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Optimal Control Analysis of Influenza Epidemic Model

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Abstract

The implementation of optimal control strategies involving preventive measures and antiviral treatment can significantly reduce the number of clinical cases of influenza. In this paper, a model for the transmission dynamics of influenza is formulated and two control strategies involving preventive measures (awareness campaign, washing hand, using hand sanitizer, wearing mask) and treatment are considered and used to minimize the total number of infected individuals and associated cost of using these two controls. The resulting optimality system is solved numerically. Hamiltonian is formulated to investigate the existence of the optimal control, in the optimal control model. Pontryagin's Maximum Principle is applied to describe the control variables and the objective function is designed to reduce both the infection and the cost of interventions. From the numerical simulation, it is observed that in the case of high contact rate ($\beta = 3$), both the controls work for a longer period of time to reduce the disease burden. The optimal control analysis and numerical simulations reveal that the interventions reduce the number of exposed and infected individuals.

Keywords

Influenza, Optimal Control, Pontryagin's Maximum Principle, Transversality Condition, Hamiltonian

1. Introduction

Influenza viruses cause the infectious disease, influenza, commonly known as "the flu" and this infection primarily transmitted through respiratory droplets produced by sneezing and coughing by an infected person [1]. Symptoms range from mild to severe and often include fever, sore throat, runny nose, headache, muscle pain, coughing, and fatigue and these symptoms begin from one to four days after exposure to the virus (typically two days) and last for about 2 - 8 days. Particularly in children diarrhea and vomiting can occur. Some other complications caused by the infection include meningitis, acute respiratory distress syndrome, encephalitis and worsening of pre-existing health problems such as asthma and cardiovascular disease.

For the past few centuries, influenza remains a serious threat to public health globally [2]. During the past century, thousands of people lost their lives during three disastrous pandemics including the Spanish flu (1918), Asian flu (1958), and Hong Kong flu (1968) [2]. In 2009, the world experienced the H1N1 influenza, also known as the Swine Influenza, an epidemic that led to over 16,455 deaths globally.

In reducing the spread of influenza, frequent hand washing with soap and water, using hand sanitizers (alcohol-based) and not touching one's nose, eyes and mouth with one's hands, are highly effective. Covering nose and mouth when coughing or sneezing and staying home when sick, is important to limit influenza transmission [3]. Creating awareness among people about the aforementioned etiquette and hygiene by spreading health education through media is important. The disease can be treated with supportive measures and, in severe cases, with antiviral drugs such as oseltamivir.

In view of the serious consequences due to the H1N1 epidemic on the public health, various mathematical models have been proposed and analyzed in order to know the transmission dynamics of the H1N1 influenza [4]-[10].

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 and is a decent strategy for deciding how to control a sickness best.

To overcome H1N1 influenza, mitigation strategies are proposed in [11], an H1N1 influenza model was analyzed in [12] that accounts for the role of an imperfect vaccine and antiviral drugs that administered to infected individuals, the evolutionary model of influenza A with drift and shift was discussed in [13]. Authors in [14] discussed two strain influenza model with vaccination for strain 1 and transmission dynamics of H1N1 influenza was rigorously analyzed with optimal control in [5]. All these studies reveal the complex feature of transmission dynamics of influenza and to the author's knowledge no such model for transmission of influenza in a population has been developed in which optimal control strategies have been designed on the basis of considering all possible preventive measures and treatment and this is the novelty of this research work.

The task of identifying optimal control strategies with a simple SEIR model that minimize the impact of influenza epidemics through the use of antiviral drug in combination with aforementioned preventive measures (which is highly prioritized) like covering nose and mouth, washing hand, using hand sanitizer, creating awareness through health education are the focus of this manuscript.

Optimal control theory [15] [16] [17], is the primary tool used in the analysis. To complement the aforementioned studies by formulating a simple model and considering all possible preventive measures and treatment as control parameters to reduce the disease burden, is the main objective of this study.

This paper is organized as follows: Section 2 (Model formulation), Section 3 (Existence of an optimal control), Section 4 (Necessary conditions of the optimal control), Section 5 (The optimality system), Section 6 (Numerical simulations and discussion) and Section 7 (Conclusion).

