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Bifurcation analysis and optimal control of an infection age–structured epidemic model with vaccination and treatment

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Abstract

This paper deals with the study and control of the transmission of an infectious disease described by a Susceptible–Vaccinated–Infected (SVI) epidemiological model. This model takes into account the age structure of the infection, imperfect vaccination and therapeutic treatment of infected people who become susceptible again. We show that the rate of therapeutic treatment can lead to bistability of disease–free and an endemic equilibria. This phenomenon is known as backward bifurcation and can allow the disease to persist in a population even if the basic reproduction number is less than one. The existence of this bifurcation means that controlling this infectious disease remains extremely difficult. This is why we are developing an optimal control strategy combining vaccination and treatment in order to minimize the disease spread in the population. We then consider vaccination and treatment rates as time–dependent functions. This allows us to formulate an optimal control problem whose objective is to minimize the number of infected individuals as well as the cost of applying controls. We establish first–order necessary conditions for optimality and characterize optimal controls. Numerical simulations illustrate the fact that a combination of intervention measures can significantly reduce the transmission dynamics of infectious diseases by keeping the population of infected individuals relatively low.

Keywords: Age–structured model, Infectious disease, Bifurcation theory, Optimal control theory, Numerical simulations.

1 Introduction

Infectious diseases are one of the greatest enemies of humans in the world. Although many efforts have been made in the fight against these diseases, some of which have been eliminated, a lot of them continue to develop and are responsible of the loss of many human lives. These diseases are caused by numerous pathogens such as bacteria, viruses, parasites or fungi, which evolve over time and can harm patients if not detected and treated early at the population level. A combination of rapid and appropriate control strategies can greatly help decision–makers limit the damage caused by these diseases. Vaccination and therapeutic treatment are among the most important control strategies for reducing the spread of many infectious diseases. However, due to strain variation, vaccination may lose its effect. In view of the economic and human damage caused by these diseases, it is necessary to develop frameworks for simulating their spread in order to better understand and predict their behavior, with a view to controlling them efficiently and at lower cost. In this case, mathematical modeling is an important tool for providing valuable information in the public health decision–making process, by generating a number of scenarios through numerical simulations, taking into account different assumptions. It also makes it possible to evaluate the various intervention measures before deploying them in the population. It has been established that the infectivity of certain infectious diseases depends on the time elapsed since infection. This time is generally referred to as the infection age. This age is widely regarded as a potentially useful variable for understanding the transmission mechanisms of certain infectious diseases, such as HIV/AIDS [1, 2, 3],

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Influenza disease [4], Tuberculosis (TB) [5, 6, 7] and see also [8, 9, 10, 5, 11] and references therein for general class of epidemic models.

Recently Wang et al. [8] studied the global dynamics of an Susceptible–Vaccinated–Infectious–Recovered (SVIR) epidemiological model with continuous infection age structure and imperfect vaccination. They demonstrated that disease–free equilibrium is globally asymptotically stable when the basic reproduction rate is less than or equal to one. However, when this threshold is greater than one, there is a unique (endemic) equilibrium point that is globally asymptotically stable. Motivated by this work, we propose in this manuscript to study and control a modified version of this model in which we assume that vaccination does not confer total immunity and that the infected individuals become susceptible again after receiving treatment and can be vaccinated again. Under these conditions, the recovered class is no longer necessary. The model is as follows

$$\begin{cases} \frac{dS}{dt} = \Lambda - \mathcal{T}(\beta i(t,.))S + \mathcal{T}(\alpha i(t,.)) - (\xi+\mu)S \\ \frac{dV}{dt} = \xi S - m\mathcal{T}(\beta i(t,.))V - \mu V \\ \partial_t i(t,x) + \partial_x i(t,x) = -[\mu + \delta(x) + \alpha(x)]i(t,x) \\ i(t,0) = [S + mV]\mathcal{T}(\beta i(t,.)), \end{cases} \quad (1)$$

where the state variables $S(t)$ and $V(t)$ denote the size of susceptible and vaccinated individuals at time $t > 0$ respectively. The state variable $i(t,x)$ represents the density of infectious individuals with the infection age $x \in \mathbb{R}_+$ at time $t > 0$. All recruitment is into the susceptible class and occurs at a constant rate Λ. The susceptible individuals are vaccinated at constant rate ξ and move to the class of vaccinated at flow ξS with a vaccine efficiency $1-m$ with the parameter $m \in (0,1)$. The transmission of the disease to the susceptible and vaccinated individuals occurs due to their contact with infected individuals. Then the corresponding force of infection are given by $\mathcal{T}(\beta i)$ and $m\mathcal{T}(\beta i)$ respectively, where $\mathcal{T}(.)$ is the integral operator defined for some integrable function f on $\mathbb{R}_+$ by $\mathcal{T}(f) = \int_{\mathbb{R}_+} f(x)dx$ and $\beta(x)$ is the age–structured disease transmission rate. The natural and disease induced death of individuals are given by the rates μ and $\delta(x)$ respectively. The model considers that the therapeutic treatment do not confer a permanent immunity and the treat recipients return to the susceptible class S at flow $\mathcal{T}(\alpha i)$ where $\alpha(x)$ represents the therapeutic treatment rate of infectious individuals of infection age $x > 0$.

Our aims in this work are twofold: first, we compute the explicit expression of the basic reproduction number by the next generation method [12, 13, 14] and study the long–term dynamics of model (1) as a function of this threshold. In general, reducing the basic reproduction number below unity is a necessary and sufficient condition for eradicating infectious diseases. However, several authors (see for instance [15, 11, 16, 17] and references therein) have demonstrated that it is possible that in certain epidemiological models, when the basic reproduction number is less than unity, the disease–free stable equilibrium point coexists simultaneously with an endemic stable equilibrium point. This phenomenon, known as backward bifurcation, reveals that to eradicate a disease, it's not enough to reduce the basic reproduction number below unity, but below a much smaller value. Determining the causes of this bifurcation in epidemiological models has attracted the attention of many researchers [15, 11, 16, 17, 18]. By using the Lyapunov–Schmidt theory introduced recently by Martcheva and Inaba in [18], we show that the system (1) can exhibit the phenomenon of backward bifurcation and we determine its cause. Secondly, we are implementing an optimal control strategy to minimize the number of people infected and the cost of implementing vaccination and therapeutic treatment. In the literature several researches have explored optimal control problems for age–structured systems. See for instance [19, 20, 21] for general optimal control theory of such systems, and also [10, 5, 22, 23, 24, 25, 26, 27, 28] for applications of this theory in many branches of science such as competing species, harvesting control, birth control, epidemic disease and plant–pest interactions.

The remaining parts of this manuscript are organized as follows. In Section 2, the model (1) is rigorously analyzed. These results include the calculation of the basic reproduction number, the existence and stability of stationary states, and bifurcation analysis. Section 3 is devoted to formulating the optimal control problem and establishing the existence and characterization of optimal control. Numerical simulations are provided in Section 4, to illustrate the theoretical results and we end the paper with a brief conclusion.

2 Mathematical properties of model

This section is devoted to the main results of this manuscript about the qualitative analysis of system (1). These include the well–posedness of the model, as well as the existence and stability of equilibrium points. Before stating our results, we make the following realistic assumptions on the positivity of the parameters and functions involved in system (1). More precisely, we assume that

Assumption 2.1. *The parameters Λ, ξ, μ, m are all positives and initial conditions $S(0)$ and $V(0)$ are nonnegatives. Moreover, the functions $\alpha(.)$, $\beta(.)$ and $\delta(.)$ belong in $L^{\infty}_{+}(0,\infty)$, and the boundary condition $i(0,.) = i_0(.) \in L^1_+(0,\infty)$. Here $L^p_+(0,\infty)$ with $1 \le p \le \infty$ denotes the space of nonnegative functions in $L^p(0,\infty)$.*

2.1 Well–posedness

Since the system (1) has a nonlinear initial condition on the variable $i(t,x)$, we use the integrated semigroup theory introduced recently by Thieme [29] in the context of age–structured models to establish the well–posedness of model. It consists of removing the nonlinearity from the domain and incorporates it into the Lipschitz continuous perturbation function. Let us introduce the Banach space $X = \mathbb{R}\times\mathbb{R}\times L^1(0,\ \infty)\times\mathbb{R}$ endowed with the usual product norm. The positive cone of space X is defined by $X_+ = \mathbb{R}_+\times\mathbb{R}_+\times L^1_+(0,\infty)\times\mathbb{R}_+$. We set $X_0 = \mathbb{R}\times\mathbb{R}\times L^1(0,\infty)\times\{0\}$ and denote by $X_{0+} = X_0\cap X_+$. The system (1) can be rewritten in the following abstract Cauchy problem

$$\frac{dz(t)}{dt} = \mathcal{A}z(t) + H(z(t)), \quad \forall t\ge 0 \quad and \quad z(0) = z_0 \in X_{0+}, \tag{2}$$

where $z(t) = (S(t), V(t), i(t,.), 0)^{\top}$ with "$\top$" denoting the transposition symbol, the linear differential operator $\mathcal{A} : D(\mathcal{A}) \subset X \longrightarrow X$ defined as follows:

$$\mathcal{A}\begin{pmatrix} S\\ V\\ i\\ 0\end{pmatrix} = \begin{pmatrix} -\mu S\\ -(\mu+\xi)V\\ -i' - pi\\ -i(0)\end{pmatrix}, \tag{3}$$

where $p(x) = \mu + \delta(x) + \alpha(x)$, the domain $D(\mathcal{A}) = \mathbb{R}\times\mathbb{R}\times \mathsf{W}^{1,1}(0,\infty)\times\{0\}$ and $\mathsf{W}^{1,1}(0,\infty) = \{f \in L^1(0,\infty) :\ D^k f \in L^1(0,\infty), \forall |k| \le 1\}$ is a Sobolev space. Note that the domain $D(\mathcal{A})$ is not dense in X since it can be seen that $X_0 = \overline{D(\mathcal{A})} \neq X$. Finally the nonlinear map $H :\ X_0 \subset X \longrightarrow X$ is defined by

$$H\begin{pmatrix} S\\ V\\ i\\ 0\end{pmatrix} = \begin{pmatrix} \Lambda - \mathcal{T}(\beta i)S + \mathcal{T}(\alpha i)\\ \xi S - m\mathcal{T}(\beta i)V\\ 0_{L^1(0,\infty)}\\ [S+mV]\mathcal{T}(\beta i)\end{pmatrix}. \tag{4}$$

Now, we are ready to establish the well–posedness of the system (1) which is given by the following result:

Theorem 2.1. *The system (1) represented by the abstract Cauchy problem (2) has a unique strongly continuous semiflow $\{\Phi(t,.)\}_{t\ge 0}$ on X_{0+} such that for each $z_0 \in X_{0+}$, the map $z(.) \in C([0,\infty), X_{0+})$ defined by $z(.) : t \longrightarrow z(t) = \Phi(t,z_0)$ is an integrated (or mild) solution of system (2) satisfying $\int_0^t z(s)ds \in \mathfrak{D}$ for all $t\ge 0$ and $z(t) = z_0 + \int_0^t z(s)ds + \int_0^t F(z(s))ds$. In addition, the non-empty domain*

$$\Omega = \{(S,V,i,0) :\ S(t) + V(t) + \mathcal{T}(i(t,.)) \le \Lambda/\mu\}, \tag{5}$$

is positively invariant and attracts all nonnegative solutions. Moreover, the semiflow $\{\Phi(t,.)\}_{t\ge0}$ is bounded dissipative, that is, there exists a bounded set $B \subset X_0$ such that for any bounded set $U \subset X_0$, we can find $\kappa = \kappa(U,B)$ such that $\Phi(t,U) \subset B$ for all $t \ge \kappa$.

