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Backward bifurcation and optimal control of an SVI age-structured epidemic model

Yves Fotso Fotso* Josué Tchouanti † Janvier P. Ntahomvukiye‡ Samuel Bowong §

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Abstract

In this work, we study a Susceptible–Vaccinated–Infectious (SVI) epidemiological model with an infection age structure, an imperfect preventive vaccine administered to susceptible individuals and a therapeutic treatment of infectious ones. First, using integrated semigroup theory, we handle the well-posedness property of the model proposed and derive the explicit expression of the basic reproduction number \mathcal{R}_0 that determines whether the disease dies out or persists. Using the Lyapunov–Schmidt type technique, we derive a necessary and sufficient condition for the occurrence of a backward bifurcation. Second, we extend the model by considering the vaccination and therapeutic treatment as time-dependent control variables. An optimal control problem is formulated with the aim of minimizing the number of infected individuals and the cost associated with vaccination and treatment. The existence of an optimal control pair is proved and the first-order necessary condition for optimality are established. Finally, the optimal control problem is solved numerically and simulations are provided. They show that the combination of these two control strategies considerably reduce the spread of the disease by keeping the population of infected individuals relatively low.

Keywords: Age-structured model, infectious disease, bifurcation theory, optimal control theory, numerical simulations.

1 Introduction

The human population is going through a period of emergence and re-emergence of infectious diseases of particular concern, causing enormous human losses worldwide. Understanding the transmission dynamics and management of these diseases has been of great interest to the scientific community in recent decades. Mathematical modeling has become a powerful and widely used tool to facilitate the evaluation of infectious diseases management activities. The interest of the models lies in their capacity to study different scenarios in order to anticipate the consequences of a disease incursion and test new control strategies. 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. The age of infection (time elapsed since the infection) is known as an important factor in the transmission of infectious diseases. The importance of age structure in epidemiological models has been emphasized by many authors in the literature (see for instance [1, 2, 3, 4] and references therein).

In this work, we focus on the Susceptible–Vaccinated–Infectious (SVI) epidemic model with age of infection described by the following differential equations:

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

In the system (1), the states $S(t)$ and $V(t)$ denote the size of susceptible and vaccinated individuals at time $t > 0$ respectively. The term $i(t, \theta)$ represents the density of infectious individuals with the age-since-infection $\theta \in \mathbb{R}_+$ at time $t > 0$. All recruitment is into the susceptible class and occurs at a constant rate Λ . The transmission of the disease to the susceptibles and vaccinated individuals occurs due to their contact with infected individuals, with the force of infection $\mathcal{T}(\beta i)$ and $m\mathcal{T}(\beta i)$ respectively, where $\mathcal{T}(\cdot)$ is the integral operator defined for some integrable function h on \mathbb{R}_+ by $\mathcal{T}(h) = \int_{\mathbb{R}_+} h(\theta)d\theta$. These functions represent the age-since-infection structured transmission rates and m is the modification parameter. It is biologically

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acceptable to assume that the modification parameter $m \in (0,1)$ which is based on the fact that the vaccinated individuals are thought to have partial immunity and hence the effective contacts with infectious individuals may decrease compared to those of susceptible individuals. The susceptibles are vaccinated at constant rate ξ and move to the class of vaccinated at rate ξS . The natural and disease induced death of individuals are given by the rates μ and $\delta(\theta)$ 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 rate $\mathcal{T}(\alpha i)$ where $\alpha(\theta)$ represents the therapeutic treatment rate of infectious individuals of age–since–infection θ . We assume that, all constant parameters of system (1) are positives and we introduce the following technical hypotheses that are necessary to place the system in a biological reasonable framework and sufficient to establish its properties.

Assumption 1.1. *The parameter functions of system (1) satisfy the following properties: The function $\alpha(\cdot) \in L_+^\infty(\mathbb{R}_+)$ and $\beta(\cdot)$ is nonnegative bounded and uniformly continuous on \mathbb{R}_+ . The initial conditions $S(0), V(0)$ are nonnegatives and the initial condition $i(0, \cdot) = i_0(\cdot) \in L_+^1(\mathbb{R}_+)$.*

Here $L_+^p(\mathbb{R}_+)$ with $1 \leq p \leq \infty$ denotes the space of functions $L^p(\mathbb{R}_+)$ which are nonnegatives. Since the exit rate of infectious individuals class is given by $p(\theta) = \mu + \alpha(\theta) + \delta(\theta)$, the probability of still being infectious after an age of infection θ is given by $\pi(\theta) = e^{-\int_0^\theta p(s) ds}$. It is clear that, $\pi(\cdot)$ is a decreasing function that satisfies $\pi(0) = 1$ and the differential equation $\partial_\theta \pi(\theta) = -p(\theta)\pi(\theta)$. Compared to the model proposed in [5], our system includes age–since–infection structure which turns our system into a partial differential equations and take into account the mortality induced by the disease. However, if therapeutic treatment is not effective (*i.e.* $\alpha(\theta) \equiv 0$ for all $\theta \in \mathbb{R}_+$), then the system (1) can be reduced to the model studied in [1].

Our aims in this work are twofold: firstly, we handle the well–posedness of system (1) using the integrated semigroup theory which provides a flexible mathematical framework for determining the existence and uniqueness of evolution equations (see for instance [6, 7, 8]). The explicit expression of basic reproduction number is calculated by the next generation operator approach (see *e.g.* [9, 10, 11]). This threshold is well known in epidemiology as an important parameter which determines if the disease can vanish or persist in the community. The existence and stability of steady states that are infection age–dependent solutions of system (1) are investigated. By using the Lyapunov–Schmidt theory introduced recently by Martcheva and Inaba in [12], we show that the system can exhibit the phenomenon of backward or forward bifurcations. See for instance [13, 14, 15, 16] for more details on such bifurcations. Secondly, we propose and implement an optimal control strategy in order to minimize the number of infected individuals in the community while at the same time keeping the cost of implementing vaccination and therapeutic treatment very low. Several researches have explored optimal control problems for age–structured systems. See for instance [17, 18, 19] for general optimal control theory of such systems, and also [3, 4, 20, 21, 22, 23, 24, 25, 26] 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 Sect. 2, the model (1) is rigorously analyzed. Those results include the existence and uniqueness of a bounded solution, the existence and stability of stationary states, and bifurcation analysis. Sect.3 is devoted to the formulation of optimal control problem. We characterize the optimal control pair by using the maximum principle introduced by Feichtinger et al.[27] for the systems with age structure. Numerical simulations are provided in Sect.4, to illustrate the theoretical results. In the last section, we give some brief summaries and discussions of our results.

2 Qualitative analysis of model

2.1 Well–posedness of the System (1)

Since the system (1) has a nonlinear boundary condition, we use the integrated Semigroup theory introduced by Thieme [7] (see also [8] and references therein) in the context of age–structured models. It consists of removing the nonlinearity from the domain and incorporates it into the Lipschitz continuous perturbation function. To do so, we 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 $X_{0+} = X_0 \cap X_+$. Let us consider the linear differential operator $\mathcal{A}: D(\mathcal{A}) \subset X \rightarrow X$ defined as follows:

$$\mathcal{A} \begin{pmatrix} S \\ V \\ i \\ 0 \end{pmatrix} = \begin{pmatrix} -\mu S \\ -(\mu + \xi)V \\ -i' - p(\theta)i \\ -i(0) \end{pmatrix}, \quad (2)$$

where the domain $D(\mathcal{A}) = \mathbb{R} \times \mathbb{R} \times W^{1,1}(0, \infty) \times \{0\}$, where $W^{1,1}(0, \infty) = \{f \in L^1(0, \infty) : D^k f \in L^1(0, \infty), \forall |k| \leq 1\}$ is a Sobolev space. Remark that the domain $D(\mathcal{A})$ is not dense in X since it can be seen that $X_0 = \overline{D(\mathcal{A})} \neq X$. Let us introduce the nonlinear map $H: X_0 \subset X \rightarrow X$ defined by

$$H \begin{pmatrix} S \\ V \\ i \\ 0 \end{pmatrix} = \begin{pmatrix} \Lambda - \mathcal{T}(\beta i)S + \mathcal{T}(\alpha i) \\ \xi S - m\mathcal{T}(\beta i)V \\ 0_{L^1(0, \infty)} \\ [S + mV]\mathcal{T}(\beta i) \end{pmatrix}. \quad (3)$$