2. Model Formulation

The total population is divided into four mutually exclusive compartments, namely susceptible ($S(t)$), exposed ($E(t)$), infected ($I(t)$), and recovered ($R(t)$) at any time t. Thus, the total population can be written as $N(t) = S(t) + E(t) + I(t) + R(t)$.

The corresponding system of nonlinear ODEs is,

$$\begin{aligned} S'(t) &= bN(t) - \beta S(t)I(t) - \mu_1 S(t), \\ E'(t) &= \beta S(t)I(t) - (\mu_1 + \gamma)E(t), \\ I'(t) &= \gamma E(t) - (\mu_1 + \mu_2 + r)I(t), \\ R'(t) &= rI(t) - \mu_1 R(t), \\ N'(t) &= (b - \mu_1)N(t) - \mu_2 I(t). \end{aligned} \tag{1}$$

with initial conditions

$$S(0) = S_0 \geq 0, E(0) = E_0 \geq 0, I(0) = I_0 \geq 0, R(0) = R_0 \geq 0, N(0) = N_0 \geq 0 \tag{2}$$

Here b is the recruitment rate, γ is the transmission rate from exposed class to infected class, r is the recovery rate and μ_1, μ_2 are natural death rate and disease induced death rate respectively. Susceptible individuals acquire infection at a per capita rate $\beta I(t)$, where β is the transmission coefficients.

To control various types of diseases, optimal control techniques are of great use in developing optimal strategies. In this model two control strategies are introduced namely $v_1(t)$, which represents the preventive measures like covering nose and mouth, washing hand, using hand sanitizer, awareness campaign among the community and $v_2(t)$, which represents the treatment of infectious people. The modified model to estimate the effect of controlling strategies, is given below,

$$\begin{aligned} S'(t) &= bN(t) - \beta S(t)I(t) - (v_1 + \mu_1)S(t), \\ E'(t) &= \beta S(t)I(t) - (\mu_1 + \gamma)E(t), \\ I'(t) &= \gamma E(t) - (\mu_1 + \mu_2 + r + v_2)I(t), \\ R'(t) &= v_1 S(t) + v_2 I(t) + rI(t) - \mu_1 R(t), \end{aligned} \tag{3}$$

with initial conditions

$$S(0) = S_0 \geq 0, E(0) = E_0 \geq 0, I(0) = I_0 \geq 0, R(0) = R_0 \geq 0 \tag{4}$$

To limit the number of infectious individuals and minimize the cost of applied controls v_1, v_2, the required objective functional J is defined as follows,

$$J(v_1, v_2) = \int_0^T \left(YI(t) + \frac{1}{2}\left(w_1 v_1^2 + w_2 v_2^2\right) \right) \mathrm{d}t \tag{5}$$

and the control set is, $V = \left\{ \left(v_1(t), v_2(t)\right) : 0 \le v_1(t) \le 1, 0 \le v_2(t) \le 1, t \in [0, T] \right\}$.

A linear combination of quadratic terms $\left(v_i^2, i = 1, 2\right)$ are used to model the control efforts, and the constants Y, w_1, w_2 are a measure of the relative cost of the interventions over [0, T]. Here the problem is to find optimal controls, $\left(v_1^*, v_2^*\right)$ such that

$$J\left(v_1^*(t), v_2^*(t)\right) = \min_V J\left(v_1(t), v_2(t)\right) \tag{6}$$

3. Existence of an Optimal Control

From the model (3), $N'(t) \le (b - \mu_1) N(t)$. Then there exists $M \in \mathbb{R}^+$ such that

$$N(t) \le N_0 \mathrm{e}^{(b-\mu_1)T} = M, t \in [0, T]$$

Since, $N(t) = S(t) + E(t) + I(t) + R(t)$ and the state variables, $S(t), E(t), I(t)$, and $R(t)$ are bounded above, then there exists solution for the system (3).

To prove the existence of the optimal control, it's required to check the following hypotheses [15].

(M_1) The set consisting of controls and corresponding state variables is nonempty.

(M_2) The admissible control set V is convex and closed.

(M_3) R.H.S of state system (3) is bounded by a linear function in the state and control variables.

(M_4) J, the objective functional, has a convex integrand on V and the integrand is bounded below by $-b_1 + b_2 \left|\left(v_1, v_2\right)\right|^\eta$ with $b_1 > 0, b_2 > 0$ and $\eta > 1$.

