A Mathematical Modelling of the Effect of Treatment in the Control of Malaria in a Population with Infected Immigrants

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Abstract

In this work, we developed a compartmental bio-mathematical model to study the effect of treatment in the control of malaria in a population with infected immigrants. In particular, the vector-host population model consists of eleven variables, for which graphical profiles were provided to depict their individual variations with time. This was possible with the help of MathCAD software which implements the Runge-Kutta numerical algorithm to solve numerically the eleven differential equations representing the vector-host malaria population model. We computed the basic reproduction ratio $R_0$ following the next generation matrix. This procedure converts a system of ordinary differential equations of a model of infectious disease dynamics to an operator that translates from one generation of infectious individuals to the next. We obtained $R_0 = \sqrt{R_{0m} \times R_{0h}}$, i.e., the square root of the product of the basic reproduction ratios for the mosquito and human populations respectively. $R_{0m}$ explains the number of humans that one mosquito can infect through contact during the life time it survives as infectious. $R_{0h}$ on the other hand describes the number of mosquitoes that are infected through contacts with the infectious human during infectious period. Sensitivity analysis was performed for the parameters of the model to help us know which parameters in particular have high impact on the disease transmission, in other words on the basic reproduction ratio $R_0$.

Keywords

Malaria Control, Infected Immigrants, Basic Reproduction Ratio, Differential Equations, MathCAD Simulation
1. Introduction

Malaria is a highly prevalent infectious disease especially in the tropical and subtropical areas. **Figure 1** below is a map obtained from WHO Malaria Report 2010 [1], depicting the countries where malaria was endemic in 2009 (shaded region).

In addition to being widespread, malaria is also a deadly disease. This is because statistics has shown that for Africa in particular, annually 145,000 million to 150,000 million infections are reported, among which, 800 to 850 cases result in deaths as shown in **Table 1**. Most of the deaths are either children under five or pregnant women. Typical symptoms of malaria infections start with headache, followed by periodic bouts of fevers and chills, and sometimes even coma. The period of cyclical fevers lasts several days, during which time a high probability of dying has been observed for children, since their immune systems are weak. Such fever can also lead to abortions in pregnant women.

1.1. Brief Analysis of Malaria Data

It is interesting to do a quick statistical analysis of the data in **Table 1**, for the malaria cases in Africa as provided by WHO (**Figure 2**). We perform a nonlinear regression analysis for both the reported cases (C) and deaths (D) against time (T). The result follows from SPSS.

![Figure 1. Malaria endemic countries 2009.](image)

**Table 1.** Estimates of malaria cases and deaths in Africa by WHO, 2000-2009.

<table>
<thead>
<tr>
<th>Year</th>
<th>2000</th>
<th>2001</th>
<th>2002</th>
<th>2003</th>
<th>2004</th>
<th>2005</th>
<th>2006</th>
<th>2007</th>
<th>2008</th>
<th>2009</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases ($\times 10^3$)</td>
<td>173,000</td>
<td>178,000</td>
<td>181,000</td>
<td>185,000</td>
<td>187,000</td>
<td>188,000</td>
<td>187,000</td>
<td>186,000</td>
<td>181,000</td>
<td>176,000</td>
</tr>
<tr>
<td>Deaths ($\times 10^3$)</td>
<td>900</td>
<td>893</td>
<td>885</td>
<td>880</td>
<td>870</td>
<td>853</td>
<td>832</td>
<td>802</td>
<td>756</td>
<td>709</td>
</tr>
</tbody>
</table>
Figure 2. Quadratic regression model for malaria cases 2000-2009.

Model Summary and Parameter Estimates. Dependent Variable: C (Numbers of cases)

<table>
<thead>
<tr>
<th>Equation</th>
<th>Model Summary</th>
<th>Parameter Estimates</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>R Square</td>
<td>F df1 df2 Sig.</td>
</tr>
<tr>
<td>Quadratic</td>
<td>0.981</td>
<td>180.044 2 7 0.000</td>
</tr>
</tbody>
</table>

The independent variable is T.

Observation: It is quite clear from the WHO data, for the number of malaria cases reported over the 10 year period that the incidence of malaria infection follows a parabolic curve, rising sharply initially, to reach a maximum and then declining sharply thereafter (Figure 3). The equation of the parabola is given by:

\[ C = 165283.3 + 7609.85T - 647.73T^2 \]

with goodness of fit \( R^2 = 0.981 \).

Model Summary and Parameter Estimates. Dependent Variable: D (Number of deaths)

<table>
<thead>
<tr>
<th>Equation</th>
<th>Model Summary</th>
<th>Parameter Estimates</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>R Square</td>
<td>F df1 df2 Sig.</td>
</tr>
<tr>
<td>Quadratic</td>
<td>0.992</td>
<td>438.638 2 7 0.000</td>
</tr>
</tbody>
</table>

The independent variable is T.

Observation: The number of malaria related deaths over the 10 year period as depicted in the above graph, follows a parabolic curve, rising from a high value initially, then reaching a maximum and then declining sharply thereafter. The equation of the parabola is given by:

\[ D = 882.883 + 12.07T - 2.89T^2 \]

with goodness of fit \( R^2 = 0.992 \).
1.2. Life Cycle of Malaria Parasites

Malaria is a vector-borne disease [2]. Malaria parasites are transferred between humans through mosquitoes. The malaria parasite life cycle is divided into two parts, one is within host (human) body and the other is within vector (mosquito) body.

