A Malaria Model with Controls on Mass Treatment and Insecticide

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Abstract

In this paper we derive a mathematical model for malaria transmission in population. We use controls on mass treatment and insecticide to reduce the number of infected hosts and infected vectors. The model considers human, larvae and mosquito populations. The host population is assumed constant, but the larvae and vector populations vary. First, we investigated the existence and stability of equilibria of the model without control based on the basic reproduction ratio. Then, the Pontryagins maximum principle is used to characterize the optimal control. The optimality system is derived and solved numerically for several scenarios.

Mathematics Subject Classification: 92D30, 93A15

Keywords: mathematical model, optimal control, malaria, basic reproduction ratio, stability, mass treatment, insecticide
1 Introduction

Malaria is still endemic in many countries. The disease is caused by *Plasmodium spp.* which transmitted to humans through the bites of infected female *Anopheles* mosquitoes. The female *Anopheles* mosquitoes require some protein in human blood for their breeding.

Malaria is a disease other than tuberculosis and HIV/AIDS which is a part of Millennium Development Goals (MDG’s) commitments. In the MDG’s, it is targeted to halt the spread of malaria and reduce the incidence of malaria by 2015. Many interventions have been done to reduce the malaria transmission, such as larvacide, insecticide, mass treatment (mass drug administration), and insecticide-treated bed nets [17]. In mass treatment, each person in population receive an antimalarial drug. For the susceptible or recovered hosts, the drug acts as prevention or prophylaxis. The antimalarial drug serves as treatment for the infected hosts.

One obstacle in mass treatment is necessary at considerable cost to reach the entire population. In addition, the use of mass treatment should be done with careful planning, because poor implementation of the plan could lead to the resistance of *Plasmodium spp.* to antimalarial drugs in the population [14].

Mathematical models are useful tools for studying the dynamics of the spread of infectious diseases. Understanding the dynamics of the spread of malaria in a population using mathematical models of epidemiology has been done by several researchers [6, 3, 2, 12, 9]. With a mathematical model, it can be determined the important factors in malaria transmission.

Mathematical models with optimal control can be used to control disease transmission. Many mathematical models using optimal control have been developed to measure the malaria control. Blayneh et al. [2] and Okosun et al. [11] have studied the effect of treatment and vaccination in the prevention of malaria. In fact, a vaccine against malaria is still in the stage of laboratory research. In [12], the authors used optimal control to investigate the malaria disease with drug resistant in the infective. The authors [9] proposed and analyze a malaria model with the inflow of infected immigrants as control parameter.

In this paper we construct a new model with optimal control to explore the effect of mass treatment and insecticide. The aim of this control is to minimize the number of malaria infected hosts and vectors with optimal cost of mass treatment and insecticide using Pontryagin’s Maximum Principle.

2 Model formulation

Here, host population is classified into the susceptible class ($S_H$), infectious class ($I_H$), and the recovered class ($R_H$). Here we consider larvae class ($L_V$).
Meanwhile, the vector population is partitioned into the susceptible class \((S_V)\) and infectious class \((I_V)\).

Human population is assumed homogeneous, closed and constant. We do not consider the spatial aspect and age structure of population. We consider the mass treatment control \(u_1\) and the insecticide control \(u_2\). These control functions \(u_1\) and \(u_2\) are bounded and Lebesgue integrable.

We use transmission diagrams for host population and vector population as in Figure 1 and Figure 2, where \(N_H\) is the total population of host. The parameters used in 1 and Figure 2 could be seen in Table 1. All parameters are assumed constant.

![Figure 1: Transmission diagram in human population.](image)

![Figure 2: Transmission diagram in vector population.](image)

Using the above assumptions and transmission diagrams, we derive following model.

\[
\begin{align*}
\frac{dS_H}{dt} &= \delta_H N_H - (1-u_1)\lambda_H \frac{I_V}{N_H} S_H - \delta_H S_H + \alpha R_H, \\
\frac{dI_H}{dt} &= (1-u_1)\lambda_H \frac{I_V}{N_H} S_H - (\delta_H + \gamma + \mu u_1) I_H, \\
\frac{dR_H}{dt} &= (\gamma + \mu u_1) I_H - (\delta_H + \alpha) R_H, \\
\frac{dL_V}{dt} &= \Lambda - (\eta + \varepsilon_L + \delta_L) L_V, \\
\frac{dS_V}{dt} &= \eta L_V - (1-u_1)\lambda_V \frac{I_H}{N_H} S_V - (\varepsilon_V u_2 + \delta_V) S_V, \\
\frac{dI_V}{dt} &= (1-u_1)\lambda_V \frac{I_H}{N_H} S_V - (\varepsilon_V u_2 + \delta_V) I_V.
\end{align*}
\]
The region of biological interest of model (1) is

\[
\Omega = \{(S_H, I_H, R_H, L_V, S_V, I_V) \in \mathbb{R}_+^6 : S_H + I_H + R_H = N_H \},
\]

where \(N_H\) is constant.

