ISSN 1 746-7233, England, UK
World Journal of Modelling and Simulation
Vol. 12 (2016) No. 4, pp. 307-319

Analysis of a simple influenza A (H1N1) model with optimal control*

Akhil Kumar Srivastav[1] , Mini Ghosh[2†]

Division of Mathematics, School of Advanced Sciences, VIT University Chennai Campus, Vandalur-Kelambakkam Road, Chennai-600 127, India

(*Received March 15 2016, Accepted August 12 2016*)

Abstract. In this paper, a deterministic non-linear $SEIHR$ type epidemic model for the transmission dynamics of Influenza A (H1N1) is proposed and analyzed. The existence and stability of different equilibria of this model are discussed in detail. The basic reproduction number R_0 of the model is computed, and it is found that for $R_0 < 1$, the disease free equilibrium of the model is globally stable. The endemic equilibrium exists only when $R_0 > 1$, and is globally asymptotically stable. The globally stability results are proved using Lyapunov method and LaSalle's invariance principle [9].

Further, this model is extended to an optimal control problem by introducing two types of controls. First control aims to reduce the interaction between susceptibles and infections while the second one aims to provide timely hospitalization for critically ill infections. Our main aim is to reduce the transmission rate of this disease which will lead to the reduction in the number of infections. The optimal control problem is analyzed using Pontryagin's Maximum Principle and is solved numerically using MATLAB. The effectiveness of optimal control is demonstrated by comparing the levels of infected populations with and without optimal control. It has been found that the optimal control strategy gives better result as it reduces the number of infections significantly in the desired period of control. Additionally, it is observed that the optimal control profiles of the control parameters are very much dependent on the cost associated with implementation of these controls. When the weight constants associated with these control parameters increase, optimal control decreases leading to the increase in the number of influenza infections. Finally, numerical simulation is performed to demonstrate the analytical findings.

Keywords: flu, mathematical model, basic reproduction number, stability analysis, optimal control

1 Introduction

Infectious diseases are the leading cause of morbidity and mortality in the World. Especially the developing countries and low-income countries are more affected by the infectious diseases such as HIV, TB, Malaria etc. In recent years, mathematical modeling has become an effective tool to analyze the transmission dynamics of an infectious disease. Mathematical modelling helps in understanding the disease dynamics and to find suitable control strategies to control the disease.

Influenza, more commonly known as "Flu" is a viral infection which affects mainly nose, throat bronchi and occasionally lung. When the people infected with flu cough, sneeze, or talk, these viruses spread through air to other person in the neighborhood of infected person. The best way to reduce the chance of becoming infected from influenza virus is vaccination. There are three types of Influenza virus, namely, Influenza A, influenza B, Influenza C.

In 2009, world faced Swine flu pandemic, which was an influenza pandemic initially spread in Mexico and then very rapidly it captured different parts of the world due to its high transmission rate and movement

* The authors thank the handling editor and anonymous referees for their valuable comments and suggestions which led to an improvement of our original manuscript.
† Corresponding author. *E-mail address*: akil.ksrivastav2014@vit.ac.in, minighosh@vit.ac.in

of infected individuals from one country to another by air travel. This virus is thought to be a mutation of four known strains of the influenza A virus, subtype H1N1: one endemic in (normally infecting) humans, one endemic in birds, and two endemic in pigs (swine).

On August 10 2010, flu was officially declared pandemic by the World Health Organization (WHO)[5].

Several mathematical models are developed to understand the transmission dynamics and control of flu (H1N1) disease[2, 10, 13]. In [2], authors emphasized on importance of fast test kit for pandemic flu through a stochastic model. In [10], authors have formulated a mathematical model of swine flu by considering standard incidence type interaction between susceptibles and infections. Here authors had assumed that the total population is constant. The rates of transmission due to symptomatic and asymptomatic patients were considered different. This model had six compartments and authors could analyze only the local stability of the equilibria and they illustrated some results using numerical simulation. The global stability of the equilibria is not explored. Similarly, in [13], authors have given a more generalized model with 15 compartments, and they used standard incidence type interaction between susceptible and infections. Here too global analysis of the full model is not performed due to the complexity of the model. Here we observed that some of the compartments are unnecessary and can be merged or ignored without much compromise with the objective of the work. Keeping these aspects in view we have formulated a new mathematical model which is based on the flow diagram provided in [2]. Unlike the stochastic model discussed in [2], our model is deterministic compartment model which is formulated using the system of differential equations. Further, we extended our model to optimal control problem to see the effect of optimal control on the transmission dynamics of the disease.

This paper is organized as follows: Section 2 describes the basic model and the basic reproduction number R_0, Section 3 elaborates the existence of equilibria and their stability. Section 4 deals with the numerical simulation of the basic model which verifies our analytical findings. Section 5 describes the optimal control problem. Section 6 describes the analytic and numerical solutions of the optimal control problem. And finally, we have discussed our results in Section 7.

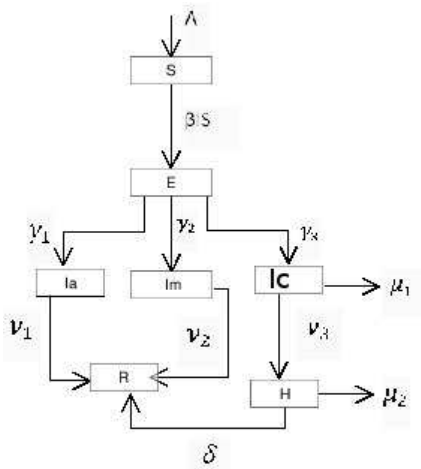

Fig. 1: Flow diagram of the SEIHR mathematical model for H1N1 transmission dynamics.

