

Optimal control of vaccination and treatment for an SIR epidemiological model*

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Abstract. We consider an SIR model with variable size population and formulate an optimal control problem subject to the model with vaccination and treatment as controls. Our aim is to find the optimal combination of vaccination and treatment strategies that will minimize the cost of the two control measures as well as the number of infectives. Our model analyses show that the disease free equilibrium is globally asymptotically stable if the basic reproduction number is less than unity while the endemic equilibrium exists and it is globally asymptotically stable whenever the basic reproduction number is greater than unity. We used Pontryagin's maximum principle to characterize the optimal levels of the two controls. The resulting optimality system is solved numerically. The results show that the optimal combination of vaccination and treatment strategy required to achieve the set objective will depend on the relative cost of each of the control measures. The results from our simulation is discussed.

Keywords: basic reproduction number, Pontryagin's maximum principle, optimality system, Transversality condition, optimal control, Hamiltonian

1 Introduction

Most infectious diseases could be driven towards eradication, if adequate and timely steps (e.g. vaccination, treatment, educational and enlightenment campaign, etc.) are taken in the course of the epidemic. However, many of these diseases eventually become endemic in our society due to lack of adequate policies and timely interventions to mitigate the spread of the diseases. Consequently, there is the need for proactive steps towards controlling the spread of infectious diseases, particularly those ones for which both vaccine and cure are available. Moreover, it is often cheaper to prevent the occurrence of a disease than to cure it.

For some diseases, medical treatments can be given to patients to cure the infection but there may not be vaccine to immunize susceptible individuals (e.g. Malaria and Cold). For a few other diseases, there is no cure but individuals can be vaccinated against getting infected (e.g. Polio). Nevertheless, diseases like Measles, Influenza, Cholera, and Tuberculosis all have approved medical treatment options and vaccine^[4]. Surprisingly, it remains a puzzle why diseases for which both treatment and vaccine are available are still endemic in some of our societies.

Mathematical models have become important tools in analyzing the spread and control of infectious diseases. Some examples on the use of mathematical model for the analyses of treatment and control of infectious disease can be found in [4, 5, 8–10, 15, 17], etc. For instance, Granich et al [5], based on results from the analysis and simulations of their HIV model, suggested universal HIV testing followed by an immediate

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commencement of antiretroviral therapy for those infected as a strategy to drive HIV epidemic towards elimination. Also, Wang et al. [20] proposed an improved Hepatitis B virus (HBV) model for the treatment of the disease and they claimed that their model control strategy could help reduce death due to HBV remarkably.

Optimal control theory is another area of mathematics that is used extensively in controlling the spread of infectious diseases. It is a powerful mathematical tool that can be used to make decisions involving complex biological situation^[13]. It is often used in the control of the spread of most diseases for which either vaccine or treatment is available. For example, Gaff and Schaefer [4] applied optimal control theory to a set of epidemiological models in their attempt to find the most effective control strategy to minimize the number of individuals who become infected in the course of an epidemic using both treatment and vaccination as control measures. Zaman et al. [22] did a related work to the one by Gaff and Schaefer but concentrated on an SIR model using only vaccination as their control. Also, the work by Kirschner et al. [11] used optimal control theory to determine the optimal treatment strategy for the administration of antiretroviral drug (Reverse Transcriptase Inhibitors) in HIV positive individuals. Fister and Donnelly [2] also used optimal control theory to determine the condition for the elimination of tumor cells in an individuals under treatment for Cancer.

In this paper, we address the question of how to optimally combine the vaccination and the treatment strategies such that the cost of the implementation of the two interventions is minimized while the disease is eradicated within specified period. It is important to mention here that our work is different from some of the other related works cited in this paper because the model uses bilinear incidence with a variable size total population which tends to an asymptotic limit while the objective functional minimizes the number of infectives at the end of the control period (terminal time) to a level - herd immunity level - at which the disease can naturally die out without any subsequent intervention. Note that in this paper, we shall deal with the mathematical analysis of the model as well as the optimal control of the disease. This approach is different from the ones in most of the papers cited which concentrate on either of the two parts. Also, most of the papers cited used constant population size but we are considering a variable population size (tending to a limit) which is more realistic. Moreover, we made the optimal control problem a fixed terminal time problem because most governments can not continue the implementation of the interventions indefinitely; rather they want the disease eradicated or driven below specified level within a set time frame.

The paper is organized as follows. In section 2, we present the SIR model to be investigated. In section 3, we carry out local and global stability analysis on the model equilibria. In section 4, we formulate an optimal control problem subject to the SIR model, characterize the optimal controls, and derive the optimality system using Pontryagin's maximum principle. In section 5, we solve the resulting optimality system numerically and discuss our results.

