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Mathematical modelling of the transmission dynamics of malaria infection with optimal control

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Abstract

In this study, we formed a mathematical model for the transmission of malaria infection in other to explore the transmission dynamics and optimal control. We considered the $S_h, E_h, I_h, R_h, S_v, E_v, I_v$ model with optimal control considering the effect of two optimal controls (Use of bed net and Treatment). The positivity and boundedness, reproduction number, stability and optimal control analysis were carried out accordingly. Numerical simulations were done. We further discovered the conditions necessary for the stability of both disease-free equilibrium (DFE) and endemic equilibrium. The DFE is asymptotically stable. Also, the endemic equilibrium is stable. The numerical simulation also shows the effective use of bed net and Treatment on the curve. Finally, we deduce that the use of bed nets and treatment over a long period can eventually help to flatten the curve of infection. However, this control intervention has no significant impact on the mosquito population.

Keywords: Stability; Reproduction Number; SEIR-SEI model; Optimal control

1. Introduction

According to [5] it was discovered that malaria is a disease of universal significance that results in about 600 million cases yearly and has an estimation of 2.2 billion people getting infected. Malaria is a deadly infectious disease that is caused by the plasmodium parasite that transmits to people through the bites of an infected female anopheles mosquito which initiates its protists via saliva into the circulatory system and finally into the liver where it grows and recreates. [5] also observed that more than a century after the resignation of the parasite and finding effective, repellants, insecticides, and drugs, it was discovered that the infection is as old as humanity itself. In Africa mostly in young children, malaria is the most life-threatening protozoan disease (numerically). It is accountable for over 750,000 deaths recorded annually [4].

According to Finkel [1], the rate at which children die per day is as a result of malaria. Malaria is preventable and curable,229 million cases of malaria were recorded in 2019 [7]. The accumulated population of malaria mortality rate stood at 409,000 in 2019, compared with 411 000 deaths in 2018. Children under the range of 5 years are the most exposed and vulnerable group affected by the infectious disease; it was recordedthat our if the 94% mortality cases recorded, they account for 67% out of it [7].

Mathematical modeling has become an important tool in understanding the dynamics of disease transmission and in decision-making processes regarding intervention programs for disease control according to [2]. It can predict if the infectious disease (malaria) will increase or decrease in the population. Control measures, vaccines, and treatment with useful information or guidelines can be estimated by mathematical models to the masses to eliminate the disease. Malaria can be eliminated if the mosquito population is decreased to a below certain threshold according to Ronald Ross. The model of Ronald Ross was improved after some years by MacDonald. MacDonald proved and show that a decrease in the mosquito population has little effect on the epidemiology of malaria in an area with the severe and chronic transmission. Various features and traits of malaria to the model of MacDonald were stated by J.L Aron and R.M May which includes reproduction and growth phase in mosquito, infection, and time of human immunity. Mathematical modeling also provides a structure for knowing the transmission Dynamics for malaria and can be used for optimal allocation of different prevention against malaria [8]

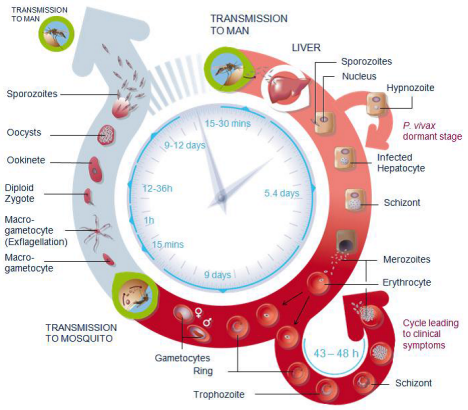

Figure 1: Life cycle of *P. falciparum* parasite.

2. Model formulation

The mathematical model for the transmission dynamics was formulated as follows: N is the total population density which is divided into seven sub classes. The susceptible human class S_h, comprising those people who are capable of contracting the dis-

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Therefore we have

$$E_h(t) \geq E_h(0)e^{(\alpha_{1h}+\mu_h)t} \tag{3}$$

Also in the third equation

$$\frac{dI_h}{dt} = \alpha_{1h}E_h - (\alpha_{2h} + \mu_h + \delta)\, I_h$$

$$\frac{dI_h}{dt} \geq -(\alpha_{2h} + \mu_h + \delta)\, I_h$$

Therefore we have

$$I_h(t) \geq I_h(0)e^{((\alpha_{2h}+\mu_h+\delta)t}$$

Also in the fourth equation

$$\frac{dR_h}{dt} = \alpha_{2h}I_h - (\mu_h + \sigma)R_h$$

$$\frac{dR_h}{dt} \geq -(\mu_h + \sigma)R_h$$

$$R_h(t) \geq R_h(0)e^{(\mu_h+\sigma)\,t}$$

Also, we have the fifth equation

$$\frac{dS_v}{dt} \geq \pi_v - \lambda_v S_v I_h - \mu_v S_v$$

Therefore we have

$$S_v(t) = \frac{-\pi_v}{\mu_v} + \left(S_v(0) + \frac{\pi_v}{\mu_v}\right) e^{\mu_v t} \tag{4}$$

