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Mathematical Model of Preventing The Spread of Dengue Disease in Yogyakarta Using Wolbachia Mosquitoes

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ABSTRACT

The purpose of this study is to explain the mathematical model of preventing the spread of dengue fever in the Special Region of Yogyakarta by involving Wolbachia mosquitoes, explain the equilibrium point and stability analysis and conduct numerical simulations. The model used in this study is SIS-SI model, using population data of Yogyakarta Special Region Province in 2023. The steps involved include forming the SIS-SI mathematical model, determining the disease-free and endemic equilibrium points, calculating the basic reproduction number, analyzing the stability of the equilibrium point, and conducting numerical simulation. The results showed that the disease-free equilibrium point is asymptotically stable when $R_0 < 1$. The endemic equilibrium point is asymptotically stable when $R_0 > 1$. Research has shown that R_0 is related to the inhibitory effect of Wolbachia bacteria (r). When $r = 0.34$, $R_0 = 1$, the threshold for disease spread. If $r < 0.34$, the disease will not spread in the population, conversly if $r \geq 0.34$, the disease will spread. Based on the numerical simulations conducted, it was observed that the smaller the inhibitory effect of Wolbachia bacteria on dengue replication in mosquitoes, the more effective Wolbachia bacteria are in suppressing the spread of dengue virus. As a result, this leads to the disappearance of dengue disease from the population.

Tujuan dari penelitian ini adalah untuk menjelaskan model matematika pencegahan penyebaran penyakit Demam Berdarah Dengue (DBD) di Daerah Istimewa Yogyakarta dengan melibatkan nyamuk Wolbachia, menjelaskan titik ekuilibrium dan analisis kestabilan serta melakukan simulasi numerik. Model yang digunakan yaitu SIS-SI dengan data penduduk Provinsi Daerah Istimewa Yogyakarta tahun 2023. Tahapan yang dilakukan yaitu membentuk model matematika SIS-SI, menentukan titik ekuilibrium bebas penyakit dan endemik, menentukan bilangan reproduksi dasar, menganalisis kestabilan titik ekuilibrium, serta simulasi numerik. Hasil penelitian diperoleh titik ekuilibrium bebas penyakit stabil asimtotik saat $R_0 < 1$. Sedangkan titik ekuilibrium endemik stabil asimtotik saat $R_0 < 1$. Dalam penelitian ini ditemukan bahwa R_0 memiliki hubungan dengan efek penghambat Wolbachia (r). Ketika $r = 0.34$, $R_0 = 1$, yang menjadi ambang batas penyebaran penyakit. Jika $r < 0.34$, penyakit tidak akan menyebar dalam populasi, sedangkan jika $r \geq 0.34$, penyakit akan menyebar. Berdasarkan simulasi numerik yang dilakukan, ditemukan bahwa semakin kecil efek penghambat Wolbachia pada replikasi demam berdarah pada nyamuk Wolbachia, semakin efektif Wolbachia dari populasi.

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INTRODUCTION

Dengue fever has emerged as a health issue in many countries. In 2019, the World Health Organization (WHO) identified dengue fever as one of the top ten global health threats, especially in tropical and subtropical regions (WHO, 2024). In Indonesia, the first recorded cases occurred in Surabaya and DKI Jakarta in 1968 (Suwandono, 2019). Dengue Homorrhagic Fever (DHF) has now spread to all provinces and become endemic in cities and towns, including Yogyakarta. The Provincial Health Office of Yogyakarta Special Region (DIY) recorded the first DHF case reported in Yogyakarta since 1972. The highest number of DHF cases was reported in 2016, with 6.318 cases and 32 deaths (Dinkes Provinsi DIY, 2016).

Many dengue control programs have been implemented, but most have been unsuccessful. These programs involve methods such as the use of insecticides, fogging, eradication of mosquito nests, and vaccination (Saraswati, et al., 2023). Strategies for dengue control have also been carried out, but have not been sufficient to reduce the number of sufferers. Therefore, a new strategy is needed to stop the cycle of DHF spread. An innovative strategy to control the spread of dengue is biological control using Wolbachia bacteria (Kemenkes, 2023). Wolbachia is a natural bacterium that can infect mosquitoes. Wolbachia can limit the mosquito's ability to spread dengue virus by suppressing virus replication in the mosquito's body. Wolbachia-carrying Aedes aegypti mosquitoes are considered an effective biological control strategy (Lusiyana, 2015).

In Indonesia, Aedes aegypti mosquitoes carrying Wolbachia were first released in Sleman District, Yogyakarta Special Region in early 2014 using the adult mosquito release method. This initiative was initiated by the Eliminate Dengue Project (EDP), now known as the World Mosquito Program (WMP) Yogyakarta, in collaboration with a university in Australia (Artanto, et al., 2019). WMP developed Wolbachia technology to control dengue hemorrhagic fever vectors. In December 2014, the research was expanded to Bantul Regency by placing buckets of Wolbachia-infected Aedes aegypti eggs (Nuraeni, Ahmad, & Utarini, 2020). Based on the results obtained from the previous phase, WMP Yogyakarta released Wolbachia-infected mosquitoes to a wider area to prove its effectiveness in reducing dengue fever cases. To achieve this goal, WMP Yogyakarta conducted the release in Yogyakarta City in August 2016 (Universitas Gajah Mada, 2017).

Formulating real problems into mathematical language is a method to explain the solution of problems that arise in the real world (Widowati, 2007). Therefore, to understand the prevention of dengue disease spread using Wolbachia mosquitoes, a mathematical model was developed to help provide solutions related to this issue. One mathematical model for analyzing the prevention of dengue disease spread is the SIS (Susceptible, Infectious, Susceptible) model.