Model (1) is well-posed in the non-negative region \(\mathbb{R}_+^6\) because the vector field on the boundary does not point to the exterior. So, if it is given an initial condition in the region, then the solution is defined for all time \(t \geq 0\) and remains in the region.

We seek to minimize the number of malaria infected host and the cost of applying mass treatment and insecticide controls. We consider an optimal control problem with the objective function given by

\[
J(u_1, u_2) = \int_0^{t_f} \left( I_H + I_V + \frac{c_1}{2} u_1^2 + \frac{c_2}{2} u_2^2 \right) dt,
\]

where \(c_1\) and \(c_2\) are the weighting constants for mass treatment and insecticide efforts, respectively. The costs of the mass treatment and insecticide are nonlinear and take quadratic forms.

We seek an optimal control \(u_1^*\) and \(u_2^*\) such that

\[
J(u_1^*, u_2^*) = \min_{\Gamma} J(u_1, u_2),
\]

where \(\Gamma = \{(u_1, u_2)|0 \leq u_i \leq 1, i = 1, 2\}\).

<table>
<thead>
<tr>
<th>Description</th>
<th>Parameter</th>
</tr>
</thead>
<tbody>
<tr>
<td>Natural death rate of host</td>
<td>(\delta_H)</td>
</tr>
<tr>
<td>Immunity lose rate</td>
<td>(\alpha)</td>
</tr>
<tr>
<td>Recovery rate from treatment</td>
<td>(\mu)</td>
</tr>
<tr>
<td>Oviposition rate</td>
<td>(\Lambda)</td>
</tr>
<tr>
<td>Natural death rate of larvae</td>
<td>(\delta_L)</td>
</tr>
<tr>
<td>Larvae death rate from larvacide</td>
<td>(\varepsilon_L)</td>
</tr>
<tr>
<td>Maturation rate of larvae</td>
<td>(\eta)</td>
</tr>
<tr>
<td>Natural death rate of vector</td>
<td>(\delta_V)</td>
</tr>
<tr>
<td>Vector death rate from insecticide</td>
<td>(\varepsilon_V)</td>
</tr>
<tr>
<td>Infection rate for vector</td>
<td>(\lambda_V)</td>
</tr>
<tr>
<td>Infection rate for host</td>
<td>(\lambda_H)</td>
</tr>
<tr>
<td>Natural recovery period of host</td>
<td>(1/\gamma)</td>
</tr>
</tbody>
</table>

Table 1: Parameters for the model.
3 Model Analysis

First, we analyze model (1) without the control functions $u_1$ and $u_2$, that is, without treatment and insecticide interventions. Let

$$T = \frac{\Lambda}{\delta V} \frac{\eta}{\delta L + \varepsilon L + \eta} \frac{\lambda_V}{\delta V} \frac{\lambda_H}{N_H (\gamma + \delta_H)}.$$ 

Parameter $T$ above is a multiplication of four terms. The first term can be interpreted as the average number of larvae produced by a female mosquito during its life. The second term can be interpreted as the probability of a larvae will succeed to become a mosquito. The third term and the fourth term can be interpreted as the average number of infected mosquitoes and hosts respectively.

Moreover, parameter $R_0 = \sqrt{T}$ can be interpreted as the basic reproduction ratio with larvacide intervention. Basic reproduction ratio represents the expected numbers of secondary cases of infection per primary case of infection in a virgin population during the infectious period of primary case [4, 5].

