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SIMPLE VACCINATION AND PREVENTION MODEL OF RESPIRATORY SYNCYTIAL VIRUS

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Abstract

We present a simple model for vaccination and prevention of respiratory syncytial virus (RSV) in the form of system of differential equations. In this model, the population is divided into three compartments: susceptible, infected and recovery. RSV control simulation consists of vaccination, campaign program and the combination of these two controls. Among these controls, the combination of vaccination and campaign program are the most effective strategy for controlling the disease. We conclude that vaccination parameter plays an important role in controlling the disease. The parameter has a more significant impact on the reduction of the infected compartment compared to campaign program one. We also found the appropriate period of time for the vaccination to obtain effective results. We also discussed the phase portrait between susceptible and infected in the presence of vaccination and campaign program. In addition, as case study, we conduct curve fitting the model with the data respiratory syncytial virus disease in North Carolina, USA.

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1. Introduction

Syncytial virus, or RSV, is respiratory virus that causes infections in the lungs and breathing passages [6]. It is common in infancy and almost all children in the age of two experienced this virus at least one time. The incubation period of RSV is about two to eight days and then infected person will get symptoms like coughing, sneezing, running nose, fever and less appetite [7, 8]. Especially, for infected young infants, the symptoms are less activity, irritability and breathing difficulties. The RSV is not a serious problem in infected healthy people because the immune system can handle this effectively [7]. Reinfection can occur during lifetime, but less severe after the first infection [9]. High risk exists in premature infants and persons under medical treatment such as of congenital heart disease, chronic lung disease [5, 9].

Bronchiolitis and pneumonia are important problems of lower infection respiratory and most of them caused by RSV that generally require hospitalization [8]. About 40% of RSV infection in infancy are cases of both diseases [9]. Pneumonia itself is a serious disease for children that requires attention of the government. According to WHO report in 2015, as many as 16% of deaths of children under five are caused by pneumonia. Moreover, pneumonia ranks second cause of child mortality after preterm birth complications [13]. Unfortunately, currently RSV vaccine is not yet available due to under development [14]. However, the high risk of severe illness such as infants who are premature or have chronic lung disease or congenital heart disease can be reduced by administration of drug such as palivizumab before and over season [5]. Administration of the drug can reduce hospitalization by 55% [15]. Occurrence and epidemic RSV can be reduced by campaign program that promotes healthy life such as making poster not to share utensils or cups, avoid kissing others, covering cough and sneezes and washing hand frequently and correctly [7]. The impact of the program is to contact people so that the virus be less. Thus the possibility of people infected by RSV is also less.

The disease can occur throughout the year, however, it has a regular

pattern that depends on the season as well as is closely related to climate [1-5, 9-11]. In sub-tropic region, the peak of RSV is usually observed in the winter season [9]. In tropic region like Singapore [11], RSV infection usually occurs in January-September reaching its peak in June. In other tropic regions like Kuala Lumpur, Malaysia, the peak is in September-December. The rainy season has become a significant factor for the monthly RSV case. In addition, the relative humidity and the temperature vary inversely with disease [12].

To get a better understanding of RSV epidemiology, researchers seek to study and investigate the disease transmission through mathematical modeling. This model allows the prediction of population dynamics of infected compartment either in the absence or presence of treatment. The results of this model are important and can be considered by the government for the implementation of policy or strategy to minimize outbreaks of disease. Of course, this is an alternative way in terms of economic cost.

In 2001, Weber et al. in [1] proposed the model of RSV taking into account the incidence of reinfection. Their model was built using a system of differential equations in the framework *MSEIRS*4. They divided the human population into five groups: maternal (*M*), susceptible (*S*), exposed (*E*), infected (*I*) and recovery (*R*). Group *M* newborn is protected by maternal immunity, while the *S*, *E*, *I* and *R* have the usual meaning *SEIR* model commonly used for epidemiological modeling. Reinfection in the model will be followed by a gradual acquisition of partial immunity. Qualitatively, the results of their simulations matched with a simple model of *SIRS* and empirical data from several countries such as the Gambia, the United States, Finland and Singapore. RSV model analysis has been developed by Jódar et al. [2]. They discussed the criteria for the existence and uniqueness of periodic solutions by using a continuation theorem based on coincidence degree theory. Using Lyapunov function, they found a unique periodic solution which is globally asymptotically stable.