Also the sixth equation

$$\frac{dE_v}{dt} = \lambda_v S_v I_h - (\alpha_{1v} + \mu_v)\, E_v$$

$$\frac{dE_v}{dt} \geq -(\alpha_{1v} + \mu_v)\, E_v$$

Therefore we have

$$E_v(t) \geq E_v(0)e^{(\alpha_{1v}+\mu_v)t} \tag{5}$$

Also the seventh equation

$$\frac{dI_v}{dt} = \alpha_{1v}E_v - \mu_v I_v$$

$$\frac{dI_v}{dt} \geq -\mu_v I_v$$

Therefore we have

$$I_v(t) \geq I_v(0)e^{\mu_v t} \tag{6}$$

2.2. Disease free equilibrium (DFE)

In other to determine the stability of the disease-free equilibrium point, we first need to find the equilibrium points (DFE)
By equating the systems to zeros we have
Thus DFE of the SEIR-SEI model is given by

$$P_0 = \left(\frac{\pi_h}{\mu_h}, 0, 0, 0, \frac{\pi_v}{\mu_v}, 0, 0\right) \tag{7}$$

2.3. Basic reproduction number

Let P and V be the non-negative matrix of the infection and the non-singular matrix of transition terms calculated at E_0respectively

$$P = \begin{bmatrix} \lambda_h S_h I_v \\ 0 \\ \lambda_v S_v I_h \\ 0 \end{bmatrix} \tag{8}$$

$$V = \begin{bmatrix} (\alpha_{1h} + \mu_h)E_h \\ -\alpha_{1h}E_h + (\alpha_{2h} + \mu_h + \delta)I_h \\ (\alpha_{1v} + \mu_v)E_v \\ -\alpha_{1v}E_v + \mu_v I_v \end{bmatrix} \tag{9}$$

Consequently , applying the next generation matrix PV^{-1} we have

$$PV^{-1} = \begin{bmatrix} 0 & 0 & \frac{\lambda_h \pi_h (\alpha_{1v})}{\mu_h(\alpha_{1v}\mu_v + \mu_v^2)} & \frac{\lambda_h \pi_h}{\mu_h \mu_v} \\ 0 & 0 & 0 & 0 \\ \frac{\lambda_v \pi_v (\alpha_{1h})}{\mu_v(\alpha_{1h}+\mu_h)(\alpha_{2h}+\mu_h+\delta)} & \frac{\lambda_v \pi_v}{\mu_v(\alpha_{2h}+\mu_h+\delta)} & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix} \tag{10}$$

$$\rho(PV^{-1}) = \sqrt{\frac{\lambda_v \lambda_h (\alpha_{1v})(\alpha_{1h})\pi_v \pi_h}{\mu_v \mu_h (\alpha_{1h} + \mu_h)(\alpha_{2h} + \mu_h + \delta)(\alpha_{1v}\mu_v + \mu_v^2)}} \tag{11}$$

$$R_0 = \sqrt{\frac{\lambda_v \lambda_h (\alpha_{1v})(\alpha_{1h})\pi_v \pi_h}{\mu_v \mu_h (\alpha_{1h} + \mu_h)(\alpha_{2h} + \mu_h + \delta)(\alpha_{1v}\mu_v + \mu_v^2)}} \tag{12}$$

2.4. Stability of the disease free equilibrium (DFE)

We proof the stability of the disease-free equilibrium from the dynamic system by proving the following lemma

Lemma 1. *The disease-free equilibrium point of the system is locally stable if the reproduction number* $R_o < 1$

$$\begin{aligned}
\frac{dS_h}{dt} &= \pi_h - \lambda_h S_h I_v - \mu_h S_h + \sigma R_h \\
\frac{dE_h}{dt} &= \lambda_h S_h I_v - (\alpha_{1h} + \mu_h) E_h \\
\frac{dI_h}{dt} &= \alpha_{1h} E_h - (\alpha_{2h} + \mu_h + \delta) I_h \\
\frac{dR_h}{dt} &= \alpha_{2h} I_h - (\mu_h + \sigma) R_h \\
\frac{dS_v}{dt} &= \pi_v - \lambda_v S_v I_h - \mu_v S_v \\
\frac{dE_v}{dt} &= \lambda_v S_v I_h - (\alpha_{1v} + \mu_v) E_v \\
\frac{dI_v}{dt} &= \alpha_{1v} E_v - \mu_v I_v
\end{aligned} \tag{13}$$

$$J_0(F) = \begin{bmatrix}
-\mu_h & 0 & 0 & 0 & 0 & 0 & -\lambda_h \frac{\pi_h}{\mu_h} \\
0 & -(\alpha_{1h} + \mu_h) & 0 & 0 & 0 & 0 & \lambda_h \frac{\pi_h}{\mu_h} \\
0 & \alpha_{1h} & -(\alpha_{2h} + \mu_h + \delta) & 0 & 0 & 0 & 0 \\
0 & 0 & \alpha_{2h} & -(\mu_h + \sigma) & 0 & 0 & 0 \\
0 & 0 & -\lambda_v \frac{\pi_v}{\mu_v} & 0 & -\mu_v & 0 & 0 \\
0 & 0 & \lambda_v \frac{\pi_v}{\mu_v} & 0 & 0 & -(\alpha_{1v} + \mu_v) & 0 \\
0 & 0 & 0 & 0 & 0 & \alpha_{1v} & -\mu_v
\end{bmatrix} \tag{14}$$

