Sensitivity and Stability Analysis of a SEIR Epidemic Model with Information

Robiatul Witari Wilda¹, Trisilowati^{2*}, Moch. Aruman Imron³

¹Master Program of Mathematics, Faculty of Mathematics and Natural Sciences, University of Brawijaya, Malang, Indonesia

^{2,3}Department of Mathematics, Faculty of Mathematics and Natural Sciences, University of Brawijaya, Malang, Indonesia

Abstract

In this paper, the construction and stability analysis of a SEIR epidemic model with information are discussed. This model contains information about how to prevent the spread of infectious diseases which is transmitted by infected individuals to susceptible individuals. Furthermore, the dynamical analysis of the model which includes determination of equilibrium points terms of existence, stability analysis of the equilibrium points and sensitivity analysis are observed. Local stability of the equilibrium point is determined by linearizing the system around the equilibrium point and checking for the eigenvalue sign of Jacobian matrix at each equilibrium point. Sensitivity analysis is performed by using a sensitivity index to measure the relative change of basic reproduction number on each parameter. Based on the analysis result, there are two equilibrium points namely disease-free equilibrium point and endemic equilibrium point. The disease-free equilibrium point always exists and is locally asymptotically stable if the basic reproduction number is less than one. Moreover, the endemic equilibrium point exists and is locally asymptotically stable under certain conditions. From sensitivity analysis, it is found that the rate of mortality is the most sensitive parameter and the least sensitive parameter is the rate of exposed individual becomes infected individual. Finally, numerical simulation is conducted to support the analysis result.

Keywords: Epidemic, information, sensitivity analysis, SEIR, stability analysis.

INTRODUCTION

A disease is defined as a condition where the function of one of the parts of the body gets disrupted so that it cannot work normally. In medical scope, a disease is categorized into two types, namely infectious disease and noninfectious disease. The disease caused by microbes such as virus, bacterium, parasite or fungus is categorized as infectious disease. There are many factors which cause infectious disease spreads extensively. For instance, dislocation of people, lifestyle, sexual practice, traveling abroad, and lack of information about the threat of the disease.

One of the strategies in reducing the risk of an individual to be infected is by using information [1]. Information, as a form of non-medical intervention, is able to publish an outbreak of disease so that prevention of disease can be anticipated as soon as possible. Practically, as people know more about prevention knowledge, the better they can protect themselves by adopting the suitable

action derived from the spreading information [2].

The dynamical of the infectious disease transmission can be illustrated by a mathematical model. In 1927, Kermack and Mc Kendrick introduced a simple transmission model of disease that consists of three sub-populations: susceptible (S), infected (I) and recovered (R). Susceptible is the susceptible sub-population, while infected is the infected sub-population and recovered is the healed sub-population. This model is known as a SIR classic model [3].

The mathematical models related to the disease transmissions have been developed especially those which included information effect in disease infection prevention. In 2008, Buonomo et al. modeled and analyzed the stability of the disease transmission model using information. In this research, the disease transmission model was divided into three compartments: susceptible individual compartment (S), infected individual compartment (I), and information media compartment (Z). The relation among those compartments explained the disease transmission model which was stated in the non-linear differential equation system. The disease was transmitted through interaction between a susceptible individual (S) and infected individual (I) [4].

*Correspondence address:

Trisilowati

Email : trisilowati@ub.ac.id

Address : Dept. Mathematics, Faculty of Mathematics and Natural Science, University of Brawijaya, Veteran Malang, Malang 65145

Some mathematical models that include latent period, infected individual sub-population who could not spread the disease, have been studied by many researchers. For example, in 2008, Cui et al. investigated the stability of disease transmission epidemic model by involving exposed individual (E). The infected individual sub-population was the individual sub-population who received medical treatment in a hospital once they were identified as infected. When this sub-population recovered, they did not spread the disease to the susceptible individual. The effect of media coverage toward infectious disease transmissions was explored. The model in the research aimed to analyze the impact of media on disease transmission [5].