Acedo et al. in [3] proposed the model of RSV taking into account the age structure. They divided the population into two groups such as the *G*1

according to children aged 0-1 years and $G2$ in accordance with the rest of the population. Models equipped with the data from the Spanish region of Valencia are presented. Then they explored and applied the model to estimate the cost of hospitalization and the cost of the vaccine program. Like the earlier work, Moore et al. [4] developed the model of RSV and matched with data from metropolitan Western Australia. They also introduced statistical parameter F (fit statistics) which measures the deviation between models and empirical data.

In this paper, we present the simple model of *SIRS* to study dynamics of RSV disease in the presence of vaccination and campaign program. The organization of this work is as follows: The discussion of the model is presented in Section 2. In Section 3, we run the simulation of the model in the presence of control and prevention in the form vaccination alone, campaign alone and a combination of both. In addition, we discuss phase portrait between susceptible and infected. In the next section, the curve fitting of the model is presented and discussed. The paper concluded with the discussion in the last section.

2. Model Formulation

In the model, population is divided into three compartments: susceptible (S), infected (I) and recovery (R). Susceptible is a compartment of healthy people. We assume that every newborn is healthy so that they will enter the compartment. If the birth rate per day is denoted by μ and the total population is denoted by N, then the susceptible will rise μN per day. The transmission of the disease will occur after contact between susceptible and infected. If the number of individual contacts per day is represented by β, then it occurred as βI contact between infected to people in the other compartment. These contacts lead to as many as $\frac{\beta IS}{N}$ people in the susceptible moved into infected. In this model, we assume that the population is constant, so the birth rate is equal to the natural death rate. Therefore, susceptible will be reduced as much as μS per day. Since there is no long-

term antibody, after a period of recovery, people would go to susceptible. If the infected period is ω^{-1} days, then the rate of transfer of infected to recovery per day is ω and as many as ωI people will move into the recovery. Reinfection may occur because antibodies to the virus are temporary after the first infection. If the recovery period is γ^{-1} per day, then γR people per day will be returned to the susceptible. Either infected or recovery will be deducted per day with a natural death rate of μS and μR, respectively. The rate of change of each compartment per day is formulated as follows:

$$\dot{S} = \mu N - \mu S - \frac{\beta SI}{N} + \gamma R, \tag{1}$$

$$\dot{I} = \frac{\beta SI}{N} - \omega I - \mu I, \tag{2}$$

$$\dot{R} = \omega I - \gamma R - \mu R. \tag{3}$$

The whole process of the above is illustrated in Figure 1. For simplicity, we introduce the proportion for state variables

$$x = \frac{S}{N}, \quad y = \frac{I}{N}, \quad z = \frac{R}{N} \tag{4}$$

and on the substitution of these into (1)-(3), we have

$$\dot{x} = \mu - \mu x - \beta xy + \gamma z, \tag{5}$$

$$\dot{y} = -\beta xy - \omega y - \mu y, \tag{6}$$

$$\dot{z} = \omega y - \gamma z - \mu z, \tag{7}$$

where $x + y + z = 1$. In order to represent RSV as a seasonal disease, contact rate β is expressed in a time-varying formula $\beta = b_0(1 + b_1 \cos(2\pi t + \phi))$ [1, 2]. The parameter of $b_0 \geq 0$ is the baseline of transmission parameter, $0 < b_1 \leq 1$ is an amplitude of the seasonal variational in the transmission parameter and ϕ is the phase angle.

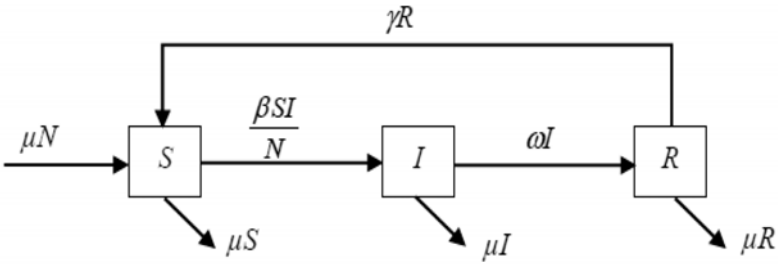


Figure 1. Compartment transmission diagram.