Human infection starts from a blood meal of an infectious female mosquito. The parasites existing in the infectious mosquito’s saliva, called sporozoites at this stage, enter the bloodstream of the human through mosquito bites and migrate to the liver. Within minutes after entering in the human body, sporozoites infect hepatocytes, and multiply asexually and asymptptomatically in liver cells for a period of 5 - 30 days [3]. This period is called the exo-erythrocytic stage. At the end of this stage, thousands of merozoites (schizonts) emerge inside an infected liver cell. These merozoites rupture their host cells undetectably by wrapping themselves in the membrane of infected liver cells. Then, merozoites escape into the bloodstream and get ready to infect red blood cells. Once entering the bloodstream, free merozoites undergo the so-called erythrocytic stage, in which merozoites invade red blood cells to develop ring forms before experiencing asexual or sexual maturation. Within the red blood cells, a proportion of parasites keep multiplying asexually and periodically break out of infected old red blood cells to invade fresh red blood cells. Such amplification cycles may cause the symptom of waves of fever. The remaining parasites follow sexual maturation and produce male (micro-) and female (macro-) gametocytes which may be taken up by bites of female mosquitoes. Finally, when it has developed into an infectious form, it spreads the disease to a new mosquito that bites the infectious human.
1.3. Malaria Control and Treatments

According to the transmission procedure of malaria, there are three conditions for the prevalence of the disease:

1) High density of Anopheles mosquitoes,
2) High density of human population,
3) Large rate of transmission of parasites between human beings and mosquitoes.

Obviously, not too much can be done in respect to (2). So, (1) and (3) are naturally targeted. That is, either controlling the population of Anopheles female mosquitoes at a lower level, or avoiding biting by mosquitoes can reduce the chance of malaria becoming endemic. In the middle of the last century, people in Africa have already knew how to remove or poison the breeding grounds of mosquitoes or the aquatic habitats of the larva stages, such as by filling or applying oil to places with standing water, to control the population of mosquitoes \[4\]. Later, pesticide was widely employed to eliminate mosquitoes. On the other hand, mosquito nets, bedclothes and mosquito-repellent incense (indoor residual spraying) also help to keep mosquitoes far away from people and minimize the biting rate, greatly reducing the chance of infection and transmission of malaria. There are some effective drugs for malaria patients currently. For example, Chloroquine, Quinine, Primaquine and combinations of some other drugs like sulfadoxine and pyrimethamine (SP) are effective medicines for treating infections caused by the five major parasites. Although malaria is an entirely preventable or curable disease thanks to these effective medicines, there are still millions of people suffering from this disease, who are too poor to afford full treatments. Moreover, insufficient treatments due to poor economic conditions, may result in drug resistance and lead to emergence of new (drug resistant) strains of malaria parasites. For instance, the first case of resistance to Chloroquine was documented in 1957. Chloroquine, Quinine and Sulfadoxine-pyrimethamine resistance cases have been reported in almost all disease endemic areas \[5\].

1.4. Control of Mosquito-Borne Infections

In order to control mosquito-borne infections one can adopt the following measures;

- Reduce vector population: Make environment less mosquito-friendly by draining stagnant water.
- Use insecticides; not without problems: for example some mosquitoes become insecticide resistant.
- Prevent mosquitoes biting people. Insecticide-laced bed nets, although this is ineffective against mosquitoes that mainly bite during the day (e.g. *A. aegypti*).
- Vaccines and drug treatments. Not always available, there are problems with drugs and drug resistance.
1.5. The Ross-Macdonald Malaria Model

The first and simplest model of malaria was developed by [6] Ross and later extended by Macdonald [7]. This so-called Ross-Macdonald model is the best-known and most widely used model. Despite its simple structure as shown below, it enables us to interpret and compare a broad range of epidemiological models.

1.6. Remark

In the Ross-Macdonald model of malaria transmission, the flow of human from a susceptible class to an infected class and through recovery from infection, the reverse is shown in the upper part of the Figure 4. The flow of mosquitoes from susceptible class to an infected class, and finally to an infectious class is shown further down. The human and mosquito population are linked through the transmission process.

1.7. Statement of the Problem

The development of the means intended to reduce the spread of malaria infections and eradication necessitates decisive measures to curb the malaria epidemic. In particular, sustained minimization of the number of humans with incidence of malaria as a result of adequate control, can be attained by developing a suitable mathematical model which can enable us to understand better the dynamics and control of the vector-host endemic.

In developing the model, the human population is compartmentalized into seven classes including the susceptible, infected, exposed, treated, non-treated, recovered, and protected classes. For the mosquito population, we have four classes, namely; class of mosquito larva, susceptible mosquitoes, infected mosquitoes and exposed mosquitoes. We assume free interaction between the vector and host populations. The mathematical analysis of the compartmental models leads us to eleven coupled systems of nonlinear ordinary differential equations.

2. Construction of the Compartmental Model

In this section we develop a compartmental bio-mathematical model (Figure 5)
to study the effect of treatment in the control of malaria in a population with infected immigrants.

From the above compartmental model we obtain the following equations for the dynamics of the human-mosquito interaction.

### 2.1. Human Population

\[
\frac{dS_H}{dt} = (1-q)\Lambda_H + \alpha_J A + \rho R_H - \frac{\beta_H I_H S_H}{N_H} - \alpha_S S_H - \delta_H S_H \\
\frac{dE_H}{dt} = \frac{\beta_H I_H S_H}{N_H} - gE_H - \delta_E E_H \\
\frac{dI_H}{dt} = gE_H + q\Lambda_H - k_I I_H - k_2 I_H - \delta_H I_H \\
\frac{dE_H}{dt} = k_I I_H - (\omega_H + \delta_H) I_H \\
\frac{dT_H}{dt} = k_I I_H - \gamma T_H - \delta_H T_H \\
\frac{dR_H}{dt} = \gamma T_H - (\mu + \rho + \delta_H) R_H \\
\frac{dA}{dt} = \alpha_A S_H + \mu R_H - \alpha_A A - \delta_H A
\]  

### 2.2. Mosquito Population

\[
\frac{dL_M}{dt} = \lambda_M - mL_M - \delta_M L_M \\
\frac{dS_M}{dt} = mL_M - \beta_M I_M S_M - \delta_M S_M \\
\frac{dE_M}{dt} = \beta_M I_M S_M - \phi E_M - \delta_M E_M \\
\frac{dI_M}{dt} = \phi E_M - \delta_M I_M
\]
2.3. Remark

The state variables and parameters are defined in Table 2 and Table 3 respectively.