2 The model

We first divide the total population $N(t)$ into seven compartments, namely, Susceptible (S), Exposed (E), Asymptotic Infective (I_a), Moderate sick (I_m), Critically ill (I_c), Hospitalized (H), Recovered (R). Hence $N = S + E + I_a + I_m + I_c + H + R$. It is assumed that the total population is varying and homogeneously mixed i.e., all people are equally likely to be infected by the infectious individuals if they come into contact. It is assumed that susceptible individuals after being exposed to the infection can move to any one of the

following infective classes, namely, asymptotic infective, moderate sick, critically sick. Individuals who are critically ill may need hospitalization and can move to class of hospitalized individuals. After hospitalization individual may recover and move to recovered class. Individuals who are asymptotic infections or moderately sick can also recover and can join recovered class upon recovery. However the rates of recovery may vary from one compartment to another. Keeping the above facts/assumptions in mind, a mathematical model is proposed as follows:

$$\frac{dS}{dt} = \Lambda - \mu S - \beta IS, \tag{1a}$$
$$\frac{dE}{dt} = \beta IS - \gamma_1 E - \gamma_2 E - \gamma_3 E - \mu E, \tag{1b}$$
$$\frac{dI_a}{dt} = \gamma_1 E - \nu_1 I_a - \mu I_a, \tag{1c}$$
$$\frac{dI_m}{dt} = \gamma_2 E - \nu_2 I_m - \mu I_m, \tag{1d}$$
$$\frac{dI_c}{dt} = \gamma_3 E - \nu_3 I_c - \mu I_c - \mu_1 I_c, \tag{1e}$$
$$\frac{dH}{dt} = \nu_3 I_c - \mu H - \mu_2 H - \delta H, \tag{1f}$$
$$\frac{dR}{dt} = \nu_1 I_a + \nu_2 I_m + \delta H - \mu R. \tag{1g}$$

Table 1: Description of parameters

Parameter	Description
Λ	Recruitment rate
μ	Natural death rate
β	Contact rate
γ_1	Progression rate from exposed to infectious class
γ_2	Progression rate from exposed to infectious class
γ_3	Progression rate from exposed to infectious class
ν_1	Recovery rate for non-hospitalized asymptotic infectious
ν_2	Recovery rate for non-hospitalized moderate sick infectious
ν_3	rate of hospitalization for critically ill infectious person
δ	progression rate for hospitalized to recover
μ_1	Death rate for critically ill infectious person without hospitalized.
μ_2	Death rate for hospitalized person
u_1	control parameter on the transmission rate
u_2	control parameter on the critically ill infectious person
a_t	additional recovery rate

2.1 The basic reproduction number r_0

Let $(S, E, I_a, I_m, I_c, H, R)$ be any solution with positive initial condition. then we have the total population $N = S + E + I_a + I_m + I_c + H + R$ and the time derivative of N in the above equation along with the solution of given system of differential equation is

$$\frac{dN}{dt} = \Lambda - \mu N - \mu_1 I_c - \mu_2 H.$$

The disease free equilibrium E_0 corresponds to the stage when infection dies out from the population and for our proposed model it is given by

$$E_0 = (S^0, E^0, {I_a}^0, {I_m}^0, {I_c}^0, H^0, R^0) = (\frac{\Lambda}{\mu}, 0, 0, 0, 0, 0, 0).$$

To find the basic the reproduction number R_0, we follow the same method as discussed in [3, 4] and using the same notations, the matrices F and V, for the new infection terms and the remaining transfer terms respectively, corresponding to the system (1) are computed as follows:

$$\mathcal{F} = \begin{pmatrix} \beta IS \\ 0 \\ 0 \\ 0 \end{pmatrix} = \begin{pmatrix} \beta(I_a + I_m + I_c) \\ 0 \\ 0 \\ 0 \end{pmatrix}$$

and

$$\mathcal{V} = \begin{pmatrix} \gamma_1 E + \gamma_2 E + \gamma_3 E + \mu E \\ -\gamma_1 E + \mu I_a + \nu_1 I_a \\ -\gamma_2 E + \mu I_m + \nu_2 I_m \\ -\gamma_3 E + \mu I_c + \nu_3 I_c + \mu_1 I_c \end{pmatrix}.$$

We can write F= Jacobian of $\mathcal{F}$ at E_0 as

$$F = \begin{pmatrix} 0 & \beta S^0 & \beta S^0 & \beta S^0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix},$$

and V=Jacobian of $(\mathcal{V})$ at E_0 as

$$\mathrm{V} = \begin{pmatrix} \gamma_1 + \gamma_2 + \gamma_3 + \mu & 0 & 0 & 0 \\ -\gamma_1 & \mu + \nu_1 & 0 & 0 \\ -\gamma_2 & 0 & \mu + \nu_2 & 0 \\ -\gamma_3 & 0 & 0 & \mu + \nu_3 + \mu_1 \end{pmatrix},$$

and it follows that

$$FV^{-1} = \begin{pmatrix} m_{11} & m_{12} & m_{13} & m_{14} \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix},$$

where $m_{11} = \dfrac{\beta S^0}{\gamma_1 + \gamma_2 + \gamma_3 + \mu} \left(\dfrac{\gamma_1}{\mu + \nu_1} + \dfrac{\gamma_2}{\mu + \nu_2} + \dfrac{\gamma_3}{\mu + \nu_3 + \mu_1}\right)$,
$m_{12} = \dfrac{\beta S^0}{\mu + \nu_1}$, $m_{13} = \dfrac{\beta S^0}{\mu + \nu_2}$, $m_{14} = \dfrac{\beta S^0}{\mu + \nu_3 + \mu_1}$.
The largest eigenvalue of FV^{-1} is the basic reproduction number R_0, and is given by

$$R_0 = \left(\frac{\beta S^0}{\gamma_1 + \gamma_2 + \gamma_3 + \mu}\right)\left(\frac{\gamma_1}{\mu + \nu_1} + \frac{\gamma_2}{\mu + \nu_2} + \frac{\gamma_3}{\mu + \nu_3 + \mu_1}\right)$$

The reproduction number R_0 gives the average number of infected humans generated by the one infected human in a fully susceptible population.

3 Equilibria and their stability

The endemic equilibrium point $E_1 = (S^*, E^*, {I_a}^*, {I_m}^*, {I_c}^*, H^*, R^*)$ is given as

$$
\begin{aligned}
S^* =& \frac{\gamma_1+\gamma_2+\gamma_3+\mu}{\beta(d_1+d_2+d_3)},\\
E^* =& \frac{\Lambda-\mu\, S^*}{\beta(d_1+d_2+d_3)\, S^*} = \frac{\Lambda-\mu\, S^*}{\gamma_1+\gamma_2+\gamma_3+\mu},\\
{I_a}^* =& d_1\, E^*, {I_m}^* = d_2\, E^*, {I_c}^* = d_3\, E^*,\\
H^* =& d_4\, E^*, R^* = d_5 E^*,
\end{aligned}
$$

where $d_1 = \frac{\gamma_1}{\mu+\nu_1}, d_2 = \frac{\gamma_2}{\mu+\nu_2}, d_3 = \frac{\gamma_3}{\mu+\nu_3+\mu_1}, d_4 = \frac{\nu_3}{\mu+\delta+\mu_2}, d_5 = \frac{\nu_1 d_1+\nu_2 d_2+\delta d_4}{\mu}$. Here it is easy to visualize that the value of E^* is positive for $R_0 > 1$ as when $R_0 > 1$ then $\frac{\Lambda}{\mu} \geq \frac{\gamma_1+\gamma_2+\gamma_3+\mu}{\beta(d_1+d_2+d_3)}$. Hence the endemic equilibrium point E^* exists for $R_0 > 1$.