Several researchers have conducted research using mathematical models to analyze the spread of dengue disease involving Wolbachia. Al Faruqy & Prawoto (2024), discussed the SIW SIR mathematical model for the spread of dengue disease by including the effect of the spread of Wolbachia bacteria and calculating the basic reproduction number. Another study was conducted by Sa'adah & Sari (2023) which used vaccination and Wolbachia parameters in an effort to control the spread of dengue fever. However, this study introduces a novelty by developing the SIS-SI model, which was had not been explored in earlier studies dan was modified from the journal by Li & Liu (2021). This model describes the conditions in which individuals who recover from infection can be susceptible to infection again, as well as the spread of infected mosquitoes carrying both dengue viruses and Wolbachia bacteria.

METHOD

The data used was partially obtained from the Health Office of the Special Region of Yogyakarta (DIY), DIY Central Statistics Agency, World Mosquito Program Indonesia, and several other websites.

The data in this study include human and mosquito population data in Yogyakarta City, Sleman Regency, and Bantul Regency in 2023. The research was carried out through the following steps:

a. Collecting data
b. Definition of variables and parameters
c. Mathematical model construction d. Determination of equilibrium point
d. Determination of basic reproduction number
e. Stability analysis of equilibrium point
f. Numerical simulation
g. Conclusion drawing

RESULTS AND DISCUSSION

In this section, the results of the research are presented which include model assumptions, model formation process, equilibrium point stability analysis, basic reproduction number calculation, and simulation to evaluate the dynamics of the system according to the conditions in Yogyakarta City, Sleman Regency, and Bantul Regency.

Mathematical Model

The assumptions of the mathematical model of dengue disease prevention through Wolbachia mosquitoes are as follows:

a. There are two populations, namely humans and mosquitoes. The mosquitoes in this study are Aedes Aegypti and Wolbachia mosquitoes.
b. There is an interaction between susceptible and infected mosquitoes with Wolbachia that makes some of the susceptible and infected population become Wolbachia mosquitoes.
c. All populations are assumed to be closed, which means that the total population is constant as there are no individuals entering or leaving the population.
d. Susceptible class individuals can become Infectious class and transmit the disease to other human individuals through mosquito bites.
e. Natural birth and natural death rates are assumed to be equal, so the total population is always constant.
f. Mosquitoes infected with dengue or infected with Wolbachia cannot recover or revert to susceptible mosquitoes. Mosquitoes with Wolbachia can still transmit dengue virus to humans.
g. The human population infected with dengue has temporary immunity.
h. There is a factor that reduces the birth rate of Aedes Aegypti mosquitoes based on the proportion of Wolbachia mosquitoes in the total mosquito population. If the number of Wolbachia mosquitoes increases, the birth rate of Aedes Aegypti mosquitoes decreases.

The variables and parameters used are presented in Table 1, as follows:

Table 1. Variables and Parameters Used in the SIS-SI Model

Variable/ Parameter	Description	Terms
$N_h(t)$	Total human population at time t	$N_h(t) \geq 0$
$N_m(t)$	Total mosquito population at time t	$N_m(t) \geq 0$
$N_v(t)$	Total population of dengue virus-carrying mosquitoes at time t	$N_v(t) \geq 0$
$N_w(t)$	Total population of mosquitoes carrying Wolbachia bacteria at time t	$N_w(t) \geq 0$

$S_h(t)$	Number of healthy but susceptible human subpopulations infected with dengue virus at time t	$S_h(t) \geq 0$
$I_h(t)$	Number of human subpopulations that have been infected with dengue virus at time t	$I_h(t) \geq 0$
$S_v(t)$	Number of susceptible mosquito subpopulations infected with dengue virus at time t	$S_v(t) \geq 0$
$I_v(t)$	Number of subpopulations of mosquitoes infected with dengue virus at time t	$I_v(t) \geq 0$
$S_w(t)$	Number of susceptible mosquito subpopulations infected with Wolbachia bacteria at time t	$S_w(t) \geq 0$
$I_w(t)$	Number of subpopulations of mosquitoes infected with Wolbachia bacteria at time t	$I_w(t) \geq 0$
α_h	Birth rate in a human population	$0 \leq \alpha_h \leq 1$
μ_h	Death rate in a human population	$0 \leq \mu_h \leq 1$
β_h	Probability of a human contracting dengue fever from a mosquito infected with dengue virus	$0 \leq \beta_h \leq 1$
$\bar{\beta}_h = r\beta_h$ $(r < 1)$	Probability of humans contracting dengue fever from mosquitoes infected with Wolbachia bacteria. r inhibitory effect of Wolbachia bacteria on dengue replication (Li & Liu, 2021)	$0 \leq \underline{\beta}_h \leq 1$
ω_h	Rate of loss of immunity to dengue virus infection	$0 \leq \omega_h \leq 1$
α_m	Birth rate in a population of mosquitoes infected with dengue virus	$0 \leq \alpha_m \leq 1$
$\underline{\alpha}_m$	Birth rate in a population of mosquitoes infected with Wolbachia bacteria	$0 \leq \underline{\alpha}_m \leq 1$
μ_m	Mortality rate in a mosquito population	$0 \leq \mu_m \leq 1$
β_m	Probability of mosquitoes contracting dengue virus from infected humans	$0 \leq \beta_m \leq 1$

The spread of dengue disease involving Wolbachia mosquitoes in a population can be represented through the transfer diagram in Figure 1.