Proof. The existence, uniqueness and positiveness of the integrated solution of system (2) can be obtained by apply a similar approach as in [30, 9, 31]. Let $z_0 \in X_{0+}$, then $\|\Phi(t,z_0)\|_X = S(t) + V(t) + \mathcal{T}(i(t,.))$. By integrating the third equation of system (1) on $\mathbb{R}_+$ with respect to x and combining with the first–second equation of (1), one can easily get

$$\frac{d\|\Phi(t,z_0)\|_X}{dt} \le \Lambda - \mu\|\Phi(t,z_0)\|_X. \tag{6}$$

Then, using the Grönwall–Bellman inequality we have

$$\|\Phi(t,z_0)\|_X \le \Lambda/\mu - (\Lambda/\mu - \|z_0\|_X)\, e^{-\mu t}, \tag{7}$$

which shows that $\Phi(t,z_0) \in \Omega$ holds for every solution of (2) satisfying $z_0 \in \Omega$. Hence the set Ω is positively invariant. Furthermore, we have the bound $\limsup_{t\to+\infty} \|\Phi(t,z_0)\|_X \le \Lambda/\mu$ which implies that the semiflow $\{\Phi(t,z_0)\}_{t\ge0}$ is bounded dissipative and Ω attracts all point of space X_{0+}. ◻

2.2 Basic reproduction number and equilibria

System (1) has always a disease–free equilibrium point $E_0 = (S^0, V^0, 0, 0) \in X_{0+}$ where $S^0 = \Lambda/(\mu + \xi)$ and $V^0 = \xi S^0/\mu$, corresponding to the equilibrium point without disease. In order to study the long run behaviour of system (1), we need to compute the *basic reproduction number* denoted $\mathcal{R}_0$. It is obtained by the so–called *next generation operator*, that gives the distribution of secondary infections as a function of the distribution of the primary infected individuals. In order to compute $\mathcal{R}_0$, we use the methodology developed in references [12, 14] where $\mathcal{R}_0$ corresponds to the spectral radius of the next generation operator. Specifically, we linearize system (1) around the disease–free equilibrium point E_0 and obtain the following equations for the dynamics of the infected population:

$$\begin{cases} \partial_t i(t,x) + \partial_x i(t,x) = -p(x) i(t,x) \\ i(t,0) = [S^0 + mV^0]\mathcal{T}(\beta i). \end{cases} \tag{8}$$

Using the characteristics method, the solution of system (1) can be expressed as

$$i(t,x) = i_0(x-t)\frac{\pi(x)}{\pi(x-t)}\mathbb{1}_{\{x>t\}} + i(t-x,0)\pi(x)\mathbb{1}_{\{x<t\}}, \tag{9}$$

where we defined $\pi(x) = e^{-\int_0^x p(\sigma)d\sigma}$ which denotes the probability to leave the infected compartment. Let $\hbar(t) = i(t,0)$ be the number of newly infectious individuals at time $t > 0$. Inserting expression (9) into the boundary condition of (8), we get the renewal equation:

$$\hbar(t) = \varphi(t) + \int_0^t \Psi(x)\hbar(t-x)dx, \tag{10}$$

where $\varphi(t) := [S^0 + mV^0] \int_t^\infty \beta(x)\frac{\pi(x)}{\pi(x-t)} i_0(x-t)dx$ and $\Psi(x) := [S^0 + mV^0]\beta(x)\pi(x)$. According to [12, 14], the basic reproduction number is calculated as the spectral radius of the next generation operator $\int_0^\infty \Psi(x)dx$. Hence, the explicit expression of $\mathcal{R}_0$ is given by

$$\mathcal{R}_0 = [S^0 + mV^0]\mathcal{T}(\beta\pi). \tag{11}$$

This threshold depends on the epidemiological parameters of the model, that ensures or not the outbreak of an epidemic process and measures the expected number of secondary cases produced by a typical infected individual during its entire period of infectiousness in a susceptible population [32, 12, 13]. However this threshold is used to measure the transmission potential of an infectious diseases. In general, it plays an important role on the determination and the stability of equilibrium points. We have the following result:

Theorem 2.2. *Let Assumption 2.1 be satisfied. If $\mathcal{R}_0 < 1$, the disease–free equilibrium point E_0 is locally asymptotically stable and is unstable when $\mathcal{R}_0 > 1$.*

Proof. Linearizing the system (1) at equilibrium point E_0 with $y(t)$, $z(t)$ and $\omega(t,x)$ being the small perturbations, that is $y(t) = S(t) - S^0$, $z(t) = V(t) - V^0$ and $\omega(t,x) = i(t,x)$. We obtain the following abstract Cauchy problem:

$$\frac{du(t)}{dt} = \mathcal{A}u(t) + DHE_0(u(t)), \quad \forall t \geq 0 \quad and \quad u(0) \in X_{0+}, \tag{12}$$

where $u(t) = (y(t), z(t), \omega(t,.), 0)^\top$ and the linear operator $DHE_0 : X_0 \subset X \longrightarrow X$ is defined for $u \in X_0$ by

$$DHE_0(u) = \begin{pmatrix} -\mathcal{T}(\beta\omega)S^0 + \mathcal{T}(\alpha\omega) \\ \xi y - m\mathcal{T}(\beta\omega)V^0 \\ 0_{L^1(0,\infty)} \\ [S^0 + mV^0]\mathcal{T}(\beta\omega) \end{pmatrix}. \tag{13}$$

Let us denote by $\mathcal{A}_0$ the restriction of the linear operator $\mathcal{A}$ in X_0, *i.e.* $\mathcal{A}_0 : \psi \in X_0 \longrightarrow \mathcal{A}_0\psi = \mathcal{A}\psi \in X_0$ and let $\{T_{\mathcal{A}_0}(t)\}_{t\geq 0}$ the semigroup generated by the linear operator $\mathcal{A}_0$. It is easy to check, by adapting the proof of Proposition 1 of [33], that $\|T_{\mathcal{A}_0}(t)\| \leq e^{-\mu t}$, $\forall t \geq 0$. It follows that $\omega_{ess}(\mathcal{A}_0)$, the essential growth rate of $\{T_{\mathcal{A}_0}(t)\}_{t\geq 0}$ is less than or equal to $-\mu$. Let $\{T_{(\mathcal{A}+DHE_0)_0}(t)\}_{t\geq 0}$ be the semigroup generated by $(\mathcal{A}+DHE_0)_0$, the restriction of the linear operator $\mathcal{A}+DHE_0$ in X_0. Since DHE_0 is a compact operator, it follows from the result in [34, Theorem 1.2] that $\omega_{ess}((\mathcal{A}+DHE_0)_0) \leq \omega_{ess}(\mathcal{A}_0) \leq -\mu < 0$. According to the results obtained in [29, Corollary 4.3], the equilibrium point E_0 is locally asymptotically stable if all eigenvalues of the linear operator $(\mathcal{A}+DHE_0)_0$ have negative real part. In this case, the trajectories which start sufficiently close to E_0 remain close and converge to the equilibrium point when time tends towards infinity. However, if at least one eigenvalue of $(\mathcal{A}+DHE_0)_0$ has strictly positive real part, then E_0 is an unstable equilibrium point. Now, we consider the exponential solutions of the linearized system (12) at disease–free equilibrium point E_0 by $y(t) = \overline{y}e^{\lambda t}$, $z(t) = \overline{z}e^{\lambda t}$ and $\omega(t) = \overline{\omega}(x)e^{\lambda t}$ with $(\overline{y}, \overline{z}, \overline{\omega}(.)) \in \mathbb{R}\times\mathbb{R}\times \mathsf{W}(0,\infty)\backslash\{0\}$ and $\lambda \in \mathbb{C}$ with $\mathfrak{Re}\lambda > -\mu$ (here the symbol $\mathfrak{Re}$ denotes the real part), to derive the characteristic equation. We get the following linear eigenvalue problem:

$$\begin{cases} (\lambda+\mu+\xi)\overline{y} = -S^0\mathcal{T}(\beta\overline{\omega}) + \mathcal{T}(\alpha\overline{\omega}) \\ (\lambda+\mu)\overline{z} = \xi\overline{y} - mV^0\mathcal{T}(\beta\overline{\omega}) \\ \overline{\omega}'(x) = -[\lambda + p(x)]\overline{\omega}(x) \\ \overline{\omega}(0) = [S^0 + mV^0]\mathcal{T}(\beta\overline{\omega}). \end{cases} \tag{14}$$

Since $\overline{y}$ and $\overline{z}$ do not interact on $\overline{\omega}$–equation, we can determine λ follows the three–four equations of (14). From the third equation of (14), we get $\overline{\omega}(x) = \overline{\omega}(0)\pi(x)e^{-\lambda x}$. Putting this expression in the last equation of (14) and canceling $\overline{\omega}(0)$, we obtain the following characteristic equation:

$$G(\lambda) := [S^0 + mV^0]\int_0^\infty \beta(x)\pi(x)e^{-\lambda x}dx = 1. \tag{15}$$

Assume that $\mathcal{R}_0 < 1$ and $\lambda \in \mathbb{C}$ with $\mathfrak{Re}\lambda \geq 0$, we have $1 = |G(\lambda)| \leq G(\mathfrak{Re}\lambda) \leq G(0) = \mathcal{R}_0 < 1$ which is a contradiction. Hence the equation $G(\lambda) = 1$ does not have a root with a nonnegative real part when $\mathcal{R}_0 < 1$. We conclude that the disease–free equilibrium point E_0 is locally asymptotically stable whenever $\mathcal{R}_0 < 1$. Now, assume that $\mathcal{R}_0 > 1$ and $\lambda \in \mathbb{R}_+$, we have $G(0) = \mathcal{R}_0 > 1$. Moreover $\lim_{\lambda\to+\infty} G(\lambda) = 0$. Since $G(.)$ is a decreasing function, there exists a unique $\lambda_0 > 0$ such that $G(\lambda_0) = 1$. Therefore E_0 is unstable whenever $\mathcal{R}_0 > 1$. This completes the proof. □

