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An Optimal Control Analysis of Dengue Fever

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Abstract

Dengue fever is one of the most infectious diseases in the world, according to data issued by the World Health Organization in 2014. It is responsible for a huge number of deaths each year around the world, particularly in tropical nations. The dengue virus (DENV) causes dengue fever, which is spread by the female Aedes aegypti mosquito. We provide a mathematical model of dengue fever transmission through hospitalization with optimal management in this paper. Before being simulated in MATLAB, this optimum control problem is numerically resolved. Vaccination, pesticide use, and prevention are all examples of optimal control in this study. The simulation results demonstrate that dengue infection can be considerably reduced by vaccination, pesticide use, and prevention.
Keywords: Dengue fever; Mathematical modelling; Optimal control.

Abstrak

Demam berdarah adalah salah satu penyakit paling menular di dunia, menurut data yang dikeluarkan oleh Organisasi Kesehatan Dunia pada tahun 2014. Penyakit ini menyebabkan banyak kematian setiap tahun di seluruh dunia, terutama di negara-negara tropis. Virus dengue (DENV) menyebabkan demam berdarah, yang disebarkan oleh nyamuk Aedes aegypti betina. Kami menyediakan model matematis penularan demam berdarah melalui rawat inap dengan penatalaksanaan optimal dalam makalah ini. Masalah kontrol optimal ini diselesaikan secara numerik sebelum disimulasikan di MATLAB. Vaksinasi, penggunaan pestisida, dan pencegahan merupakan contoh pengendalian yang optimal dalam penelitian ini. Hasil simulasi menunjukkan bahwa infeksi dengue dapat dikurangi dengan vaksinasi, penggunaan pestisida, dan pencegahan.
Kata Kunci: *Demam berdarah; Pemodelan matematika; Kontrol optimal.*

2020MSC: 00A71, 92B05.

1. INTRODUCTION

Dengue fever is transmitted to humans by female Aedes aegypti and Aedes albopictus mosquitoes, according to WHO (World Health Organization) data from 2012 [1]. When a person is afflicted with dengue fever, the virus is carried in his body and transmitted to uninfected mosquitoes when the insect bites the human. Once a mosquito has been infected with dengue fever, it can spread the disease for the rest of its life. This is owing to mosquitoes' relatively short lifespan (1-2 months [2]). The dengue virus can be transferred vertically through birth with a 75 percent likelihood [3], in addition to a mosquito that can be infected by biting an infected human.

DENV-1, DENV-2, DENV-3, and DENV-4 are the four known dengue viruses. Although recovery from dengue fever caused by one of the above viruses can provide lifelong immunity to that virus, it does not provide lifelong protection to the other three. A second infection by a different virus may put victims at increased risk [1]. The dengue virus is the primary cause of dengue fever, also known as vector-borne illness. The main mode of transmission to the human population is through

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mosquito bites carrying the dengue virus (female mosquito) [4]. The virus is spread by infected mosquitoes who take a blood meal from an affected person and then pass it on to other healthy people. Furthermore, recovery from one DENV serotype makes a person immune to the other serotypes permanently and partially or temporarily [5].

Vaccination is one of the treatments available for the dengue virus. Dengue fever vaccinations have been licensed for use in preventing dengue transmission with efficacy ranging from 54 to 77 percent [6]. The vaccine's effectiveness is strongly reliant on the age group and transmission level [7]. In places with high transmission rates, Ferguson et al.[7] discovered that immunization benefited all groups (seronegative and seropositive). Secondary infections may be more common in locations with low and moderate transmission rates. Furthermore, Zheng et al.[8] conducted a cost-benefit study of dengue vaccine use and discovered that widespread vaccination would cut annual disease costs in Latin American and Asian countries by roughly 22-23 percent.

In the literature [9][10] and references therein, there exist different mathematical models that address dengue dynamics. In [11] is a list of current research publications that have reported on dengue infection using real data. Many studies involving more components, such as age structure factors [12], human population variables [13][14], and models of dengue fever in the human body involving multiple strains, have been inspired by [14][15]. Dengue modeling is briefly treated in [16], both in a deterministic and stochastic sense. In addition to showing the pattern of dengue fever spread, whether in a closed community or not, mathematical models have been widely employed to develop techniques for preventing dengue fever. Many of these studies have centered on mosquito population management. Laboratory research [17][18][19] preceded these studies, which were followed by the development of mathematical models that could be used to forecast the long-term dynamics of dengue fever [20][21] while taking human intervention into account. Dengue fever is a mosquito-borne disease. To determine the most efficient preventative approach, several mathematical models were developed as a preliminary study [22][23]. In [24] investigates a hybrid technique for predicting dengue fever. In [25], the dynamics of dengue fever are proposed in the context of temperature and mosquito control, as well as human migration. In [26] the dengue model using human instances has been reported. Researchers have applied the optimal control technique to a range of issues [27][28]. For example, in [27], the authors used the spectral linear filter approach to solve stochastic optimum control problems and presented their findings. In [29] investigated the dynamics of dengue fever in asymptomatic carriers, as well as the use of appropriate control techniques. In [28] considers a SIR epidemic model with the best impulse control. In [11] consider a mathematical model of dengue in East Java, Indonesia, where in this study only two optimal controls were given.

The authors are encouraged to undertake a study on the mathematical model of dengue disease by proposing three optimal controls in the form of prevention, pesticide, and immunization based on these investigations. Based on the literature review, the state of the art from this study is a mathematical model of dengue fever with three optimal controls, which will be solved numerically and simulated using MATLAB software. This control is expected to offer information to readers, particularly the government in the field of health, to make decisions about dengue fever cases in Indonesia, as well as researchers in the field of applied mathematics as a reference for the creation of future research.