By identifying $z(t)$ together with state vector $(S(t), V(t), i(t, \cdot), 0)^\top$ where " \top " denotes the transposition symbol and by setting $z(0) = (S(0), V(0), i_0(\cdot), 0)^\top$ one obtains that, the system (1) can be rewritten in the following abstract Cauchy problem.

$$\frac{dz(t)}{dt} = \mathcal{A}z(t) + H(z(t)), \quad \forall t \geq 0 \quad \text{and} \quad z(0) = z_0 \in X_{0+}. \quad (4)$$

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

Theorem 2.1. *Let Assumption 1.1 be satisfied. Then there exists a unique strongly continuous semiflow $\{\Phi(t, \cdot)\}_{t \geq 0}$ on X_{0+} such that for each $z_0 \in X_{0+}$, the map $z(\cdot) \in \mathcal{C}([0, +\infty), X_{0+})$ defined by $z(\cdot) : t \rightarrow z(t) = \Phi(t, z_0)$ is an integrated (or mild) solution of the Cauchy problem (4). It satisfies for all $t \geq 0$, $\int_0^t z(s) ds \in X_0$ and $z(t) = z_0 + \mathcal{A} \int_0^t z(s) ds + \int_0^t H(z(s)) ds$. Moreover, the non-empty compact set*

$$\Omega := \left\{ (S, V, i, 0) \in X_{0+} : S(t) + V(t) + \mathcal{T}(i) \leq \frac{\Lambda}{\mu} \right\}, \quad (5)$$

is positively invariant under the semiflow $\{\Phi(t, \cdot)\}_{t \geq 0}$ and attracts all points of space X_{0+} .

Proof. We notice that the map $H(\cdot)$ is Lipschitz continuous on the bounded sets. It is easy to check that the operator $(\mathcal{A}, D(\mathcal{A}))$ satisfies the Hille–Yosida properties [6]. Then, classical techniques apply to provide the existence and uniqueness of an integrated solution to system (4), see e.g. [8, 2, 28, 7]. Let $z_0 \in X_{0+}$, then $\|\Phi(t, z_0)\|_X = S(t) + V(t) + \mathcal{T}(i)$. By integrating the third equation of system (1) on \mathbb{R}_+ with respect to θ and combining with the first–second equation of (1), one can easily get

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

Thus, using the Grönwall–Bellman inequality we have

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

which shows that $\Phi(t, z_0) \in \Omega$ holds for every solution of (1) satisfying $z_0 \in \Omega$. Hence the set Ω is positively invariant. Furthermore we have the bound $\limsup_{t \rightarrow +\infty} \|\Phi(t, z_0)\|_X \leq \Lambda/\mu$ which implies that the semiflow $\{\Phi(t, z_0)\}_{t \geq 0}$ is bounded and Ω attracts all point of space X_{0+} . \square

2.2 Basic reproduction number and steady states

System (1) has always a disease-free steady state $E_0 = (S^0, V^0, 0, 0) \in X_{0+}$ where $S^0 = \Lambda/(\mu + \xi)$ and $V^0 = \xi S^0/\mu$, corresponding to the steady state without disease. In order to study the long time behaviour of system (1), we need to compute a key threshold parameter called *the basic reproduction number* denoted \mathcal{R}_0 . 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 completely susceptible population [29, 9, 10]. It is based on 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 Dieckmann et al. [9] (see also Inaba [11] and references therein) where \mathcal{R}_0 coincides with the spectral radius of the next generation operator. Specifically, we linearize system (1) around the disease-free steady state E_0 to obtain the following equations for the dynamics of the infected population:

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

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

$$i(t, \theta) = \begin{cases} i_0(\theta - t) \frac{\pi(\theta)}{\pi(\theta - t)} & \text{if } \theta \geq t \\ i(t - \theta, 0) \pi(\theta) & \text{if } \theta < t. \end{cases} \quad (9)$$

Let $\bar{h}(t) = i(t, 0)$ 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:

$$\bar{h}(t) = \varphi(t) + \int_0^t \Psi(\theta) \bar{h}(t - \theta) d\theta, \quad (10)$$

where $\varphi(t) := [S^0 + mV^0] \int_t^\infty \beta(\theta) \frac{\pi(\theta)}{\pi(\theta - t)} i_0(\theta - t) d\theta$ and $\Psi(\theta) := [S^0 + mV^0] \beta(\theta) \pi(\theta)$. According to [9, 11], the basic reproduction number is calculated as the spectral radius of the next generation operator $\int_0^\infty \Psi(\theta) d\theta$. Hence, the explicit expression of \mathcal{R}_0 is given by

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

Let $E^*(\theta) = (S^*, V^*, i^*(\theta), 0)$ be an arbitrary steady state of system (1). Then to analyze the local stability of system in the neighbourhood of $E^*(\theta)$, we linearize the system around $E^*(\theta)$ with $x(t)$, $y(t)$ and $\omega(t, \theta)$ being the small perturbations, that is $x(t) = S(t) - S^*$, $y(t) = V(t) - V^*$ and $\omega(t, \theta) = i(t, \theta) - i^*(\theta)$. We obtain the following linear system written in the abstract Cauchy problem form:

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

where $u(t) = (x(t), y(t), \omega(t, \theta), 0)^\top$ and the linear operator $DHE^*: X_0 \subset X \rightarrow X$ is defined for $\phi \in X_0$ by

$$DHE^*(u(t)) = \begin{pmatrix} -\mathcal{T}(\beta\omega)S^* - \mathcal{T}(\beta i^*)x + \mathcal{T}(\alpha\omega) \\ \xi x - m\mathcal{T}(\beta\omega)V^* - m\mathcal{T}(\beta i^*)y \\ 0_{L^1(0, \infty)} \\ [x + my]\mathcal{T}(\beta i^*) + [S^* + mV^*]\mathcal{T}(\beta\omega) \end{pmatrix}. \quad (13)$$

Let us denote by \mathcal{A}_0 the restriction of the linear operator \mathcal{A} in X_0 , i.e. $\mathcal{A}_0: \psi \in X_0 \rightarrow \mathcal{A}_0\psi = \mathcal{A}\psi \in X_0$ 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 [30], 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 $\{T_{(\mathcal{A} + DHE^*)_0}(t)\}_{t \geq 0}$ be the semigroup generated by $(\mathcal{A} + DHE^*)_0$, the part of linear operator $\mathcal{A} + DHE^*$. Since DHE^* is compact operator, it follows using the result in [31, Theorem 1.2] that $\omega_{ess}((\mathcal{A} + DHE^*)_0) \leq \omega_{ess}(\mathcal{A}_0) \leq -\mu < 0$. Therefore, according to the results obtained in [7, Corollary 4.3] that the steady state $E^*(\theta)$ is locally asymptotically stable if all eigenvalues of linear operator $(\mathcal{A} + DFE^*)_0$ have negative real part. In this case, the trajectories which start sufficiently close to $E^*(\theta)$ remain close and converge to this steady state when time tends towards infinity. However, if at least one eigenvalue of $(\mathcal{A} + DFE^*)_0$ has strictly positive real part, then $E^*(\theta)$ is unstable steady state.

