Journal of the Nigerian Association of Mathematical Physics
Volume28, No. 1, **(***November, 2014***), pp 163 – 176**

A Model for the Transmission Dynamics of Malaria with Infective Immigrants And it's Optimal Control Analysis

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Abstract

In this article, we proposed an optimal control model that includes constant immigration of individuals into the susceptible population out of which a fraction is infective. Seeking to minimize the number of infectious humans and mosquitoes, we use controls to represent the screening of infected immigrants coming into the population, the use of prophylactic drugs on susceptible human and use of gametes destroying drugs on infectious human. A characterization of the optimal control via adjoint variables is established. The optimality system is solved numerically using an iterative method with Runge-Kutta fourth order scheme. Finally, numerical simulations of the optimal control problem is carried out to investigate the effectiveness of the proposed control measures. Parameter values have been taken from available literature.

Keywords: Infective, immigrants, optimal control, malaria, transmission dynamics

1.0 Introduction

Over the years, malaria disease has always been a great concern of human kind. It is one of the leading causes of death and remains a major challenge for many countries in the world. Malaria is a life-threatening disease caused by the parasite *plasmodium falciparum,* this parasite are transmitted to people through the bite of infected female anopheles mosquitoes. It is only the female anopheles mosquito that feeds on human blood. This is because; the blood is needed for the production of eggs. Malaria is endemic in 109 countries and territories in tropical and sub-tropical regions, spanning all continents of the world except Antarctica and Australia [1].

Human migration is present through the world; this has greatly affected the transmission dynamics of infectious diseases like malaria. [2] asserted that, there is a close connection between vector-borne disease and movement of people. Immigration has been known to play a key role in disease dynamics and this has been linked to increases in the incidence of malaria in some countries.It has been shown in [3, 4] that malaria models that include a constant flow of infective immigrant cannot eliminate the disease through any standard control measures. Usually these control measures are based on the basic or effective reproduction number, which cannot be applied to model with a constant inflow of infective individuals since the disease-free equilibrium can never be achieved.[5] asserted that one of the reasons for the failure of strategies to eradicate infectious disease is because of their neglect of the mobility pattern of the host, and that the importance of the role of human migration is evident in the recent increase in malaria incidence not only in the endemic areas, but also in areas where malaria had been eradicated

Several models have been formulated to study the dynamics of malaria. For example, [6] proposed a model by including constant immigration of susceptible human population and exclude direct human recovery from the infectious to susceptible class. The model does not include immigration of infectious humans, as they assume that sick people do not travel. [7] proposed a mathematical model that tracks the dynamics of malaria disease. Their model incorporates immigration of infective human and ignore vertical transmission. However, all these works did not put into consideration the optimality, costs and cost-effectiveness of the treatment, prevention and vector control interventions, which are mainly hampered by the availability of resources. In view of this, [8] applied optimal control to study the epidemiology of malaria. In their study, they

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used optimal control theory to investigate the optimal strategies for controlling the spread of malaria disease using treatment, insecticide, treated bed nets and spray of mosquito insecticide as the system control variables. [9] applied optimal control to investigate the fundamental role of three type of control, personal protection, treatment and mosquito reduction strategies in controlling malaria. [10] applied optimal control to study vector borne disease with a particular reference to dengue disease. [11] applied optimal control to a mathematical model with infected and infectious immigrants to investigate the role of inflow of infected immigrants in malaria transmission.

In this paper, we proposed a model that includes a constant influx of immigrants into the susceptible class out of which a fraction p is considered infective. The model differs from the model of [7] by excluding the direct recovery from the infectious class to the susceptible class which was evident in [7]. The model will be extended to assess the impact of the anti-malaria control measures (immigrant screening, use of Prophylactic drugs and gametocytes destroying drugs) by reformulating the model as an optimal control problem. This will entail the use of three control functions namely;, immigrant screening strategies, use of Prophylactic drugs and gametocyte destroying drugs. Our goal is to minimize the number of infectious human and infectious mosquitoes at a minimum cost. Using analytical method, the existence of an optimal control and the optimality of the system will be proved. The numerical simulation of the optimal control model will be done using MATLAB.

