A deterministic model of measles with imperfect vaccination and quarantine intervention

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Abstract. A modified SVIQR (Susceptible-Vaccinated-Infected-Quarantine-Recovered) deterministic model for measles infection will be discussed in this article. An intervention of two times vaccination (one of them is imperfect to protect measles infection) is implemented along with the quarantine intervention in a purpose to controlling the spread of measles among human population. A measles-free and measles endemic equilibrium, for a complete and a simplified model, established analytically. A basic-reproduction number ($R_0$) as the endemic indicator is performed using the next-generation matrix approach. We find that the disease-free equilibrium is locally stable if $R_0 < 1$ and the endemic equilibrium of measles is achieved when $R_0 > 1$. Some numerical simulation regarding the sensitivities of $R_0$ and simulation for the autonomous model is given to give a better interpretation for the analytical results.

1. Introduction
Measles is a highly infectious disease caused by a virus in the paramyxovirus family. The virus is spread by coughing and sneezing, or direct contact with the infected [1]. The virus first comes in contact with host lung tissue, where it infects immune cells and it spread throughout the body. As the virus travels in the blood, it infects capillaries in the skin that causes a rash on the skin [7].

Before the rash appears, measles has an incubation period for about 8-12 days followed by fever ($39^\circ-40,5^\circ$C), cough, coryza, conjunctivitis, and Koplik's spots [2] (small white spots in the mouth). These symptoms are followed by the appearance of a rash that starts on the face and neck and later it will spread to the body [1, 2, 8].

In some cases, measles can cause complications. Most deaths from measles are caused by complications. Serious complications often occur in children under five years of age and adults over the age of 30 years, especially those with insufficient vitamin A, or whose immune systems have been weakened by other diseases [1]. Those serious complications include blindness, severe diarrhea, severe respiratory infections such as pneumonia, or severe neurological infections such as encephalitis [1, 2].

To prevent measles, all health institutions recommend children to get the measles vaccine. Measles vaccine can be accepted by children and adults through MMR (Mumps, Measles, and Rubella) vaccines, MR (Measles and Rubella) vaccines and MMRV (Mumps, Measles, Rubella, and Varicella) vaccines. All of those vaccines consist of two doses. According to Centers for Disease Control and Prevention (CDC), one dose of MMR vaccine is 93% effective against measles and two doses of MMR vaccine are 97% effective against measles [8].
An estimated 90,000 people died from the disease measles in 2016. In 2016 also for the first time deaths caused by measles is decreased by 84%. The decrease in mortality was due to the implementation of vaccinations for measles to individuals [1].

In addition to getting the measles vaccine, quarantine can be carried out to prevent measles. Quarantine has been used to reduce the transmission of infectious diseases such as leprosy, plague, cholera, typhus, yellow fever, smallpox, diphtheria, tuberculosis, measles, mumps, Ebola and Lassa fever [3].

Some mathematical models have been introduced by many authors to describe the spread of measles, such as [4, 5, 6]. Different with previous model, we construct a mathematical model of measles that accommodates two-step of vaccination and quarantine in this article. The model differentiates individual who already get one time vaccination and two time vaccination into two different compartments. In the other hand, quarantine strategy is also involved into the model to understand how important and crucial is the quarantine to control the spread of measles, if it is compared with the vaccination strategy.

The layout of this article is given as follows. In Section 2, the mathematical model will be introduced followed with the analysis of it. Some numerical simulations are given in Section 3. Finally in Section 4, some conclusions are given.

2. Mathematical model and analysis

Let the human population divided into 6 subpopulations, let define them as susceptible class denoted by $S(t)$, vaccinated class $V_1(t)$ and $V_2(t)$ denoted as human population who get vaccinated once and twice, respectively, Infected class and quarantined class denoted by $I(t)$ and $Q(t)$, respectively, and recovered class $R(t)$. The transmission and transition process in this model is following the process in a standard SVIQR model. Even though, there are some comments need to be stated as a foundation for the model development.

(i) The first assumption is that the vaccination is given two times ($u_1$ and $u_2$) to make people protected by measles 100%, that is why we have two classes for the vaccinated population, i.e $V_1(t)$ and $V_2(t)$.

(ii) The human in the class of $V_1(t)$ does not get a 100% protection from measles infection, we denote the reduction of infection probability by $p$.