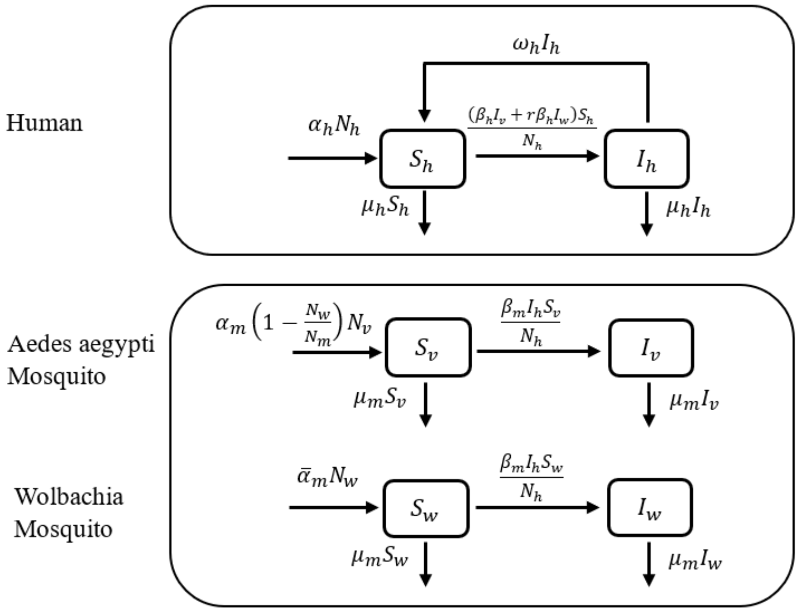

Figure 1. Transfer Diagram of SIS-SI Model

Figure 1 is a modified version of the model developed in the study by Zhang, Liu, Li, & Wang (2023). Based on Figure 1, the SIS-SI model can be stated as follows:

$$\begin{aligned}
\frac{dS_h}{dt} &= \alpha_h N_h + \omega_h I_h - \left(\frac{(\beta_h I_v + r\beta_h I_w)}{N_h} + \mu_h\right) S_h \\
\frac{dI_h}{dt} &= \frac{(\beta_h I_v + r\beta_h I_w)}{N_h} S_h - (\omega_h + \mu_h) I_h \\
\frac{dS_v}{dt} &= \alpha_m \left(1 - \frac{N_w}{N_m}\right) N_v - \left(\frac{\beta_m I_h}{N_h} + \mu_m\right) S_v \\
\frac{dI_v}{dt} &= \frac{\beta_m I_h}{N_h} S_v - \mu_m I_v \\
\frac{dS_w}{dt} &= \bar{\alpha}_m N_w - \left(\frac{\beta_m I_h}{N_h} + \mu_m\right) S_w \\
\frac{dI_w}{dt} &= \frac{\beta_m I_h}{N_h} S_w - \mu_m I_w
\end{aligned} \tag{1}$$

with $N_h = S_h + I_h$ and $N_m = N_v + N_w$, where $N_v = S_v + I_v$ and $N_w = S_w + I_w$.

The system in Equation (1) can be rescaled based on the total population to simplify and facilitate the analysis. The proportions of individuals and mosquitoes in each class are expressed as follows:

$$s_h = \frac{S_h(t)}{N_h}, i_h = \frac{I_h(t)}{N_h}, s_v = \frac{S_v(t)}{N_v}, i_v = \frac{I_v(t)}{N_v}, s_w = \frac{S_w(t)}{N_w}, i_w = \frac{I_w(t)}{N_w}$$

Thus, after simplifying notation, the system of equations becomes:

$$\begin{aligned}
\frac{ds_h}{dt} &= \alpha_h + \omega_h i_h - ((\beta_h i_v n_v + r\beta_h i_w n_w) + \mu_h) s_h \\
\frac{di_h}{dt} &= (\beta_h i_v n_v + r\beta_h i_w n_w) s_h - (\omega_h + \mu_h) i_h \\
\frac{ds_v}{dt} &= \alpha_m \left(1 - \frac{N_w}{N_m}\right) - (\beta_m i_h + \mu_m) s_v \\
\frac{di_v}{dt} &= \beta_m i_h s_v - \mu_m i_v \\
\frac{ds_w}{dt} &= \bar{\alpha}_m - (\beta_m i_h + \mu_m) s_w \\
\frac{di_w}{dt} &= \beta_m i_h s_w - \mu_m i_w
\end{aligned} \tag{2}$$

with $n_v = \frac{N_v}{N_h}$, $n_w = \frac{N_w}{N_h}$, and $s_h + i_h = 1$ and $N_v + N_w = 2$, where $s_v + i_v = 1$ and $s_w + i_w = 1$

The disease-free equilibrium point is obtained when $i_h = i_v = i_w = 0$ from Equation (2) as follows

$$E_0 = (s_h^*, i_h^*, s_v^*, i_v^*, s_w^*, i_w^*) = \left(\frac{\alpha_h}{\mu_h}, 0, \frac{\alpha_m(N_m - N_w)}{N_m \mu_m}, 0, \frac{\bar{\alpha}_m}{\mu_m}, 0\right) \tag{3}$$

Furthermore, to obtain the endemic equilibrium point, it is assumed as $i_h \neq 0$, $i_v \neq 0$, and $i_w \neq 0$. Based on Equation (2), the endemic equilibrium point is obtained

$$E_1 = (s_h^*, i_h^*, s_v^*, i_v^*, s_w^*, i_w^*)$$

$$E_1 = \left(\begin{array}{c} \frac{(\beta_m \alpha_h + \mu_h \mu_m)(\omega_h + \mu_h)\mu_m N_m}{\beta_m \mu_h A}, \frac{B}{\beta_m \mu_h A}, \frac{\alpha_m (N_m - N_w)\mu_h A}{N_m C} \\ \frac{\alpha_m (N_m - N_w) B}{\mu_m N_m C}, \frac{\bar{\alpha}_m \mu_h A}{C}, \frac{\bar{\alpha}_m B}{\mu_m C} \end{array}\right) \tag{4}$$

where

$$A = \beta_h n_v \alpha_m N_m + r\beta_h n_w \bar{\alpha}_m N_m - \beta_h n_v \alpha_m N_w + \mu_h \mu_m N_m + \omega_h \mu_m N_m$$

$$B = \beta_h\beta_m n_v\alpha_m\alpha_h N_m + r\beta_h\beta_m n_w\bar{\alpha}_m\alpha_h N_m - \beta_h\beta_m n_v\alpha_m\alpha_h N_w - \mu_m^2\mu_h^2 N_m - \omega_h\mu_m^2\mu_h N_m$$
$$\begin{aligned} C = {} & \beta_h\beta_m n_v\alpha_m\alpha_h N_m + r\beta_h\beta_m n_w\bar{\alpha}_m\alpha_h N_m - \beta_h\beta_m n_v\alpha_m\alpha_h N_w + \beta_h n_v\alpha_m\mu_m\mu_h N_m \\ & + r\beta_h n_w\bar{\alpha}_m\mu_m\mu_h N_m - \beta_h n_v\alpha_m\mu_m\mu_h N_w \end{aligned}$$