2.0 Modelformulation with Immigration of Infective

Let A (a constant) be the number of new members arriving into the population in unit time with the fraction p of A arriving infected with malaria such that $0 \le p \le 1$ We assume that the members $(1-p)A$ are free from the malaria disease. The new model is given below:

$$\frac{dS_h}{dt} = \Lambda_h + (1-p)A + \rho_h R_h - \frac{\beta_h I_m S_h}{N_h} - \mu_h S_h \quad (1a)$$

$$\frac{dI_h}{dt} = pA + \frac{\beta_h I_m S_h}{N_h} - (\mu_h + \gamma_h + \delta_h) I_h \quad (1b)$$

$$\frac{dR_h}{dt} = \gamma_h I_h - (\mu_h + \rho_h) R_h \quad (1c)$$

$$\frac{ds_m}{dt} = \Lambda_m - \frac{\beta_m I_h S_m}{N_h} - \mu_m S_m \quad (1d)$$

$$\frac{dI_m}{dt} = \frac{\beta_m I_h S_m}{N_h} - \mu_m I_m \quad (1e)$$

where

Λ_h = birth rate of humans

Λ_m = birth rate of mosquitoes

ρ_h = rate of loss of immunity

β_h = rate of transmission of infection from infectious mosquito to humans

γ_h = recovery rate of humans

δ_h = disease-induced death rate of humans

β_m = of transmission of infection from infectious humans to mosquitoes

μ_h = Natural death rate for humans

A = immigrant rate

P = fraction of infective immigrants

μ_m = natural death rate for mosquitoes

S_h = Number of susceptible humans

I_h = Number of infectious humans

R_h = Number of immune humans

S_m = Number of susceptible mosquitoes

I_m = Number of infectious mosquitoes

N_h = Total Number of humans

N_m = Total Number of mosquitoes

The equation in (1) represents the rate of change, with respect to time, of the different compartments.
Equation (1a) describes the rate of change of the susceptible human population, S_H. the first term on the right hand side of (1a) is the recruitment term Λ_h. The second term is the change in the S_H population due to the influx of immigrants into the population. Since p represents the fractions of immigrants (with a constant value A) having active malaria parasite, then (1-p) will be the fraction of A who are susceptible and therefore join the S_H class. The third term is the change in the S_H population due to the loss of immunity. That is, those in recovered population who lose immunity and return to the susceptible class. The fourth term of equation (1a) is the interaction between the susceptible human S_H and the infectious mosquitoes I_M that leads to new cases of malaria in human. This leaves the susceptible human class, S_H and moves into the infective class, I_H. The final term is the natural mortality rate for the susceptible class $\mu_h S_h$.
Equation (1b) describes the rate of change of the infectious human class I_H. The first term on the right hand side is the number of infective immigrant coming into the population. The second term represents the number of new malaria cases. The last term of equation (1b) is the recovery rate, γ_h , natural mortality rate, μ_h , and disease induced death rate, δ_h . All these reduce the infectious class, I_H.
Equation (1c) describes the rate of change of the recovered class, R_H. The first term on the right hand side is the number of infectious humans that recovered per unit time. The last term represents those that lose immunity and returned to the susceptible class and the natural death rate in the recovered class .
Equation (1d) describes the rate of change of the susceptible class S_M for mosquito populations. The first term on the right hand side is the recruitment term for mosquitoes, Λ_m .The second term of equation (1d) is the interactions between the susceptible mosquitoes, I_M and the infectious human I_H that leads to new cases of infectious mosquitoes. This leaves the susceptible mosquito population to the infectious mosquito class, I_M. The last term of equation (1d) is the natural mortality rate for susceptible mosquitoes.
Equation (1e) describes the rate of change of the infections mosquito class I_M. The first term represents the number of new infectious mosquito cases and the last term is the natural mortality rate for infectious mosquitoes.

