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Modelling and simulation of Influenza with Screening

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Abstract*— Influenza, generally known as common cold or flu is a highly infectious disease caused by influenza virus. It is transmitted through coughing or sneezing by an infected person. Generally, it is not taken seriously by people at initial stage. But in present scenario, after emergence and re-emergence of influenza virus causing more severe illnesses such as swine flu, bird flu etc., and the simple looking cough-cold may turn life threatening as well. Here, in this research work, we have formulated two deterministic models for influenza. The first one is simple model with four compartments namely Susceptible (S), Infectious (I), Infected with Swine flu (I_{sw}), and Recovered (R). Here patients move to swine flu class through screening. A relation for basic reproduction number is established. Then a further complex model is formulated with various effects of vaccination. In this model the entire population is divided into eight compartments. These compartments are Unvaccinated Susceptible (S_u), Vaccinated Susceptible (S_v), Unvaccinated Infectious (I_u), Vaccinated Infectious (I_v), Unvaccinated and Infected with Swine flu (I_{swu}), Vaccinated and Infected with Swine flu (I_{swv}), Unvaccinated Recovered population (R_u), Vaccinated Recovered population (R_v). Model is formulated using ordinary differential equations. A relation for basic reproduction number, R_0, is deduced for both vaccinated population as well as unvaccinated population. Steady state conditions are derived giving that the disease free equilibrium is stable if $R_{u0} + R_{v0} < 1$ otherwise unstable. Sensitivity analysis and simulation is done using MATLAB giving us a vision of future disease scenario and right direction for working towards disease control.

***Index Terms*—Mathematical model, Influenza, Sensitivity analysis, Simulation, Swine flu.**

I. INTRODUCTION

Influenza is a highly infectious disease of respiratory system. It can induce mild to critical ailment. Grievous consequences of this disease can result in hospitalization and death. Influenza virus is broadly classified into three classes namely influenza-virus A, influenza-virus B and influenza-virus C. Type B and type are less common. The most active out of three is type A. Its natural hosts are wild aquatic birds. But it mutates very easily. Influenza viruses were the first animal viruses found capable of combining with human red blood cells. Current subtypes of influenza A viruses found in human beings are H0N1 (seasonal flu), H1N1 (swine flu) and H3N2 (bird flu) and the latest one H5N1. Seasonal flu is the most common out of all. Next dominating influenza is swine flu. Bird flu occurs to those who are working in poultry farms where infected birds are present. Therefore evolution of virus is making the scenario worse. Many vaccines are being developed for the disease but as the virus evolves, the vaccine becomes obsolete and new research is required again. Many researches have been done from various directions. Simon *et al.* discussed various vaccine effects with the help of mathematical model [1]. Shim *et al.* formulated vaccination model on the basis of public interest [2]. Coburn *et al.* reviewed the present scenario and various researches and concluded that more intense research is required [3]. Beauchemin and Handel reviewed mathematical models of virus dynamics in human body [4]. Kamate *et al.* provide detailed scenario of disease in India and used for extracting data.

II. SIMPLE MATHEMATICAL MODEL

Here, we formulate an epidemic model similar to SIR. In order to formulate a simple model with screening and without vaccination, we divide the entire population into four compartments as susceptibles (S), infectious (I), infected with swine flu (I_{sw}) and recovered (R). Here, it is assumed that as soon as the patient loses the symptoms, moves to recovered class and does not spread infection any more. The transfer of population from one compartment to the other is depicted in figure 1.