3. Numerical Results

Vaccination and healthy living campaign are attempts to control and prevent the spread of disease. In vaccination or known as immunization, a vaccine is injected to the body based on the medical guide, while a healthy living campaign can reduce the risk of disease transmission. In this section, we will explore a model for studying the population dynamics of infection under the vaccination and the campaign program. To do this, we perform simulations for vaccination, the campaign program, and a combination of both. The parameter values required to perform it are available in [1].

3.1. Vaccination

In this subsection, we study the effect of vaccination to dynamics of infected population. It is an action to prevent a person from a particular disease because there is immunity in the body. Here, we assume that the vaccine in the model is hypothetical, the result is perfect and has a lasting immunity effect. For this simulation, we introduce vaccination parameter p, where $p \in [0, 1]$ that represents a fraction of newborns vaccinated. In the presence of vaccination, the system (5)-(7) becomes

$$\dot{x} = \mu(1 - p) - \mu x - \beta xy - \gamma z, \tag{8}$$

$$\dot{y} = \beta xy - \omega y - \mu y, \tag{9}$$

$$\dot{z} = \omega y + \gamma z + \mu p - \mu z. \tag{10}$$

Next, we present two scenarios simulations. The first is aimed at to

investigate the effect of variation of p values to the dynamics of infected population, while the second one is to investigate as to when it is right time to give the vaccine. The first simulation starts with the initial conditions $x(0) = 0.68$, $y(0) = 0.05$ and $z(0) = 0.27$ and the vaccine is administered at $t = [2.5 + i, 3 + i]$, where $i = 0, 1, 2, 4, ..., t$ in years, with p values varying 0.01, 0.02 and 0.03. As shown in Figure 2, the epidemic peak depends on the parameter p. The peak decreases as the p value rises. The maximum decrease of 56.13% occurs when the value $p = 0.03$. The results show that vaccination has a significant effect on disease epidemic control. In the second simulation, we set a constant p value at 0.03 and the vaccination time is denoted by t_v. Here, we vary t_v following infected compartment dynamics patterns such as $t_{v1} = [1.75 + i, 2.25 + i]$ in RSV season, $t_{v2} = [2 + i, 2.5 + i]$ when RSV decreases, $t_{v3} = [2.25 + i, 2.75 + i]$ when there is no outbreak, and $t_{v4} = [2.5 + i, 3 + i]$ before season until the peak of the RSV season, where $i = 1, 2, 3, ...$ Simulation results demonstrate that every t_{vj} can reduce the peak of RSV outbreak, where $j = 1, 2, 3, 4$ as shown in Figure 3. However, the infected compartment decreased most significantly at t_{v4} and the peak decreased to 43.87%, while the infected compartment decreased significantly when t_{v2} and the peak decreased to 83.29%. This suggests that the timing of vaccination plays an important role in the effectiveness of disease control. We also present a phase portrait between susceptible and infected with various values of p. The simulation results show the cycle limit with its size depends on the parameter p as we can see in Figure 4. This represents that the infected population is periodic. The smallest cycle size occurs when the value of $p = 0.03$. This means that the p value successfully decreases the largest number of infected population.

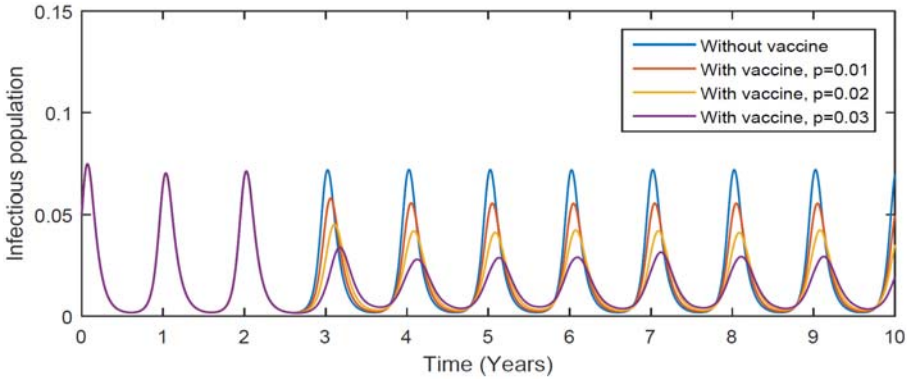


Figure 2. Vaccination by varying parameter of p.