2 Model formulation

There are several variations of models for describing epidemics with different properties with respect to mortality, immunity, and time horizon^[4, 14, 19, 21, 23]. In this paper, one of these variations is examined. Precisely, we considered a standard SIR model with bilinear incidence and variable total population. Suppose S represents the number of susceptibles, I represents the number of individuals who are infected, and R represents the number of individuals who are removed due to vaccination or recovery from the disease which confers permanent immunity to reinfection. *It is important to note that this model is applicable to a class of diseases that is fatal, despite the availability of treatment and vaccination (e.g. measles).* Also, individuals can acquire immunity against the disease either through vaccination or recovery after treatment for the disease. We now consider the SIR model below:

$$\dot{S} = b - \beta SI - dS - u_1 S, \quad \dot{I} = \beta SI - u_2 I - dI - \alpha I, \quad \dot{R} = u_1 S + u_2 I - dR. \quad (1)$$

In the model, b is the recruitment rate, β is the disease transmission rate, d is the natural death rate, u_1 is the proportion of the susceptible that is vaccinated per unit time, u_2 is the proportion of the infectives that is treated per unit time, and α is the disease-induced death rate.

The total population $N(t)$ can be obtained from $N(t) = S(t) + I(t) + R(t)$ or from Eq. (2)

$$\dot{N} = b - Nd - \alpha I. \quad (2)$$

Here, it is important to note that in the absence of the disease, $N(t) \rightarrow \frac{b}{d}$.

Moreover, under the dynamics described by Eqs. (1) and (2), the region

$$\Omega = \left\{ x = (S, I, N) \in \mathbb{R}_+^3 \mid S \geq 0, I \geq 0, S + I \leq N \leq \frac{b}{d} \right\},$$

is positively invariant. Hence, the system is both mathematically and epidemiologically well-posed. Therefore, for initial starting point $x \in \mathbb{R}_+^3$; the trajectory lies in Ω . Thus, we can restrict our analysis to the region Ω .

3 Stability analysis

We consider the first two equations in Eq. (1) together with Eq. (2) for the model stability analysis, since $R(t)$ can always be obtained by the equation $R(t) = N(t) - S(t) - I(t)$. Subsequently, we will use the system below in place of Eq. (1) in our analysis:

$$\dot{S} = b - \beta SI - dS - u_1 S, \quad \dot{I} = \beta SI - u_2 I - dI - \alpha I, \quad \dot{N} = b - Nd - \alpha I. \quad (3)$$

3.1 Equilibrium solutions

The system Eq. (3) has two equilibrium solutions:

(1) a disease-free equilibrium solution

$$\mathcal{E}_0 = \left(\frac{b}{d + u_1}, 0, \frac{b}{d} \right).$$

(2) an endemic equilibrium solution

$$\mathcal{E}_1 = (S^*, I^*, N^*),$$

where

$$\begin{aligned} S^* &= \frac{u_2 + d + \alpha}{\beta}, \\ I^* &= \frac{b\beta - (u_1 + d)(u_2 + d + \alpha)}{\beta(u_2 + d + \alpha)} = (\mathcal{R}_0 - 1) \frac{u_1 + d}{\beta}, \\ N^* &= \frac{b\beta(u_2 + d) + \alpha(d + u_1)(u_2 + d + \alpha)}{d\beta(u_2 + d + \alpha)}, \\ \mathcal{R}_0 &= \frac{b\beta}{(d + u_1)(u_2 + d + \alpha)} = \left(\frac{b}{d + u_1} \right) \left(\frac{\beta}{u_2 + d + \alpha} \right). \end{aligned}$$

The basic reproduction number \mathcal{R}_0 is computed using the *next generation matrix approach* (see [1]) or by simply imposing the non-negativity condition on the infected compartment I . \mathcal{R}_0 is the average number of secondary infections produced when one single infected individual is introduced into a host population where everyone is susceptible^[1, 6, 7]. Note that our model \mathcal{R}_0 above is a product of the average number susceptible per unit time (in the presence of vaccination and possibility of natural death) and the rate of the disease transmission by an infective over the period of his/her infectivity. It is indeed a threshold quantity that helps to determine whether an outbreak of infectious disease dies out or spreads in a community. When $\mathcal{R}_0 < 1$, the disease die out without any medical interventions but when $\mathcal{R}_0 > 1$, the disease becomes endemic and this necessitates the introduction of some control measures in order to curtail the situation^[7].

3.2 Local stability of the equilibria

Theorem 1. *The disease free equilibrium is locally asymptotically stable if $\mathcal{R}_0 < 1$.*

Proof. The Jacobian matrix J of the system Eq. (3) is

$$J = \begin{pmatrix} -\beta I - d - u_1 & -\beta S & 0 \\ \beta I & \beta S - u_2 - d - \alpha & 0 \\ 0 & -\alpha & -d \end{pmatrix}.$$

Evaluating matrix J at the disease free equilibrium gives

$$J_0 = \begin{pmatrix} -d - u_1 & -\frac{\beta b}{d+u_1} & 0 \\ 0 & \frac{\beta b}{d+u_1} - u_2 - d - \alpha & 0 \\ 0 & -\alpha & -d \end{pmatrix}.$$