Model (1) has two equilibria (with respect to the coordinate $(S_H, I_H, R_H, L_V, S_V, I_V)$), these are, the disease-free equilibrium $E^0 = (S^0_H, 0, 0, L^0_V, S^0_V, 0)$, where $S^0_H = N_H$, $I^0_H = \frac{\Lambda}{\delta L + \varepsilon L + \eta}$, $S^0_V = \frac{\eta}{\delta V} L^0_V$, and the endemic equilibrium $E^1 = (S^1_H, I^1_H, R^1_H, L^1_V, S^1_V, I^1_V)$, where

$$S^1_H = \frac{N_H \delta V (\alpha + \gamma + \delta_H)}{T \delta V (\alpha + \gamma + \delta_H) + \lambda_V (\alpha + \delta_H)},$$

$$I^1_H = \frac{N_H \delta V (T - 1)(\alpha + \delta_H)}{T \delta V (\alpha + \gamma + \delta_H) + \lambda_V (\alpha + \delta_H)},$$

$$R^1_H = \frac{N_H \gamma \delta V (T - 1)}{T \delta V (\alpha + \gamma + \delta_H) + \lambda_V (\alpha + \delta_H)},$$

$$L^1_V = \frac{\Lambda}{\delta L + \varepsilon L + \eta},$$

$$S^1_V = \frac{\eta [T \delta V (\alpha + \gamma + \delta_H) + \lambda_V (\alpha + \delta_H)] L^1_V}{T \delta V (\alpha + \gamma + \delta_H) \delta V + \lambda_V (\alpha + \delta_H)},$$

$$I^1_V = \frac{(T - 1)(\alpha + \delta_H) \eta \lambda_V}{T \delta V (\alpha + \gamma + \delta_H) \delta V + \lambda_V (\alpha + \delta_H)} L^1_V.$$

The equilibrium $E^0$ always exists. It does not depend on the threshold parameter $T$. Meanwhile, the equilibrium $E^1$ exists if $T > 1$ or equivalently $R_0 > 1$. The following theorem gives the stability criteria of the disease-free equilibrium $E^0$.

**Theorem 3.1** For $R_0 < 1$, the disease-free equilibrium $E^0$ is locally asymptotically stable. Otherwise, it is unstable.
Proof. For the local stability of the disease-free equilibrium $E_0$, we linearized model (1) at $E_0$. From the linearization, we get the eigenvalues as $-\delta_H, -\delta_V, -(\alpha + \delta_H), -(\delta_L + \varepsilon_L + \eta)$ and the roots of quadratic equation $x^2 + (\delta_H + \delta_V + \gamma)x + \delta_V(\delta_H + \gamma)(1 - T) = 0$. In order that the quadratic equation has negative roots, the constant coefficient should be positive, that is, $T < 1$ or equivalently $R_0 < 1$. So, if $R_0 < 1$, the equilibrium $E_0$ is locally asymptotically stable. Otherwise, it is unstable. \hfill \Box

Stability of the endemic equilibrium $E_1$ is not easy to confirm analytically because it involves a quartic equation. Numerically, the endemic equilibrium is locally asymptotically stable. This can be seen in Figure 3. We use three different initial conditions for the simulation. Those orbits tend to a same point as time evolves.

Conjecture 3.2 For $R_0 > 1$, the endemic equilibrium $E_1$ is locally asymptotically stable.

![Figure 3: Phase portrait of model (1) in $S_V - I_V$ plane.](image)

4 Analysis of Optimal Control

In this section, we analyze model (1), that is, model of the spread of malaria in population using optimal control strategy. Consider again the objective function (2) to model (1). Necessary conditions to determine the optimal control $u_1^*$ and $u_2^*$ that satisfy the condition (3) with constraint model (1) will be solved by the Pontryagin's Maximum Principle [13]. This principle converts (1), (2) and (3) into a problem of minimizing pointwise a Hamiltonian $H$, with respect to $(u_1, u_2)$, that is

$$H(S_H, I_H, R_H, L_V, S_V, I_V, u_1, u_2, \lambda_1, \lambda_2, \lambda_3, \lambda_4, \lambda_5, \lambda_6)$$

$$= I_H + I_V + \frac{c_1}{2} u_1^2 + \frac{c_2}{2} u_2^2 + \sum_{i=1}^{6} \lambda_i g_i,$$
where $g_i$ is the right-hand side of the differential equation (1) of the $i$-th state variable.

