Parameter Estimation and Sensitivity Analysis of Malaria Model

Fatmawati¹*, Utami Dyah Purwati¹, Jonner Nainggolan²

¹Department of Mathematics, Faculty of Science and Technology, Universitas Airlangga, Surabaya, Indonesia
²Department of Mathematics, Faculty of Mathematics and Natural Science, Universitas Cenderawasih, Jayapura, Indonesia

E-mail: fatmawati@fst.unair.ac.id

Abstract. In this work, we present a model dynamic of malaria disease transmission in Papua province, Indonesia. The parameters of the model are estimated based on the monthly cumulative data of malaria cases in the Papua province in 2018. We use the least-square fitting technique to estimate the parameters. The basic reproduction number \( R_0 \) of the model is estimated as \( R_0 \approx 1.2929 \). Furthermore, the sensitivity analysis is done to determine the significance of the biological parameters in the disease spread. The numerical simulation indicates that the disease can be minimized by reduces the contact between human and mosquito.

1. Introduction

Malaria is an infectious disease caused by the Plasmodium parasite which transmitted to humans through the bite of Anopheles infected with the Plasmodium parasite. Anopheles female mosquito needs human blood for their reproductive processes [1]. Malaria has become one of the main health problems in the world, including in Indonesia. This disease can cause death especially in high-risk groups, namely infants, children under five, and pregnant women. Besides malaria directly causes anemia and can reduce work productivity.

In 2016 there were 216 million cases of malaria in 91 countries with a mortality rate reaching 445,000 people [1]. In Indonesia, there are around 1.5 million people indicated as having malaria and 252,027 confirmed malaria cases until 2014 [2]. In 2017 there were still 10.7 million people living in medium and high malaria-endemic areas [3].

The target of malaria elimination areas in Indonesia from year to year continues to grow. In 2016 the government succeeded in eliminating malaria in 247 districts/cities, in 2017 as many as 266 districts cities, and in 2018, it is targeted to have 285 districts/cities. The high malaria-endemic areas are in Papua, West Papua, and East Nusa Tenggara. The acceleration of achieving malaria-free needs to be done in the Provinces [3]. At present, Papua is one of the provinces with the largest number of malaria sufferers in Indonesia. In 2018, there were 432,331 sufferers suspected of malaria and 137,265 cases tested positive for malaria based on results of blood smear examination in Papua [4].

Mathematical modeling is a powerful tool for designing malaria control programs and analyzing various difficulties in implementing malaria treatment. The researchers have been developed mathematical models to investigate the spread dynamics of malaria. Tasman et al. [5] proposed a malaria model to explore the effect of the proportion of treatment on the spread of the resistance. Okosun et al.
[6] analyzed a malaria model by incorporating treatment and vaccination. The model for the impacts of bed-net on the dynamics of malaria infection was proposed by Agusto et al. [7]. Fatmawati and Tasman [8] discussed a malaria model considering mass treatment and insecticide. The authors in [9] developed a model in [8] by taking into account the malaria resistance.

An accurate model can be utilized to predict and control infectious disease outbreaks effectively. The availability of data for infectious diseases will also increase the estimation of model parameters. In this paper, we adopt the epidemic model as in [7] that considers the malaria infection in mosquito and human populations. This study discusses the parameter estimation of the model to investigate the dynamics of malaria transmission using the cumulative monthly number of malaria cases reported in the Papua province in 2018. We use the least-square fitting technique to estimate the biological parameters of the model. Furthermore, sensitivity analysis is done to identify the parameters that have a great influence on disease transmission. The numerical simulation is then performed using the estimated parameter values.