Table 2. State variables of the basic malaria model.

<table>
<thead>
<tr>
<th>Symbol</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>$S(t)$</td>
<td>Susceptible human population at time $t$</td>
</tr>
<tr>
<td>$E(t)$</td>
<td>Exposed human population at time $t$</td>
</tr>
<tr>
<td>$I(t)$</td>
<td>Infected human population at time $t$</td>
</tr>
<tr>
<td>$I_{nt}(t)$</td>
<td>Non-treated infected human population at time $t$</td>
</tr>
<tr>
<td>$T(t)$</td>
<td>Treated human population at time $t$</td>
</tr>
<tr>
<td>$R(t)$</td>
<td>Recovered human population at time $t$</td>
</tr>
<tr>
<td>$A(t)$</td>
<td>Protected human population at time $t$</td>
</tr>
<tr>
<td>$L(t)$</td>
<td>Population of mosquito larva at time $t$</td>
</tr>
<tr>
<td>$S_m(t)$</td>
<td>Population of susceptible mosquitoes at time $t$</td>
</tr>
<tr>
<td>$E_m(t)$</td>
<td>Population of exposed mosquitoes at time $t$</td>
</tr>
<tr>
<td>$I_m(t)$</td>
<td>Population of infected mosquitoes at time $t$</td>
</tr>
<tr>
<td>$N_H$</td>
<td>Total population size of humans</td>
</tr>
<tr>
<td>$N_M$</td>
<td>Total population size of mosquitoes</td>
</tr>
</tbody>
</table>

Table 3. Parameters of the basic malaria model.

<table>
<thead>
<tr>
<th>Symbol</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\Lambda_H$</td>
<td>Birth and immigrant rate of humans</td>
</tr>
<tr>
<td>$\Lambda_M$</td>
<td>Birth rate of mosquitoes</td>
</tr>
<tr>
<td>$\rho$</td>
<td>Rate of loss of immunity</td>
</tr>
<tr>
<td>$\beta_H$</td>
<td>Transmission rate of infection from infected mosquitoes to susceptible human</td>
</tr>
<tr>
<td>$\alpha_H$</td>
<td>Loss of immunity of protected class</td>
</tr>
<tr>
<td>$q$</td>
<td>Fraction of infective immigrants</td>
</tr>
<tr>
<td>$\alpha_L$</td>
<td>Progression rate of susceptible human to protected class</td>
</tr>
<tr>
<td>$k_H$</td>
<td>Treatment rate of human from infected state to treated class</td>
</tr>
<tr>
<td>$k_L$</td>
<td>Transmission rate of human from infected state to infectious none treated class</td>
</tr>
<tr>
<td>$g$</td>
<td>Progression rate of human from exposed to infected compartments</td>
</tr>
<tr>
<td>$\gamma$</td>
<td>Recovery rate of human from treated class</td>
</tr>
<tr>
<td>$\delta_H$</td>
<td>Natural death rate of human from exposed to infected</td>
</tr>
<tr>
<td>$\mu$</td>
<td>Progression rate of human from recovery class to protected class</td>
</tr>
<tr>
<td>$M$</td>
<td>Progression rate of mosquitoes from larva to susceptible</td>
</tr>
<tr>
<td>$\beta_M$</td>
<td>Transmission rate of infection from infected human to susceptible mosquitoes</td>
</tr>
<tr>
<td>$\delta_M$</td>
<td>Natural death rate of mosquitoes</td>
</tr>
<tr>
<td>$\phi$</td>
<td>Progression rate of exposed mosquitoes to infected mosquitoes</td>
</tr>
<tr>
<td>$\omega_H$</td>
<td>Disease-induced death rate of human</td>
</tr>
</tbody>
</table>
2.4. Invariant Region

The total population sizes $N_H$ and $N_M$ can be determined by

$$N_H = S_H + E_H + I_H + I_{HN} + T_H + A + R_H \quad \text{and} \quad N_M = L_M + S_M + E_M + I_M.$$  

Thus

$$\frac{dN_H}{dt} = \Lambda_H - \delta_H N_H - \alpha_H I_{HN}$$  

Without loss of generality, we can write

$$\frac{dN_H}{dt} \leq \Lambda_H - \delta_H N_H, \quad \frac{dN_M}{dt} \leq \Lambda_M - \delta_M N_M$$  

2.5. Lemma

The model system has solution which are contained in the feasible $\Omega = \Omega_H \times \Omega_M$.

Proof: let $\Omega = \{S_H, E_H, I_H, I_{HN}, T_H, A, R_H, L_M, S_M, E_M, I_M\} \in \mathbb{R}^{11}_+$ be any solution of the system with non-negative initial conditions. From Equation (13)

$$\frac{dN_H}{dt} \leq \Lambda_H - \delta_H N_H$$  

Adopting Birhoff and Rotta [8] theorem on differential inequality, we have

$$0 \leq N_H \leq \frac{\Lambda_H}{\delta_H}, \quad \Lambda_H - \delta_H N_H \geq C e^{-\delta_H t}$$  

where $C$ is a constant.