The matrix J_0 has eigenvalues $\lambda_1 = -d < 0$, $\lambda_2 = -(d + u_1) < 0$, $\lambda_3 = \frac{\beta b}{d+u_1} - (u_2 + d + \alpha)$. For local asymptotic stability, we require $\lambda_3 < 0$ (i.e. $\frac{\beta b}{d+u_1} - (u_2 + d + \alpha) < 0$) which is equivalent to

$$\frac{b\beta}{(d + u_1)(u_2 + d + \alpha)} = \mathcal{R}_0 < 1.$$

Thus, the disease free equilibrium \mathcal{E}_0 is locally asymptotically stable if $\mathcal{R}_0 < 1$. \square

Remark 1. The case $\mathcal{R}_0 = 1$ is a critical threshold point where the disease free equilibrium \mathcal{E}_0 loses its asymptotic stability and simply becomes (neutrally) stable. Moreover, it becomes unstable immediately $\mathcal{R}_0 > 1$ and this will lead to the existence of a stable endemic equilibrium \mathcal{E}_1 . Note that $\mathcal{R}_0 = 1$ can literally be viewed as a transcritical bifurcation point where stability is exchanged between \mathcal{E}_0 and \mathcal{E}_1 .

Theorem 2. *The endemic equilibrium is locally asymptotically stable if $\mathcal{R}_0 > 1$.*

Proof. The Jacobian matrix J evaluated at the endemic equilibrium gives

$$J_1 = \begin{pmatrix} -\mathcal{R}_0(u_1 + d) & -(u_2 + d + \alpha) & 0 \\ (\mathcal{R}_0 - 1)(u_1 + d) & 0 & 0 \\ 0 & -\alpha & -d \end{pmatrix}.$$

The eigenvalues of J_1 are $\lambda_1 = -d$,

$$\lambda_{2,3} = \frac{-\mathcal{R}_0(d + u_1) \pm \sqrt{\mathcal{R}_0^2(d + u_1)^2 - 4(\mathcal{R}_0 - 1)(d + u_2 + \alpha)}}{2}.$$

Hence, if $\mathcal{R}_0 > 1$, then $\lambda_2 < 0$ and $\lambda_3 < 0$. \square

3.3 Global stability

Theorem 3. *If $\mathcal{R}_0 \leq 1$, then the disease free equilibrium \mathcal{E}_0 is globally asymptotically stable on Ω .*

Proof. Given that $\mathcal{R}_0 \leq 1$, then there exist only the disease free equilibrium $\mathcal{E}_0 = (\bar{S}, \bar{I}, \bar{N}) = (\frac{b}{d+u_1}, 0, \frac{b}{d})$.

Considering the Lyapunov function candidate $V(S, I, N) : \mathbb{R}^3 \rightarrow \mathbb{R}^+$ defined as

$$V(S, I, N) = \omega I \quad \omega \geq 0$$

Differentiating $V(S, I, N)$ with respect to time yields

$$\dot{V} = \omega \dot{I}. \quad (4)$$

Substituting the system Eq. (3), we have

$$\begin{aligned}
 \dot{V} &= \omega(\beta SI - u_2 I - dI - \alpha I) \\
 &= \omega(\beta S - (u_2 + d + \alpha))I \\
 &\leq \omega\left(\frac{\beta b}{d+u_1} - (u_2 + d + \alpha)\right)I \quad \text{since } S \leq \bar{S} = \frac{b}{d+u_1} \\
 &= \omega(u_2 + d + \alpha)\left(\frac{\beta b}{(d+u_1)(u_2+d+\alpha)} - 1\right)I \quad \left(\text{using } \omega = \frac{1}{u_2+d+\alpha}\right) \\
 &= (\mathcal{R}_0 - 1)I \\
 &\leq 0
 \end{aligned} \tag{5}$$

It is important to note that, $\dot{V} = 0$ only when $I = 0$. However, substituting $I = 0$ into the equations for \dot{S} and \dot{N} in Eq. (3) shows that $S \rightarrow \frac{b}{d+u_1}$ and $N \rightarrow \frac{b}{d}$ as $t \rightarrow \infty$. Therefore, the maximum invariant set in $\{(S, I, N) \in \Omega \mid \dot{V} \leq 0\}$ is the singleton set $\{\mathcal{E}_0\}$. Hence, the global stability of \mathcal{E}_0 when $\mathcal{R}_0 \leq 1$ follows from LaSalle's invariance principle (see [12, 19]). \square

Theorem 4. *If $\mathcal{R}_0 > 1$, then there exist an endemic equilibrium \mathcal{E}_1 (in addition to the disease-free equilibrium) and it is globally stable.*

Proof. Given that $\mathcal{R}_0 > 1$, then the existence of the endemic equilibrium is guaranteed.

