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Control of Infectious Diseases through Vaccination and Treatment

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Abstract. *In this study, an SVIR compartmental model is proposed and analysed which accounts for the effect of two stage vaccination (vaccination of new born and immigrants, and vaccination of susceptible population) and treatment. Stability of steady states has been established. Disease free steady state has been found globally asymptotically stable when $\mathcal{R}_0$ is less than unity. Transcritical bifurcation has been found at $\mathcal{R}_0 = 1$. For $\mathcal{R}_0 > 1$ a unique endemic steady state exists and it is found to be globally asymptotically stable under certain conditions. Further, an optimal control problem is proposed considering vaccinations (both) and treatment as controls. Existence of optimal controls is established which minimize the total cost incurred and characterized analytically using Pontryagin's Maximum Principle. Comparative study has been performed for following control strategies: Strategy A- Implementation of both the vaccinations, Strategy B- Implementation of vaccination of new born and immigrants with treatment, Strategy C- Implementation of vaccination of susceptible population with treatment and Strategy D- Combination of all the policies. Our study accentuates that Strategy A is expensive (with respect to defined cost) with a significant impact on vaccinated population. Strategy B and Strategy C work well and better than the Strategy A, and are found very effective in reducing the infective population with high prevalence of vaccinated population and minimum cost. Strategy D is found highly effective and economically feasible than all other applied control strategies and keeps a tab on infective population.*

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Key words: Stability analysis; Transcritical bifurcation; Vaccination; Treatment; Optimal control.

1 Introduction

A large number of mathematical models have been proposed after the pioneer work of Kermack and McKendrick [1] to analyse and understand the dynamics of diseases so that suitable control interventions can be devised to curtail or control the spread of the disease (one can see in [2, 3, 4] and few of the recent works in [5, 6, 7, 8, 9, 10]). Some important control interventions such as vaccination, treatment, quarantine and isolation, etc. have been studied to control the disease transmission and prevalence in [9, 10, 11, 12, 13]. Among them, vaccination and treatment have been found to be very useful due to their own practical advantages. Note that both the interventions complement each other as vaccination reduces the number of susceptible which in turn will reduce the burden on treatment and similarly treatment will reduce the infective and that will reduce the number of people to be vaccinated. There are about 25 diseases that can be prevented by WHO approved available vaccination [14]. In the following we are presenting some of the works related to our proposed model.

Vaccination as an intervention has been used by many researchers to control the spread of influenza, measles *etc*., [5, 7, 8, 10, 15]. In [5], Alexander *et al*. proposed an SVIR model for the dynamics of influenza where they considered the vertical growth for infective population and assumed that implemented vaccine does not confer 100% immunity to the population. They observed that influenza spread can be controlled if the vaccine efficacy and vaccination rate crosses a threshold quantity. They also noted that model system exhibits bistable equilibria under certain parametric conditions. Effect of continuous and impulsive vaccination has been studied by Liu *et al*. [7] in an SVIR model. They observed that if the basic reproduction number of the model system is below one then disease dies out otherwise it persists in both cases. They also noted that vaccination is helpful in reducing the disease burden but with certain condition on the basic reproduction number. In [8], Qiu *et al*. proposed and analysed a model for influenza dynamics using vaccination and antiviral treatment to control the spread. They determined two threshold parameters that measure persistence or extinction of disease.

In 2013, Hu *et al*. proposed following SVIR model of influenza [16]:

$$\begin{aligned}
\frac{dS}{dt} &= k(1-p) - (u+\mu)S - \beta SI,\\
\frac{dV}{dt} &= pk + uS - \mu V,\\
\frac{dI}{dt} &= \beta SI - (\mu + d + r)I,\\
\frac{dR}{dt} &= rI - \mu R.
\end{aligned} \tag{1.1}$$

Here S, V, I and R are the densities of susceptible, vaccination, infective and removed populations, respectively. Parameter k is the recruitment rate of new individuals (*i.e*. new recruits may include new born and immigrants). Parameters p and u are vaccination rate of the newly recruited and susceptible individuals respectively, with $p, u \in [0,1]$ *i.e*. a proportion of newly recruited and susceptible individuals move to vaccination class. Parameter μ is the natural death rate and d represents disease caused death rate. r is the recovery rate and β is the disease transmission rate when infective population make contacts with susceptible one. For the detailed description of these parameters see [16].

They [16] observed that the disease will die out if the basic reproduction number is less than unity whereas disease will persist if it is greater than unity. They further formulated an optimal control problem to investigate an optimal way for vaccination of susceptible population. It is important to note here that they have assumed that influenza vaccination confers full immunity to vaccinated population *i.e*. vaccine efficacy is of 100% and the vaccinated population *will not* take part in the disease transmission. As per the CDC report, there is no vaccine of flu or influenza with 100% efficacy level and does not confer full immunity

[17]. Thus, in this study, we assume that vaccination does not confer the full immunity *i.e*. the level of vaccine efficacy is not 100%. Also, during the period to get immunity, vaccinated population can make contact with infected individuals and can contract disease with rate β_1 with $\beta_1 \leq \beta$ [7]. Once, vaccinated individuals obtain vaccine-induced immunity during or after the vaccination process, they will move to the removed class with the rate γ [7]. In [16], authors considered only natural recovery with rate r. Practically, only natural recovery can not reduce the disease prevalence significantly. Thus, we consider an additional recovery to infective population via treatment with rate u_3. These treated individuals will move to the removed class after treatment. The corresponding proposed compartmental model is given as follows:

$$\begin{aligned}
\frac{dS}{dt} &= k(1-u_1) - \mu S - \beta SI - u_2 S, \\
\frac{dV}{dt} &= ku_1 + u_2 S - \beta_1 VI - \gamma V - \mu V, \\
\frac{dI}{dt} &= \beta SI + \beta_1 VI - (r+d+\mu)I - u_3 I, \\
\frac{dR}{dt} &= \gamma V + rI + u_3 I - \mu R
\end{aligned} \tag{1.2}$$

with initial conditions $S(0) \geq 0, V(0) \geq 0, I(0) \geq 0$ and $R(0) \geq 0$. Here all parameters are taken to be non-negative. Here, we denote vaccination rate p by u_1 and u by u_2 and have same meaning as in the model (1.1).

The rest of the paper is divided into two parts. In the first part, a temporal dynamical analysis of the proposed model system (1.2) has been performed. In the second part, an optimal control problem, using vaccinations and treatment as controls, corresponding to the model (1.2) is proposed and analysed to minimize the total cost incurred due to applied control interventions as well as the disease burden. Finally we conclude our findings.

2 Part - I : Model analysis

In this section, we present the stability analysis of the steady states for the model system (1.2). Since our model involves human population, therefore the positivity of the populations in different compartments must be guaranteed. Here, first we shall show the positivity and boundedness of the populations. Note from the model system:

$$\left.\frac{dS}{dt}\right|_{S=0,V>0,I>0,R>0} = k(1-u_1) > 0, \quad \left.\frac{dV}{dt}\right|_{V=0,S>0,I>0,R>0} = ku_1 + u_2 S > 0,$$

$$\left.\frac{dI}{dt}\right|_{I=0,S>0,V>0,R>0} = 0, \quad \left.\frac{dR}{dt}\right|_{R=0,S>0,V>0,I>0} = \gamma V + (r+u_3)I \geq 0.$$

It is easy to see that all the above rates are non-negative on bounding planes of the non-negative cone of $\mathbb{R}^4$. Thus if we begin in the interior of this cone, we shall always remain in this cone as the direction of vector field is inward on all the bounding planes of the cone. Hence the positivity of populations is ensured.