2. METHODS

This section describes a host-vector paradigm for mosquito-borne diseases. Five human (host) populations, recovered (R_m), hospitalized and/or notified infectious (P_m), infectious (I_m), exposed (E_m), susceptible (S_m) and three mosquito populations, infectious (I_n), exposed (E_n), susceptible (S_n), and make up the host-vector model. As a result, $N_m = S_m + E_m + I_m + P_m + R_m$ denotes the whole human population. Here, we address a new class of persons known as hospitalized individuals who have been alerted of an infection, as demonstrated by P_m. The participants in P_m class are thought to be those who have been registered at the hospital and have been identified as confirmed dengue sufferers. We believe, however, that the population in I_m class can recover without entering P_m class. All human hosts in the $P_m(t)$ class are completely protected, meaning they do not transmit disease to mosquitos or contribute to disease transmission. The dynamics of host-vector dengue fever are described by a dynamic function of differential human mathematical formulas, that is provided as [11]:

$$\frac{dS_n}{dt} = \Lambda_n - \beta\alpha_n S_n \frac{I_m}{N_m} - \mu_n S_n, \tag{1}$$

$$\frac{dE_n}{dt} = \beta\alpha_n S_n \frac{I_m}{N_m} - (\gamma_n + \mu_n)E_n, \tag{2}$$

$$\frac{dI_n}{dt} = \gamma_n E_n - \mu_n I_n, \tag{3}$$

$$\frac{dS_m}{dt} = \Lambda_m - \beta\alpha_m I_n \frac{S_m}{N_m} - \mu_m S_m, \tag{4}$$

$$\frac{dE_m}{dt} = \beta\alpha_m I_n \frac{S_m}{N_m} - (\gamma_m + \mu_m)E_m, \tag{5}$$

$$\frac{dI_m}{dt} = \gamma_m E_m - (\eta + q_1 + \mu_m)I_m, \tag{6}$$

$$\frac{dP_m}{dt} = \eta I_m - (\delta + q_2 + \mu_m)P_m, \tag{7}$$

$$\frac{dR_m}{dt} = q_1 I_m + q_2 P_m - \mu_m R_m. \tag{8}$$

Initially $S_n(0) = S_{n0} \geq 0, E_n(0) = E_{n0} \geq 0, I_n(0) = I_{n0} \geq 0, \quad S_m(0) = S_{m0} \geq 0, E_m(0) = E_{m0} \geq 0, I_m(0) = I_{m0} \geq 0, P_m(0) = P_{m0} \geq 0, R_m(0) = R_{m0} \geq 0$.

The recruitment rates of the vector Λ_n and Λ_m host are given by vand and h in the above model, respectively (see Figure 1). The biting rate of mosquitos is the variable β. α_n depicts the chance of transmission between infected humans and mosquitos. Humans have a natural death rate of μ_m, whereas mosquitos have a rate of μ_n. The parameter γ_n denotes the mosquito population's incubation period, while γ_m denotes the human incubation period. α_m is the chance of transmission between infected mosquitos and susceptible people. The confirmed dengue-infected cases that have been notified or hospitalized are displayed η. The natural recovery of infected persons is provided by q_1, whereas confirmed dengue patients are recovered at a rate of q_2. δ demonstrates the fatalities caused by dengue fever infection. Table 1 summarizes the comprehensive definitions including the input variables to model (1)-(8).

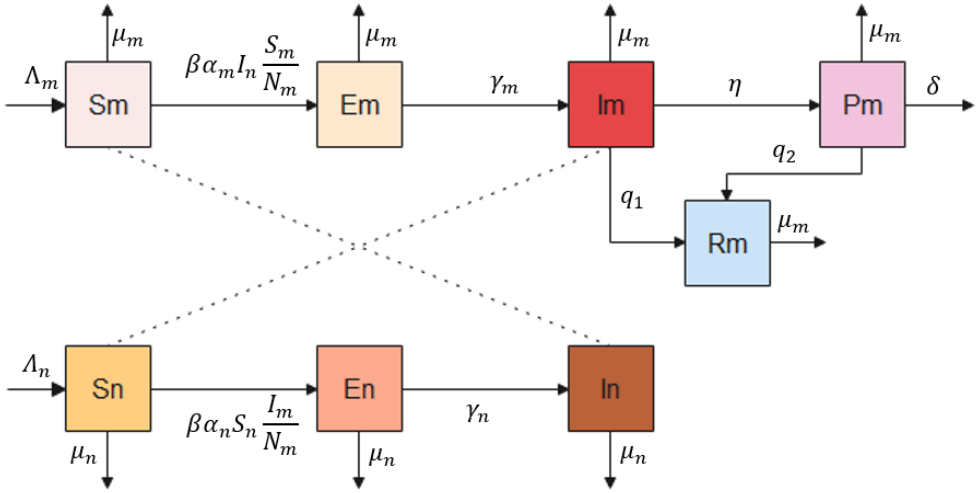

Figure 1. Social hierarchy-structured dengue model.

3. RESULTS AND DISCUSSION

3.1 Model Analysis

In this part, we examine the stability findings for the model that was suggested at the disease-free equilibrium (DFE) E_0. The following expressions are produced when we put the right side of the dengue model (1)-(8) equal to zero.

$$E_0 = (S_n^0, 0,0, S_m^0, 0,0,0,0) = \left(\frac{\Lambda_n}{\mu_n}, 0,0, \frac{\Lambda_m}{\mu_m}, 0,0,0,0\right).$$

For the dengue model, we use the next-generation matrix technique to get the fundamental reproduction number or r. Take into consideration that the dengue model's (1)-(8) infected compartments are P_m, Im, E_m, I_n, E_n. By following the directions provided in [31] and applying them in [32, 33], the following matrices were produced:

$$F = \begin{pmatrix} 0 & 0 & \frac{\beta\alpha_n\mu_m\Lambda_n}{\Lambda_m\mu_n} & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & \beta\alpha_m & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{pmatrix}, \; V = \begin{pmatrix} k_1 & 0 & 0 & 0 & 0 \\ -\gamma_n & \mu_n & 0 & 0 & 0 \\ 0 & 0 & k_2 & 0 & 0 \\ 0 & 0 & -\gamma_m & k_3 & 0 \\ 0 & 0 & 0 & -\eta & k_4 \end{pmatrix},$$