Biologically speaking, this result means that the disease can be eradicate (when $\mathcal{R}_0 < 1$) when initial sizes of each subpopulation in the system (1) is within the basin of attraction of the stable point E_0. W now examine the existence of the endemic equilibrium points. For this, let $E^\star(x) = (S^\star, V^\star, i^\star(x), 0)$ be any arbitrary equilibrium point of system (1). To find conditions for the existence of equilibrium points for which disease is endemic in the population we set the derivatives with respect to time in (2) equal to zero (*i.e.* by solving the abstract algebraic equation $\mathcal{A}E^\star + H(E^\star) = 0$), that is

$$\begin{cases} \Lambda - \mathcal{T}(\beta i^\star)S^\star + \mathcal{T}(\alpha i^\star) - (\xi+\mu)S^\star = 0 \\ \xi S^\star - m\mathcal{T}(\beta i^\star)V^\star - \mu V^\star = 0 \\ \partial_x i^\star(x) = -[\mu + \delta(x) + \alpha(x)]i^\star(x) \\ i^\star(0) = [S^\star + mV^\star]\mathcal{T}(\beta i^\star), \end{cases} \tag{16}$$

Then, equilibrium point $E^\star$ with positive components is such that

$$S^\star = \frac{\Lambda + \mathcal{T}(\alpha i^\star)}{\mathcal{T}(\beta i^\star) + \mu + \xi}, \qquad V^\star = \frac{\xi S^\star}{m\mathcal{T}(\beta i^\star) + \mu}, \qquad i^\star(x) = i^\star(0)\pi(x),$$

and $i^\star(0)$ is the positive real solution of the quadratic equation

$$a_2(i^\star(0))^2 + a_1 i^\star(0) + a_0 = 0, \tag{17}$$

where

$$\begin{aligned} a_2 &= m[\mathcal{T}(\beta\pi)]^2[1-\mathcal{T}(\alpha\pi)]; \quad a_0 = \mu(\mu+\xi)(1-\mathcal{R}_0); \\ a_1 &= m\mathcal{T}(\beta\pi)[\mu - \Lambda\mathcal{T}(\beta\pi)] + (\mu + m\xi)\mathcal{T}(\beta\pi)[1-\mathcal{T}(\alpha\pi)]. \end{aligned}$$

We see that the coefficients a_2 and a_0 are positives (respectively negatives) if and only if $\mathcal{T}(\alpha\pi) < 1$ and $\mathcal{R}_0 < 1$ (respectively $\mathcal{T}(\alpha\pi) > 1$ and $\mathcal{R}_0 > 1$) respectively. Using the Descartes' rule of signs on the quadratic polynomial (17), the existence for the possible positive real roots of equation (17) are summarized in Table 1. It follows that under the condition $\mathcal{R}_0 < 1$, it is possible to have one or two endemic equilibrium points. In this case, it is possible to have a backward bifurcation phenomenon in system (1) *i.e.* the locally asymptotically stable disease–free equilibrium E_0 coexists with a locally asymptotically stable endemic equilibrium when $\mathcal{R}_0 < 1$. To check this, the discriminant of quadratic equation (17) $a_1^2 - 4a_2a_1$ is set to zero and solved for the critical value of $\mathcal{R}_0$ denoted $\mathcal{R}_0^{\#}$ is given by $\mathcal{R}_0^{\#} = 1 - a_1^2/4a_2\mu(\mu+\xi)$. Thus the backward bifurcation phenomenon would occur for the values of threshold $\mathcal{R}_0$ satisfying the relation $\mathcal{R}_0^{\#} < \mathcal{R}_0 < 1$. It would be very interesting to analyze the system's bifurcations to see if it is possible to have a bistability phenomenon, and if so, to determine its cause.

Table 1: Number of possible positive real roots of the equation (17) according of the sign of the coefficients a_k, $k = 0, 1, 2$.

a_2	a_1	a_0	$\mathcal{R}_0$	Number of positive solutions of (17)
−	−	−	$\mathcal{R}_0 > 1$	0
+	−	−	$\mathcal{R}_0 > 1$	1
+	+	−	$\mathcal{R}_0 > 1$	1
−	+	−	$\mathcal{R}_0 > 1$	0 or 2
−	−	+	$\mathcal{R}_0 < 1$	1
−	+	+	$\mathcal{R}_0 < 1$	1
+	+	+	$\mathcal{R}_0 < 1$	0
+	−	+	$\mathcal{R}_0 < 1$	0 or 2

2.3 Bifurcation analysis

In this subsection, we study the existence of bifurcations of system (1) around the disease–free equilibrium E_0. To this end, we use a recent result introduced by Martcheva and Inaba [18] to detect the presence of bifurcations in partial differential equations, and define the necessary and sufficient conditions for them to occur. Let us set $\beta(x) = \bar{\beta}\beta_0(x)$ where the function $\beta_0(x)$ is normalized as $[S^0 + mV^0]\mathcal{T}(\beta_0\pi) = 1$, which suggests that $\mathcal{R}_0 = 1$ is equivalent to $\bar{\beta} = 1$. In what follows, we consider $\bar{\beta}$ as the bifurcation parameter. Let us introduce the important threshold

$$\Theta := -\left[\left(1 + m\frac{\xi}{\mu}\right)\frac{S^0}{\xi+\mu} + \frac{m^2}{\mu}V^0\right]\mathcal{T}(\beta_0\pi) + \left(1 + m\frac{\xi}{\mu}\right)\frac{\mathcal{T}(\alpha\pi)}{\xi+\mu}. \tag{18}$$

Then, we have the following main result:

Theorem 2.3. *Let Assumption 2.1 be satisfied. If $\Theta > 0$, the system (1) undergoes a backward bifurcation at $(E_0, \bar{\beta} = 1)$. Otherwise, the system (1) exhibits a forward bifurcation at $(E_0, \bar{\beta} = 1)$ when $\Theta < 0$.*

Proof. It is based on the Lyapunov–Schmidt method. For this purpose, let us set $z = (z_1, z_2, z_3, 0) \in X_0$ and introduce the nonlinear map $F(z, \bar{\beta}) := \mathcal{A}z + H(z)$ where the linear operator $\mathcal{A}$ and map $H(z)$ are defined in (3) and (4) respectively. The linearized operator $\mathcal{B} := D_zF(E_0, \bar{\beta})$ acting on X is given by

$$\mathcal{B}z = \begin{pmatrix} -\bar{\beta}S^0\mathcal{T}(\beta_0 z_3) + \mathcal{T}(\alpha z_3) - (\xi+\mu)z_1 \\ \xi z_1 - \bar{\beta}mV^0\mathcal{T}(\beta_0 z_3) - \mu z_2 \\ -z_3' - p(x)z_3 \\ -z_3(0) + \bar{\beta}[S^0 + mV^0]\mathcal{T}(\beta_0 z_3) \end{pmatrix}, \tag{19}$$

where its domain is given by $D(\mathcal{B}) = D(\mathcal{A})$. Let us define by $\lambda \in \mathbb{C}$ the eigenvalue of the operator $\mathcal{B}$ and solving the differential equation $\mathcal{B}z = \lambda z$ for $z \in X_0$, we have $z_3(x) = z_3(0)\pi(x)e^{-\lambda x}$. Inserting the expression of $z_3(x)$ into the four equation in $\mathcal{B}z = \lambda z$ and canceling $z_3(0)$, we get the characteristic equation

$$\bar{\beta}[S^0 + mV^0]\int_0^\infty \beta_0(x)\pi(x)e^{-\lambda x}dx = 1, \tag{20}$$

which has $\lambda = 0$ as a simple isolated eigenvalue when $\bar{\beta} = 1$ and each of the remaining solutions has negative real part thanks to the proof of Theorem 2.2. To find the eigenvector $\widehat{v}_0$ associated with eigenvalue zero, we need to solve the equation $\mathcal{B}z = 0$. We can choose $z_3(x) = \pi(x)$ and the boundary condition of the four equation of $\mathcal{B}z = 0$ is trivially satisfied at $\bar{\beta} = 1$. From the first equation of $\mathcal{B}z = 0$, we get $z_1^0 := z_1 = \frac{-\bar{\beta}S^0\mathcal{T}(\beta_0\pi)+\mathcal{T}(\alpha\pi)}{\xi+\mu}$ and the second equation gives $z_2^0 := z_2 = -\frac{\bar{\beta}m}{\mu}V^0\mathcal{T}(\beta_0\pi) + \frac{\xi}{\mu}z_1^0$. Therefore, we set the vector $\widehat{v}_0 = (z_1^0, z_2^0, \pi(x), 1)$. Now, we seek the adjoint operator $\mathcal{B}^*$. To do so, let us consider the vector $\Psi = (\Psi_1, \Psi_2, \Psi_3, \Psi_4) \in X^* := \mathbb{R}^2 \times L^1(0,\infty) \times \mathbb{R}$. Then, we have the relation

$$\begin{aligned}\langle \Psi,\ \mathcal{B}z\rangle &= \left[-\bar{\beta}S^0\mathcal{T}(\beta_0 z_3) + \mathcal{T}(\alpha z_3) - (\xi+\mu)z_1\right]\Psi_1 + \left[\xi z_1 - \bar{\beta}mV^0\mathcal{T}(\beta_0 z_3) - \mu z_2\right]\Psi_2\\ &+ \int_0^\infty \left[-z_3' - p(x)z_3\right]\Psi_3(x)dx + \left[-z_3(0) + \bar{\beta}[S^0+mV^0]\mathcal{T}(\beta_0 z_3)\right]\Psi_4.\end{aligned}$$

Notice that, by integrating by part assuming that $\Psi_3(\infty) = 0$ we get

$$\int_0^\infty \left[-z_3' - p(x)z_3\right]\Psi_3(x)dx = z_3(0)\Psi_3(0) + \int_0^\infty \left[\Psi_3' - p(x)\Psi_3\right]z_3(x)dx.$$

Hence we have

$$\begin{aligned}\langle \Psi,\ \mathcal{B}z\rangle &= \left[\xi\Psi_2 - (\xi+\mu)\Psi_1\right]z_1 - \mu\Psi_2 z_2 + (\Psi_3(0) - \Psi_4)z_3(0)\\ &+ \int_0^\infty [\Psi_3' - p\Psi_3 + (-\bar{\beta}S^0\beta_0 + \alpha)\Psi_1 - \bar{\beta}mV^0\beta_0\Psi_2 + \bar{\beta}(S^0+mV^0)\beta_0\Psi_4]z_3(x)dx\\ &= \langle \mathcal{B}^*\Psi, z\rangle,\end{aligned}$$

which should hold for $\Psi \in D(\mathcal{B}^*)$ and $z \in D(\mathcal{B}) \subset X_0$. We take the domain of the operator $\mathcal{B}^*$ as follows

$$D(\mathcal{B}^*) = \left\{\Psi \in \mathbb{R}^2 \times \mathrm{W}^{1,\infty}(0,\infty) \times \mathbb{R} :\ \Psi_3(\infty) = 0, \Psi_4 = \Psi_3(0)\right\}.$$

Therefore, the adjoint operator $\mathcal{B}^*$ is defined for $\Psi \in D(\mathcal{B}^*) \subset X^* = \mathbb{R}^2 \times L^\infty(0,\infty) \times \mathbb{R}$ by

$$\mathcal{B}^*\Psi = \begin{pmatrix} \xi\Psi_2 - (\xi+\mu)\Psi_1\\ -\mu\Psi_2\\ \Psi_3' - p\Psi_3 + (-\bar{\beta}S^0\beta_0 + \alpha)\Psi_1 - \bar{\beta}mV^0\beta_0\Psi_2 + \bar{\beta}[S^0+mV^0]\beta_0\Psi_4\\ \Psi_3(0)\end{pmatrix}. \tag{21}$$