The basic reproduction number (R_0) is calculated using the Next Generation Matrix (NGM) method. By linearizing the infected classes i_h, i_v, and i_w as follows

$$J = \begin{bmatrix} -(\omega_h + \mu_h) & \beta_h n_v s_h & r\beta_h n_w s_h \\ \beta_m s_v & -\mu_m & 0 \\ \beta_m s_w & 0 & -\mu_m \end{bmatrix}$$

Substitute Equation (4) so as to obtain the following

$$J(E_0) = \begin{bmatrix} -(\omega_h + \mu_h) & \dfrac{\beta_h n_v \alpha_h}{\mu_h} & \dfrac{r\beta_h n_w \alpha_h}{\mu_h} \\ \dfrac{\beta_m \alpha_m (N_m - N_w)}{\mu_m N_m} & -\mu_m & 0 \\ \dfrac{\beta_m \bar{\alpha}_m}{\mu_m} & 0 & -\mu_m \end{bmatrix}$$

Jacobian matrix decomposition

$$F = \begin{bmatrix} 0 & \dfrac{\beta_h n_v \alpha_h}{\mu_h} & \dfrac{r\beta_h n_w \alpha_h}{\mu_h} \\ \dfrac{\beta_m \alpha_m (N_m - N_w)}{\mu_m N_m} & 0 & 0 \\ \dfrac{\beta_m \bar{\alpha}_m}{\mu_m} & 0 & 0 \end{bmatrix}$$

$$V = \begin{bmatrix} \omega_h + \mu_h & 0 & 0 \\ 0 & \mu_m & 0 \\ 0 & 0 & \mu_m \end{bmatrix}$$

The value of the basic reproductive number (R_0) is calculated using the formula $R_0 = \rho(FV^{-1})$, so that the value of R_0 is obtained, namely

$$R_0 = \frac{\beta_h\beta_m\alpha_h(n_v\alpha_m N_m - n_v\alpha_m N_w + n_w r\bar{\alpha}_m N_m)}{\mu_h\mu_m^2(\omega_h + \mu_h)N_m} \quad (5)$$

Analysis of Equilibrium Point Stability

Analysis of the stability of the equilibrium point is determined based on the eigenvalues obtained by first forming the Jacobian matrix of Equation (2) which is obtained

$$J(E) = \begin{bmatrix} -(\beta_h i_v n_v + r\beta_h i_w n_w + \mu_h) & \omega_h & 0 & -\beta_h n_v s_h & 0 & -r\beta_h n_w s_h \\ \beta_h i_v n_v + r\beta_h i_w n_w & -(\omega_h + \mu_h) & 0 & \beta_h n_v s_h & 0 & r\beta_h n_w s_h \\ 0 & -\beta_m s_v & -(\beta_m i_h + \mu_m) & 0 & 0 & 0 \\ 0 & \beta_m s_v & \beta_m i_h & -\mu_m & 0 & 0 \\ 0 & -\beta_m s_w & 0 & 0 & -(\beta_m i_h + \mu_m) & 0 \\ 0 & \beta_m s_w & 0 & 0 & \beta_m i_h & -\mu_m \end{bmatrix} \quad (6)$$

Stability Analysis of Disease-Free Equilibrium Point

Properties. If $R_0 < 1$, then disease free equilibrium point is locally asymptotically stable.

Proof. To find the stability of the disease-free equilibrium point, substitute E_0 into Equation (6) to obtain the Jacobian matrix $J(E_0)$ as follows

$$J(E_0) = \begin{bmatrix} -\mu_h & \omega_h & 0 & -\frac{\beta_h n_v \alpha_h}{\mu_h} & 0 & -\frac{r\beta_h n_w \alpha_h}{\mu_h} \\ 0 & -(\omega_h + \mu_h) & 0 & \frac{\beta_h n_v \alpha_h}{\mu_h} & 0 & \frac{r\beta_h n_w \alpha_h}{\mu_h} \\ 0 & -\frac{\beta_m \alpha_m (N_m - N_w)}{N_m \mu_m} & -\mu_m & 0 & 0 & 0 \\ 0 & \frac{\beta_m \alpha_m (N_m - N_w)}{N_m \mu_m} & 0 & -\mu_m & 0 & 0 \\ 0 & -\frac{\beta_m \bar{\alpha}_m}{\mu_m} & 0 & 0 & -\mu_m & 0 \\ 0 & \frac{\beta_m \bar{\alpha}_m}{\mu_m} & 0 & 0 & 0 & -\mu_m \end{bmatrix}$$

Then the eigenvalues of $J(E_0)$, so that the characteristic equation is obtained

$$(\lambda + \mu_h)(\lambda + \mu_m)(\lambda + \mu_m)(\lambda + \mu_m)(q_0\lambda^2 + q_1\lambda + q_2) = 0 \tag{7}$$

where

$q_1 = \omega_h + \mu_h + \mu_m$

$q_2 = \mu_m(\omega_h + \mu_h) - \dfrac{n_v \beta_m \beta_h \alpha_h \alpha_m (N_m - N_w)}{\mu_h \mu_m N_m} - \dfrac{\beta_m r \beta_h n_w \alpha_h \bar{\alpha}_m}{\mu_h \mu_m}$

