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Different Vaccination Strategies for Measles Diseases: A Simulation Study

I.A. Moneim

Abstract. Vaccination strategies are designed and applied to control or eradicate an infection from the population. This paper studies three different vaccination strategies used world wide for many infectious diseases including measles. These strategies are the conventional constant vaccination strategy, the periodic step (pulse) vaccination strategy and finally the mixed vaccination strategy of both the constant and the periodic one. Simulation of the different vaccination programs is been conducted. The Poincar section is playing as a **filter** of our simulation results to show a wide range of possible behavior of our model. critical vaccination parameter is been estimated from the results to prevent sever epidemics.

1. Introduction

Vaccination programs are frequently used as a tool to control the spread of epidemics. The simplest vaccination strategy is to vaccinate all susceptible individuals at a constant rate. This may also be combined with vaccination of a fixed fraction of very young children at the smallest possible age where maternal antibodies no longer confound the effect of the vaccine, commonly 9-18 months for measles. In the absence of vaccination cases, many common childhood diseases show a regular periodic oscillation with period a whole number of years [12, 18]. We ignore the effect of maternal antibodies in this paper, so children subject to be vaccinated from birth. Much work has been done analysing seasonal periodic outbreaks of infectious diseases considering seasonal variation in the contact rate [12, 18].

Recently it has been postulated that in some circumstances a periodic vaccination strategy, for example pulse vaccination, can be a more efficient use of limited immunisation resources than continuous constant vaccination effort [1, 17, 19]. Many recent works studied epidemic models with pulse vaccination strategy. The pulse vaccination was the main aim of these epidemiological investigations [8, 9, 5, 6, 20, 21].

*Key words and phrases.*Simulation; SEIR model; Periodic vaccination; Poincar section; Filter; Epidemics.

In this paper we study a general continuous periodic vaccination strategy $r(t)$. This is combined with vaccination of a given proportion of newborn individuals. As in many real diseases there is a time delay between an individual becoming infected and becoming infectious we introduced an exposed or latent class into the model. We consider the model both with a periodic disease transmission rate and a constant one.

If the combined vaccination strategy is applied in the situation where no disease is present then the number of susceptibles eventually reaches a unique periodic solution. Our results lead us to conjecture that this combined periodic and fixed vaccination strategy is sufficient to eliminate disease from the population exactly when the weighted time-averaged disease-free susceptible population is less than a certain threshold value.

2. **The SEIR model with vaccination**

The SEIR model of the spread of infectious diseases makes the following assumptions:

(1) The total population size is N and the per capita birth rate is a constant μ. As births balance deaths we must have that the per capita death rate is also μ.
(2) The population is uniform and mixes homogeneously.
(3) The population is divided into susceptible, exposed, infective and recovered individuals. The total number of individuals in each of these classes are respectively $S \equiv S(t)$, $E \equiv E(t)$, $I \equiv I(t)$ and $R \equiv R(t)$.
(4) The infection rate $\beta(t)$ is defined as the total rate at which potentially infectious contacts occur between two individuals. So the total rate at which susceptibles become exposed is $\beta(t)SI$. Biological considerations mean that $\beta(t)$ is continuous. We also assume that $\beta(t)$ is not identically zero, positive, non-constant and periodic of period T.
(5) The susceptibles move from the exposed class to the infective class at a constant rate σ.
(6) The infectives move from the infective class to the recovered class at a constant rate γ
(7) A fraction p $(0 \leq p \leq 1)$ of all new-born children are vaccinated. In addition all susceptibles in the population are vaccinated at a time dependent periodic rate $r(t)$. This is the periodic vaccination strategy. We shall suppose that $r(t)$ is periodic with period LT. The case where $r(t)$ has period T can be obtained by setting $L = 1$.

Our SEIR model with time dependent vaccination strategy can be written as a set of four coupled non-linear ordinary differential equations as follows

[12, 18, 13]:

$$\frac{dS}{dt} = \mu N(1-p) - \beta(t)SI - (\mu + r(t))S, \tag{1}$$

$$\frac{dE}{dt} = \beta(t)SI - (\mu + \sigma)E, \tag{2}$$

$$\frac{dI}{dt} = \sigma E - (\mu + \gamma)I, \tag{3}$$

and

$$\frac{dR}{dt} = \mu Np + r(t)S + \gamma I - \mu R, \tag{4}$$

with

$$S + E + I + R = N. \tag{5}$$

Here the disease transmission rate $\beta(t)$ and the vaccination rate $r(t)$ are non-zero, positive, continuous periodic functions. The system (1)-(5) has no equilibrium points but a disease free solution (DFS), with $E(t) = I(t) = 0$ is still possible.

