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OPTIMAL CONTROL PROBLEM OF VACINATION FOR THE SPREAD OF MEASLES DISEASES MODEL

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ABSTRACT

Measles is a disease in humans that is very contagious. Before the vaccine was known, the incidence of measles was very high, even the measles mortality rate reached 2.6 million every year. With the introduction of vaccines, the mortality rate in 2000-2016 can be reduced to 20.4 million deaths. Therefore, vaccination programs are very useful in reducing the incidence of measles. Unfortunately, we cannot know the optimal conditions for administering vaccines. The study of optimal control analysis of vaccination is needed in optimizing the prevention of the spread of measles. In this paper, a mathematical model which is a third-order differential equation system is constructed based on characteristic information on measles. The existence and locally stability of the equilibrium point are analyzed here. In addition, optimal control of the vaccination program also occurred. The results of our analysis suggest that the incidence of measles can decrease as the effectiveness of vaccination increases. But the effectiveness of vaccination is directly proportional to the costs incurred. If the cost incurred for the vaccination program more significant, the incidence of measles will decrease.

Keywords: Measles diseases, Basic reproduction number, existance and stability, optimal control

1 Introduction

Measles, caused by the paramyxovirus virus of the genus measles virus, is an infectious disease in humans that can cause serious illness, lifelong complications and death [1]. This Diseases that can infect the respiratory tract are transmitted through droplets aerosols that contain viral particles. The symptoms of measles are high fever, reddish patches on the skin accompanied by coughing [2]. Humans are the only host of measles, although monkeys can also be infected but do not play a role in transmission [2].

Before the vaccination program was known, the incidence of measles was very high, even the number of measles deaths was approximately 2.6 million every year, mostly children under the age of

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5 years. This has encouraged governments in various parts of the world to plan measles immunization programs [3, 4]. In Indonesia, in 2010 to 2015, the incidence of measles was estimated at 23,164 cases. However, after the vaccination program, the incidence of measles decreased, reaching 2,949 in 2016. Unfortunately, anemo community to the vaccination program was not as high as the costs incurred by the government, as a result in the following year, the incidence of measles increased to 15,104 cases [5, 6].

Mathematical models have an important role in analyzing the dynamics of the spread of measles. Some examples of mathematical models used to analyze and describe the spread of measles can be found in [7, 8, 9, 10]. In [11], mathematical models is built based on discrete time so that the analysis carried out is a discrete study. Meanwhile, in [12] a mathematical modeling was carried out describing the spread of measles by dividing human groups into four groups, namely susceptible, Exposed, infection and recovery.

This paper is a continuation of the previous paper [12]. But in this paper, the model is built by ignoring the exposed human group. This is done because the focus of this paper study is on the optimal aspects of control. In practice, human groups consisting of three groups, namely susceptible, infection and recovery, can be reduced to just two groups.

The paper is organized as follows. In section 2, we introduce a mathematical model to be analyzed. In addition, stability analysis of equilibrium points and optimal control formulations carry out here. In section 3, numerical simulations are represented.

2 Results and Discussion

In the construction of the model, based on the status of infected or not by measles diseases, the humans are grouped into three groups. The first is a susceptible group that is likely to get measles diseases. The second is an infected group where the human has been infected and can transmit measles diseases. The third is a recovery group who recover from an infection. An important note that must be considered in model construction is the characteristic of measles diseases, i.e. the people who have recovered from measles diseases cannot be infected for the second time.

2.1 Model Formulation

A flow chart showing transmission of measles can be seen in the figure 2.1. The assumptions used in this model are as follows: (i) The status of recruitment rate (Λ) is susceptible; (ii) The mortality rate for each group (μ) is the same; (iii) Total population is constant such that $\Lambda = \mu N$; (iv) The population that has been vaccinated and recovered from measles diseases never be infected again.

From the flow chart in the figure 2.1 and the assumptions, we obtain a three dimensional system of differential equations as follows:

$$\begin{cases} \dfrac{d\tilde{S}}{dt} &= \Lambda - \beta(1-u(t))\dfrac{\tilde{S}\tilde{I}}{N} - (u(t)+\mu)\tilde{S} \\ \dfrac{d\tilde{I}}{dt} &= \beta(1-u(t))\dfrac{\tilde{S}\tilde{I}}{N} - (\gamma+\mu)\tilde{I} \\ \dfrac{d\tilde{R}}{dt} &= u(t)\tilde{S} + \gamma\tilde{I} - \mu\tilde{R} \\ N(t) &= \tilde{S}(t) + \tilde{I}(t) + \tilde{R}(t) \end{cases} \tag{1}$$

where β is the infection rate, γ is recovery rate and $u(t) \in [0,1)$ is a vaccination control rate. Furthermore, for scaling purposes, suppose $S = \dfrac{\tilde{S}}{N}, I = \dfrac{\tilde{I}}{N}, R = \dfrac{\tilde{R}}{N}$ such that $S+I+R = 1$. The recovery compartemen R can be searched from $R(t) = 1 - S(t) - I(t)$, as a results the model (1) can be reduced