(iii) Human who get a quarantine intervention (with the rate of $u_3$) should be separated in the specific class, i.e. $Q(t)$ and do not permanently avoid contact with another human. Therefore, there is a reduction of the capability of this class to spread measles, we denote it by $q$.

(iv) Quarantine intervention does not make the human stay in the quarantine place until this infected human get cured by measles. There is a possibility that they do not finish the quarantine intervention and come back to the infected class, denote it as $u_4$. Different from $u_1, u_2$ and $u_3$ which it should be implemented massively to avoid the spread of measles, $u_4$ should be kept in a small value to make sure the infected human do not spread measles easily to susceptible human.

(v) The human who separated in the quarantined class do not get an extra medical treatment that will make them recovered from measles faster than usual. The recovery rate is given by $\gamma$.

With these assumptions, the mathematical model of measles spread with two-step vaccination...
intervention and quarantine intervention is given by:

\[
\begin{align*}
\frac{dS}{dt} &= A - \frac{\beta SI}{N} - \frac{\beta qSQ}{N} - u_1 S - \mu S, \\
\frac{dV_1}{dt} &= u_1 S - \frac{\beta pV_1 I}{N} - \frac{\beta qV_1 Q}{N} - \mu V_1 - u_2 V_1, \\
\frac{dV_2}{dt} &= -\mu V_2 + u_2 V_1, \\
\frac{dI}{dt} &= \frac{\beta SI}{N} + \frac{\beta pV_1 I}{N} + \frac{\beta qSQ}{N} + \frac{\beta qV_1 Q}{N}\mu - u_3 I - \gamma I - \mu I + u_4 Q, \\
\frac{dQ}{dt} &= u_3 I - Q\mu - u_4 Q, \\
\frac{dR}{dt} &= \gamma I + Q\gamma - R\mu.
\end{align*}
\]

(1)

Where \( A \) is the recruitment rate from newborn, \( \mu \) is the natural death rate, and \( N \) is the total human population. Since we assume that no migration is involved in the model, the dynamic of total for human population is given by

\[
\frac{dN}{dt} = A - \mu N.
\]

To avoid the exponential growth or decrease of the total of human population, we assume that the number of newborn is the same with number of death. Therefore, we have that \( A - \mu N \). Please note that all parameters are positive.

System (1) has one trivial equilibrium, let us call it as measles-free equilibrium point which given by:

\[
\Omega_1 = (S^1, V^1_1, V^1_2, I^1, Q^1, R^1) = \left( \frac{A}{\mu + u_1}, \frac{u_1 A}{(\mu + u_2)(\mu + u_1)}, \frac{u_1 A u_2}{(\mu + u_1)(\mu + u_2)\mu}, 0, 0, 0 \right).
\]

This measles-free equilibrium describes a situation when all human population is not infected. Therefore, only \( S, V_1 \) and \( V_2 \) are positive, while \( I, Q \) and \( R \) are zero. From the form of \( \Omega_1 \), we can see that \( S^1 + V^1_1 + V^1_2 + I^1 + Q^1 + R^1 = \frac{A}{\mu} \), which describe that total of the human population is always constant and not depending on other parameters, except newborn and death rate. We also can see that when there is no vaccination intervention, we have that \( \Omega_1 \) reduced into \((\frac{A}{\mu}, 0, 0, 0, 0, 0)\). Using the next generation matrix approach, system (1) has a basic reproduction number as the endemic indicator of measles spread given by:

\[
\mathcal{R}_0 = \frac{\beta \mu (pu_1 + \mu + u_2)(qu_3 + \gamma + \mu + u_4)}{(\mu + u_2)(\mu + u_1)(\gamma + \mu)(\gamma + u_3 + u_4 + \mu)}.
\]

(2)

Basic reproduction number \( (\mathcal{R}_0) \) describes the expected number of secondary cases of measles caused by one primary case of measles during one infection period in a completely susceptible population. From this definition, it means that when \( \mathcal{R}_0 > 1 \), then the disease will spread among the population when \( t \to \infty \). On the other hand, the disease will disappear from population when \( \mathcal{R}_0 < 1 \). Please see [9] for further detail about the construction of the basic reproduction number, and for more example of the construction of basic reproduction number with these approaches.