Let

$$\lambda_h \frac{\pi_h}{\mu_h} = m_1 (\alpha_{1h} + \mu_h) = m_2 \mu_h + \sigma = \mu \mu_v = \eta (\alpha_{2h} + \mu_h + \delta) = m_3 \lambda_v \frac{\pi_v}{\mu_v} = m_4$$

$$(\alpha_{1v} + \mu_v) = m_5 \alpha_{1h} = \alpha \alpha_{2h} = \gamma \alpha_{1v} = \sigma \tag{15}$$

$$J_0(F) = \begin{bmatrix}
-\mu & 0 & 0 & 0 & 0 & 0 & -m_1 \\
0 & -m_2 & 0 & 0 & 0 & 0 & m_1 \\
0 & \alpha & -m_3 & 0 & 0 & 0 & 0 \\
0 & 0 & \gamma & -\mu & 0 & 0 & 0 \\
0 & 0 & -m_4 & 0 & -\eta & 0 & 0 \\
0 & 0 & m_4 & 0 & 0 & -m_5 & 0 \\
0 & 0 & 0 & 0 & 0 & \sigma & -\eta
\end{bmatrix} \tag{16}$$

Since we know that the eigenvalue λas stated under the

$$\left| J(f^0) - \lambda E \right| = 0$$

$$\begin{bmatrix}
-m_2 & 0 & 0 & m_1 \\
\alpha & -m_3 & 0 & 0 \\
0 & m_4 & -m_5 & 0 \\
0 & 0 & \sigma & -\eta
\end{bmatrix} \tag{17}$$

$$\lambda^4 + P_1 \lambda^3 + P_2 \lambda^2 + P_3 \lambda + P_4 = 0$$

$$\begin{aligned}
P_1 &= \eta + m_5 + m_3 + m_2 \\
P_2 &= \eta m_5 + \eta m_3 + \eta m_2 + m_5 m_3 + m_5 m_2 + m_3 m_2 \\
P_3 &= \eta m_5 m_3 + \eta m_5 m_2 + \eta m_3 m_2 + m_5 m_3 m_2 \\
P_4 &= \eta m_5 m_3 m_2 - \sigma m_4 \alpha m_1
\end{aligned} \qquad
\begin{aligned}
P_1 &= \eta + m_5 + m_3 + m_2 \\
P_2 &= \eta m_5 + \eta m_3 + \eta m_2 + m_5 m_3 + m_5 m_2 + m_3 m_2 \\
P_3 &= \eta m_5 m_3 + \eta m_5 m_2 + \eta m_3 m_2 + m_5 m_3 m_2 \\
P_4 &= \eta m_5 m_3 m_2 - \sigma m_4 \alpha m_1
\end{aligned} \tag{18}$$

$$P_4 = \mu_v (\alpha_{1v} + \mu_v)(\alpha_{2h} + \mu_h + \delta)(\alpha_{1h} + \mu_h) - \alpha_{1v} \left(\frac{\lambda_v \pi_v}{\mu_v} \right) \alpha_{1h} \left(\frac{\lambda_h \pi_h}{\mu_h} \right) \tag{19}$$

$$= \mu_v (\alpha_{1v} + \mu_v)(\alpha_{2h} + \mu_h + \delta)(\alpha_{1h} + \mu_h) \left(1 - \frac{\lambda_v \lambda_h \pi_v \pi_h \alpha_{1v} \alpha_{1h}}{\mu_h (\alpha_{2h} + \mu_h + \delta)(\alpha_{1h} + \mu_h)(\alpha_{1v} \mu_v + \mu_v^2)} \right) \tag{20}$$

$$= \mu_v (\alpha_{1v} + \mu_v)(\alpha_{2h} + \mu_h + \delta)(\alpha_{1h} + \mu_h)(1 - R_0^2) \tag{21}$$

Where

$$R_0 = \sqrt{\frac{\lambda_v \lambda_h (\alpha_{1v})(\alpha_{1h}) \pi_v \pi_h}{\mu_v \mu_h (\alpha_{1h} + \mu_h)(\alpha_{2h} + \mu_h + \delta)(\alpha_{1v} \mu_v + \mu_v^2)}}$$

Thus the eigenvalues of the model are real and negative if therefore the DFE R_0^2 is Locally Asymptotically stable.

2.5. Stability of endemic equilibrium

In this section, we show the stability of the endemic equilibrium by proving the following lemma

Lemma 2. *The endemic equilibrium of the dynamic model is globally asymptotically stable if* $R_0 > 1$.

$$\begin{bmatrix} -(p_1+\mu_h) & 0 & 0 & \sigma & 0 & 0 & -p_2 \\ p_1 & -(\alpha_{1h}+\mu_h) & 0 & 0 & 0 & 0 & p_2 \\ 0 & \alpha_{1h} & -(\alpha_{2h}+\mu_h+\delta) & 0 & 0 & 0 & 0 \\ 0 & 0 & \alpha_{2h} & -(\mu_h+\sigma) & 0 & 0 & 0 \\ 0 & 0 & -p_3 & 0 & -(p_4+\mu_v) & 0 & 0 \\ 0 & 0 & p_3 & 0 & p_4 & -(\alpha_{1v}+\mu_v) & 0 \\ 0 & 0 & 0 & 0 & 0 & \alpha_{1v} & -\mu_v \end{bmatrix} \tag{22}$$

One eigen value $= -\mu_v$ which the remaining eigen values can be obtained from

$$\begin{bmatrix} -(p_1+\mu_h) & 0 & 0 & \sigma & 0 & 0 \\ p_1 & -(\alpha_{1h}+\mu_h) & 0 & 0 & 0 & 0 \\ 0 & \alpha_{1h} & -(\alpha_{2h}+\mu_h+\delta) & 0 & 0 & 0 \\ 0 & 0 & \alpha_{2h} & -(\mu_h+\sigma) & 0 & 0 \\ 0 & 0 & -p_3 & 0 & -(p_4+\mu_v) & 0 \\ 0 & 0 & p_3 & 0 & p_4 & -(\alpha_{1v}+\mu_v) \end{bmatrix} \tag{23}$$