Consider the region D in $\mathscr{R}^4$ defined by

$$D = \{(S, E, I, R) \in [0, N]^4 \mid S + E + I + R = N\}.$$

The system of differential equations (1)-(4) is well posed on D [16].

3. **The disease free solution**

In the case that $r(t)$ is a non-constant bounded continuous periodic function, there is no equilibrium point for the system (1)-(5). So there is no disease free equilibrium point. But still there is a periodic DFS corresponding to the case that $E(t) = I(t) = 0$. In this case DFS is given by:

$$\begin{aligned} S^*(t_0) = \Bigg(& N[\mu(1-p)] \exp\left[-\mu LT - \int_0^{LT} r(\tau) d\tau \right] \\ & \times \int_{t_0}^{t_0+LT} \exp\left[\mu(\zeta - t_0) + \int_{t_0}^{\zeta} r(\tau) d\tau \right] d\zeta \Bigg) \\ & \times \frac{1}{1 - \exp\left[-\mu LT - \int_0^{LT} r(\tau) d\tau \right]}. \end{aligned} \tag{6}$$

Hence $S^*(t_0 + LT) = S^*(t_0)$. So S^* is a periodic function of t. Differentiating (6) $S^*(t_0)$ is continuously differentiable with respect to t_0 and $\hat{S}(t) = S^*(t)$, $\hat{E} = \hat{I} = 0$ and $\hat{R}(t) = R^*(t) = N - S^*(t)$ is a disease free periodic solution of the system (1)-(5) which repeats itself every LT years; see [15]. We have the following result:

Theorem 1. *Equations* (1)-(5) *have a disease free periodic solution of period LT which is continuously differentiable and* this is the only disease free periodic solution to (1)-(5)*, and any disease free solution to* (1)-(5) *approaches this one as time becomes large.*

Proof. See [14] for the case $L = 1$. □

4. **The simulation**

In this paper the simulations of the SEIR model with three different vaccination strategies have been conducted using the XPPAUT package and data estimated from the literature. Parameter values corresponding to the measles disease have been used.

A constant population size of $N = 1,000,000$ has been considered. We also supposed that $\mu = 0.02$/year corresponding to an average human lifetime of 50 years [18] and [4]. We chose this value to be consistent with previous studies even though the actual value of the average lifetime in many countries is higher. For example the average lifetime in the UK is around 70.0 years. We do not feel that this will have much effect on the results of our simulations as we are mainly considering childhood diseases and the proportion of individuals who catch the disease at 50 years or later is negligible. Mainly the following specific values of σ^{-1} and γ^{-1} have been taken as in [11], [7], [2], [3] and [10] for our model:

Measles $\sigma^{-1} = 9.49$ days and $\gamma^{-1} = 3.65$ days;

We have taken also β_0 as estimated from the literature, for our simulations results for all of the bifurcation diagrams presented and for the three diseases under investigation as flows: $\beta_0 = 0.0018$/year for measles, 0.00113/year for chickenpox and 0.0007/year for rubella respectively.

The key parameter in the analytical results was the basic reproduction number R_0 [16] and [14]. So the computer simulations of our model were performed using values of $R_0 > 1$ to insure that the disease is in the endemic state. The values of R_0 were determined by the value of β_0, the mean level of the disease transmission function, and β_1 which determines the amplitude parameter of the periodic transmission rate $\beta(t)$.

This paper targeted the long term behaviour of the system in response to changes in the vaccination parameter, (the value the vaccination rate of the convection strategy, the amplitude of the vaccination function of both the pulse and the mixed one), which is our bifurcation parameter. The basic idea of this study is simply that, given a set of parameter values compound with appropriate initial values then the endemic equilibrium solution is obtained by running the system for a long time to eliminate transient solutions. Filtering the equilibrium solutions by looking at Poincar sections of them taken every year (recall that the underlying seasonal variation in the contact rate has period one year). So in this paper the vaccination parameter is used as a **filter** of the long term equilibrium solution. By plotting the sections of the long term endemic equilibrium solutions against the vaccination parameter we obtain a number of points in a vertical line corresponding to each value chosen for the vaccination parameter. These points on the filter, represent the period of the stable long term periodic solution of our model. For example a single point indicates a solution of period one year, two points a solution of period two years, n points a solution of period n years and an infinite number of points a chaotic solution. In the following simulation results which represent global bifurcation diagrams for SEIR model with vaccination using our filter are given. We say global because the filter described above is used to plot the bifurcation diagrams for a large range of values of the vaccination parameter. The comparison of the simulation results of our model show that the type of vaccination parameter affecting the pattern of the dynamics of the disease. The pattern of the mixed vaccination is the simplest and the most controllable one.