Again, from the model equations we have $S+V+I+R \leq \frac{k}{\mu}$. Hence the biological feasible region (which is a positively invariant set of the model system (1.2)) is given as

$$\Omega = \left\{ (S,V,I,R) \in \mathbb{R}^4_+ : 0 \leq S,\, V,\, I,\, R \leq \frac{k}{\mu} \right\}.$$

2.1 Existence of the disease free steady state and the basic reproduction number

Equating the rate equations of the model system (1.2), we find that the disease free steady state $E_0 = (S_0, V_0, 0, \frac{\gamma V_0}{\mu})$, where $S_0 = \frac{k(1-u_1)}{\mu+u_2}$ and $V_0 = \frac{ku_1+u_2S_0}{\gamma+\mu}$ always exists. Further using the next generation matrix method [18], the basic reproduction number is given as,

$$\mathcal{R}_0 = \frac{\beta S_0 + \beta_1 V_0}{r+\mu+d+u_3}.$$

2.2 Stability of the disease free steady state

Theorem 1. The disease free steady state E_0 is locally asymptotically stable when $\mathcal{R}_0 < 1$ and unstable when $\mathcal{R}_0 > 1$.

Proof. The proof of this theorem follows from Theorem 2 of Van den Driessche *et al*. [18].

Theorem 2. The disease free steady state E_0 is globally asymptotically stable when $\mathcal{R}_0 < 1$.

Proof. To show the global stability of disease free steady state E_0, we use the method explained in [19]. Choosing $X = (S,V,R)^T$ and $Y = (I)$ so that $E_0 = (X_0, 0)$ is the disease free steady state of the model system (1.2) with $X_0 = (S_0, V_0, R_0)$. Define,

$$\begin{aligned} F(X,Y) &= (k(1-u_1) - \beta SI - (\mu+u_2)S,\ ku_1 + u_2S - \beta_1 VI - (\mu+\gamma)V,\ \gamma V + (r+u_3)I - \mu R)^T, \\ G(X,Y) &= (\beta SI + \beta_1 VI - (r+\mu+d+u_3)I). \end{aligned}$$

The global asymptotic stability of E_0 is guaranteed if the following two conditions are satisfied:

(H_1) For the system $\frac{dX}{dt} = (k(1-u_1) - \beta SI - (\mu+u_2)S,\ ku_1 + u_2S - \beta_1 VI - (\mu+\gamma)V,\ \gamma V + (r+u_3)I - \mu R)^T$, X_0 is globally asymptotically stable,

(H_2) $G(X,Y) = \mathcal{A}I - \hat{G}(X,Y)$, here $\hat{G}(X,Y) = (\beta(S_0 - S) + \beta_1(V_0 - V))I \geq 0$ as $S \leq \frac{k(1-u_1)}{\mu+u_2}$ and $V \leq \frac{k(u_1\mu+u_2)}{(\mu+u_2)(\mu+\gamma)}$ for $(X,Y) \in \Omega$, where matrix $\mathcal{A} = (\beta S_0 + \beta_1 V_0 - (r+d+\mu+u_3))$ is a scalar M-matrix and Ω is the biologically feasible region of the model system (1.2).

Note, when the basic reproduction number $\mathcal{R}_0 < 1$, condition (H_2) is satisfied. Further, for $I = Y = 0$, one can easily see from the first component of the system $\frac{dX}{dt}$ that as $t \to \infty$, $S \to S_0$ and similarly $V \to V_0$ and $R \to R_0$ as $t \to \infty$. Hence X_0 is globally asymptotically stable as $X \to X_0$ whenever $t \to \infty$. Thus condition (H_1) is fulfilled. Hence the theorem.

2.3 Existence of endemic steady states

Equating the right hand side of the rate equations of the model system (1.2) to zero, we find that it has a unique endemic steady state $E_* = (S_*, V_*, I_*, R_*)$. The components of E_* are $S_* = \frac{k(1-u_1)}{\beta I_* + \mu + u_2}$, $V_* = \frac{ku_1+u_2S_*}{\beta_1 I_* + \mu + \gamma}$, $R_* = \frac{(r+u_3)I_* + \gamma V_*}{\mu}$, and I_* is the positive root of equation

$$f(I_*) = A_1 I_*^2 + A_2 I_* + A_3 = 0.$$

The coefficients are $A_1 = \beta\beta_1(r+\mu+d+u_3)$, $A_2 = (r+\mu+d+u_3)(\beta_1(\mu+u_2) + \beta(\mu+\gamma)) - \beta\beta_1 k$, and $A_3 = (r+\mu+d+u_3)(\mu+\gamma)(\mu+u_2) - \beta_1 k u_1(\mu+u_2) - \beta_1 k u_2(1-u_1) - \beta k(1-u_1)(\mu+\gamma) \equiv (r+\mu+d+u_3)(\mu+\gamma)(\mu+u_2)\left(1 - \frac{\beta S_0 + \beta_1 V_0}{r+\mu+d+u_3}\right) \equiv (r+\mu+d+u_3)(\mu+\gamma)(\mu+u_2)(1-\mathcal{R}_0)$.

Thus for $\mathcal{R}_0 > 1$ quadratic equation $f(I_*) = 0$ always has a unique positive root $I_* = \frac{-A_2 + \sqrt{A_2^2 - 4A_1A_3}}{2A_1}$, and hence there exists a unique endemic steady state E_*.

2.4 Stability of unique endemic steady state

In this section we discuss the stability of endemic steady state E_* using eigen values of the Jacobian matrix. The jacobian matrix evaluated at E_*, is given as:

$$J_{E_*} = \begin{pmatrix} -\beta I_* - \mu - u_2 & 0 & -\beta S_* & 0 \\ u_2 & -\beta_1 I_* - \mu - \gamma & -\beta_1 V_* & 0 \\ \beta I_* & \beta_1 I_* & \beta S_* + \beta_1 V_* - (r+\mu+d+u_3) & 0 \\ 0 & \gamma & r+u_3 & -\mu \end{pmatrix}.$$

The characteristic equation is given as,

$$(\lambda+\mu)(\lambda^3 + D_1\lambda^2 + D_2\lambda + D_3) = 0,$$

where $D_1 = \beta I_* + \beta_1 I_* + 2\mu + \gamma + u_2$, $D_2 = (\beta_1 I_* + \mu + \gamma)(\beta I_* + \mu + u_2) + \beta_1^2 I_* V_* + \beta^2 S_* I_*$, $D_3 = \beta_1^2 I_* V_* (\beta I_* + \mu + u_2) + \beta\beta_1 u_2 S_* I_* + \beta^2 S_* I_* (\beta_1 I_* + \mu + \gamma)$. Clearly D_1 and D_3 are always positive. Using Routh-Hurwitz criteria, we note that all roots of above equation will be with negative real part if $D_1 D_2 > D_3$ and thus E_* will be locally asymptotically stable. The result is summarized in the following theorem.

Theorem 3. The unique endemic steady state E_* is locally asymptotically stable for $\mathcal{R}_0 > 1$ and $D_1 D_2 > D_3$.

Further, we show that this endemic equilibrium is in fact globally asymptotically stable.