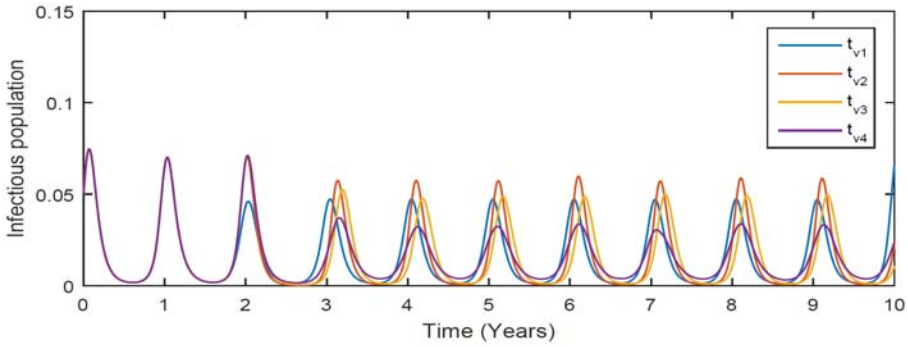


Figure 3. Vaccination by varying parameter of t_v.

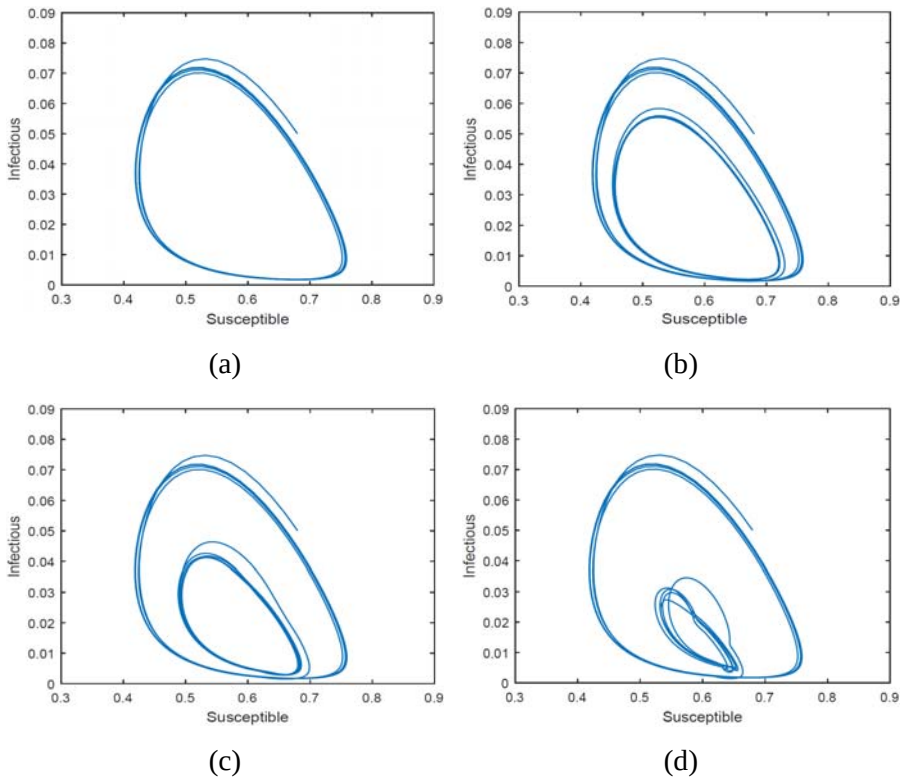


Figure 4. Phase portrait between susceptible and infected: (a) $p = 0.00$, (b) $p = 0.01$, (c) $p = 0.02$ and (d) $p = 0.03$.

3.2. Campaign program

In this subsection, we study the relationship between the campaign program and the infected compartment. The aim is to reduce the infected compartment in presence of the campaign program. Here, we consider that the campaign program may reduce RSV transmission. Therefore, it can be associated with b_0 parameters. We introduce the u parameter representing the success rate of the program, where $u \in [0, 1]$. We also call this campaign program parameter. The baseline of transmission parameter becomes $(1-u)b_0$. We run simulations with initial conditions $x(0) = 0.77$, $y(0) = 0.02$, $z(0) = 0.21$ and u values vary as 0.1, 0.2 and 0.3. The parameter u

is involved in the simulation only in t_{v4} and the result is shown in Figure 5. The smallest reduction of the infected compartment is generated when $u = 0.1$, while the maximum decrease occurs when $u = 0.3$. Obviously, the greater the value of u, the greater the effect on the infected compartment. We also present simulations with the same u parameter values as before, but the campaign program runs all the time after 2.5 years. The results showed that the reduction of the infected compartment was more significant than the previous simulation as we can see in Figure 6. Phase portrait for the same conditions as Figure 6 and $u = 0.3$ can be seen in Figure 7. The results show that the campaign program all the time after 2.5 years gives a smaller cycle size compared to t_{v4}. In addition, the limit cycle has a further position shift, see Figures 7(a) and 7(b).