To find the vector $\widehat{v}_0^*$, the unique positive vector satisfying the relation $\langle \mathcal{B}z, \widehat{v}_0^*\rangle = 0$ for all $z \in X$, it suffices to solve the equation $\mathcal{B}^*\Psi = 0$ with $\bar{\beta} = 1$. It is easy to see that $\Psi_1 = \Psi_2 = 0$. Solving the differential equation in $\mathcal{B}^*\Psi = 0$, we get $\Psi_3(x) = [S^0+mV^0]\Psi_3(0)\int_x^\infty \beta_0(s)\frac{\pi(s)}{\pi(x)}ds$. Hence, the eigenfunction $\widehat{v}_0^* = (0, 0, \Psi_3(x), \Psi_3(0))$ where $\Psi_3(0) > 0$. Computing the second derivative for F with respect to z and $\bar{\beta}$, we obtain

$$D^2_{z\bar{\beta}}F(E_0, 1)\widehat{v}_0 = \begin{pmatrix} -S^0\mathcal{T}(\beta_0\pi)z_1^0\\ -mV^0\mathcal{T}(\beta_0\pi)z_2^0\\ 0\\ [S^0+mV^0]\mathcal{T}(\beta_0\pi)\end{pmatrix}. \tag{22}$$

Therefore, one obtains

$$b = \langle D^2_{z\bar{\beta}}F(E_0, 1)\widehat{v}_0, \widehat{v}_0^*\rangle = [S^0+mV^0]\Psi_3(0)\mathcal{T}(\beta_0\pi) > 0. \tag{23}$$

On the order hand, the second derivative $D^2_{zz}F(E_0,\ 1)[\widehat{v}_0, \widehat{v}_0]$ can be computed with the following formula:

$$D^2_{zz}F(E_0, 1)[\widehat{v}_0, \widehat{v}_0] = \partial^2_{hk}F(E_0 + (h+k)\widehat{v}_0, 1) = \begin{pmatrix} -2\mathcal{T}(\beta_0\pi)z_1^0\\ -2m\mathcal{T}(\beta_0\pi)z_2^0\\ 0\\ 2[z_1^0+mz_2^0]\mathcal{T}(\beta_0\pi)\end{pmatrix}. \tag{24}$$

Thus, we have

$$a = \langle D^2_{zz}F(E_0, 1)[\widehat{v}_0, \widehat{v}_0], \widehat{v}_0^*\rangle = 2[z_1^0+mz_2^0]\mathcal{T}(\beta\pi)\Psi_3(0) = 2\Theta\mathcal{T}(\beta\pi)\Psi_3(0). \tag{25}$$

It follows that $a < 0$ (respectively $a > 0$) if and only if $\Theta < 0$ (respectively $\Theta > 0$). According to [18, Theorem 2.1] (see Appendix A), the bifurcation is backward if and only if $\Theta > 0$ and forward if and only if $\Theta < 0$. This completes the proof. □

The appearance of a backward bifurcation in the epidemiological model (1) can lead to the persistence of disease in the population even if the basic reproduction number is less than unity. In such a scenario, the condition $\mathcal{R}_0 < 1$ becomes only a necessary but not sufficient condition for disease eradication. This important property of the model is caused by the therapeutic treatment rate of infectious individuals since $\Theta < 0$ when $\alpha(x) = 0$ for all $x \in \mathbb{R}_+$. In this case, the coefficients of quadratic equation (17) $a_2 > 0$ and $a_0 < 0$ when $\mathcal{R}_0 > 1$. Consequently, the system (1) admits a unique endemic equilibrium. Moreover, the global asymptotic stability of the disease–free equilibrium of the model (1) is given below for the special case $\alpha(x) = 0$.

Theorem 2.4. *Assume that the therapeutic treatment is not effective (i.e. $\alpha(x) = 0$ for all $x \in \mathbb{R}_+$). Then, the system (1) always admits a disease–free equilibrium point E_0 which is globally asymptotically stable whenever $\mathcal{R}_0 \leq 1$.*

Proof. To establish the global stability of disease–free equilibrium E_0, we use the Lyapunov function approach. For this, we consider the function $q(x) = \int_x^\infty \beta(s)\frac{\pi(s)}{\pi(x)}ds$. Note that $q \in L_+^\infty(0,\infty)$, $q(0) = \mathcal{T}(\beta\pi)$ and its satisfies the differential equation for all $x > 0$, $q'(x) - (\mu + \delta(x))q(x) + \beta(x) = 0$. Let us introduce the Volterra–type function which takes the form $h(z) = z - \ln z - 1$. Obviously, $h'(z) = 1 - (1/z)$ and $h(z) \geq 0$ for all $z > 0$. Thus $h(.)$ is decreasing function on $(0,1)$ and increasing on $(1,+\infty)$. In addition to the fact that $h''(z) > 0$ for all $z > 0$, then $h(.)$ has a unique global minimum at $z_0 = 1$ satisfying $h(z_0) = 0$. Let us consider the following Lyapunov function:

$$\mathsf{W}[t] = S_0 h\left(\frac{S(t)}{S^0}\right) + V^0 h\left(\frac{V(t)}{V_0}\right) + [S^0 + mV^0]\mathcal{T}(qi(t,.)). \tag{26}$$

It follows that the function $\mathsf{W}[.]$ is nonnegative and well defined with respect to the disease–free equilibrium E_0 which is a global minimum. Differentiating the function $\mathsf{W}[.]$ along the solution of the system (1), we have

$$\begin{aligned}\frac{d\mathsf{W}[t]}{dt} &= \left(1 - \frac{S^0}{S}\right)\frac{dS}{dt} + \left(1 - \frac{V^0}{V}\right)\frac{dV}{dt} + [S^0 + mV^0]\int_0^\infty q(x)\partial_t i(t,x)dx \\ &= \left(1 - \frac{S^0}{S}\right)(\Lambda - \mathcal{T}(\beta i)S + \mathcal{T}(\alpha i) - (\xi + \mu)S) + \left(1 - \frac{V^0}{V}\right)(\xi S - m\mathcal{T}(\beta i)V - \mu V) \\ &+ [S^0 + mV^0]\int_0^\infty q(x)(-\partial_x i(t,x) - (\mu + \delta(x)))dx.\end{aligned}$$

By using the fact that $\Lambda = (\xi + \mu)S^0$ and $\xi S^0 = \mu V^0$, we get after a few algebraic calculations

$$\begin{aligned}\frac{d\mathsf{W}[t]}{dt} &= \mu S^0\left(2 - \frac{S^0}{S} - \frac{S}{S^0}\right) + \xi S^0\left(3 - \frac{V}{V^0} - \frac{S^0}{S} - \frac{S}{S_0}\frac{V^0}{V}\right) + [S^0 + mV^0]\mathcal{T}(\beta i) \\ &- [S + mV]\mathcal{T}(\beta i) + [S^0 + mV^0]\int_0^\infty q(x)(-\partial_x i(t,x) - (\mu + \delta(x)))dx.\end{aligned} \tag{27}$$

Using the integration by parts formula, we have

$$\int_0^\infty q(x)\partial_x i(t,x)dx = [q(x)i(t,x)]_0^\infty - \int_0^\infty q'(x)i(t,x)dx = -q(0)i(t,0) - \int_0^\infty q'(x)i(t,x)dx. \tag{28}$$

Combining the relations (27) and (28), we have after calculation

$$\begin{aligned}\frac{d\mathsf{W}[t]}{dt} &= \mu S^0\left(2 - \frac{S^0}{S} - \frac{S}{S^0}\right) + \xi S^0\left(3 - \frac{V}{V^0} - \frac{S^0}{S} - \frac{S}{S_0}\frac{V^0}{V}\right) + (1 - \mathcal{R}_0)i(t,0) \\ &+ [S^0 + mV^0]\int_0^\infty [q'(x) - (\mu + \delta(x))q(x) + \beta(x)]i(t,x)dx.\end{aligned} \tag{29}$$

Finally we get,

$$\frac{d\mathsf{W}[t]}{dt} = \mu S^0\left(2 - \frac{S^0}{S} - \frac{S}{S^0}\right) + \xi S^0\left(3 - \frac{V}{V^0} - \frac{S^0}{S} - \frac{S}{S_0}\frac{V^0}{V}\right) + (1 - \mathcal{R}_0)i(t,0). \tag{30}$$

According to the arithmetic–geometric mean inequality, both terms $2 - \frac{S^0}{S} - \frac{S}{S^0}$ and $3 - \frac{V}{V^0} - \frac{S^0}{S} - \frac{S}{S_0}\frac{V^0}{V}$ are nonnegatives and the equality holds if and only if $S = S^0$ and $V = V^0$. Therefore, the function $\mathsf{W}[.]$ is nonincreasing since $\frac{d\mathsf{W}[t]}{dt} \leq 0$ when $\mathcal{R}_0 \leq 1$. By the boundedness of function $\mathsf{W}[.]$, the alpha limit set of $(S(t), V(t), i(t,.))$ must be contained in the maximal compact invariant subset defined by $\Gamma = \left\{(S, V, i) : \frac{d\mathsf{W}[t]}{dt} = 0\right\}$. However, the equality $\frac{d\mathsf{W}[t]}{dt} = 0$ holds if and only if $S = S^0$, $V = V^0$ and $i(t, 0) = 0$. Integrating the $i(t, x)$–equation of system (1) using the characteristics method, it follows that $i(t, x) = 0$ for all $t > x$. Hence, we get $i(t, x) \longrightarrow 0$ as $t \to +\infty$. Therefore, the set Γ is reduced to singleton $\{E_0\}$ and by means of the Lasalle's invariant principle [35], we can conclude that the disease–free equilibrium E_0 is globally asymptotically stable when $\mathcal{R}_0 \leq 1$. □

Epidemiologically speaking, Theorem 2.4 means that in the absence of therapeutic treatment, a flow of infectious individuals for all age of infection will not generate outbreak of the disease unless $\mathcal{R}_0 > 1$ where the disease will persist. Therefore, reduce the basic reproduction number below the unity become a necessary and sufficient condition to eradicate the disease in the population. Treatment of infected individuals can lead to non–eradication of the disease when the basic reproduction rate is less than one. It is therefore important to develop an optimal combined control strategy aimed at reducing the spread of the disease through appropriate vaccination and treatment protocols at the lowest possible cost.