2. Model formulation
In the present section, we formulate the malaria transmission in the form of the nonlinear ordinary differential equation system. The total human population $N_h(t)$ is split into two-compartment denoted by susceptible $S_h(t)$ and infectious $I_h(t)$, while the total mosquito (vector) population $N_v(t)$ is also split into two-compartment namely susceptible $S_v(t)$ and infectious $I_v(t)$. The susceptible humans get the infection through contact with the infectious mosquitoes. Conversely, the susceptible mosquitoes acquire malaria through contact with infectious humans. The mathematical model of malaria spread can be stated in the differential equation as follows:

$$\begin{align*}
\frac{dS_h}{dt} &= \Lambda_h - \frac{p_1 \beta I_v}{N_h} S_h + \gamma_h I_h - \mu_h S_h \\
\frac{dI_h}{dt} &= \frac{p_1 \beta I_v}{N_h} S_h - (\mu_h + \gamma_h + \delta_h) I_h \\
\frac{dS_v}{dt} &= \Lambda_v - \frac{p_2 \beta I_h}{N_h} S_v - \mu_v S_v \\
\frac{dI_v}{dt} &= \frac{p_2 \beta I_h}{N_h} S_v - \mu_v I_v,
\end{align*}$$

with the initial conditions $S_h(0) > 0, I_h(0) \geq 0, S_v(0) > 0, I_v(0) \geq 0$.

Furthermore, the total population of human and mosquito populations can be expressed as $N_h = S_h + I_h$ and $N_v = S_v + I_v$, respectively. The description of the parameters is given in Table 1.

| Parameter | Interpretation |
|-----------|----------------|
| $\Lambda_h$ | Recruitment rate of human |
| $\Lambda_v$ | Recruitment rate of mosquito |
| $\gamma_h$ | Recovery rate of infectious human |
| $\mu_h$ | Natural death rate of human |
| $\delta_h$ | Disease induced death rate of human |
| $\beta$ | Mosquito–human contact rate |
| $\mu_v$ | Natural death rate of mosquito |
| $p_1$ | Probability of disease spread from mosquito to human |
| $p_2$ | Probability of disease spread from human to mosquito |
3. Parameter estimation

In this section, we estimate the parameters of the model (1) associated with the malaria disease in Papua. Data on malaria-infected individuals discussed here are data from people who have confirmed the laboratory and tested positive for malaria. The data were obtained from the Papua Health Office from January-December 2018 [10] as given in Figure 1. We use cumulative data on malaria cases per month from January to December 2018 that shown in Figure 2.

In this paper, we solve the parameter estimation problem using the least-square fitting technique except for parameters $\mu_h$ and $\Lambda_h$, are obtained from the local demographic. The natural death rate of human, $\mu_h$, is obtained from the inverse of the average life expectancy in Papua. The average life expectancy in Papua is 65.36 years [11], therefore, $\mu_h = \frac{1}{65.36}$ per year. For parameter, $\Lambda_h$, recruitment rate of the human is computed as follows: we consider the year 2018, the population of Papua province is given 2,264,615 [10]. Hence, $\frac{\Lambda_h}{\mu_h} = 2,264,615$, which is the total human population without the disease, so that $\Lambda_h = 34,648,3323$ per year. The remaining of the model parameters is estimated using the least-square fitting technique. Model (1) can be written as follows:

$$\frac{dx}{dt} = f(t, x, \Theta), \quad x(t_0) = x_0$$  \hspace{2cm} (2)

where $x$ and $\Theta$ are the vectors of variables and unknown parameters respectively. Therefore the sum-of-square error is represented by

$$\psi(\Theta) = \sum_{i=1}^{n}(x_i - \bar{x}_i)^2$$ \hspace{2cm} (3)

where $\bar{x}_i$ is the real data and $x_i = x(t_i, \Theta)$ is the solution of the model (2) and $n$ denotes the number of the data. In order to obtain the parameter, the goal is to minimize the objective function

$$\min \psi(\Theta)$$ \hspace{2cm} (4)

Subject to Eq. (2).

The algorithm of the parameter estimation based on [12] can be outlined as follows.

1) Set the initial values of parameter and variables.
2) Calculate the numerical solution of model (2) using the fourth-order Runge-Kutta
3) Check error using (3)
4) Minimize (4) using an optimization algorithm presented in [13] to find the parameter values that fit to the real data.
5) Examine convergence criteria. If not converged, go back to step (2).

6) Update the new parameter and numerical solution till convergence criteria for the parameters are met.