This paper looked at bifurcation diagrams for three different vaccination function one of them is the constant strategy. These three vaccination programs are applied for the SEIR model with the seasonally periodic transmission function the more realistic reparameterised step function as, $\beta(t) = \beta_0 + \beta_1\Delta_1(t)$, with mean value β_0, of period one year [16] and [14], where

$$\Delta_1(t) = \begin{cases} -2 & \text{when } (t - [t]) \in (1/3, 2/3), \\ 1 & \text{otherwise.} \end{cases}$$

Our three different vaccination strategies are of the following forms:

(1) The constant vaccination function $P(t) = p_1$ to vaccinate the newborns as many as possible all the time.

(2) The periodic binary step vaccination function $p(t) = p_1\Delta(t)$ with period one year to vaccinate the susceptible population $S(t)$, where

$$\Delta(t) = \begin{cases} 1 & \text{when } (t - [t]) = 2/3, \\ 0 & \text{otherwise.} \end{cases}$$

(3) The mixed vaccination strategy which is compromised of the periodic function $p(t) = p_1\Delta(t)$, in combined with the constant vaccination one $P(t) = p$ in all of our simulations we have taken $p = 0.5$.

The simulation study is been designed to start off just before school opening days. It means that the disease transmission rate is at its highest value. Therefore at this critical moment we start our vaccination to control the disease dynamics or possibly prevent severe epidemics to occur. We simulate our model with the three different vaccination strategies under consideration by varying the vaccination parameter p_1 from 0 to 1 in value. Then plotting the long term solution against the vaccination parameter to have wide range of possible behaviour of the disease under consideration. From the obtained patterns we can decide easily which vaccination strategy is more effective than the others.

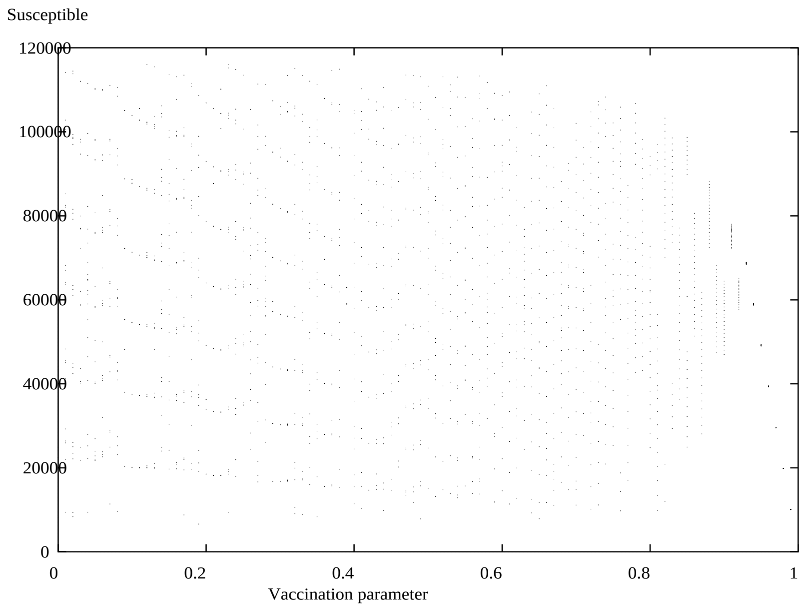

Figure 1. The bifurcation diagrams of measles parameter values of number of susceptibles against vaccination parameter value of p_1 of the convection constant vaccination strategy $P(t) = p_1$.

We start off our simulation of measles disease with the constant vaccination strategy. Figure 1 represents the bifurcation diagram of measles when the vaccination strategy is the convection constant one. This pattern shows that at low level of vaccination rate measles have long period solutions, these solution tend to chaos behaviour by a series of period doubling. This complicated pattern is interrupted by six, ten and twelve years periodic solutions. Increasing the value of p_1 we obtained a region of long period or aperiodic solutions until p_1 reaches the value 0.9 approximately then a long period, 20 years or more, periodic solution appears up to the value $p_1 = 0.96$. Increasing the value of p_1 slightly again a one year periodic solution appears and persists to decrease and tends to its limiting value at the end of range. These results agree with the previous results [2] and [1] which predict that, the effective value of p_1 of the convection constant vaccination strategy should exceed 0.95 in value. In other words the percentage of the number of vaccinated newborns should exceed 95% to prevent sever epidemics to occur. This proportion of newborns is very difficult to be vaccinated for different reasons [16].