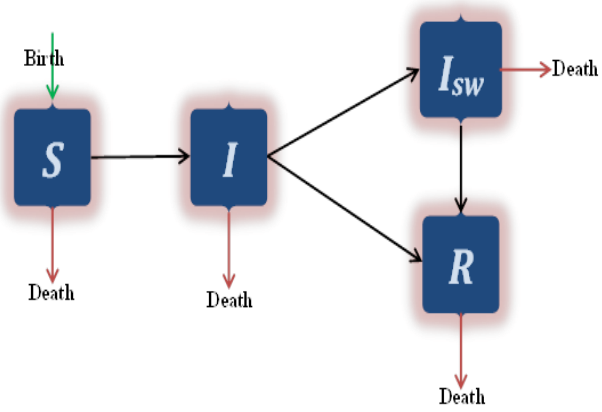

Fig 1: Flow of population from one compartment to other

The person enters the susceptible compartment by birth. When he gets exposed to the infection and shows symptoms of disease, he moves to infectious class. At this stage screening is done (by means of some tests) in order to see if it is influenza or swine flu. After screening if the test turns positive the person moves to swine flu compartment. In either case person receives the treatment and moves to recovered class. Natural death can take place at any stage but disease induced death is possible in I/I_{sw} compartments only.

The state variables and parameters used in simple model are given below:

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S: Number of susceptibles
I: Population infected with influenza virus
I_{sw}: Population infected with swine flu
R: Number of patients recovered
N: Total population
B: Birth rate
β: Probability of transmission of infection
μ: Natural death rate
δ: Disease induced death rate
c: Contact rate
γ: Treatment rate
σ: Rate of screening

Taking assumptions into account and using ordinary differential equations, the model takes the form as given below:

$$\frac{dS}{dt} = B - \frac{\beta cSI}{N} - \frac{\beta cSI_{sw}}{N} - \mu S \quad (1)$$

$$\frac{dI}{dt} = \frac{\beta cSI}{N} + \frac{\beta cSI_{sw}}{N} - (\sigma + \gamma + \mu + \delta) I \quad (2)$$

$$\frac{dI_{sw}}{dt} = \sigma I - (\gamma + \mu + \delta) I_{sw} \quad (3)$$

$$\frac{dR}{dt} = \gamma I + \gamma I_{sw} - \mu R \quad (4)$$

with

$$N = S + I + I_{sw} + R \quad (5)$$

Adding above four equations, we have

$$\frac{d}{dt}(S + I + I_{sw} + R) = B - \mu(S + I + I_{sw} + R) - \delta(I + I_{sw})$$

$$\Rightarrow (S + I + I_{sw} + R)' \le B - \mu(S + I + I_{sw} + R)$$

Then $$\limsup_{t \to \infty} (S + I + I_{sw} + R) \le \frac{B}{\mu}$$

So, the feasible region for the system is

$$\Lambda = \left\{ (S, I, I_{sw}, R) : S + I + I_{sw} + R \le \frac{B}{\mu}, \; S > 0, I \ge 0, I_{sw} \ge 0, R \ge 0 \right\} \quad (6)$$

Since R does not appear in any of the first three equations, so we can drop the fourth in analysis and use first three equations giving a reduced system consisting of equations (1) – (3).

Let $E(\bar{S}, \bar{I}, \bar{I}_{sw})$ be an equilibrium point of the reduced system of equations. The system will have a disease free equilibrium at

$$E_0(\bar{S}, \bar{I}, \bar{I}_{sw}) = \left(\frac{B}{\mu}, 0, 0 \right)$$

Let $E' = (I, I_{sw}, S)^T$.

Therefore $E' = \frac{dE}{dt} = \mathcal{F}(E) - \mathcal{V}(E)$

where

$$\mathcal{F}(E) = \begin{bmatrix} \frac{\beta cSI}{N} + \frac{\beta cSI_{sw}}{N} \\ 0 \\ 0 \end{bmatrix}$$

and $$\mathcal{V}(E) = \begin{bmatrix} (\sigma + \gamma + \mu + \delta) I \\ -\sigma I + (\gamma + \mu + \delta) I_{sw} \\ -B + \frac{\beta cS}{N}(I + I_{sw}) + \mu S \end{bmatrix}$$