Therefore we get that the eigen values from the matrix are

$$\begin{aligned} &(\mu_h+\sigma), (\alpha_{2h}+\mu_h+\delta), (\alpha_h+\mu_h), \\ &(\alpha_v+\mu_v), (p_4+\mu_v) \ \ and \ \ (p_1-\mu_h) \end{aligned} \tag{24}$$

Now, it is easy to see that $Trace(M*)<0$

$$\begin{aligned} trace(M*) = &-p_1 - 4\mu_h - \alpha_{1h} - \alpha_{2h} \\ &- \delta - \sigma - p_4 - \alpha_v < 0 \end{aligned} \tag{25}$$

The Determinant

$$\begin{aligned} (M*) = &(-P_1-\mu_h)(-\alpha_h-\mu_h)(-\alpha_{2h}-\mu_h-\delta) \\ &(-\mu_h-\sigma)(-p_4-\mu_v)(-\alpha_v-\mu_v) \end{aligned} \tag{26}$$

$$That \ is \ Det(M*) > 0$$

According to Routh-Hurwitz condition, all eigenvalues of matrix M* are real and negative if Trace (M*)<0 and Det (M*) >0. Thus All eigenvalues are real and negative so the endemic equilibrium is asymptotically stable and unstable if $R_0 > 1$.

2.6. Mathematical analysis of the model with control measures

Using Pontryagin's Maximum Principle, we formulated an objective functional and present the existence of optimal control. Given the optimal control problem, the objective functional J formulates the optimization problem of identifying the most elective strategies. The overall preselected objective involves the minimization of the number of quarantined, exposed, infectious individuals and the viral spread in the environment over a finite time interval [0, T].

$U = \{(u_1, u_2) \in U\}$is Lebesgue measurable on [0,1], $0 \leq u_i(t) \leq 1 \in [0, T], i = 1, 2$

We define the objective functional J, as follows:

$$J(u_1, u_2) = \int_0^T \left(A_1 I + A_2 E + \frac{1}{2}\left(B_1 {u_1}^2 + B_2 {u_2}^2 \right) \right) dt \tag{27}$$

Subject to

$$\begin{aligned} \frac{dS_h}{dt} &= \pi_h - (1-u_1) b\beta_h S_h I_v - \mu_h S_h + \sigma R_h \\ \frac{dE_h}{dt} &= (1-u_1) b\beta_h S_h I_v - (\alpha_{1h}+\mu_h) E_h \\ \frac{dI_h}{dt} &= \alpha_{1h} E_h - (\alpha_{2h}+\mu_h+\delta) I_h - u_2 I_h \\ \frac{dR_h}{dt} &= u_2 I_h + \alpha_{2h} I_h - (\mu_h+\sigma) R_h \\ \frac{dS_v}{dt} &= \pi_v - \beta_v S_v I_h - \mu_v S_v \\ \frac{dE_v}{dt} &= \beta_v S_v I_h - (\alpha_{1v}+\mu_v) E_v \\ \frac{dI_v}{dt} &= \alpha_{1v} E_v - \mu_v I_v \end{aligned} \tag{28}$$

$S_h(0) > 0$, $E_h(0) > 0$, $I_h(0) > 0$, $R_h(0) > 0$, $S_v(0) > 0$, $E_v(0)>0$ and $I_v(0) > 0$

In the objective function ?? is the final time and quantitiesA_1, $A_2$are weights constants of the virus in the environment, infected individuals, exposed individuals and quarantined respectively.

In other to achieve the objective of the control problem, we seek the functions $({u_1}^*(t), {u_2}^*(t))$ such that

$$J({u_1}^*(t), {u_2}^*(t)) = \min\{J(u_1, u_2), (u_1, u_2) \in U\} \tag{29}$$

2.7. Existence of an optimal control

Theorem 3. *Given the objective functional* $J(u_1, u_2)$ *as in* (27) *above, where the control set U is measurable subject to with initial conditions given at t = 0, then there exists an optimal control* $u^* = ({u_1}^*(t), {u_2}^*(t))$ *such that*

$$J({u_1}^*(t), {u_2}^*(t)) = \min\{J(u_1, u_2), (u_1, u_2) \in U\}$$

Proof. Due to the convexity of the integrand of J to control measuresu_1, u_2, the priori boundedness of the solutions of both the state and adjoint equations and the Lipchitz property of the state system with respect to the state variables, then the optimal control exist. □

Now we need to show the optimal solution. To achieve this, we need the Lagrangian (L) and Hamiltonian (H) for the optimal control problem.

The Lagrangian is given as

$$L = A_1 I + A_2 E + \frac{1}{2}\left(B_1 {u_1}^2 + B_2 {u_2}^2 \right) \tag{30}$$

Then the Hamiltonian function for the system is

$$\begin{aligned} H &= A_1 I_h + A_2 E_h + \tfrac{1}{2}\left(B_1 {u_1}^2 + B_2 {u_2}^2\right) \\ &+\Omega_{S_h}\left[\pi_h - (1-u_1) b\beta_h S_h I_v - \mu_h S_h + \sigma R_h\right] \\ &+\Omega_{E_h}\left[(1-u_1) b\beta_h S_h I_v - (\alpha_{1h} + \mu_h) E_h\right] \\ &+\Omega_{I_h}\left[\alpha_{1h} E_h - (\alpha_{2h} + \mu_h + \delta) I_h - u_2 I_h\right] + \\ &\Omega_{R_h}\left[u_2 I_h + \alpha_{2h} I_h - (\mu_h + \sigma) R_h\right] \\ &+\Omega_{S_V}\left[\pi_v - \beta_v S_v I_h - \mu_v S_v\right] \\ &+\Omega_{E_V}\left[\beta_v S_v I_h - (\alpha_{1v} + \mu_v) E_v\right] + \Omega_{I_v}\left[\alpha_{1v} E_v - \mu_v I_v\right] \end{aligned} \tag{31}$$

where $\Omega_j, j \in \{S_h, E_h, I_h, R_h, S_v, E_v, I_v\}$ are the disjoint variables.