3.0 Optimal Control Model Formulation

Here, we reformulate system (1) as an optimal control problem.
The control functions, $u_1(t)$, $u_2(t)$, $u_3(t)$, are bounded, *Lebesgue* integrable functions, where the control $u_1(t)$ is a control that allows for medical testing/screening of new immigrants coming into the population. The control $u_2(t)$ is a control on susceptible human that allows for the use of Prophylactic drugs by the susceptible individuals. The control $u_3(t)$ is a control on infected humans that allows for the use of drugs that not only treat the disease but prevent the formation of gametocytes in the human host.
The differential equation incorporating optimal control terms is given below

$$\frac{dS_h}{dt} = \Lambda_h + \left[1-\left(1-u_1(t)\right)p\right]A + \rho_h R_h - \frac{\beta_h S_h I_m \left(1-u_2(t)\right)}{N_h} - \mu_h S_h \qquad (2a)$$

$$\frac{dI_h}{dt} = \left(1-u_1(t)\right)pA + \frac{\beta_h S_h I_m \left(1-u_2(t)\right)}{N_h} - \left(\mu_h + \gamma_h + \delta_h\right) I_h \qquad (2b)$$

$$\frac{dR_h}{dt} = \gamma_h I_h - \left(\mu_h + \rho_h\right) R_h \qquad (2c)$$

$$\frac{ds_m}{dt} = \Lambda_m - \frac{\beta_m S_m I_h \left(1-u_3(t)\right)}{N_h} - \mu_m S_m \tag{2d}$$

$$\frac{dI_m}{dt} = \frac{\beta_m S_m I_h \left(1-u_3(t)\right)}{N_h} - \mu_m I_m \tag{2e}$$

The equations in (2) represent the rate of change, with respect to time of the different compartments with control terms.
In equation (2a), the term $\left[1-\left(1-u_1(t)\right)p\right]A$ represent the number of susceptible immigrants coming into the population in the presence of a time dependent control, $u_1(t)$. The control $u_1(t)$ is a control that allows for medical testing/screening of new immigrants coming into the population before they are allowed into the population, while the coefficient $1 – u_1(t)$ is the effort that sustains such a testing policy; $u_1(t)$ near 0 indicates that the policy is "loose," it does not prevent the infected immigrants from entering the population while $u_1(t)$ near 1, indicates a very strict testing policy that prevents the infected immigrants from increasing the size of the infected class I_H. The control $u_2(t)$ is a drug controlthat prevent the malaria parasite from developing in susceptible human, after the use of Prophylactic drugs. The coefficient $1 – u_2(t)$ is the effectiveness of the drug;$u_2(t)$ near 0 indicates that the specific prophylactic drug does not prevent the infected mosquito from infecting the susceptible individuals, while $u_2(t)$ near 1, indicate that the prophylactic drugs effectively prevents the infected mosquito from infecting the susceptible individuals following a bite or blood meal. The control $u_3(t)$ is a drug combination for treating malaria and prevent the forming of gametocytes in the human host that could be ingested by the mosquitoes after a blood meal, thereby infecting the mosquitoes. The coefficient $1\text{-}u_3(t)$ is the effectiveness of the gametocytes destroying drug; $u_3(t)$ near 0, indicate that the specific drug does not affect the formation of gametocytes in the body, while $u_3(t)$ near 1 indicate that the drug is effective in preventing the forming of gametes and hence reducing the likelihood of having infected mosquitoes.
The objective function to be minimized is

$$J\left(u_1,u_2,u_3\right) = \int_0^T \left(I_H + I_M + \frac{1}{2}\left(c_1u_1^2 + c_2u_2^2 + c_3u_3^2\right)\right) dt \tag{3}$$

We minimize the infectious human and infectious mosquito population. Hence we will minimize an objective functional of a form that shows the trade-off we need in minimizing the number of infectious humans and mosquitoes, and the associated relevant cost of doing this. The associated relevant cost is made up of the cost of immigrant screening, the cost on the use of prophylactic drugs and cost of the use of gametocytes destroying drugs. Here, we assume that the associated cost with immigrant screening, the use of prophylactic drugs and gametocytes destroying drugs are nonlinear and take a quadratic form. The coefficients C_1, C_2 and C_3 are balancing cost factors due to the size and importance of the parts making up the objective functional.