To prove the above statements the following theorem is required,

Theorem 1. If each of the functions $\tilde{F}_i$, for $i = 1, \cdots n$ and the partial derivatives $\frac{\partial \tilde{F}_i}{\partial x_j}$ for $i, j = 1, \cdots n$, are continuous in $\mathcal{R}^{n+1}$ space, then there exists a unique solution $\left(x_1 = \phi_1(t), \cdots, x_n = \phi_n(t)\right)$ of the system of differential equations, $x_i' = \tilde{F}_i\left(t, x_1, \cdots, x_n\right)$ for $i = 1, \cdots n$, with initial conditions $x_i(t_0) = x_i^0$ for $i = 1, \cdots n$, and the solution also satisfies the initial conditions [15].

To prove the hypotheses (M_1-M_4), let us consider the system,

$$\begin{aligned} \frac{\mathrm{d}S}{\mathrm{d}t} &= \tilde{F}_1(t, S, E, I, R), \\ \frac{\mathrm{d}E}{\mathrm{d}t} &= \tilde{F}_2(t, S, E, I, R), \\ \frac{\mathrm{d}I}{\mathrm{d}t} &= \tilde{F}_3(t, S, E, I, R), \\ \frac{\mathrm{d}R}{\mathrm{d}t} &= \tilde{F}_4(t, S, E, I, R), \end{aligned} \tag{7}$$

where $\tilde{F}_1, \tilde{F}_2, \tilde{F}_3$ and $\tilde{F}_4$ represent the right side of the system (3) and for some constants c_1 and c_2, let $v_1(t) = c_1$ and $v_2(t) = c_2$. The functions $\tilde{F}_i$ for $i = 1, \cdots 4$, must be linear and their partial derivatives with respect to all state variables are constants. Hence the functions and their partial derivatives are continuous everywhere. So, according to the theorem 1 we can say that, there exists a unique solution $S(t) = \phi_1(t), E(t) = \phi_2(t), I(t) = \phi_3(t), R(t) = \phi_4(t)$, which satisfies the initial conditions. Therefore, the consisting set of controls and corresponding state variables is nonempty.

Now for any two controls $v_1, v_2 \in V$ and $\theta \in [0,1]$, $0 \le \theta v_1 + (1-\theta) v_2 \le 1$. Therefore, the set V is convex and closed (by definition).

Now comparing (7) with (3),

$$\tilde{F}_1 \le bN - v_1 S$$
$$\tilde{F}_2 \le KI$$
$$\tilde{F}_3 \le \gamma E - v_2 I$$
$$\tilde{F}_4 \le v_1 S + v_2 I + rI$$

in matrix form,

$$\bar{F}(t, \bar{X}, V) \le \bar{m}_1\left(t, \begin{bmatrix} S \\ E \\ I \\ R \end{bmatrix}\right) \bar{X}(t) + \bar{m}_2\left(t, \begin{bmatrix} S \\ E \\ I \\ R \end{bmatrix}\right) V \tag{8}$$

where,

$$\bar{m}_1\left(t, \begin{bmatrix} S \\ E \\ I \\ R \end{bmatrix}\right) = \begin{bmatrix} 0 & 0 & 0 & 0 \\ 0 & 0 & K & 0 \\ 0 & \gamma & 0 & 0 \\ 0 & 0 & r & 0 \end{bmatrix} \text{ and } \bar{m}_2\left(t, \begin{bmatrix} S \\ E \\ I \\ R \end{bmatrix}\right) = \begin{bmatrix} -S \\ 0 \\ -I \\ S+I \end{bmatrix}$$

Here all the parameters are constant and nonnegative. Therefore from (8),

$$\left|\bar{F}(t, \bar{X}, V)\right| \le \|\bar{m}_1\|\left|\bar{X}\right| + |S + I|\left|(v_1(t), v_2(t))\right| \le q\left(\left|\bar{X}\right| + \left|(v_1(t), v_2(t))\right|\right)$$

Therefore, the right side of the state system (3) is bounded by a linear function in the state and control variables.