Now we can apply the necessary conditions to the Hamiltonian (H).

Theorem 4. *Given an optimal control $u^* = ({u_1}^*(t), {u_2}^*(t))$and a solution $y^* = ({S_h}^*, {E_h}^*, {I_h}^*, {R_h}^*, {S_v}^*, {E_v}^*, {I_v}^*)$of the corresponding state system, there exists adjoint variable $\Omega_j, j \in \{S_h, E_h, I_h, R_h, S_v, E_v, I_v\}$satisfying*

$$\begin{aligned} \frac{d\Omega_{S_h}}{dt} &= \left[\Omega_{S_h}\left[(1-u_1) b\beta_h I_v - \mu_h\right] - \Omega_{E_h}\left[(1-u_1) b\beta_h I_v\right]\right] \\ \frac{d\Omega_{E_h}}{dt} &= -A_2 + \left[\Omega_{E_h}\left[(\alpha_{1h} + \mu_h)\right] - \Omega_{I_h}(\alpha_{1h})\right] \\ \frac{d\Omega_{I_h}}{dt} &= -A_1 + \left[\Omega_{I_h}\left[(\alpha_{2h} + \mu_h + \delta) + u_2\right] - \Omega_{R_h}(u_2 + \alpha_{2h}) + \Omega_{S_v}(\beta_v S_v) - \Omega_{E_v}(\beta_v S_v)\right] \\ \frac{d\Omega_{R_h}}{dt} &= \left[-\Omega_{S_h}(\sigma) + \Omega_{R_h}(\mu_h + \sigma)\right] \\ \frac{d\Omega_{S_v}}{dt} &= \left[\Omega_{S_v}(\beta_v I_v + \mu_v) - \Omega_{E_v}(\beta_v I_h)\right] \\ \frac{d\Omega_{E_v}}{dt} &= \left[\Omega_{E_v}(\alpha_{1v} + \mu_v) - \Omega_{I_v}(\alpha_{1v})\right] \\ \frac{d\Omega_{I_v}}{dt} &= \left[(\Omega_{S_h}(1-u_1) b\beta_h S_h) - \Omega_{E_h}\left[(1-u_1) b\beta_h S_h\right] + \Omega_{I_v}(\mu_v)\right] \end{aligned} \tag{32}$$

With transversality conditions $\Omega_j, j(T) \in \{S_h, E_h, I_h, R_h, S_v, E_v, I_v\}$
Therefore the control function are given by

$$\begin{aligned} {u_1}^* &= \min\left\{1, \max\left\{0, \Lambda_1\right\}\right\}, \quad {u_1}^* = \min\left\{1, \max\left\{0, \Lambda_1\right\}\right\}, \\ {u_2}^* &= \min\left\{1, \max\left\{0, \Lambda_2\right\}\right\}, , \quad {u_2}^* = \min\left\{1, \max\left\{0, \Lambda_2\right\}\right\}, , \end{aligned} \tag{33}$$

Where

$$\begin{aligned} \Lambda_1 &= \frac{(\Omega_{E_h} - \Omega_{S_h})\lambda S_h I_v}{B_1} \\ \Lambda_2 &= \frac{(\Omega_{E_h} - \Omega_{S_h}) I_h}{B_2} \end{aligned} \tag{34}$$

To determine the adjoint equation and the transversality condition, we make use of the Halmitonian H. we differentiate the Halmitonian with respect to $S_h, E_h, I_h, R_h, S_v, E_v, I_v$. Then we have the adjoins equation to be

$$\begin{aligned} \frac{d\Omega_{S_h}}{dt} &= -\frac{\partial H}{dS_h} = \left[\Omega_{S_h}\left[(1-u_1) b\beta_h I_v - \mu_h\right] - \Omega_{E_h}\left[(1-u_1) b\beta_h I_v\right]\right] \\ \frac{d\Omega_{E_h}}{dt} &= -\frac{\partial H}{dE_h} = -A_2 + \left[\Omega_{E_h}\left[(\alpha_{1h} + \mu_h)\right] - \Omega_{I_h}(\alpha_{1h})\right] \\ \frac{d\Omega_{I_h}}{dt} &= -\frac{\partial H}{dI_h} = -A_1 + \left[\Omega_{I_h}\left[(\alpha_{2h} + \mu_h + \delta) + u_2\right] - \Omega_{R_h}(u_2 + \alpha_{2h}) + \Omega_{S_v}(\beta_v S_v) - \Omega_{E_v}(\beta_v S_v)\right] \\ \frac{d\Omega_{R_h}}{dt} &= -\frac{\partial H}{dR_h} = \left[-\Omega_{S_h}(\sigma) + \Omega_{R_h}(\mu_h + \sigma)\right] \\ \frac{d\Omega_{S_v}}{dt} &= -\frac{\partial H}{dS_v} = \left[\Omega_{S_v}(\beta_v I_v + \mu_v) - \Omega_{E_v}(\beta_v I_h)\right] \\ \frac{d\Omega_{E_v}}{dt} &= -\frac{\partial H}{dE_v} = \left[\Omega_{E_v}(\alpha_{1v} + \mu_v) - \Omega_{I_v}(\alpha_{1v})\right] \\ \frac{d\Omega_{I_v}}{dt} &= -\frac{\partial H}{dI_v} = \left[(\Omega_{S_h}(1-u_1) b\beta_h S_h) - \Omega_{E_h}\left[(1-u_1) b\beta_h S_h\right] + \Omega_{I_v}(\mu_v)\right] \end{aligned} \tag{35}$$