Furthermore, in 2017, Kumar et al. explained the effect of information toward the infectious disease transmission using a SIR epidemic model and added information compartment (Z). This information induced the behavior change in the susceptible individual to protect themselves from infection of the disease. The process of infectious disease transmission happened through interaction between a susceptible individual and infected individual. Kumar et al. added the optimum control problem in the model by selecting treatment combination control (pharmacy control) and information effect (non – pharmacy control) [6].

In 2017, Njankou and Nyabadza constructed and analyzed the stability of Ebola disease model using information. The model of disease transmission was divided into seven compartments which were susceptible individual compartment (S), exposed individual (E), infected individual with no symptom (I_a), infected individual with symptom (I_s), recovered individual (R), died individual (D), and information media (Z). In contrast with Kumar et al. in this model susceptible and exposed sub-population are affected by the information [7].

In this paper, we construct a *SEIRZ* disease transmission model. In contrast with Kumar et al. in this model, it is assumed that information affect susceptible and exposed sub-populations as in Njankou and Nyabadza research. Moreover, this model is also different from the research of Njankou and Nyabadza because in this study, we use saturation rate in the information compartment. A dynamical analysis is carried out by determining the equilibrium point and the conditions of its existence and analyzing the stability of the equilibrium point and its basic reproduction number. Then, sensitivity analysis is

performed using a sensitivity index to measure the relative changes of R_0 to each parameter. The results of the stability analysis of the equilibrium point are illustrated through numerical simulations using several parameter values.

MATERIAL AND METHOD

Construction Model

We develop a *SEIRZ* disease transmission model by combining the model used in Kumar et al. [6] and Njankou and Nyabadza [7]. This research adopts the information change rate model from Kumar et al. [6] and information affecting susceptible or exposed sub-population stated in Njankou and Nyabadza [7]. The infectious disease transmission model in this research is stated in five compartments: susceptible individual (S), exposed individual (E), infected individual (I), recovered individual (R) and information compartment (Z).

Stability Analysis of Equilibrium Point

Local stability analysis can be determined by linearizing of the model around its equilibrium points using the Taylor series. The equilibrium point is stable if the real part of the characteristic roots are negative or equal to zero [8].

Basic Reproduction Number

In disease transmission epidemic model, basic reproduction number is used as a parameter to identify the occurrence of disease outbreaks transmission in a population. The basic reproduction number (R_0) states the average number of individuals infected by others who have been infected before.

Disease transmission occurs when $R_0 > 1$. It is because on average, an infected individual causes more than one new infected individual. If $R_0 < 1$, the disease transmission doesn't occur due to the average infected individual causes less than one new infected individual [9].

Sensitivity Analysis

A sensitivity analysis of *SEIR* (Susceptible, Exposed, Infectious and Recovered) epidemic model is conducted to determine the influential of parameters on the basic reproduction number [10]. Normalized sensitivity index which is obtained by differentiating R_0 against parameters α_i with $i = 1, \dots, n$ can be formulated as below:

$$\gamma_{\alpha_i}^{R_0} = \frac{\partial R_0}{\partial \alpha_i} \times \frac{\alpha_i}{R_0}$$

Sensitivity index on all parameters that have a high influence on R_0 can be an indicator of intervention in order to control the spread of disease [11]. Sensitivity analysis is important as it can be used to determine which parameter is the most important in reducing the level of a disease.

Numerical Simulation

Numerical simulation begins with determining the parameter values that meet the conditions of existence and the stability requirements of the equilibrium point.