Therefore, all feasible solutions of the human population only of the model system are in the region.

$$\Omega_H = \left\{ (S_H, E_H, I_H, I_{HN}, T_H, A, R_H) \in \mathbb{R}^7_+ : N_H \leq \frac{\Lambda_H}{\delta_H} \right\}$$

Similarly the feasible set for model of the mosquitoes population only are in the region

$$\Omega_M = \left\{ (L_M, S_M, E_M, I_M) \in \mathbb{R}^4_+ : N_M \leq \frac{\Lambda_M}{\delta_M} \right\}$$

Therefore the feasible set for the model system is given by

$$\Omega = \left\{ (S_H, E_H, I_H, I_{HN}, T_H, A, R_H, L_M, S_M, E_M, I_M) \in \mathbb{R}^{11}_+ : N_H \leq \frac{\Lambda_H}{\delta_H} = N_H^*, \quad N_M \leq \frac{\Lambda_M}{\delta_M} = N_M^* \right\}$$

2.6. Mathematical Analysis of the Model

The nonlinear system (1)-(11) will be qualitatively analyzed so as to find the conditions for existence and stability of disease free equilibrium points. Analysis of the model allows us to determine the impact of treatment on the transmission of malaria infection in a population. Also on finding the reproductive number $R_0$, one can determine if the disease become endemic in a population or not [9]. However, one can see that adding the human equation of the model, with the case that there is no disease -induced death. From Equation (13)
Thus $\frac{\Lambda_H}{\delta_H}$ is the upper bound of $N_H(t)$ provided that $N_H(0) \leq \frac{\Lambda_H}{\delta_H}$. Similarly, $\frac{dN_M}{dt} = \Lambda_M - \delta_M N_M \Rightarrow N_M(t) \rightarrow \frac{\Lambda_M}{\delta_M}$ as $t \rightarrow \infty$.

Thus $\frac{\Lambda_M}{\delta_M}$ is the upper bound of $N_M(t)$ provided that $N_M(0) \leq \frac{\Lambda_M}{\delta_M}$.

Hence the invariant region is

$$\Omega = \left\{ \left( S_H, E_H, I_H, t_H, T_H, A, R_H, L_M, S_M, E_M, I_M \right) \in \mathbb{R}^{11}_+: N_H \leq \frac{\Lambda_H}{\delta_H} = N_H^*, \right. $$

$$\left. N_M \leq \frac{\Lambda_M}{\delta_M} = N_M^* \right\}$$

is positively invariant. Hence no solution path leaves through and boundary of $\Omega$. Since path cannot leave $\Omega$, solution remains non-negative for non negative initial conditions. This means that the solution exists for all positive time $t$. Therefore the model (1)-(11) is mathematically and epidemiological well-posed [10].

For convenience and to simplify the analysis of our model, we rewrite the model system (1)-(11) in terms of the proportions of individual in each class. Let

$$s_h = \frac{S_H}{N_H}, e_h = \frac{E_H}{N_H}, i_h = \frac{I_H}{N_H}, r_h = \frac{T_H}{N_H}, i_m = \frac{R_H}{N_H},$$

$$z = \frac{A}{N_H}, s_m = \frac{L_M}{N_H}, e_m = \frac{S_M}{N_H}, i_m = \frac{I_M}{N_H}.$$ 

Let $\pi = \frac{N_M}{N_H}$ be the female mosquito–human ratio, that is, the number of female mosquito per human host. The ratio $\pi = \frac{N_M}{N_H}$ is constant because a mosquito takes a fixed number of blood meals per unit independent of the population density of the host [11]. Also let

$$\Lambda_H = \Lambda_h, \Lambda_M = \Lambda_m, \beta_H = \beta_h, \delta_H = \delta_h, \beta_M = \beta_m, \delta_M = \delta_m, \omega_H = \omega_h.$$ 

The simplified model now becomes modified human and mosquito population models.

### 2.7. Modified Human Population

$$\frac{ds_h}{dt} = (1-q)\Lambda_h + \alpha z + \rho r_h - \beta_h i_m s_h - \alpha_i s_h - \delta_h s_h \quad (17)$$

$$\frac{de_h}{dt} = \beta_h i_m s_h - \delta_h e_h \quad (18)$$

$$\frac{di_h}{dt} = \delta e_h + q\Lambda_h - k_i i_h - k_s i_h - \delta h s_h \quad (19)$$
\[
\frac{di_h}{dt} = k_s i_h - (\omega_h + \delta_h) i_{ln}
\]
(20)

\[
\frac{dt_h}{dt} = k_t i_h - \gamma t_h - \delta_t t_h
\]
(21)

\[
\frac{dr_h}{dt} = \gamma t_h - (\mu + \rho + \delta_h) r_h
\]
(22)

\[
\frac{dz}{dt} = \alpha s_h + \mu r_h - \alpha z - \delta_h z
\]
(23)

### 2.8. Modified Mosquitoes Population

\[
\frac{dl_m}{dt} = \Lambda_m - ml_m - \delta_m l_m
\]
(24)

\[
\frac{ds_m}{dt} = ml_m - \beta_m s_m - \delta_m s_m
\]
(25)

\[
\frac{de_m}{dt} = \beta_m s_m - \phi e_m - \delta_m e_m
\]
(26)

\[
\frac{di_m}{dt} = \phi e_m - \delta_m i_m
\]
(27)

### 2.9. Positivity of Solutions

It is necessary to prove that all solutions of system (17)-(27) with positive initial data will remain positive for all times \( t > 0 \). This will be established by the following theorem.

#### 2.10. Theorem

Let the initial data be

\[
\begin{align*}
    s_h(0) &\geq 0, t_h(0) \geq 0, l_{ln}(0) \geq 0, i_{ln}(0) \geq 0, z(0) \geq 0, r_h(0) \geq 0, \\
    e_h(0) &\geq 0, s_m(0) \geq 0, t_m(0) \geq 0, e_m(0) \geq 0, i_m(0) \geq 0 \\
    &\in \Omega
\end{align*}
\]

Then the solution set \((s_h, e_h, i_h, l_{ln}, t_h, z, r_h, l_m, s_m, e_m, i_m)(t)\) of the model system (4) is positive for all \( t > 0 \).