With transversality conditions $\Omega_j, j(T) \in \{S_h, E_h, I_h, R_h, S_v, E_v, I_v\}$. To minimize the Halmitonian, H, with respect to the optimal controls, we differentiate H with respect tou_1, u_2. We then obtain the solution by equating the results to zero. This gives the optimal control required and applying the boundary condition of each of these controls, the solution becomes

$$\begin{aligned} {u_1}^* &= \min\left\{1, \max\left\{0, \Lambda_1\right\}\right\}, \quad {u_1}^* = \min\left\{1, \max\left\{0, \Lambda_1\right\}\right\}, \\ {u_2}^* &= \min\left\{1, \max\left\{0, \Lambda_2\right\}\right\}, \quad {u_2}^* = \min\left\{1, \max\left\{0, \Lambda_2\right\}\right\}, \end{aligned}$$

$$\begin{aligned} \text{Where} \quad \Lambda_1 &= \frac{(\Omega_{E_h} - \Omega_{S_h})\lambda S_h I_v}{B_1} \\ \Lambda_2 &= \frac{(\Omega_{E_h} - \Omega_{S_h}) I_h}{B_2} \qquad \text{Proved.} \end{aligned} \tag{36}$$

3. Numerical simulation

To observe the dynamics mathematical modelling of the spread of malaria disease with control over time, numerical simulations were done using MATLAB (2018) software. We make use of the variables in Table 1 and the parameters given in Table 2 in simulation, based on the data provided. Some values assigned to the parameters were derived from epidemiological literature while others were estimated.

Table 1: Description of variables in the system.

State variables	Description
$S_h\,(t)$	Susceptible Human
$E_h\,(t)$	Exposed Humans
$I_h\,(t)$	Infectious Human
$R_h\,(t)$	Recovered Humans
$S_v\,(t)$	Susceptible Human
$E_v\,(t)$	Exposed Humans
$I_v\,(t)$	Infectious Human

4. Discussion

In this paper, we formulated a mathematical model for the transmission dynamics of malaria with two time-dependent control measures. We first consider control parameters to be zero and perform mathematical analysis of the model. The analysis showed that there exists a domain where the model is epidemiologically and mathematically well-posed. Stability analysis of the model showed that the disease-free equilibrium is locally asymptotically stable if the reproduction number$R_0 < 1$. If $R_0 > 1$, the unique endemic equilibrium exist and is globally asymptotically stable.

We then consider the case of time-dependent control variable from where we formulated an optimal control problem and derived expressions for the optimal control for the malaria model with two control variables to minimize the number of malaria infections in human. In the optimal control problem, the use of one control and a combination of interventions can be explored to investigate and compare the effects of control strategies on malaria eradication for different transmission settings. The analysis of the model showed that the state and optimal control can be calculated using the optimal system.

The findings showed that, for the epidemic-prone areas, the optimal control for reducing the infected human and mosquito population was the use of bed nets and treatment. Findings from each graph are outlined as follows

Fig 2: The mathematical modeling dynamics of the SEIR-SEI model considering only the Human population before intervention strategies. From the graph, we observe that the susceptible rate reduces very fast as people get exposed to the infection. However, people can recover through natural immunity from the disease.

Fig 3: The mathematical modeling dynamics of the SEIR-SEI model considering only the Mosquitoes population before intervention strategies. Our observation showed that, without control strategies in place, the mosquito population gets exposed within a short time and hereby leads to infection.

Fig 4: shows the effect of control interventions on the Exposed human population. Varying the control measures (use of mosquito net and treatment). We observed that the interventions of control measures help to reduce the exposed population.

Fig 5: shows the effect of control interventions on the Infected human population. Varying the control measures (use of mosquito net and treatment). We observed that the interventions of control measures help to reduce the infected population.

Fig 6: shows the effect of control interventions on the Recovered human population. Varying the control measures (use of mosquito net and treatment). It was observed that the interventions of control measures help to increase the recovered population.

Fig 7: shows the effect of control interventions on the exposed mosquito population. Varying the control measures (use of mosquito net and treatment), we observed that the interventions of control measures do not affect the exposed mosquito population.

Fig 8: shows the effect of control interventions on the infected mosquito population. Varying the control measures (use of mosquito net and treatment), we observed that the interventions of control measures have no effect on the infected mosquito population.

Therefore, it is observed that the control intervention is adequate in reducing the rate of spread malaria infection in the human population.

5. Conclusion

The research work aims to explore the transmission dynamics and optimal control of malaria infection. This study considered the effect of two optimal controls (Use of bed net and Treatment). numerical simulations were done using MATLAB (2018) software. We make use of the variables in Table 1 and the parameters given in Table 2 in simulation based on the data provided. Some values assigned to the parameter were derived from epidemiological literature while others were estimated. The result from the numerical simulations shows that interventions of control measures help to increase the recovered population.