Moreover, the integrand, $YI(t) + \frac{1}{2}\left(w_1 v_1^2 + w_2 v_2^2\right)$ of the objective functional J, is convex and satisfies $J(v_1, v_2) = -b_1 + b_2\left|(v_1, v_2)\right|^2$ where $b_1 > 0, b_2 > 0$ and $\eta = 2 > 1$, according to [18] [19] [20].

Hence, we have the following theorem.

Theorem 2 For $V = \{(v_1(t), v_2(t)) : 0 \le v_1(t) \le 1, 0 \le v_2(t) \le 1, t \in [0, T]\}$ subject to Equation (3) having the initial conditions and $J(v_1, v_2) = \int_0^T \left(YI(t) + \frac{1}{2}\left(w_1 v_1^2 + w_2 v_2^2\right)\right) dt$, there is an optimal control (v_1^*, v_2^*) such that $J(v_1^*(t), v_2^*(t)) = \min_V J(v_1(t), v_2(t))$ [7].

For the solution of the system (3), it's Hamiltonian has to be defined.

4. Necessary Conditions of the Optimal Control

Let $\tilde{X}=(S,E,I,R), V=(v_1,v_2)$ and $\lambda=(\lambda'_S,\lambda'_E,\lambda'_I,\lambda'_R)$. Then the Hamiltonian H for the optimal control problem is,

$$\begin{aligned} H(\tilde{X},V,\lambda) &= YI(t)+\frac{1}{2}(w_1v_1^2+w_2v_2^2)+\lambda_S(bN-\beta SI-(v_1+\mu_1)S) \\ &+\lambda_E(\beta SI-(\mu_1+\gamma)E)+\lambda_I(\gamma E-(\mu_1+\mu_2+r+v_2)I) \\ &+\lambda_R(v_1S+v_2I+rI-\mu_1R) \end{aligned} \tag{9}$$

Pontryagin's maximum principle [17] is used to derive the necessary conditions for the optimal control, which (Pontryagin's maximum principle) converts the problem (6) into the problem of minimizing the Hamiltonian.

Hamiltonian H is used for determining the adjoint equations and transversality conditions.

The following can be derived from the differentiation of H, with respect to each state variables

$$\lambda'_S=-\frac{\partial H}{\partial S}=\lambda_S(\beta I+(v_1+\mu_1))-\beta I\lambda_E-v_1\lambda_R,$$

$$\lambda'_E=-\frac{\partial H}{\partial E}=(\mu_1+\gamma)\lambda_E-\gamma\lambda_I,$$

$$\lambda'_I=-\frac{\partial H}{\partial I}=\beta S\lambda_S-\beta S\lambda_E+(\mu_1+\mu_2+r+v_2)\lambda_I-(v_2+r)\lambda_R-Y,$$

$$\lambda'_R=-\frac{\partial H}{\partial R}=\mu_1\lambda_R$$

with transversality conditions, $\lambda_S(T)=\lambda_E(T)=\lambda_I(T)=\lambda_R(T)=0$.

With the help of controls and conditions of optimality,

$$\left.\frac{\partial H}{\partial v_1}\right|_{v_1=v_1^*}=0$$

$$\Rightarrow v_1^*w_1-S\lambda_S+S\lambda_R=0$$

$$\Rightarrow v_1^*=\frac{S(\lambda_S-\lambda_R)}{w_1}$$

and

$$\left.\frac{\partial H}{\partial v_2}\right|_{v_2=v_2^*}=0$$

$$\Rightarrow v_2^*w_2-I\lambda_I+I\lambda_R=0$$

$$\Rightarrow v_2^*=\frac{I(\lambda_I-\lambda_R)}{w_2}$$

5. The Optimality System

The resulting optimality system is given as follows,

State equations with initial conditions,

$$\begin{aligned} S'(t) &= bN(t) - \beta S(t) I(t) - (v_1 + \mu_1) S(t), \\ E'(t) &= \beta S(t) I(t) - (\mu_1 + \gamma) E(t), \\ I'(t) &= \gamma E(t) - (\mu_1 + \mu_2 + r + v_2) I(t), \\ R'(t) &= v_1 S(t) + v_2 I(t) + rI(t) - \mu_1 R(t), \end{aligned} \tag{10}$$

with initial conditions

$$S(0) = S_0 \geq 0, E(0) = E_0 \geq 0, I(0) = I_0 \geq 0, R(0) = R_0 \geq 0 \tag{11}$$