Theorem 4. If $\mathcal{R}_0 > 1$, the unique endemic steady state E_* is globally asymptotically stable in Ω when following equality is satisfied:

$$\frac{\beta_1(r+d+u_3+\beta S_*)}{\beta} = (r+d+\gamma+u_3+\beta S_*) + \frac{\gamma\beta_1 V_*}{u_2}.$$

Proof. Consider a positive definite function, $L_1 = \frac{1}{2}(S - S_* + V - V_* + I - I_*)^2 + m(I - I_* - I_* ln\frac{I}{I_*}) + \frac{1}{2}(S - S_*)^2 + \frac{m_1}{2}(V - V_*)^2$, where m and m_1 are positive constants to be determined later. The derivative of L_1 along the solution trajectories of the model system is given as,

$$\begin{aligned}
L_1' &= (S - S_* + V - V_* + I - I_*)(S' + V' + I') + \frac{mI'}{I}(I - I_*) + (S - S_*)S' \\
&\quad + m_1(V - V_*)V', \\
&= (S - S_* + V - V_* + I - I_*)(k - \mu(S+V+I) - (r+d+u_3)I - \gamma V) \\
&\quad + m(I - I_*)(\beta S + \beta_1 V - (r+d+\mu+u_3)) + (S - S_*)(k(1-u_1) - \beta SI \\
&\quad - (\mu+u_2)S) + m_1(V - V_*)(ku_1 + u_2 S - \beta_1 VI - (\gamma+\mu)V), \\
&= (S - S_* + V - V_* + I - I_*)(-\mu(S - S_*) - (r+d+\mu+u_3)(I - I_*) - (\gamma+\mu)(V - V_*)) \\
&\quad + m(I - I_*)(\beta(S - S_*) + \beta_1(V - V_*)) + (S - S_*)(-\beta(SI - S_*I + S_*I - S_*I_*) \\
&\quad - (\mu+u_2)(S - S_*)) + m_1(V - V_*)(u_2(S - S_*) - \beta_1(VI - V_*I + V_*I - V_*I_*) \\
&\quad - (\gamma+\mu)(V - V_*)), \\
&= -\mu(S - S_*)^2 - \mu(S - S_*)(V - V_*) - \mu(S - S_*)(I - I_*) - (r+d+\mu+u_3)(S - S_*)(I - I_*) \\
&\quad - (r+d+\mu+u_3)(V - V_*)(I - I_*) - (r+d+\mu+u_3)(I - I_*)^2 - (\mu+\gamma)(S - S_*)(V - V_*) \\
&\quad - (\mu+\gamma)(V - V_*)^2 - (\mu+\gamma)(V - V_*)(I - I_*) + m\beta(S - S_*)(I - I_*) + m\beta_1(I - I_*)(V - V_*) \\
&\quad - \beta I(S - S_*)^2 - \beta S_*(S - S_*)(I - I_*) - (\mu+u_2)(S - S_*)^2 + m_1 u_2(S - S_*)(V - V_*) \\
&\quad - m_1\beta_1 I(V - V_*)^2 - m_1\beta_1 V_*(V - V_*)(I - I_*) - m_1(\gamma+\mu)(V - V_*)^2,
\end{aligned}$$

$$\begin{aligned}
L_1' &= -\mu(S-S_*+V-V_*+I-I_*)^2-(r+d+u_3)(S-S_*)(I-I_*)-(r+d+u_3)(I-I_*)^2\\
&\quad -(r+d+u_3)(V-V_*)(I-I_*)-\gamma(S-S_*)(V-V_*)-\gamma(V-V_*)^2-\gamma(V-V_*)(I-I_*)\\
&\quad +m\beta(S-S_*)(I-I_*)+m\beta_1(V-V_*)(I-I_*)-\beta I(S-S_*)^2-\beta S_*(S-S_*)(I-I_*)\\
&\quad -(\mu+u_2)(S-S_*)^2+m_1u_2(S-S_*)(V-V_*)-m_1\beta_1 I(V-V_*)^2-m_1\beta_1V_*(V-V_*)(I-I_*)\\
&\quad -m_1(\gamma+\mu)(V-V_*)^2,\\
&= -\mu(S-S_*+V-V_*+I-I_*)^2-(r+d+u_3)(I-I_*)^2-(\beta I+\mu+u_2)(S-S_*)^2\\
&\quad -(\gamma+m_1(\gamma+\mu)+m_1I\beta_1)(V-V_*)^2-(r+d+u_3+\beta S_*-m\beta)(S-S_*)(I-I_*)\\
&\quad -(r+d+u_3+\gamma-m\beta_1+m_1\beta_1V_*)(V-V_*)(I-I_*)-(\gamma-m_1u_2)(S-S_*)(V-V_*).
\end{aligned}$$

Choose $m=\frac{r+d+u_3+\beta S_*}{\beta}$ and $m_1=\frac{\gamma}{u_2}$. When $\frac{\beta_1(r+d+u_3+\beta S_*)}{\beta}=(r+d+\gamma+u_3+\beta S_*)+\frac{\gamma\beta_1V_*}{u_2}$, the derivative $L_1'\leq 0$. Hence using Lyapunov LaSalle Theorem [20] the theorem follows.

Remark 1. The same Lyapunov function will also work choosing $m=\frac{r+d+u_3+\beta S_*}{\beta}$ and $m_1=\frac{m}{V_*}$ along with the following set of parametric conditions:

$$(\gamma\beta V_*-u_2(r+d+u_3+\beta S_*))^2<2\beta V_*(\mu+u_2)(\beta\gamma V_*+(\beta_1I_*+\mu+\gamma)(r+d+u_3+\beta S_*)),$$

and

$$(r+d+\mu+u_3)^2<\frac{2}{\beta V_*}(\mu+u_2)(\beta\gamma V_*+(\beta_1I_*+\mu+\gamma)(r+d+u_3+\beta S_*)).$$

2.5 Direction of bifurcation at $\mathcal{R}_0=1$

One of the root of the characteristic equation of matrix J at E_0 becomes zero when $\mathcal{R}_0=1$, and the disease free steady state E_0 of the model system (1.2) becomes non-hyperbolic steady state. Using center manifold theory approach as discussed in [21], we establish the direction of bifurcation at E_0 by considering transmission rate $\beta=\beta^*$ as bifurcation parameter corresponding to $\mathcal{R}_0=1$.

Define $S=x_1$, $V=x_2$, $I=x_3$, $R=x_4$, using the vector $X_1=(x_1,x_2,x_3,x_4)^T$ (T represents the transpose of vector), the model system (1.2) can be written as $\frac{dX_1}{dt}=f=(f_1,f_2,f_3,f_4)^T$, where the components of f are as follows:

$$\begin{aligned}
f_1 &= k(1-u_1)-\beta x_1x_3-(\mu+u_2)x_1,\\
f_2 &= ku_1+u_2x_1-\beta x_2x_3-(\mu+\gamma)x_2,\\
f_3 &= \beta x_1x_3+\beta_1x_2x_3-(r+\mu+d+u_3)x_3,\\
f_4 &= \gamma x_2+(r+u_3)x_3-\mu x_4.
\end{aligned}\tag{2.1}$$

The jacobian matrix at disease free steady state E_0 for bifurcation parameter $\beta=\beta^*$ *i.e.* $\mathcal{R}_0=1$ is given as:

$$J_{E_0}=\begin{pmatrix}
-\mu-u_2 & 0 & -\beta S_0 & 0\\
u_2 & -\mu-\gamma & -\beta_1V_0 & 0\\
0 & 0 & 0 & 0\\
0 & \gamma & r+u_3 & -\mu
\end{pmatrix}.$$