The derivatives of $\mathcal{F}(E)$ and $\mathcal{V}(E)$ at disease free equilibrium E_0 are partitioned as

$$D\mathcal{F}(E_0) = \begin{bmatrix} F & 0 \\ 0 & 0 \end{bmatrix} \quad \text{and} \quad D\mathcal{V}(E_0) = \begin{bmatrix} V & 0 \\ J_1 & J_2 \end{bmatrix}$$

where F and V are 2×2 matrices given by

$$F = \begin{bmatrix} \frac{\beta cB}{\mu N} & \frac{\beta cB}{\mu N} \\ 0 & 0 \end{bmatrix}$$

and $$V = \begin{bmatrix} (\sigma + \gamma + \mu + \delta) & 0 \\ -\sigma & (\gamma + \mu + \delta) \end{bmatrix}$$

$$\Rightarrow \quad FV^{-1} = \begin{bmatrix} \frac{\beta cB}{\mu N(\gamma + \mu + \delta)} & \frac{\beta cB}{\mu N(\gamma + \mu + \delta)} \\ 0 & 0 \end{bmatrix}$$

This gives basic reproduction number to be

$$R_0 = \frac{\beta cB}{\mu N(\gamma + \mu + \delta)} \quad (7)$$

III. MODEL WITH VACCINATION

Here, we introduced vaccination among the population. We broadly bifurcated the entire population as vaccinated and unvaccinated then further divided both the populations into four compartment each, as in the above model. We give the list of new state variables as below:

S_u: Number of unvaccinated susceptibles
S_v: Number of vaccinated susceptibles
I_u: Unvaccinated population infected with influenza virus
I_v: Vaccinated population infected with influenza virus
I_{swu}: Unvaccinated population infected with swine flu
I_{swv}: Vaccinated population infected with swine flu
R_u: Number of unvaccinated patients recovered
R_v: Number of vaccinated patients recovered

The transfer diagram of the model is given in fig 2.

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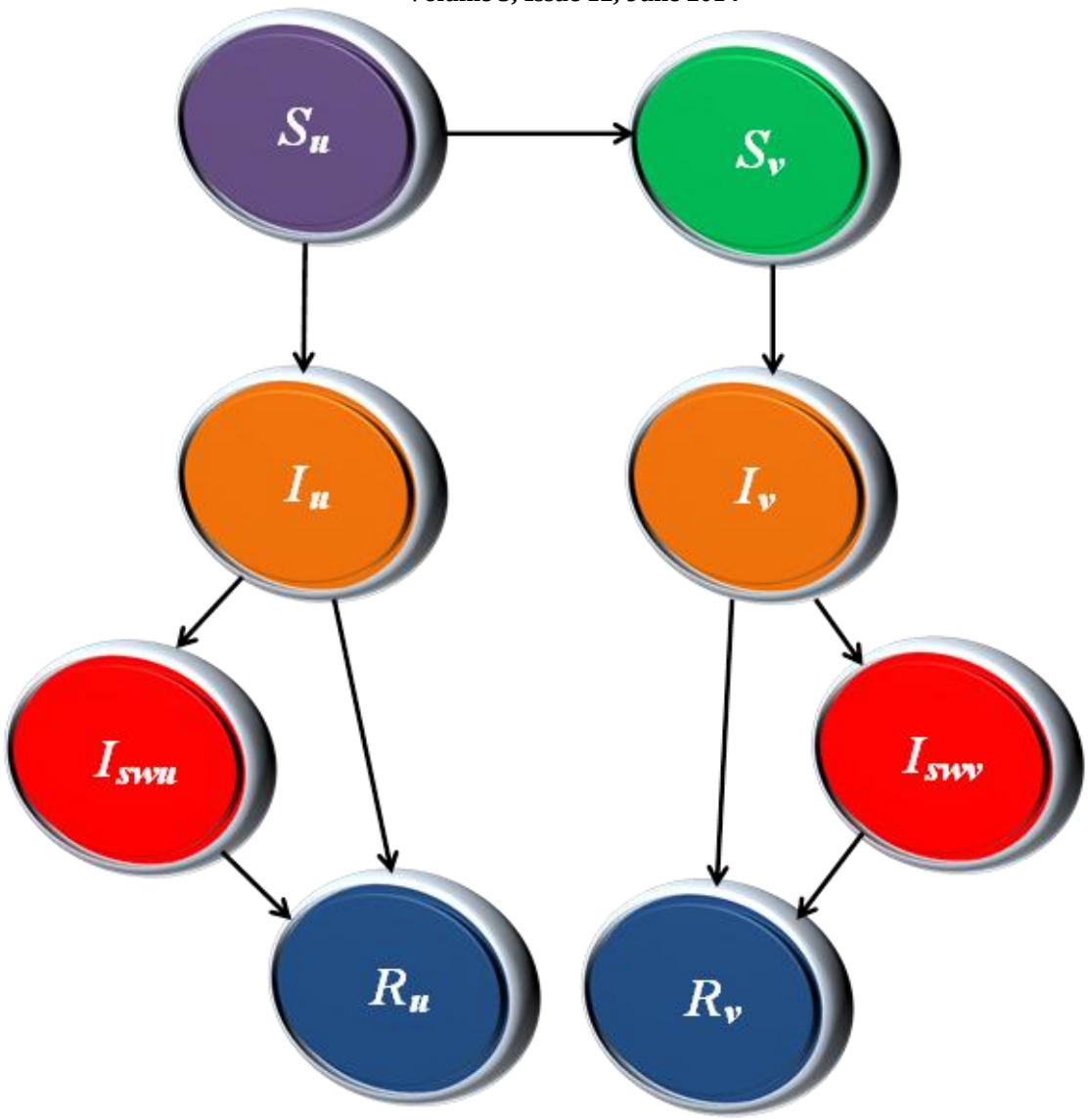