Adjoint system with transversality conditions,

$$\begin{aligned} \lambda_S' &= -\frac{\partial H}{\partial S} = \lambda_S \left(\beta I + (v_1 + \mu_1)\right) - \beta I \lambda_E - v_1 \lambda_R, \\ \lambda_E' &= -\frac{\partial H}{\partial E} = (\mu_1 + \gamma) \lambda_E - \gamma \lambda_I, \\ \lambda_I' &= -\frac{\partial H}{\partial I} = \beta S \lambda_S - \beta S \lambda_E + (\mu_1 + \mu_2 + r + v_2) \lambda_I - (v_2 + r) \lambda_R - Y, \\ \lambda_R' &= -\frac{\partial H}{\partial R} = \mu_1 \lambda_R \end{aligned} \tag{12}$$

and,

$$\lambda_S(T) = \lambda_E(T) = \lambda_I(T) = \lambda_R(T) = 0 . \tag{13}$$

Controls v_1^* and v_2^* are given by,

$$v_1^* = \begin{cases} 0, & \text{if } \dfrac{S(\lambda_S - \lambda_R)}{w_1} < 0 \\ \dfrac{S(\lambda_S - \lambda_R)}{w_1}, & \text{if } 0 \leq \dfrac{S(\lambda_S - \lambda_R)}{w_1} \leq 1 \\ 1, & \text{if } \dfrac{S(\lambda_S - \lambda_R)}{w_1} > 1 \end{cases} \tag{14}$$

and

$$v_2^* = \begin{cases} 0, & \text{if } \dfrac{I(\lambda_I - \lambda_R)}{w_2} < 0 \\ \dfrac{I(\lambda_I - \lambda_R)}{w_2}, & \text{if } 0 \leq \dfrac{I(\lambda_I - \lambda_R)}{w_2} \leq 1 \\ 1, & \text{if } \dfrac{I(\lambda_I - \lambda_R)}{w_2} > 1 \end{cases} \tag{15}$$

6. Numerical Simulations and Discussion

For the numerical solution of the system (10), the Runge-Kutta method is used. The simulation of the model is done with different scenarios. For this, the considered initial population size for susceptible class, exposed class, infected class and recovered class are $S_0 = 0.8, E_0 = 0.06, I_0 = 0.05$ and $R_0 = 0.05$ respectively and total number of years, $T = 8$.

Here intead of whole numbers the proportions are used. Description of the variables of the model and other parameter values are given in Table 1 and Table 2 respectively.

Figure 1 shows the density of the susceptible, exposed, infected and recovered population with and without control. It is noticed that, the extinction of infected and exposed class is possible if the control parameters are kept. Otherwise the infection reaches to the maximum level.

Figure 2 and Figure 3 show a comparative situation with varying effective contact rate. For low contact rate ($\beta = 0.4$) there is a significant increase in the recovered compartment, compared to the high contact rate ($\beta = 3$). In the case of high contact rate, both the controls v_1 and v_2 work for a longer period of time to reduce the disease burden. Figure 4 and Figure 5 portray the solution of the optimal control problem with different control weights ($w_1 = 0.2, w_2 = 0.5$) and ($w_1 = 0.5, w_2 = 0.2$) respectively and there are no significant changes in the infected and exposed class. Applying more awareness control does not significantly bring down the number of exposed and infected individuals as compared to the case when applying more of the treatment control. In both cases there are increase in the infected individuals after the time $t = 7.4$ years.

Table 1. Description of the model variables.

Variable	Description
$S(t)$	Susceptible Population at time t
$E(t)$	Exposed Population at time t
$I(t)$	Infected Population at time t
$R(t)$	Recovered Population at time t

Table 2. Description and nominal value of the model parameter.