We seek to find an optimal control triple u_1^*, u_2^*, u_3^* such that

$$J\left(u_1^*,u_2^*,u_3^*\right) = \min J\left(u_1,u_2,u_3\right) \in U \tag{4}$$

Subject to the system describe in (2)
Where the control set is defined as

$$U = \left\{\left(u_1,u_2,u_3\right): u_i(t) \in [0,1], 0 \le u_i(t) \le 1, i = 1,2,3\right\}.$$

4.0 A Note on the Transmission Dynamics of Malaria with Infective Immigrants

Before we analyse the optimal control model (2), we give the analysis of model (1)that has no time-dependent control.
The coupled system of ordinary differential equations which describe the progress of the disease with immigration of infective is given by

$$\begin{aligned}
\frac{dS_h}{dt} &= \Lambda_h + (1-p)A + \rho_h R_h - \frac{\beta_h I_m S_h}{N_h} - \mu_h S_h \\
\frac{dI_h}{dt} &= pA + \frac{\beta_h I_m S_h}{N_h} - \left(\mu_h + \gamma_h + \delta_h\right) I_h \\
\frac{dR_h}{dt} &= \gamma_h I_h - \left(\mu_h + \rho_h\right) R_h \\
\frac{ds_m}{dt} &= \Lambda_m - \frac{\beta_m I_h S_m}{N_h} - \mu_m S_m \\
\frac{dI_m}{dt} &= \frac{\beta_m I_h S_m}{N_h} - \mu_m I_m
\end{aligned} \tag{5}$$

A suitable domain for model (5) is

$$D=\left\{\left(S_H, I_H, R_H, S_M, I_M\right)\in R^5 : S_H + I_H + R_H \le \frac{\Lambda_h + A}{\mu_h}, S_M + I_M \le \frac{\Lambda_m}{\mu_m}\right\}$$

It can be shown that the set D is positively invariant set and a global attractor of this system. Hence a phase trajectory initiated anywhere in the non-negative region of the space eventually enters the region D and remains in D afterwards

The rate of change of the total human population N_H is given by

$$\frac{dN_H}{dt}=\left(\Lambda_H + A\right)-\mu_H N_H - \delta_H I_H$$

Without loss of generality, we can write that

$$\frac{dN_H}{dt}\le\left(\Lambda_H + A\right)-\mu_H N_H$$

Since the right-hand side of the equation for the rate of change of N_H, is bounded by $\left(\Lambda_H + A\right)-\mu_H N_H$, a standard comparison theorem can be used to show that

$$N_H(t)\le N_H(0)e^{-\mu_H t}+\frac{\left(\Lambda_H + A\right)}{\mu_H}(1-e^{-\mu_H t})$$

If $N_H(0)\le\frac{\left(\Lambda_H + A\right)}{\mu_H}$

Then $N_H(\mathrm{t})\le\frac{\left(\Lambda_H + A\right)}{\mu_H}$

Similarly $N_m(\mathrm{t})\le\frac{\Lambda_m}{\mu_m}$

Thus, D is a positively invariant set under the flow described in system (5). Hence no solution path leaves through any boundary of D. Since path cannot leave D, solutions remain non-negative for non-negative initial conditions. This means that the solution exists for all positive time t. Therefore, the model (5) is mathematically and epidemiologically well-posed, [12].

For convenience and to simplify the analysis of our model, we rewrite equation (5) in terms of the proportions of individual in each class.

Let $s_h=\frac{S_H}{N_H}, i_h=\frac{I_H}{N_H}, r_h=\frac{R_H}{N_H}, s_m=\frac{S_M}{N_M}, i_m=\frac{I_M}{N_M}$ be the proportions for the classes S_H, I_H, R_H, S_M and I_M, respectively.

Let $m=\frac{N_m}{N_H}$ be the female mosquito-human ratio, that is, the number of female mosquito per human host.

The ratio $m=\frac{N_m}{N_H}$ is a constant because a mosquito takes a fixed number of blood meals per unit time independent of the population density of the host. [13].