Figure 2 represents the bifurcation diagram of measles when the vaccination parameter is the amplitude of the periodic step function $p(t) = p_1\delta(t)$. This pattern start off by long period periodic solution at low values of the amplitude of the vaccination function. Increasing the value of p_1 aperiodic solutions interrupted

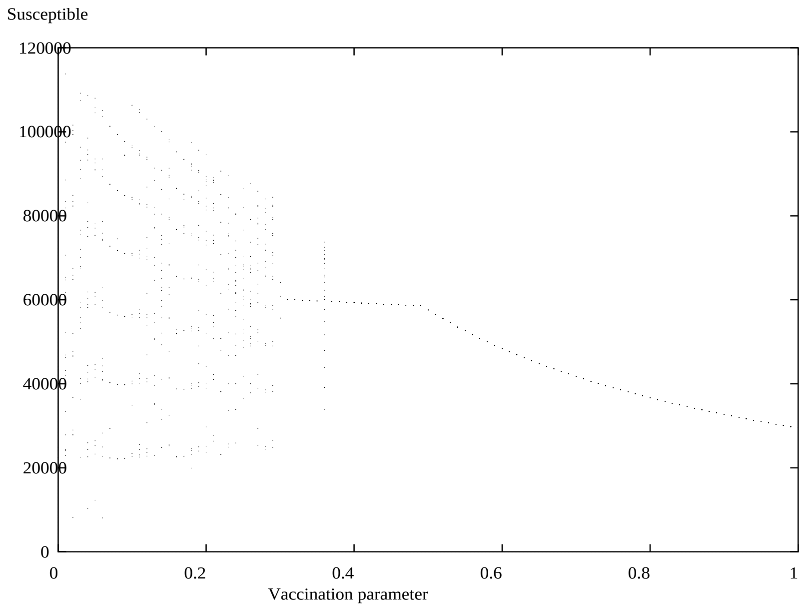

Figure 2. The bifurcation diagrams of measles parameter values of number of susceptibles against vaccination parameter, the amplitude p_1 of the non constant periodic vaccination function $p(t) = p_1\delta(t)$.

with long period solutions appear until the value of the amplitude reaches the value 0.3. Unlike the convection vaccination strategy, increasing the amplitude slightly a three years periodic solution obtained flowed by a one year periodic solution which persists until the value of p_1 becomes 0.5 in value. This one year periodic solution is been interrupted with a long period periodic solution. Increasing the value of p_1 more the one year periodic solution persists but decreases to it limiting value as the p_1 tends to the end of its range. It is important to note that, the step periodic vaccination force the behavior of the system to be simply more than the convection one. and the control of the dynamics of the disease is possible for a lower values of p_1 compared with the convection strategy.

Figure 3 represents the corresponding bifurcation diagram of measles when the vaccination strategy is the mixed strategy and amplitude p_1 of the periodic step function $p(t) = p_1\delta(t)$ is vaccination parameter. In this vaccination strategy there is another proportion of vaccinated newborns, this proportion is been taken as 50%. This pattern starts with a ban of long period periodic solutions followed by six years periodic solutions then a one year periodic solutions interrupted with long period periodic solutions. When the value of p_1 exceeds 0.2 a one year periodic solution appears and persists until the of p_1 reaches 0.5 in value. Increasing the value p_1 further the one year periodic solution decreases monotonically to its limiting value as the amplitude parameter tends to its end of range. It is