Considering a Lyapunov function candidate

$$V(S, I, N) = \frac{1}{2}(N - N^*)^2 + \frac{1}{2}(S - S^*)^2 + \epsilon \left(I - I^* - I^* \ln \left(\frac{I}{I^*} \right) \right) \quad \epsilon \geq 0. \tag{6}$$

The derivative of V along the solution curve of the system Eq. (3) yields

$$\dot{V} = (N - N^*)\dot{N} + (S - S^*)\dot{S} + \epsilon \left(1 - \frac{I^*}{I} \right) \dot{I}. \tag{7}$$

Substituting the model Eq. (3) into the relation Eq. (7) gives

$$\dot{V} = (N - N^*)(b - dN - \alpha I) + (S - S^*)(b - \beta SI - dS - u_1 S) + \epsilon \left(1 - \frac{I^*}{I} \right) (\beta SI - u_2 I - dI - \alpha I). \tag{8}$$

We recall that, at the endemic equilibrium, we have

$$\begin{aligned}
 b &= \beta S^* I^* + dS^* + u_1 S^* = dN^* + \alpha I^*, \\
 \beta S^* I^* &= (u_2 + d + \alpha) I^* = b - dS^* - u_1 S^*.
 \end{aligned} \tag{9}$$

Using the equilibrium condition Eq. (9) above, Eq. (8) becomes

$$\begin{aligned}
 \dot{V} &= (N - N^*)(b - dN - \alpha I) + (S - S^*)(b - \beta SI - dS - u_1 S) + \frac{\epsilon}{I} (I - I^*)(\beta SI - u_2 I - dI - \alpha I) \\
 &= (N - N^*)(dN^* + \alpha I^* - dN - \alpha I) + (S - S^*)(\beta S^* I^* + dS^* + u_1 S^* - \beta SI - dS - u_1 S) \\
 &\quad + \frac{\epsilon}{I} (I - I^*)(\beta SI - \beta S^* I) \\
 &= -d(N - N^*)^2 + \alpha(N - N^*)(I^* - I) - (u_1 + d)(S - S^*)^2 + \beta(S - S^*)(S^* I^* - SI) \\
 &\quad + \beta \epsilon (I - I^*)(S - S^*) \\
 &= -d(N - N^*)^2 - \alpha(N - N^*)(I - I^*) - (u_1 + d)(S - S^*)^2 \\
 &\quad + \beta S^*(I^* - I)(S - S^*) - \beta I(S - S^*)^2 + \beta \epsilon (I - I^*)(S - S^*) \\
 &= -d(N - N^*)^2 - (u_1 + d + \beta I)(S - S^*)^2 - \alpha(N - N^*)(I - I^*) \\
 &\quad + \beta(\epsilon - S^*)(S - S^*)(I - I^*) \quad \text{setting } \epsilon = S^*, N \leq N^*, I \leq I^* \\
 &\leq 0
 \end{aligned} \tag{10}$$

We note that $\dot{V} = 0$ holds only at \mathcal{E}_1 . By LaSalle's invariant principle [12], every solution to the system Eq. (3), with the initial conditions in Ω , approaches \mathcal{E}_1 as $t \rightarrow \infty$ if $\mathcal{R}_0 > 1$. Hence, the endemic equilibrium \mathcal{E}_1 is globally asymptotically stable in Ω if $\mathcal{R}_0 > 1$. \square

4 Optimal control

We define our objective functional as

$$\mathbb{Z} = \min_{u_1, u_2} I(T) + \frac{1}{2} \int_0^T (C_1 u_1^2 + C_2 u_2^2) dt, \quad (11)$$

subject to system of Eq. (3) with appropriate states initial conditions while the control set \mathbb{U} is Lebesgue measurable and it is defined as

$$\mathbb{U} = \{(u_1(t), u_2(t)) \mid 0 \leq u_1 \leq u_{1max} \leq 1, 0 \leq u_2 \leq u_{2max} \leq 1, t \in [0, T]\}, \quad (12)$$

where C_1 and C_2 are the relative weights attached to the cost of vaccination and treatment respectively, u_{1max} is maximum attainable value for u_1 and u_{2max} is maximum attainable value for u_2 .

The control u_1 is the proportion of the susceptible that is vaccinated per unit time while the control u_2 is the proportion of the infectives that is treated per unit time. Thus, u_1 and u_2 lie between 0 and 1 while u_{1max} and u_{2max} will depend on the amount of resources available to implement each of the control measures. The weights C_1 and C_2 will depend on the relative importance of each of the control measures in mitigating the spread of the disease as well as the cost (human effort, material resources, infrastructural resources, etc.) of implementing each of the control measures per unit time. Thus, the terms $C_1 u_1^2$ and $C_2 u_2^2$ describe the costs associated with vaccination and treatment respectively. The vaccination cost could include the cost of the vaccine, the vaccine storage cost, other related overheads, etc. The treatment cost could include the cost of the medical tests and diagnosis, drug cost, hospitalization cost, etc. (see [4, 16, 22]).

Here, we used quadratic for the cost as estimate for nonlinear function based on the assumption that the costs take nonlinear form. The term $I(T)$ is so constructed as a terminal cost because it seems more realistic to minimize the number of infective at end of the implementation of the control programme than at each time unit within the implementation period. This will also be economical if the minimum level of the infective attained at the terminal time is such that will lead to the extinction of the disease even if the intervention is stopped at that time.