Based on Equation (7), $\lambda_1 = -\mu_h$ and $\lambda_{2,3,4} = -\mu_m$ are obtained. Since μ_h and μ_m are positive, the real part of the four eigenvalues is negative. As for the other eigenvalues, the Routh-Hurwitz Criterion will be used to determine the type of stability of the characteristic equation

$$q_0\lambda^2 + q_1\lambda + q_2 = 0 \tag{8}$$

Equation (8) is satisfied if the following conditions are obtained

a. It is clear that q_0 is positive ($q_0 > 0$)
b. $q_1 = \omega_h + \mu_h + \mu_m > 0$
c. $\Delta_2 = q_1 q_2 - q_0 q_3$

$$= (\omega_h + \mu_h + \mu_m)\left(\mu_m(\omega_h + \mu_h) - \frac{n_v \beta_m \beta_h \alpha_h \alpha_m (N_m - N_w)}{\mu_h \mu_m N_m} - \frac{\beta_m r \beta_h n_w \alpha_h \bar{\alpha}_m}{\mu_h \mu_m}\right)$$

$= \mu_m(\omega_h + \mu_h)(1 - R_0) > 0$, if $R_0 < 1$

Based on the Routh-Hurwitz Criterion, it can be seen that λ_5 and λ_6 in Equation (8) have negative values. This shows that all eigenvalues of Equation (7) have negative values, so the disease-free equilibrium point E_0 is locally asymptotically stable under the condition $R_0 < 1$.

Stability Analysis of Endemic Equilibrium Point

Properties. If $R_0 > 1$, then endemic equilibrium point is locally asymptotically stable.

Proof. To find the stability of the endemic equilibrium point, substitute E_1 into Equation (6) to obtain the Jacobian matrix $J(E_1)$ as follows

$$J(E_1) = \begin{bmatrix} -(\beta_h i_v n_v + r\beta_h i_w n_w + \mu_h) & \omega_h & 0 & -\beta_h n_v s_h & 0 & -r\beta_{h_h} n_w s_h \\ \beta_h i_v n_v + r\beta_h i_w n_w & -(\omega_h + \mu_h) & 0 & \beta_h n_v s_h & 0 & r\beta_h n_w s_h \\ 0 & -\beta_m s_v & -(\beta_m i_h + \mu_m) & 0 & 0 & 0 \\ 0 & \beta_m s_v & \beta_m i_h & -\mu_m & 0 & 0 \\ 0 & -\beta_m s_w & 0 & 0 & -(\beta_m i_h + \mu_m) & 0 \\ 0 & \beta_m s_w & 0 & 0 & \beta_m i_h & -\mu_m \end{bmatrix} \tag{9}$$

Suppose

$x = \beta_h i_v n_v + r\beta_h i_w n_w = \dfrac{\beta_h n_v \alpha_m (N_m - N_w) B}{\mu_m N_m C} + \dfrac{r\beta_h n_w \bar{\alpha}_m B}{\mu_m C}$

$y = \beta_h n_v s_h = \dfrac{\beta_h n_v (\beta_m \alpha_h + \mu_h \mu_m)(\omega_h + \mu_h)\mu_m N_m}{\beta_m \mu_h A}$

$$z = r\beta_h n_w s_h = \frac{r\beta_h n_w(\beta_m \alpha_h + \mu_h \mu_m)(\omega_h + \mu_h)\mu_m N_m}{\beta_m \mu_h A}$$
$$l = \beta_m s_v = \frac{\beta_m \alpha_m (N_m - N_w)\mu_h A}{N_m C}$$
$$m = \beta_m i_h = \frac{\beta_m B}{\beta_m \mu_h A}$$
$$j = \beta_m s_w = \frac{\beta_m \bar{\alpha}_m \mu_h A}{C}$$

Then Equation (9) can be expressed as

$$J(E_1) = \begin{bmatrix} -(x+\mu_h) & \omega_h & 0 & -y & 0 & -z \\ x & -(\omega_h+\mu_h) & 0 & y & 0 & z \\ 0 & -l & -(m+\mu_m) & 0 & 0 & 0 \\ 0 & l & m & -\mu_m & 0 & 0 \\ 0 & -j & 0 & 0 & -(m+\mu_m) & 0 \\ 0 & j & 0 & 0 & m & -\mu_m \end{bmatrix}$$

Then the eigenvalues of $J(E_1)$, so that the characteristic equation is obtained

$$(\lambda + m + \mu_m)(\lambda + \mu_m)(k_0\lambda^4 + k_1\lambda^3 + k_2\lambda^2 + k_3\lambda + k_4) = 0 \tag{10}$$

with

$$k_1 = m + 2\mu_m + \omega_h + \mu_h + x$$
$$k_2 = \mu_m m + \mu_m^2 + 2\mu_m\omega_h + 3\mu_h\mu_m + 2x\mu_m + 3\omega_h m + xm + x\omega_h + x\mu_h + \mu_h\omega_h + \mu_h^2 - yl - zj - x\omega_h$$
$$k_3 = 3m\omega_h\mu_m + \mu_m^2\omega_h + 2\mu_h\mu_m^2 + xm\mu_m + x\mu_m^2 + 2x\mu_h\mu_m + 2\mu_h\omega_h\mu_m + 2\mu_h^2\mu_m + x\mu_h m + \mu_h\omega_h m + \mu_h^2 m - 2ylm - yl\mu_m - 2ylx - yl\mu_h - zj\mu_m - zjx - zj\mu_h - 2\mu_m x\omega_h - mx\omega_h - xjz^2$$
$$k_4 = x\mu_h m\mu_m + x\mu_h\mu_m^2 + \mu_h\omega_h m\mu_m + \mu_h\omega_h\mu_m^2 + \mu_h^2 m\mu_m + \mu_h^2\mu_m^2 - 4mylx - 2myl\mu_h - 2ylx\mu_m - yl\mu_m\mu_h - 2zjx\mu_m - zj\mu_m\mu_h - x\omega_h m\mu_m - x\omega_h\mu_m^2 - 2xjzm$$