3.1 Global stability results

To prove the global stability of disease-free equilibrium, we are using the theorem by Castillo-chavez et al.[1].

Theorem 1. *If the given mathematical model can be written in this form:*

$$\frac{dX}{dt} = F(X,Y),\ and\quad \frac{dY}{dt} = G(X,Y),\quad G(X,0) = 0 \qquad (*)$$

where $X = S, Y = (E, I_a, I_m, I_c)^T$, denoting the number of uninfected and denoting the number of flu infected people respectively.

then the DFE is represented here by $E_0 = (X_0, 0) = (\frac{\lambda}{\mu}, 0)$, For the global asymptotically stable, the condition (H_1) and (H_2) given below must be satisfied.

$H_1 : for \frac{dX}{dt} = F(X_0, 0), X_0$ *is globally asymptotically stable,*

$H_2 : G(X,Y) = AY - \widehat{G}(X,Y),\ \widehat{G}(X,Y) \geq 0\ here\ A = D_Y G(X_0, 0)$*is M- matrix (In M-matrix, all the off diagonal element of matrix are non-negative) . If the given system of differential equation in mathematical model satisfies the given condition in $(*)$ then the point $E_0 = (X_0, 0)$ is globally asymptotically stable equilibrium provided $R_0 < 1$. And for the given mathematical model, the result is shown in the next theorem.*

Theorem 2. *The equilibrium point $E_0 = (X_0, 0)$ is globally asymptotically stable (G.A.S.) provided $R_0 < 1$.*

Proof. Using Theorem 1 to our mathematical model, we have

$$F(X_0, 0) = \Lambda - \mu S,\ \ G(X,Y) = AY - \widehat{G}(X,Y),$$

where

$$A = \begin{pmatrix} a_{11} & \beta S^0 & \beta S^0 & \beta S^0 \\ \gamma_1 & a_{22} & 0 & 0 \\ \gamma_2 & 0 & a_{33} & 0 \\ \gamma_3 & 0 & 0 & a_{44} \end{pmatrix}$$

and $a_{11} = -(\gamma_1+\gamma_2+\gamma_3+\mu), a_{22} = -(\nu_1+\mu)$, $a_{33} = -(\nu_2+\mu), a_{44} = -(\nu_3+\mu+\mu_1)$.
Then

$$\widehat{G}(X,Y) = \begin{pmatrix} \widehat{G}_1(X,Y) \\ \widehat{G}_2(X,Y) \\ \widehat{G}_3(X,Y) \\ \widehat{G}_4(X,Y) \end{pmatrix} = \begin{pmatrix} \beta(I_a+I_m+I_c)(S^0-S) \\ 0 \\ 0 \\ 0 \end{pmatrix}.$$

Here we can easily see that $S^0 \geq S$, implying $\widehat{G}(X,Y) \geq 0$ for all (X,Y). Additionally, the matrix A is M matrix (by definition of M matrix). Hence the DFE (E_0) is globally asymptotically stable.

Theorem 3. *The endemic equilibrium* $E_1 = (S^*, E^*, I_a{}^*, I_m{}^*, I_c{}^*, H^*, R^*)$ *of the system (1) is globally asymptotically stable whenever it exists.*

Proof. To prove the global stability result, we consider the following Lyapunov function[6]:

$$\begin{aligned} V_1 =& K_1(S - S^* - S^* ln\frac{S}{S^*}) + K_2(E - E^* - E^* ln\frac{E}{E^*}) + K_3(I_a - I_a{}^* - I_a{}^* ln\frac{I_a}{I_a{}^*}) \\ &+ K_4(I_m - I_m{}^* - I_m{}^* ln\frac{I_m}{I_m{}^*}) + K_5(I_c - I_c{}^* - I_c{}^* ln\frac{I_c}{I_c{}^*}). \end{aligned}$$

The time derivative of V_1 is given by,

$$\begin{aligned} \frac{dV_1}{dt} =& K_1(1 - \frac{S^*}{S})\frac{dS}{dt} + K_2(1 - \frac{E^*}{E})\frac{dE}{dt} + K_3(1 - \frac{I_a{}^*}{I_a})\frac{dI_a}{dt} + K_4(1 - \frac{I_m{}^*}{I_m})\frac{dI_m}{dt} \\ &+ K_5(1 - \frac{I_c{}^*}{I_c})\frac{dI_c}{dt}. \end{aligned}$$

Putting the values of $\frac{dS}{dt}, \frac{dE}{dt}, \frac{dI_a}{dt}, \frac{dI_m}{dt}, \frac{dI_c}{dt}$ in the above equation, we get,

$$\begin{aligned} \frac{dV_1}{dt} =& K_1(1 - \frac{S^*}{S})[\Lambda - \mu S - \beta IS] + K_2(1 - \frac{E^*}{E})[\beta IS - (\gamma_1 + \gamma_2 + \gamma_3 + \mu)E] \\ &+ K_3(1 - \frac{I_a{}^*}{I_a})[\gamma_1 E - (\nu_1 + \mu)I_a] + K_4(1 - \frac{I_m{}^*}{I_m})[\gamma_2 E - (\nu_2 + \mu)I_m] \\ &+ K_5(1 - \frac{I_c{}^*}{I_c})[\gamma_3 E - (\nu_3 + \mu + \mu_1)I_c]. \end{aligned}$$

The mathematical model system satisfies the following relation at the equilibrium point.

$$\begin{aligned} &\Lambda = \mu S^* + \beta I^* S^*, (\gamma_1 + \gamma_2 + \gamma_3 + \mu) = \frac{\beta I^* S^*}{E^*}, \\ &(\nu_1 + \mu) = \frac{\gamma_1 E^*}{I_a{}^*}, (\nu_2 + \mu) = \frac{\gamma_2 E^*}{I_m{}^*}, (\nu_3 + \mu + \mu_1) = \frac{\gamma_3 E^*}{I_c{}^*}. \end{aligned}$$