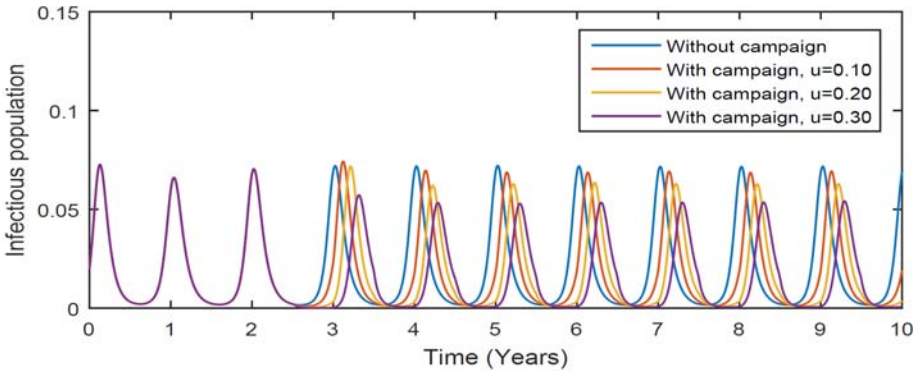


Figure 5. Campaign program is given at t_{v4} with varying u values.

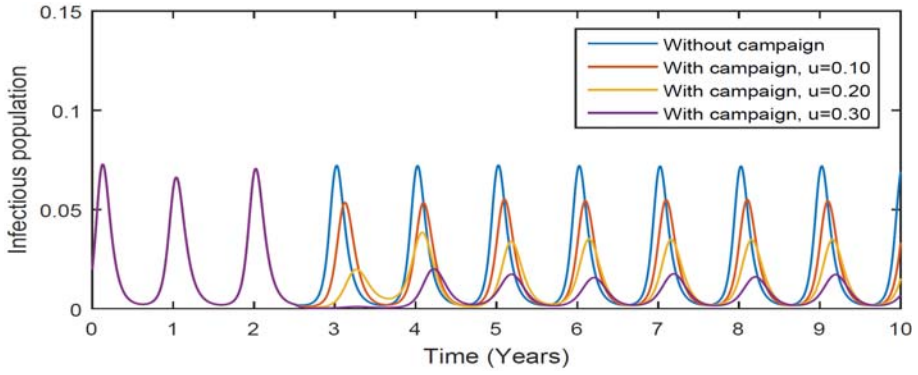
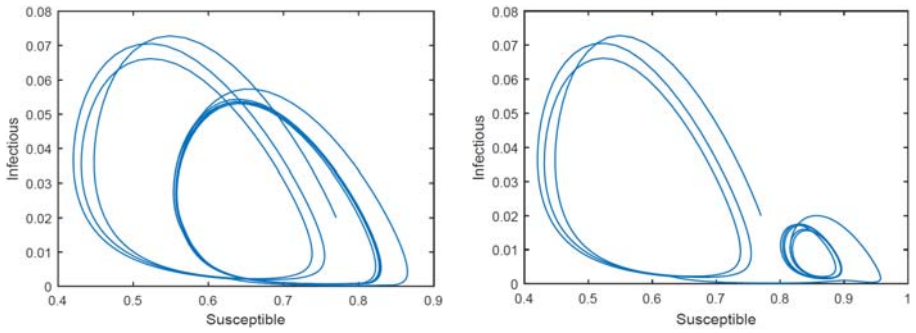


Figure 6. Campaign program all the time after 2.5 years.



(a) (b)

Figure 7. Phase portrait: (a) campaign at t_{v4}, (b) campaign all the time.