Proposition 2.1. *Let Assumption 1.1 be satisfied. If $\mathcal{R}_0 < 1$, the disease-free steady state E_0 is locally asymptotically stable and is unstable when $\mathcal{R}_0 > 1$.*

Proof. We consider the exponential solutions of the linearized system (12) at disease-free steady state E_0 by $x(t) = \bar{x}e^{\lambda t}$, $y(t) = \bar{y}e^{\lambda t}$ and $\omega(t) = \bar{\omega}(\theta)e^{\lambda t}$ with $(\bar{x}, \bar{y}, \bar{\omega}(\theta)) \in \mathbb{R} \times \mathbb{R} \times \mathbf{W}(0, \infty) \setminus \{0\}$ and $\lambda \in \mathbb{C}$ with $\Re \lambda > -\mu$ (here the symbol \Re denotes the real part), to derive the characteristic equation. We get the following linear eigenvalue problem:

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

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

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

Consider that $\lambda \in \mathbb{C}$ with $\Re \lambda \geq 0$, we have $1 = |G(\lambda)| \leq G(\Re \lambda) \leq G(0) = \mathcal{R}_0 < 1$ which is a contradiction. hence the equation $G(\lambda) = 1$ does not have a root with a nonnegative real part when $\mathcal{R}_0 < 1$. Hence, the disease-free steady state 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 $\lim_{\lambda \rightarrow +\infty} G(\lambda) = 0$. Since $G(\cdot)$ 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. \square

Now, we examine the existence of the endemic steady states. For this, Let $E^*(\theta) = (S^*, V^*, i^*(\theta), 0)$ be any arbitrary steady state of system (1). To find conditions for the existence of steady states for which disease

Table 1: Number of possible positive real roots of the equation (16) according of the sign of the coefficient a_k , $k=0,1,2$.

a_2	a_1	a_0	Number of possible positive real roots
-	-	-	0
+	-	-	1
+	+	-	1
-	+	-	0 or 2
-	-	+	1
-	+	+	1
+	+	+	0
+	-	+	0 or 2

is endemic in the population (*i.e.* steady state with disease is endemic) we set the derivatives with respect to time in (14) equal to zero (*i.e.* by solving the abstract equation $\mathcal{A}z^* + H(z^*) = 0$). Then, steady state E^* with positive components is such that

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

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

$$a_2(i^*(0))^2 + a_1 i^*(0) + a_0 = 0, \quad (16)$$

where

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

Clearly the coefficients a_2 and a_0 are positives (resp. negatives) if and only if $\mathcal{T}(\alpha\pi) < 1$ and $\mathcal{R}_0 < 1$ (resp. $\mathcal{T}(\alpha\pi) > 1$ and $\mathcal{R}_0 > 1$) respectively. Thus the number of possible real roots of the polynomial (16) depend of the signs of coefficients a_2 , a_1 and a_0 . This can be analyzed using the Descartes' rule of signs on the quadratic polynomial (16). The different possibilities of existence for the positive real roots of equation (16) are summarized in Table 1. This table shows that under the condition $\mathcal{R}_0 < 1$, it is possible to have one or more endemic steady states. In this case, it is interesting to analyze the system's bifurcations to see if it is possible to have a bi-stability phenomenon, and if so, to determine its cause.

2.3 Bifurcation analysis

In this subsection, we study the existence of bifurcations in the system (1). For this, we start by recalling an analogue result of the Castillo Chavez and Song Theorem [32] designed for the partial differential equations introduced recently by Martcheva and Inaba [12] in order to detect the presence of backward and forward bifurcations and driving a necessary and sufficient conditions for its occurrence. This result is somewhat easier to use but it is based on more abstract approach and its proof is based on the Lyapunov-Schmidt theory. For more details, we refer readers to the article [12].

Theorem 2.2 (Martcheva and Inaba [12]). *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*

$$\frac{dx}{dt} = F(x, q), \quad F: Y \times \mathbb{R} \longrightarrow Z. \quad (17)$$

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 equilibrium 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. $F(x, q) \in \mathcal{C}^2(U_0 \times I_0, Z)$ for some neighbourhood U_0 of 0 and interval I_0 containing q_0 .
3. Assume Z^* is the dual of Z and $\langle \cdot, \cdot \rangle$ 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 $\dim(\ker A^*) = 1$ where A^* is the adjoint of A and $\ker A^* = \text{span}\{\widehat{v}_0^*\}$.
4. Assume $\langle D_{xq}^2 F(0, q_0)\widehat{v}_0, \widehat{v}_0^* \rangle \neq 0$ where $D_{xq}^2 F(0, q_0)$ is the second derivative of F with respect to x and q .

Then, the direction of the bifurcation is determined by the numbers $a = \langle D_{xx}^2 F(0, q_0)[\widehat{v}_0, \widehat{v}_0], \widehat{v}_0^* \rangle$ and $b = \langle D_{xq}^2 F(0, q_0)\widehat{v}_0, \widehat{v}_0^* \rangle$, where $D_{xx}^2 F(0, q_0)[h_1, h_2]$ 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 $a < 0$.

In order to examine the bifurcations of system (1) at disease-free steady state E_0 . Let us set $\beta(\theta) = \bar{\beta}\beta_0(\theta)$ where $\beta_0(\theta)$ is a normalized function such that $[S^0 + mV^0]\mathcal{T}(\beta_0\pi) = 1$, which suggests that $\mathcal{R}_0 = 1$ is equivalent to $\bar{\beta} = 1$ and it is used to be a bifurcation parameter for deriving the existence of bifurcations. To use the Lyapunov Schmidt method, we 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 (2) and (13) respectively. Then, it is easy to see that $F(z^*, \bar{\beta}) = 0$ if $z^* = E_0$. Then the linearized operator $\mathcal{B} := D_z F(E_0, \bar{\beta})$ acting on X is calculated as follows:

$$\mathcal{B}z = \begin{pmatrix} -\bar{\beta}S^0\mathcal{T}(\beta_0z_3) + \mathcal{T}(\alpha z_3) - (\xi + \mu)z_1 \\ \xi z_1 - \bar{\beta}mV^0\mathcal{T}(\beta_0z_3) - \mu z_2 \\ -z_3' - p(\theta)z_3 \\ -z_3(0) + \bar{\beta}[S^0 + mV^0]\mathcal{T}(\beta_0z_3) \end{pmatrix}, \quad (18)$$

where its domain is given by $D(\mathcal{B}) = D(\mathcal{A})$. Let us consider the eigenvalues of \mathcal{B} and solving the differential equation form $\mathcal{B}z = \lambda z$ for $z \in X_0$. Then, we have $z_3(\theta) = z_3(0)\pi(\theta)e^{-\lambda\theta}$. Inserting the expression of $z_3(\theta)$ into the four equation in $\mathcal{B}z = \lambda z$ and canceling $z_3(0)$. Thus we get the characteristic equation:

$$\bar{\beta}[S^0 + mV^0] \int_0^\infty \beta_0(\theta)\pi(\theta)e^{-\lambda\theta} d\theta = 1, \quad (19)$$

which has a single eigenvalue of zero when $\bar{\beta} = 1$. To find the eigenvector \widehat{v}_0 associated with eigenvalue zero, we need to solve the equation $\mathcal{B}z = 0$. We can choose $z_3(\theta) = \pi(\theta)$ and the boundary condition (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 of $\mathcal{B}z = 0$ 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 $\widehat{v}_0 = (z_1^0, z_2^0, \pi(\theta), 1)$. 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

$$\begin{aligned} \langle \Psi, \mathcal{B}z \rangle &= [-\bar{\beta}S^0\mathcal{T}(\beta_0z_3) + \mathcal{T}(\alpha z_3) - (\xi + \mu)z_1] \Psi_1 + [\xi z_1 - \bar{\beta}mV^0\mathcal{T}(\beta_0z_3) - \mu z_2] \Psi_2 \\ &\quad + \int_0^\infty [-z_3' - p(\theta)z_3] \Psi_3(\theta) d\theta + [-z_3(0) + \bar{\beta}[S^0 + mV^0]\mathcal{T}(\beta_0z_3)] \Psi_4. \end{aligned}$$