$k_1 = (\gamma_n + \mu_n), k_2 = (\gamma_m + \mu_m), k_3 = (\eta + q_1 + \mu_m), k_4 = (\delta + q_2 + \mu_m)$. The spectral radius of the matrix $\mathcal{R}_0 = \rho(FV^{-1})$, which can be obtained by the formula that follows, can be used to derive the basic reproduction that is necessary for the given model $\mathcal{R}_0^2 = \frac{\beta^2\alpha_m\gamma_m\mu_m\alpha_n\gamma_n\Lambda_n}{k_1k_2k_3\Lambda_m\mu_n^2}$.

The virus will propagate across the population if $\mathcal{R}_0 > 1$; otherwise, it won't when $\mathcal{R}_0 < 1$ for biological modelling. In general, it is more difficult to contain an epidemic when the value of $\mathcal{R}_0$ is high. The following examples show the disease-free equilibrium's (DFE) local stability at E_0.

Theorem 1. When $0 > 1$, the DFE E_0 is a locally stable asymptotically equilibrium for the system (1)-(8).

Proof. We must evaluate model (1)-(8) at the DFE E_0 to obtain the Jacobian matrix, and we have to do this to establish the provided theorem.

$$J(E_0) = \begin{pmatrix} -\mu_n & 0 & 0 & 0 & 0 & -\frac{\beta\alpha_n\mu_m\Lambda_n}{\Lambda_m\mu_n} & 0 & 0 \\ 0 & k_1 & 0 & 0 & 0 & \frac{\beta\alpha_n\mu_m\Lambda_n}{\Lambda_m\mu_n} & 0 & 0 \\ 0 & \gamma_n & -\mu_n & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & -\beta\alpha_m & -\mu_m & 0 & 0 & 0 & 0 \\ 0 & 0 & \beta\alpha_m & 0 & -k_2 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & \gamma_m & -k_3 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & \eta & -k_4 & 0 \\ 0 & 0 & 0 & 0 & 0 & q_1 & q_2 & -\mu_m \end{pmatrix}.$$

The eigenvalues $-k_4, -\mu_m, -\mu_m, -\mu_n$ of the preceding matrix $J(E_0)$ are negative, but the other four eigenvalues with negative real portions can be found by solving the equations that follow:

$$\lambda^4 + (k_1 + k_2 + k_3 + \mu_n)\lambda^3 + \big(k_3\mu_n + k_2(k_3 + \mu_n) + k_1(k_2 + k_3 + \mu_n)\big)\lambda^2 + \Big(k_2k_3\mu_n + k_1\big(k_3\mu_n + k_2(k_3 + \mu_n)\big)\Big)\lambda + \big(k_1k_2k_3\mu_n(1 - \mathcal{R}_0^2)\big) = 0.$$

For the given circumstances, the coefficient should meet the Rough-Hurtwiz requirements, which can be done with ease. This criteria is met and provided through,

$$\begin{aligned} \beth = {} & k_1^2(k_2 + k_3 + \mu_n)[k_2(2k_3(1 + \mathcal{R}_0^2)\mu_n + k_3^2 + \mu_n^2) + k_2^2(k_3 + \mu_n) + k_3\mu_n(k_3 + \mu_n)] \\ & + k_1^3[k_2(k_3(2 + \mathcal{R}_0^2)\mu_n + k_3^2 + \mu_n^2) + k_2^2(k_3 + \mu_n) + k_3\mu_n(k_3 + \mu_n)] \\ & + k_1\big(k_2^3(k_3(2 + \mathcal{R}_0^2)\mu_n + k_3^2 + \mu_n^2) + k_3k_2(2 + \mathcal{R}_0^2)\mu_n(k_3 + \mu_n)^2 \\ & + k_3^2\mu_n^2(k_3 + \mu_n)\big) + k_1k_2^2(k_3 + \mu_n)(k_3(2\mathcal{R}_0^2 + 3)\mu_n + k_3^2 + \mu_n^2) \\ & + k_2k_3(k_2 + k_3)\mu_n(k_2 + \mu_n)(k_3 + \mu_n). \end{aligned}$$

The dengue model provided by (1)-(8) is thus guaranteed to be locally asymptotically stable at the DFE E_0 under the Rough-Hurtwiz criterion.

3.2 Controllability Analysis

The optimal control problem solution may not be obtained if the system is not controlled. So it is necessary to analyze the controllability of the system.

Theorem 2. If there is a state matrix equation as follows: $\dot{x}(t) = Ax(t) + Bu(t)\ y(t) = Cx(t)$. The necessary and sufficient conditions for a system to be said to be controlled are: The matrix $Mc = [B|AB|A^2B|\cdots|A^{n-1}B]$ has a rank equal to n [11].