Also let $\beta_H=\beta_h, \Lambda_H=\Lambda_h, \mu_H=\mu_h, \rho_H=\rho_h, \beta_M=\beta_m, \mu_M=\mu_m, \Lambda_M=\Lambda_m$

Differentiating the above proportions with respect to time t, we have that

$$\frac{ds_h}{dt}=\frac{1}{N_H}\frac{dS_H}{dt}-\frac{s_h}{N_H}\frac{dN_H}{dt}$$

$$\frac{di_h}{dt}=\frac{1}{N_H}\frac{dI_H}{dt}-\frac{i_h}{N_H}\frac{dN_H}{dt}$$

$$\frac{dr_h}{dt} = \frac{1}{N_H}\frac{dR_H}{dt} - \frac{r_h}{N_H}\frac{dN_H}{dt}$$
$$\frac{ds_m}{dt} = \frac{1}{N_M}\frac{dS_M}{dt} - \frac{s_m}{N_M}\frac{dN_M}{dt} \quad (6)$$
$$\frac{di_m}{dt} = \frac{1}{N_M}\frac{dI_M}{dt} - \frac{i_m}{N_M}\frac{dN_M}{dt}$$

Using equation (6), the system (5) can be written as

$$\frac{ds_h}{dt} = \frac{\Lambda_h}{N_H} + \frac{A(1-p)}{N_H} + \rho_h r_h - \left(\frac{\Lambda_h + A}{N_H} + \beta_h m i_m - \delta_h i_h\right) s_h$$
$$\frac{di_h}{dt} = \frac{pA}{N_H} + \beta_h m i_m s_h - \left(\frac{\Lambda_h + A}{N_H} + \gamma_h + \delta_h - \delta_h i_h\right) i_h$$
$$\frac{dr_h}{dt} = \gamma_h i_h - \left(\frac{\Lambda_h + A}{N_H} + \rho_h - \delta_h i_h\right) r_h \quad \frac{ds_m}{dt} = \frac{\Lambda_m}{N_m} - \left(\frac{\Lambda_m}{N_m} + \beta_m i_h\right) s_m \quad (7)$$
$$\frac{di_m}{dt} = \beta_m i_h s_m - \frac{\Lambda_m i_m}{N_m}$$

4.1 Existence of the equilibria of the malaria Model (7)

Since malaria can be introduced into the population by the recruitment of infected immigrants, it is more realistic to consider the malaria model with p > 0.

To findthe steady states of (7), we set the derivatives with respect to time in (7) to zero and using the fact that

$\frac{dN_H}{dt} = \left(\frac{\Lambda_h + A}{N_H} - \mu_h - \delta_h i_h\right) N_H = 0$, that is $\frac{\Lambda_h + A}{N_H} = \mu_h + \delta_h i_h$, $\frac{\Lambda_m}{N_m} = \mu_m$, $s_h + i_h + r_h = 1$,

$s_m + i_m = 1$ and $\frac{A}{N_H} = a$

This yield the endemic equilibrium $E^1 = \left(s_h^*, i_h^*, r_h^*, s_m^*, i_m^*\right)$

Where

$$s_h^* = \frac{\mu_h + \delta_h i_h - pA + \rho_h r_h}{\mu_h + \beta_h m i_m} \quad (8a)$$
$$i_h^* = \frac{pA + \beta_h m i_m (1 - r_h)}{\mu_h + \gamma_h + \delta_h + \beta_h m i_m} \quad (8b)$$
$$r_h^* = \frac{\gamma_h i_h}{\mu_h + \rho_h} \quad (8c)$$
$$s_m^* = \frac{\mu_m}{\mu_m + \beta_m i_h} \quad (8d)$$
$$i_m^* = \frac{\beta_m i_h}{\beta_m i_h + \beta_m} \quad (8e)$$

4.2 Disease-Free Equilibrium point

In order to understand the implications of having a constant influx of infected immigrants on the dynamics of the system in (7), we present conditions for the existence of positive equilibria with or without the infected immigrants.

Let $E^0 = \left(s_h^o, i_h^o, r_h^o, s_m^o, i_m^o\right)$ be the disease-free equilibrium points of model (7)

In the absence of the disease, that is when $i_h = i_m = p = 0$, the model (7) reduces to

$s_h = 1$, $i_h = 0$, $r_h = 0$, $s_m = 1$ and $i_m = 0$

Therefore $E^0 = \left(s_h^o, i_h^o, r_h^o, s_m^o, i_m^o\right) = (1,0,0,1,0)$ (9)

This implies that at the disease-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.