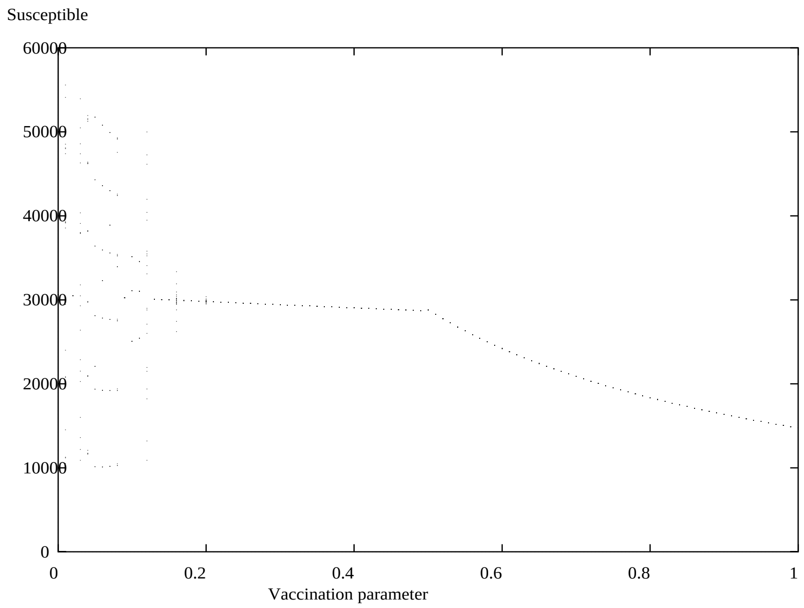

Figure 3. The bifurcation diagrams of measles parameter values of number of susceptibles against vaccination parameter, p_1 the amplitude of the mixed vaccination strategy of both the constant and periodic step one.

important to note that the level of susceptible population is half the value of the corresponding value of the susceptible population when the vaccination strategy is the step periodic one only. This result is expected and obtained in several previous works. The most important result here and it seems to be a novel result is the simple pattern of measles with the mixed vaccination strategy. This patterns shows disappearance of very long period solutions and the pattern does not contain any chaotic behaviour.

Therefore we can claim that the mixed vaccination strategy is the most effective policy to control measles disease. Moreover using this mixed vaccination strategy reduces the number of the susceptibles in the system by a fraction p which is the rate at which the newborns are vaccinated.

5. **Summary and discussion**

It is important to simulate our model with exposed or latent class and with different vaccination strategy, to evaluate which strategy is more efficient. We have simulated the control of the dynamics of three childhood infectious disease by using three different types of vaccination strategies. We perform these simulations for an SEIR model with a seasonally varying disease transmission rate. Using a periodic vaccination strategy in such an SEIR model seems to lead to periodicity in the disease dynamics [16]. In this paper we try to control or possibly eradicate diseases by applying the most efficient vaccination strategy. Efficiency means some times less number of vaccinated individuals leads to perfect control of the disease.

However the simulation results have indicated that using different functional forms of vaccination strategies generates different patterns of solutions for the measles disease parameter set. The bifurcation diagrams show that the simplest pattern is that of the mixed vaccination strategy. Apart from some of the results this diagram show a one year solution for the whole diagram except the first quarter of range of the vaccination parameter. The most complicated Diagram is corresponding to the constant vaccination parameter which show a wide range of periodic and aperiodic solutions all over this pattern.

It is interesting to note the difference between the bifurcation diagrams in the case of using a periodic step vaccination function and the constant convection vaccination strategy. The bifurcation diagram for the periodic step vaccination shows that the disease reaches the DFS at a vaccination level less than 60% of the total number of the susceptible population. On the other hand the constant vaccination strategy failed to control the disease before the vaccination rate exceeds 95%.

Finally we point out the difference between the bifurcation diagrams, when using the periodic step vaccination function and using the mixed vaccination strategy. The patterns show that, the level of vaccinated population at which the disease starts to be controlled, in the case of using the mixed vaccination strategy is much fewer than that of the only step periodic vaccination strategy. The diagrams show that, the effective vaccination parameter p_1 in the case of the mixed vaccination is about a third of the that of the only step periodic vaccination strategy. Using a continuous periodic vaccination strategy in conjunction with vaccination of a fixed proportion of newborn individuals, reduces the proportion of newborns who need to be immunised to a more realistic level. Moreover from (6) one can see easily that using such a mixed vaccination strategy uniformly reduces the level of fluctuation of susceptible in the DFS compared with a purely periodic vaccination function ($p = 0$). This agree with our simulation results. As the diagrams show that at the end of range of the vaccination parameter, the number of susceptible population in the system when the mixed vaccination strategy is used, is approximately half its corresponding number of susceptible population in the system when the purely step vaccination strategy is used. Hence it is more optimal to use a combined vaccination approach in order to prevent major outbreaks of infectious disease occurring.

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I.A. Moneim, *Department of Basic and Applied Science, Unaizah Community College, Qaseem University, Unaizah, 51911, P.O. 4394, Saudi Arabia*.
E-mail: moneim97@yahoo.com

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