Proof. To carry out controllability analysis in the tuberculosis disease model, a matrix B will be formed with the following steps. With $\bar{x} = (S, V, L, I, T)$, then the matrix B is separated to obtain the following matrix A and B:

$$A = \begin{bmatrix} -(1-\varsigma_1)\beta\alpha_n\frac{I_m}{N_m} - \mu_n - b\varsigma_2 & 0 & 0 & 0 & 0 & -(1-\varsigma_1)\beta\alpha_n S_n\frac{1}{N_m} & 0 & 0 \\ (1-\varsigma_1)\beta\alpha_n S_n\frac{I_m}{N_m} & -(\gamma_n+\mu_n)E_n - b\varsigma_2 E_n & -\mu_n I_n - b\varsigma_2 I_n & -(1-\varsigma_1)\beta\alpha_m I_n\frac{S_m}{N_m} - \mu_m S_m - \varsigma_3 S_m & 0 & (1-\varsigma_1)\beta\alpha_n S_n\frac{I_m}{N_m} & 0 & 0 \\ 0 & \gamma_n E_n & 0 & (1-\varsigma_1)\beta\alpha_m I_n\frac{S_m}{N_m} & -(\gamma_m+\mu_m) & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & \gamma_m & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & -(\eta+q_1+\mu_m) & -(\delta+q_2+\mu_m) & 0 \\ 0 & 0 & 0 & 0 & 0 & \eta & q_2 & -\mu_m \\ 0 & 0 & 0 & \varsigma_3 & 0 & q_1 & & \end{bmatrix}$$

,

$$B = \begin{bmatrix} b_1 & 0 & 0 \\ b_2 & b_3 & 0 \\ 0 & b_4 & 0 \\ b_5 & 0 & b_6 \\ b_7 & 0 & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \\ 0 & 0 & b_8 \end{bmatrix}, \; M_c = [B|AB|A^2B|A^3B|A^4B|A^5B|A^6B|A^7B],$$

by using Matlab software it was found that rank $M_c = 8$ so it can be concluded that the system is controlled.

3.3 Analysis of Global Sensitivity

To identify the most significant variable that influences the fundamental reproduction number 0, we conducted the global sensitivity analysis utilizing the partial rank correlation coefficient (PRRC). μ_n is the most sensitive parameter, with, α_m, Λm, Λn, β, etc. Being the remaining sensitive parameters. Dengue infection can be decreased by raising the mosquito mortality rate. Additionally, using an air conditioner to regulate the temperature of the location and locking the doors while entering will lessen the likelihood of a mosquito bite. Eliminating superfluous container habitats that gather water (such as plastic jars, bottles, cans, tires, and buckets) where Aedes aegyptians lay eggs to hatch is a realistic and advised environmental management method. By utilizing a bed net and other required precautions, the bite of the mosquito can be minimized.

The population of sick and hospitalized persons is reduced by lowering the mosquito population's rate through the use of bed nets and other preventative strategies. The long-term impact of sensitive parameters such as μ_n, α_m, β, can reduce the number of infected and hospitalized people. The value μ_n, which measures how quickly the virus spreads among sick and hospitalized people, and the parameter α_m, which indicates the likelihood of transmission within susceptible and infected humans, work in the same way.

3.4 Mathematical Model Formulation with Optimal Control

Applying suitable control measures to detect the disease's possible elimination from society is the epidemic model with the optimal control strategy. The models of epidemics and their prevention were already developed in mathematical biology when addressing various diseases [11][30][31]. Through this section, we give a dengue model (1)-(8) extension with control variables to create an optimization approach for the examined model (1)-(8). In the model as control variables, we include three intervention strategies: preventive (ς_1), pesticide (ς_2), and vaccine (ς_3). Mosquito nets, DEET-based mosquito repellent, and repellent-treated clothing are among the preventative measures, while insecticides include mosquito spraying and fogging. The controlled model is described by a system of differential equations expressed as,

$$\frac{dS_n}{dt} = \Lambda_n - (1-\varsigma_1)\beta\alpha_n S_n \frac{I_m}{N_m} - \mu_n S_n - b\varsigma_2 S_n, \tag{9}$$

$$\frac{dE_n}{dt} = (1-\varsigma_1)\beta\alpha_n S_n \frac{I_m}{N_m} - (\gamma_n + \mu_n)E_n - b\varsigma_2 E_n, \tag{10}$$

$$\frac{dI_n}{dt} = \gamma_n E_n - \mu_n I_n - b\varsigma_2 I_n, \tag{11}$$

$$\frac{dS_m}{dt} = \Lambda_m - (1-\varsigma_1)\beta\alpha_m I_n \frac{S_m}{N_m} - \mu_m S_m - \varsigma_3 S_m, \tag{12}$$

$$\frac{dE_m}{dt} = (1-\varsigma_1)\beta\alpha_m I_n \frac{S_m}{N_m} - (\gamma_m + \mu_m)E_m, \tag{13}$$

$$\frac{dI_m}{dt} = \gamma_m E_m - (\eta + q_1 + \mu_m)I_m, \tag{14}$$

$$\frac{dP_m}{dt} = \eta I_m - (\delta + q_2 + \mu_m)P_m, \tag{15}$$

$$\frac{dR_m}{dt} = q_1 I_m + q_2 P_m - \mu_m R_m + \varsigma_3 S_m. \tag{16}$$

The goal of the research is to lower the number of disease hosts and vectors even though retaining control $\varsigma_1, \varsigma_2, \varsigma_3$ expenditures is low. The following objective function can be used to express this goal:

$$J(\varsigma_1, \varsigma_2, \varsigma_3) = \int_0^{t_f} \left(E_n + I_n + S_m + E_m + I_m + \frac{A_1}{2}\varsigma_1^2 + \frac{A_2}{2}\varsigma_2^2 + \frac{A_3}{2}\varsigma_3^2\right) dt, \tag{17}$$

$A_1, A2, A_3$ are positive weights, while t_f is the final time.

We utilize a quadratic objective function that determines responsibilities effectively in this study because the expenses upon the treatment are nonlinear. The hypothesis is predicated on the rationale that for infective populations, there is no linear link between intervention outcomes and intervention costs; writers have commonly used quadratic costs, see [32][33]. See [34][35][36] and the references therein for a more relevant paper in which the researchers tackled the nonlinear objective leads to efficiency. The terms $\varsigma_1^2, \varsigma_2^2, \; and \; \varsigma_3^2$ describe the cost of preventative, pesticide, and vaccine control measures, respectively.