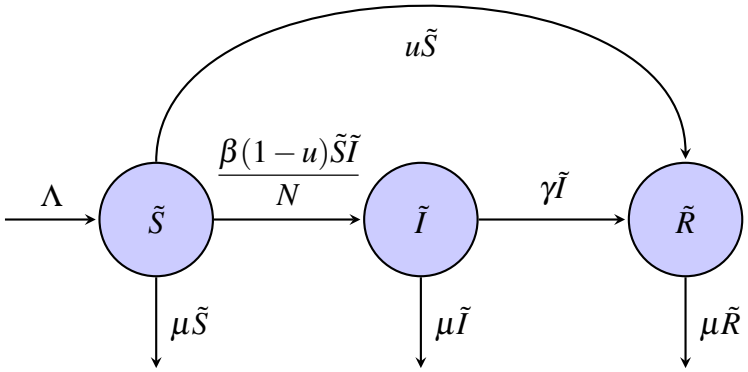


Figure 1: Transmission diagram of measles diseases

to two dimensional system of differential equations as follows:

$$\begin{cases} \frac{dS}{dt} &= \mu - \beta(1-u(t))SI - (u(t)+\mu)S \\ \frac{dI}{dt} &= \beta(1-u(t))SI - (\gamma+\mu)I \end{cases} \tag{2}$$

with initial condition $S(0) = S_0$ and $I(0) = I_0$. The feasible set of the system which has biological meaning is given by

$$\Omega = \left\{x = (S,I) \in \mathbb{R}^2_+ : 0 < S+I < 1\right\}$$

that positivity invariant. Therefore the trajectory lies in Ω for initial starting point $x \in \mathbb{R}^2_+$. By regulating the rate of infection positive in the origin population, from the system (2), we obatain the basic reproduction number $\mathscr{R}_0 = \dfrac{\beta\mu(1-u)}{(u+\mu)(\gamma+\mu)}$. That is the average number of secondary infection when one single infected individual where every one is susceptible [13, 14]. $\mathscr{R}_0$ depending on the rate of infection, the rate of individual recovery and the effectiveness of vaccination. It can be used as a threshold to see outbreaks or not. if it biger than one, then the outbreak of measles disease occure. But, if it less than one, the deases is extinction.

2.2 Existence and Stability Analysis

To obtain an equilibrium point, we assume that the vaccination control parameter u is constant. By making zero the right segment of the system (2), we get two different constant solutions. The first solution is diseases free equilibrium (DFE) where the infection compartment is zero and the second solution is endemic equilibrium (EE) that is a solution where all compartments are not zero. The expressions of diseases free and endemic equilibrium points are given by:

$$DFE := \left\{S = \frac{\mu}{(u+\mu)}, I = 0\right\} \tag{3}$$

$$EE := \left\{S = \frac{\gamma+\mu}{\beta(1-u)}, I = \frac{(\mathscr{R}_0-1)(u+\mu)}{\beta(1-u)}\right\} \tag{4}$$

The existence and stability of each equilibria are presented in the theorem 2.1.

Theorem 2.1. ***Existance and stability of equilibria***

(i) The existance of DFE is not depand on $\mathscr{R}_0$. If $\mathscr{R}_0 < 1$ then the DFE is locally asymtotically stable. If $\mathscr{R}_0 > 1$ then the DFE is unstable saddle.

(ii) The point of EE exist and locally asymtotically stable if $\mathscr{R}_0 > 1$. If $\mathscr{R}_0 < 1$ the EE is not exist.

PROOF. The following is proof of the theorem 2.1

(i) The Jacobian matrix that is evaluated on the DFE is

$$J_1 = \begin{pmatrix} -(\mu+u) & -\dfrac{\beta\mu(1-u)}{\mu+u} \\ 0 & \dfrac{\beta\mu(1-u)}{\mu+u} - (\mu+\gamma) \end{pmatrix} \tag{5}$$

The eigenvalues of J_1 are $\lambda_1 = -(u+\mu)$ and $\lambda_2 = (\mathscr{R}_0 - 1)(\gamma+\mu)$ in term of $\mathscr{R}_0$. We can see that the λ_1 always negative and the eigenvalues $\lambda_2 < 0$ if $\mathscr{R}_0 < 1$. Thus the DFE point is locally asymtotically stable.