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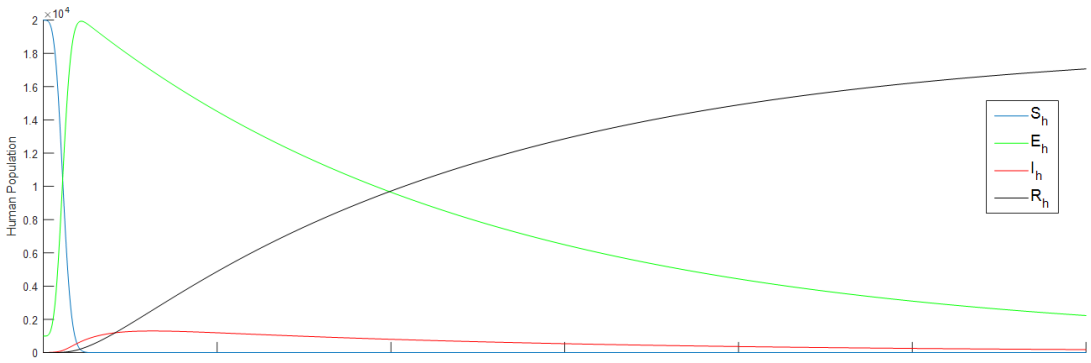

Figure 2: Transmission dynamics of malaria infection (Human population) over time.

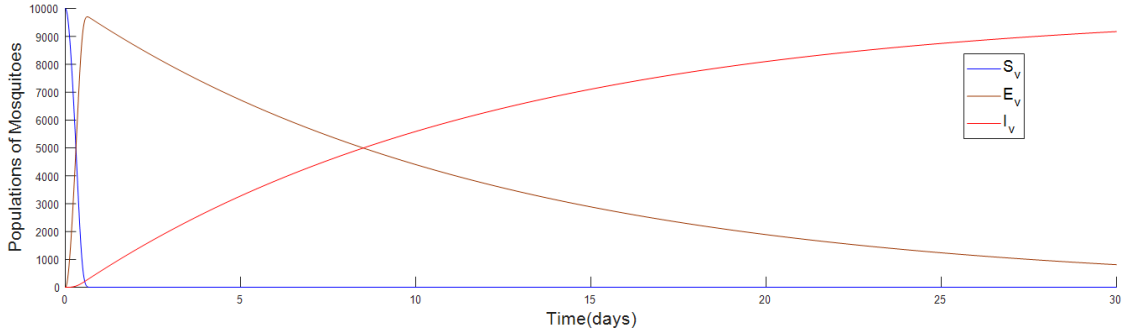

Figure 3: Transmission dynamics of malaria infection (Mosquito population) over time.

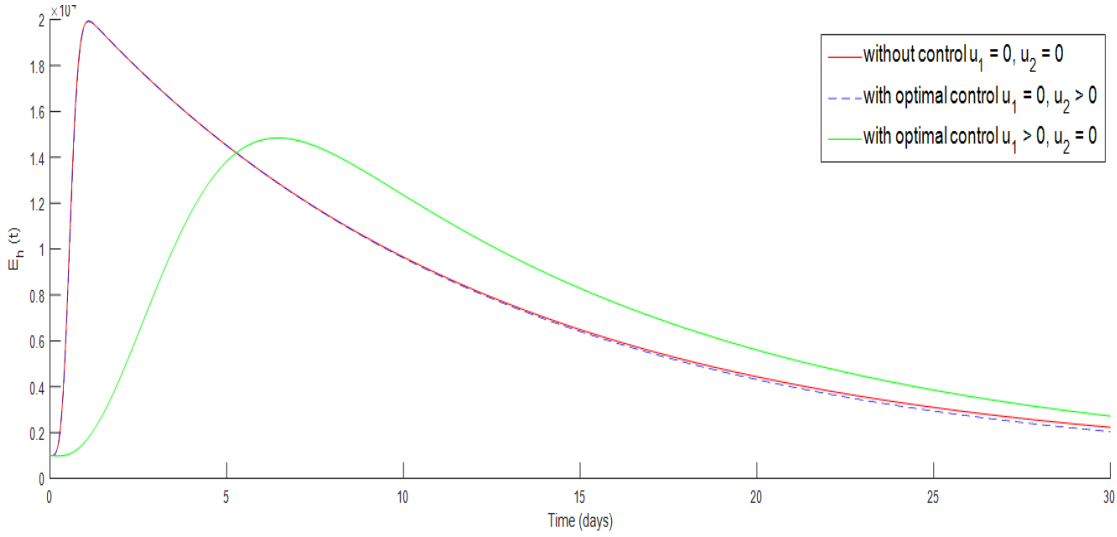

Figure 4: Solution trajectories for Exposed human individuals with optimal control.

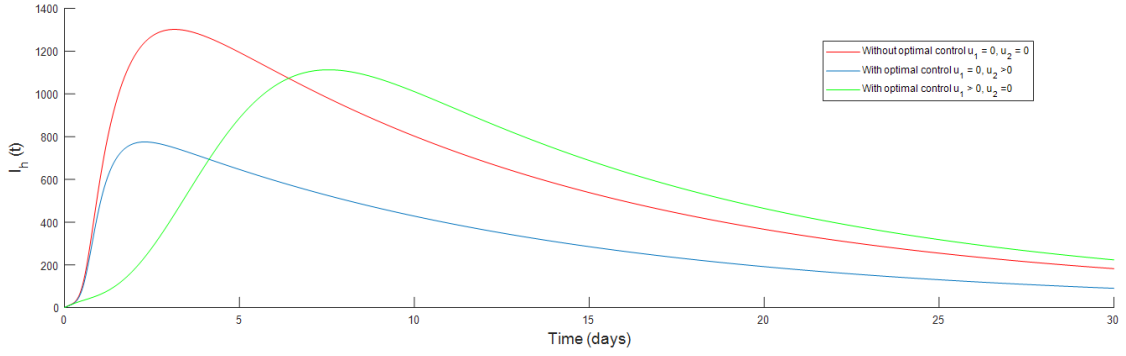

Figure 5: Solution trajectories for Infected human individuals with optimal control.