The goal of this study is to discover the best control combination $\varsigma_1^*, \varsigma_2^*, \varsigma_3^*$ such that

$$J(\varsigma_1^*, \varsigma_2^*, \varsigma_3^*) = \underbrace{min}_{\tau} J(\varsigma_1, \varsigma_2, \varsigma_3), \tag{18}$$

which $\tau = (\varsigma_1, \varsigma_2, \varsigma_3) | 0 \leq \varsigma_1 \leq \varsigma_1^*, 0 \leq \varsigma_2 \leq \varsigma_2^*, 0 \leq \varsigma_3 \leq \varsigma_3^*$.

3.2 Existence of The Optimal Control

We prove the existence of an optimal control with an initial condition of $t = 0$ in this section by stating and proving the following theorem and studying the properties of the model (9)-(16) with all non-negative initial circumstances $t > 0$. We'll also utilize model (9)-(16) to examine if there's an optimal control that meets all of Pontryagin's Maximum Principle's requirements [37]–[41]. By using Pontryagin's Maximum Principle, Eqs. (9)-(18) can be transformed into a problem of minimizing the Lagrange point, L, with regard to $\varsigma_1, \varsigma_2, \varsigma_3$. The control problem's Lagrangian is provided by

$$L = E_n + I_n + E_m + I_m + S_m + \frac{A_1}{2}\varsigma_1^2 + \frac{A_2}{2}\varsigma_2^2 + \frac{A_3}{2}\varsigma_3^2, \tag{19}$$

The Pontryagin Maximum Principle [37] will be used to find the requirements needed to establish the optimal control $\varsigma_1^*, \varsigma_2^*, \varsigma_3^*$ that fulfills condition (18) with the constraint model (9)-(16). Equations (9)-(16), (17), and (18) are transformed into problems of minimizing the Hamiltonian function, pointing to the $(\varsigma_1, \varsigma_2, \varsigma_3)$, that is,

$$H = L + \sum_{i=1}^{8} \vartheta_i g_i, \tag{20}$$

where g_i signifies the model's right side (9)-(16). The adjoint variable ϑ_i fulfills the following co-state system for $i = 1, 2, \ldots, 8$. Equation (19) and model (9)-(16) are substituted into equation (20), so that

$$\begin{aligned} H = {} & E_n + I_n + E_m + I_m + S_m + \frac{A_1}{2}\varsigma_1^2 + \frac{A_2}{2}\varsigma_2^2 + \frac{A_3}{2}\varsigma_3^2 + \vartheta\_1\left(\Lambda_n - (1-\varsigma_1)\beta\alpha_n S_n \frac{I_m}{N_m} - \right. \\ & \left. \mu_n S_n - b\varsigma_2 S_n\right) + \vartheta\_2\left((1-\varsigma_1)\beta\alpha_n S_n \frac{I_m}{N_m} - (\gamma_n + \mu_n)E_n - b\varsigma_2 E_n\right) + \vartheta\_3(\gamma_n E_n - \mu_n I_n - \\ & b\varsigma_2 I_n) + \vartheta\_4\left(\Lambda_m - (1-\varsigma_1)\beta\alpha_m I_n \frac{S_m}{N_m} - \mu_m S_m - \varsigma_3 S_m\right) + \vartheta\_5\left((1-\varsigma_1)\beta\alpha_m I_n \frac{S_m}{N_m} - \right. \\ & \left. (\gamma_m + \mu_m)E_m\right) + \vartheta\_6(\gamma_m E_m - (\eta + q_1 + \mu_m)I_m) + \vartheta\_7(\eta I_m - (\delta + q_2 + \mu_m)P_m) + \\ & \vartheta\_8(q_1 I_m + q_2 P_m - \mu_m R_m + \varsigma_3 S_m). \end{aligned} \tag{21}$$

The theorem would be used to determine whether the model (9)-(16) has optimal control.

Theorem 3. There exists an optimal control $\varsigma^* = (\varsigma_1^*, \varsigma_2^*, \varsigma_3^*) \in \tau$ such that; the control model (9)-(16) with initial conditions at $t = 0$ and

$$J(\varsigma_1^*, \varsigma_2^*, \varsigma_3^*) = \underbrace{min}_{\tau} J(\varsigma_1, \varsigma_2, \varsigma_3). \tag{22}$$

Proof. The model's state and control variables are both positive, and the control set is small and convex. The integrand of the objective function J given in model (9)-(16) is thus a convex function of

$(\varsigma_1, \varsigma_2, \varsigma_3)$ on the control set τ. The Lipschitz property of the state system with regard to the state variables is satisfied because the state solutions are bounded. Positive numbers $\varepsilon_1, \varepsilon_2$ and a constant $\epsilon > 1$ can also be interpreted as follows:

$$J(\varsigma_1, \varsigma_2, \varsigma_3) \geq \varepsilon_1(|\varsigma_1|^2|\varsigma_2|^2|\varsigma_3|^2)^{\epsilon/2} - \varepsilon_2. \tag{23}$$

As a result, the state variables are bounded, indicating that the model (9)-(16) has optimal control.

3.3 The Optimal Control's Uniqueness

The necessary conditions for this optimal control are revealed using Pontryagin's Maximum Principle. This is due to the availability of an optimal control when minimizing the cost functional in eq. (17) subject to the model (9)-(16). If (x, u) is an optimal solution of an optimal control problem, then a non-trivial vector function $\vartheta = (\vartheta_1, \vartheta_2, \vartheta_3, \vartheta_4, \vartheta_5, \vartheta_6, \vartheta_7, \vartheta_8)$ must satisfy the following equations, according to [42][43].

$$\frac{dx}{dt} = \frac{\partial H(t,x,\varsigma,\vartheta)}{\partial \vartheta}, \tag{24}$$

$$0 = \frac{\partial H(t,x,\varsigma,\vartheta)}{\partial \varsigma}, \tag{25}$$

$$\dot{\vartheta} = \frac{\partial H(t,x,\varsigma,\vartheta)}{\partial x}. \tag{26}$$

As a result, the requisite conditions can now be applied to the Hamiltonian, H, in eq (21).

