Mathematics model of measles and rubella with vaccination

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Abstract. Measles and rubella are two contagious diseases in human population which are caused by viruses. Measles and rubella can be prevented by vaccination. In this article, a mathematical model of the spread of measles and rubella with vaccination was constructed and analyzed. The population was divided into 9 classes. It was obtained four equilibrium points, these were the disease-free equilibrium point, the measles-free equilibrium point, the rubella-free equilibrium point, and the endemic equilibrium point. There were two basic reproduction numbers, corresponding to spread of measles and rubella. These numbers correspond to the stability of the equilibrium points. Numerical simulation is done to see the dynamics of population and to confirm the analytical result.

Keywords: Epidemiological model, measles, rubella, equilibrium point, basic reproduction number, stability analysis

1. Introduction
Measles is a contagious disease caused by virus. This disease is one of the top-ten diseases causes death that occur in children aged 5 and below in developing countries. World Health Organization (WHO) stated that in 2015 measles had caused death of 134,200 people (367 people a day and 15 people per hour) [1].

Rubella is also a disease caused by virus. Rubella is very dangerous disease when infected a pregnant woman. The child who born from an infected mom can caused Congenital Rubella Syndrome [2].

In 2016, there were 6,880 measles cases in Indonesia. The government is campaigning the MR (Measles-Rubella) vaccine to all children around the country. The government’s target is to eliminate measles and rubella in Indonesia in 2020 [3].

MR vaccine is given to prevent the outbreak of measles and rubella. MR vaccine is the best way to protect against measles and rubella virus. In Indonesia, MR vaccine is given three times, those are a nine-month-old baby, an 18-month-old baby, and a 6–7 year old children [3].

In mathematics field, there are some studies about the outbreak of measles such as in [4, 5] and rubella in [6, 7]. In our observation, the study of measles and rubella combined in one paper has not done yet. In this paper, a model of measles and rubella with vaccination is constructed and analyzed.
2. Methodology

2.1. Assumptions
Model of measles and rubella with vaccination is constructed under five assumptions. These are:

a) New-born babies are free from the disease and counted as susceptible subpopulation.

b) Only susceptible can receive MR vaccine.

c) Anyone who has already receive three doses of MR vaccine has permanent immunity of measles and rubella.

d) The population is constant and closed.

e) There is no death caused by the diseases.

2.2. Parameters and variables
Parameters which are used in this model are presented in table 1. In model of measles and rubella with vaccination, the population is divided into 9 subpopulations as following.

a) Susceptible ($S$): subpopulation which has not be infected by measles or rubella virus yet.

b) Vaccinated ($V$): subpopulation which has receive one or two doses of MR vaccine.

c) Infectious of measles ($I_m$): subpopulation which has been infected by measles virus and can transmit measles virus to others.

d) Infectious of rubella ($I_r$): subpopulation which has been infected rubella virus and can transmit rubella virus to others.

e) Infectious of measles after rubella ($I_{mr}$): subpopulation which has been infected by measles virus after recovered from rubella and can transmit measles virus to others.

f) Infectious of rubella after measles ($I_{rm}$): subpopulation which has been infected by rubella virus after recovered from measles and can transmit rubella virus to others.

g) Recovered from measles ($R_m$): subpopulation which has recovered from measles and has immunity of measles.

h) Recovered from rubella ($R_r$): subpopulation which has recovered from rubella and has immunity of rubella.

i) Permanent immunity of measles and rubella ($R_2$): subpopulation which has permanent immunity of measles and rubella after receiving three doses of MR vaccine.

3. Model formulation

3.1. Model construction
Figure 1 showed the transmission diagram of the diseases spread. The explanation of construction the model of measles and rubella with vaccination according to figure 1 are as following.

a) Susceptible ($S$) increases by natural birth process (assumption a) and without migration (assumption d). It decreases by natural death or being infected by measles and rubella virus and being vaccinated.

b) Infectious of measles ($I_m$) increases by susceptible who being infected measles virus and vaccinated whose immunity has decrease and being infected measles virus. Infectious of measles hosts will decrease by natural death and recovering from measles.

c) Recovered from measles ($R_m$) will increases by recovering from measles and decreases by natural death and being infected by rubella virus.