(ii) The Jacobian matrix J_2 that is evaluated on the point of EE is

$$\begin{pmatrix} -(\mu+u+(\mathscr{R}_0-1)(\mu+u)) & -(\gamma+\mu) \\ (\mathscr{R}_0-1)(\mu+u) & 0 \end{pmatrix} \tag{6}$$

The characteristic polynomials of the Jacobian matrix are evaluated on EE is

$$P(\lambda) = \lambda^2 + \mathscr{R}_0(u+\mu)\lambda + (\mathscr{R}_0-1)(u+\mu)(\gamma+\mu) \tag{7}$$

Suppose $\mathscr{R}_0 > 1$. We can see that the coeffisien of $P(\lambda)$ are positive. It shows that the sum of the polynomial roots is negative and the multiplication of the roots is positive. As a result, the two roots of the polynomial are negative then the equilibrium EE is locally asymtotically stable □.

2.3 Optimal Control Problem

Our goal in this model is to minimize the number of individuals infected with measles virus. We define the objective function of an optimal control problem as follows:

$$\mathbb{Z} = \min_u \int_0^{T_f} I(t) + \frac{1}{2}\alpha u^2(t)dt \tag{8}$$

subject to system (2) where α is relative weight associated with the cost of vaccination. While control u is the proportion of individuals susceptible that is vaccinated per unit time. To obtain the optimal condition, we use Pontraigan's maximum principle [15, 16].

Theorem 2.2. *If u^* is an optimal control corresponding to state S^* and I^* which minimize the objective functional* (8)*, then there exist an adjoint variables λ_1 and λ_2 which satisfy:*

$$\begin{cases} \lambda_1' &= \beta(\lambda_1-\lambda_2)(1-u)I + \lambda_1(\mu+u) \\ \lambda_2' &= \beta(\lambda_1-\lambda_2)(1-u)S + \lambda_2(\gamma+\mu) - 1 \end{cases} \tag{9}$$

and the transversality conditions $\lambda_1(T_f) = \lambda_2(T_f) = 0$. Furthermore, we obtain the optimal control as

$$u^* = \min\left\{\max\left(0, \frac{S\lambda_1 - \beta(\lambda_1-\lambda_2)SI}{\alpha}\right), u_{max}\right\} \tag{10}$$

PROOF. We define the Hamiltonian function $\mathscr{H}$ which contains the integration of the objective function and the inner product between the adjoin variables and the right hand side of the system (2) as follows:

$$\mathscr{H} = I + \frac{1}{2}\alpha u^2 + \lambda_1(\mu - \beta(1-u)SI - (u+\mu)S) + \lambda_2(\beta(1-u)SI - (\gamma+\mu)) \tag{11}$$

by using Pontriagin's maximum principle [16], we obtain an adjoint equation (9) corresponding to the system (2) that is taken from partial derivative of the Hamiltonian

$$\lambda_1' = -\frac{\partial \mathscr{H}}{\partial S}, \qquad \lambda_2' = -\frac{\partial \mathscr{H}}{\partial I} \tag{12}$$

where the transversality conditions are $\lambda_1(T_f) = \lambda_2(T_f) = 0$. The optimality condition is obtained from differentiate Hamiltonian $\mathscr{H}$ with respect to u, such that we have

$$\frac{\partial \mathscr{H}}{\partial u} = \alpha u - S\lambda_1 + \beta(\lambda_1 - \lambda_2)SI = 0 \tag{13}$$

and solving (13), we obtain that

$$u^* = \frac{S\lambda_1 - \beta(\lambda_1 - \lambda_2)SI}{\alpha} \tag{14}$$

We consider that $0 \leq u \leq u_{max}$ on the control to yield (10) as required $\square$.

We obtain the optimal system as follows:

$$\begin{cases} \frac{dS}{dt} &= \mu - \beta(1-u^*)SI - (u^*+\mu)S \\ \frac{dI}{dt} &= \beta(1-u^*)SI - (\gamma+\mu)I \\ S(0) &= S_0, I(0) = I_0 \\ \lambda_1' &= \beta(\lambda_1 - \lambda_2)(1-u^*)I + \lambda_1(\mu+u^*) \\ \lambda_2' &= \beta(\lambda_1 - \lambda_2)(1-u^*)S + \lambda_2(\gamma+\mu) - 1 \\ \lambda_1(T_f) &= \lambda_2(T_f) = 0 \end{cases} \tag{15}$$