3 Optimal control Problem

3.1 Control problem statement

Given the seriousness of the damage caused by infectious diseases in many countries, it is important to know how much and when vaccination and treatment should be applied, in order to control the dynamics of disease transmission effectively and at minimum cost. For this purpose, we consider that the vaccination and treatment are represented by Lebesgue measurable functions on finite time horizon $[0, T]$, denoted $\xi(t)$ and $\alpha(t, x)$ respectively and where $T > 0$ is the final time of intervention strategies. In addition, we replace the upper limit of the integral with respect to infection age by a finite number $x_+ > 0$ for practical consideration, *i.e.* the integral function $\mathcal{T}(f) = \int_0^{x_+} f(x)dx$. Let us introduce the set $Q = [0, T] \times [0, x_+]$. Given the limited resources and time available to implement strategies to control this infectious disease, policies must be limited to a predefined objective. For this reason, we consider by $\mathfrak{D} := \mathcal{L}^\infty(0, T; [0, \xi_+]) \times \mathcal{L}^\infty(Q; [0, \alpha_+])$ the set of admissible control pair which is the space of measurable and bounded functions pair $(\xi(.), \alpha(.,.))$ defined by $\xi(.) : [0, T] \longrightarrow [0, \xi_+]$ and $\alpha(.,.) : Q \longrightarrow [0, \alpha_+]$. The positive constants ξ_+ and α_+ represent the maximum rates at which individuals may be vaccinated and treated respectively. Hence, implementing both time–dependent controls in system (1), we obtain the following controlled system:

$$\begin{cases} \frac{dS}{dt} = \Lambda - \mathcal{T}(\beta i(t,.))S + \mathcal{T}(\alpha(t,.)i(t,.)) - (\xi(t) + \mu)S \\ \frac{dV}{dt} = \xi(t)S - m\mathcal{T}(\beta i(t,.))V - \mu V \\ \partial_t i(t,x) + \partial_x i(t,x) = -[\mu + \delta(x) + \alpha(t,x)]i(t,x) \\ i(t,0) = [S + mV]\mathcal{T}(\beta i(t,.)). \end{cases} \tag{31}$$

Our main objective is to minimize the total number of infected individuals and the necessary cost of vaccination and therapeutic treatment. To achieve this goal, we work together with system (31), the following objective functional:

$$\mathcal{J}(\xi, \alpha) = \int_Q \chi(x)i(t,x)dtdx + \frac{C_1}{2}\|\xi\|^2_{L^2(0,T)} + \frac{C_2}{2}\|\alpha\|^2_{L^2(Q)}, \tag{32}$$

where $\chi(.) \in L^\infty_+(0, x_+)$, $C_1 > 0$ and $C_2 > 0$ are balancing coefficients transforming the integral into a cost spent over the interval $[0, T]$. Quadratic expression of the control in (32) is included to indicate the nonlinearity of the implementation cost as it is more costly to increase the control efficiency when it is already high. As mentioned before, our optimal control problem reads as follows: *find an admissible control pair $(\xi^\star(.), \alpha^\star(.,.)) \in \mathfrak{D}$ steering the optimal trajectory $(S^\star(.), V^\star(.), i^\star(.,.))$ satisfying the optimization problem*

$$\mathcal{J}(\xi^\star, \alpha^\star) = \min_{(\xi,\alpha)\in\mathfrak{D}} \mathcal{J}(\xi, \alpha). \tag{OCP}$$

3.2 First–order necessary optimality conditions

In this subsection, we start by showing the existence of an optimal solution to the optimization problem (OCP) subject to the age–structured system (31).

Theorem 3.1. *Under Assumption 2.1, there exists at least one optimal control pair* $(\xi^\star, \alpha^\star) \in \mathfrak{D}$ *at which corresponds the state variable* $(S^\star, V^\star, i^\star)$*, solution of the optimization problem (OCP).*

Proof. The objective functional $\mathcal{J}(\xi, \alpha) \geq 0$ since the state variables and controls are all nonnegatives. Then, it follows that $d = \inf\{\mathcal{J}(\xi, \alpha) : \ (\xi, \alpha) \in \mathfrak{D}\}$ is finite and nonnegative. So there is a minimizing sequence $(\xi_n, \alpha_n) \in \mathfrak{D}$ such that for $n \geq 1$ we have

$$d \leq \mathcal{J}(\xi_n, \alpha_n) \leq d + \frac{1}{n}. \tag{33}$$

As the sequence (ξ_n, α_n) is bounded, there exists a subsequence still denoted (ξ_n, α_n) that converges to some $(\xi^\star, \alpha^\star)$ for the weak–$\star$ topology of $L^\infty(0,T) \times L^\infty(Q)$. The set $\mathfrak{D}$ is a closed convex subset of $L^\infty(0,T) \times L^\infty(Q)$, so it is weakly closed. Therefore $(\xi^\star, \alpha^\star) \in \mathfrak{D}$. Denote by (S_n, V_n, i_n) the solution of state system (31) corresponding to control pair (ξ_n, α_n). The sequence (S_n, V_n) is uniformly bounded and equicontinuous on $[0, T]$. Using Arzerla–Ascoli's Theorem, we can extract a subsequence still denoted (S_n, V_n) which converges uniformly to the limit $(S^\star, V^\star)$ in $C(0, T)$. Let us denote by $\pi_{\alpha_n}(t, x) = e^{-\int_0^x [\mu + \delta(s) + \alpha_n(t - x + s, s)] ds}$. It is easy to see that the function π_{α_n} is Lipschitz in the following sense, for (α^1, α^2), there exists a constant $k \geq 0$ such that $|\pi_{\alpha^1}(t, x) - \pi_{\alpha^2}(t, x)| \leq k\mathcal{T}(|\alpha^1(t, .) - \alpha^2(t, .)|)$. As consequence, we have the convergence $\pi_{\alpha_n}(t, x) \longrightarrow \pi_{\alpha^\star}(t, x)$ as $n \to \infty$ almost everywhere in Q. By using the method of characteristics, we get explicit expression of $i_n(t, x)$–equation

$$i_n(t, x) = i_0(x - t) \frac{\pi_{\alpha_n}(t, x)}{\pi_{\alpha_n}(t, x - t)} \mathbb{1}_{\{x > t\}} + i_n(t - x, 0) \pi_{\alpha_n}(t, x) \mathbb{1}_{\{x < t\}}.$$

This sequence is bounded since the sequences (S_n), (V_n), $(\mathcal{T}(i_n))$ and (α_n) are all bounded. Then we can extract a subsequence still denoted (i_n) that converges weakly to $i^\star(t, x)$ in $L^2(Q)$ defined as follows

$$i^\star(t, x) = i_0(x - t) \frac{\pi_{\alpha^\star}(t, x)}{\pi_{\alpha^\star}(t, x - t)} \mathbb{1}_{\{x > t\}} + i^\star(t - x, 0) \pi_{\alpha^\star}(t, x) \mathbb{1}_{\{x < t\}}.$$

Since the sequence $(\mathcal{T}(i_n))$ is bounded, it converges to $\mathcal{T}(i^\star)$ by the uniqueness of the limit. Moreover, passing to the limit in the differential equations satisfied by the subsequences (S_n) and (V_n) in controlled system (31), we obtain:

$$\begin{cases} \frac{dS}{dt} = \Lambda - \mathcal{T}(\beta i^\star) S^\star + \mathcal{T}(\alpha(t, .) i^\star) - (\xi^\star(t) + \mu) S^\star \\ \frac{dV}{dt} = \xi^\star(t) S^\star - m\mathcal{T}(\beta i^\star) V^\star - \mu V^\star. \end{cases} \tag{34}$$

Passing to the limit as $n \longrightarrow \infty$ in (33) and lower semicontinuity of objective functional $\mathcal{J}(., .)$, we obtain $\lim\limits_{n \to \infty} \mathcal{J}(\xi_n, \alpha_n) = \mathcal{J}(\xi^\star, \alpha^\star) = d$. Hence, $((S^\star, V^\star, i^\star), (\xi^\star, \alpha^\star))$ is an optimal solution of the optimization problem (OCP). This achieves the proof. □

Now, we derive the first–order necessary conditions for optimality of a control pair must satisfy in order to be optimal. Using the framework of Barbu [36], we derive the optimal control as a combination of the state and adjoint variables. In fact, the adjoint variables are determined by first introducing the sensitivity functions. For this purpose, let us denote by $\Psi := (S, V, i)$ and define the solution map $(\xi, \alpha) \longmapsto \Psi(\xi, \alpha)$ of the system (31). The sensitivity functions $\varphi_S(t)$, $\varphi_V(t)$ and $\varphi_i(t, x)$ associated to state variables $S(t)$, $V(t)$ and $i(t, x)$, are obtained by the Gâteaux derivatives $\varepsilon^{-1}[\Psi((\xi, \alpha) + \varepsilon(q, p)) - \Psi(\xi, \alpha)] \longrightarrow (\varphi_S, \varphi_V, \varphi_i)$ as $\varepsilon \to 0^+$ in $(L^\infty(0, T))^2 \times L^\infty(Q)$, where $(\xi, \alpha) + \varepsilon(q, p) \in \mathfrak{D}$ and $(q, p) \in L^\infty(0, T) \times L^\infty(Q)$. By using the explicit expression of state variables of system (31), it is easy to establish that the map $(\xi, \alpha) \longmapsto \Psi(\xi, \alpha)$ is Lipschitz in L^∞. Then according to result in Barbu [36, page 17], the existence of sensitivity functions is guaranteed. In addition, the sensitivity functions satisfy the following system of differential equations:

$$\begin{cases} \frac{d\varphi_S}{dt} = -\mathcal{T}(\beta\varphi_i) + \mathcal{T}(\alpha\varphi_i) + \mathcal{T}(pi) - qS - [\mathcal{T}(\beta i) + \xi + \mu]\varphi_S \\ \frac{d\varphi_V}{dt} = \xi\varphi_S + qS - m\mathcal{T}(\beta i)\varphi_V - m\mathcal{T}(\beta\varphi_i)V - \mu\varphi_V \\ \partial_t\varphi_i + \partial_x\varphi_i = -[\mu + \delta + \alpha]\varphi_i - pi \\ \varphi_i(t, 0) = [S + mV]\mathcal{T}(\beta\varphi_i) + [\varphi_S + m\varphi_V]\mathcal{T}(\beta i). \end{cases} \tag{35}$$

Next, we introduce the adjoint variables $\mathcal{Z}_S(t)$, $\mathcal{Z}_V(t)$ and $\mathcal{Z}_i(t,x)$ corresponding to the state variables $S(t)$, $V(t)$ and $i(t,x)$ of system (31), respectively. The adjoint system satisfied by the adjoint variables is then derived by using the adjoint operator associated with the sensitivity system (35) together with appropriated transversality and boundary conditions (see for instance [20] for more details). Specifically, the adjoint system is given by:

$$\begin{cases} \frac{d\mathcal{Z}_S}{dt} = [\mathcal{T}(\beta i)+\mu]\mathcal{Z}_S + \xi(t)[\mathcal{Z}_S - \mathcal{Z}_V] - \mathcal{Z}_i(t,0)\mathcal{T}(\beta i) \\ \frac{d\mathcal{Z}_V}{dt} = [m\mathcal{T}(\beta i)+\mu]\mathcal{Z}_V - m\mathcal{T}(\beta i)\mathcal{Z}_i(t,0) \\ \partial_t\mathcal{Z}_i + \partial_x\mathcal{Z}_i = -\chi(x) + [\beta(x)S - \alpha(t,x)]\mathcal{Z}_S + m\beta(x)\mathcal{Z}_V V \\ \qquad\qquad -[S+mV]\beta(x)\mathcal{Z}_i(t,0) + [\mu+\delta(x)+\alpha(t,x)]\mathcal{Z}_i, \end{cases} \tag{36}$$

endowed with the following transversality and boundary conditions for $(t,x)\in Q$:

$$\mathcal{Z}_S(T)=0, \quad \mathcal{Z}_V(T)=0, \quad \mathcal{Z}_i(T,x)=0, \quad \mathcal{Z}_i(t,x_+)=0. \tag{37}$$