The right eigen vector of above jacobian matrix is $V_1=(-\beta S_0,\ v_2,\ \mu+u_2,\ v_4)^T$ and $W_1=(0,0,1,0)^T$ is left eigen vector, where components v_2 and v_4 are given as

$$\begin{aligned}
v_2 &= -\frac{\beta\mu S_0+\beta_1V_0(\mu+u_2)}{\mu+\gamma},\\
v_4 &= \frac{(r+u_3)(\mu+u_2)+\gamma v_2}{\mu}.
\end{aligned}$$

Further, we evaluate the constants a and b (see [21]) as,

$$a = \Sigma_{k,i,j=1}^{4} w_k v_i v_j \left.\frac{\partial^2 f_k}{\partial x_i x_j}\right|_{(E_0,\beta^*)} = -2\beta^{*2} S_0(\mu+u_2) + 2\beta_1(\mu+u_2)v_2 < 0$$

and

$$b = \Sigma_{k,i=1}^{4} w_k v_i \left.\frac{\partial^2 f_k}{\partial x_i \partial \beta^*}\right|_{(E_0,\beta^*)} = (\mu+u_3)S_0 > 0.$$

Clearly $a < 0$ and $b > 0$. Using the Theorem 4.1.(iv) of [21] we conclude the following.

Theorem 5. When β crosses β^* *i.e.* $\mathcal{R}_0$ crosses unity, the disease free steady state E_0 changes its stability from stable to unstable. Correspondingly a negative unstable endemic steady state becomes positive and locally asymptotically stable. Thus the direction of bifurcation is forward (transcritical) at $R_0 = 1$.

Example 1. Here, we verify the Theorem (5), and for that we consider a set of representative parameters as: $k = 0.1, \mu = 0.1, \gamma = 0.01, \beta_1 = 0.6, d = 0.01$, $u_1 = 0.3$, $u_2 = 0.5$, $u_3 = 0.5$, and $r = 0.01$. We vary β form 0.601 to 1.75 for varying $\mathcal{R}_0$ through 1. The occurrence of transcritical bifurcation has been shown in the left panel of Fig. 1. Note that as $\mathcal{R}_0$ crosses one a unique positive steady state appears and is stable while the stable disease free steady state becomes unstable. We further plot the solution trajectories to depict this in right panel of Fig. 1. Fix $\beta = 0.601$ so that $\mathcal{R}_0 = 0.89 < 1$. In this case only disease free steady state exists and we find that solution trajectories that start with initial population $(0.8, 0.18, 0.005, 0.015)$, move to disease free steady state *i.e.* disease dies out. Again fix $\beta = 1.745$, so that $\mathcal{R}_0 = 1.1 > 1$, and note that a unique endemic steady state exists and in this case trajectories move to stable endemic steady state.

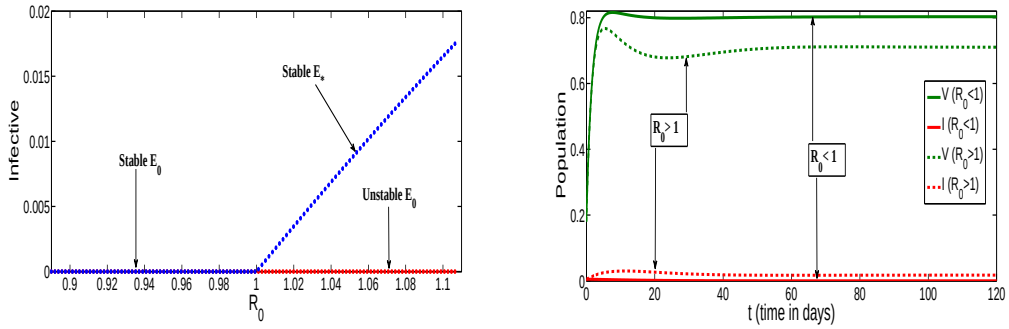

Fig. 1 Left Panel: Existence of Transcritical bifurcation when $\mathcal{R}_0$ crosses one. Right Panel: Dynamics of V and I populations for initial population size $(0.8, 0.18, 0.005, 0.015)$. Here solid line represents the dynamics when $\mathcal{R}_0 = 0.89 < 1$ (for $\beta = 0.601$) whereas dashed line represents the dynamics when $\mathcal{R}_0 = 1.1 > 1$ (for $\beta = 1.745$).

In this section we observed that disease always dies out whenever basic reproduction number $\mathcal{R}_0$ is less than one whereas it persists for $\mathcal{R}_0 > 1$ and a transcritical bifurcation is observed at $\mathcal{R}_0 = 1$. Further it is also noted that $\frac{\partial \mathcal{R}_0}{\partial u_3} < 0$ and hence it is possible to eradicate the disease by providing treatment but question is, is it available adequately? Also, $\frac{\partial \mathcal{R}_0}{\partial u_1}$ and $\frac{\partial \mathcal{R}_0}{\partial u_2}$ are not always negative but can be made negative employing the parameter dependent possibility of disease eradication. Hence it is clear that the controls in form of vaccination and treatment can not be used arbitrarily for eradication rather we may need to choose them appropriately depending on availability of resources.

3 Part - II : Extension of model 1.2 to optimal control problem

In the previous section, the controls on disease (vaccination and treatment) are considered as constants and hence no cost determination is taken care of which will be incurred in their implementation. In this section, we formulate a corresponding optimal control problem for the model system (1.2) considering the two vaccinations and treatment as control interventions to minimize the disease prevalence and corresponding economic burden. Optimal control technique has been used successfully to determine the relevant control strategy with optimal cost [9, 10, 15, 22, 23]. A few of the studies relevant to control problems are described in the following.

Lee *et al*. [10] studied antiviral treatment and isolation as control measures for pandemic influenza for various combination of the controls. They designed and analysed five control strategies using various combinations of antiviral treatment and isolation that are under resource restrictions. They found that integrated strategy reduces maximum pandemic peak whereas isolation works well when antiviral resources are limited. Yan *et al*. [22] studied an optimal control problem considering quarantine and isolation as control measures for SARS epidemic model of Gumel *et al*. [6]. In [9], Gaff *et al*. formulated epidemiological models using vaccination and treatment as control measures. They observed that comprehensive use of vaccination and treatment plays a critical role in the reduction of disease burden whereas vaccination only is found more effective than treatment only strategy. Zeiler *et al*. [24] formulated a model in which force of infection was modified through behavioural change and further considered an optimal control problem with screening policy for infective. Recently, Kassa *et al*. [23] proposed and studied the impact of self-protective measures via education on an optimal control problem using various control policies. They found that optimal treatment along with behavioural changes through education plays a central role on the dynamics of diseases.

In the follwoing, first we introduce the control policies that are to be implemented.

(i) Vaccination to new born and immigrant population: As new born and immigrant population increase the density of susceptible population (prone to get infection), we implement a vaccination control at the inflow of new born and immigrant population so that they will not participate in the disease transmission. In the model system (1.2), u_1 is constant vaccination, which we consider as a variable control function $u_1(t)$.

(ii) Vaccination to susceptible population: The vaccination to susceptible u_2 is chosen as another time dependent control intervention as $u_2(t)$. We are interested in determining the optimal fraction of susceptible population which needs to be vaccinated.

(iii) Treatment to infective population: As treatment has practical advantages in the reduction of the disease prevalence during the epidemic outbreaks. A constant treatment u_3 that is provided to infective in the model system (1.2) is chosen be third variable control function $u_3(t)$.