Using the above relation, the expression for $\frac{dV_1}{dt}$ simplifies to,

$$\begin{aligned} \frac{dV_1}{dt} =& - K_1(\frac{(S^* - S)^2}{S})\mu + K_1(1 - \frac{S^*}{S})[\beta I^* S^* - \beta IS] + K_2(1 - \frac{E^*}{E})[\beta IS - (\frac{\beta I^* S^*}{E^*})E] \\ &+ K_3(1 - \frac{I_a{}^*}{I_a})[\gamma_1 E - (\frac{\gamma_1 E^*}{I_a{}^*})I_a] + K_4(1 - \frac{I_m{}^*}{I_m})[\gamma_2 E - (\frac{\gamma_2 E^*}{I_m{}^*})I_m] \\ &+ K_5(1 - \frac{I_c{}^*}{I_c})[\gamma_3 E - (\frac{\gamma_3 E^*}{I_c{}^*})I_c] \\ \frac{dV_1}{dt} =& - K_1(\frac{(S^* - S)^2}{S})\mu + f(x_1, x_2, x_3, x_4, x_5) \end{aligned}$$

where $\frac{S}{S^*} = x_1, \frac{E}{E^*} = x_2, \frac{I_a}{I_a{}^*} = x_3, \frac{I_m}{I_m{}^*} = x_4, \frac{I_c}{I_c{}^*} = x_5, S^* I_a{}^* = a, S^* I_m{}^* = b, S^* I_c{}^* = c, \gamma_1 E^* = d, \gamma_2 E^* = e, \gamma_3 E^* = f$, and

$$
\begin{aligned}
f(x_1,x_2,x_3,x_4,x_5) =& K_1\beta(a+b+c) - K_1\beta(ax_1x_3+bx_1x_4+cx_1x_5) - K_1\beta(a+b+c)\frac{1}{x_1}\\
&+ K_1\beta(ax_3+bx_4+cx_5) + K_2\beta(ax_1x_3+bx_1x_4+cx_1x_5)\\
&- K_2x_2\beta(a+b+c) - K_2\beta(ax_1x_3+bx_1x_4+cx_1x_5)\frac{1}{x_2}\\
&+ K_2\beta(a+b+c) + K_3dx_2 + K_3dx_3 - K_3d\frac{x_2}{x_3} + K_3d + K_4ex_2\\
&- K_4x_4e - K_4e\frac{x_2}{x_4} + K_4e + K_5fx_2 - K_5x_5f - K_5f\frac{x_2}{x_5} + K_5f,\\
&= (-K_1\beta a + K_2\beta a)x_1x_3 + (-K_1\beta b + K_2\beta b)x_1x_4 + (-K_1\beta c + K_2\beta c)x_1x_5\\
&+ x_2(-K_2\beta(a+b+c) + K_3d + K_4e + K_5f) + x_4(K_1\beta b - K_4e)\\
&+ x_5(K_1\beta c - K_5f) + x_3(K_1\beta a - K_3d) + K_1\beta(a+b+c)\\
&- K_1\beta(a+b+c)\frac{1}{x_1} - K_2\beta(ax_1x_3+bx_1x_4+cx_1x_5)\frac{1}{x_2} + K_2\beta(a+b+c)\\
&- K_3d\frac{x_2}{x_3} + K_3d - K_4e\frac{x_2}{x_4} + K_4e - K_5f\frac{x_2}{x_5} + K_5f.
\end{aligned}
$$

Now for the following choice of K_1, K_2, K_3, K_4 and K_5, the coefficients of $x_1x_3, x_1x_4, x_1x_5, x_4, x_3, x_5$ equal to zero, $K_1 = K_2$; $K_3 = \frac{K_1\beta a}{d}$; $K_4 = \frac{K_1\beta b}{e}$; $K_5 = \frac{K_1\beta c}{f}$.
Choosing $K_1 = K_2 = 1$, we get

$$
f(x_1,x_2,x_3,x_4,x_5) = \beta a(3 - \frac{1}{x_1} - \frac{x_1x_3}{x_2} - \frac{x_2}{x_3}) + \beta b(3 - \frac{1}{x_1} - \frac{x_1x_4}{x_2} - \frac{x_2}{x_4}) + \beta c(3 - \frac{1}{x_1} - \frac{x_1x_5}{x_2} - \frac{x_2}{x_5}).
$$

Since the arithmetic mean (A.M.) is greater than or equal to geometric mean (G.M.), we have $\frac{1}{x_1} + \frac{x_1x_3}{x_2} + \frac{x_2}{x_3} \geq 3$, $\frac{1}{x_1} + \frac{x_1x_4}{x_2} + \frac{x_2}{x_4} \geq 3$ and $\frac{1}{x_1} + \frac{x_1x_5}{x_2} + \frac{x_2}{x_5} \geq 3$.

Finally, we get

$$
\frac{dV_1}{dt} = -\frac{(S^*-S)^2}{S}\mu + \beta a(3 - \frac{1}{x_1} - \frac{x_1x_3}{x_2} - \frac{x_2}{x_3}) + \beta b\left(3 - \frac{1}{x_1} - \frac{x_1x_4}{x_2} - \frac{x_2}{x_4}\right) + \beta c\left(3 - \frac{1}{x_1} - \frac{x_1x_5}{x_2} - \frac{x_2}{x_5}\right).
$$

Thus $\frac{dV_1}{dt} \leq 0$ and the equality $\frac{dV_1}{dt} = 0$ hold only for
$x_1 = x_2 = x_3 = x_4 = x_5 = 1$ for which $S = S^*$, $E = E^*$, $I_a = {I_a}^*$, $I_m = {I_m}^*$, $I_c = {I_c}^*$. Hence from the LaSalle's invariance principle[7], the equilibrium E_1 of the given system is globally asymptotically stable for $R_0 > 1$.

4 Numerical simulation

In this section, numerical simulation is performed to verify our analytical findings. Most of our parameter values are taken from the reference[12], and remaining parameters are assumed. All the parameters are in day. The given mathematical model is simulated for the following set of parameters using MATLAB: $\Lambda = 3$, $\mu = 0.0075$, $\beta = 0.0001$, $\gamma_1 = 0.1$, $\gamma_2 = 0.1$, $\gamma_3 = 0.1$, $\nu_1 = 0.03$, $\nu_2 = 0.03$, $\nu_3 = 0.02$, $\delta = 0.02, \mu_1 = 0.04227, \mu_2 = 0.027855$.

For this set of parameters $R_0 = 0.8802$ and DFE equilibrium point E_0 is $(400,\ 0,\ 0,\ 0,\ 0,\ 0,\ 0)$. Here Figure 2 demonstrate the stability of DFE (E_0). The stability of the endemic equilibrium (E_1) is demonstrated in Fig. 4 using the following set of parameters: $\Lambda = 7$, $\mu = 0.0075$, $\beta = 0.0001$, $\gamma_1 = 0.1$, $\gamma_2 = 0.1$, $\gamma_3 = 0.1$, $\nu_1 = 0.03$, $\nu_2 = 0.03$, $\nu_3 = 0.02$, $\delta = 0.02, \mu_1 = 0.04227, \mu_2 = 0.027855$.