But if $i_h = i_m = 0, p \neq 0$ The model (7) has no disease-free equilibrium, since there will always be infected human migration into the population.

Again if we substitute equations (8c) and (8e) into (8b), we have the following quadratic equation in i_h^*.

$$\left(B_2B_3\beta_m + B_2\beta_m^2 m + B_1 m\gamma_h\right)i_h^{*2} + \left(B_2B_3\mu_m - B_1B_2 m - paB_2\beta_m\right)i_h^* - paB_2\mu_m = 0 \quad (10)$$

Where $B_1 = \beta_h\beta_m, B_2 = \mu_h + \rho_h, B_3 = \mu_h + \gamma_h + \delta_h$

Case 1: $(p = 0)$, in this case, equation (10) reduces to

$$\left(B_2B_3\beta_m + B_2\beta_m^2 m + B_1 m\gamma_h\right)i_h^{*2} - \left(B_1B_2 m - B_2B_3\mu_m\right)i_h^* = 0 \quad (11)$$

Which has two roots:

$i_h^* = 0$, for which the disease is absent.(Disease-free equilibrium)

and

$i_h^* = \dfrac{B_1B_2 m - B_2B_3\mu_m}{B_1B_2\beta_m + B_2\beta_m^2 m + B_1 m\gamma_h}$ for which the disease persists. This is positive provided

$\sigma = B_1B_2 m - B_2B_3\mu_m > 0$

Now

$$i_h^* = \frac{B_2B_3\mu_m\left(\dfrac{B_1 m}{B_3\mu_m} - 1\right)}{B_1B_2\beta_m + B_2\beta_m^2 m + B_1 m\gamma_h} = \frac{B_2B_3\mu_m\left(R_0^2 - 1\right)}{B_1B_2\beta_m + B_2\beta_m^2 m + B_1 m\gamma_h}$$

Where

$$R_0^2 = \frac{m\beta_h\beta_m}{\mu_m\left(\mu_h + \gamma_h + \delta_h\right)}$$

If $R_0 > 1$ the disease will persists in the population.That is, if $p = 0$, the model has a disease-free equilibrium and an endemic equilibrium point, with the former existing when $R_0 > 1$ while the latter exists and is unique when $R_0 > 1$

Case 2: $p > 0$, in this , (10) can be re-written as

$$\left(B_2B_3\beta_m + B_2\beta_m^2 m + B_1 m\gamma_h\right)i_h^{*2} - \left(\sigma + paB_2\beta_m\right)i_h^* - paB_2\mu_m = 0 \quad (12)$$

Clearly, there is no disease-free solution to equation (12). Instead, (12) has one positive root given by

$$i_h^* = \frac{\sigma + paB_2\beta_m + \sqrt{\left(\sigma + paB_2\beta_m\right)^2 + 4\left(B_2B_3\beta_m + B_2\beta_m^2 m + B_1 m\gamma_h\right)paB_2\mu_m}}{2\left(B_2B_3\beta_m + B_2\beta_m^2 m + B_1 m\gamma_h\right)} \quad (13)$$

This means that for $p=0$, there exist a disease-free equilibrium when $R_0<1$and a unique endemic equilibrium point when $R_0>1$. However, if $p>0$, There is no disease-free equilibrium, instead, an endemic equilibrium point exist.

5.0 Analysis of Optimal Control

The necessary conditions that an optimal control u_1,u_2,u_3 must satisfy comes from the Pontryagin's maximum principle [14]. This principle converts equations (2), (3) and (4) into a problem of minimizing pointwise a Hamiltonian H, with respect to u_1,u_2,u_3.