Fig 2: Transfer diagram for the model with vaccination

Generally, we assume that after vaccination a person attains full protection against the disease. Practically, when vaccination is done, in some cases 100% sterilization is not achieved i.e. even after vaccination for a disease, there is a certain amount of possibility for the person to catch the infection. So, as used by Simon [1] in his paper, we discuss all possible effects of vaccination here and use them for our influenza model. These effects are explained below:

- **Sterilizing immunity** (ω): The person attains full protection against the disease-causing microorganism.
- **Reduced susceptibility effect** (ω_s): It means that if a microorganism is transmitted to a person who has received vaccination but not achieved sterilizing effect, there are reduced chances that this infectious agent will find a suitable place to grow rapidly.
- **Infectiousness effect** (ω_c): If the infectious agent begins to grow, the speed of proliferation would be slower and therefore there would be fewer microorganisms available for getting transmitted to others i.e. the person would be less contagious.
- **Disease duration effect** (ω_d): The person would have boosted immune response to the agent that would reduce the duration of infection.

Let the fraction p of the population be vaccinated. Taking all four effects and other considerations into account we formulate the model as follows:

$$\frac{dS_u}{dt} = (1-p)B - \beta c \frac{S_u I_u}{N} - \omega_c \beta c \frac{S_u I_v}{N} - \mu S_u \quad (8)$$

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$$\frac{dS_v}{dt} = pB - \omega_s \beta c \frac{S_v I_u}{N} - \omega_s \omega_c \beta c \frac{S_v I_v}{N} - (\mu + \omega p) S_v \quad (9)$$

$$\frac{dI_u}{dt} = \beta c \frac{S_u I_u}{N} + \omega_c \beta c \frac{S_u I_v}{N} - (\sigma + \gamma + \mu + \delta) I_u \quad (10)$$

$$\frac{dI_v}{dt} = \omega_s \beta c \frac{S_v I_u}{N} + \omega_s \omega_c \beta c \frac{S_v I_v}{N} - \frac{(\mu + \gamma)}{\omega_d} I_v - (\sigma + \mu + \delta) I_v \quad (11)$$

$$\frac{dI_{swu}}{dt} = \sigma I_u - (\gamma + \mu + \delta) I_{swu} \quad (12)$$

$$\frac{dI_{swv}}{dt} = \sigma I_v - \frac{(\mu + \gamma)}{\omega_d} I_{swv} - (\gamma + \mu + \delta) I_{swv} \quad (13)$$