Execution of such control interventions involve huge amount of money and resources. Thus, our main objective is to investigate the optimal way for these control policies which minimizes the economic load as well as disease prevalence. The admissible set of these control variables $u_1(t), u_2(t)$ and $u_3(t)$ is given as follows and these control functions are considered as measurable and bounded.

$$U=\{u_1(t),u_2(t),u_3(t): \ 0\le u_1(t)\le u_{1max},\ 0\le u_2(t)\le u_{2max} \text{ and } 0\le u_3(t)\le u_{3max},\ t\in[0,T]\}.$$

Here, T is the final or end time of implemented control policies. This time T may vary as per the duration of disease prevalence and applied interventions or the time of study.

3.1 Determination of the total cost

We first determine the total cost incurred due to implemented control policies and disease burden which ultimately is to be minimized. In the following, the weighted sum of the total cost incurred due control policies and disease burden is described.

(i) Cost incurred due to the disease: The cost incurred due to the disease burden is the weighted cost due to opportunity loss [25] of the infected individuals and given as

$$\int_0^T AI(t)dt.$$

This opportunity loss includes many factors which are related with loss in productivity due to sickness, loss of manpower, loss generated in searching treatment and protection, patient caring, etc. [9, 15, 23, 26].

(ii) Cost incurred in vaccination: The weighted sum of cost generated in vaccination coverage which includes the cost of both vaccination of new born and immigrants, and vaccination of susceptible is given as

$$\int_0^T [B_1u_1^2(t) + B_2u_2^2(t)]dt.$$

The total cost of vaccination involves the cost of vaccine, cost of man power needed, cost of vaccination coverage or campaign, etc. A nonlinear relationship between cost and efforts made on vaccination coverage has been considered in this cost construction that follows from [9, 10, 11, 23].

(iii) Cost incurred in treatment: The cost in providing treatment to infective population during the epidemic outbreak is taken as

$$\int_0^T B_3u_3^2(t)dt.$$

The total weighted cost incurred in treatment includes the costs of efforts made on treatment process, cost of medicine, diagnosis charges and cost of hospitalization etc. in the period of providing treatment. On the basis of severity and effect of treatment on population, we consider second order nonlinearity in corresponding cost of treatment [9, 10, 11, 15, 23].

In the following, we define the control problem as per the above discussion for control policies and cost incurred. The cost functional which has to be minimized is

$$J_1[u_1(t),u_2(t),u_3(t)] = \int_0^T [AI(t) + B_1u_1^2(t) + B_2u_2^2(t) + B_3u_3^2(t)]dt \tag{3.1}$$

subject to the model system

$$\begin{aligned}
\frac{dS}{dt} &= k(1-u_1(t)) - \beta SI - \mu S - u_2(t)S,\\
\frac{dV}{dt} &= ku_1(t) + u_2(t)S - \beta_1 VI - \gamma V - \mu V,\\
\frac{dI}{dt} &= \beta SI + \beta_1 VI - (r+d+\mu)I - u_3(t)I,\\
\frac{dR}{dt} &= \gamma V + rI - \mu R + u_3(t)I,
\end{aligned} \tag{3.2}$$

along with the initial conditions $S(0) \geq 0, V(0) \geq 0, I(0) \geq 0$ and $R(0) \geq 0$. The cost functional J_1 represents the total cost incurred due to applied control plans and disease burden. Whereas the temporal cost is measured by the integrand $L(S,V,I,R,u_1,u_2,u_3) = AI(t) + B_1u_1^2(t) + B_2u_2^2(t) + B_3u_3^2(t)$. Here A, B_1, B_2 and B_3 are positive weight constants related with the cost in unit effort and also balance the units of integrand. In the rest of the paper, for convenience we consider $u_1(t) = u_1, u_2(t) = u_2$ and $u_3(t) = u_3$.

3.2 Existence of optimal controls

In this section, we shall establish the existence of optimal control functions for the control problem (3.1)-(3.2). For the existence, we follow the result given in [9, 15, 27].

Theorem 1. There exist optimal control functions u_1^*, u_2^* and u_3^* in U such that $J_1[u_1^*, u_2^*, u_3^*] = min[J_1[u_1, u_2, u_3]]$ corresponding to the control system (3.1)-(3.2).

Proof. In order to show the existence, we follow the Theorem 4.1 (pp. 68 in [27]) and note that the following conditions must be satisfied:

(i) Solutions set to the system (3.2) with control variables in U is non empty.
(ii) U is closed and convex, and state system can be written as linear function of control variables with coefficients depending on time and state variables.
(iii) Integrand $L(S,V,I,R,u_1,u_2,u_3)$ of the equation (3.1) is convex on U and $L(S,V,I,R,u_1,u_2,u_3) \geq g(u_1,u_2,u_3)$ where g is continuous and $\frac{g(u_1,u_2,u_3)}{|(u_1,u_2,u_3)|} \to \infty$ as $|\ (u_1,u_2,u_3)\ | \to \infty$, here $|\ .\ |$ represents the $l^2(0,T)$ norm.

The total population $N = S+V+I+R$ follows the following differential equation:

$$\frac{dN}{dt} = k - \mu N - dI.$$

This gives that $\limsup_{t\to\infty} N \leq \frac{k}{\mu}$. Thus, for each bounded control variables in U, the state solutions of the system (3.2) are bounded *i.e.* $S+V+I+R \leq \frac{k}{\mu}$. Clearly the right hand side functions of the system (3.2) satisfies the Lipschitz condition with respect to state variables. Hence using Picard-Lindelöf theorem [28], condition (i) is fulfilled.

Clearly, by definition, the control set U is closed and convex, and the model system (3.2) is linear in control variables u_1, u_2 and u_3 with coefficients depending on state variables. Thus we reached to condition (ii). Quadratic nature of control variables u_1, u_2 and u_3 assures the convex property of the integrand $L(S,V,I,R,u_1,u_2,u_3)$. Further, $L(S,V,I,R,u_1,u_2,u_3) = AI + B_1u_1^2 + B_2u_2^2 + B_3u_3^2 \geq B_1u_1^2 + B_2u_2^2 + B_3u_3^2$. Now choose $c = min(B_1,B_2,B_3) > 0$ and $g(u_1,u_2,u_3) = c(u_1^2+u_2^2+u_3^2)$ then $L(S,V,I,R,u_1,u_2,u_3) \geq g(u_1,u_2,u_3)$, clearly g is continuous and satisfy $\frac{g(u_1,u_2,u_3)}{|(u_1,u_2,u_3)|} \to \infty$ whenever $|\ (u_1,u_2,u_3)\ | \to \infty$ hence condition (iii) is fulfilled. Thus, using results of [9, 15, 27], there exist optimal control functions u_1^*, u_2^* and u_3^* such that $J_1[u_1^*, u_2^*, u_3^*] = min[J_1[u_1,u_2,u_3]]$. Hence the theorem.