RESULT AND DISCUSSION

Model Formulation

We formulate a compartmental model which includes the effect of information. The schematic diagram takes the form:

Figure 1. Schematic diagram of SEIRZ model

The SEIRZ epidemic model consists of susceptible (S), infected (I), removed (R), and information (Z) where the recovered individual will not get infected again. In susceptible individual, the population of the individual will increase along the recruitment rate Λ and natural death can cause the decline of susceptible population with the rate μ . The susceptible individual is able to turn into exposed as the effect of interaction with infected population with the rate $\kappa(t)$. The exposed individual is able to decline also when there is natural death with the rate μ and the rate of exposed individual becomes infected individual is represented by σ . The infected individual population will increase when the rate of exposed individual becomes infected individual is represented by σ . This infected individual may also decline when there is either a natural death with the rate μ or death caused by disease with the rate δ . Meanwhile, recovered individual can increase when infected individual gets recovered with the recovery rate γ . In contrast, the degradation of recovered individual happens because of natural death. The information can increase proportionally with the infected population density as $\frac{aI}{1+bI}$, where the growth rate of information is represented by a

and b represents saturation constant. The decreasing of information is affected by degradation of the information which is represented by a_0 . This degradation can happen due to expired information. The effect of information $Z(t)$ is a reduction factor notated by $f(t) = (1 - Z(t))$, $0 < Z(t) < 1$, $\forall t \geq 0$.

The following is the rate of infected disease infection toward time $\kappa(t) = c\beta (1 - Z(t))I(t)$. Based on that explanation, the model of infectious disease transmission with information can be formulated as below:

$$\begin{aligned}\frac{dS(t)}{dt} &= \Lambda - (\mu + \kappa(t))S(t), \\ \frac{dE(t)}{dt} &= \kappa(t)S(t) - (\mu + \sigma)E(t), \\ \frac{dI(t)}{dt} &= \sigma E(t) - (\mu + \delta + \gamma)I(t), \\ \frac{dR(t)}{dt} &= \gamma I(t) - \mu R(t), \\ \frac{dZ(t)}{dt} &= \frac{aI(t)}{(1 + bI(t))} - a_0 Z(t),\end{aligned}\quad (1)$$

with initial condition:

$$S(0) > 0, E(0) > 0, I(0) > 0, R(0) > 0, \\ Z(0) > 0.$$

Existence of the Positive Equilibrium

The system (1) has following equilibrium:

1. The disease-free equilibrium point $E_1 \left(\frac{\Lambda}{\mu}, 0, 0, 0 \right)$ always exists.

The basic reproduction number R_0 , which represents the expected average number of new disease infections produced by a single infected individual when in contact with a completely susceptible population. The basic reproduction number for system (1) is easily computed by van den Driessche [12]. The formula is given by:

$$R_0 = \frac{\Lambda \sigma c \beta}{\mu(\mu + \sigma)(\mu + \delta + \gamma)}$$

2. The unique equilibrium point $E_2 (S^*, E^*, I^*, R^*, Z^*)$ exists if $a < a_0 b$, where $S^* = \frac{\Lambda}{(\mu + c\beta(1 - Z^*)I^*)}$, $E^* = \frac{(\mu + \delta + \gamma)I^*}{\sigma}$, $R^* = \frac{\gamma I^*}{\mu}$, $Z^* = \frac{aI^*}{a_0(1 + bI^*)}$ and I^* is the positive root of the following equation:

$$g(I) = AI^2 + BI + C = 0,$$

with

$$A = \frac{1}{R_0} (a - a_0) \frac{\sigma \Lambda c^2 \beta^2}{\mu},$$

$$B = -\sigma\Lambda a_0 b c \beta \left(\frac{1}{R_0} - 1 \right) - c \beta a \sigma \Lambda$$

$$-a_0((\mu + \sigma)(\mu + \delta + \gamma)),$$

$$C = -\sigma\Lambda a_0 c \beta \left(\frac{1}{R_0} - 1 \right).$$

Note that $C > 0$ and $A < 0$ if $R_0 > 1$ and hence $g(I) = 0$ has a unique positive root if $R_0 > 1$. Thus the system (1) has a unique infected equilibrium E_2 if and only if $R_0 > 1$.