To analyze the local stability of \( \Omega_1 \), we analyze this equilibrium in the Jacobian matrix of system (1). The eigenvalue of this matrix is taken from the root of a characteristic polynomial:

\[
(a_2 \lambda^2 + a_1 \lambda + a_0)(\lambda + \mu)^2(\lambda + \mu + u_2)(\lambda \mu + u_1) = 0.
\]
measles spread, the numerator of $R$ and only if the basic reproduction number is less than 1. This result indicates that to control unstable otherwise.

Theorem 1. Measles model in (1) has a measles-free equilibrium given by $\Omega_1$ which always exist ($\Omega_1 \in \mathbb{R}^+_0$) without any condition. $\Omega_1$ will locally asymptotically stable if and only if $R_0 < 1$ and unstable otherwise.

Theorem 1 tells us that the measles-free equilibrium will be locally asymptotically stable if and only if the basic reproduction number is less than 1. This result indicates that to control measles spread, the numerator of $R_0$ should be reduced (one of many ways is to reduce the infection probability $\beta$), while the de-numerator should be increased (one of many ways is to increase $u_1$, $u_2$ and $u_3$). Further discussion about the basic reproduction number will be discussed in the next section.

The second equilibrium is the endemic equilibrium where measles is existed among the human population. This equilibrium is not in a simple form to be shown explicitly. Therefore, the existence of this equilibrium will be presented as a function depending on $I$. This second equilibrium is given by:

$$\Omega_2 = (S^2, V_1^2, V_2^2, I^2, Q^2, R^2)$$

where

$$S^2 = \frac{AN (\gamma + u_4 + \mu)}{I^* \beta (qu_3 + \gamma + \mu + u_4) + N (u_1 + \mu) (\gamma + u_4 + \mu)},$$

$$V_1^2 = f_1(I^*),$$

$$V_2^2 = f_2(I^*),$$

$$Q^2 = \frac{u_3 I^*}{\gamma + \mu + u_4},$$

$$R^2 = \frac{\gamma I^* (\gamma + u_3 + u_4 + \mu)}{\mu (\gamma + \mu + u_4)}$$

while $I^*$ is taken from the positive root of two degrees polynomial of $I$ which is given by:

$$f_3(I^*) = a_2 I^2 + a_1 I + a_0,$$

where

$$a_2 = -\beta^2 p(\gamma + \mu)(\gamma + \mu + u_3 + u_4)(qu_3 + \gamma + \mu + u_4)^2,$$

$$a_1 = \beta(\gamma + \mu + u_4)(qu_3 + \gamma + \mu + u_4)N(\gamma + \mu)(\gamma + u_3 + u_4)(\mu p + pu_1 + \mu + u_2)(R_2 - 1),$$

$$a_0 = N(\gamma + u_4)^2(\gamma + \mu)(\gamma + u_3 + u_4)(\mu + u_2)(\mu + u_1)(R_0 - 1),$$
where $R_2 = \frac{\beta Ap(qu_3 + \mu + u_4 + \gamma)}{N(\gamma + \mu)(\gamma + \mu + u_3 + u_4)(\mu p + pu_1 + \mu + u_2)}$. From polynomial of $f_3(I)$, it can be seen that we will have a unique endemic equilibrium of $\Omega_2$ if $R_0 > 1$, two positive endemic equilibrium is $\Omega_2$ if $R_0 < 1 < R_2$ and no endemic equilibrium if $R_2 < R_0 < 1$. These results are given in the following theorem.

**Theorem 2.** Measles model in (1) has

(i) Unique endemic equilibrium if $R_0 > 1$, and

(ii) No endemic equilibrium if $R_2 < R_0 < 1$,

where $R_2 = \frac{\beta Ap(qu_3 + \mu + u_4 + \gamma)}{N(\gamma + \mu)(\gamma + \mu + u_3 + u_4)(\mu p + pu_1 + \mu + u_2)}$ and

$R_0 = \frac{\beta \mu (pu_3 + \mu + u_2)(qu_3 + \gamma + \mu + u_4)}{(\mu + u_2)(\mu + u_1)(\gamma + \mu)(\gamma + u_3 + u_4 + \mu)}$.