By using the algorithm, we get the parameter values of the model (1) which given in Table 2. The result of fitting data and the model (1) compared in Figure 3.

| Table 2. Fitted or estimated values of the parameters |
|----------------------------------------|
| Parameter | Value (days) | Source |
| Λ_h      | 94.9269     | Estimated |
| Λ_v      | 474.8190    | Fitted   |
| γ_h      | 0.0074      | Fitted   |
| μ_h      | 1           | Estimated |
| δ_h      | 0.00044653  | Fitted   |
| β        | 0.6370      | Fitted   |
| μ_v      | 0.0250      | Fitted   |
| p_1      | 0.7300      | Fitted   |
| p_2      | 0.1327      | Fitted   |

4. Basic reproduction number
The basic reproduction number is the important threshold in the epidemic model because the capability to quantify the disease transmission. It is thought as the expected number of secondary cases per primary case in a “virgin” population [14]. This threshold parameter is computed by using the next-generation matrix.

In this study, we determine the basic reproduction number (R_0) as presented in [15]. We begin by calculating the disease-free equilibrium of the model (1). We set the right-hand sides of the equations in the model (1) to zero and I_h = I_v = 0, then we obtain the disease-free equilibrium E_0 = \( \left( \frac{\Lambda_h}{\mu_h}, 0, \frac{\Lambda_v}{\mu_v}, 0 \right) \).

Thus, the next generation matrices at E_0 are given by:

\[
F = \begin{pmatrix} 0 & p_1 \beta \\ \frac{p_2 \Lambda_v \mu_h}{\mu_v \Lambda_h} & 0 \end{pmatrix}, \quad V = \begin{pmatrix} \gamma_h + \delta_h + \mu_h & 0 \\ 0 & \mu_v \end{pmatrix}.
\] (5)

Therefore, the reproduction number is given by
where $\rho$ is the spectral radius. Based on the parameter values in Table 2, the value of $R_0$ for the malaria cases in Papua is $R_0 \approx 1.2929 > 1$ which mean the disease will persist in the province.

5. Sensitivity analysis
In this present section, we consider the sensitivity analysis to identify the parameter that can impact the basic reproduction number. To determine sensitivity analysis, we followed the technique outlined by [16]. The sensitivity analysis that associate to the parameters is measured by the sensitivity index. The sensitivity index $R_0$ with respect to some parameter, say $\alpha$ is given by $\mathcal{Y}_\alpha^{R_0} = \frac{\partial R_0}{\partial \alpha} \times \frac{\alpha}{R_0}$. Now, we can compute the sensitivity indexes of $R_0$ using the parameter values in Table 2. The results are stated in Table 3.

| Parameter | Sensitivity index |
|-----------|-------------------|
| $\Lambda_h$ | -0.5 |
| $\Lambda_v$ | 0.5 |
| $\gamma_h$ | -0.469040 |
| $\mu_h$ | 0.497343 |
| $\delta_h$ | -0.028303 |
| $\beta$ | 1 |
| $\mu_v$ | -1 |
| $p_1$ | 0.5 |
| $p_2$ | 0.5 |

The sensitivity index can be interpreted as follows. The positive sensitivity index shows that when the values of the parameter are raised, the value of $R_0$ will increase as well. Conversely, the negative sensitivity index shows that when the values of the parameter are raised, the value of $R_0$ will decrease. For example, for $\mathcal{Y}_\beta^{R_0} = 1$, increasing the value of mosquito–human contact rate $\beta$ by 10%, increases the reproduction number $R_0$ by 10%. Thus, increasing the natural death rate of mosquito $\mu_v$ by 10% decreases $R_0$ by 10%. In the same way for the other indexes.

The parameters that have highly sensitive should be considered carefully due to small variations in these parameters will cause large quantitative changes. From Table 3, it can be seen that the parameters which have the greatest influence on basic reproduction are parameters $\beta$ and $\mu_v$. The implication is that an increase the parameter $\beta$, increases the spread of malaria disease in the population, while the increasing of parameter $\mu_v$, decrease the malaria transmission in the community.

6. Numerical simulation
In the present section, we perform the numerical simulation of the malaria model (1) using the parameter displayed in Table 2. The initial values of the model (1) are carried out as follows. According to [10], the total population of Papua province in 2018 is estimated 2,264,615. The initial value used is the malaria case data in January 2018, where $S_h(0) = 2,223,198$ and $I_h(0) = 20,711$ with five people dying of malaria. We assume that the initial population of mosquitoes are given as $S_v(0) = 100,000$ and $I_v(0) = 1000$.