Proof: From first equation of (17)

\[
\frac{ds_h}{dt} = (1-q) \Lambda_h + \alpha z + \rho r_h - \beta i_m s_h - \alpha_i s_h - \delta_h s_h \geq -\left(\beta i_m + \alpha_i + \delta_h\right) s_h
\]

\[
\Rightarrow \int_{s_h}^{s_h(t)} d(s_h) \geq -\left(\beta i_m + \alpha_i + \delta_h\right) dt
\]

\[
\therefore \quad s_h(t) \geq s_h(0) e^{-\left(\beta i_m + \alpha_i + \delta_h\right) t} \geq 0
\]

Following the above procedure, from equations (18)-(23), we obtain respectively the positivity conditions;

\[
\begin{align*}
    e_h(t) &\geq e_h(0) e^{-\left(\delta_i t + \delta_h\right) t} \geq 0, \\
    i_h(t) &\geq i_h(0) e^{-\left(\delta_i t + \delta_h\right) t} \geq 0, \\
    l_{ln}(t) &\geq l_{ln}(0) e^{-\left(\delta_i t + \delta_h\right) t} \geq 0, \\
    i_{ln}(t) &\geq i_{ln}(0) e^{-\left(\delta_i t + \delta_h\right) t} \geq 0, \\
    r_h(t) &\geq r_h(0) e^{-\left(\delta_i t + \delta_h\right) t} \geq 0, \\
    z(t) &\geq z(0) e^{-\left(\delta_i t + \delta_h\right) t} \geq 0.
\end{align*}
\]
Similarly for the modified mosquito population, equations (20)-(27) gives the positivity conditions:
\[
\begin{align*}
& l_m(t) \geq l_m(0) e^{-(\delta_{ih}+\delta_{h})t} \geq 0, \\
& e_m(t) \geq e_m(0) e^{-(\delta_{ie}+\delta_{e})t} \geq 0, \\
& i_m(t) \geq i_m(0) e^{-\delta_{i}t} \geq 0.
\end{align*}
\]

2.11. Existence and Stability of Steady-State Solutions

Let \( E^0 = \{ s_h^0, i_h^0, e_h^0, i_m^0, e_m^0, s_m^0, e_m^0, i_m^0 \} \) be the steady-state of the system (17)-(27) which can be calculated by setting the right hand side of the model (17)-(27) to zero, giving us the following:
\[
\begin{align*}
(1-q)\Lambda_h + \alpha r_h - \beta_{ih}s_h - \alpha_i s_h - \delta_i i_h &= 0 \\
\beta_{ih}i_h s_h - g e_h - \delta_h e_h &= 0 \\
ge_h + q\Lambda_h - k_i i_h - k s_h - \delta_i i_h &= 0 \\
k_i i_h - (\omega_h + \delta_h) i_h &= 0 \\
k_i i_h - (\gamma_h + \delta_h) t_h &= 0 \\
\gamma_h - (\mu + \rho + \delta_h) r_h &= 0 \\
\alpha_i s_h + \mu r_h - \alpha z - \delta_i z &= 0 \\
\Lambda_m - m l_m - \delta_i l_m &= 0 \\
ml_m - \beta_m i_m s_m - \delta_m s_m &= 0 \\
\beta_m i_m s_m - \phi e_m - \delta_m e_m &= 0 \\
\phi e_m - \delta_m i_m &= 0
\end{align*}
\]

2.12. Disease-Free Equilibrium Point

Disease-free equilibrium points (DFE) are steady-state solutions where there is no disease (malaria). The disease free equilibrium of the normalized model (17)-(27) is obtained by setting
\[
\begin{align*}
\frac{d s_h}{dt} &= \frac{d e_h}{dt} = \frac{d i_h}{dt} = \frac{d s_m}{dt} = \frac{d e_m}{dt} = \frac{d i_m}{dt} = \frac{d z}{dt} = \frac{d l_m}{dt} = \frac{d s_m}{dt} = \frac{d e_m}{dt} = \frac{d i_m}{dt} = 0
\end{align*}
\]

At disease free equilibrium we have,
\[
\begin{align*}
s_h &= \frac{\Lambda_h}{\delta_h}, \\
 s_m &= \frac{m \Lambda_m}{\delta_m (m + \delta_m)}, \\
e_h &= i_h = i_m = t_h = r_h = L_m = e_m = i_m = z = q = 0.
\end{align*}
\]

Therefore the disease free equilibrium (DFE) denoted by \( E^0 \) of the system (28)-(38) is given by
\[
E^0 = \left( s_h^0, i_h^0, e_h^0, i_m^0, e_m^0, s_m^0, e_m^0, i_m^0 \right)
\]
\[
= \left( \frac{\Lambda_h}{\delta_h}, 0, 0, 0, 0, 0, 0, 0, \frac{m \Lambda_m}{\delta_m (m + \delta_m)} \right)
\]

that represents the state in which there is no infection in the society and is known as the disease-free equilibrium point (DFE). This implies that at the dis-
ease-free equilibrium, the susceptible human population is equal to the total human population and the susceptible mosquito population is equal to the total mosquito population.

### 2.13. Local Stability of DFE

The disease free equilibrium of the model (17)-(27) was given by

\[
E^0 = \left( \delta_h^0, \epsilon_h^0, \tau_h^0, \lambda_h^0, \phi_h^0, \lambda_m^0, \phi_m^0, \epsilon_m^0, \epsilon_m^0, \frac{m \Lambda_m}{\delta_m (m + \delta_m)}, 0, 0 \right)
\]

### 2.14. Basic Reproduction Ratio

\( R_0 \) is often found through the study and computation of the eigenvalues of the Jacobian at the disease- or infectious-free equilibrium Diekmann [12] follow a different approach which is the next generation matrix method. This procedure converts a system of ordinary differential equations of a model of infectious disease dynamics to an operator (or matrix) that translate from one generation of infectious individuals to the next. The basic reproductive number is then defined as the spectral radius (dominant eigenvalue) of this operator. Van den Driessche and Watmough [9] describe such a method in detail for general deterministic compartmental models.