d) Infectious of rubella after measles ($I_{mr}$) will increases by recovered from measles being infected by rubella virus and will decreases by natural death and recovering from rubella.

e) Infectious of rubella ($I_r$) will increases by susceptible and vaccinated who being infected by rubella virus and will decreases by natural death and recovering from rubella.
f) Recovered from rubella ($R_r$) will increases by recovering from rubella and will decreases by natural death and being infected by measles virus.

g) Infectious of measles after rubella ($I_{mr}$) will increases by recovered from rubella being infected by measles virus and will decreases by natural death and recovering from measles.

h) Vaccinated ($V$) increases by vaccination which done only for susceptible (assumption b). Vaccinated hosts will decrease by natural death, being infected by both measles and rubella, and being fully vaccinated.

i) Permanent immunity of measles and rubella ($R_2$) will increase by full three-dose vaccination (assumption c), recovering from measles, and recovering from rubella. Permanent immunity will decrease by natural death.

In figure 1, we use force of infection parameters such as $\lambda_m, \lambda_r, \theta_m, \theta_r$ in order to make the diagram as simple as possible. In model construction, we detailed the parameters.

Table 1. List of parameters

| Parameter | Description                        | Unit        |
|-----------|------------------------------------|-------------|
| $\mu$     | Per capita natural birth/death rate| 1/year      |
| $\alpha$  | Per capita one or two dose vaccination rate | 1/year |
| $\rho$    | Per capita transmission of measles rate | 1/year |
| $\omega$  | Per capita rubella transmission rate | 1/year |
| $\phi$    | Three-dose vaccination rate        | 1/year      |
| $\varepsilon$ | Immunity failed proportion     | -           |
| $\gamma$  | Per capita measles recovering rate | 1/year      |
| $\pi$     | Per capita rubella recovering rate | 1/year      |

Figure 1. Transmission diagram
Based on the assumptions and transmission diagram in figure 1, we constructed a 9-d dynamical system of the spread of measles and rubella with vaccination in population as follows:

\[
\begin{align*}
\frac{dS}{dt} &= \mu N - \frac{\rho S(I_m + I_{rm})}{N} - \frac{\omega S(I_r + I_{mr})}{N} - (\alpha + \mu)S, \\
\frac{dI_m}{dt} &= \frac{\rho S(I_m + I_{rm})}{N} + \frac{\varepsilon \rho V(I_m + I_{rm})}{N} - (\gamma + \mu)I_m, \\
\frac{dR_m}{dt} &= \gamma I_m - \frac{\omega R_m(I_r + I_{mr})}{N} - \mu R_m, \\
\frac{dI_{mr}}{dt} &= \frac{\omega R_m(I_r + I_{mr})}{N} - (\pi + \mu)I_{mr}, \\
\frac{dI_r}{dt} &= \frac{\omega S(I_r + I_{mr})}{N} + \frac{\varepsilon \omega V(I_r + I_{mr})}{N} - (\pi + \mu)I_r, \\
\frac{dR_r}{dt} &= \pi I_r - \frac{\rho R_r(I_m + I_{rm})}{N} - \mu R_r, \\
\frac{dI_{rm}}{dt} &= \frac{\rho R_r(I_m + I_{rm})}{N} - (\gamma + \mu)I_{rm}, \\
\frac{dV}{dt} &= \alpha S - \frac{\varepsilon \rho V(I_m + I_{rm})}{N} - \frac{\varepsilon \omega V(I_r + I_{mr})}{N} - (\varphi + \mu)V, \\
\frac{dR_2}{dt} &= \varphi V + \pi I_{mr} + \gamma I_{rm} - \mu R_2,
\end{align*}
\]

where \( N = S + I_m + R_m + I_{mr} + I_r + R_r + I_{rm} + V + R_2 \) is constant (assumption d).