3.3 Characterization of optimal controls

Using Pontryagin's Maximum Principle we shall derive the necessary conditions for optimal control functions obtained in the previous section and also characterize the optimal control functions analytically for the control problem (3.1)-(3.2) [27, 29]. In order to derive the necessary conditions, we first define the Hamiltonian which is given as follows.

$$\begin{aligned} H(S,V,I,R,u_1,u_2,u_3,\lambda) &= L(S,V,I,R,u_1,u_2,u_3) + \lambda_1\frac{dS}{dt} + \lambda_2\frac{dV}{dt} + \lambda_3\frac{dI}{dt} + \lambda_4\frac{dR}{dt} \\ &= AI + B_1u_1^2 + B_2u_2^2 + B_3u_3^2 + \lambda_1(k(1-u_1) - \beta SI - \mu S - u_2S) \\ &\quad + \lambda_2(ku_1 + u_2S - \beta_1VI - \gamma V - \mu V) + \lambda_3(\beta SI + \beta_1VI - (r+d+\mu+u_3)I) \\ &\quad + \lambda_4(\gamma V + rI - \mu R + u_3I). \end{aligned} \tag{3.3}$$

Here $\lambda = (\lambda_1,\lambda_2,\lambda_3,\lambda_4) \in \mathbb{R}^4$ is known as adjoint variable. Using adjoint variable, Pontryagin's Maximum Principle adjoins the cost functional with state equations. In the following, we shall characterize the analytical paths of optimal controls.

Theorem 2. Let u_1^*, u_2^* and u_3^* be the optimal control functions and S^*, V^*, I^* and R^* are corresponding optimal state variables of the control problem (3.1)-(3.2). Then there exists adjoint variable $\lambda = (\lambda_1,\lambda_2,\lambda_3,\lambda_4) \in \mathbb{R}^4$ which satisfy the following canonical equations:

$$\begin{aligned}
\frac{d\lambda_1}{dt} &= (\mu+\beta I+u_2)\lambda_1 - u_2\lambda_2 - \beta I\lambda_3,\\
\frac{d\lambda_2}{dt} &= (\beta_1 I+\gamma+\mu)\lambda_2 - \beta_1 I\lambda_3 - \gamma\lambda_4,\\
\frac{d\lambda_3}{dt} &= -A+\beta S\lambda_1+\beta_1 V\lambda_2 - (\beta S+\beta_1 V-d-r-\mu-u_3)\lambda_3 - (r+u_3)\lambda_4,\\
\frac{d\lambda_4}{dt} &= \mu\lambda_4,
\end{aligned} \tag{3.4}$$

with transversality conditions

$$\lambda_1(T)=0,\lambda_2(T)=0,\lambda_3(T)=0 \text{ and } \lambda_4(T)=0. \tag{3.5}$$

The corresponding optimal control functions are given as

$$\begin{aligned}
u_1^* &= min\left\{max\left\{0,\frac{k(\lambda_1-\lambda_2)}{2B_1}\right\},u_{1max}\right\},\\
u_2^* &= min\left\{max\left\{0,\frac{S^*(\lambda_1-\lambda_2)}{2B_2}\right\},u_{2max}\right\},\\
u_3^* &= min\left\{max\left\{0,\frac{I^*(\lambda_3-\lambda_4)}{2B_3}\right\},u_{3max}\right\}.
\end{aligned} \tag{3.6}$$

Proof. Let u_1^*,u_2^* and u_3^* be the given optimal control functions and S^*,V^*,I^* and R^* are corresponding optimal state variables of the system (3.2) that minimize the cost functional (3.1). Then by Pontryagin's Maximum Principle, there exist adjoint variables $\lambda_1,\lambda_2,\lambda_3$ and λ_4 which satisfy following canonical equations

$$\frac{d\lambda_1}{dt}=-\frac{\partial H}{\partial S},\ \frac{d\lambda_2}{dt}=-\frac{\partial H}{\partial V},\ \frac{d\lambda_3}{dt}=-\frac{\partial H}{\partial I} \text{ and } \frac{d\lambda_4}{dt}=-\frac{\partial H}{\partial R}$$

with transversality conditions $\lambda_1(T)=0,\lambda_2(T)=0,\lambda_3(T)=0$ and $\lambda_4(T)=0$. Here H is known as the Hamiltonian and is as given in (3.3). Thus, we get the adjoint system (3.4) with transversality conditions (3.5). Now, applying the optimality condition $\frac{dH}{du_i}=0, i=1-4$ and property of the control set U, we obtained required optimal control functions as given in (3.6).

3.4 Optimality System

Using the optimal control functions which are characterized as above, this section summarises the optimality system corresponding to the control problem (3.1)-(3.2). The optimality system with minimized Hamiltonian H^* at $(S^*,V^*,I^*,R^*,u_1^*,u_2^*,u_3^*,\lambda)$ is given as follows.

$$\begin{aligned}
\frac{dS^*}{dt} &= k(1-u_1^*)-\beta S^*I^*-\mu S^*-u_2^*S^*,\\
\frac{dV^*}{dt} &= ku_1^*+u_2^*S^*-\beta_1 V^*I^*-\gamma V^*-\mu V^*,\\
\frac{dI^*}{dt} &= \beta S^*I^*+\beta_1 V^*I^*-(r+d+\mu)I^*-u_3^*I^*,\\
\frac{dR^*}{dt} &= \gamma V^*+rI^*-\mu R^*+u_3^*I^*,
\end{aligned} \tag{3.7}$$

with initial conditions $S^*(0)\geq 0, V^*(0)\geq 0,\ I^*(0)\geq 0$ and $R^*(0)\geq 0$. The corresponding adjoint system is

$$\begin{aligned}
\frac{d\lambda_1}{dt} &= (\mu+\beta I^*+u_2^*)\lambda_1 - u_2^*\lambda_2 - \beta I^*\lambda_3,\\
\frac{d\lambda_2}{dt} &= (\beta_1 I^*+\gamma+\mu)\lambda_2 - \beta_1 I^*\lambda_3 - \gamma\lambda_4,\\
\frac{d\lambda_3}{dt} &= -A+\beta S^*\lambda_1+\beta_1 V^*\lambda_2 - (\beta S^*+\beta_1 V^*-d-r-\mu-u_3^*)\lambda_3 - (r+u_3^*)\lambda_4, \qquad (3.8)\\
\frac{d\lambda_4}{dt} &= \mu\lambda_4,
\end{aligned}$$

with transversality conditions (3.5), and the optimal control functions u_1^*, u_2^* and u_3^* are as in (3.6).

3.5 Numerical experiments with discussion

To validate the analytical results obtained in the previous section we performed numerical simulations using MATLAB. To explore the effect of applied control interventions numerically on the dynamics of diseases, we shall execute various combinations of applied controls and design following strategies.

Strategy A: Implementation of both the vaccination policies (u_1, u_2).
Strategy B: Implementation of vaccination of new born and immigrants with treatment (u_1, u_3).
Strategy C: Implementation of vaccination of susceptible population with treatment (u_2, u_3).
Strategy D: Combination of all the policies, both vaccinations and treatment (u_1, u_2, u_3).

For our numerical simulations, we consider the implementation time period for controls $T = 120$ days. Parametric values are taken as: $k = 0.1, \mu = 0.1, \gamma = 0.01, \beta = 0.9, \beta_1 = 0.6, d = 0.01$ and $r = 0.01$ along with the initial population size $S(0) = 0.8, V(0) = 0.18, I(0) = 0.005$, $R(0) = 0.015$. Positive weight constants are considered as: $A_1 = 10, B_1 = 0.75, B_2 = 1$ and $B_3 = 25$ [12]. In order to investigate the effect of above designed strategies numerically, we simulate the optimality system (3.7)-(3.8). For this, we use the forward-backward sweep method starting with an initial guess for optimal controls and solve the optimal state system forward in time and after that solve the adjoint system backward in time, due to transversality conditions, using the optimal state variables and initial guess of optimal controls. Further, optimal control functions are updated using adjoint variables and optimal state variables, and the same process is continued till a pre-defined convergence criteria is met (for complete details see [13]).