Our goal is to characterize an optimal control $(u_1^*, u_2^*) \in \mathbb{U}$ which minimizes the cost of the vaccination and the cost of the treatment over the specified time interval as well as minimizes the number of infectives at terminal time.

4.1 Characterization of the optimal control pair

We shall now characterize the optimal control pair (u_1^*, u_2^*) , which accomplish the set objectives, and the corresponding states (S^*, I^*) . The existence of an optimal control pair is guaranteed by the compactness of the control and the states spaces, and the convexity in the problem based on Theorem 4.1 of Chapter III in Fleming and Rishel [3]. The non-trivial requirement from Fleming and Rishel's theorem are listed below:

(1) The set of all solutions to system Eq. (3) with corresponding control functions in \mathbb{U} (as given in Eq. (12)) is nonempty.

(2) The state system can be written as a linear function of the control variables with coefficients dependent on time and the state variables.

(3) The integrand L in Eq. (11) is convex on \mathbb{U} and additionally satisfies

$$L(t, S, I, u_1, u_2) \geq k_1 |(u_1, u_2)|^\delta - k_2 \text{ where } k_1 > 0, k_2 > 0, \text{ and } \delta > 1.$$

We applied Pontriagin's maximum principle [18] to obtain the following results.

Theorem 5. If u_1^*, u_2^* is an optimal control pair corresponding to states S^* and I^* which minimizes the objective functional Eq. (11), then there exist an adjoint variables λ_1 and λ_2 which satisfy:

$$\begin{aligned} \lambda_1' &= - \frac{\partial \mathbb{H}}{\partial S} = \lambda_1(\beta I + d + u_1) - \lambda_2 \beta I, \\ \lambda_2' &= - \frac{\partial \mathbb{H}}{\partial I} = \lambda_1 \beta S - \lambda_2(\beta S - u_2 - d - \alpha). \end{aligned} \quad (13)$$

and the transversality conditions

$$\lambda_1(T) = 0, \quad \lambda_2(T) = 1. \quad (14)$$

Furthermore, we obtain the optimal control pair (u_1^*, u_2^*) as

$$u_1^* = \min \left\{ \max\left(0, \frac{\lambda_1 S}{C_1}\right), u_{1\max} \right\}, \quad u_2^* = \min \left\{ \max\left(0, \frac{\lambda_2 I}{C_2}\right), u_{2\max} \right\}. \quad (15)$$

Proof. We form the Hamiltonian \mathbb{H} as below:

$$\mathbb{H} = \frac{1}{2}C_1 u_1^2 + \frac{1}{2}C_2 u_2^2 + \lambda_1(b - \beta SI - dS - u_1 S) + \lambda_2(\beta SI - u_2 I - dI - \alpha I). \quad (16)$$

Using Pontriagin's maximum principle [18], we derive the system Eq. (13) from

$$\lambda_1' = -\frac{\partial \mathbb{H}}{\partial S}, \quad \lambda_2' = -\frac{\partial \mathbb{H}}{\partial I}. \quad (17)$$

The transversality conditions give $\lambda_1(T) = 0$ and $\lambda_2(T) = 1$ as in Eq. (14) since $S(T)$ is free at the terminal time T while $I(T)$ occur in the objective functional as a terminal cost^[13, 16]. The Hamiltonian is maximized with respect to the controls at the optimal control pair, thus we differentiate \mathbb{H} with respect to u_1 and u_2 in the interior of \mathbb{U} to obtain the optimality conditions that follows:

$$\frac{\partial \mathbb{H}}{\partial u_1} = C_1 u_1 - \lambda_1 S = 0, \quad \frac{\partial \mathbb{H}}{\partial u_2} = C_2 u_2 - \lambda_2 I = 0. \quad (18)$$

Substituting $u_1 = u_1^*$ and $u_2 = u_2^*$ and solving for the optimal control pair (u_1^*, u_2^*) , we obtain

$$u_1^* = \frac{\lambda_1 S}{C_1}, \quad u_2^* = \frac{\lambda_2 I}{C_2}, \quad (19)$$

Now, We impose the bounds $0 \leq u_1 \leq u_{1\max}$ and $0 \leq u_2 \leq u_{2\max}$ on the controls to yield Eq. (15) as required. \square

Therefore, our resulting optimality system is:

$$\begin{cases} \dot{S} = b - \beta SI - dS - u_1^* S, \\ \dot{I} = \beta SI - u_2^* I - dI - \alpha I, \\ S(0) = S_0, \quad I(0) = I_0, \\ \dot{\lambda}_1 = \lambda_1(\beta I + d + u_1^*) - \lambda_2 \beta I, \\ \dot{\lambda}_2 = \lambda_1 \beta S - \lambda_2(\beta S - u_2^* - d - \alpha), \\ \lambda_1(T) = 0, \quad \lambda_2(T) = 1, \end{cases} \quad (20)$$

Remark 2. It is important to note that we do not include the $N(t)$ state equation and its corresponding adjoint equation in the Hamiltonian above because $N(t)$ does not appear explicitly in the objective functional and in the first two states equations. Therefore, this reduction will not affect our result in anyway.