Parameter	Description	Value
b	Birth rate	0.03 [assumed]
μ_1	Natural death rate	0.02 [5]
μ_2	Disease induced death rate	0.01 [5]
β	Effective contact rate	0.9 [5]
γ	Transmission rate from $E(t)$ to $I(t)$ class	0.53 [5]
r	Recovery rate	0.2 [5]
Y	Weight parameter	10 [assumed]
w_1	Weight parameter	0.2 [assumed]
w_2	Weight parameter	0.3 [assumed]

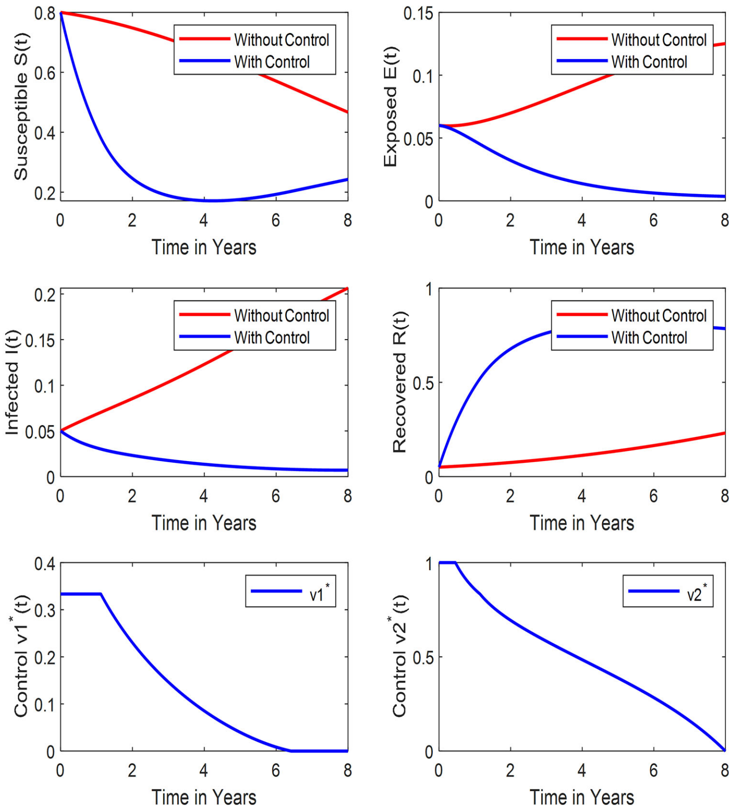

Figure 1. The graph shows the comparison of changes in population with and without control.

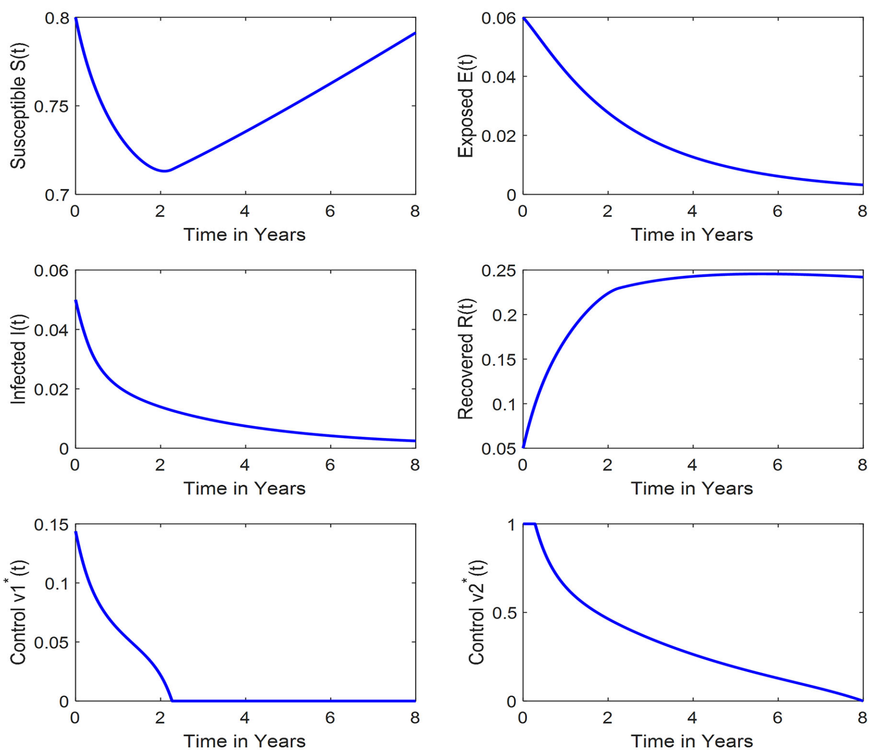

Figure 2. The graph shows the effect of low contact rate ($\beta = 0.4$).