3.3. Combination of vaccination and campaign program

Here, we study the effect of a combination of the two controls on the previous section on the dynamics of the infected compartment. We performed simulations with vaccination program parameters and campaign parameters, $p = 0.02$ and $u = 0.2$. Both controls are given at t_{v4}. As we can see in Figure 8, the maximum infected compartment reduction occurs when vaccinations and campaigns are conducted simultaneously. However, the combined effects of these two controls are not significant when compared with vaccination controls alone where the high peak difference is about 14.26%. Furthermore, we present a combination of both controls with different campaign times. The first is a campaign program running at t_{v4}, while the second is a campaign program implemented throughout the year starting after 2.5 years. As we can see in Figure 9, the simulation shows that the difference of the infected compartment is significant, where the difference is 45.30%. In addition, we also present a phase portrait simulation for the previous case in Figure 10. Long-term controls produce smaller cycle sizes than controls at time t_{v4}.

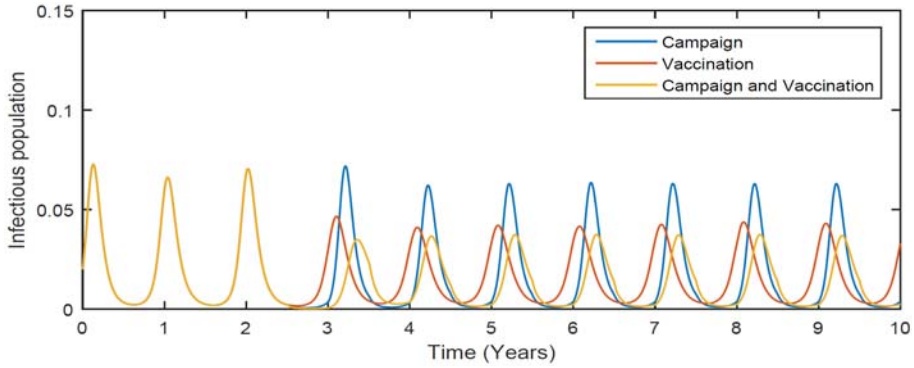


Figure 8. Vaccination, campaign program and combination of both controls.

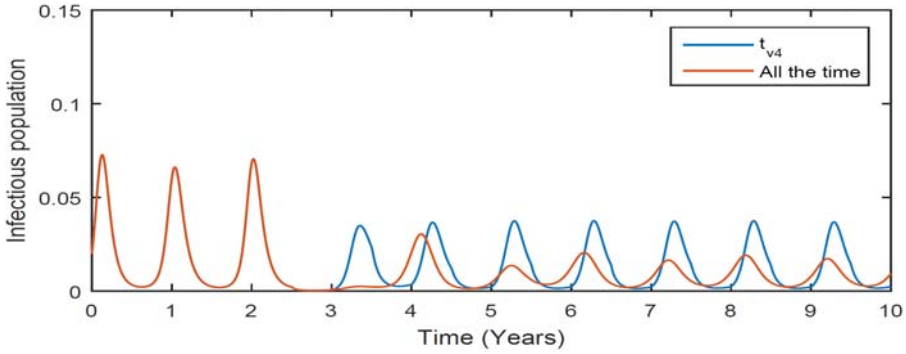
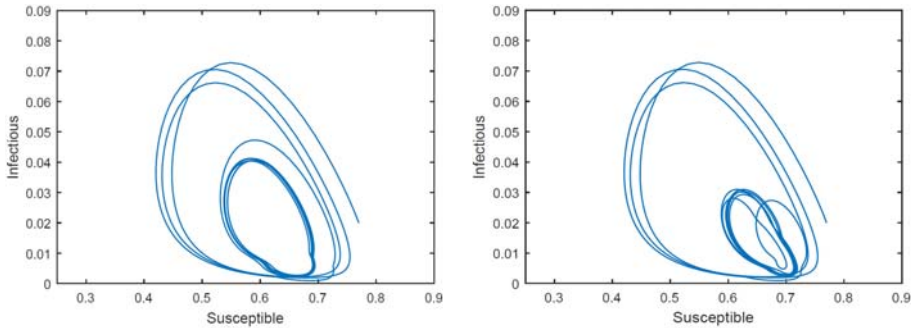


Figure 9. Combination of vaccination and campaign program.



(a) (b)

Figure 10. Phase portrait: (a) campaign in year t_{v4}, (b) campaign all the time after in year 2.5.