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

$$\int_0^\infty [-z_3' - p(\theta)z_3] \Psi_3(\theta) d\theta = z_3(0)\Psi_3(0) + \int_0^\infty [\Psi_3' - p(\theta)\Psi_3] z_3(\theta) d\theta.$$

Hence we have

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

which should hold for $\Psi \in D(\mathcal{B}^*)$ and $z \in D(\mathcal{B}) \subset X_0$. Thus we choose the domain of \mathcal{B}^* as

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

Therefore, the adjoint operator \mathcal{B}^* is defined on $D(\mathcal{B}^*) \subset X^* = \mathbb{R}^2 \times L^\infty(0, \infty) \times \mathbb{R}$ as follows:

$$\mathcal{B}^*\Psi = \begin{pmatrix} \xi \Psi_2 - (\xi + \mu)\Psi_1 \\ -\mu \Psi_2 \\ \Psi_3' - p\Psi_3 + (-\bar{\beta}S^0\beta_0 + \alpha)\Psi_1 - \bar{\beta}mV^0\beta_0\Psi_2 + \bar{\beta}[S^0 + mV^0]\beta_0\Psi_4 \\ \Psi_3(0) \end{pmatrix}, \quad (20)$$

with $\Psi \in D(\mathcal{B}^*)$. To find \widehat{v}_0^* , we solve the equation $\mathcal{B}^*\Psi = 0$ with $\bar{\beta} = 1$. We have $\Psi_1 = \Psi_2 = 0$. Solving the differential equation in $\mathcal{B}^*\Psi = 0$, we get $\Psi_3(\theta) = [S^0 + mV^0]\Psi_3(0) \int_\theta^\infty \beta_0(s) \frac{\pi(s)}{\pi(\theta)} ds$. Hence, we have the eigenfunction $\widehat{v}_0^* = (0, 0, \Psi_3(\theta), \Psi_3(0))$ where $\Psi_3(0) > 0$. Computing the second derivative for F with respect to z and $\bar{\beta}$, we obtain

$$D_{z\bar{\beta}}^2 F(E_0, 1)\widehat{v}_0 = \begin{pmatrix} -S^0\mathcal{T}(\beta_0\pi)z_1^0 \\ -mV^0\mathcal{T}(\beta_0\pi)z_2^0 \\ 0 \\ [S^0 + mV^0]\mathcal{T}(\beta_0\pi) \end{pmatrix}. \quad (21)$$

Therefore, one obtains

$$b = \langle D_{z\bar{\beta}}^2 F(E_0, 1)\widehat{v}_0, \widehat{v}_0^* \rangle = [S^0 + mV^0]\Psi_3(0)\mathcal{T}(\beta_0\pi) > 0. \quad (22)$$

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

$$D_{zz}^2 F(E_0, 1)[\widehat{v}_0, \widehat{v}_0] = \partial_{hk}^2 F(E_0 + (h+k)\widehat{v}_0, 1) = \begin{pmatrix} -2\mathcal{T}(\beta_0\pi)z_1^0 \\ -2m\mathcal{T}(\beta_0\pi)z_2^0 \\ 0 \\ 2[z_1^0 + mz_2^0]\mathcal{T}(\beta_0\pi) \end{pmatrix}. \quad (23)$$

Thus, we have

$$a = \langle D_{zz}^2 F(E_0, 1)[\widehat{v}_0, \widehat{v}_0], \widehat{v}_0^* \rangle = 2[z_1^0 + mz_2^0]\mathcal{T}(\beta_0\pi)\Psi_3(0). \quad (24)$$

Let us introduce the threshold

$$\Theta := z_1^0 + mz_2^0 = - \left[\left(1 + m\frac{\xi}{\mu}\right) \frac{S^0}{\xi + \mu} + \frac{m^2}{\mu} V^0 \right] \mathcal{T}(\beta_0\pi) + \left(1 + m\frac{\xi}{\mu}\right) \frac{\mathcal{T}(\alpha\pi)}{\xi + \mu}. \quad (25)$$

Hence it follows that $a < 0$ (respectively $a > 0$) if and only if $\Theta < 0$ (respectively $\Theta > 0$). According to Theorem 2.2, we obtain the following result:

Theorem 2.3. *If $\Theta > 0$, then system (1) undergoes a backward bifurcation at $(E_0, 1)$. Otherwise, when $\Theta < 0$, the system (1) exhibits a forward bifurcation at $(E_0, 1)$.*

Remark 2.1. *We see that 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 [12].*

The occurrence of a backward bifurcation in the transmission dynamics of an infectious disease where stable disease-free steady state coexists with one or more stable endemic steady states when the basic reproduction rate is smaller than unity makes it difficult to control effectively in a community. In such a scenario, the fact that the basic reproduction rate is below one becomes only a necessary but not sufficient condition for disease eradication. It is worth noting that we always have $\Theta < 0$ when the therapeutic treatment rate is zero *i.e.* $\alpha(\theta) = 0$ for all $\theta \in [0, +\infty)$. Thus, the backward bifurcation property of the model is caused by the treatment of infectious individuals. To further confirm the above, the global asymptotic stability of the steady states of the model are given below for the special case $\alpha(\theta) = 0$ (the proofs are given in [1]).

Theorem 2.4. *Assume that the therapeutic treatment is not effective (*i.e.* $\alpha(\theta) = 0$ for all $\theta \in \mathbb{R}_+$). Then the system (1) always admits a disease-free steady state E_0 which is globally asymptotically stable whenever $\mathcal{R}_0 \leq 1$. Moreover, if $\mathcal{R}_0 > 1$, the system (1) has a unique endemic steady state $E^*(\theta)$ which is globally asymptotically stable.*

3 Optimal control

3.1 Control problem statement

Because of the seriousness of infectious diseases, a time-independent vaccination and treatment policy may not be a good choice in the socio-economic context of many countries. However, it is important to know how much and when these control strategies should be applied in order to control the spread of the disease at low cost. In addition, the implementation of these control strategies remains very costly and difficult. For this purpose, we consider that the vaccination and therapeutic treatment are represented by Lebesgue measurable functions on finite time horizon $[0, T]$, denoted $\xi(t)$ and $\alpha(t, \theta)$ 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 $\theta_{\max} > 0$ for practical consideration, *i.e.* the integral function $\mathcal{T}(f) = \int_0^{\theta_{\max}} f(\theta) d\theta$. Let us introduce the set $Q = [0, T] \times [0, \theta_{\max}]$. Due to the limited resources and time available to implement these control strategies, policies must be constrained to a predefined objective. For this reason, we consider by $\mathfrak{D} := \mathcal{L}^\infty(0, T; [0, \xi_{\max}]) \times \mathcal{L}^\infty(Q; [0, \alpha_{\max}])$ the set of admissible control pair which is the space of measurable and bounded functions pair $(\xi(\cdot), \alpha(\cdot, \cdot))$ defined by $\xi(\cdot) : [0, T] \rightarrow [0, \xi_{\max}]$ and $\alpha(\cdot, \cdot) : Q \rightarrow [0, \alpha_{\max}]$. The positive constants ξ_{\max} and α_{\max} 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:

$$\begin{cases} \frac{dS}{dt} = \Lambda - \mathcal{T}(\beta i)S + \mathcal{T}(\alpha(t, \cdot))i - (\xi(t) + \mu)S \\ \frac{dV}{dt} = \xi(t)S - m\mathcal{T}(\beta i)V - \mu V \\ \frac{\partial i}{\partial t}(t, \theta) + \frac{\partial i}{\partial \theta}(t, \theta) = -[\mu + \delta(\theta) + \alpha(t, \theta)]i(t, \theta) \\ i(t, 0) = [S + mV]\mathcal{T}(\beta i). \end{cases} \quad (26)$$