Stability of the Equilibrium

In this section, we investigate the local stability analysis of the system of nonlinear ordinary differential. The variational matrix J of the system (1) at any point (S, E, I, R, Z) is given by,

$$J(E) = \begin{pmatrix} -(\mu + c\beta(1-Z)I) & 0 & -c\beta(1-Z)S & 0 & c\beta IS \\ c\beta(1-Z)I & -(\mu + \sigma) & c\beta(1-Z)S & 0 & -c\beta IS \\ 0 & \sigma & -(\mu + \delta + \gamma) & 0 & 0 \\ 0 & 0 & \gamma & -\mu & 0 \\ 0 & 0 & \frac{a}{(1+bI)^2} & 0 & -a_0 \end{pmatrix}$$

The stability conditions of equilibrium E_1 and E_2 are stated in the following theorems.

Theorem 1. The equilibrium point $E_1(\frac{\Lambda}{\mu}, 0, 0, 0, 0)$ of system (1) is locally asymptotically stable if $R_0 < 1$.

Proof. The stability of the disease-free equilibrium point can be determined by substituting equilibrium point E_1 in the Jacobian matrix of system (1), so that it is obtained

$$J(E_1) = \begin{pmatrix} -\mu & 0 & -\frac{\Lambda c \beta}{\mu} & 0 & 0 \\ 0 & -(\mu + \sigma) & \frac{\Lambda c \beta}{\mu} & 0 & 0 \\ 0 & \sigma & -(\mu + \delta + \gamma) & 0 & 0 \\ 0 & 0 & \gamma & -\mu & 0 \\ 0 & 0 & a & 0 & -a_0 \end{pmatrix}$$

The eigenvalues of $J(E_1)$ are $\lambda_1 = \lambda_2 = -\mu$, $\lambda_3 = -a_0$ and the other two eigenvalues $\lambda_{4,5}$ are the roots of the following equation

$$\lambda^2 + \zeta_1 \lambda + \zeta_2 = 0,$$

where $\zeta_1 = -(2\mu + \delta + \sigma + \gamma)$ and $\zeta_2 = (\mu + \sigma)(\mu + \delta + \gamma) - \frac{\Lambda c \beta \sigma}{\mu}$. E_1 will be locally asymptotically stable if $\lambda_{4,5} < 0$, which is $(\mu + \sigma)(\mu + \delta + \gamma) - \frac{\Lambda c \beta \sigma}{\mu} > 0$ that gives $\frac{\Lambda c \beta \sigma}{\mu(\mu + \sigma)(\mu + \delta + \gamma)} < 1$, where $\frac{\Lambda c \beta \sigma}{\mu(\mu + \sigma)(\mu + \delta + \gamma)}$ is basic reproduction number (R_0).

Theorem 2. The equilibrium point $E_2(S^*, E^*, I^*, R^*, Z^*)$ of system (1) is locally

asymptotically stable if $\frac{\Lambda}{\mu} > S^*$, $\varphi_1 \varphi_2 - \varphi_3 > 0$, and $(\varphi_1 \varphi_2 - \varphi_3) \varphi_3 - \varphi_1(\varphi_1 \varphi_4) > 0$.

Proof. The stability of the endemic equilibrium point can be determined by substituting the equilibrium point E_2 in the Jacobian matrix of system (1) as follows

$$J(E_2) = \begin{pmatrix} -(\mu + c\beta(1-Z^*)I^*) & 0 & -c\beta(1-Z^*)S^* & 0 & c\beta I^* S^* \\ c\beta(1-Z^*)I^* & -(\mu + \sigma) & c\beta(1-Z^*)S^* & 0 & -c\beta I^* S^* \\ 0 & \sigma & -(\mu + \delta + \gamma) & 0 & 0 \\ 0 & 0 & \gamma & -\mu & 0 \\ 0 & 0 & \frac{a}{(1+bI)^2} & 0 & -a_0 \end{pmatrix}$$