For this set of parameters, the basic reproduction number $R_0 = 2.0538$ and equilibrium point is $(454.43,\ 11.68,\ 31.14,\ 31.14,\ 16.74,\ 6.048,\ 265.31)$. The impact of ν_3 which is the rate of hospitalization for critically ill infections on I_a, I_m, I_c is demonstrated in the Figs. 4-4 respectively. It is observed that with the increase in the parameter ν_3 the number of infections in I_a, I_m and I_c class decreases.

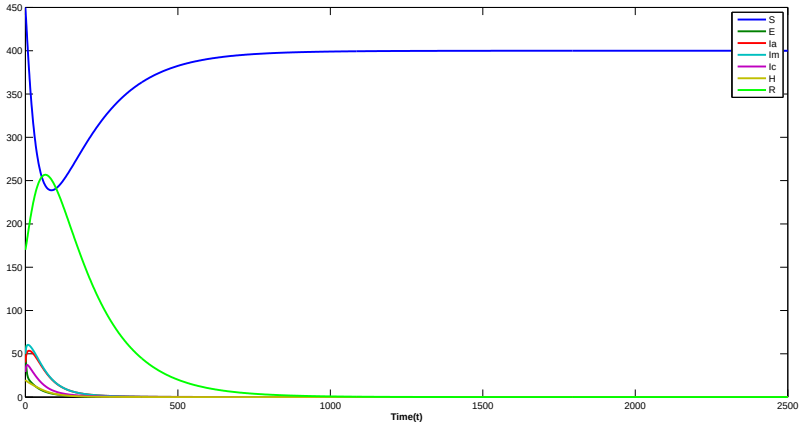

Fig. 2: Variation of S E ,I_a, I_m, I_c, H and R with time, showing the stability of disease free equilibrium point.

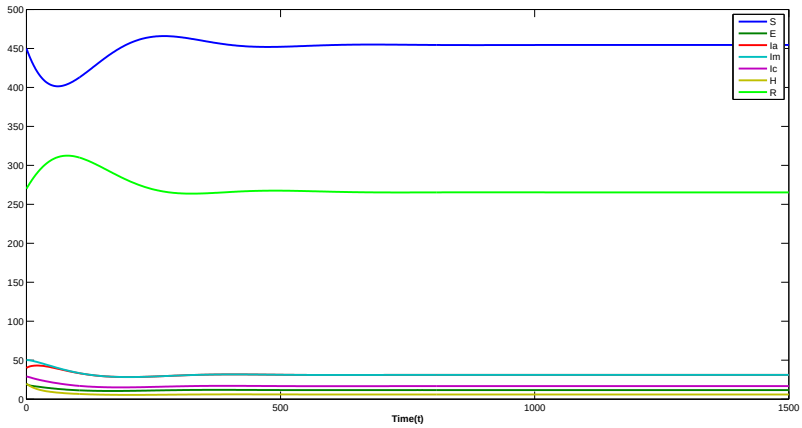

Fig. 3: Variation of S E ,I_a, I_m, I_c, H and R with time, showing the stability of endemic equilibrium point.

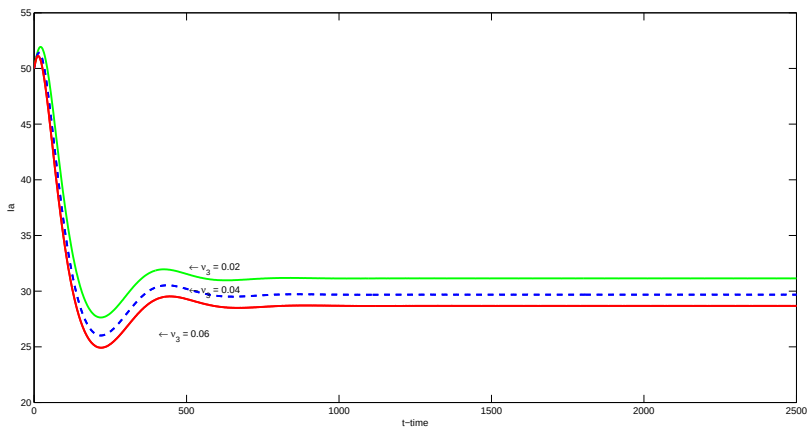

Fig. 4: Variation of I_a with time for different values of ν_3.

5 Optimal control model

Here the mathematical model (1) is extended to formulate optimal control problem. Two types of control parameters, namely, u_1 and u_2 are added to the existing model (1). By the control u_1, we are reducing effective transmission rate (β) and by control u_2, we are reducing critically ill individuals as they recover fast and move to the recovered class. Both control functions are bounded and Lebesgue integrable on the interval [0, t_f],

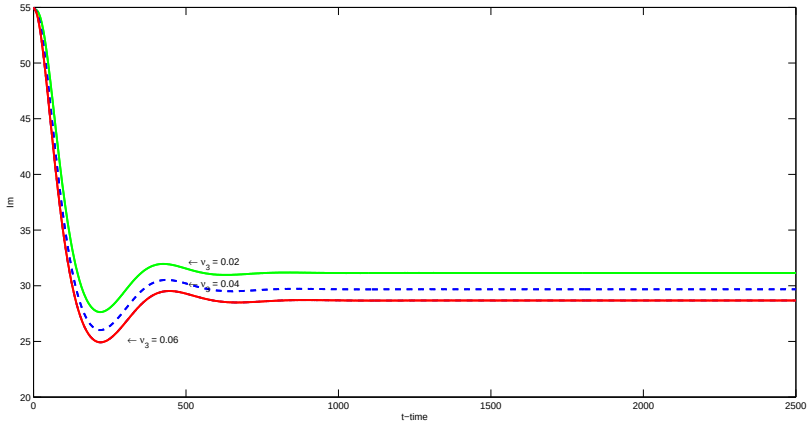

Fig. 5: Variation of I_m with time for different values of ν_3.