### 3. Numerical simulation

In this section, system (1) is simulated using the parameter in Table 1 to illustrate the theoretical results contained in this article.

| Parameters | Description                                       | Value          |
|------------|---------------------------------------------------|----------------|
| $A$        | Birth rate.                                       | 1000           |
| $\mu$      | Natural death rate.                               | $\frac{1}{65.365}$ |
| $\beta$    | Infection rate.                                   | 0.33 $[10]$    |
| $p$        | The proportion of infections in individuals with one stage of vaccination. | 0.1            |
| $q$        | Proportion of infections in infected individuals quarantined. | 0.01          |
| $\gamma$   | Recovery rate.                                    | $\frac{1}{30}$ |

#### 3.1. The sensitivity of basic reproduction number

From Figure 1(a), 1(b), and 1(c), we can see that $R_0$ will continue to decrease as the control values $u_1$, $u_2$, and $u_3$ increase respectively. Furthermore, it can be seen that the decrease in $R_0$ against the value of $u_3$ occurs linearly, but nonlinear against $u_1$ and $u_2$. This means that $R_0$ can be reduced significantly for values that are close to zero but decreases when the values of $u_1$, and $u_2$ are close to one. On the other hand, the $R_0$ increases when the rate of the $u_4$ increases. This indicates that the quarantine period for individuals who are affected by measles needs to be increased so that the outbreaks of measles can be reduced.

#### 3.2. Simulation of the autonomous system

From Figure 2, we can see that when $u_1 = 0.9$, there is a vaccination process, so that the number of healthy population will continue to increase while the number of infected population will decrease, but when $u_1 = 0$, there is no vaccination process, so that the number of healthy population will decrease while the number of infected population will increase.
Figure 1: The sensitivity of basic reproduction number ($R_0$) curve refers to (a) the first step of vaccination, (b) the second step of vaccination, (c) infected individuals quarantined, (d) infected individuals who stop quarantine and the y-axis is the $R_0$.

Figure 2: The dynamics of total healthy ($S + V_1 + V_2 + R$) and infected ($I + Q$), with $u_1 = 0.9$ for $R_0 = 0.9891664722$ (blue); $u_1 = 0$ for $R_0 = 9.887497369$ (red) and $t \in [0, 365]$ days.
Table 2: Total healthy and infected at $t = 365$ with and without vaccination.

|                      | Without vaccination | With vaccination |
|----------------------|---------------------|------------------|
| Total healthy at $t = 365$ | 999.9883            | 998.7266         |
| Total infected at $t = 365$  | 0.0117              | 1.2734           |

Although there is no vaccination process in the population, when $u_1 = 0$, the total healthy does not always decrease, but also can increase because individuals who have been infected with measles will not be re-infected with measles and belong to healthy. From Table 2, we can see that total infected with a vaccination process at $t = 365$. From table 2, it can be seen that total infected with a vaccination process at $t = 365$ is greater than total infected without a vaccination process, but from Figure 2, showed that there will be no measles outbreak with a vaccination process, whereas without a vaccination process, total infected will increase before decreasing due to the healing of infected who become immune to measles.

![Figure 3: The dynamics of total healthy ($S + V_1 + V_2 + R$) and infected ($I + Q$), with $u_3 = 0.5$ for $R_0 = 0.1557066249$ (blue); $u_3 = 0$ for $R_0 = 1.027835147$ (red) and $t \in [0, 365]$ days.](image)

From Figure 3, we can see that when $u_3 = 0.5$, there is a quarantine process, that makes the number of healthy population increases faster because the quarantine process can reduce the infection. Because measles is a highly contagious disease, when $u_3 = 0$, there is no quarantine process so that the number of healthy population will decrease.

Table 3: Total healthy and infected at $t = 365$ with and without quarantine.

|                      | Without quarantine | With quarantine |
|----------------------|---------------------|------------------|
| Total healthy at $t = 365$ | 999.9883            | 999.9937         |
| Total infected at $t = 365$  | 0.0116              | 0.006372         |
As we can see from Table 3, the number of infected population with the quarantine process at $t = 365$ is less than the number of infected population without the quarantine process. It means, the quarantine process is important to reduce the number of infected. Even though there is no quarantine process in the population, when $u_3 = 0$, the number of healthy population does not always decrease, but also can increase because individuals who have been infected with measles will not be re-infected with measles and belong to healthy.