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 (26), the following objective functional:

$$\mathcal{J}(\xi, \alpha) = \int_Q \chi(\theta) i(t, \theta) dt d\theta + \frac{C_1}{2} \|\xi\|_{L^2(0, T)}^2 + \frac{C_2}{2} \|\alpha\|_{L^2(Q)}^2, \quad (27)$$

where $\chi(\cdot) \in L_+^\infty(0, \theta_{\max})$, $C_1 > 0$ and $C_2 > 0$ measure the relative costs of infection and the applied control interventions. Quadratic expression of the control in (27) 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 $(\xi^*(\cdot), \alpha^*(\cdot, \cdot)) \in \mathfrak{D}$ steering the optimal trajectory $(S^*(\cdot), V^*(\cdot), i^*(\cdot, \cdot))$ satisfying the optimization problem*

$$\mathcal{J}(\xi^*, \alpha^*) = \min_{(\xi, \alpha) \in \mathfrak{D}} \mathcal{J}(\xi, \alpha). \quad (\text{OCP})$$

3.2 Existence of an optimal solution

Here, we establish the existence of a solution for optimization problem (OCP) subject to the controlled age-structured system (26).

Theorem 3.1. *Under Assumption 1.1, there exists at least one optimal control pair $(\xi^*, \alpha^*) \in \mathfrak{D}$ at which corresponds the state variable (S^*, V^*, i^*) , solution of the optimization problem (OCP).*

Proof. Since the state variables $S(\cdot)$, $V(\cdot)$, $\mathcal{T}(i)$ and controls are uniformly bounded, then it follows that $d = \inf\{\mathcal{J}(\xi, \alpha) : (\xi, \alpha) \in \mathfrak{D}\}$ is finite. Thus, there exists a minimizing sequence $(\xi_n, \alpha_n) \in \mathfrak{D}$ such that

$$d \leq \mathcal{J}(\xi_n, \alpha_n) \leq d + \frac{1}{n}. \quad (28)$$

Since the sequence (ξ_n, α_n) is bounded, there exists a subsequence still denoted (ξ_n, α_n) that converges to some (ξ^*, α^*) for the weak- \star topology of $L^\infty(0, T) \times L^\infty(Q)$. The limit $(\xi^*, \alpha^*) \in \mathfrak{D}$ since the set \mathfrak{D} is a closed convex subset of $L^\infty(0, T) \times L^\infty(Q)$ and so it is weakly closed. Let (S_n, V_n, i_n) be the state variables associated with control pair (ξ_n, α_n) . The sequence (S_n, V_n) is uniformly bounded and equicontinuous on $[0, T]$. Then, by the Arzela-Ascoli's theorem, we can extract a subsequence still denoted (S_n, V_n) which converges uniformly to the limit (S^*, V^*) in $\mathcal{C}(0, T)$. Let us denote by $\pi_{\alpha_n}(t, \theta) = e^{-\int_0^\theta [\mu + \delta(s) + \alpha_n(t - \theta + s, s)] ds}$. 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 $|\pi_{\alpha^1}(t, \theta) - \pi_{\alpha^2}(t, \theta)| \leq k\mathcal{T}(|\alpha^1(t, \cdot) - \alpha^2(t, \cdot)|)$. As consequence, we have the convergence $\pi_{\alpha_n}(t, \theta) \rightarrow \pi_{\alpha^*}(t, \theta)$ as $n \rightarrow \infty$ almost everywhere in Q . By using the method of characteristics, we get explicit expression of $i_n(t, \theta)$ -equation

$$i_n(t, \theta) = \begin{cases} i_0(\theta - t) \frac{\pi_{\alpha_n}(t, \theta)}{\pi_{\alpha_n}(t, \theta - t)} & \text{if } \theta > t \\ i_n(t - \theta, 0) \pi_{\alpha_n}(t, \theta) & \text{if } \theta < t. \end{cases}$$

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 $i^*(t, \theta)$ in $L^2(Q)$ defined as follows

$$i^*(t, \theta) = \begin{cases} i_0(\theta - t) \frac{\pi_{\alpha^*}(t, \theta)}{\pi_{\alpha^*}(t, \theta - t)} & \text{if } \theta > t \\ i^*(t - \theta, 0) \pi_{\alpha^*}(t, \theta) & \text{if } \theta < t. \end{cases}$$

Since the sequence $(\mathcal{T}(i_n))$ is bounded, it converges to $\mathcal{T}(i^*)$ 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 (26), we obtain:

$$\begin{cases} \frac{dS}{dt} = \Lambda - \mathcal{T}(\beta i^*) S^* + \mathcal{T}(\alpha(t, \cdot)) i^* - (\xi^*(t) + \mu) S^* \\ \frac{dV}{dt} = \xi^*(t) S^* - m \mathcal{T}(\beta i^*) V^* - \mu V^*. \end{cases} \quad (29)$$

Passing to the limit as $n \rightarrow \infty$ in (28), we obtain $\lim_{n \rightarrow \infty} \mathcal{J}(\xi_n, \alpha_n) = \mathcal{J}(\xi^*, \alpha^*) = d$. Hence, $((S^*, V^*, i^*), (\xi^*, \alpha^*))$ is an optimal solution of the optimization problem (OCP). This achieves the proof. \square

3.3 Optimality conditions

In this section, we use the maximum principle for general age-structured systems on a finite horizon established by Feichtinger et al.[27] to derive the first-order necessary conditions for optimality and characterize the optimal control pair solution of (OCP). To this end, we set state vector $x(t) = (S(t), V(t))^T$ to rewrite controlled system (26) in the following compact form:

$$\begin{cases} \frac{dx(t)}{dt} = G(t, x(t), q(t), \xi(t)) =: G(t) \\ \partial_t i(t, \theta) + \partial_\theta i(t, \theta) = F(t, \theta, i(t, \theta), \alpha(t, \theta)) =: F(t, \theta) \\ i(t, 0) = \psi(t, x(t), q(t)) =: \psi(t), \end{cases} \quad (30)$$

where $q(t) = (q_1(t), q_2(t))^T$ derives from the vector function $h(t, \theta) = (h_1(t, \theta), h_2(t, \theta))^T$ with $h_1(t, \theta) = \beta(\theta)i(t, \theta)$ and $h_2(t, \theta) = \alpha(t, \theta)i(t, \theta)$, and $q_j(t) = \mathcal{T}(h_j(t, \cdot))$ for $j = \{1, 2\}$. The functions $G(t) = (G_1(t), G_2(t))^T$, $F(t, \theta)$ and $\psi(t)$ represent the right hand side of the controlled system (26) for $S(t)$ -, $V(t)$ -, $i(t, \theta)$ - and $i(t, 0)$ -equations, respectively. We also define the following functional $L(t, \theta) = \chi(\theta)i(t, \theta) + \frac{C_1}{2}\xi^2(t) + \frac{C_2}{2}\alpha^2(t, \theta)$. Below ∇_z denotes differentiation with respect to state variable z . Let us introduce the adjoint functions $\mathcal{Z}_x(\cdot) = (\mathcal{Z}_S(\cdot), \mathcal{Z}_V(\cdot)) \in L^\infty(0, T; \mathbb{R}^2)$ and $\mathcal{Z}_i(\cdot, \cdot) \in L^\infty(Q; \mathbb{R})$ corresponding to the state vector $x(t)$ and variable $i(t, \theta)$ respectively. Then, from [27] the adjoint functions satisfy the following adjoint system:

$$\begin{cases} -\frac{d\mathcal{Z}_x(t)}{dt} = \mathcal{Z}_x(t)\nabla_x G(t) + \mathcal{Z}_i(t, 0)\nabla_x \psi(t) \\ -\partial_t \mathcal{Z}_i(t, \theta) - \partial_\theta \mathcal{Z}_i(t, \theta) = \nabla_i L(t, \theta) + \mathcal{Z}_i(t, \theta)\nabla_i F(t, \theta) \\ \quad + \mathcal{Z}_x(t)\nabla_q G(t)\nabla_i h(t, \theta) + \mathcal{Z}_i(t, 0)\nabla_q \psi(t)\nabla_i h(t, \theta) \\ \mathcal{Z}_i(T, \theta) = 0, \quad \mathcal{Z}_i(t, \theta_{\max}) = 0, \quad \mathcal{Z}_x(T) = (0, 0). \end{cases} \quad (31)$$