In order to comprehend the comparative study for the designed control strategies, we first solve the model system in the absence of any control interventions *i.e.* $u_1 = u_2 = u_3 = 0$. The corresponding outcomes are plotted in Fig. 2 with blue in color. As there is no vaccination in the system, so vaccinated population decreases very fast to zero (and model is essentially SIR model) and in this case rapid growth of infective population is found with high prevalence. This high prevalence is due to absence of cure or treatment in the system and hence it causes high morbidity and mortality.

Further, we deployed the Strategy A *i.e.* both the vaccinations are executed simultaneously in the absence of treatment $u_3 = 0$. The corresponding population trajectories are plotted in Fig. 2 with red in color. At the beginning, a rapid growth in vaccinated population is observed in comparison with the case of no controls but after about 10 days there is a sharp decay due to presence of infective population. Hence, in this case infective increases (as no treatment is applied) and settle at higher level (but less than the case of no controls). The corresponding paths of optimal controls u_1^* and u_2^* are depicted in Fig. 3(b) and Fig. 4(a) respectively. One can observe that initially vaccination of susceptible population u_2^* is more feasible than the u_1^* while after about two weeks vaccination of new born and immigrants u_1^* is required to keep the count of vaccinated individuals at higher level with less potential of u_2^*. Hence Strategy A works well in increasing the vaccinated population but with less impact on infective population.

Profiles of the populations corresponding to the Strategy B (vaccination of new born with treatment where $u_2 = 0$) are plotted in Fig. 2 with green in color. A significant impact of Strategy B is found on vaccinated population and in this case the count of infective population is found very small than the Strategy A. One can easily observe that, in this case, the prevalence of vaccinated population is found higher in entire duration of the epidemic than the Strategy A. The corresponding paths of optimal controls u_1^* and u_3^* are

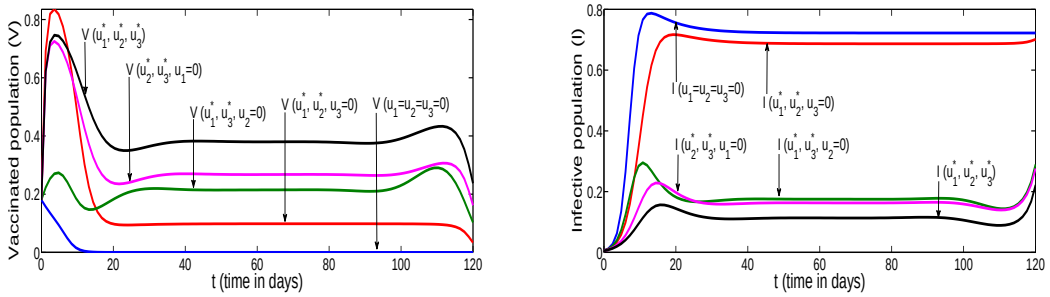

Fig. 2 (a) Profiles of V under various optimal control strategies. (b) Profiles of I under various optimal control strategies.

given in Fig. 3(b) and Fig. 4(b). In this Strategy B, vaccination of new born u_1^* has to be deployed with high potential than the treatment u_3^* during the epidemic to minimize the disease prevalence.

Now we can explore the individual effect of both the controls of Strategy B. Vaccination of new born u_1^* minimizes the count of susceptible population and hence increases the vaccinated one but does not affect the average life time of infectious individuals. Whereas treatment u_3^* reduces the average life time of infective individual via increasing the recovery rate of infective population. Thus, treatment is found an important control which helps in the reduction of disease prevalence.

Further, we execute the Strategy C (vaccination of susceptible population with treatment where $u_1 = 0$) and the profiles of the populations with magenta in color are plotted in Fig. 2. We found that Strategy C works more or less similar as Strategy B. In this case, vaccinated population is found slightly higher than the Strategy B. Profiles of optimal controls u_2^* and u_3^* are depicted in Fig. 4(a) and Fig. 4(b) respectively. Here the impact of both the optimal controls, on control of disease transmission and prevalence, are same as in Strategy B. Hence, policy makers can choose either Strategy B or Strategy C for reduction of disease prevalence *i.e.* either of vaccination (*i.e.* u_1 or u_2) with treatment is required for eradication of disease.

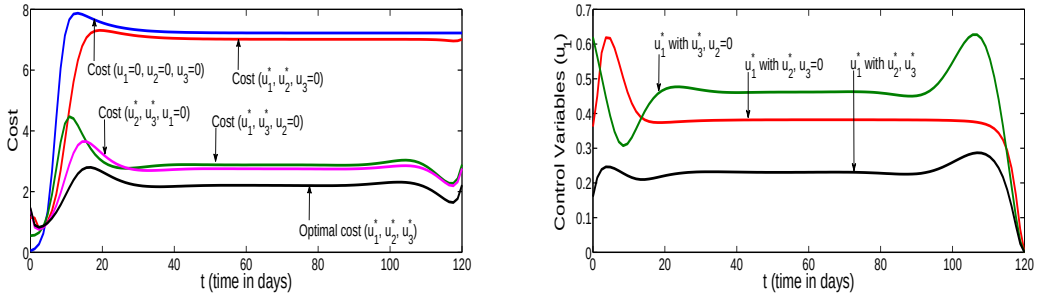

Fig. 3 (a) Cost profiles under various optimal control strategies. (b) Paths of optimal control u_1^* under various optimal control strategies.

Profiles of the populations corresponding to the Strategy D *i.e.* both vaccination and treatment are applied simultaneously are given in Fig. 2 with black in color. In this case prevalence of vaccinated population is found higher than any other applied strategies and prevalence of the infective population is found lowest among others. Hence Strategy D is found highly effective in elimination of disease prevalence. Profiles of optimal controls u_1^*, u_2^* and u_3^* are given in Fig. 3(b) and Fig. 4. Almost equal contribution of each of the control interventions is noted to keep the vaccinated population at maximum level with minimum disease prevalence.

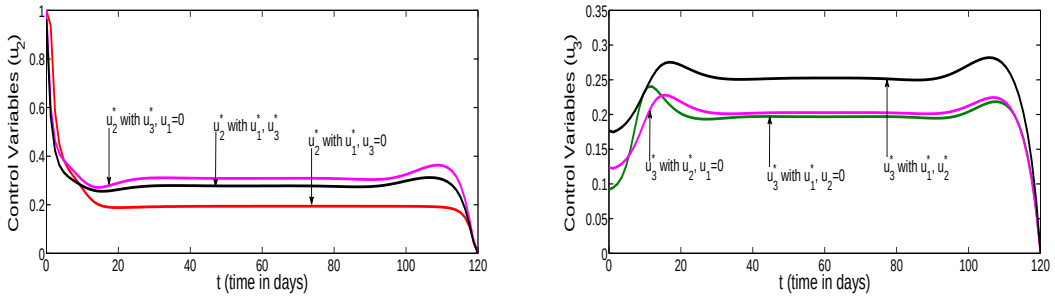

Fig. 4 (a) Paths of optimal control u_2^* under various optimal control strategies. (b) Paths of optimal control u_3^* under various optimal control strategies.