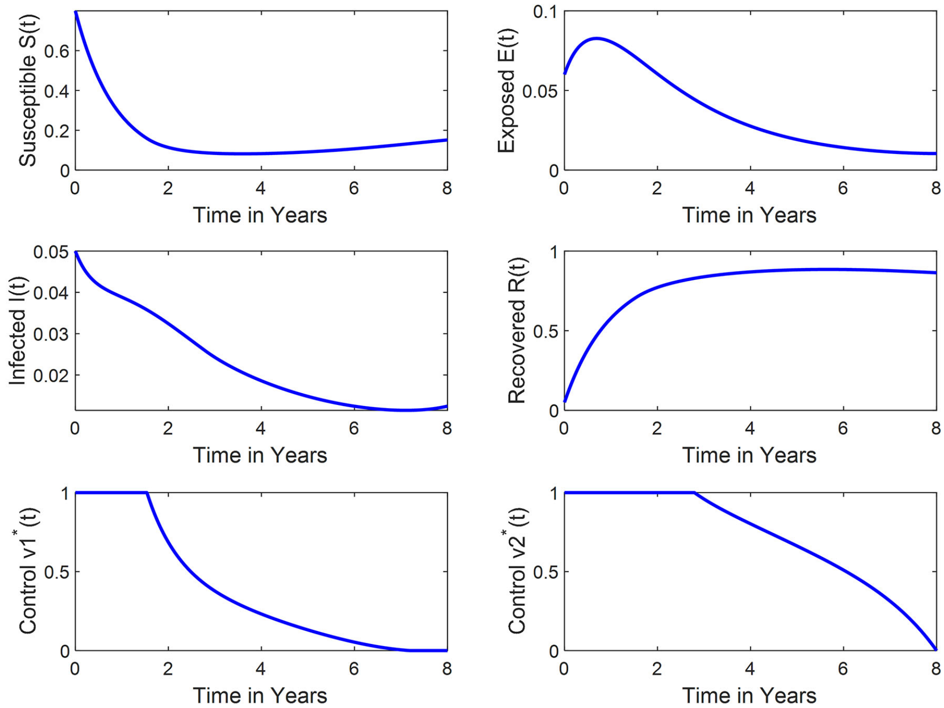

Figure 3. The graph shows the effect of high contact rate ($\beta = 3$).