This leads to the following adjoint system:

$$\begin{cases} \frac{d\mathcal{Z}_S}{dt} = [\mathcal{T}(\beta i) + \mu]\mathcal{Z}_S + \xi[\mathcal{Z}_S - \mathcal{Z}_V] - \mathcal{Z}_i(t, 0)\mathcal{T}(\beta i) \\ \frac{d\mathcal{Z}_V}{dt} = [m\mathcal{T}(\beta i) + \mu]\mathcal{Z}_V - m\mathcal{T}(\beta i)\mathcal{Z}_i(t, 0) \\ \partial_t \mathcal{Z}_i + \partial_\theta \mathcal{Z}_i = -\chi(\theta) + [\beta(\theta)S - \alpha(t, \theta)]\mathcal{Z}_S + m\beta(\theta)\mathcal{Z}_V V \\ \quad - [S + mV]\beta(\theta)\mathcal{Z}_i(t, 0) + [\mu + \delta(\theta) + \alpha(t, \theta)]\mathcal{Z}_i \\ \mathcal{Z}_S(T) = 0, \quad \mathcal{Z}_V(T) = 0, \quad \mathcal{Z}_i(T, \theta) = 0, \quad \mathcal{Z}_i(t, \theta_{\max}) = 0. \end{cases} \quad (32)$$

From the solution $S(t)$, $V(t)$ and $i(t, \theta)$ of system (26) and the corresponding solution $\mathcal{Z}_S(t)$, $\mathcal{Z}_V(t)$ and $\mathcal{Z}_i(t, \theta)$ of adjoint system (32), we introduce the following distributed Hamiltonian functional associated with the optimization problem (OCP) by:

$$\mathcal{H}(t, \theta) := L(t, \theta) + \mathcal{Z}_S(t)G_1(t) + \mathcal{Z}_V(t)G_2(t) + \mathcal{Z}_i(t, \theta)F(t, \theta) + \mathcal{Z}_i(t, 0)\psi(t). \quad (33)$$

Applying Pontryagin's Maximum Principle introduced in [27], which consists in solving equations $\partial_\xi \mathcal{H}(t, \theta) = 0$ and $\partial_\alpha \mathcal{H}(t, \theta) = 0$, and taking into account the boundaries of each control strategies, we obtain the characterization of optimal control pair by:

$$\xi(t) = \mathcal{P}_1\left(\frac{[\mathcal{Z}_S(t) - \mathcal{Z}_V(t)]S(t)}{C_1}\right) \quad \text{and} \quad \alpha(t, \theta) = \mathcal{P}_2\left(\frac{[-\mathcal{Z}_S(t) + \mathcal{Z}_i(t, \theta)]i(t, \theta)}{C_2}\right), \quad (34)$$

where $\mathcal{P}_j(\cdot)$ denotes the projection map on \mathfrak{D} defined as follows:

$$\mathcal{P}_j(z) = \begin{cases} 0, & \text{if } z < 0 \\ z, & \text{if } 0 \leq z \leq z_{j\max} \\ z_{j\max}, & \text{if } z > z_{j\max}, \end{cases}$$

with $j \in \{1, 2\}$, $z_{1\max} = \xi_{\max}$ and $z_{2\max} = \alpha_{\max}$.

Remark 3.1. *A the final time $T > 0$, the optimal controls defined in (34) vanish, that are $\xi(T) = 0$ and $\alpha(T, \theta) = 0$ for all $\theta \in [0, \theta_{\max}]$, since the adjoint state variables are all equal to zero at time T .*

3.4 Uniqueness of solution to (OCP)

Note that the Theorem 3.1 only shows the existence of an optimal control pair, but does not guarantee its uniqueness. However using the optimal control structure (34) this uniqueness can be obtained using the procedure based on Ekeland's variational principle [33, 34]. This principle consists in generating a sequence of controls and its corresponding state variables that converge towards the optimal controls and its corresponding state variables using the convergence of a minimizing sequence of approximate objective functional. For this purpose, we embed the objective functional $\mathcal{J}(\xi, \alpha)$ into $L^1(0, T) \times L^1(Q)$ by defining the following functional:

$$\tilde{h}(\xi, \alpha) = \begin{cases} \mathcal{J}(\xi, \alpha), & \text{if } (\xi, \alpha) \in \mathfrak{D} \\ +\infty & \text{otherwise.} \end{cases} \quad (35)$$

Let us introduce the following technical lemma that we shall use to establish the uniqueness result of the optimal control pair of (OCP).

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 $(\xi, \alpha) \in \mathfrak{D} \rightarrow (S, V, i)$ is Lipschitz in the following ways:*

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

where (S^k, V^k, i^k) is a solution of (26) 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 (32) 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

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

2. The functional $\bar{h}(\dots)$ is lower semi-continuous with respect to (ξ, α) in $L^1(0, T) \times L^1(Q)$.

Proof. See Appendix A. □

Since the functional $\bar{h}(\dots)$ is lower semi-continuous in L^1 , then according to Ekeland's variational principle [34, 33], 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:

- (i) $\bar{h}(\xi_\varepsilon, \alpha_\varepsilon) \leq \inf_{(\xi, \alpha) \in \mathfrak{D}} \bar{h}(\xi, \alpha) + \varepsilon$
- (ii) $\bar{h}(\xi_\varepsilon, \alpha_\varepsilon) = \inf_{(\xi, \alpha) \in \mathfrak{D}} \{\bar{h}(\xi, \alpha) + \sqrt{\varepsilon} \|(\xi, \alpha) - (\xi_\varepsilon, \alpha_\varepsilon)\|_{L^1}\}$.

Note that, the perturbed functional $\bar{h}_\varepsilon(\xi, \alpha) = \bar{h}(\xi, \alpha) + \sqrt{\varepsilon} \|(\xi, \alpha) - (\xi_\varepsilon, \alpha_\varepsilon)\|_{L^1}$ attains its infimum at the control pair $(\xi_\varepsilon, \alpha_\varepsilon)$. From item (ii) and a similar argument as that in Subsection 3.3 give the characterization of control pair $(\xi_\varepsilon, \alpha_\varepsilon)$ by

$$\xi_\varepsilon(t) = \mathcal{P}_1 \left(\frac{[\mathcal{Z}_S^\varepsilon - \mathcal{Z}_V^\varepsilon] S^\varepsilon - \sqrt{\varepsilon} \vartheta_1^\varepsilon}{C_1} \right) \quad \text{and} \quad \alpha_\varepsilon(t, \theta) = \mathcal{P}_2 \left(\frac{[-\mathcal{Z}_S^\varepsilon + \mathcal{Z}_i^\varepsilon] i^\varepsilon - \sqrt{\varepsilon} \vartheta_2^\varepsilon}{C_2} \right), \quad (36)$$

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 $\mathcal{M}: \mathfrak{D} \rightarrow \mathfrak{D}$ 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

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

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

$$\mathfrak{C}_{3T} = K_1 \mathfrak{C}_{1T} + K_2 \mathfrak{C}_{2T}, \quad (37)$$

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 $(\xi^*, \alpha^*) \in \mathfrak{D}$ 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 $S^\varepsilon, V^\varepsilon$ 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

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

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

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

which gives passing to the limit as $\varepsilon \rightarrow 0$ the convergence $(\xi_\varepsilon, \alpha_\varepsilon) \rightarrow (\xi^*, \alpha^*)$. Since \bar{h} is lower semi-continuous and using property (i) of Ekeland's principle, the inequality $\bar{h}(\xi_\varepsilon, \alpha_\varepsilon) \leq \inf_{(\xi, \alpha) \in \mathcal{D}} \bar{h}(\xi, \alpha) + \varepsilon$ implies (as $\varepsilon \rightarrow 0$) that $\bar{h}(\xi^*, \alpha^*) \leq \inf_{(\xi, \alpha) \in \mathcal{D}} \bar{h}(\xi, \alpha)$. Therefore, we have $\bar{h}(\xi^*, \alpha^*) = \inf_{(\xi, \alpha) \in \mathcal{D}} \bar{h}(\xi, \alpha)$. We can summarize the uniqueness of optimal control pair in the following result.