$$\frac{dR_u}{dt} = \gamma (I_u + I_{swu}) - \mu R_u \quad (14)$$

$$\frac{dR_v}{dt} = \frac{(\mu + \gamma)}{\omega_d} (I_v + I_{swv}) - \mu R_v + \omega p S_v \quad (15)$$

with $N = S_u + S_v + I_u + I_v + I_{swu} + I_{swv} + R_u + R_v$

$$\Rightarrow \frac{dN}{dt} = B - \mu (S_u + S_v + I_u + I_v + I_{swu} + I_{swv} + R_u + R_v) - \delta (I_u + I_v + I_{swu} + I_{swv})$$

$$\Rightarrow \quad \frac{dN}{dt} \le B - \mu N$$

$$\Rightarrow \quad \limsup_{t \to \infty} N \le \frac{B}{\mu}$$

So, the feasible region for the system is

$$\Lambda = \left\{ (S_u, S_v, I_u, I_v, I_{swu}, I_{swv}, R_u, R_v) : S_u + S_v + I_u + I_v + I_{swu} + I_{swv} + R_u + R_v \le \frac{B}{\mu}, \; S_u > 0, S_v > 0, I_u \ge 0, I_v \ge 0, I_{swu} \ge 0, I_{swv} \ge 0, R_u \ge 0, R_v \ge 0 \right\}$$

Leaving both the recovered compartments namely R_u and R_v, we use reduced system of equations consisting of equations (8) to (13).

Let $E_v(\bar{S}_u, \bar{S}_v, \bar{I}_u, \bar{I}_v, \bar{I}_{swu}, \bar{I}_{swv})$ be an equilibrium point of the above reduced system of equations. The system will have a disease free equilibrium at

$$E_{v0}(\bar{S}_u, \bar{S}_v, \bar{I}_u, \bar{I}_v, \bar{I}_{swu}, \bar{I}_{swv}) = ((1-p), p(1-\omega), 0, 0, 0, \omega p)$$

Let $X' = E_v(I_u, I_v, I_{swu}, I_{swv}, S_u, S_v)$.

Therefore $X' = \frac{dX}{dt} = \mathcal{F}(X) - \mathcal{V}(X)$

where $\mathcal{F}(X) = \begin{bmatrix} \beta c \frac{S_u I_u}{N} + \omega_c \beta c \frac{S_u I_v}{N} \\ \omega_s \beta c \frac{S_v I_u}{N} + \omega_s \omega_c \beta c \frac{S_v I_v}{N} \\ 0 \\ 0 \\ 0 \\ 0 \end{bmatrix}$

and

$$\mathcal{V}(X) = \begin{bmatrix} (\sigma + \gamma + \mu + \delta) I_u \\ \frac{(\mu + \gamma)}{\omega_d} I_v + (\sigma + \mu + \delta) I_v \\ -\sigma I_u + (\gamma + \mu + \delta) I_{swu} \\ -\sigma I_v + \frac{(\mu + \gamma)}{\omega_d} I_{swv} + (\mu + \delta) I_{swv} \\ -(1-p) B + \beta c \frac{S_u I_u}{N} + \omega_c \beta c \frac{S_u I_v}{N} + \mu S_u \\ -pB + \omega_s \beta c \frac{S_v I_u}{N} + \omega_s \omega_c \beta c \frac{S_v I_v}{N} + (\mu + \omega p) S_v \end{bmatrix}$$

The derivatives of $\mathcal{F}(X)$ and $\mathcal{V}(X)$ at disease free equilibrium are partitioned as

$$D\mathcal{F}(E_0) = \begin{bmatrix} F & 0 \\ 0 & 0 \end{bmatrix} \quad \text{and} \quad D\mathcal{V}(E_0) = \begin{bmatrix} V & 0 \\ J_1 & J_2 \end{bmatrix}$$

where

$$F = \begin{bmatrix} \frac{\beta c (1-p)}{N} & \frac{\omega_c \beta c (1-p)}{N} & 0 \\ \frac{\omega_s \beta c p (1-\omega)}{N} & \frac{\omega_s \omega_c \beta c p (1-\omega)}{N} & 0 \\ 0 & 0 & 0 \end{bmatrix}$$

and

$$V = \begin{bmatrix} (\sigma + \gamma + \mu + \delta) & 0 & 0 \\ 0 & \frac{(\mu + \gamma)}{\omega_d} + (\sigma + \mu + \delta) & 0 \\ -\sigma & 0 & (\gamma + \mu + \delta) \end{bmatrix}$$