4. Curve Fitting

In this subsection, we are interested to curve fitting the model with data from the United States. These data were collected from four hospitals: Forsyth Medical Center, High Point Regional Hospital, Moses H. Cone Memorial Hospital and Baptist Medical Center - in North Carolina State. The hospital reported data on patients with RSV in percentage monthly for more than 3 years, starting from September 2003 to August 2006 [5]. These data are available in Table 1. In simulation, we introduce scale factor denoted by s which scales the number of infected compartments to empirical data. We choose the value is 600. The plot of the simulation model and empirical data can be seen in Figure 11. The results show simulation models and empirical data, each showing that the outbreak has the same periodic pattern at the same time where both curves have three peaks of the RSV season in January. The peak represents the epidemic of that period. Therefore, qualitatively, this model is able to show the dynamic behaviour of infected compartment similar to empirical data, although at some point, the data is quite far from the model especially in July to September because, at interval time, RSV data is zero. Statistically, we also calculate the deviation between model and empirical data (D) as follows:

$$D = \frac{1}{36}\sum_{i=1}^{36} | x_i - y_i | = 3.99\%,$$

where x is data from [5] and y is data from model.

Table 1. Percent positive of RSV from North Carolina, USA [5]

No.	Month	2003-2004	2004-2005	2005-2006
1	September	9	0	0
2	October	24.9	4.4	5.1
3	November	21.1	10.1	18.1
4	December	18.2	27.3	31
5	January	28.6	32	33.7
6	February	26.5	23.1	23.4
7	March	15.9	8.6	23.6
8	April	5.8	12.4	13.9
9	May	5.6	7	8.6
10	June	0	0	3.3
11	July	0	0	9.4
12	August	0	0	0

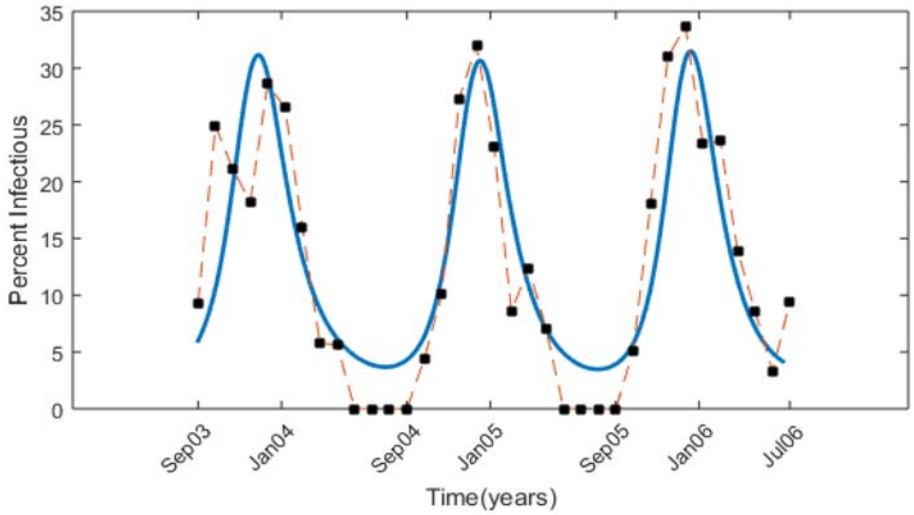


Figure 11. Curve fitting between model and empirical data.

5. Discussion and Conclusion

We have presented the *SIRS* model to study RSV transmission in human populations simulating RSV controls under the influence of vaccination and

campaign program. In simulation of vaccination, the p parameter is important to control epidemic. The greater the value of p, the smaller the infected compartment as is shown in Figure 2. However, more vaccinations are not necessarily an effective strategy because cost factors need to be considered. This factor is not involved in this model. We have also shown that the appropriate time for vaccination is at the time interval before the RSV season to the peak of the outbreak. This will reduce the largest infected compartment. In addition, the phase portrait of susceptible and infected is presented in Figure 4. The limit cycle shows the dynamics of the infected compartment periodically throughout the year. Its size is controlled by the p parameter. Implicitly, the limit cycle that exists agrees with Jódar et al. in [2]. In a simulated campaign program, u parameter is able to control disease epidemics. However, the results are not significant when compared to vaccination controls, see Figures 2 and 5. The campaign program will have significant effects if given over time as we can see in Figure 6. Better results will be obtained if vaccination and campaign programs are combined simultaneously, see Figure 8. Finally, we compare simulations and data. The results in Figure 3 show that the fit models and empirical data are good [5] with deviations of 3.99%.

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