The dynamical behavior of the model (1), when $R_0 = 1.2929$ and $\beta = 0.6370$ is displayed in Figures 4-5. Based on Figure 4, it can be seen that the number of susceptible humans tends to decrease, while the infectious humans tend to increase. From Figure 5, it is observed that the number of susceptible mosquitoes goes down; meanwhile, infectious mosquitoes tend to increase. In Figure 6, we depict the
dynamic of the infected human population ($I_h$) for $\beta = 0.6$, $\beta = 0.5$ and $\beta = 0.4$. From Figure 6, we can see that as $\beta$ is decreased, the number of infected humans also decrease.

![Figure 4](image1.png)  
**Figure 4.** Dynamic of human population for $R_0 > 1$ and $\beta = 0.6370$.

![Figure 5](image2.png)  
**Figure 5.** Dynamic of mosquito population for $R_0 > 1$ and $\beta = 0.6370$.

![Figure 6](image3.png)  
**Figure 6.** Dynamic of infected human population for different values of $\beta$.

### 7. Conclusion
In this work, we proposed the dynamics of malaria transmission in Papua province. The model was fitted to the malaria cases per month in Papua from January to December 2018. The parameters were estimated by fitting the model to the malaria data using the least-square technique. Based on the parameter estimation result, the value of $R_0$ is $R_0 \approx 1.2929$ which indicate that the malaria is still endemic in the province. The sensitivity analysis of the basic reproduction number shows that the parameters $\beta$ and $\mu_v$ have the greatest influence on the model. Finally, the numerical simulation was performed to illustrate the effect of the important model parameter.

### Acknowledgments
Part of this work is supported by DRPM RISTEKDIKTI through “Penelitian Dasar” Universitas Airlangga, 2019.
References

[1] WHO 2018 Malaria [Accessed on August 18th, 2018]

[2] WHO 2017 World Malaria Statistics [Accessed on August 18th, 2018]

[3] Kementerian Kesehatan RI 2018 Wilayah Indonesia Dominan Bebas Malaria [Accessed on August 18th, 2018]

[4] Kementerian Kesehatan RI 2018 Pusat Data dan Informasi Kementerian Kesehatan Republik Indonesia (Jakarta).

[5] Tasman H, Soewono E, Sidarto K A, Syafruddin D, Rogers, W O 2009 A model for transmission of partial resistance to anti-malarial drugs Math. Biosci. Eng. 6 649

[6] Okosun K O, Ouifki R, Marcus N 2011 Optimal control analysis of a malaria disease transmission model that includes treatment and vaccination with waning immunity Biosystem, 106 136

[7] Agusto B F, Del Valle S Y, Blayneh K W, Ngonghala, N C, Goncalves M J, Li N, Zhao R, Gong H 2013 The impact of bed-net use on malaria prevalence J. Theor. Biol. 320 58

[8] Fatmawati, Tasman H 2013 A malaria model with controls on mass treatment and insecticide Applied Mathematical Sciences 7 3379

[9] Fatmawati, Tasman H, 2015 An optimal control strategy to reduce the spread of malaria resistance Math. Biosci. 262 73

[10] The Health Office (Dinas Kesehatan) of the Papua Province, 2018, Indonesia.

[11] Indonesia Central Bureau of Statistics 2018 Life expectancy of Papua 2018, [Accessed on August 18th, 2018]

[12] Samsuzzoha M, Singh M, Lucy D 2013 Parameter estimation of influenza epidemic model Appl. Math. Comput. 220 616

[13] Kristensen M R 2014 Parameter estimation in nonlinear dynamical systems Master’s Thesis, Technical University of Denmark, Kongens.

[14] Diekmann O, Heesterbeek J A P 2000 Mathematical Epidemiology of Infectious Diseases, Model Building, Analysis and Interpretation (New York: John Wiley & Son)

[15] van den Driessche P, Watmough J 2002 Reproduction numbers and sub-threshold endemic equilibria for compartmental models of disease transmission Math. Biosci. 180 29

[16] Chitnis N, Hyman J M, Cushing J M 2008 Determining important parameters in the spread of malaria through the sensitivity analysis of a mathematical model Bull. Math. Biol. 70 1272