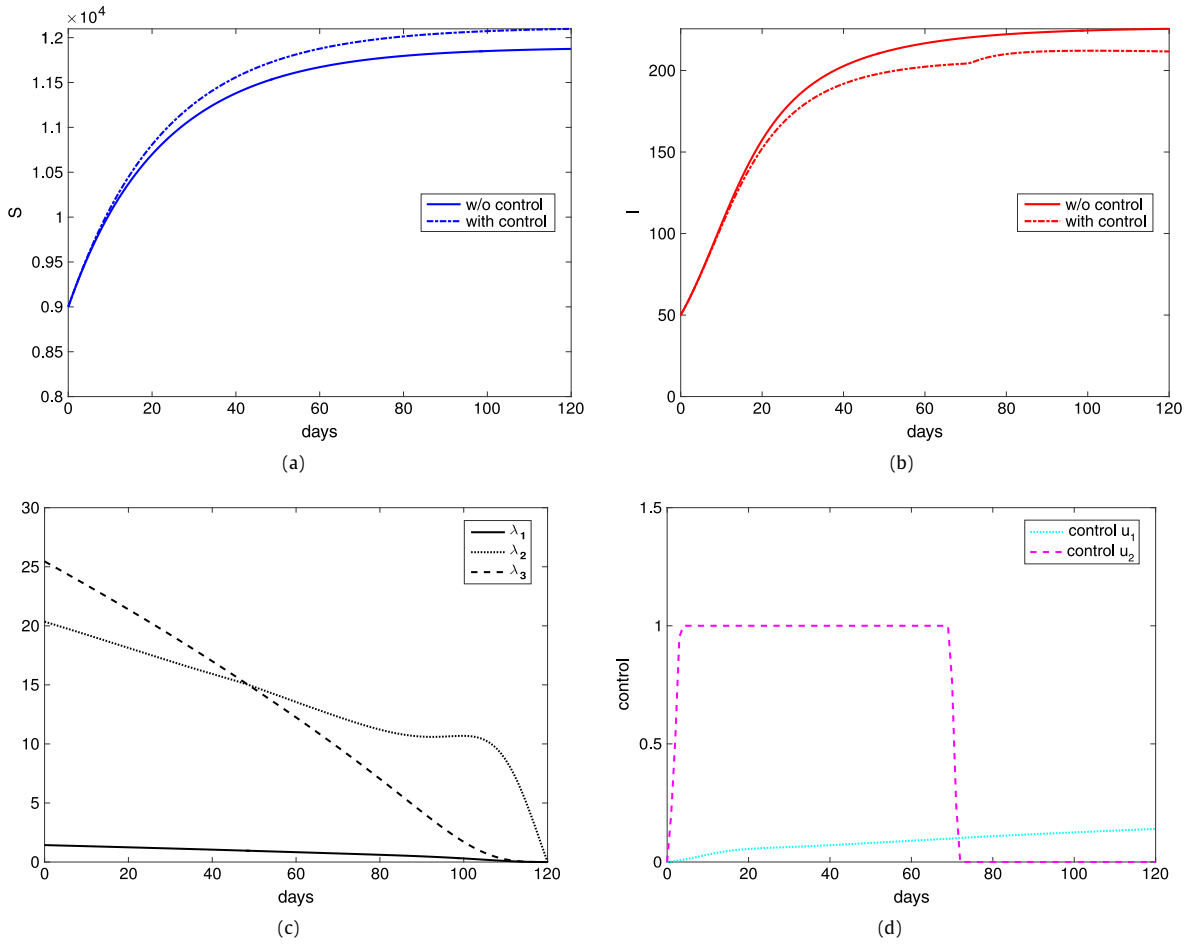

Fig. 6. The third scenario. The values of parameters are given in Table 2. Weight factors: $b = 1000$ and $c = 0.1$.

When we analyze Figs. 4b, 5b and 6b, we clearly see a decrease in the number of infective individuals with an increase in the number of susceptible individuals (see Figs. 4a, 5a and 6a). Here, we have presented to you, three different scenarios, where weight factors b and c play a key role.

The first scenario. We consider that both interventions' weight factors are the same, that is we set $b = c = 1$. We observe that, during a period of 90 days, it is optimal to keep a maximum amount of both interventions: therapeutic treatment and awareness campaigns. After this period, we must stop awareness campaigns and maintain the treatment at its maximum. We target only infectious people to avoid any unstable or sudden increase in their number.

The second scenario. We assume that the weight factor of costs associated to awareness campaigns is higher than the one related to the preventive intervention, that is $b = 0.01$ and $c = 10$. It is optimal, to keep a maximum treatment rate and barely use some awareness campaigns.

The third scenario. Now, we assume that the weight factor of costs associated to treatment is much higher than the one related to the awareness campaigns intervention, that is $b = 1000$ and $c = 0.1$. It is now optimal to maintain an important awareness campaign during almost three months, with a little number of therapeutic intervention. It is allowed to use only a small rate of therapeutic treatment because its cost is very high. It is imperative for any government or decision maker to think carefully about the best intervention strategy to choose so as to limit the spread of infection and optimize the costs.

8. Conclusion

In this work, we proposed and analyzed a nonlinear SIRS epidemic model taking relapse and cure rates into account. Also, a nonlinear incidence rate was considered. The aim of our study is to explore infectious diseases where infected individuals may recover permanently or become infected again. The global dynamics of system (5) has been completely established, we have shown that if the basic reproduction number $\mathcal{R}_0$ is less than unity, the disease free-equilibrium state E_f is globally

exponentially asymptotically stable. E_f is globally asymptotically stable when $\mathcal{R}_0 = 1$. Also, if $\mathcal{R}_0$ is greater than unity, we have shown, by means of a suitable Lyapunov functional, that a unique globally asymptotically stable endemic state exists.

A controlled model with preventive campaigns to avoid relapse and therapeutic treatment was built with a threshold level to simulate realistic conditions. The system was solved numerically using a backward finite difference scheme. According to numerical simulations, the number of infected individuals significantly decreases and the disease is controlled but not eradicated.

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