The existence of the adjoint solutions can be proved thanks to a fixed point argument mapping principle, see for instance [36]. In what follows, we employ tangent normal cone techniques in nonlinear functional analysis (see [36, 37, 21]) to deduce the first–order necessary conditions for optimality of optimal control. To do so, let us denote by $\mathcal{T}_{\mathfrak{D}}(\xi,\alpha)$ and $\mathcal{N}_{\mathfrak{D}}(\xi,\alpha)$, the tangent and normal cone of space $\mathfrak{D}$ at control pair (ξ,α) respectively. We have the following result:

Theorem 3.2. *Let $(\xi,\alpha)\in\mathfrak{D}$ be an optimal admissible solution of the optimization problem (OCP) to which the trajectory $(S(t),V(t),i(t,x))$ is associated and let $(\mathcal{Z}_S(t),\mathcal{Z}_V(t),\mathcal{Z}_i(t,x))$ be an adjoint vector satisfying the system (36)–(37). Then, we have the following optimal control structure:*

$$\xi(t) = \mathcal{P}_1\left(\frac{[\mathcal{Z}_S(t)-\mathcal{Z}_V(t)]S(t)}{C_1}\right) \quad \textit{and} \quad \alpha(t,x) = \mathcal{P}_2\left(\frac{[-\mathcal{Z}_S(t)+\mathcal{Z}_i(t,x)]i(t,x)}{C_2}\right), \tag{38}$$

where the projection maps $\mathcal{P}_j(x) = \min\{\max\{0,x\},x_{j\max}\}$ for $j=1,2$ with $x_{1\max}=\xi_+$ and $x_{2\max}=\alpha_+$.

Proof. For any element of the tangent cone $(q,p)\in\mathcal{T}_{\mathfrak{D}}(\xi,\alpha)$ and let us denote by $(\xi^\varepsilon,\alpha^\varepsilon) := (\xi,\alpha)+\varepsilon(q,p)$, then we have $(\xi^\varepsilon,\alpha^\varepsilon)\in\mathfrak{D}$ for $\varepsilon>0$ small enough. Let $(S^\varepsilon,V^\varepsilon,i^\varepsilon)$ be the solution of the optimization problem (OCP) corresponding to the control pair $(\xi^\varepsilon,\alpha^\varepsilon)$. Since $\mathcal{J}(.,.)$ is minimal on (ξ,α), it follows that $\mathcal{J}(\xi^\varepsilon,\alpha^\varepsilon)\geq\mathcal{J}(\xi,\alpha)$ and then

$$\int_Q \chi(x)\,(i^\varepsilon(t,x)-i(t,x))dtdx + \frac{C_1}{2}\int_0^T \left(\xi^{\varepsilon 2}(t)-\xi^2(t)\right)dt + \frac{C_2}{2}\int_Q \left(\alpha^{\varepsilon 2}(t,x)-\alpha^2(t,x)\right)dtdx \geq 0. \tag{39}$$

Passing to the limit as $\varepsilon\to 0^+$ in the inequality above, we obtain

$$\int_Q \chi(x)\varphi_i(t,x)dtdx + C_1\int_0^T q(t)\xi(t)dt + C_2\int_Q p(t,x)\alpha(t,x)dtdx \geq 0. \tag{40}$$

Let us multiply the first three equations in (35) by the variables $\mathcal{Z}_S(t)$, $\mathcal{Z}_V(t)$, $\mathcal{Z}_i(t,x)$ and the equations in (36) by the variables $\varphi_S(t)$, $\varphi_V(t)$ and $\varphi_i(t,x)$, respectively. Then, we obtain thanks to the relationship between the sensitive and adjoint operators (see for instance [20]) the relation

$$\varphi_S\frac{d\mathcal{Z}_S}{dt} + \varphi_V\frac{d\mathcal{Z}_V}{dt} + \int_0^{x_+}\varphi_i\,(\partial_t\mathcal{Z}_i+\partial_x\mathcal{Z}_i)\,dx + \mathcal{Z}_S\frac{d\varphi_S}{dt} + \mathcal{Z}_V\frac{d\varphi_V}{dt} + \int_0^{x_+}\mathcal{Z}_i\,(\partial_t\varphi_i+\partial_x\varphi_i)\,dx = 0.$$

By expanding the above equation and using integration by parts, the initial and boundary conditions, we obtain the following relationship

$$\int_0^{x_+}\chi(x)\varphi_i(t,x)dtdx - \int_0^{x_+}[\mathcal{Z}_S(t)-\mathcal{Z}_i(t,x)]\,p(t,x)i(t,x)dx + [\mathcal{Z}_S(t)-\mathcal{Z}_V(t)]\,q(t)S(t) = 0. \tag{41}$$

Integrating (41) over $[0,T]$, we deduce that

$$\int_Q \chi(x)\varphi_i(t,x)dtdx = \int_Q [\mathcal{Z}_S(t)-\mathcal{Z}_i(t,x)]\,p(t,x)i(t,x)dtdx + \int_0^T [-\mathcal{Z}_S(t)+\mathcal{Z}_V(t)]\,q(t)S(t)dt. \tag{42}$$

Consequently, inequality (3.2) becomes

$$\int_Q [(-\mathcal{Z}_S + \mathcal{Z}_i)i - C_2\alpha]p(t,x)dtdx + \int_0^T [(\mathcal{Z}_S - \mathcal{Z}_V)S - C_1\xi]q(t)dt \le 0 \tag{43}$$

for all $(q,p) \in \mathcal{T}_{\mathfrak{D}}(\xi,\alpha)$. Hence it follows according to the structure of normal cone (see for instance [36, 37] for more details) that the expression $([\mathcal{Z}_S - \mathcal{Z}_V]S - C_1\xi, [-\mathcal{Z}_S + \mathcal{Z}_i]i - C_2\alpha) \in \mathcal{N}_{\mathfrak{D}}(\xi,\alpha)$. By the standard optimality arguments[1] and taking into account the boundaries of each control strategies, we obtain the representation given in (38) which gives the desired result. This achieves the proof. □

Remark 3.1. *At the final time $T > 0$, the optimal controls defined in (38) vanish, that are $\xi(T) = 0$ and $\alpha(T,x) = 0$ for all $x \in [0,x_+]$ since the adjoint state variables are all equal to zero at final time T by (37).*

Note that Theorem 3.1 does not guarantee the uniqueness of optimal control pair. However, using the optimal control structure (38), this uniqueness can be obtained using the standard procedure based on Ekeland's variational principle [36, 38]. This principle is used in order to generate a sequence of controls and its corresponding states that converge to the optimal control and its corresponding state via the use of the convergence of a minimizing sequence of approximate objective functional. More precisely, we have the following result

Theorem 3.3. *There is a positive real constant K_T that depends on the final time T such that for $K_T < 1$, the optimization problem (OCP) has a unique optimal control pair $(\xi,\alpha) \in \mathfrak{D}$ characterized by (38).*

Before starting the proof of the Theorem above, we embed the objective functional $\mathcal{J}(\xi,\alpha)$ into $L^1(0,T) \times L^1(Q)$ by defining the following functional:

$$\hbar(\xi,\alpha) = \begin{cases} \mathcal{J}(\xi,\alpha), & \text{if} \quad (\xi,\alpha) \in \mathfrak{D} \\ +\infty & \text{otherwise.} \end{cases} \tag{44}$$

Let us introduce the following technical lemma that we shall use to establish the uniqueness result of the optimal control pair of (OCP) whose its proof is described in Appendix B.

Lemma 3.1. *We have the following properties:*

1. *For $T > 0$ sufficiently small, there are positive constants $\mathfrak{C}_{1T}$ and $\mathfrak{C}_{2T}$ such that:*
   - (i) *The map $(\xi,\alpha) \in \mathfrak{D} \longrightarrow (S,V,i)$ is Lipschitz in the following ways:*

     $$\left\|(S^1,V^1,i^1) - (S^2,V^2,i^2)\right\|_{L^\infty} \le \mathfrak{C}_{1T}\left\|(\xi^1,\alpha^1) - (\xi^2,\alpha^2)\right\|_{L^\infty},$$

     where (S^k,V^k,i^k) is a solution of (31) associated to control pair (ξ^k,α^k) for $k \in \{1,2\}$.
   - (ii) *For $(\xi^k,\alpha^k) \in \mathfrak{D}$, the adjoint system (36) admits a weak solution $(\mathcal{Z}_S^k,\mathcal{Z}_V^k,\mathcal{Z}_i^k) \in L^\infty(0,T) \times L^\infty(0,T) \times L^\infty(Q)$ such that for $k \in \{1,2\}$ we have*

     $$\left\|(\mathcal{Z}_S^1,\mathcal{Z}_V^1,\mathcal{Z}_i^1) - (\mathcal{Z}_S^2,\mathcal{Z}_V^2,\mathcal{Z}_i^2)\right\|_{L^\infty} \le \mathfrak{C}_{2T}\left\|(\xi^1,\alpha^1) - (\xi^2,\alpha^2)\right\|_{L^\infty}.$$

2. *The functional $\hbar(.,.)$ is lower semi–continuous with respect to (ξ,α) in $L^1(0,T) \times L^1(Q)$.*

Proof. (of Theorem 3.3) Since the functional $\hbar(.,.)$ is lower semi–continuous in L^1, then according to Ekeland's variational principle [38, 36], it follows that for any given $\varepsilon > 0$, there exists a control pair $(\xi_\varepsilon,\alpha_\varepsilon) \in L^1(0,T) \times L^1(Q)$ such that:

$$\begin{aligned} (i) \quad & \hbar(\xi_\varepsilon,\alpha_\varepsilon) \le \inf_{(\xi,\alpha)\in\mathfrak{D}} \hbar(\xi,\alpha) + \varepsilon \\ (ii) \quad & \hbar(\xi_\varepsilon,\alpha_\varepsilon) = \inf_{(\xi,\alpha)\in\mathfrak{D}} \left\{\hbar(\xi,\alpha) + \sqrt{\varepsilon}\,\|(\xi,\alpha) - (\xi_\varepsilon,\alpha_\varepsilon)\|_{L^1}\right\}. \end{aligned}$$

[1] Refer to Barbu [36], the normal cone $\mathcal{N}_{\mathfrak{D}}(\xi,\alpha)$ is characterized as follows: for $(\omega_1,\omega_2) \in \mathcal{N}_{\mathfrak{D}}(\xi,\alpha)$, we have $\omega_1 > 0$ (resp. $\omega_2 > 0$) when $\xi = \xi_+$ (resp. $\alpha = \alpha_+$); $\omega_1 < 0$ (resp. $\omega_2 < 0$) when $\xi = 0$ (resp. $\alpha = 0$) and finally $\omega_1 = 0$ (resp. $\omega_2 = 0$) when $\xi \in [0,\xi_+]$ (resp. $\alpha \in [0,\alpha_+]$).