The dynamics of the model is specified by the IVP;

\[
\frac{dx_i}{dt} = f_i(x), \quad x(0) \in \mathbb{R}^n
\]  
(39)

We define \( \Theta_0 \) as the set of all disease-free states as

\[
\Theta_0 = \{ x \in \mathbb{R}^n : x_i = 0, 1 \leq i \leq m \}
\]  
(40)

Next we recast the IVP (4.39) in the form;

\[
\frac{dx_i}{dt} = F_i(x) - V_i(x)
\]  
(41)

where \( F_i(x) \) is the rate of new infections entering compartment \( i \), and \( V_i(x) = V_i^+(x) - V_i^-(x) \)  
(42)

where \( V_i^+(x) \) is the rate of transfer into compartment \( i \) by any other means, and \( V_i^-(x) \) is the rate of transfer out of compartment \( i \). Given a disease-free equilibrium point \( x_{\text{DFE}} \) of (39), with \( x_{\text{DFE}} \) and \( f(x) \) satisfying certain important assumptions [12], then we define the square matrices \( F \) and \( V \) of dimension \( m \times m \) as follows;

\[
F_{ij} = \frac{\partial F_i(x)}{\partial x_j} \bigg|_{x_{\text{DFE}}}, \quad V_{ij} = \frac{\partial V_i(x)}{\partial x_j} \bigg|_{x_{\text{DFE}}}, \quad \text{for } 1 \leq i, j \leq m
\]  
(43)

It then follows that \( FV^{-1} \) is the next generation matrix and the basic reproduction ratio \( R_0 \) is the spectral radius of \( FV^{-1} \),

\[
\Rightarrow R_0 = \rho(FV^{-1})
\]  
(44)
Rewriting the system (41) starting with the infected compartments for both populations; \(e_h, i_h, e_m, i_m, l_h, l_m\) and then followed by uninfected classes; \(s_h, z, r_h, l_h, s_m\) also from the two populations, gives;

\[
\begin{align*}
\frac{de_h}{dt} &= \beta_h i_h s_h - ge_h - \delta_h e_h \\
\frac{di_h}{dt} &= ge_h + q\Lambda_h - k_i i_h - k_z i_h - \delta_i i_h \\
\frac{de_m}{dt} &= \beta_m i_m s_m - \phi e_m - \delta_e e_m \\
\frac{di_m}{dt} &= \phi e_m - \delta_i i_m \\
\frac{di_m}{dt} &= k_z i_h - (\omega_h + \delta_h) i_m \\
\frac{dr_h}{dt} &= k_i i_h - \gamma_t h - \delta_h t_h \\
\frac{ds_h}{dt} &= (1-q)\Lambda_h + \alpha z z + \rho r_h - \beta_h i_h s_h - \alpha s_h - \delta_h s_h \\
\frac{dr}{dt} &= \alpha s_h + \mu r_h - \alpha z z - \delta_h z \\
\frac{dr}{dt} &= \gamma t_h - (\mu + \rho + \delta_h) r_h \\
\frac{dl_m}{dt} &= \Lambda_m - m l_m - \delta_m l_m \\
\frac{ds_m}{dt} &= m l_m - \beta_i i_m s_m - \delta_m s_m
\end{align*}
\]

The method of next generation matrix has been used to show the rate of appearance of new infection in compartments; \(e_h\) and \(e_m\), from the system (12);

\[
F = \begin{pmatrix}
\beta_h i_h s_h \\
\beta_m i_m s_m \\
0 \\
0 \\
0 \\
0
\end{pmatrix}, \quad V = \begin{pmatrix}
(g + \delta_h) e_h \\
-ge_h - q\Lambda_h + (k_i + k_z + \delta_i) i_h \\
(\phi + \delta_m) e_m \\
-\phi e_m + \delta_i i_m \\
-k_z i_h + (\omega_h + \delta_h) i_m \\
-k_i i_h + (\gamma + \delta_h) t_h
\end{pmatrix}
\]

By linearization approach, the associated matrix at disease free equilibrium is obtained as

\[
F = \begin{pmatrix}
0 & 0 & 0 & \frac{\Lambda_h \beta_h}{\delta_h} & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & 0
\end{pmatrix}
\]
Here the term \( \frac{\Lambda_s \beta_s \phi}{\delta_m (\phi + \delta_m)} \) explains the number of humans that one mosquito infect through contact during the life time it survives as infectious. On the other hand \( \frac{m \Lambda_m \beta_m g}{\delta_m (m + \delta_m)(g + \delta_i)(k_1 + k_2 + \delta_i)} \) describes the number of mosquitoes that are infected through contacts with the infectious human during infectious period. Hence

\[
R_0 = \sqrt{R_{0m} \times R_{0h}}
\]

where \( R_{0m} = \frac{\Lambda_s \beta_s \phi}{\delta_m (\phi + \delta_m)} \) and \( R_{0h} = \frac{m \Lambda_m \beta_m g}{\delta_m (m + \delta_m)(g + \delta_i)(k_1 + k_2 + \delta_i)} \).

3. Sensitivity Analysis of the Model Parameters

In this section, we carry out the sensitivity analysis of the model parameter to help us know the parameters that have high impact on the disease transmission, which is on the reproduction ratio \( R_0 \).

We used the normalized forward sensitivity index of a variable to parameter approach used in Okosun \[13\].

### 3.1. Sensitivity Analysis of \( R_0 \)

We compute the sensitivity of \( R_0 \) to each of the parameters described in Table 4. Using the formula

\[ \gamma^n_m = \frac{\partial m}{\partial n} \times \frac{n}{m} \]

where \( n \) represents the variables of the model, and \( m \) the parameters.