3.2. Disease free equilibrium point (DFE)

The disease-free equilibrium (DFE) point occurs when there is no measles and rubella infection in the population. The point, in \((S, I_m, R_m, I_{mr}, I_r, R_r, I_{rm}, V, R_2)\) coordinate, is as following.

\[
DFE = \left(\frac{\mu N}{\alpha + \mu}, 0, 0, 0, 0, 0, 0, 0, 0\right).
\]

3.3. Basic reproduction number \((R_0)\)

Basic reproduction number is obtained by construction of next generation matrix (NGM) [8]. In construction of NGM, only the subsystem of infectious of system (1) is being noticed. The subsystem is as following.

\[
\begin{align*}
\frac{dI_m}{dt} &= \frac{\rho S(I_m + I_{rm})}{N} + \frac{\varepsilon \rho V(I_m + I_{rm})}{N} - (\gamma + \mu)I_m, \\
\frac{dI_r}{dt} &= \frac{\omega S(I_r + I_{mr})}{N} + \frac{\varepsilon \omega V(I_r + I_{mr})}{N} - (\pi + \mu)I_r, \\
\frac{dI_{mr}}{dt} &= \frac{\omega R_m(I_r + I_{mr})}{N} - (\pi + \mu)I_{mr}, \\
\frac{dI_{rm}}{dt} &= \frac{\rho R_r(I_m + I_{rm})}{N} - (\gamma + \mu)I_{rm}.
\end{align*}
\]
After do the linearization of subsystem (3), it is obtained transmission matrix $F$ and transition matrix $V$. Then determine the NGM as $K = -FV^{-1}$. We obtain

$$R_{0m} = \frac{\rho \mu (\alpha \varepsilon + \mu + \phi)}{(\mu + \phi)(y + \mu)(\alpha + \mu)} \quad \text{and} \quad R_{0r} = \frac{\omega \mu (\alpha \varepsilon + \mu + \phi)}{(\mu + \phi)(\alpha + \mu)(\pi + \mu)},$$

(4)

where $R_{0m}$ is basic reproduction number for measles infection and $R_{0r}$ is basic reproduction number for rubella infection.

### 3.4. Endemic equilibrium

There are three types of endemic equilibrium point, these are the measles-free equilibrium point, the rubella-free equilibrium point, and the endemic equilibrium point.

#### 3.4.1. Measles free equilibrium point

The Measles-free equilibrium (MFE) occurs when there is no more measles virus in population. In other words, there is only rubella virus which exists in population. The MFE is as following:

$$MFE = (S^*, I_m^*, R_m^*, I_m^*, I_r^*, R_r^*, I_r^*, V^*, R_2^*)$$

$$= (S^*, 0, 0, I_r^*, R_r^*, 0, V^*, R_2^*),$$

$$S^* = \frac{N(\omega \varepsilon I_r^* + \mu \omega I_r^* + N \mu I_r^* + N \pi V^* + N \mu V^* + N \mu V^* + N \mu \phi^*)}{(N \varepsilon \alpha I_r^* + N \mu I_r^* + N \mu I_r^* + N \mu I_r^* + N \mu I_r^* + N \mu I_r^* + N \mu I_r^* + N \mu I_r^* + N \mu I_r^*)}$$

(5)

$$V^* = \frac{\pi I_r^*}{\mu},$$

and

$$R_2^* = \frac{N^2 \alpha \varepsilon (\pi + \mu)}{\mu \omega (N \varepsilon \alpha I_r^* + N \mu I_r^* + N \mu I_r^* + N \mu I_r^* + N \mu I_r^* + N \mu I_r^* + N \mu I_r^* + N \mu I_r^* + N \mu I_r^*)}.$$

Furthermore, the value of $I_r^*$ satisfies the quadratic equation

$$A_1 (I_r^*)^2 + A_2 (I_r^*) + A_3 = 0,$$

(6)

The MFE point has a biology meaning when all the variables are non-negative. All of its components are non-negative when the condition below satisfied.

$$R_{0r} = \frac{\omega \mu (\alpha \varepsilon + \mu + \phi)}{(\mu + \phi)(\alpha + \mu)(\pi + \mu)} > 1.$$

(7)