Note that, the perturbated functional $\hbar_\varepsilon(\xi,\alpha) = \hbar(\xi,\alpha) + \sqrt{\varepsilon}\,\|(\xi,\alpha)-(\xi_\varepsilon,\alpha_\varepsilon)\|_{L^1}$ attains its infimum at the control pair $(\xi_\varepsilon,\alpha_\varepsilon)$. From item (ii) and a similar argument as that in Subsection 3.2 give the characterization of control pair $(\xi_\varepsilon,\alpha_\varepsilon)$ by

$$\xi_\varepsilon(t) = \mathcal{P}_1\left(\frac{[\mathcal{Z}_S^\varepsilon - \mathcal{Z}_V^\varepsilon]S^\varepsilon - \sqrt{\varepsilon}\vartheta_1^\varepsilon}{C_1}\right) \quad \text{and} \quad \alpha_\varepsilon(t,\theta) = \mathcal{P}_2\left(\frac{[-\mathcal{Z}_S^\varepsilon + \mathcal{Z}_i^\varepsilon]i^\varepsilon - \sqrt{\varepsilon}\vartheta_2^\varepsilon}{C_2}\right), \tag{45}$$

where $(S^\varepsilon, V^\varepsilon, i^\varepsilon)$ and $(\mathcal{Z}_S^\varepsilon, \mathcal{Z}_V^\varepsilon, \mathcal{Z}_i^\varepsilon)$ are the solutions of controlled and adjoint system respectively, corresponding to the control pair $(\xi_\varepsilon,\alpha_\varepsilon)$. The functions $\vartheta_1^\varepsilon \in L^\infty(0,T)$, $\vartheta_2^\varepsilon \in L^\infty(Q)$ and $|\vartheta_j^\varepsilon| \leq 1$ for $j \in \{1,2\}$ and $(t,\theta) \in Q$. We now ready to prove our main result of this subsection concerning the uniqueness of an optimal control pair solution of optimization problem (OCP). To do so, let us consider the following map $\mathcal{M}:\ \mathfrak{D} \longrightarrow \mathfrak{D}$ defined by

$$\mathcal{M}(\xi,\alpha) = \left(\mathcal{P}_1\left(\frac{[\mathcal{Z}_S - \mathcal{Z}_V]S}{C_1}\right),\ \mathcal{P}_2\left(\frac{[-\mathcal{Z}_S + \mathcal{Z}_i]i}{C_2}\right)\right),$$

Let (S^k, V^k, i^k) and $(\mathcal{Z}_S^k, \mathcal{Z}_V^k, \mathcal{Z}_i^k)$ are the state and adjoint variables corresponding to the control pair (ξ^k, α^k) with $k \in \{1,2\}$. Using the Lipschitz properties of the state and adjoint variable established in the Lemma 3.1, we have

$$\begin{aligned}
\|\mathcal{M}(\xi^1,\alpha^1) - \mathcal{M}(\xi^2,\alpha^2)\|_{L^\infty} &= \left\|\mathcal{P}_1\left(\frac{[\mathcal{Z}_S^1 - \mathcal{Z}_V^1]S^1}{C_1}\right) - \mathcal{P}_1\left(\frac{[\mathcal{Z}_S^2 - \mathcal{Z}_V^2]S^2}{C_1}\right)\right\|_{L^\infty(0,\ T)} \\
&+ \left\|\mathcal{P}_2\left(\frac{[-\mathcal{Z}_S^1 + \mathcal{Z}_i^1]i^1}{C_2}\right) - \mathcal{P}_2\left(\frac{[-\mathcal{Z}_S^2 + \mathcal{Z}_i^2]i^2}{C_2}\right)\right\|_{L^\infty(Q)} \\
&\leq C_1^{-1}\left\|[\mathcal{Z}_S^1 - \mathcal{Z}_V^1]S^1 - [\mathcal{Z}_S^2 - \mathcal{Z}_V^2]S^2\right\|_{L^\infty(0,T)} \\
&+ C_2^{-1}\left\|[-\mathcal{Z}_S^1 + \mathcal{Z}_i^1]i^1 - [-\mathcal{Z}_S^2 + \mathcal{Z}_i^2]i^2\right\|_{L^\infty(Q)} \\
&\leq K_1\left\|(S^1,i^1) - (S^2,i^2)\right\|_{L^\infty} + K_2\left\|(\mathcal{Z}_S^1,\mathcal{Z}_V^1,\mathcal{Z}_i^1) - (\mathcal{Z}_S^2,\mathcal{Z}_V^2,\mathcal{Z}_i^2)\right\|_{L^\infty} \\
&\leq (K_1\mathfrak{C}_{1T} + K_2\mathfrak{C}_{2T})\left(\|\xi^1 - \xi^2\|_{L^\infty(0,T)} + \|\alpha^1 - \alpha^2\|_{L^\infty(Q)}\right) \\
&\leq \mathfrak{C}_{3T}\left(\|(\xi^1,\alpha^1) - (\xi^2,\alpha^2)\|_{L^\infty}\right),
\end{aligned}$$

where the constants K_1 and K_2 depend on the L^∞ bounds on the state and adjoint state variables and

$$\mathfrak{C}_{3T} = K_1\mathfrak{C}_{1T} + K_2\mathfrak{C}_{2T}, \tag{46}$$

where $\mathfrak{C}_{1T}$ and $\mathfrak{C}_{2T}$ are the Lipschitz constants obtained in Lemma 3.1. Clearly $\mathcal{M}$ is a contraction function if $\mathfrak{C}_{3T} < 1$. Hence, $\mathcal{M}$ has a unique fixed point $(\xi^\star,\alpha^\star) \in \mathfrak{D}$ by the Banach contraction theorem when $\mathfrak{C}_{3T} < 1$. We show that this fixed point is an optimal control pair by using the approximating minimizers sequence $(\xi_\varepsilon,\alpha_\varepsilon)$ from Ekeland's principle and corresponding state variables S^ε, V^ε and i^ε, and adjoint variables $\mathcal{Z}_S^\varepsilon$, $\mathcal{Z}_V^\varepsilon$ and $\mathcal{Z}_i^\varepsilon$. From Lemma 3.1 and the contraction property of the application $\mathcal{M}$, we have

$$\begin{aligned}
\|(\xi^\star,\alpha^\star) - (\xi_\varepsilon,\alpha_\varepsilon)\|_{L^\infty} &= \left\|\mathcal{M}(\xi^\star,\alpha^\star) - \left(\mathcal{P}_1\left(\frac{[\mathcal{Z}_S^\varepsilon - \mathcal{Z}_V^\varepsilon]S^\varepsilon - \sqrt{\varepsilon}\vartheta_1^\varepsilon}{C_1}\right), \mathcal{P}_2\left(\frac{[-\mathcal{Z}_S^\varepsilon + \mathcal{Z}_i^\varepsilon]i^\varepsilon - \sqrt{\varepsilon}\vartheta_2^\varepsilon}{C_2}\right)\right)\right\|_{L^\infty} \\
&\leq \|\mathcal{M}(\xi^\star,\alpha^\star) - \mathcal{M}(\xi_\varepsilon,\alpha_\varepsilon)\|_{L^\infty} \\
&+ \left\|\mathcal{M}(\xi_\varepsilon,\alpha_\varepsilon) - \left(\mathcal{P}_1\left(\frac{[\mathcal{Z}_S^\varepsilon - \mathcal{Z}_V^\varepsilon]S^\varepsilon - \sqrt{\varepsilon}\vartheta_1^\varepsilon}{C_1}\right), \mathcal{P}_2\left(\frac{[-\mathcal{Z}_S^\varepsilon + \mathcal{Z}_i^\varepsilon]i^\varepsilon - \sqrt{\varepsilon}\vartheta_2^\varepsilon}{C_2}\right)\right)\right\|_{L^\infty} \\
&\leq \mathfrak{C}_{3T}\|(\xi^\star,\alpha^\star) - (\xi_\varepsilon,\alpha_\varepsilon)\|_{L^\infty} + \sqrt{\varepsilon}(C_1^{-1} + C_2^{-1}).
\end{aligned}$$

Then for $\mathfrak{C}_{3T} < 1$, we obtain

$$\|(\xi^\star,\ \alpha^\star) - (\xi_\varepsilon,\ \alpha_\varepsilon)\|_{L^\infty} \leq \frac{\sqrt{\varepsilon}(C_1^{-1} + C_2^{-1})}{1 - \mathfrak{C}_{3T}},$$

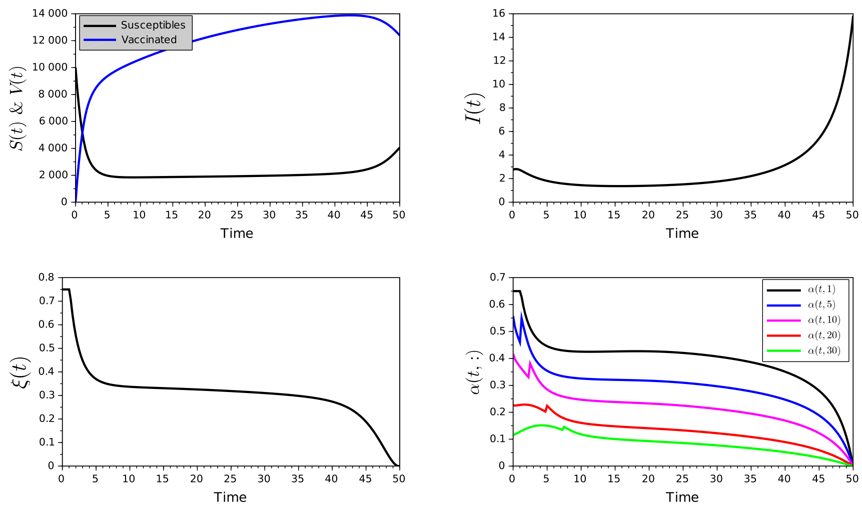

Figure 1: Simulation of system (31) with the optimal control variables for the same control costs $C_1 = C_2 = 50$.

which gives passing to the limit as $\varepsilon \to 0$ the convergence $(\xi_\varepsilon, \alpha_\varepsilon) \longrightarrow (\xi^\star, \alpha^\star)$. Since $\hbar$ is lower semi–continuous and using property (i) of Ekeland's principle, the inequality $\hbar(\xi_\varepsilon, \alpha_\varepsilon) \leq \inf\limits_{(\xi,\alpha)\in\mathfrak{D}} \hbar(\xi, \alpha) + \varepsilon$ implies (as $\varepsilon \to 0$) that $\hbar(\xi^\star, \alpha^\star) \leq \inf\limits_{(\xi,\alpha)\in\mathfrak{D}} \hbar(\xi, \alpha)$. Therefore, we have $\hbar(\xi^\star, \alpha^\star) = \inf\limits_{(\xi,\alpha)\in\mathfrak{D}} \hbar(\xi, \alpha)$. Hence, it suffices to take $K_T = \mathfrak{C}_{3T}$ and we obtain the indicated result. □

4 Numerical simulations

In this subsection, we run numerical simulations to illustrate the effect of optimal control strategies on disease transmission dynamics. Generally, it is not possible to solve optimal control problems analytically. Therefore, we use a numerical method to approximate the optimal solutions and display the results. Among the practical approaches of optimization algorithms, we use the Forward–Backward sweep method [20, 21, 28, 3] to approximate numerically the solution of problem (OCP). Our numerical simulations are done for the control time $T = 50$ and with the maximal age of infection $x_{\max} = 30$. Baseline parameters $\Lambda = 700$, $\mu = 0.04$, $m = 0.25$ and $\delta(x) \equiv \delta = 0.05$. Moreover, we use the age–dependent infection rate $\beta(x) = 0.00005(1 + x/(1 + 5x))$. The initial and boundary conditions are $S(0) = 10^4$, $V(0) = 0$ and $i_0(x) = 60(x + 20)e^{-0.4(x+50)}$. Let $I(t) = \int_0^{x_{\max}} i(t, x)dx$ be the total number of infected individuals and we further set $\xi_{\max} = 0.75$ and $\alpha_{\max} = 0.65$.