Sensitivity index of \( \phi \) given by \(-\frac{1}{2} \left( \frac{\phi}{\phi + \delta_m} \right)\)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>( \beta_s )</th>
<th>( k_1 )</th>
<th>( k_i )</th>
<th>( g )</th>
<th>( \delta_m )</th>
<th>( M )</th>
<th>( \beta_m )</th>
<th>( \delta_i )</th>
<th>( \phi )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity Index</td>
<td>0.5</td>
<td>-0.25</td>
<td>-0.156</td>
<td>-0.375</td>
<td>-0.719</td>
<td>0.125</td>
<td>0.5</td>
<td>-1.352</td>
<td>-0.272</td>
</tr>
</tbody>
</table>
Sensitivity index of $g$ given by
\[
- \frac{1}{2} \left( \frac{g}{g + \delta_g} \right)
\]
Sensitivity index of $\delta_a$ given by
\[
- \frac{1}{2} \left( -2 - \frac{\delta_a}{\phi + \delta_a} - \frac{\delta_m}{m + \delta_a} \right)
\]
Sensitivity index of $\delta_b$ given by
\[
\frac{1}{2} \left( -1 - \frac{\delta_b}{g + \delta_b} - \frac{\delta_a}{k_1 + k_2 + \delta_b} \right)
\]
Sensitivity index of $k_1$ given by
\[
- \frac{k_1}{2} \left( k_1 + k_2 + \delta_b \right)
\]
Sensitivity index of $k_2$ given by
\[
- \frac{k_2}{2} \left( k_1 + k_2 + \delta_b \right)
\]
Sensitivity index of $m$ given by
\[
\frac{1}{2} \left( - \frac{m}{m + \delta_a} \right)
\]
Sensitivity index of $\Lambda_m = \beta_m = \beta_a = \Lambda_n = \frac{1}{2}$

**Remark:** Sensitivity indices of $R_0$ evaluated at the baseline parameter values are given in the Table 5.

From Table 5, the sensitivity index may be a complex expression, depending on different parameters of the system. But it can also be a constant value. Example, the sensitivity index of $\beta_M$, $\beta_H = +0.5$, means that increasing (or decreasing) $\beta_M$, $\beta_H$ by 10% increases (or decreases) $R_0$ by 5%.

### 3.2. Math Cad Simulation of the Model

Parameter values:

$q := 0.1, \Lambda_H := 0.5, \alpha_i := 0.8, \alpha_z := 0.6, \rho := 0.02, \beta_H := 0.5, \delta_H := 0.3, g_i := 0.9, k_1 := 0.8, k_2 := 0.5, \omega_H := 0.5, \gamma := 0.7, \mu := 0.4, N_H := 100,$

$\Lambda_M := 0.2, m_i := 0.3, \delta_M := 0.1, \beta_M := 0.4, \phi := 0.12$

\[
D(t,Y) := \begin{bmatrix}
(1-q)\Lambda_H + \alpha_i Y_6 + \rho Y_7 - \frac{\beta_H Y_4 Y_6}{N_H} - \alpha_i Y_3 - \delta_H Y_4 \\
\frac{\beta_H Y_4 Y_6}{N_H} - g_i Y_3 - \delta_H Y_3 \\
g_i Y_7 + q_t\Lambda_H - k_1 Y_7 - k_2 Y_8 - \delta_H Y_2 \\
k_2 Y_2 - (\omega_H + \delta_H) Y_5 \\
k_1 Y_5 - \gamma Y_4 - \delta_H Y_4 \\
\gamma Y_4 - (\mu + \rho + \delta_H) Y_5 \\
\alpha_i Y_3 - \alpha_i Y_3 - \delta_H Y_6 \\
\Lambda_M - m_1 Y_5 - \delta_M Y_5 \\
m_1 Y_5 - \frac{\beta_H Y_6 Y_7}{N_H} - \delta_M Y_8 \\
\frac{\beta_H Y_6 Y_7}{N_H} - \phi Y_6 - \delta_M Y_7 \\
\phi Y_6 - \delta_M Y_{10}
\end{bmatrix}
\]
Vector of derivative values at any solution point \((t, Y)\):

Define additional arguments for the ODE solver:

\[ t_0 := 0 : \text{Initial value of independent variable} \]

\[ t_1 := 0 : \text{Initial value of independent variable} \]

\[ Y_0 := \begin{bmatrix} 50 & 15 & 25 & 2 & 2 & 4 & 2 & 5 & 3 & 2 & 1 \end{bmatrix}^T : \text{Vector of initial function values} \]

\( num := 1 \times 10^3 \): Number of solution values on \([t_0, t_1]\)

\( S_1 := \text{Rkadapt}(Y_0, t_0, t_1, num, D) \): Solution matrix

**Human (Table 6)**

- \( t := S_1(0) \): Independent variable values
- \( S_H := S_1(t) \): First solution function values
- \( E_H := S_1(2) \): Second solution function values
- \( I_H := S_1(3) \): Third solution function values
- \( I_{HN} := S_1(4) \): Fourth solution function values
- \( T_H := S_1(5) \): Fifth solution function values
- \( R_H := S_1(6) \): Sixth solution function values
- \( A_H := S_1(7) \): Seventh solution function values

**Table 5.** Sensitivity indices of \( R_0 \) evaluated at the baseline parameter values.

<table>
<thead>
<tr>
<th>Param ( \Lambda_\alpha \quad \Lambda_\psi \quad \rho \quad \beta_\alpha \quad \alpha_i \quad q \quad \alpha_e \quad k, k_i \quad g \quad \gamma \quad \delta_\alpha \quad \mu \quad M \quad \beta_\omega \quad \delta_\omega \quad \phi \quad \omega_\beta )</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.5</td>
<td>0.4</td>
</tr>
</tbody>
</table>