Furthermore, $\lambda_i, i = 1, 2, \ldots, 6$ are the adjoint variables or co-state variables solutions of the following adjoint system:

$$
\begin{align*}
\frac{d\lambda_1}{dt} &= \lambda_1 \left((1 - u_1) \lambda_H \frac{I_V}{N_H} + \delta_H\right) - \lambda_2 \lambda_H (1 - u_1) \frac{I_V}{N_H}, \\
\frac{d\lambda_2}{dt} &= -1 + \lambda_2 (\delta_H + \gamma + \mu u_1) - \lambda_3 (\gamma + \mu u_1) + (\lambda_5 - \lambda_6) (1 - u_1) \lambda_V \frac{S_V}{N_H}, \\
\frac{d\lambda_3}{dt} &= -\lambda_1 \alpha + \lambda_3 (\delta_H + \alpha), \\
\frac{d\lambda_4}{dt} &= \lambda_4 (\eta + \varepsilon_L + \delta_L) - \lambda_5 \eta, \\
\frac{d\lambda_5}{dt} &= \lambda_5 \left((1 - u_1) \lambda_V \frac{I_H}{N_H} + \varepsilon_V u_2 + \delta_V\right) - \lambda_6 \lambda_V (1 - u_1) \frac{I_H}{N_H}, \\
\frac{d\lambda_6}{dt} &= -1 + \lambda_1 (1 - u_1) \lambda_H \frac{S_H}{N_H} - \lambda_2 \lambda_H (1 - u_1) \frac{S_H}{N_H} + \lambda_6 (\varepsilon_V u_2 + \delta_V),
\end{align*}
$$

with transversality conditions $\lambda_i(t_f) = 0, i = 1, \ldots, 6$.

By applying Pontryagin’s Maximum Principle and the existence result for the optimal control pairs [8, 10], we obtain the following theorem.

**Theorem 4.1** The optimal control pair $(u_1^*, u_2^*)$ that minimizes $J(u_1, u_2)$ over $\Gamma$ is given by

$$
\begin{align*}
u_1^* &= \max \left\{0, \min \left\{1, \frac{\Delta}{c_1}\right\}\right\}, \\
u_2^* &= \max \left\{0, \min \left\{1, \frac{\lambda_5 \varepsilon_V S_V + \lambda_6 \varepsilon_V I_V}{c_2}\right\}\right\},
\end{align*}
$$

where $\Delta = (\lambda_2 - \lambda_1) \lambda_H \frac{I_V}{N_H} S_H + (\lambda_2 - \lambda_3) \mu I_H + (\lambda_6 - \lambda_5) \lambda_V \frac{I_H}{N_H} S_V$, and $\lambda_i, i = 1, \ldots, 6$ are solutions of the co-state equations (4).

**Proof.** First of all, we differentiate the Hamiltonian $H$ with respect to the states and then the co-state, the system can be written as

$$
\begin{align*}
\frac{d\lambda_1}{dt} &= -\frac{\partial H}{\partial S_H}, \lambda_1(t_f) = 0, \\
\vdots \\
\frac{d\lambda_6}{dt} &= -\frac{\partial H}{\partial I_V}, \lambda_6(t_f) = 0,
\end{align*}
$$

where $t_f$ is the end time of integration.
Furthermore, by equating to zero derivatives of the Hamiltonian $H$ with respect to the controls, we obtain

$$\frac{\partial H}{\partial u_1} = 0, \frac{\partial H}{\partial u_2},$$

and solving for $u_1^*, u_2^*$ subject the constraints, the characterizations $u_1^*$ and $u_2^*$ can be derived. □

5 Numerical simulation

In this section, we study the effect of optimal strategy on malaria transmission using some numerical methods. The optimal strategy is obtained by solving the state system (1) and co-state system (4). An iterative scheme is used for solving the optimality system. We start to solve the state equations with a guess for the controls over the simulated time using a forward fourth order Runge-Kutta scheme. Moreover, the co-state equations are simultaneously solved using a backward fourth order Runge-Kutta scheme with the transversality conditions. Then, the controls are updated by using a convex combination of the previous controls and the value from the characterizations of $u_1^*$ and $u_2^*$. This process is repeated and iteration is stopped if the values of unknowns at the previous iteration are very close to the ones at the present iteration [7].