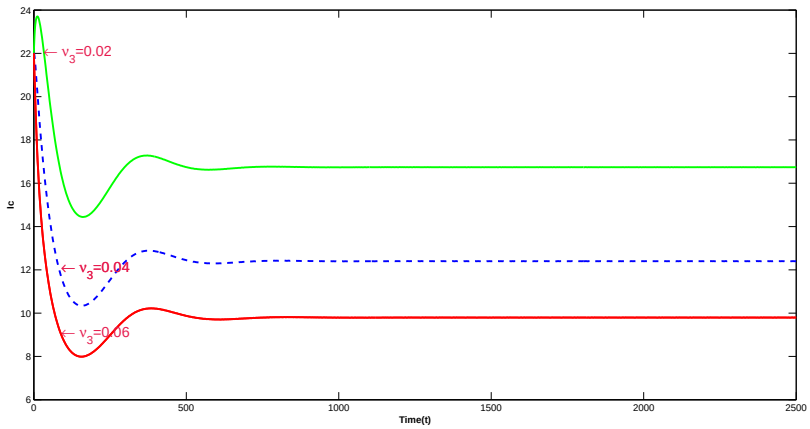

Fig. 6: Variation of I_c with time for different values of ν_3.

where t_f represent a pre-selected length of time during which these controls are applied. In the model, we are using the term $a_t u_2(t)$ where a_t is the additional recovery rate of a novel H1N1 infected individual undergoing treatment (i.e. $(\nu_3 + a_t u_2(t))$= recovery rate with treatment). It is assumed that u_1 and u_2 lie between 0 and 1. As if u_1 and u_2 are equal to zero, then there is no effort being placed in these controls at time t and if they are equal to one then maximum effort is applied.

Keeping in view of the above assumptions, the optimal control model is formulated as follows:

$$\frac{dS}{dt} = \Lambda - \mu S - (1 - u_1(t))\beta IS, \tag{2a}$$

$$\frac{dE}{dt} = (1 - u_1(t))\beta IS - \gamma_1 E - \gamma_2 E - \gamma_3 E - \mu E, \tag{2b}$$

$$\frac{dI_a}{dt} = \gamma_1 E - \nu_1 I_a - \mu I_a, \tag{2c}$$

$$\frac{dI_m}{dt} = \gamma_2 E - \nu_2 I_m - \mu I_m, \tag{2d}$$

$$\frac{dI_c}{dt} = \gamma_3 E - (\nu_3 + a_t u_2(t)) I_c - \mu I_c - \mu_1 I_c, \tag{2e}$$

$$\frac{dH}{dt} = (\nu_3 + a_t u_2(t)) I_c - \mu H - \mu_2 H - \delta H, \tag{2f}$$

$$\frac{dR}{dt} = \nu_1 I_a + \nu_2 I_m + \delta H - \mu R. \tag{2g}$$

6 The optimal control problem

In this section, we analyze the behavior of the given model by using optimal control theory. The objective functional for fixed time t_f is given below:

$$J = \int_0^{t_f} (c_1 I_a + c_2 I_m + c_3 I_c + \frac{1}{2} c_4 {u_1}^2 + \frac{1}{2} c_5 {u_2}^2) dt. \tag{3}$$

Here the parameter $c_1 \geq 0$, $c_2 \geq 0$, $c_3 \geq 0$, $c_4 \geq 0$ and $c_5 \geq 0$, and they represent the weight constants. Our objective is to find the control parameters ${u_1}^*$ and ${u_2}^*$, such that

$$J({u_1}^*, {u_2}^*) = \min_{u_1, u_2 \in \Omega} J(u_1, u_2), \tag{4}$$

where Ω is the control set and is defined as $\Omega = \{u_1, u_2 : \text{measurable and } 0 \leq u_1, u_2 \leq 1\}$ and $t \in [0, t_f]$.

The Lagrangian of this problem is defined as :

$$L(I_a, I_m, I_c, u_1, u_2) = c_1 I_a + c_2 I_m + c_3 I_c + \frac{1}{2} c_4 {u_1}^2 + \frac{1}{2} c_5 {u_2}^2$$

For our problem, we formed Hamiltonian $\mathcal{H}$:

$$\mathcal{H} = L(I_a, I_m, I_c, u_1, u_2) + \lambda_1 \frac{dS}{dt} + \lambda_2 \frac{dE}{dt} + \lambda_3 \frac{dI_a}{dt} + \lambda_4 \frac{dI_m}{dt} + \lambda_5 \frac{dI_c}{dt} + \lambda_6 \frac{dH}{dt} + \lambda_7 \frac{dR}{dt},$$

where λ_i are the adjoint variables and $i = 1$ to 7. Now adjoint variables in the form of differential equation can be written as follows:

$$\begin{aligned}
\frac{d\lambda_1}{dt} = -\frac{\partial \mathcal{H}}{\partial S} &= \lambda_1 \mu + (1 - u_1(t)) \beta I (\lambda_2 - \lambda_1), && (5a)\\
\frac{d\lambda_2}{dt} = -\frac{\partial \mathcal{H}}{\partial E} &= \lambda_2 \mu + \gamma_1 (\lambda_2 - \lambda_3) \\
&\quad + \gamma_2 (\lambda_2 - \lambda_4) + \gamma_3 (\lambda_2 - \lambda_5), && (5b)\\
\frac{d\lambda_3}{dt} = -\frac{\partial \mathcal{H}}{\partial I_a} &= -c_1 + (1 - u_1(t)) \beta S (\lambda_1 - \lambda_2) \\
&\quad + \nu_1 (\lambda_3 - \lambda_7) + \lambda_3 \mu, && (5c)\\
\frac{d\lambda_4}{dt} = -\frac{\partial \mathcal{H}}{\partial I_m} &= -c_2 + (1 - u_1(t)) \beta S (\lambda_1 - \lambda_2) \\
&\quad + \nu_2 (\lambda_4 - \lambda_7) + \lambda_4 \mu, && (5d)\\
\frac{d\lambda_5}{dt} = -\frac{\partial \mathcal{H}}{\partial I_c} &= -c_3 + (1 - u_1(t)) \beta S (\lambda_1 - \lambda_2) \\
&\quad + (\nu_3 + a_t u_2(t)) (\lambda_5 - \lambda_6) \\
&\quad + \lambda_5 (\mu + \mu_1), && (5e)\\
\frac{d\lambda_6}{dt} = -\frac{\partial \mathcal{H}}{\partial H} &= (\lambda_6 - \lambda_7) \delta + \lambda_6 (\mu + \mu_2), && (5f)\\
\frac{d\lambda_7}{dt} = -\frac{\partial \mathcal{H}}{\partial R} &= \mu \lambda_7. && (5g)
\end{aligned}$$