Theorem 4. For the optimal control issue in model (9)-(16). $S_n^*, E_n^*, I_n^*, S_m^*, E_m^*, I_m^*, P_m^*, R_m^*$ be optimal state solutions associated with optimal control $(\boldsymbol{\varsigma_1^*}, \boldsymbol{\varsigma_2^*}, \boldsymbol{\varsigma_3^*})$. There are co-states that prove with the transversality criteria $\vartheta_i(t_f) = 0$ for $i = 1, 2, 3, 4, 5, 6, 7, 8$ and the control variables $(\boldsymbol{\varsigma_1^*}, \boldsymbol{\varsigma_2^*}, \boldsymbol{\varsigma_3^*})$.

Proof. Differentiate Hamiltonian, H, with respect to $S_n, E_n, I_n, S_m, E_m, I_m, P_m, R_m$ to get eq.(21). We can also consider the state variables:

$$\dot{\vartheta_1} = \vartheta_1\left(\frac{(1-\varsigma_1)\beta\alpha_n I_m}{N_m} + \mu_m + b\varsigma_2\right) - \frac{\vartheta_2(1-\varsigma_1)\beta\alpha_n I_m}{N_m}, \tag{27}$$

$$\dot{\vartheta_2} = -1 + \vartheta_2(b\varsigma_2 + \gamma_n + \mu_m) + \vartheta_3\gamma_n, \tag{28}$$

$$\dot{\vartheta_3} = -1 + \vartheta_3(b\varsigma_2 + \mu_n) + \frac{\vartheta_4(1-\varsigma_1)\beta\alpha_m S_m}{N_m} - \frac{\vartheta_5(1-\varsigma_1)\beta\alpha_m S_m}{N_m}, \tag{29}$$

$$\dot{\vartheta_4} = (\vartheta_2 - \vartheta_1)\frac{(1-\varsigma_1)\beta\alpha_n S_n I_m}{N_m^2} + (\vartheta_4 - \vartheta_5)\frac{(1-\varsigma_1)\beta\alpha_m I_n}{N_m} + (\vartheta_5 - \vartheta_4)\frac{(1-\varsigma_1)\beta\alpha_m I_n S_m}{N_m^2} + \vartheta_4(\mu_m + S_m) - \vartheta_8 S_m, \tag{30}$$

$$\dot{\vartheta_5} = -1 + (\vartheta_2 - \vartheta_1)\frac{(1-\varsigma_1)\beta\alpha_n S_n I_m}{N_m^2} + (\vartheta_5 - \vartheta_4)\frac{(1-\varsigma_1)\beta\alpha_m I_n S_m}{N_m^2} + (\vartheta_5 - \vartheta_6)\gamma_m + \mu_m\vartheta_5, \tag{31}$$

$$\dot{\vartheta}_6 = -1 + (\vartheta_1 - \vartheta_2)\frac{(1-\varsigma_1)\beta\alpha_n S_n}{N_m} + (\vartheta_2 - \vartheta_1)\frac{(1-\varsigma_1)\beta\alpha_n S_n I_m}{N_m^2} + (\vartheta_5 - \vartheta_4)\frac{(1-\varsigma_1)\beta\alpha_m I_n S_m}{N_m^2} - \vartheta_7\eta - \vartheta_8 q_1 + \vartheta_6(\eta + q_1 + \mu_h), \quad (32)$$

$$\dot{\vartheta}_7 = (\vartheta_2 - \vartheta_1)\frac{(1-\varsigma_1)\beta\alpha_n S_n I_m}{N_m^2} + (\vartheta_5 - \vartheta_4)\frac{(1-\varsigma_1)\beta\alpha_m I_n S_m}{N_m^2} + \vartheta_7(\delta + q_2 + \mu_m) - \vartheta_8 q_2, \quad (33)$$

$$\dot{\vartheta}_8 = (\vartheta_2 - \vartheta_1)\frac{(1-\varsigma_1)\beta\alpha_n S_n I_m}{N_m^2} + (\vartheta_5 - \vartheta_4)\frac{(1-\varsigma_1)\beta\alpha_n S_n I_m}{N_m^2} + \vartheta_8\mu_m, \quad (34)$$

under the conditions of transversality, $\vartheta_1(t_f) = \vartheta_2(t_f) = \vartheta_3(t_f) = \vartheta_4(t_f) = \vartheta_5(t_f) = \vartheta_6(t_f) = \vartheta_7(t_f) = \vartheta_8(t_f) = 0$.

To determine the control variable set's optimal control, where $\varsigma_i = (1,2,3)$. Differentiate the Hamiltonian in the second equation., H, in eq.(7) with regard to control variables $\varsigma_1, \varsigma_2, \varsigma_3$ to get $S_n = S_n^*, E_n = E_n^*, I_n = I_n^*, S_m = S_m^*, E_m = E_m^*, I_m = I_m^*, P_m = P_m^*, R_m = R_m^*$.