Therefore

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$$FV^{-1} = \begin{bmatrix} \dfrac{\beta c(1-p)}{N(\sigma+\gamma+\mu+\delta)} & \dfrac{\omega_c \beta c(1-p)}{N\left[\dfrac{(\mu+\gamma)}{\omega_d}+(\sigma+\mu+\delta)\right]} & 0 \\ \dfrac{\omega_s \beta cp(1-\omega)}{N(\sigma+\gamma+\mu+\delta)} & \dfrac{\omega_s \omega_c \beta cp(1-\omega)}{N\left[\dfrac{(\mu+\gamma)}{\omega_d}+(\sigma+\mu+\delta)\right]} & 0 \\ 0 & 0 & 0 \end{bmatrix}$$

Therefore, basic reproduction number

$$R = \left(\frac{\beta c(1-p)}{N(\sigma+\gamma+\mu+\delta)}, \frac{\omega_s \omega_c \beta cp(1-\omega)}{N\left[\dfrac{(\mu+\gamma)}{\omega_d}+(\sigma+\mu+\delta)\right]} \right) = (R_{0u}, R_{0v})$$

IV. STABILITY OF DISEASE FREE EQUILIBRIUM

The Jacobian of system under consideration can be written as

$$J = \begin{bmatrix} -\mu & 0 & 0 & 0 & 0 & 0 \\ 0 & -(\mu+\omega p) & 0 & 0 & 0 & 0 \\ 0 & 0 & \dfrac{\beta c(1-p)}{N} - (\sigma+\gamma+\mu+\delta) & \dfrac{\omega_s \beta c(1-p)}{N} & 0 & 0 \\ 0 & 0 & \dfrac{\omega_s \beta cp(1-\omega)}{N} & \dfrac{\omega_s \omega_c \beta cp(1-\omega)}{N} - \dfrac{(\mu+\gamma)}{\omega_d} - (\sigma+\mu+\delta) & 0 & 0 \\ 0 & 0 & \sigma & 0 & -(\gamma+\mu+\delta) & 0 \\ 0 & 0 & 0 & \sigma & 0 & -\dfrac{(\mu+\gamma)}{\omega_d} - (\mu+\delta) \end{bmatrix}$$

Clearly, trace (J) is negative.

Now, for det (J) to be positive, we simplify $|J|$ and get the relation as

$$\omega_s \omega_c \beta cp \frac{(1-\omega)}{N}(\sigma+\gamma+\mu+\delta) < \left[\frac{(\mu+\gamma)}{\omega_d}+(\sigma+\mu+\delta)\right] \times \left((\sigma+\gamma+\mu+\delta) - \frac{\beta c(1-p)}{N}\right) \quad (16)$$

$$\Rightarrow \quad R_{0v} < 1 - R_{0u}$$

$$\Rightarrow \quad R_{0v} + R_{0u} < 1$$

This shows that the disease free equilibrium is locally asymptotically stable if total basic reproduction number of both the populations (i.e. vaccinated and unvaccinated) is less than one.

V. MINIMUM FRACTION OF POPULATION TO BE VACCINATED

If we provide vaccination for some virus or bacteria to a significant fraction of population, then it provide protection to those individuals also who have not taken vaccine for developing immunity to that agent as there are very few susceptibles left in the population. This is termed as community immunity or herd immunity. This is a very effective method to stop the spread of a particular disease in the population. On rewriting relation (16) in terms of p, we get a relation as follows:

$$p > \frac{\left(1 - \dfrac{N}{\beta c}(\sigma+\gamma+\mu+\delta)\right)}{\left[\dfrac{\omega_s \omega_c \omega_d (1-\omega)(\sigma+\gamma+\mu+\delta)}{(\mu+\gamma)+\omega_d(\sigma+\mu+\delta)} - 1\right]} \quad (17)$$

The relation (17) provides us the optimum size of the population to be vaccinated in order to achieve disease free scenario.