5 Simulation results and discussion

Numerical solutions to the optimality system Eq. (20) are executed using MATLAB with the following realistic hypothetical parameter values and initial conditions:

$$b = 0.03, \quad d = 0.02, \quad \alpha = 0.1, \quad \beta = 0.75, \quad S(0) = 0.95, \quad I(0) = 0.05, \quad N(0) = 1.0.$$

It is important note that the parameters values above were chosen such that the total population never goes into extinction and it yields $\mathcal{R}_0 > 1$ in the absence of vaccination and treatment (i.e. when $u_1 = 0$ and $u_2 = 0$).

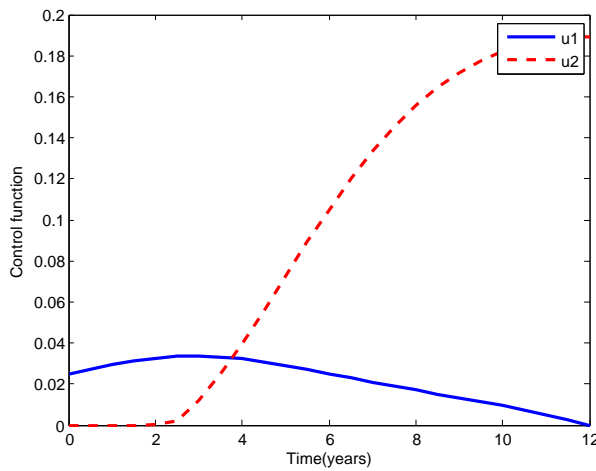


Fig. 1. The control functions u_1 and u_2 for $C_1 = 4, C_2 = 1$

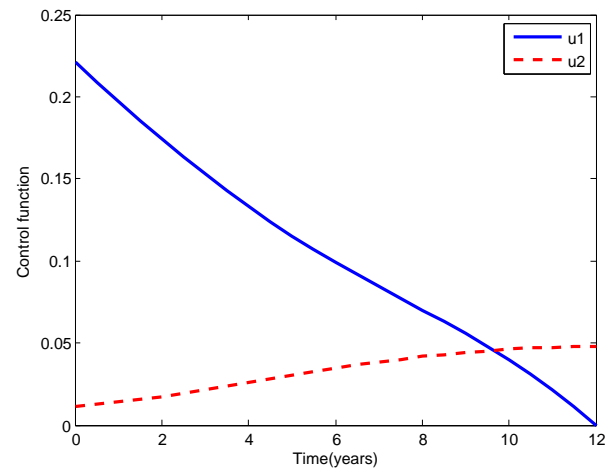


Fig. 2. The control functions u_1 and u_2 for $C_1 = 1, C_2 = 4$

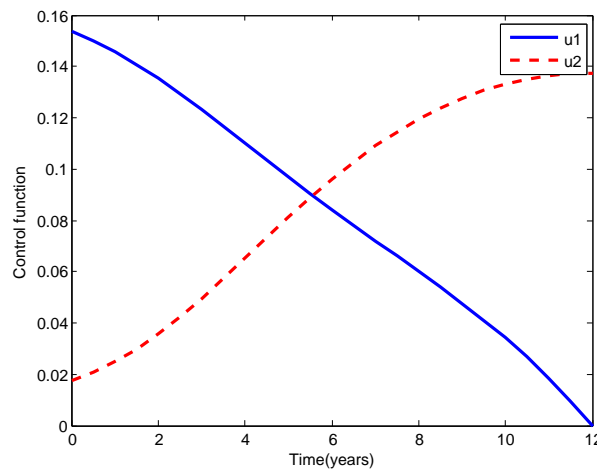


Fig. 3. The control functions u_1 and u_2 for $C_1 = 1, C_2 = 1$

We used the forward-backward sweep scheme; starting with an initial guess for the optimal controls u_1 and u_2 . The state system is solved forward in time while the solution to the states together with the initial guess for the controls are then used to solve the co-state system backward in time. Subsequently, we determine controls u_1 and u_2 as given in Eq. (19) while the iteration continues until convergence is achieved. The results from our simulations are displayed in the figures that follow:

In Figs. 1, 2, and 3; we show the the profile of the control functions u_1 and u_2 with weights ($C_1 = 4, C_2 = 1$), ($C_1 = 1, C_2 = 4$), and ($C_1 = 1, C_2 = 1$) respectively. We observe that for optimality, we mostly use less of the control with the bigger weight and more of the control with the lesser weight. However, in the case where both weights are equal, initially we have to apply more of the vaccination control to reduce the susceptible to below certain threshold, afterwhich we gradually start to apply more of the treatment control with less of the vaccination.