$$\frac{\partial H}{\partial \varsigma_1} = 0, \quad (35)$$

$$\frac{\partial H}{\partial \varsigma_2} = 0, \quad (36)$$

$$\frac{\partial H}{\partial \varsigma_3} = 0, \quad (37)$$

to derive ς_i^* for $i = 1, 2, 3$ topic of formula

$$\varsigma_1^* = \left(\frac{(\vartheta_1 - \vartheta_2)\beta\alpha_n S_n I_m + (\vartheta_5 - \vartheta_4)\beta\alpha_m I_n S_m}{A_1 N_m}\right), \quad (38)$$

$$\varsigma_2^* = \left(\frac{b(\vartheta_1 S_n + \vartheta_2 E_n + \vartheta_3 I_n}{A_2}\right), \quad (39)$$

$$\varsigma_3^* = \left((\vartheta_8 - \vartheta_4)S_m\right), \quad (40)$$

$$\varsigma_1^* = max\left\{0, min\left(\varsigma_1^{max}, \frac{(\vartheta_1 - \vartheta_2)\beta\alpha_n S_n I_m + (\vartheta_5 - \vartheta_4)\beta\alpha_m I_n S_m}{A_1 N_m}\right)\right\}, \quad (41)$$

$$\varsigma_2^* = max\left\{0, min\left(\varsigma_2^{max}, \frac{b(\vartheta_1 S_n + \vartheta_2 E_n + \vartheta_3 I_n}{A_2}\right)\right\}, \quad (42)$$

$$\varsigma_3^* = max\{0, min\left((\vartheta_8 - \vartheta_4)S_m\right)\}. \quad (43)$$

This demonstrates that for small t_f, the model's optimal control is unique due to the state variables' prior boundedness as well as the adjoint variables' prior boundedness. The use of the Lipschitz property of ordinary differential equations allows for this.

3.4 Numerical Solution

The simulation's initial variables, are based on the population of East Java province in 2018 in [11] The initial conditions we used in [11]. The state variables and optimal control can be computed using this optimality system. By substituting ς_i^* for model (9)-(16), we get:

$$\frac{dS_n}{dt} = \Lambda_n - \left(1 - \left(max\left\{0, min\left(\varsigma_1^{max}, \frac{(\vartheta_1-\vartheta_2)\beta\alpha_n S_n I_m + (\vartheta_5-\vartheta_4)\beta\alpha_m I_n S_m}{A_1 N_m}\right)\right\}\right)\right)\beta\alpha_n S_n \frac{I_m}{N_m} - \mu_n S_n - b\left(max\left\{0, min\left(\varsigma_2^{max}, \frac{b(\vartheta_1 S_n + \vartheta_2 E_n + \vartheta_3 I_n}{A_2}\right)\right\}\right) S_n, \quad (44)$$

$$\frac{dE_n}{dt} = \left(1 - \left(max\left\{0, min\left(\varsigma_1^{max}, \frac{(\vartheta_1-\vartheta_2)\beta\alpha_n S_n I_m + (\vartheta_5-\vartheta_4)\beta\alpha_m I_n S_m}{A_1 N_m}\right)\right\}\right)\right)\beta\alpha_n S_n \frac{I_m}{N_m} - (\gamma_n + \mu_n)E_n - b\left(max\left\{0, min\left(\varsigma_2^{max}, \frac{b(\vartheta_1 S_n + \vartheta_2 E_n + \vartheta_3 I_n}{A_2}\right)\right\}\right) E_n, \quad (45)$$

$$\frac{dI_n}{dt} = \gamma_n E_n - \mu_n I_n - b\left(max\left\{0, min\left(\varsigma_2^{max}, \frac{b(\vartheta_1 S_n + \vartheta_2 E_n + \vartheta_3 I_n}{A_2}\right)\right\}\right) I_n, \quad (46)$$

$$\frac{dS_m}{dt} = \Lambda_m - \left(1 - \left(max\left\{0, min\left(\varsigma_1^{max}, \frac{(\vartheta_1-\vartheta_2)\beta\alpha_n S_n I_m + (\vartheta_5-\vartheta_4)\beta\alpha_m I_n S_m}{A_1 N_m}\right)\right\}\right)\right)\beta\alpha_m I_n \frac{S_m}{N_m} - \mu_m S_m - \left(max\{0, min\left((\vartheta_8 - \vartheta_4)S_m\right)\}\right)S_m, \quad (47)$$

$$\frac{dE_m}{dt} = \left(1 - \left(max\left\{0, min\left(\varsigma_1^{max}, \frac{(\vartheta_1-\vartheta_2)\beta\alpha_n S_n I_m + (\vartheta_5-\vartheta_4)\beta\alpha_m I_n S_m}{A_1 N_m}\right)\right\}\right)\right)\beta\alpha_m I_n \frac{S_m}{N_m} - (\gamma_m + \mu_m)E_m, \quad (48)$$

$$\frac{dI_m}{dt} = \gamma_m E_m - (\eta + q_1 + \mu_m)I_m, \quad (49)$$

$$\frac{dP_m}{dt} = \eta I_m - (\delta + q_2 + \mu_m)P_m, \quad (50)$$

$$\frac{dR_m}{dt} = q_1 I_m + q_2 P_m - \mu_m R_m + \left(max\{0, min\left((\vartheta_8 - \vartheta_4)S_m\right)\}\right)S_m. \quad (51)$$

To optimize the objective function J, we used $\varsigma_1 \neq 0, \varsigma_2 \neq 0, \varsigma_3 \neq 0$. The initial conditions are in [11] and the parameter value for the numerical simulation are in Table 1.

Table 1. Description and Parameter Value

Parameter	Description	Value	Units
μ_m	The natural death rate of human	$1/70.97 \times 365$	day^{-1}
δ	Human disease-related death rate	0.0969	day^{-1}
q_1	Hospitalized and/or alerted afflicted humans' recovery rates	0.0840	day^{-1}
q_2	Infected people's natural healing rate	0.0154	day^{-1}
η	Hospitalization and/or notification of affected people rates	0.0904	day^{-1}
γ_m	Extrinsic human incubation	0.5550	day^{-1}
α_m	Probability of infection from an infected mosquito to a vulnerable individual	0.6794	
Λ_m	Human recruitment rate	1525.1426	day^{-1}
γ_n	Extrinsic mosquito incubation	0.7186	day^{-1}
μ_n	The natural death rate of mosquito	0.0244	day^{-1}
α_n	Transmission probability from infected human to susceptible mosquito	0.8541	
β	Average mosquito biting rate per person	1.1971	day^{-1}
Λ_n	Mosquito recruitment rate	3839.9	day^{-1}