Parameters	**Description**	**Unit**	**Value**	
			$\mathscr{R}_0 < 1$	$\mathscr{R}_0 > 1$
μ	natural mortality rate	$time^{-1}$	0.01	0.01
β	infection rate	$time^{-1}$	0.2	0.3
γ	natural recovery rate	$time^{-1}$	0.03	0.01
u	vaccination rate	$time^{-1}$	0.06	0.05
α	vaccination cost	-	$[0,1]$	$[0,1]$

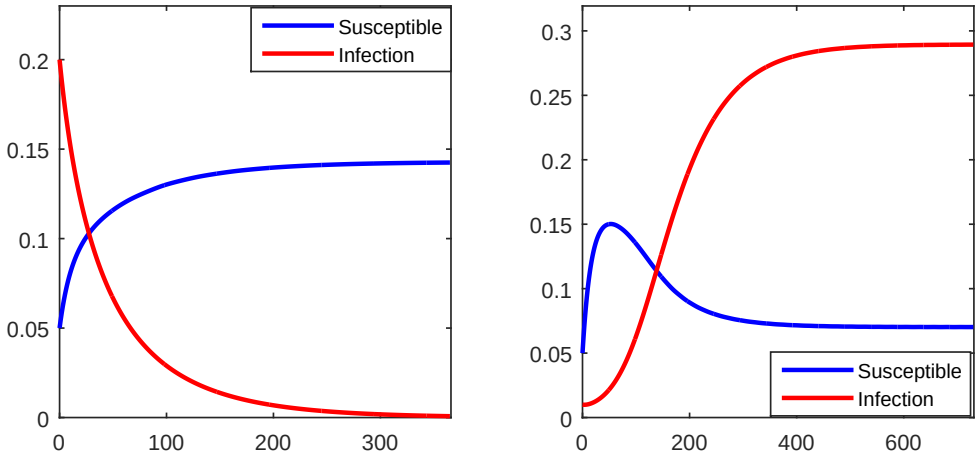
Table 1: The description and value of parameters

3 Numerical Simulation

In this section, we represent a numerical simulation of the infection dynamics of the spread of measles with constant control and with optimal control on vaccination (u^*) by using the 4^{th} order Runge Kutta scheme. Note that the optimal control simulation on vaccination uses data and initial

conditions in the table 2.3 that satisfy $\mathscr{R}_0 > 1$. The meaning is the infection population and susceptible are not going to zero. The performance of optimal control is presented with a variety of costs.

In figure 2(a), we can see the extinction of infected humans. Infection rate $\beta = 0.2$ per unit time and the effectiveness of vaccination is given any value. Figure 2(a) confirm the theorem 2.1-(i) which states that if the basic reproduction number is less than one ($\mathscr{R}_0 < 1$), then the infected population goes to zero, while the susceptible population is heading towards its equilibrium. However, in figure 2(b) we change the value of the infection rate parameter $\beta = 0.3$ and the rate of disease recovery $\gamma = 0.01$. In addition, the effectiveness of vaccination dropped to $u = 0.05$ per unit time. This parameter change is conducted to confirm the outbreak of measles when the rate of infection increases and the rate of recovery and vaccination decreases such that the basic reproduction number is bigger than one ($\mathscr{R}_0 > 1$) . The result we can see in the figure 2(b) that the proportion of humans infected is higher than susceptible. It should be noted that the proportion of susceptible will never be zero because humans who recover from measles will not be re-infected. This condition confirms the theorem 2.1-(ii) which states that if the basic reproduction number is greater than one, which is equivalent to a high infection rate while vaccine effectiveness is low, the endemic equilibrium is stable that equivalent with the infected population is increasingly large.