In Figs. 4, 5, and 6, we display numerical solution for our model S and I compartments with control weights ($C_1 = 4, C_2 = 1$), ($C_1 = 1, C_2 = 4$), and ($C_1 = 1, C_2 = 1$) respectively. The results show that applying more of the treatment control does not appreciably bring down the number of infected individuals which peaks at about 0.4 thousand as compared to the case when we applied more of the vaccination which makes the infected compartment to peak at about 0.2 thousand. However, the peak attained in the latter case does not seems to be significantly different from the case when the two controls are equally weighted (see Fig. 6).

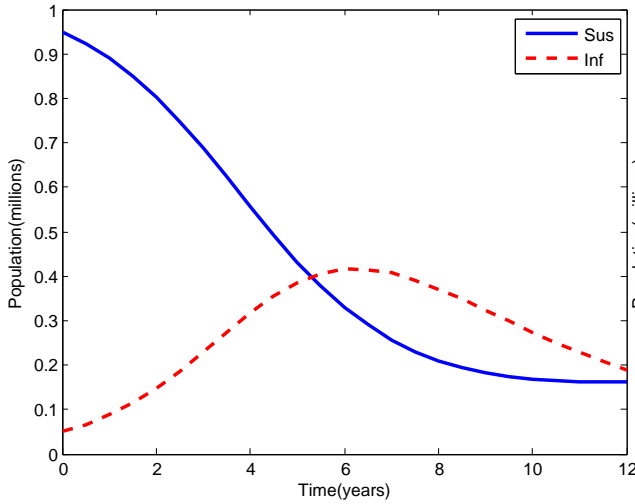


Fig. 4. The population of S and I for $C_1 = 4, C_2 = 1$

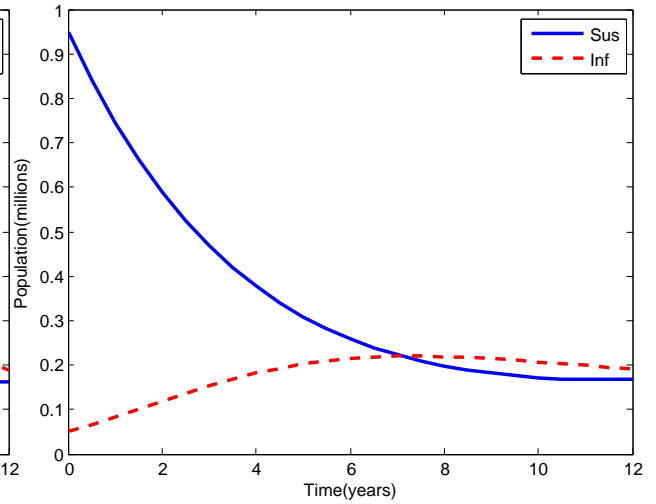


Fig. 5. The population of S and I for $C_1 = 1, C_2 = 4$

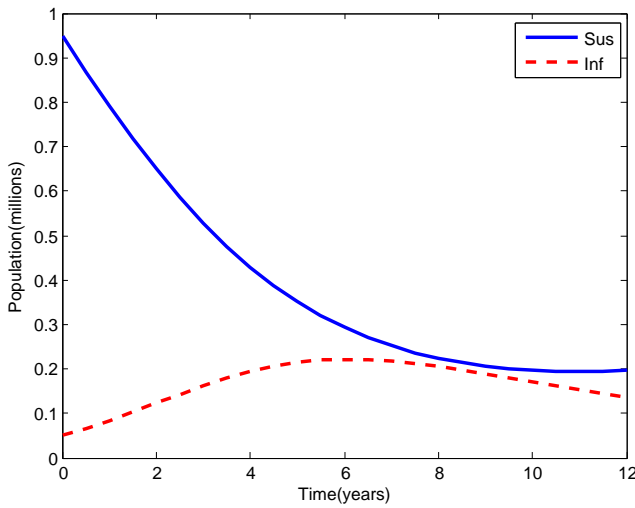


Fig. 6. The population of S and I for $C_1 = 1, C_2 = 1$

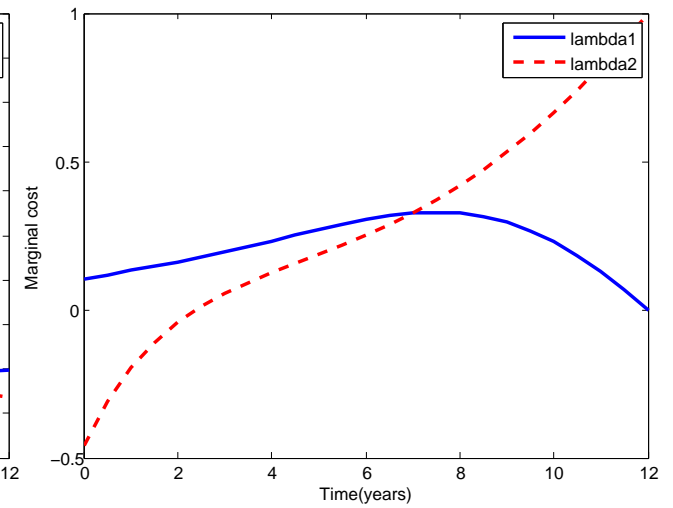


Fig. 7. The marginal cost λ_1 and λ_2 for $C_1 = 4, C_2 = 1$

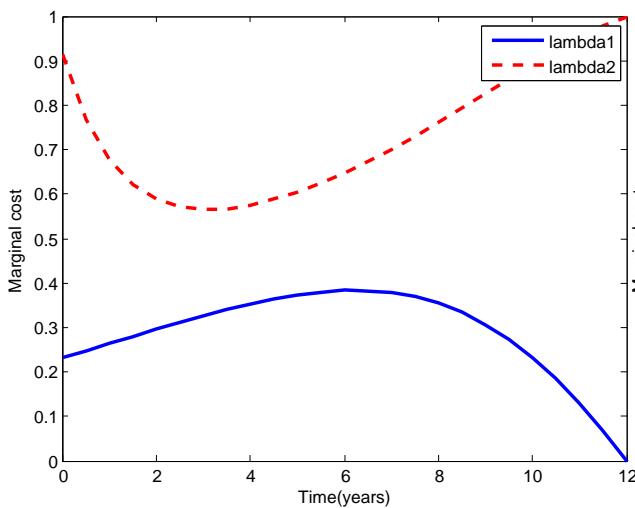


Fig. 8. The marginal cost λ_1 and λ_2 for $C_1 = 1, C_2 = 4$

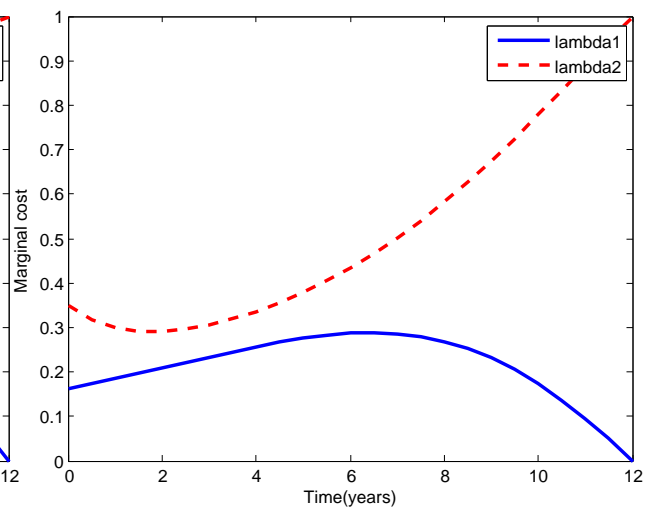


Fig. 9. The marginal cost λ_1 and λ_2 for $C_1 = 1, C_2 = 1$

In Figs. 7, 8, and 9; we show the numerical solutions for the adjoint variables λ_1 and λ_2 . In the case with $C_1 = 4$ and $C_2 = 1$, we found that the marginal cost for the vaccination and the treatment increases within the first few years, though the increase in the latter is more significant. However, after the intersection of the two costs, the marginal cost for the vaccination begins to fall while the marginal cost for the treatment continues to increase. Since, the marginal cost of the treatment continues to increase over time, this strategy may not be too economical to adopt except it is absolutely unavoidable. In the case with $C_1 = 1$ and $C_2 = 4$, the marginal cost for vaccination increases moderately in first few years after which it starts to fall significantly while the marginal cost for the treatment