VI. SENSITIVITY ANALYSIS

For checking the sensitivity of basic reproduction number to each parameter, we use parameter values as: $\beta = 0.008$; $c = 100$; $\mu = 0.008$; $\delta = 0.06$; $\gamma = 0.5$; $\sigma = 0.23$; $p = 0.6$; $\omega = 0.75$; $\omega_s = 0.6$; $\omega_c = 0.6$; $\omega_d = 0.6$. Most of the parameter values are taken from previous research works and government websites. But some values, like four vaccine effects, have been chosen reasonably feasible. The results of sensitivity analysis are given in table 1 and table 2.

Table 1. Sensitivity indices for R_{0u}

Parameter	Sign	Index
β	+	1.0000
c	+	1.0000
σ	-	0.2882
γ	-	0.6266
μ	-	0.0100
δ	-	0.0752
p	-	1.5000

Table 2. Sensitivity indices for R_v

Parameter	Sign	Index
β	+	1.0000
c	+	1.0000
σ	-	0.2009
γ	-	0.7280
μ	-	0.0187
δ	-	0.0524
ω	-	3.0000
ω_s	+	1.0000
ω_c	+	1.0000
ω_d	+	0.7397

These indices show that the transmission rate has positive impact on disease spread. On the other hand vaccination widely helps in controlling the disease. 25000 to see the population trends in various compartments and foresee the impact of screening and vaccination on the disease. These results are shown in

VII. NUMERICAL SIMULATION

Numerical simulation is done for a sample population of

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figure 3.

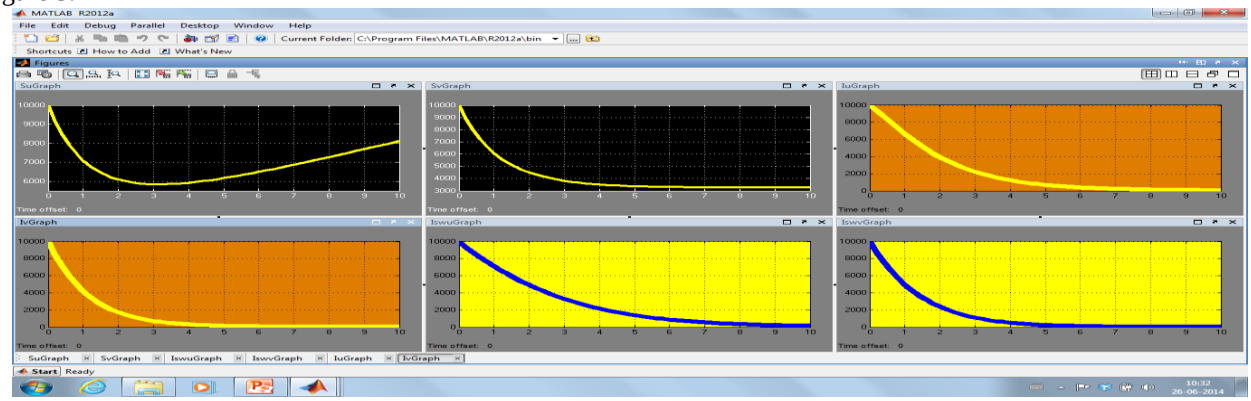

Fig 3. Population dynamics in various compartments

VIII. RESULTS AND DISCUSSION

In this study, we formulated two models for influenza parallel to SIR epidemic model – one simple model with screening and without vaccination and then the other with vaccination. A relation for basic reproduction is established for both the models. Steady state conditions are derived for model with vaccination giving that the disease free equilibrium will be locally asymptotically stable if total basic reproduction number is less than one. Sensitivity analysis result shows that vaccination is highly effective in case of this disease. Also, simulation results show that those who have received vaccination and have not achieved sterilizing immunity, recover faster than others. So, if we need to bring awareness among the population and motivate them for vaccination.

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