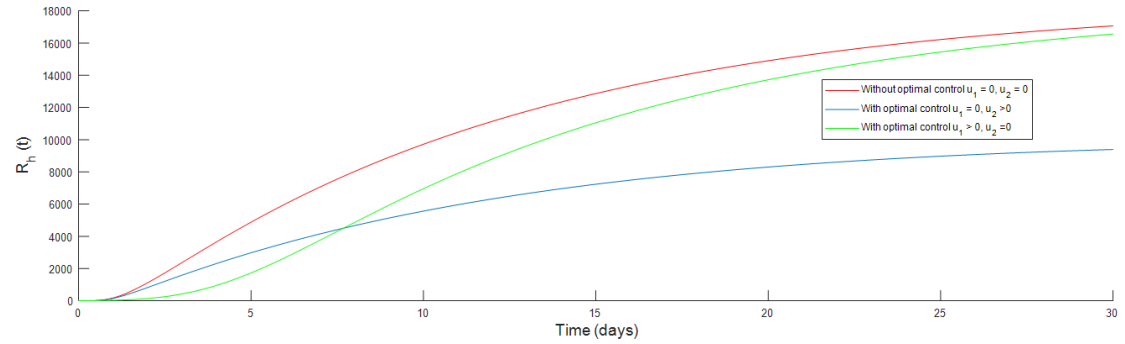

Figure 6: Solution trajectories for Recovered human individuals with optimal control.

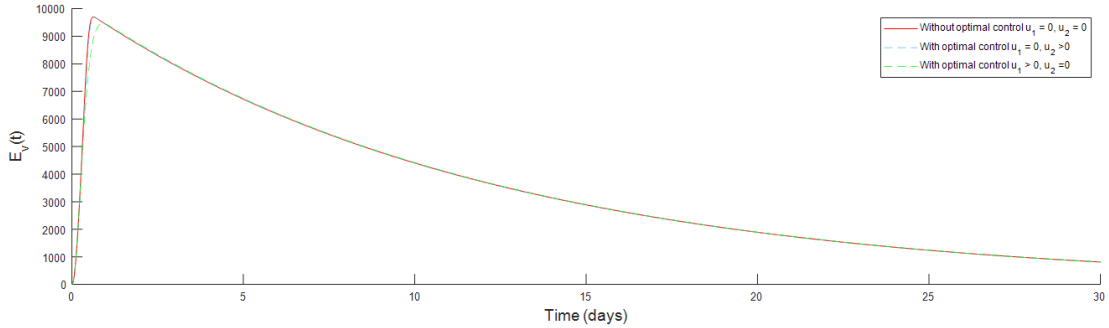

Figure 7: Solution trajectories for Exposed population with optimal control.

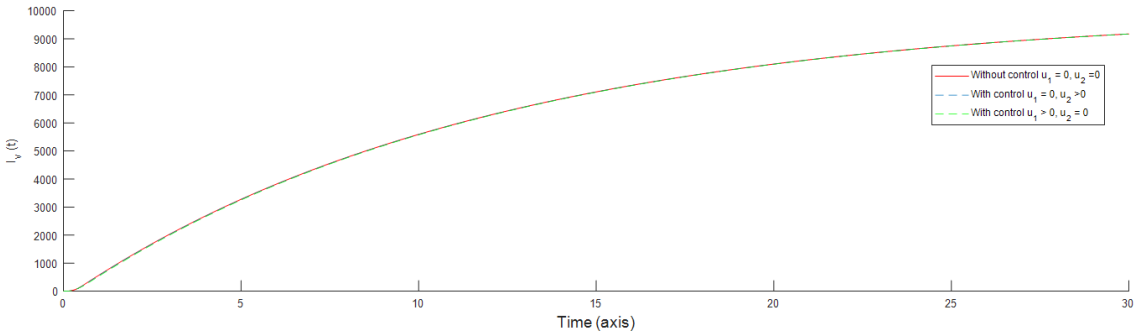

Figure 8: Solution trajectories for Infected mosquito population with optimal control.

Table 2: Symbols and Values of parameters used in the model.

Description of parameter	Symbols	Value
Recruitment rate (human population)	π_h	0.0043
Recruitment rate (Mosquito population)	π_v	0.0071
Probability of Infection	b	0.39
Natural death rate for humans	μ_h	0.0000472
Natural death rate of mosquitoes	μ_v	0.0000472
Rate of progressive recovered human individual to the susceptible class	σ	0.00274
Rate of progressive susceptible human individuals to the exposed class	β_h	0.000025
Rate of progressive susceptible mosquito individuals to the exposed class	β_v	0.000034
Rate of progressive Exposed human individuals to the infectious class	α_{1h}	0.08333
Rate of progressive Infected human individuals to the recovered class	α_{2h}	0.48
Rate of progressive Exposed mosquito individuals to the recovered class	α_{1v}	0.0845
Death Rate of humans caused by Infection	δ	0.083