Theorem 3.2. *If $\mathfrak{C}_{3T} < 1$, then there exists only one admissible optimal control pair $(\xi, \alpha) \in \mathcal{D}$ which is given by (34) solution of optimization problem (OCP).*

4 Numerical Simulations

In this section, we perform the numerical simulations that illustrate the effect of the optimal strategies on the spread of the disease. 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. We apply the semi-implicit finite difference scheme for partial differential equations based on finding solutions along characteristic curves to system (26) involved, for simplicity in numerical setup and ease of code development. In addition, the integral terms are discretized using an explicit composite trapezoidal rule. Among the practical approaches of optimization algorithms, we use the Forward-Backward sweep method [18, 19] to approximate numerically the solution of problem (OCP). The algorithm proceeds as follows. Firstly, the state variables of controlled system (26) are approximated using the forward difference method in time and backward difference method in age with an initial guess for the control. Secondly, the adjoint system (32) is solved by using the backward difference in time and forward difference in age using the solution of the state variables. After these two steps, the control function values are updated with the new values of the state and adjoint variables, thanks to equation (34) that characterize the optimal strategy. This procedure is repeated until successive values of all state, adjoint and control variables are sufficiently close, that is $\|\hat{x} - \hat{x}_{old}\| \leq \varepsilon \|\hat{x}\|$ where $\varepsilon > 0$ is the accepted tolerance fixed here at 10^{-4} ; $\hat{z} = (x, \mathcal{Z}, (\xi, \alpha))$ is the state vector of current values (state, adjoint and control variables), \hat{x}_{old} is the vector from the previous iteration and finally $\|\cdot\|$ refers to the norm of vector \hat{x} . Our numerical simulations are done for the control time $T = 50$ and with the maximal age of infection $\theta_{max} = 30$. Baseline parameters $\Lambda = 700$, $\mu = 0.04$, $m = 0.25$ and $\delta(\theta) \equiv \delta = 0.05$. Moreover, we use the age-dependent infection rate $\beta(\theta) = 0.00005(1 + \theta/(1 + 5\theta))$. The initial and boundary conditions are $S(0) = 10^4$, $V(0) = 0$ and $i_0(\theta) = 60(\theta + 20)e^{-0.4(\theta + 50)}$. Let $I(t) = \int_0^{\theta_{max}} i(t, \theta) d\theta$ be the total number of infected individuals and we further set $\xi_{max} = 0.75$ and $\alpha_{max} = 0.65$. The simulation results of optimization problem (OCP) are illustrated in Figure 1 where we assume that the cost weighting factors for the two control strategies are the same, that is $C_1 = C_2 = 50$ and in Figure 2 where we assume that the weighting factor for the cost of vaccination is lower than that of therapeutic treatment, that is $C_1 = 50$ and $C_2 = 200$.

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. 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.

5 Conclusion

In this work, we have formulated an age-structured model describing the transmission dynamics of an infectious disease and taking into account imperfect vaccination and therapeutic treatment as control measures. The model was rigorously analyzed to better understand its qualitative dynamics. These include mainly the calculation of explicit expression of basic reproduction number \mathcal{R}_0 , the study of existence and stability of steady states which shown that the disease-free steady state is locally asymptotically stable when $\mathcal{R}_0 < 1$. However, this steady state may not be globally asymptotically stable for $\mathcal{R}_0 < 1$ since the model exhibits the backward bifurcation phenomenon where the stable disease-free steady state coexists with a stable endemic steady state. It is shown that this dynamics feature (backward bifurcation) is caused by the rate of therapeutic treatment of infectious individuals. An optimal control problem is then formulated, aiming at minimizing the total

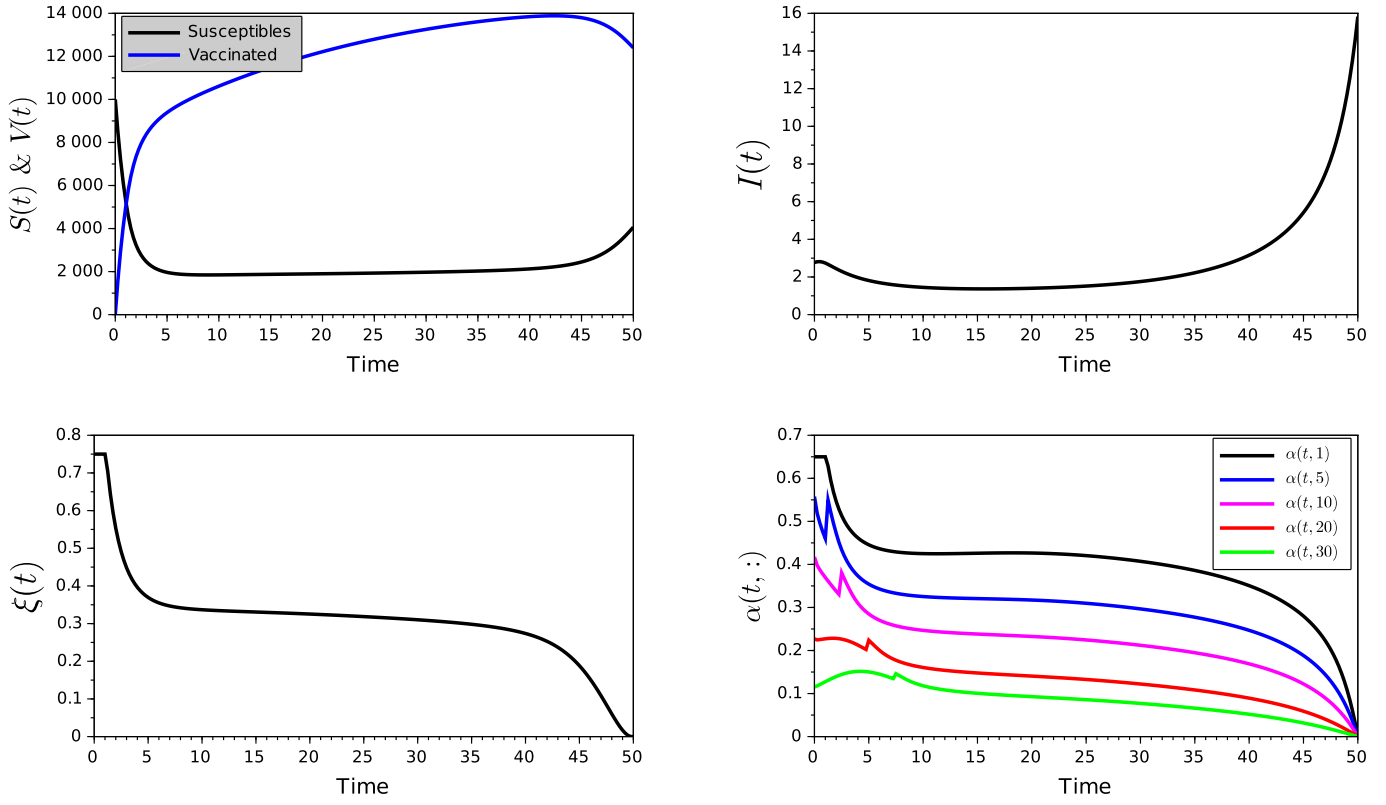


Figure 1: Simulation of system (26) with the optimal control variables for the same control costs $C_1 = C_2 = 50$.