decreases significantly in the first few years after which it starts to increase. However, the marginal cost for the vaccination and the treatment do not overlap, rather the marginal cost for the treatment is always higher than the marginal cost for the vaccination. This implies that it will be more economical to expand the vaccination coverage than to expand the treatment coverage. Nevertheless, the case with $C_1 = 1$ and $C_2 = 1$; showed similar behaviour as that of the case with $C_1 = 1$ and $C_2 = 4$.

6 Concluding remarks

In this paper, we studied optimal combination of vaccination and treatment strategies for driving infectious diseases with cure and vaccine towards eradication within a specified period. We considered an SIR model with varying size population using vaccination and treatment as control measures. We established the conditions for the local and global stability of the model equilibria. We used Pontryagin's maximum principle to characterize the controls and derive the optimality system. Numerical simulations of the resulting optimality system showed that, in the case where it is more expensive to vaccinate than to treat, resources should be invested in treating the disease until the disease prevalence begins to fall. This option, however, does not reduce the number of susceptibles quickly enough, thus resulting in an overall increase in the infected population. On the other hand, if it is more expensive to treat than to vaccinate, then more resource must be put into vaccination. This latter case resulted in a rapid reduction in the susceptibles as well as an appreciable reduction in the number of infectives. Nevertheless, the case where both measures are equally expensive showed that the optimal way to drive the epidemic towards eradication within the specified period is to use more of the vaccination control and less of the treatment control initially to drive the epidemic to below certain threshold after which we can then apply less of vaccination control and more of the treatment control.

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