![Graph](image)

Figure 4: The dynamics of total healthy ($S + V_1 + V_2 + R$) and infected ($I + Q$), with $u_2 = 0.9$ for $R_0 = 0.0008797384461$ (blue); $u_2 = 0$ for $R_0 = 0.9894998315$ (red) and $t \in [0, 365]$ days.

From Figure 4, we can see that when $u_2 = 0.9$, there is a second step of the vaccination process, so that the number of healthy increases faster and the number of infected decreases faster. When $u_2 = 0$, there is no second step of the vaccination process, but the number of healthy increases slowly because there is a first step of the vaccination process in the individuals, and without the second step of the vaccination process, the number of infected will also decrease slowly because there is a first step of the vaccination process.

|                          | Without the second step of vaccination | With the second step of vaccination |
|--------------------------|----------------------------------------|-----------------------------------|
| Total healthy at $t = 365$ | 999.0898                               | 999.9992                          |
| Total infected at $t = 365$ | 0.9102                                | 0.0008                            |

As we can see from Table 4, with the second step of the vaccination process, the number of infected is less than without the second step of the vaccination process at $t = 365$. It means the second step of the vaccination process is essential to reduce the infected. Even though there is no second step of the vaccination process in the population, when $u_2 = 0$, the number of healthy will increase slowly because the individual has received the first step of the vaccination process.
4. Conclusion
In this paper, a mathematical model of the spread of measles disease involving quarantine and two steps of vaccination has been developed. The model has two equilibrium points, i.e., the measles-free equilibrium and the measles endemic equilibrium point. The basic reproduction number ($R_0$) for the model is obtained using the next generation matrix and we find that the measles free equilibrium will LAS if $R_0 < 1$. From the numerical simulation, we know that receiving two steps of vaccine can reduce measles transmission much better rather than only with one step vaccination. Because measles is a highly contagious disease, it can be seen that protecting susceptible individual from infected individual with quarantine intervention is another option to control the spread of measles.

In this article, the vaccination and quarantine interventions are given as a constant parameter which could be not optimal to control the spread of measles. Changing this parameters as a time dependent parameters is a good option to control measles in a optimal way since the intervention will depend on the needs. Reconstruct the model as an optimal control problem might be one of the option for future work.

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References
[1] World Health Organization (2018), Measles. Retrieved from http://www.who.int/news-room/fact-sheets/detail/measles
[2] Robert T. Perry and Neal A. Halsey. (2004), The Clinical Significance of Measles: A Review. The Journal of Infectious Diseases.
[3] Hethcote, H., Zhien, M., & Shengbing, L. (2002). Effects of quarantine in six endemic models for infectious diseases. Mathematical Biosciences, 180(1-2), 141-160. doi:10.1016/s0025-5564(02)00111-6
[4] B.P.Prawoto (2017), Stability and simulation of measles transmission model with and without vaccination. Far East Journal of Mathematical Sciences, 102(2), pp. 271-281.
[5] Momoh, A.A., Ibrahim, M.O., Uwanta, I.J., Manga, S.B. (2013), Modelling the effect of vaccination on the transmission dynamics of measles, International Journal of Pure and Applied Mathematics, 88(3), pp. 381-390.
[6] Oghre, E.O., Ako, I.I. (2011), A mathematical model for measles disease, Far East Journal of Mathematical Sciences, 54(1), pp. 47-63
[7] David S. (2015). What does measles actually do?. Retrieved from http://www.sciencemag.org/news/2015/01/what-does-measles-actually-do
[8] Centers for Disease Control and Prevention (2018), Measles, Mumps, and Rubella (MMR) Vaccination: What Everyone Should Know. Retrieved from https://www.cdc.gov/vaccines/vpd/mmr/public/index.html
[9] Diekmann, O., Heesterbeek, J. A., & Roberts, M. G. (2009). The construction of next-generation matrices for compartmental epidemic models. Journal of The Royal Society Interface, 7(47), 873-885. doi:10.1098/rsif.2009.0386
[10] Pang, L., Ruan, S., Liu, S., Zhao, Z., & Zhang, X. (2015). Transmission dynamics and optimal control of measles epidemics. Applied Mathematics and Computation, 256, 131-147. doi:10.1016/j.amc.2014.12.096