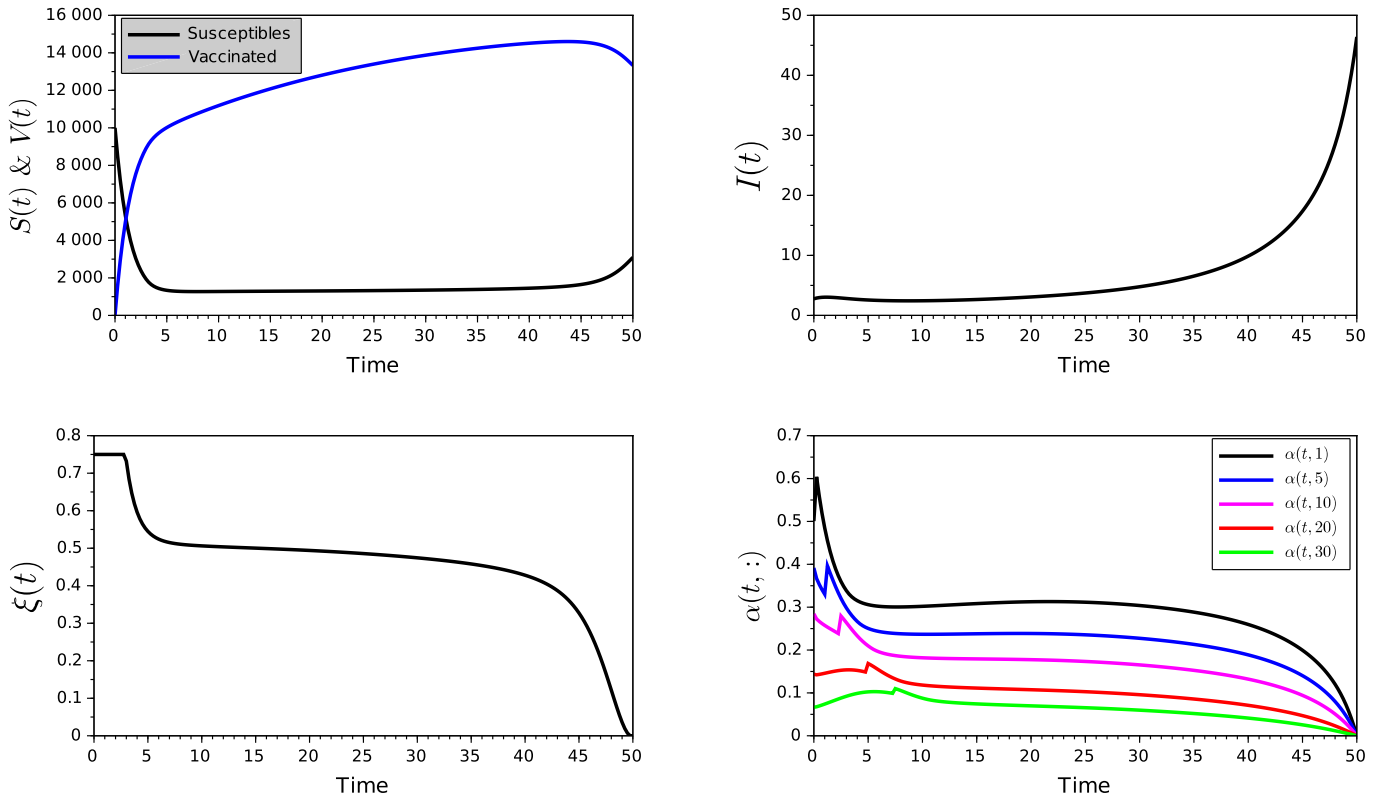


Figure 2: Simulation of system (26) with the optimal control variables for the control costs $C_1 = 50$ and $C_2 = 200$.

number of infected individuals and cost associated to vaccination and therapeutic treatment. We establish the existence of an optimal solution, which we characterize using the maximum principle for general age-structured systems. The problem is solved numerically using a Forward-Backward sweep method. Our numerical results show that optimal vaccination and therapeutic treatment can significantly reduce the prevalence of the disease and slow the spread of infection in the population. These optimal protocols are highly dependent on the cost of the interventions, and the optimal treatment depends considerably on the age of the infection.

A Proof of Lemma 3.1

- 1.(i) Let us consider the functions $h_r^{(1)}(i, \xi) = e^{-\int_r^t [\mathcal{T}(\beta i(\sigma, \cdot)) + \xi(\sigma) + \mu] d\sigma}$ and $h_r^{(2)}(i) = e^{-\int_r^t [\mathcal{T}(\beta i(\sigma, \cdot)) + \mu] d\sigma}$ 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, ξ^k) with $k \in \{1, 2\}$, the following inequalities, $|h_r^{(1)}(i^1, \xi^1) - h_r^{(1)}(i^2, \xi^2)| \leq K_1 \int_0^t |\mathcal{T}(i^1(\sigma, \cdot)) - \mathcal{T}(i^2(\sigma, \cdot))| d\sigma + K_2 \int_0^t |\xi^1(\sigma) - \xi^2(\sigma)| d\sigma$ and $|h_r^{(1)}(i^1) - h_r^{(1)}(i^2)| \leq K_3 \int_0^t |\mathcal{T}(i^1(\sigma, \cdot)) - \mathcal{T}(i^2(\sigma, \cdot))| d\sigma$. 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 (26) respectively, we obtain the following expression of state variables:

$$\begin{aligned} S(t) &= S_0 h_0^{(1)}(i, \xi) + \int_0^t [\Lambda + \mathcal{T}(\alpha(r, \cdot) i(r, \cdot))] h_r^{(1)}(i, \xi) dr; \\ V(t) &= V_0 h_0^{(2)}(i) + \int_0^t \xi(r) S(r) h_r^{(2)}(i) dr; \\ i(t, \theta) &= i_0(\theta - t) \frac{\pi_\alpha(t, \theta)}{\pi_\alpha(t, \theta - t)} \mathbb{1}_{\{\theta > t\}} + i(t - \theta, 0) \pi_\alpha(t, \theta) \mathbb{1}_{\{\theta \leq t\}} \end{aligned} \quad (38)$$

From the above representation of solutions of system (26) 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 [3, 35].

(ii) Follows like in Item (i).

2. Let $(\xi_n, \alpha_n) \rightarrow (\xi, \alpha)$ as $n \rightarrow \infty$, (S_n, V_n, i_n) and (S, V, i) be the state of system (26) 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 $(\xi_n^2, \alpha_n^2) \rightarrow (\xi^2, \alpha^2)$ almost everywhere in $[0, T] \times Q$ as $n \rightarrow \infty$. Thus, Lebesgue's dominated convergence theorem yields that $\|\xi_n\|_{L^1(0, T)}^2 \rightarrow \|\xi\|_{L^1(0, T)}^2$ and $\|\alpha_n\|_{L^1(Q)}^2 \rightarrow \|\alpha\|_{L^1(Q)}^2$ as $n \rightarrow \infty$. On the other hand, it follows that $\int_Q \chi(\theta) i_n(t, \theta) dt d\theta \rightarrow \int_Q \chi(\theta) i(t, \theta) dt d\theta$ as $n \rightarrow \infty$. By Fatou's Lemma, it follows that $\tilde{h}(\xi, \alpha) \leq \liminf_{n \rightarrow \infty} \tilde{h}(\xi_n, \alpha_n)$. Hence, the functional $\tilde{h}(\dots)$ is lower semi-continuous. This achieves the proof \square

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