#### 3.4.2. Rubella free equilibrium point

The rubella free equilibrium (RFE) occurs when there is no more rubella virus in population, only measles virus which is exists in population. The RFE is as following:

$$RFE = (S^{**}, I_m^{**}, R_m^{**}, I_m^{**}, I_r^{**}, R_r^{**}, I_r^{**}, V^{**}, R_2^{**})$$

$$= (S^{**}, I_m^{**}, R_m^{**}, 0, 0, 0, V^{**}, R_2^{**})$$

(8)
where \( S^{**} = \frac{N(y \mu e t_m^* + \mu \rho e t_m^* + N \alpha e + N \alpha \phi + N \mu^2 + N \mu \phi)}{(N \alpha e + \rho e t_m^* + N \mu + N \phi)(\mu)} \), \( R_m^{**} = \frac{y t_m^*}{\mu} \),

\[
\psi^{**} = \frac{N^2 \alpha(\gamma + \mu)}{(N \alpha e + \rho e t_m^* + N \mu + N \phi)(\mu)} \quad \text{and} \quad R_2^{**} = \frac{N^2 \alpha(\gamma + \mu)}{\mu \rho(N \alpha e + \rho e t_m^* + N \mu + N \phi)(\mu)}
\]

and the value of \( I_m^* \) satisfy the quadratic equation

\[
B_1(I_m^*)^2 + B_2(I_m^*) + B_3 = 0,
\]

The RFE has a biology meaning when all the variables are non-negative. All of its components are non-negative when the condition below satisfied.

\[
R_{0m} = \frac{\rho \mu(\alpha e + \mu + \phi)}{(\mu + \phi)(\gamma + \mu)(\alpha + \mu)} > 1.
\] (9)

3.4.3. Endemic equilibrium point. It is not easy to determine the endemic equilibrium point (EE) analytically. So, a numerical simulation is done to find the existence of the endemic equilibrium point. The result of that simulation is shown in table 2.

Since \( N \) is total population, the equilibrium point of measles and rubella endemic exists and has a biological meaning.

3.5. Stability analysis

3.5.1. Stability analysis of disease-free equilibrium point. The linearization around DFE point produced nine eigenvalues. The nine eigenvalues must be negative, so that DFE point is stable. That condition is satisfied when

\[
R_{0m} = \frac{\rho \mu(\alpha e + \mu + \phi)}{(\mu + \phi)(\gamma + \mu)(\alpha + \mu)} < 1 \quad \text{and} \quad R_{0r} = \frac{\omega \mu(\alpha e + \mu + \phi)}{(\alpha + \mu)(\gamma + \mu)(\alpha + \mu)} < 1.
\] (10)

3.5.2. Stability analysis of endemic equilibrium point. Three others equilibrium point are determined by numeric simulation. The result of the simulation is shown in table 3.

There are 4 cases of the value of \( R_0 \) in table 3. Those are \( R_{0m} < 1 \) and \( R_{0r} < 1 \), \( R_{0m} < 1 \) and \( R_{0r} > 1 \), \( R_{0m} > 1 \) and \( R_{0r} < 1 \), also \( R_{0m} > 1 \) and \( R_{0r} > 1 \). The equilibrium point is locally asymptotically stable from the analysis of the eigenvalues of Jacobian matrix.

| Parameter list | \( R_{0m} \) | \( R_{0r} \) | Equilibrium point |
|---------------|--------------|--------------|-------------------|
| \( \mu = 0.015; \rho = 150; \) | 1.385 | 1.149 | \( (S_{s0}, I_{s0}, R_{s0}, I_{s0}, I_{r0}, R_{r0}, I_{m0}, V, R_2) \) |
| \( \omega = 150; \gamma = 2.607; \) | | | \( (0.006N, 0.002N, 0.012N, 0.001N, 0.001N, 0.008N, 0.001N, 0.004N, 0.965N) \) |
| \( \pi = 3.65; \alpha = 0.9; \) | | | |
| \( \phi = 0.7; \epsilon = 0.9 \) | | | |