In order to measure the applicability and criticality of control strategies, comparative study has been performed for corresponding costs incurred due to applied control interventions and disease burden. Various cost profiles are given in Fig. 3(a). In the absence of any controls, the incurred productivity loss due to disease only is plotted in blue color. This productivity loss is found high because in the absence of controls infective will increase rapidly and hence so productivity loss will be high. Whereas combinations of all the controls required minimum cost (*i.e.* optimal cost) in reducing the disease prevalence. Execution of vaccination only (Strategy A) is found expensive (curve in red color in Fig. 3(a)) during epidemic outbreak. Moreover, Strategy B and Strategy C are found economically feasible with almost same cost burden (curves in green and magenta color in Fig. 3(a)) but less than the Strategy A and greater than Strategy D. Thus comprehensive use all the controls (Strategy D) is found highly economical feasible during the disease outbreaks and reduces the disease prevalence.

Effect of vaccine efficacy on optimal controls

In this subsection, we shall determine the sensitivity of the parameter β_1 (related to vaccine efficacy level) on infective and vaccinated population, and on all optimal controls (Strategy D). For this, we vary the parameter β_1 in the range $(0-0.9)$. The corresponding outcome is plotted in Fig. 5. One can observe from Fig. 5(a) that as vaccine efficacy decreases (β_1 increases) the corresponding prevalence of vaccinated population also decreases *e.g.* at $\beta_1 = 0$ (full immunity), vaccinated population is at higher level whereas low prevalence of vaccinated population is found at $\beta_1 = 0.9$ (less immunity). Moreover, a reverse pattern is found for infective population as given in Fig. 5(b). For example, a high prevalence of infective is found at $\beta_1 = 0.9$ (less immunity) whereas vaccine with high efficacy level (*i.e.* $\beta_1 = 0$) minimizes the count of infective population under Strategy D. Hence, vaccination with high efficacy level leads the eradication of infection from the population under control Strategy D.

We plotted the corresponding profiles of cost for various values of β_1 under Strategy D in Fig. 6(a). We infer that if vaccination with high efficacy (β_1=0) is implemented along with treatment *i.e.* Strategy D, minimum cost will be incurred whereas high economic burden will pose if implemented vaccine is of low efficacy (as can be seen from plotted black colored curve in Fig. 6(a)). Paths of optimal controls u_1^*, u_2^* and u_3^* are given in Fig. 6(b) and Fig. 7. Our study accentuates that policy makers have to focus on treatment if the implemented vaccine is of low efficacy to balance the disease burden and economic load and vice-versa.

4 Conclusion

In this work, we proposed an SVIR compartmental model based on the model proposed by Hu *et al.* [16]. Model accounts for the effect of two stage vaccination *i.e.* vaccination of new born and immigrants, and

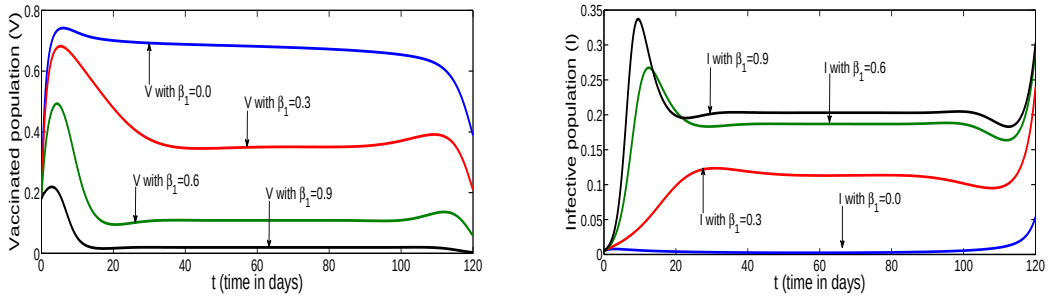

Fig. 5 (a) Profiles of V for various values of β_1 under optimal controls (Strategy D). (b) Profiles of I for various values of β_1 under optimal controls (Strategy D).

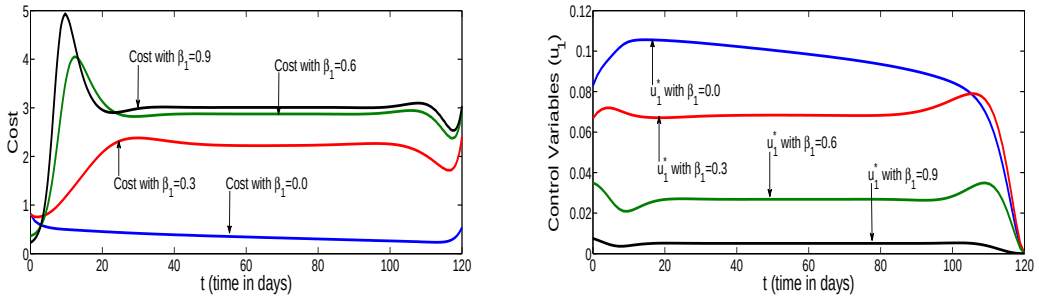

Fig. 6 (a) Cost profiles for various values of β_1 with optimal controls (Strategy D). (b) Paths of optimal control u_1^* for various values of β_1 under Strategy D.

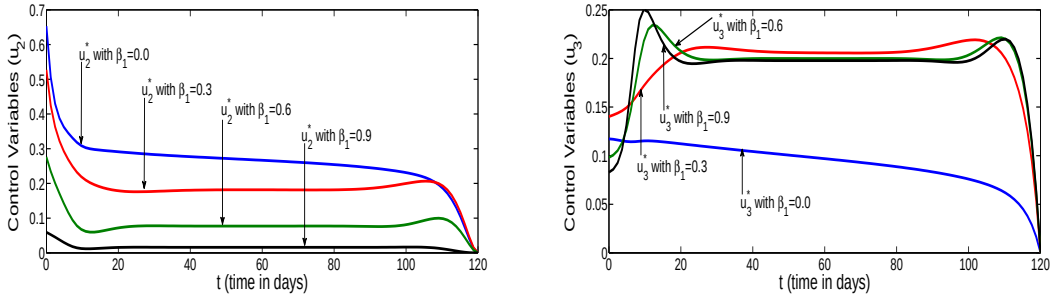

Fig. 7 (a) Paths of optimal control u_2^* for various values of β_1 under Strategy D. (b) Paths of optimal control u_3^* for various values of β_1 under Strategy D.

vaccination of susceptible population along with treatment of infective. Model analysis has been performed and stability of steady states has been established. The disease free steady state has been found globally asymptotically stable when basic reproduction number $\mathcal{R}_0$ is less than one. A transcritical bifurcation (forward bifurcation) is observed at $\mathcal{R}_0 = 1$. Further, for $\mathcal{R}_0 > 1$ a unique endemic steady state exists which is found to be globally asymptotically stable under certain conditions.

Further, we extended our proposed model to corresponding an optimal control problem considering both the vaccinations and treatment as control interventions. In the designed cost functional, a nonlinear relationship between cost and efforts made on implementation of controls is considered which also includes

opportunity loss. Existence of such optimal control paths is established and characterized analytically using Pontryagin's Maximum Principle which minimize the cost functional. We made a comparative study numerically for the following designed control strategies: Strategy A- Implementation of both the vaccinations, Strategy B- Implementation of vaccination of new born and immigrants with treatment, Strategy C- Implementation of vaccination of susceptible population with treatment and Strategy D- Combination of all the policies, both vaccination and treatment. Strategy A is found expensive with a significant impact on vaccinated population. Whereas Strategy B and Strategy C work well and better than the Strategy A and found very effective in reducing the count of infective with minimum cost. Impact of both the strategies B and C is found similar on the dynamics of disease. Moreover, comprehensive use of all the controls (Strategy D) is found highly effective and highly economically feasible than the all other applied control strategies during the outbreaks. In this case, count of infective population is observed at a very low level with high prevalence of vaccinated population.

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