The numerical simulations of the optimization problem (OCP) are illustrated in Figure 1–2 for various weight factors C_1 and C_2. We observe that the application of optimal controls keeps susceptible individuals at a relatively low level and increases the population of vaccinated individuals for almost the entire intervention period. In addition, it is optimal to start vaccination at the maximum rate. However, when the cost of therapeutic treatment is higher than that of vaccination (see figure 2), more effort should be devoted to vaccination than when control costs are identical (see figure 1). The application of the controls decreases with time and cancels out at the final instant in both figures, which is consistent with the theoretical result of the remark 3.1. As a result, the total population of infected people, which had remained relatively low, increased at the end of the intervention campaign, but not enough. This increase in the number of infected people is due to the fact that controls are decreasing. Optimal therapeutic treatment differs according to the age of infection. In fact, it is higher in people who have been infected for a short time, and decreases over time. This means that to fight this disease effectively, we need to treat people from the very beginning of their infection.

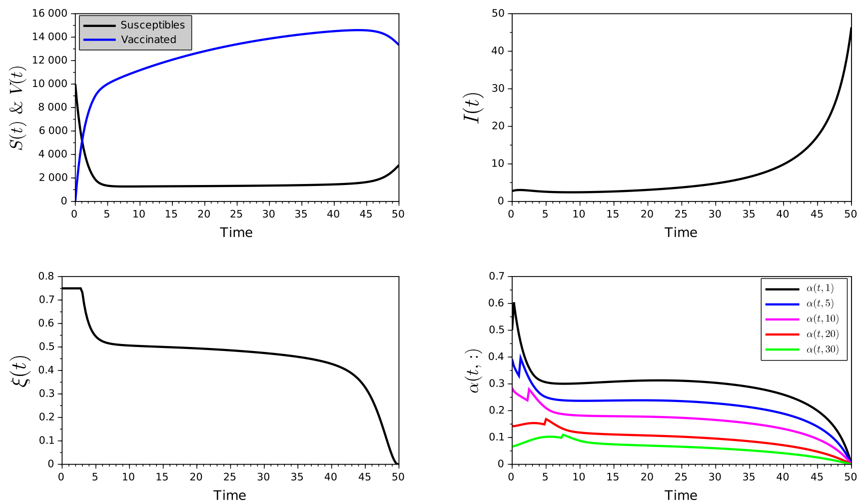

Figure 2: Simulation of system (31) with the optimal control variables for the control costs $C_1 = 50$ and $C_2 = 200$.

5 Conclusion

In this study, we have formulated and analyzed an SVI age–structured model describing the dynamics of an infectious disease in a population and taking into account imperfect vaccine and therapeutic treatment as control measures. We highlighted the expression for the basic reproduction number $\mathcal{R}_0$ and carried out a model stability analysis (1). We showed that when $\mathcal{R}_0 < 1$, the model exhibits the phenomenon of backward bifurcation, where the stable equilibrium point coexists with a stable endemic equilibrium point. As a consequence, the condition $\mathcal{R}_0 < 1$ is only a necessary but not sufficient condition for the disease to disappear. We deduce from Theorem 2.4 that this bifurcation is caused by the rate of therapeutic treatment of infected people. Assuming that vaccination and treatment rates are time-dependent functions, we have formulated and solved an optimal control problem aiming to minimize the number of infected individuals and the costs associated with vaccination and treatment. This problem is solved numerically using the Backward–Forward sweep method. Numerical results illustrate the fact that optimal vaccination and therapeutic treatment can significantly reduce disease prevalence and slow the spread of infection in the population, while keeping the number of infected individuals relatively low. In addition, optimal control strategies remain dependent on control costs and age of infection.

A Appendix A

We present in this appendix, the recent result establish by Martcheva and Inaba [18] in order to detect the presence of backward and forward bifurcations and driving a necessary and sufficient conditions for its occurence in the infinite dynamical system.

Theorem A.1 (Martcheva and Inaba [18])**.** *Let Y and Z be Banach spaces, $x \in Y$ and $q \in \mathbb{R}$ is a parameter. We consider the following abstract differential equation*

$$\frac{dx}{dt} = F(x,q), \qquad F : Y \times \mathbb{R} \longrightarrow Z. \tag{47}$$

Without loss of generality, we assume that 0 is an equilibrium point of the system (that is $F(0,q) = 0$ for all $q \in \mathbb{R}$) and assume

1. *$A := D_x F(0,q_0)$ is the linearization around the equilibium 0 evaluated at a critical value of parameter q_0, such that A is a closed operator with a simple isolated eigenvalue zero and remaining eigenvalues having negative real part. Let $\widehat{v}_0$ be the unique (up to a constant) positive solution of $Av = 0$.*
2. *$F(x,q) \in C^2(U_0 \times I_0,\ Z)$ for some neighbourhood U_0 of 0 and interval I_0 containing q_0.*

3. *Assume Z^* is the dual of Z and $\langle .,. \rangle$ is the pairing between Z and Z^*. Assume $\widehat{v}_0^* \in Z^*$ is the unique (up to a constant) positive vector satisfying $\langle Ax,\ \widehat{v}_0^* \rangle = 0$ for all $x \in Y$, that is $dim(kerA^*) = 1$ where A^* is the adjoint of A and $kerA^* = span\{\widehat{v}_0^*\}$.*

4. *Assume $\langle D^2_{xq}F(0,q_0)\widehat{v}_0, \widehat{v}_0^* \rangle \neq 0$ where $D^2_{xq}F(0,q_0)$ is the second derivative of F with respect to x and q.*

Then, the direction of the bifurcation is determined by the numbers $a = \langle D^2_{xx}F(0,q_0)[\widehat{v}_0, \widehat{v}_0], \widehat{v}_0^* \rangle$ and $b = \langle D^2_{xq}F(0,q_0)\widehat{v}_0, \widehat{v}_0^* \rangle$, where $D^2_{xx}F(0,q_0)[h_1,h_2]$ is the second derivative of F with respect to x applied to the function h_1 and h_2. If $b > 0$, then the bifurcation is backward if and only if $a > 0$ and forward if and only if $a < 0$.

Remark A.1. *The components of the eigenvector $\widehat{v}_0$, that corresponds to positive entries in the disease–free steady state, may be negative. This is in general the case with the partial differential equations as well [18].*

B Proof of Lemma 3.1

1. (i) Let us consider the functions $h_r^{(1)}(i,\xi) = e^{-\int_r^t [\mathcal{T}(\beta i(\sigma,.))+\xi(\sigma)+\mu]d\sigma}$ and $h_r^{(2)}(i) = e^{-\int_r^t [\mathcal{T}(\beta i(\sigma,.))+\mu]d\sigma}$ for $r > 0$ and $t \in [0,T]$. Then by direct computation based on the following arguments: for all $x,y \in \mathbb{R}_+$, we have $|e^{-x} - e^{-y}| \leq |x-y|$, there exists the positive constants K_k with $k \in \{1,2,3\}$ such that the functions $h_r^{(1)}$ and $h_r^{(2)}$ satisfy for $(i^k,\ \xi^k)$ with $k \in \{1,2\}$, the following inequalities, $|h_r^{(1)}(i^1,\xi^1) - h_r^{(1)}(i^2,\xi^2)| \leq K_1 \int_0^t |\mathcal{T}(i^1(\sigma,.)) - \mathcal{T}(i^2(\sigma,.))|d\sigma + K_2 \int_0^t |\xi^1(\sigma) - \xi^2(\sigma)|d\sigma$ and $|h_r^{(1)}(i^1) - h_r^{(1)}(i^2)| \leq K_3 \int_0^t |\mathcal{T}(i^1(\sigma,.)) - \mathcal{T}(i^2(\sigma,.))|d\sigma$. Using the method of integrating factors on the ordinary differential equations and the method of characteristic on the first–second and third equations of system (31) respectively, we obtain the following expression of state variables:

$$
\begin{aligned}
S(t) &= S_0 h_0^{(1)}(i,\xi) + \int_0^t [\Lambda + \mathcal{T}(\alpha(r,.)i(r,.))]\, h_r^{(1)}(i,\xi)dr;\\
V(t) &= V_0 h_0^{(2)}(i) + \int_0^t \xi(r)S(r)h_r^{(2)}(i)dr;\\
i(t\ \theta) &= i_0(\theta - t)\frac{\pi_\alpha(t,\ \theta)}{\pi_\alpha(t,\theta-t)}\mathbb{1}_{\{\theta>t\}} + i(t-\theta,0)\pi_\alpha(t,\theta)\mathbb{1}_{\{\theta\leq t\}}
\end{aligned} \tag{48}
$$

   From the above representation of solutions of system (31) and using the Lipschitz properties of the functions $h_r^{(1)}$ and $h_r^{(2)}$ for all $r \geq 0$, the proof of these estimates follow similarly as in corresponding result found in [10, 3].

   (ii) Follows like in Item (i).

2. Let $(\xi_n,\alpha_n) \longrightarrow (\xi,\alpha)$ as $n \to \infty$, (S_n,V_n,i_n) and (S,V,i) be the state of system (31) corresponding to (ξ_n,α_n) and (ξ,α), respectively. By Riez theorem, there is a subsequence still denoted (ξ_n,α_n), such that $(\xi_n^2,\alpha_n^2) \longrightarrow (\xi^2,\alpha^2)$ almost everywhere in $[0,T]\times Q$ as $n \to \infty$. Thus, Lebesgue's dominated convergence theorem yields that $\|\xi_n\|^2_{L^1(0,T)} \longrightarrow \|\xi\|^2_{L^1(0,T)}$ and $\|\alpha_n\|^2_{L^1(Q)} \longrightarrow \|\alpha\|^2_{L^1(Q)}$ as $n \to \infty$. On the other hand, it follows that $\int_Q \chi(\theta)i_n(t,\theta)dtd\theta \longrightarrow \int_Q \chi(\theta)i(t,\theta)dtd\theta$ as $n \to \infty$. By Fatou's Lemma, it follows that $\hbar(\xi,\alpha) \leq \liminf_{n\to\infty} \hbar(\xi_n,\alpha_n)$. Hence, the functional $\hbar(.,.)$ is lower semi–continuous. This achieves the proof □

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