The eigenvalue of $J(E_2)$ is $\lambda_1 = -\mu$, and the other eigenvalues are roots of the following characteristic equation

$$\lambda^4 + \varphi_1 \lambda^3 + \varphi_2 \lambda^2 + \varphi_3 \lambda + \varphi_4 \quad (2)$$

where

$$\varphi_1 = (\mu + \sigma) + \frac{\Lambda}{S^*} + (\mu + \delta + \gamma) + a_0$$

$$\varphi_2 = \frac{\Lambda}{S^*}((\mu + \sigma) + (\mu + \delta + \gamma) + a_0)$$

$$+ (\mu + \sigma)(\mu + \delta + \gamma) + a_0(\mu + \sigma)$$

$$+ (\mu + \delta + \gamma)a_0 + \frac{\sigma}{I^*}(\Lambda - \mu S^*)$$

$$\varphi_3 = \left(\frac{\Lambda}{S^*}\right)((\mu + \sigma) + (\mu + \delta + \gamma) + a_0)(\mu + \sigma)$$

$$+ (\mu + \delta + \gamma)a_0 + (\mu + \sigma)(\mu + \delta + \gamma)a_0$$

$$+ \frac{a_0 \sigma \Lambda}{I^*} + \frac{a \sigma c \beta I^* S^*}{(1+bI^*)^2} + \frac{\mu \sigma}{I^*}(\Lambda - a_0 S^* - \mu S^*)$$

$$\varphi_4 = \left(\frac{\Lambda}{S^*}\right)(\mu + \sigma)(\mu + \delta + \gamma)a_0 + \frac{a \sigma \mu \xi_1}{(1+bI^*)^2}$$

$$+ \frac{a_0 \sigma \mu}{I^*}(\Lambda - \mu S^*)$$

Clearly that $\varphi_1 > 0$, and $\varphi_4 > 0$ if $\frac{\Lambda}{\mu} > S^*$. By using Routh- Hurwitz criterion, the roots of equation (2) have negative real part if only if $\frac{\Lambda}{\mu} > S^*$, $\varphi_1 \varphi_2 - \varphi_3 > 0$, and $(\varphi_1 \varphi_2 - \varphi_3) \varphi_3 - \varphi_1(\varphi_1 \varphi_4) > 0$ [13].

Sensitivity Analysis

The sensitivity index R_0 depends on the differentiation of the parameters $\Lambda, \sigma, c, \beta, \mu, \delta$ and γ . Suppose that the parameter values are given in Table 1.

Table 1. Parameters Value

No	Point	Description
1	Λ	0.5
2	σ	0.005
3	c	1
4	β	0.0005
5	μ	0.004
6	δ	0.1
7	γ	0.005

Based on the parameter values in Table 1, this value produces $R_0 = 5.787$ and a sensitivity index of R_0 is obtained as shown in the Table 2.

Table 2. Index Sensitivity Parameters

No	Point	Description
1	μ	-1.474
2	Λ	1
3	β	1
4	c	1
5	γ	-0.499
6	δ	-0.1
7	σ	0.074

Table 2 shows the sensitivity level of the most sensitive parameters to less sensitive parameters namely mortality rate (μ), recruitment rate (Λ), transmission rate (β), number of contacts with infected individuals (c), recovery rate (γ), rate of death due to disease (δ), and the rate of exposed individual becomes infected individual (σ). The effect of changing the parameter value on the R_0 is presented in Table 3.

Table 3. Basic Reproduction Number

Parameter	R_0 Value	
	$P + 10\%$	$P - 10\%$
μ	6.747	5.021
Λ	6.365	5.208
β	6.365	5.208
c	6.365	5.739
γ	6.091	5.511
δ	5.729	5.845
σ	5.826	0.074

Table 3 shows that if one of the parameter values is increased or decreased by 10%, then the value of R_0 also increase or decrease. Therefore the endemicity of infectious diseases will increase or decrease.