Let $\widetilde{S}$, $\widetilde{E}$, $\widetilde{I_a}$, $\widetilde{I_m}$, $\widetilde{I_c}$, $\widetilde{H}$, $\widetilde{R}$ be the optimum values of S, E, I_a, I_m, I_c respectively, and $\widetilde{\lambda_1}$, $\widetilde{\lambda_2}$, $\widetilde{\lambda_3}$, $\widetilde{\lambda_4}$, $\widetilde{\lambda_5}$, $\widetilde{\lambda_6}$, $\widetilde{\lambda_7}$ be the solution of the system (3). By using [8, 9], we state and prove the following theorem:

Theorem 4. *There exist optimal controls ${u_1}^*, {u_2}^* \in \Omega$ such that $J({u_1}^*, {u_2}^*) = \min J(u_1, u_2)$ subject to system (2).*

Proof. To prove this theorem we use [11]. Here the state variables and the controls are positive. For this minimizing problem, the necessary convexity of the objective functional in (u_1, u_2) is satisfied. The control variable set $u_1, u_2 \in \Omega$ is also convex and closed by the definition. The integrand of the functional

$$(c_1 I_a + c_2 I_m + c_3 I_c + \frac{1}{2} c_4 {u_1}^2 + \frac{1}{2} c_5 {u_2}^2)$$

is convex on the control set Ω and the state variables are bounded.

Since there exists an optimal control for minimizing the functional subject to Eqs. (2)-(4), we use Pontryagin's maximum principle to derive the necessary conditions to find the optimal solutions as follows:

If (x,u) is an optimal solution of an optimal control problem, then there exist a non-trivial vector function $\lambda = \lambda_1, \lambda_2, \lambda_3, \cdots, \lambda_n$ satisfying the following:

$$\frac{dx}{dt} = \frac{\partial H(t,x,u,\lambda)}{\partial \lambda}, \quad 0 = \frac{\partial H(t,x,u,\lambda)}{\partial \lambda}, \quad \frac{d\lambda}{dt} = \frac{\partial H(t,x,u,\lambda)}{\partial \lambda}.$$

With the help of Pontryagin's maximum principle[11] and theorem (1), we prove the following theorem:

Theorem 5. *The optimal controls $({u_1}^*, {u_2}^*)$ which minimizes J over the region Ω given by*

$${u_1}^* = \min\{1, \max(0, \widetilde{u_1})\}, \quad {u_2}^* = \min\{1, \max(0, \widetilde{u_2})\},$$

where

$$\widetilde{u_1} = \frac{\beta(I_a + I_m + I_c)S(\lambda_2 - \lambda_1)}{c_4},$$
$$\widetilde{u_2} = \frac{a(\lambda_5 - \lambda_6)I_c}{c_5}.$$

Proof. Using optimally condition:

$\frac{\partial \mathcal{H}}{\partial u_1} = 0$, $\frac{\partial \mathcal{H}}{\partial u_2} = 0$ we get, $\frac{\partial \mathcal{H}}{\partial u_1} = u_1 c_4 + \lambda_1 \beta I - \lambda_2 \beta I = 0.$

This implies $u_1 = \frac{(\lambda_2 - \lambda_1)\beta I}{c_4} = \widetilde{u_1}$

And, $\frac{\partial \mathcal{H}}{\partial u_2} = u_2 c_5 - \lambda_5 a I_c + \lambda_6 a I_c = 0$ gives $u_2 = \frac{(\lambda_5 - \lambda_6) a I_c}{c_5} = \widetilde{u_2}$.

Again upper and lower bounds for these control are 0 and 1 respectively. i.e. $u_1 = u_2 = 0$ if $u_1 < 0$ and $u_2 < 0$, and $u_1 = u_2 = 1$ if $\widetilde{u_1} > 1$ and $\widetilde{u_2} > 1$, otherwise $u_1 = \widetilde{u_1}$ and $u_2 = \widetilde{u_2}$. Hence for these controls ${u_1}^*, {u_2}^*$ we get optimum value of the function J.

6.1 Simulation of optimal control model

The optimal control model is simulated using MATLAB. The weight constants for the optimal control problem are taken as $C_1 = 1, C_2 = 1, C_3 = 1, C_4 = 100, C_5 = 110$. We solve the optimality system by iterative method with the help of forward and backward difference approximations (see [8]). We consider the time interval as $[0, 150]$. First we solve the state equations by the forward difference approximation method then we use the backward difference approximation method to solve the adjoint equations in the same time interval. Figs. 7 and 8 are showing the optimal control profile of u_1 and u_2 respectively for the following set of parameters. All the parameters are in day. $\Lambda = 7$, $\mu = 0.0075$, $\beta = 0.0001$, $\gamma_1 = 0.1$, $\gamma_2 = 0.1$, $\gamma_3 = 0.1$, $\nu_1 = 0.03$, $\nu_2 = 0.03$, $\nu_3 = 0.02, \delta = 0.02, \mu_1 = 0.04227, \mu_2 = 0.027855$. The effect of weight constant C_5 on critically ill individuals is demonstrated in Fig. 9. Similarly, effect of weight constant C_4 on exposed individuals is demonstrated in Fig. 10. From these figures it is observed that increase in the values of weight constants leads to increase in the corresponding variable which is obvious as increase in cost of control causes reduction in the control measures. This fact is demonstrated in Figs. 11-12. Figure 13 is showing the variation of I_c with time with and without optimal control. These simulation results indicate the effectiveness of optimal control strategies in reducing the number of infections.

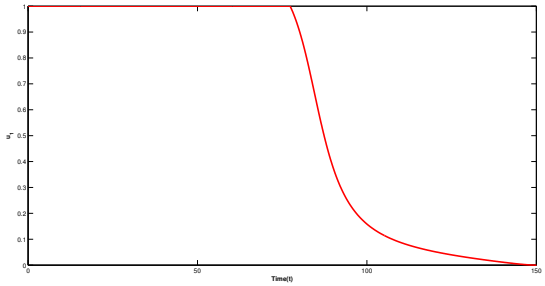

Fig. 7: Optimal control profile of u_1.

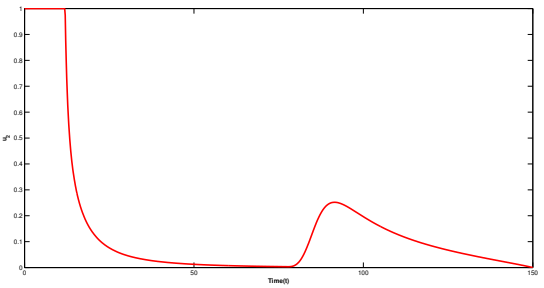

Fig. 8: Optimal control profile of u_2.