Based on Equation (10), the eigenvalues are $\lambda_1 = -m - \mu_m$ and $\lambda_2 = -\mu_m$. Since m and μ_m have positive values, the real part of the eigenvalue is negative. As for the other eigenvalues, the Routh-Hurwitz Criterion will be used to determine the type of stability of the characteristic equation

$$k_0\lambda^4 + k_1\lambda^3 + k_2\lambda^2 + k_3\lambda + k_4 = 0 \tag{11}$$

Equation (11) is satisfied if the following conditions are obtained

a. It is clear that k_0 is positive ($k_0 > 0$)
b. $k_1 = m + 2\mu_m + \omega_h + \mu_h + x > 0$
c. $k_2 = \mu_m m + \mu_m^2 + 2\mu_m\omega_h + 3\mu_h\mu_m + 2x\mu_m + 3\omega_h m + xm + x\mu_h + \mu_h\omega_h + \mu_h^2 - yl - zj > 0$, if $\mu_m m + \mu_m^2 + 2\mu_m\omega_h + 3\mu_h\mu_m + 2x\mu_m + 3\omega_h m + xm + x\mu_h + \mu_h\omega_h + \mu_h^2 > yl + zj$
d. $\Delta_2 = k_1k_2 - k_0k_3$
$$= (m + 2\mu_m + \omega_h + \mu_h + x)\big(\mu_m m + \mu_m^2 + 2\mu_m\omega_h + 3\mu_h\mu_m + 2x\mu_m + 3\omega_h m + xm + x\mu_h + \mu_h\omega_h + \mu_h^2 - yl - zj\big) - 3m\omega_h\mu_m - \mu_m^2\omega_h - 2\mu_h\mu_m^2 - xm\mu_m - x\mu_m^2 - 2x\mu_h\mu_m - 2\mu_h\omega_h\mu_m - 2\mu_h^2\mu_m - x\mu_h m - \mu_h\omega_h m - \mu_h^2 m + 2ylm + yl\mu_m + 2ylx + yl\mu_h + zj\mu_m + zjx + zj\mu_h + 2\mu_m x\omega_h + mx\omega_h + xjz^2 > 0, \text{if } R_0 > 1$$
e. $\Delta_3 = k_3\Delta_2 - k_4(k_1)^2$
$$= \big(3m\omega_h\mu_m + \mu_m^2\omega_h + 2\mu_h\mu_m^2 + xm\mu_m + x\mu_m^2 + 2x\mu_h\mu_m + 2\mu_h\omega_h\mu_m + 2\mu_h^2\mu_m + x\mu_h m + \mu_h\omega_h m + \mu_h^2 m - 2ylm - yl\mu_m - 2ylx - yl\mu_h - zj\mu_m - zjx - zj\mu_h - 2\mu_m x\omega_h - mx\omega_h - xjz^2\big)\Delta_2 - \big(x\mu_h m\mu_m + x\mu_h\mu_m^2 + \mu_h\omega_h m\mu_m + \mu_h\omega_h\mu_m^2 + \mu_h^2 m\mu_m + \mu_h^2\mu_m^2 - 4mylx - 2myl\mu_h - 2ylx\mu_m - yl\mu_m\mu_h - 2zjx\mu_m - zj\mu_m\mu_h - x\omega_h m\mu_m - x\omega_h\mu_m^2 - 2xjzm\big)(m + 2\mu_m + \omega_h + \mu_h + x)^2 > 0, \text{if } R_0 > 1$$

Based on the Routh-Hurwitz Criterion, it can be seen that λ_3, λ_4, λ_5, and λ_6 in Equation (11) have negative values. This shows that all eigenvalues of Equation (10) have negative values, so the endemic equilibrium point E_1 is locally asymptotically stable under the condition $R_0 > 1$.

Numerical Simulation

Numerical simulations were conducted to provide a clearer understanding of the mathematical model of dengue disease prevention in Yogyakarta using Wolbachia mosquitoes. Data were taken from Yogyakarta City, Sleman Regency, and Bantul Regency. The following Table 2 shows the results of the initial values, variables and parameters of Equation (2).

Table 2. Initial Values, Variables, and Parameters

Variable/ Parameter	Value	Description
$N_h(t)$	2.834.300 individuals	(BPS Provinsi DIY, 2024), (Dinkes Provinsi DIY, 2023)
$N_m(t)$	447.505 mosquitos	Assumed
$N_v(t)$	360.985 mosquitos	(World Mosquito Program, 2024)
$N_w(t)$	86.520 mosquitos	Assumed
α_h	0.0000367/day	$\alpha_h = \dfrac{1}{life\ expectancy} = 0.0000367$ (BPS Provinsi DIY, 2024)
μ_h	0.0000367/day	(BPS Provinsi DIY, 2024)
β_h	0.012/day	(Li & Liu, 2021)
$\bar{\beta}_h$	$\bar{\beta}_h = r\beta_h$	(Li & Liu, 2021)
ω_h	0.1/day	(Li & Liu, 2021)
α_m	0.077/day	Assumed
β_m	0.24/day	(Li & Liu, 2021)
μ_m	0.0385/day	$\mu_m = \frac{1}{26\ \text{day}} = 0.0385$ (Nurbaya, Maharani, & Nugroho, 2022)
$\bar{\alpha}_m$	0.0385/day	(Nurbaya, Maharani, & Nugroho, 2022)

The basic reproduction number in Equation (5) was obtained. A graph of the relationship between R_0 and r is shown.