Numerical Simulation

Numerical Simulation for $R_0 < 1$.

In this simulation, we use the parameter values $\Lambda = 0.2, \beta = 0.0001, c = 10, \delta = 0.01, \gamma = 0.5, \mu = 0.005, \sigma = 0.08, a_0 = 0.06, a = 0.01, b = 1$. Based on these parameter values, we have $R_0 = 0.0003655054255 < 1$ and $E_1 \left(\frac{\Lambda}{\mu}, 0, 0, 0, 0 \right) = (40, 0, 0, 0, 0)$. According to analysis result, E_1 is a locally asymptotically stable since $R_0 < 1$. In Figure 2, it can be seen that with initial value $(S(0), E(0), I(0), R(0), Z(0)) = (95, 55, 45, 40, 0.4)$ the numerical solution is convergent to the equilibrium point E_1 . It indicates that there is no exposed and infected individuals for a long time.

Figure 3 shows a portrait phase of the solution in the SEI space with three different initial values $(S(0), E(0), I(0), R(0), Z(0)) = (50, 23, 10, 1, 2), (S(0), E(0), I(0), R(0), Z(0)) = (15, 20, 1, 0, 0)$, and $(S(0), E(0), I(0), R(0), Z(0)) = (30, 12, 10, 10, 1)$. The simulation results show that by using the three initial values, the orbits in the SEI space is stable to the disease-free equilibrium

point (E_1). This is in accordance with the result of the analysis.

Figure 2. Solution of system (1) when $R_0 < 1$.

Figure 3. Portrait phase of the SEI space in disease-free equilibrium point

Numerical Simulation $R_0 > 1$.

In this simulation, we use the parameter values $\Lambda = 0.5, \beta = 0.0005, c = 1, \delta = 0.001, \gamma = 0.005, \mu = 0.004, \sigma = 0.05, a_0 = 0.0006, a = 0.000001, b = 1$, so that $R_0 = 5.787 > 1$.

Based on these parameter values, a disease-free equilibrium point and an endemic equilibrium point are obtained $E_1 \left(\frac{\Lambda}{\mu}, 0, 0, 0, 0 \right) = (125, 0, 0, 0, 0)$ and $E_2(S^*, E^*, I^*, R^*, Z^*) = (21.635, 7.656, 38.283, 47.854, 0.0016)$.

Furthermore, we have $\varphi_1 \varphi_2 - \varphi_3 = 0.0002128670467 > 0$ and $(\varphi_1 \varphi_2 - \varphi_3) \varphi_3 - \varphi_1(\varphi_1 \varphi_4) = 3.3756 \times 10^{-9} > 0$, $\frac{\Lambda}{\mu} - S^* = 103.635 > 0$, that satisfy the stability condition. In Figure 4, it can be seen that numerical solution with an initial value $(100, 50, 60, 30, 0.3)$ is stable to the equilibrium point E_2 .

Figure 4. Solution of system (1) when $R_0 > 1$.

Figure 5 shows a portrait phase of the solution in the SEI space with three different initial values $(S(0), E(0), I(0), R(0), Z(0)) = (40, 2, 5, 50, 0.5)$, $(S(0), E(0), I(0), R(0), Z(0)) = (1, 40, 3, 10, 0)$, and $(S(0), E(0), I(0), R(0), Z(0)) = (3, 35, 75, 1000, 0.5)$. The simulation results show that by using several different initial values, the orbits in the SEI space is stable to E_2 . This shows that when $R_0 > 1$ the equilibrium point E_2 is locally asymptotically stable. However, a disease-free equilibrium points (E_1) it is unstable.

Figure 5. Portrait phase of the SEI space in endemic equilibrium point.

Numerical Simulation of Sensitivity Analysis

In conducting a sensitivity analysis, it is done by increasing or decreasing the one parameter value while the other parameter value is constant. Numerical simulation of parameters that influence the spread of disease to the population is presented in Figure 6 and 7.