Table 2. Equilibrium point
Table 3. Stability analysis of equilibrium points

| No. | Parameter list | $R_{0m}$ | $R_{0r}$ | Equilibrium point $(S, I_m, R_m, I_{mr}, I_r, R_r, I_{rm}, V, R_2)$ | Stability |
|-----|----------------|----------|----------|-------------------------------------------------|----------|
| 1.  | $\mu = 0.015; \rho = 45.625$; $\omega = 120; \gamma = 26.07$; $\pi = 3.65; \alpha = 0.9$; $\phi = 0.7; \varepsilon = 0.9$ | 0.061    | 1.329    | DFE $= \left( \begin{array}{c} 0.016N, 0, 0, 0, 0, 0, 0, 0 \end{array} \right)$ | Unstable |
|     |                |          |          | MFE $= \left( \begin{array}{c} 0.015N, 0, 0, 0, 0.001N, 0.164N, 0, 0.017N, 0.802N \end{array} \right)$ | Locally asymptotically stable |
| 2.  | $\mu = 0.015; \rho = 90$; $\omega = 40.55; \gamma = 2.607$; $\pi = 36.5; \alpha = 0.9$; $\phi = 0.7; \varepsilon = 0.9$ | 1.201    | 0.449    | DFE $= \left( \begin{array}{c} 0.016N, 0, 0, 0, 0, 0, 0, 0.021N, 0.963N \end{array} \right)$ | Unstable |
|     |                |          |          | MFE $= \left( \begin{array}{c} 0.015N, 0.002N, 0.215N, 0, 0, 0, 0, 0, 0, 0.016N, 0.753N \end{array} \right)$ | Locally asymptotically stable |
|     |                |          |          | RFE $= \left( \begin{array}{c} 0.012N, 0, 0, 0, 0, 0, 0, 0, 0.014N, 0.974N \end{array} \right)$ | Unstable |
| 3.  | $\mu = 0.01; \rho = 150$; $\omega = 150; \gamma = 2.607$; $\pi = 3; \alpha = 0.85$; $\phi = 0.7; \varepsilon = 0.9$ | 1.385    | 1.149    | DFE $= \left( \begin{array}{c} 0.011N, 0, 0, 0, 0.001N, 0.219N, 0, 0.011N, 0.758N \end{array} \right)$ | Unstable |
|     |                |          |          | MFE $= \left( \begin{array}{c} 0.009N, 0.002N, 0.354N, 0, 0, 0, 0, 0, 0, 0.009N, 0.626N \end{array} \right)$ | Unstable |
|     |                |          |          | RFE $= \left( \begin{array}{c} 0.006N, 0.002N, 0.012N, 0.001N, 0.001N, 0.008N, 0.001N, 0.004N, 0.965N \end{array} \right)$ | Locally asymptotically stable |

4. Numeric simulations

4.1. Numerical simulation of various early vaccination parameter values

This simulation is done with four scenarios of early vaccination parameter values ($\alpha$), while the value of full vaccination parameter ($\phi$) is constant. The others parameter values are given in table 2, while initial condition of population presented in table 4.

In figure 2, when the value of early vaccination ($\alpha$) increases, the infection of measles and/or rubella decreases. In other words, early vaccination can reduce measles and rubella infection in population. This figure also confirms the existence of four equilibrium points in table 3.
4.2. Numerical simulation of various full vaccination parameter values

This simulation is done with four scenarios of full vaccination parameter values ($\varphi$), while the value of early vaccination parameter ($\alpha$) is constant. The others parameter values are given in table 2, while initial condition of population presented in table 4.

From figure 3, we obtained that higher the value of full-vaccination will make lower measles and/or rubella infection in population. This figure also confirms the existence of four equilibrium points in table 3.

| Variable | $S(0)$ | $I_m(0)$ | $R_m(0)$ | $I_{mr}(0)$ | $I_r(0)$ | $R_r(0)$ | $I_{rm}(0)$ | $V(0)$ | $R_2(0)$ |
|----------|--------|----------|----------|-------------|---------|---------|-------------|-------|---------|
| Initial  | 11,000 | 10,000   | 9,000    | 7,000       | 10,000  | 8,000   | 5,000       | 4,000 | 1,000   |
| condition|        |          |          |             |         |         |             |       |         |

Figure 2. Dynamics of subpopulations $I_m, I_{mr}, I_r, I_{rm}$ with four values of early-vaccination parameter ($\alpha$). The green, red, blue and yellow curves are for $\alpha = 0, 0.5, 2$ and 30 respectively.
5. Conclusion

In this article, a mathematical model of the spread of measles and rubella with vaccination in population was constructed and analyzed. The model used 9 non-linear differential equations. This model produced two basic reproduction numbers related with measles and rubella infection. There were four equilibrium points which correspond to the basic reproduction numbers. The existence and stability of the equilibrium points depend on the basic reproduction numbers. The numerical simulation showed that increasing the early-vaccination and full-vaccination process will reduce the measles and/or rubella infection in population.

Acknowledgments

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