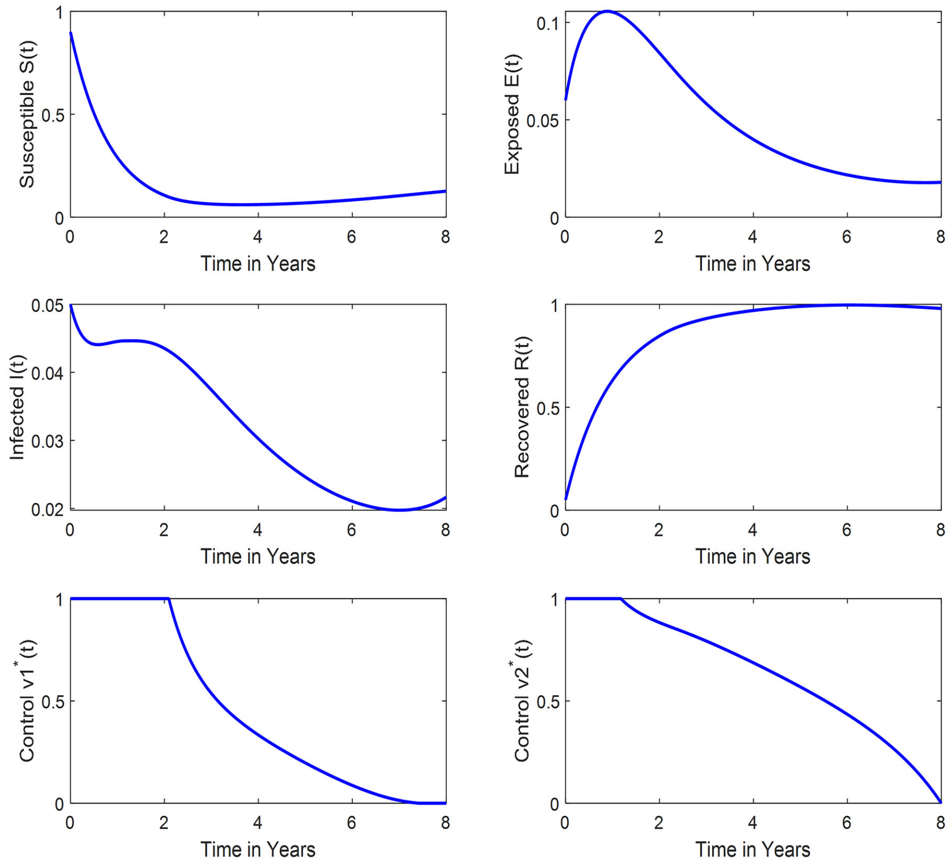

Figure 4. The graph shows the effect of weight parameters ($w_1 = 0.2, w_2 = 0.5$).

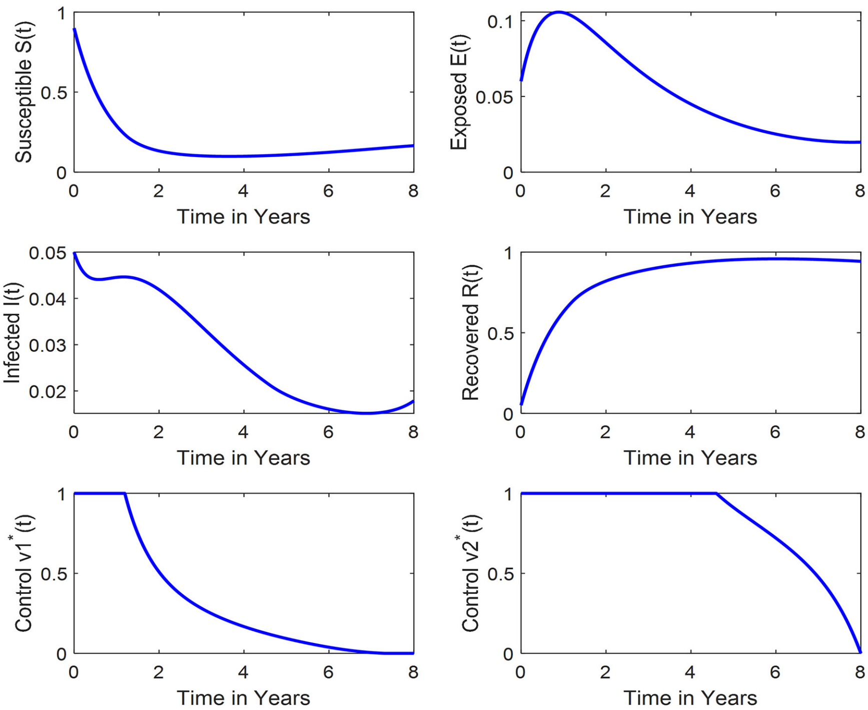

Figure 5. The graph shows the effect of weight parameters ($w_1 = 0.5, w_2 = 0.2$).

7. Conclusions

In this paper, a deterministic mathematical model of Influenza was formulated with preventive measures (awareness campaign, washing hand, using hand sanitizer, wearing mask) and treatment as interventions. It is monitored that there is a significant effect of using control strategies in reducing the exposed and infected individuals. In case of high effective contact rate, the effectiveness of the controls should last for longer period of time because of increasing disease burden. Moreover, the combination of both the controls has positive impact on reducing the disease burden and minimizing the corresponding cost. The main findings are:

For high contact rate ($\beta = 3$), to reduce disease burden both the controls, preventive measures and treatment should work for long period and in the case of low contact rate ($\beta = 0.4$), exposed and infected individuals decrease rapidly and for this, control v_1 needs to work for more than 2 years.

For different control weights ($w_1 = 0.2, w_2 = 0.5$) and ($w_1 = 0.5, w_2 = 0.2$), it is monitored that the number of recovered individuals increases more rapidly and reaches it maximum level faster whenever preventive measures get more priority and this is more economical than treatment cost.

In this study, the optimal control problem does not include vaccination, which is important and for further study, this problem extends by considering the vaccination as intervention.

Conflicts of Interest

The author declares no conflicts of interest regarding the publication of this paper.

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