In Figure 6, it is shown that by increasing the parameter value of μ by 10 % while the other parameters are fixed, the number of infected individuals will decrease. Conversely, by reducing the value of μ by 10 % the number of infected individuals will increase. Figure 7 shows that by increasing the parameter value of σ by 10 % while the other parameters are fixed, the number of infected individuals will also increase. Conversely, by decreasing the value of σ by 10 % the number of infected individuals will also decrease. The changing of these parameters will

cause the changing of the value of the basic reproduction number. It means that the endemicity of infectious diseases is greatly affected by the rate of mortality and the rate of exposed individual becomes infected individual.

Figure 6. Graphs showing the effect of varying μ on infected population.

Figure 7. Graphs showing the effect of varying σ on infected population.

CONCLUSION

In this paper, we have studied a modified SEIR epidemic model with information. The model has two equilibrium, i.e. the disease-free equilibrium point and the endemic equilibrium point. The existence of the disease-free equilibrium point always exists. The endemic equilibrium point exists under certain condition. From the sensitivity analysis, it is obtained that the most sensitive parameters are the rate of mortality and the least sensitive parameter is the rate of an exposed individual becomes an infected individual. Numerical simulation agrees with the analysis result.

REFERENCES

- [1] Buonomo, B., A. d'Onofrio, D. Lacitignola. 2008. Globally stable endemicity for infectious diseases with information-related

- changes in contact patterns. *Appl. Math. Lett.* 25(7). 1056-1060.
- [2] Cui, J., Y. Sun, H. Zhu. 2008. An SIS infection model incorporating media coverage. *Rocky Mountain J. Math.* 38(5).1323-1334.
- [3] Kermack, W.O., A.G. Mc Kendrick. 1972. A contribution to the mathematical theory of epidemics. Proceedings of the Royal Society of London. Series A, Containing Papers of a Mathematical and Physical Character. 115(772).
- [4] Buonomo, B., A. d'Onofrio, D. Lacitignola. 2008. Global stability of an SIR epidemic model with information dependent vaccination, *Math. Biosci.* 216(1). 9-16.
- [5] Cui, J., Y. Sun, H. Zhu. 2008. The impact of media on the control of infectious diseases. *J. Dyn. Differ. Equ.* 20(1). 31-53.
- [6] Kumar, A., P.K. Srivastava, Y. Takeuchi. 2017. Modeling the role of information and limited optimal treatment on disease prevalence. *J. Theor. Biol.* 414. 103-119.
- [7] Njankou, S.D.D., F. Nyabadza. 2017. Modelling the potential role of media campaigns in ebola transmission dynamics, *Int. J. Differ. Equ.* 1-13.
- [8] Boyce, W.E., R.C. DiPrima. 2010. Elementary differential equations and boundary value problem, 10th Ed. John Wiley and Sons, Inc. USA.
- [9] Brauer, F. 2004. Backward bifurcation in simple vaccination model. *J. Math. Anal. Appl.* 418-431.
- [10] Hurint, R.U., Z.N. Meksianis, M. Lobo. 2017. Analisis sensitivitas model epidemi SEIR (in Indonesian). *J. Nat. Sci.* 6(1). 22-28.
- [11] Chitnis, N., J.M. Hyman, J.M. Cushing. 2008. Determining important parameters in the spread of malaria through the sensitivity analysis of a mathematical model. *Bull. Math. Biol.* 70(5). 1272-1296.
- [12] Van den Driessche, P., J. Watmough. 2002. Reproduction numbers and subthreshold endemic equilibrium for compartmental models of disease transmission, *Math. Biosci.* 180(1-2). 29-48.
- [13] Murray, J.D. 2002. Mathematical biology I. an introduction, 3rd Ed. Springer-Verlag, Berlin Heidelberg.