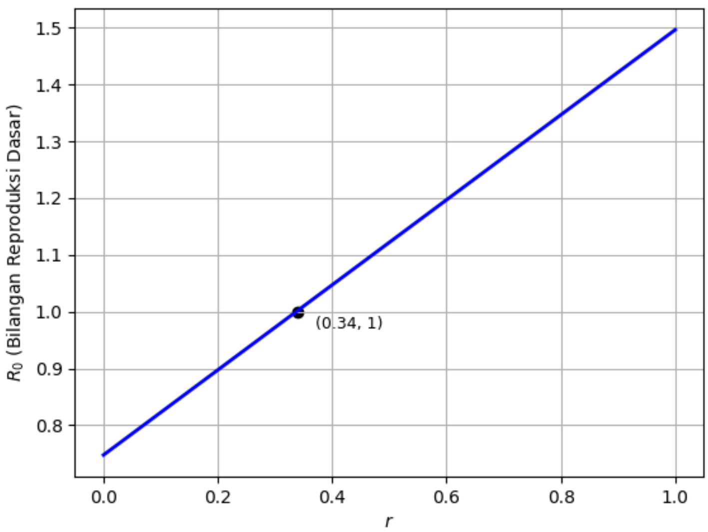

Figure 2. Diagrams of the Relationship Curve between $\boldsymbol{R_0}$ and $\boldsymbol{r}$

Figure 2 shows the curve of the relationship between the basic reproductive number (R_0) and the inhibitory effect of Wolbachia bacteria on dengue fever replication in mosquitoes (r). The curve explains that an increase in r will increase the value of R_0. The curve shows that $R_0 = 1$ occurs when

$r = 0.34$, or 34%, meaning that the inhibitory effect of Wolbachia bacteria on dengue virus replication reaches 34%, which is the threshold for disease spread. If $r < 34\%$, the value of $R_0 < 1$, which means that the disease will not spread widely in the population. On the contrary, if $r \geq 34\%$, the value of $R_0 \geq 1$, so the disease will spread. This emphasizes the importance of the inhibitory effect of Wolbachia bacteria in disease control. For Wolbachia bacteria to be effective, the inhibitory effect of Wolbachia bacteria on dengue replication must reach at least 34%. Thus, this strategy can be used to significantly stop the spread of dengue fever.

Simulation for $R_0 < 1$

Simulation for $R_0 < 1$, $r = 0.1$, the value of r represents the inhibitory effect of Wolbachia bacteria on dengue replication in mosquitoes. That is, only 10% of the probability of Wolbachia mosquitoes transmitting dengue virus compared to mosquitoes without Wolbachia. In other words, Wolbachia bacteria effectively inhibit dengue virus replication in mosquitoes, resulting in a much lower risk of transmission to humans. The parameter $\bar{\beta}_h$, which is smaller than β_h, reflects the lower probability of humans being infected with dengue due to Wolbachia mosquito bites due to the inhibitory effect of Wolbachia bacteria on dengue virus replication. Based on the parameters in Table 2, $R_0 = 0.822$ was obtained, indicating that the spread of dengue will decrease slowly and then will disappear from the population in a certain period of time.

Simulation results based on these parameters and with initial values of $s_h(0) = 0.99987, i_h(0) = 0.00013, s_v(0) = 0.65, i_v(0) = 0.35, s_w(0) = 0.9,$ and $i_w(0) = 0.1$ are presented in Figure 3.

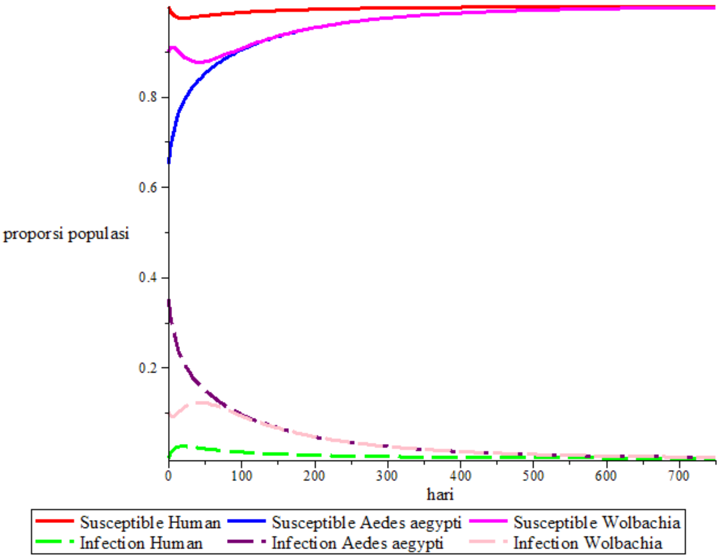

Figure 3. Simulation Graph for $\boldsymbol{R_0 < 1}$ with $\boldsymbol{r = 0.1}$

Based on the simulation in Figure 3, it can be seen that there are changes in the proportion of each population, namely human population, dengue virus-infected mosquito population, and Wolbachia bacteria-carrying mosquito population. In this graph, it can be seen that the proportion of susceptible humans, mosquitoes susceptible to dengue virus, and mosquitoes susceptible to Wolbachia bacteria will increase over time to one, while the proportion of infected humans, mosquitoes infected with dengue virus, and mosquitoes infected with Wolbachia bacteria will decrease towards zero.

The system solution starting from the initial value will move towards the equilibrium point, namely $E_0 = (s_h^*, i_h^*, s_v^*, i_v^*, s_w^*, i_w^*) = (1,0,1,0,1,0)$. This means that when $R_0 < 1$, the spread of DHF in Yogyakarta Special Region, especially Yogyakarta City, Sleman Regency, and Bantul Regency, will decrease and gradually disappear from the population in about 700 days. This simulation shows that when $R_0 < 1$ the solution of the system Equation (2) will go to the equilibrium point E_0. Thus, the simulation results are in line with the analytical results which state that the disease-free equilibrium point E_0 is asymptotically stable when $R_0 < 1$.