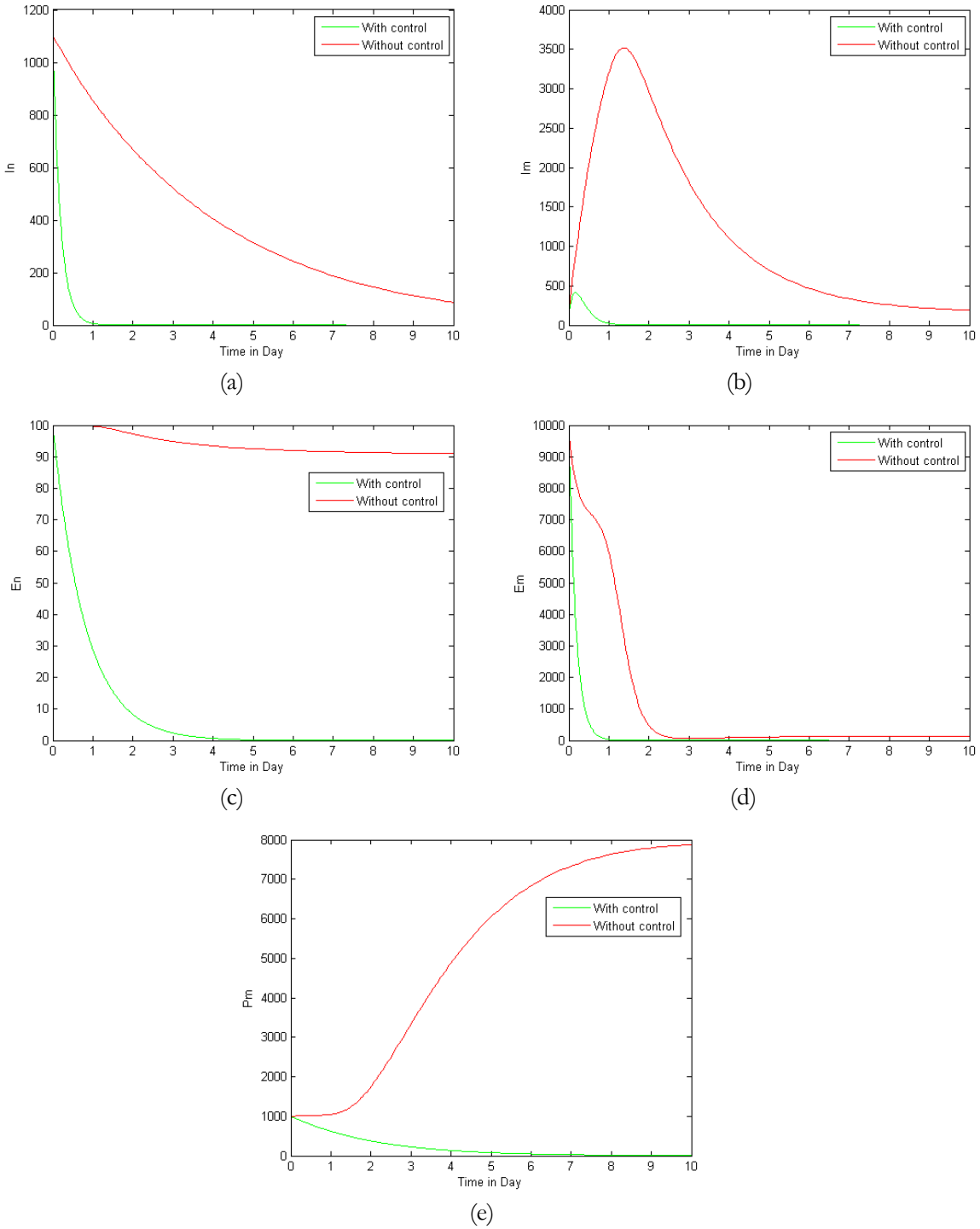

Figure 2. Simulation of the model without optimal control (**a**) Population of mosquito that infectious; (**b**) Population of human that infectious; (**c**) Population of mosquito that exposed; (**d**) Population of human that exposed; (**e**) Population of human that hospitalized and/or notified infectious.

Figure 2 shows the numerical results. Maximum prevention is carried out for about 10 days, as shown in Figure 2. According to the simulation shown in Figure 2, E_n and In dropped in the mosquito population before being provided optimal management. The E_n and I_n populations both showed a drop when optimal control was supplied, with a more significant decrease compared to before optimal control was given.

The E_m population in the human population showed a decline before and after being given optimal control, but it saw a more significant decrease after being given optimal control since the first day of monitoring. Both exhibited a rise and a drop in the days after in the I_m population at the start of the study, before and after being administered control. I_m population increased significantly before being granted control, but it decreased significantly after being given control. Figure 2 shows a large increase in the P_m population before being provided control till the last day of observation. Meanwhile, the graph shows a decline until the last day of the experiment after being provided optimal control.

4. CONCLUSIONS

We develop a mathematical model of dengue disease with hospitalization in this study, with three optimal controls. According to the sensitivity analysis done, the most sensitive factors were mosquito bite rate (β) and mosquito fatality rate (μ_n). Dengue infection can be rapidly decreased by reducing mosquito mortality and other community-wide prevention measures. Mosquito nets, insect repellant, and other critical steps can help decrease insect bites. To see the influence of vaccines, pesticide use, and prevention on dengue fever transmission in East Java, we employed optimal control approaches. The presence of optimal controls and their properties were computed and evaluated. Based on the results of the simulations, giving optimal control in the form of the vaccine, pesticide use, and prevention can lower the number of dengue fever hosts and vectors in the community, demonstrating that the optimal control offered can meet the study's objectives. This research will provide statistics to assist the government in making choices and implementing actions to combat dengue fever.

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