For numerical simulation, we use parameter values as in Table 2, the initial condition $x(0) = (400000, 40000, 10000, 150000, 50000, 20000)$ and the weighting control $c_1 = 80, c_2 = 20$. In this case, the weighting factor $c_1$ corresponding to the mass treatment control $u_1$ is greater than $c_2$ which corresponds to the insecticide control $u_2$. The cost of mass treatment include the cost of medications, monitoring, and patient care. For the time horizon, we take 100 days.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\delta_H$</td>
<td>0.00004566/day</td>
<td>$\eta$</td>
<td>0.07142/day</td>
</tr>
<tr>
<td>$\alpha$</td>
<td>0.333/day</td>
<td>$\delta_V$</td>
<td>0.07142/day</td>
</tr>
<tr>
<td>$\mu$</td>
<td>0.04/day</td>
<td>$\varepsilon_V$</td>
<td>0.1/day</td>
</tr>
<tr>
<td>$\Lambda$</td>
<td>105,000/day</td>
<td>$\lambda_V$</td>
<td>1.5/day</td>
</tr>
<tr>
<td>$\delta_L$</td>
<td>0.4/day</td>
<td>$\lambda_H$</td>
<td>1/day</td>
</tr>
<tr>
<td>$\varepsilon_L$</td>
<td>0.4/day</td>
<td>$\gamma$</td>
<td>0.01/day</td>
</tr>
</tbody>
</table>

Table 2: Value of parameters.
5.1 Mass treatment control

In this scenario, we activate only control $u_1$ on mass treatment, while the control $u_2$ on insecticide is set to zero. The profile of the optimal control $u_1$ could be seen in Figure 4. To eliminate malaria in 100 days, the treatment should be hold intensively almost 100 days.

Using the optimal control $u_1$ as in Figure 4, the dynamics of infected host and infected vector could be seen in Figure 5. The number of infected hosts and infected vectors decrease due to the mass treatment, while the number of infected hosts and infected vectors increase without mass treatment.

![Figure 4: The profile of the optimal control $u_1$](image1)

![Figure 5: The optimal solutions for infected host ($I_H$, left) and infected vector ($I_V$, right) via mass treatment only](image2)
5.2 Insecticide control

In this scenario, we set the mass treatment control $u_1$ to zero and activate only the insecticide control $u_2$. Figure 6 shows the profile of the optimal control $u_2$ on insecticide. From Figure 6, we see that to eliminate malaria in 100 days, the treatment should be hold intensively during 100 days.

![Figure 6: The profile of the optimal control $u_2$](image)

Using the optimal control $u_2$ as in Figure 6, the dynamics of infected host ($I_H$, left) and infected vector ($I_V$, right) could be seen in Figure 7. We observed that the number of infected vector is fewer in the insecticide control case than in the uncontrolled one. With this scenario, there is no a significant different in the number of infected host with optimal strategy compared to the number of infected host without control.

![Figure 7: The optimal solutions for infected host ($I_H$, left) and infected vector ($I_V$, right) via insecticide only](image)
5.3 Optimal mass treatment and insecticide controls

In this scenario, the mass treatment control $u_1$ and the insecticide control $u_2$ are both activated to optimize the objective function $J$. The profile of optimal controls $u_1$ and $u_2$ can be seen in Figure 8.

![Figure 8: The profile of the optimal control $u_1$ and $u_2$](image1)

Figure 8: The profile of the optimal control $u_1$ and $u_2$

![Figure 9: The optimal solutions for infected host ($I_H$, left) and infected vector ($I_V$, right) via mass treatment and insecticide](image2)

Figure 9: The optimal solutions for infected host ($I_H$, left) and infected vector ($I_V$, right) via mass treatment and insecticide

From Figure 8, we see that to eliminate malaria in 100 days, the mass treatment should be held intensively almost 100 days, while the insecticide should give full effort in the beginning of the disease spread and then the effort can be smoothly reduced after 15 days. Using the optimal control $u_1$ and $u_2$ as in Figure 8, the dynamics of infected host and infected vector could be seen in Figure 9. We observed that due to the control strategies, the number of infected host and infected vector decreases, while the population of infected host and infected vector increases when there is no control. This scenario shows
that the combination of mass treatment and insecticide effort can effectively reduce the number of infected host and infected vector.

6 Conclusion

In this paper, we derived and analyzed a deterministic model for the spread of malaria that includes mass treatment and insecticide. We obtain the basic reproduction ratio, $R_0$, with interventions. The ratio determine the existence and the stability of the equilibria of the model. Using optimal control strategy, we addressed the eradication of the disease in a finite time. From numerical results, we conclude that the combination of mass treatment and intervention is more effective in reducing the number of infected host and infected vector.

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References


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