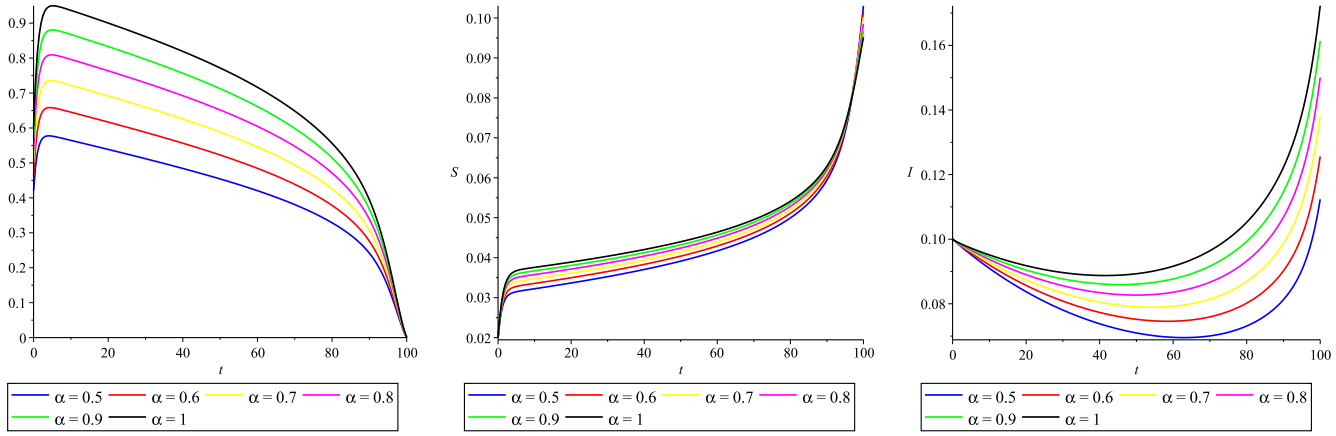
(a) (b)

Figure 2: The dynamic of susceptible and infection with the different condition (a) $\mathscr{R}_0 < 1$ with initial condition $S(0) = 0.05, I(0) = 0.2$; (b) $\mathscr{R}_0 > 1$ with initial condition $S(0) = 0.05, I(0) = 0.01$.

In figure 3(a), we can see that the cost of the vaccination program is directly proportional to the effectiveness of the vaccine. If the cost of a vaccination program is high, the effectiveness of vaccination is also high, but if the cost of the vaccination program is low, then the effectiveness of the control will also be low. For example, the lowest cost proportion in the figure 3(a) is $\alpha = 0.5$ corresponds to low effectiveness of vaccination (blue line), but the proportion of costs is high $\alpha = 1$ corresponds to the effectiveness of high vaccination rates (black line). The highest effectiveness of vaccination in the figure 3(a) is around $t = 10$, as a result the proportion of humans infected has declined, 3(c), while the proportion of susceptible humans is increasing 3(b). When the proportion of vaccination effectiveness runs out, at $t = 100$, the infected human population rises and goes to its equilibrium (see figure 3(c)). But even though the effectiveness of vaccination has run out, the proportion of humans recovering will still rise to its equilibrium (see 3(b)). This is because humans who have been exposed to measles cannot be re-infected.

Our simulation results indicate that initial vaccination with lower costs is very effective in reducing the proportion of humans infected. We can see a comparison between the proportion of humans infected with optimum vaccination control and with constant vaccination in figure 2. At $t = 80$ the

proportion of infected humans who use constant vaccination (see 2(b)) is higher than the proportion of infected humans who use the optimum vaccination control (see figure 3(c)). The results of this simulation suggest that vaccination does not need to be continuous provided the initial immunization is carried out with low effectiveness. Regarding the effectiveness of vaccination, we can see that optimum control u^* depends on the proportion of humans infected and humans susceptible (see equation (10)). This implies a biological meaning that the optimal vaccination must pay attention to the proportion of humans infected and susceptible in the field. The vaccination cannot be equated in each region, sometimes vaccination cost is high enough if the number of patients and the rate of infection is high. There are also areas that are given vaccinations at a low cost, or even not vaccinated at all. This needs to be a concern for policy makers to determine the cost of vaccination programs in areas that will be given vaccines.



(a) (b) (c)

Figure 3: The simulation with various of cost; (a) control performance; (b) susceptible dynamics with initial condition $S(0) = 0.02$; (c) infected dynamics with initial condition $I(0) = 0.1$

4 Conclusion

The deterministic mathematical model that describes the spread of measles diseases involving the control factor of vaccination has been introduced here. This model can explain well the phenomenon of the measles spread and its relationship to vaccination programs. The correlation between disease outbreak and the basic reproduction number is discussed in the theorem 2.1 which states that disease can spread if the infection rate is higher than the effectiveness of vaccination and recovery rate $(\mathscr{R}_0 > 1)$. Conversely, if the effectiveness of vaccination and recovery rate is higher than the rate of infection (imply $(\mathscr{R}_0 < 1)$), then the proportion of infected will go to zero such that the spread of the disease can be stopped. But the high effectiveness of vaccination is directly proportional to the costs used. Theorem 2.2 recommends optimal control in dealing with the spread of measles by vaccination. From the equation (10) we can see optimal control formulations that depend on the cost of the vaccination program, the vaccinated individuals and the rate of infection. When the infection rate is high, we suggest that immunization be carried out more intensively even though the program can cost a lot. The more susceptible individuals who are vaccinated will be able to reduce infected individuals so that the outbreak does not occur.

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