Simulation for $R_0 > 1$

The next simulation for $R_0 > 1$, the parameter value of r was increased to 0.7, the value of r represents the inhibitory effect of Wolbachia bacteria on dengue replication in mosquitoes. That is, 70% of the probability of Wolbachia mosquitoes transmitting dengue virus compared to mosquitoes without Wolbachia. In other words, Wolbachia bacteria did not effectively inhibit dengue virus replication in mosquitoes, resulting in a much higher risk of transmission to humans. Based on the parameters in Table 2, $R_0 = 1.271$ was obtained, indicating that the disease will spread, which means endemic.

Simulation results based on these parameters and with initial values of $s_h(0) = 0.99987, i_h(0) = 0.00013, s_v(0) = 0.65, i_v(0) = 0.35, s_w(0) = 0.9,$ and $i_w(0) = 0.1$ are presented in Figure 4.

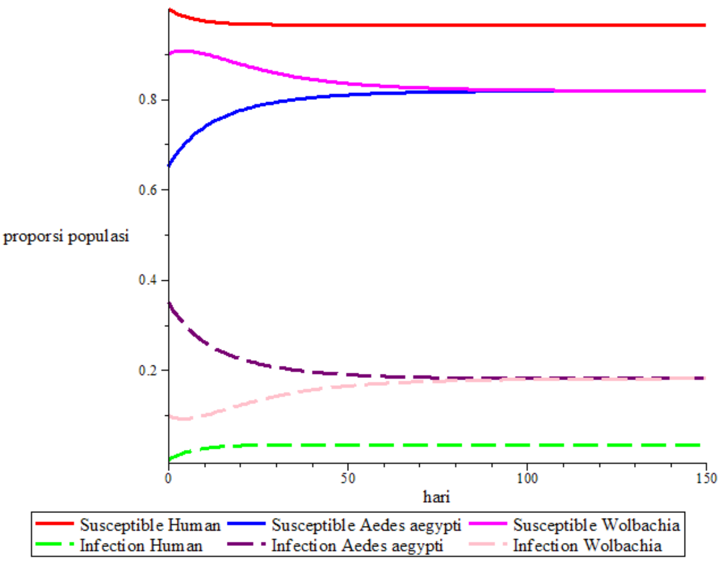

Figure 4. Simulation Graph for $\boldsymbol{R_0 > 1}$ with $\boldsymbol{r = 0.7}$

Based on the simulation in Figure 4, it can be seen that there are changes in the proportion of each population, namely the human population, the population of dengue virus-infected mosquitoes, and the population of mosquitoes carrying Wolbachia bacteria. This graph illustrates how each population changes and eventually reaches the endemic equilibrium point. In this graph, it can be seen that the proportion of susceptible humans (s_h) will decrease, while the proportion of infected humans (i_h) will increase. In mosquitoes, as the proportion of the population of dengue virus susceptible mosquitoes (s_v) and Wolbachia bacteria infected mosquitoes (i_w) increases, the proportion of the population of dengue virus infected mosquitoes (i_v) and Wolbachia bacteria susceptible mosquitoes (s_w) decreases.

The system solution starting from the initial value will move to the point $E_1 = (s_h^*, i_h^*, s_v^*, i_v^*, s_w^*, i_w^*) = (0.9638611317,\ 0.03613886832, 0.8161391470,\ 0.1838608530,$ $0.8161391470,\ 0.1838608530)$. This means that under the condition of $R_0 > 1$, the spread of dengue in the Special Region of Yogyakarta, especially Yogyakarta City, Sleman Regency, and Bantul Regency using Wolbachia mosquitoes will still exist, and the system will reach an equilibrium where the infection spreads in about 120 days. The simulation shows that when $R_0 > 1$ the solution of the system Equation (2) will lead to the equilibrium point E_1. Thus, this simulation result is in line with the analytical result that the endemic equilibrium point E_1 is asymptotically stable when $R_0 > 1$.

CONCLUSION

This model produces two equilibrium points: disease-free and endemic. The disease-free equilibrium point E_0 which is always present and is the point that is stable if the value of the basic reproduction number is $R_0 < 1$. The endemic equilibrium point E_1 where s_h^* is the number of susceptible human subpopulations infected with dengue virus, i_h^* is the number of human subpopulations that have been infected with dengue virus, s_v^* is the number of susceptible mosquito subpopulations infected with dengue virus, i_v^* is the number of subpopulations of mosquitoes infected with dengue virus, s_w^* is the number of susceptible mosquito subpopulations infected with Wolbachia bacteria, and i_w^* is the number of subpopulations of mosquitoes infected with Wolbachia bacteria. The stability of the endemic equilibrium point is guaranteed if the value $R_0 > 1$.

Based on numerical simulations in the Special Region of Yogyakarta (DIY), especially Yogyakarta City, Sleman Regency, and Bantul Regency, with the given initial values and parameters, it was found that the relationship between the basic reproductive number (R_0) and the inhibitory effect of Wolbachia bacteria (r) is linear. The critical value of $r = 0.34$, or 34% became the threshold for disease spread, where if $r < 0.34$, then $R_0 < 1$ and the disease does not spread, while if $r \geq 0.34$, then $R_0 \geq 1$ and the disease will spread in the population. Therefore, when the inhibitory effect of Wolbachia bacteria on dengue replication (r) is smaller, the greater the effectiveness of Wolbachia in inhibiting dengue virus transmission and the value of the disease-free equilibrium point E_0 will become locally asymptotically stable if $R_0 < 1$ and dengue disease in DIY will disappear. Conversely, when the inhibitory effect of Wolbachia bacteria on dengue replication (r) is greater, the potential for virus transmission from mosquitoes to humans is high and the value of the endemic equilibrium point E_1 will become locally asymptotically stable if $R_0 > 1$ and the dengue disease in DIY will spread.

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