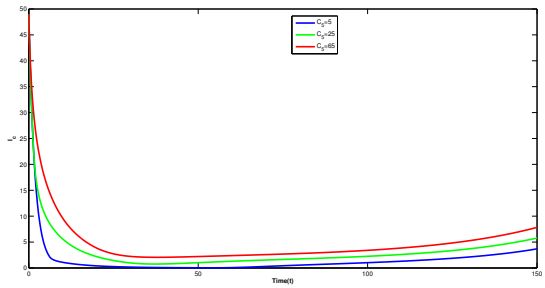

Fig. 9: Variation of I_c with time for different values of weight constant C_5.

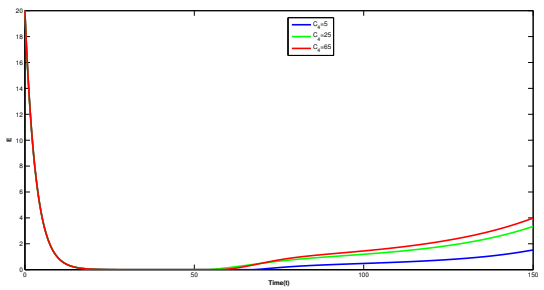

Fig. 10: Variation of E with time for different values of weight constant C_4.

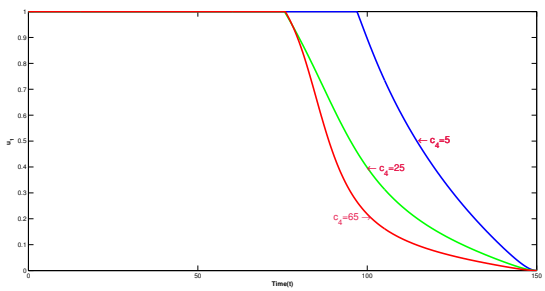

Fig. 11: Optimal control profile of u_1 for different costs of control C_4.

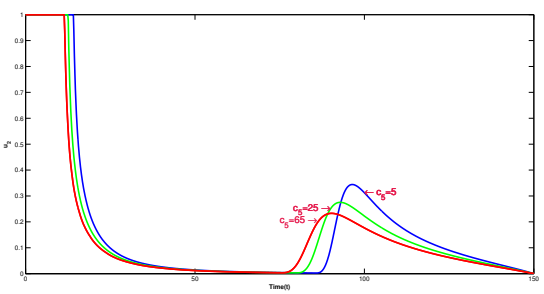

Fig. 12: Optimal control profile of u_2 for different costs of control C_5.

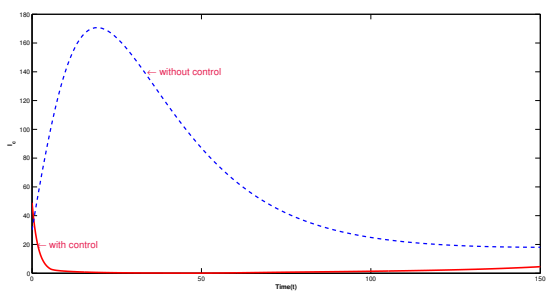

Fig. 13: Variation of I_c with time with and without control

7 Conclusion

Here an SEIHR type epidemic model for the transmission dynamics of a H1N1 (flu) disease is proposed and analyzed. The given model has a globally asymptotically stable disease free equilibrium (DFE) whenever the basic reproduction number R_0 is less than unity. The endemic equilibrium of the model is globally asymptotically stable whenever the basic reproduction number R_0 is greater than unity. Numerical simulation is performed to support our analytical findings. Also, it is observed that the increase in the parameter ν_3

which corresponds to the rate of hospitalization of critically infected individuals leads to the decrease in the equilibrium levels of I_a, I_m, and I_c.

Further the proposed model is extended to optimal control problem by introducing two types of controls which correspond to reduction in the transmission rate of this disease and timely hospitalization of critically ill infections. The optimal control problem is analyzed using Pontryagins maximum principle. The numerical simulation is performed which indicates that optimal control strategy is very effective in reducing the total number of infections.

References

[1] C. Castillo-Chavez, Z. Feng, W. Huang. On the computation of r and its role on global stability. **in:** *Mathematical Approaches for For Emerging and Reemerging Infectious Diseases*, Springer-Verlag, 2002, 229–250.

[2] J. Chin, G. Koh, D. Y. Lee. How necessary is a fast testkit for mitigation of pandemic flu? *Journal of the Royal Society Interface*, 2010, **7**(48): 1033–47.

[3] O. Diekmann, J. A. P. Heesterbeek, J. A. J. Metz. On the definition and the computation of the basic reproduction ratio r 0 in models for infectious diseases in heterogeneous populations. *Journal of Mathematical Biology*, 1990, **28**(4): 365–382.

[4] P. V. D. Driessche, J. Watmough. Reproduction numbers and sub-threshold endemic equilibria for compartmental models of disease transmission. *Mathematical Biosciences*, 2002, **180**(1-2): 29–48.

[5] D. A. Fitzgerald. Human swine influenza a [h1n1]: Practical advice for clinicians early in the pandemic. *Paediatric Respiratory Reviews*, 2009, **10**(3): 154–158.

[6] A. Korobeinikov, G. C. Wake. Lyapunov functions and global stability for sir, sirs, and sis epidemiological models. *Applied Mathematics Letters*, 2002, **15**(8): 955–960.

[7] B. J. P. Lasalle. The stability of dynamical systems. society for industrial and applied mathematics. **in:** *Artstein, Regional Conference Series in Applied Mathematics*, 2010.

[8] S. Lenhart, J. T. Workman. Optimal control applied to biological models. *Crc Press*, 2007.

[9] D. L. Lukes. Differential equations: Classical to controlled. *American Mathematical Monthly*, 1985, **92**(3).

[10] P. Pongsumpun, I. M. Tang. Mathematical model of the symptomatic and asymptomatic infections of swine flu. *International Journal of Mathematical Models & Methods in Applied Sciences*, 2011, **5**(2): 247–254.

[11] L. S. Pontryagin, V. G. Boltyanskii, R. V. Gamkrelidze, E. F. Mishchenko. *The Mathematical theory of optimal processes*. Interscience Publishers,, 1962.

[12] M. A. Safi, A. B. Gumel. Mathematical analysis of a disease transmission model with quarantine, isolation and an imperfect vaccine. *Computers & Mathematics with Applications*, 2011, **61**(10): 3044–3070.

[13] O. Sharomi, C. N. Podder, A. B. Gumel, S. M. Mahmud, E. Rubinstein. Modelling the transmission dynamics and control of the novel 2009 swine influenza (h1n1) pandemic. *Bulletin of Mathematical Biology*, 2011, **73**(73): 515–48.