**Table 6.** Solution matrix \( S_1 \) for the system of ODEs

<table>
<thead>
<tr>
<th></th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
<td>50</td>
<td>15</td>
<td>25</td>
<td>2</td>
<td>2</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>1</td>
<td>0.01</td>
<td>49.469</td>
<td>14.824</td>
<td>24.737</td>
<td>2.108</td>
<td>2.178</td>
<td>3.99</td>
<td>2.394</td>
</tr>
<tr>
<td>2</td>
<td>0.02</td>
<td>48.946</td>
<td>14.649</td>
<td>24.476</td>
<td>2.214</td>
<td>2.352</td>
<td>3.97</td>
<td>2.78</td>
</tr>
<tr>
<td>3</td>
<td>0.03</td>
<td>48.431</td>
<td>14.477</td>
<td>24.218</td>
<td>2.317</td>
<td>2.523</td>
<td>3.96</td>
<td>3.159</td>
</tr>
<tr>
<td>4</td>
<td>0.04</td>
<td>47.924</td>
<td>14.307</td>
<td>23.963</td>
<td>2.419</td>
<td>2.689</td>
<td>3.95</td>
<td>3.53</td>
</tr>
<tr>
<td>5</td>
<td>0.05</td>
<td>47.425</td>
<td>14.138</td>
<td>23.71</td>
<td>2.518</td>
<td>2.852</td>
<td>3.94</td>
<td>3.894</td>
</tr>
<tr>
<td>6</td>
<td>0.06</td>
<td>46.933</td>
<td>13.972</td>
<td>23.46</td>
<td>2.616</td>
<td>3.012</td>
<td>3.93</td>
<td>4.25</td>
</tr>
<tr>
<td>7</td>
<td>0.07</td>
<td>46.449</td>
<td>13.808</td>
<td>23.212</td>
<td>2.711</td>
<td>3.167</td>
<td>3.93</td>
<td>4.6</td>
</tr>
<tr>
<td>8</td>
<td>0.08</td>
<td>45.972</td>
<td>13.645</td>
<td>22.966</td>
<td>2.804</td>
<td>3.32</td>
<td>3.92</td>
<td>4.942</td>
</tr>
<tr>
<td>9</td>
<td>0.09</td>
<td>45.503</td>
<td>13.485</td>
<td>22.723</td>
<td>2.896</td>
<td>3.469</td>
<td>3.92</td>
<td>5.278</td>
</tr>
<tr>
<td>10</td>
<td>0.1</td>
<td>45.041</td>
<td>13.326</td>
<td>22.483</td>
<td>2.985</td>
<td>3.614</td>
<td>3.91</td>
<td>5.607</td>
</tr>
<tr>
<td>11</td>
<td>0.11</td>
<td>44.585</td>
<td>13.17</td>
<td>22.245</td>
<td>3.073</td>
<td>3.756</td>
<td>3.91</td>
<td>5.929</td>
</tr>
<tr>
<td>12</td>
<td>0.12</td>
<td>44.137</td>
<td>13.015</td>
<td>22.009</td>
<td>3.159</td>
<td>3.895</td>
<td>3.91</td>
<td>6.245</td>
</tr>
<tr>
<td>13</td>
<td>0.13</td>
<td>43.695</td>
<td>12.862</td>
<td>21.776</td>
<td>3.242</td>
<td>4.03</td>
<td>3.91</td>
<td>6.554</td>
</tr>
<tr>
<td>14</td>
<td>0.14</td>
<td>43.26</td>
<td>12.711</td>
<td>21.545</td>
<td>3.324</td>
<td>4.163</td>
<td>3.91</td>
<td>6.857</td>
</tr>
<tr>
<td>15</td>
<td>0.15</td>
<td>42.832</td>
<td>12.561</td>
<td>21.316</td>
<td>3.405</td>
<td>4.292</td>
<td>3.91</td>
<td>...</td>
</tr>
</tbody>
</table>
3.3. Results and Discussion

The susceptible human population $S_H$ against time (Figure 6(a)), clearly shows a rapid exponential decline from the initial value to zero. Similarly, the variation of exposed human population $E_H$ against time (Figure 6(b)) depicts an exponential decline from the initial value to zero. The variation of the infected human population $I_H$ against time (Figure 6(c)), also depicts an exponential decline from the initial value to zero. The graphical profile of the variation of the non treated human population $I_{HN}$ against time (Figure 6(d)), shows a sharp rise from the initial value to reach a maximum, and thereafter exhibits an exponential decline to zero. The variation of treated human population $T_H$ against time (Figure 6(e)), shows a sharp rise from the initial value to reach a maximum, and thereafter declines exponentially to zero. Similarly, the graphical profile of the variation of the removed human population $R_H$ against time (Figure 6(f)), depicts a rise from the initial value to reach a maximum, and thereafter declines exponentially to zero. The graphical profile of the variation of the protected human population $A_H$ against time (Figure 6(g)), shows a sharp rise from the initial value to reach a maximum, and thereafter declines exponentially to a steady state. From the graphical profile of the variation of population of mosquito larva $L_M$ against time (Figure 6(h)), we observe an exponential decline from the initial value to reach a steady state. The variation of the susceptible mosquito population $S_M$ against time (Figure 6(i)), depicts a rise from the initial value to reach a maximum, and thereafter exhibits a sharp decline. In the same manner, the variation of the exposed mosquito population $E_M$ against time (Figure 6(j)), shows a decline from the initial value to reach a steady state. Finally, the variation of the infected mosquito population $I_M$ against time (Figure 6(k)), depicts a rise from the initial value to reach a maximum and then exhibits a decline.

3.4. Conclusion

Despite the availability of drugs, the malaria disease is still endemic in many parts of the world including developed countries. Elimination of malaria requires maintaining the effective reproduction number $R_0$ less than unity, as well as achieving low levels of susceptibility. In this research work, we developed a compartmental bio-mathematical model to study the effect of treatment in the control of malaria in a population with infected immigrants. We obtained the basic reproduction number, $R_0$ and studied the stability of the disease-free equilibrium of the model. Sensitivity analysis of $R_0$ with respect to the model parameters was carried out on the compartmental vector-host malaria model with
Figure 6. (a) Population of susceptible humans against time; (b) Population of exposed humans against time; (c) Population of infected humans against time; (d) Population of non-treated infected human against time; (e) Population of treated humans against time; (f) Population of recovered humans against time; (g) Population of protected humans against time; (h) Population of mosquitoes larva against time; (i) Population of susceptible mosquitoes against time; (j) Population of exposed mosquitoes against time; (k) Population of infected mosquitoes against time.
eleven compartments. From the literature on modelling of vector-host malaria models, we discovered that many researchers failed to consider protective measures in their models, though some discussed it theoretically. Our major contribution to the existing body of knowledge is incorporating the protective measure in our mathematical model.

Conflicts of Interest
The authors declare no conflicts of interest regarding the publication of this paper.

References