The lagrangrian of the control problem is given by

$$L=I_H+I_M+\frac{1}{2}\left(c_1u_1^2+c_2u_2^2+c_3u_3^2\right) \tag{14}$$

We seek for the minimal value of the Lagragrian. To do this, we define the Hamiltonian H for the optimal control problem.

$$H=L\left(I_H,I_M,u_1,u_2,u_3\right)+\lambda_1\frac{dS_H}{dt}+\lambda_2\frac{dI_H}{dt}+\lambda_3\frac{dR_H}{dt}+\lambda_4\frac{dS_M}{dt}+\lambda_5\frac{dI_M}{dt} \tag{15}$$

$$\begin{aligned}H&=I_H+I_M+\frac{1}{2}\left(c_1u_1^2+c_2u_2^2+c_3u_3^2\right)\\&+\lambda_1\left(\Lambda_h+\left[1-\left(1-u_1(t)\right)p\right]A+\rho_hR_h-\frac{\beta_hS_hI_m\left(1-u_2(t)\right)}{N_h}-\mu_hS_h\right)\\&+\lambda_2\left(\left(1-u_1(t)\right)pA+\frac{\beta_hS_hI_m\left(1-u_2(t)\right)}{N_h}-\left(\mu_h+\gamma_h+\delta_h\right)I_h\right)\\&+\lambda_3\left(\gamma_hI_h-\left(\mu_h+\rho_h\right)R_h\right)\\&+\lambda_4\left(\Lambda_m-\frac{\beta_mS_mI_h\left(1-u_3(t)\right)}{N_h}-\mu_mS_m\right)\\&+\lambda_5\left(\frac{\beta_mS_mI_h\left(1-u_3(t)\right)}{N_h}-\mu_mI_m\right)\end{aligned} \tag{16}$$

In order to find the optimal solution, we apply Pontryagin's Maximum Principle. We obtain the following theorem.

Theorem 4.1

There exists an optimal control u_1^*,u_2^*,u_3^* and corresponding solutions, $S_H^*,I_H^*,R_H^*,S_M^*,I_M^*$ that minimize $J\left(u_1,u_2,u_3\right)\in U$. Furthermore, there exist adjoint functions $\lambda_1,\lambda_2,\lambda_3,\lambda_4,\lambda_5$ such that

$$\lambda_1^I=\left(\lambda_1-\lambda_2\right)\beta_h\frac{I_m}{N_h}\left(1-u_2(t)\right)+\lambda_1\mu_h \tag{17a}$$

$$\lambda_2^I=-1+\lambda_2\left(\mu_h+\gamma_h+\delta_h\right)-\lambda_3\gamma_h+\left(\lambda_4-\lambda_5\right)\frac{\beta_mS_m\left(1-u_3(t)\right)}{N_h} \tag{17b}$$

$$\lambda_3^I=\left(\lambda_3-\lambda_1\right)\rho_h+\lambda_3\mu_h \tag{17c}$$

$$\lambda_4^I=\left(\lambda_4-\lambda_5\right)\frac{\beta_mI_h\left(1-u_3(t)\right)}{N_h}+\lambda_4\mu_m \tag{17d}$$

$$\lambda_5^I = -1 + (\lambda_1 - \lambda_2)\frac{\beta_h S_h (1-u_2(t))}{N_h} + \lambda_5 \mu_m \tag{17e}$$

With transversality conditions

$\lambda_i(t) = 0, i = 1,2,...,5$ and $N_H^* = S_H^* + I_H^* + R_H^*$, $N_M^* = S_M^* + I_M^*$

The following characterization holds

$$u_1^*(t) = \min\left\{1, \max\left(0, \frac{(\lambda_2 - \lambda_1)\, pA}{C_1}\right)\right\} \tag{18a}$$

$$u_2^*(t) = \min\left\{1, \max\left(0, (\lambda_2 - \lambda_1)\frac{\beta_h S_h I_m}{C_2 N_h}\right)\right\} \tag{18b}$$

$$u_3^*(t) = \min\left\{1, \max\left(0, (\lambda_5 - \lambda_4)\frac{\beta_m S_m I_h}{C_3 N_H}\right)\right\} \tag{18c}$$

Proof

When the Pontryagin's Maximum principle is applied, we have that

$$\frac{d\lambda_1}{dt} = -\frac{\partial H}{\partial S_H}, \lambda_1(t) = 0$$

$$\frac{d\lambda_2}{dt} = -\frac{\partial H}{\partial I_H}, \lambda_2(t) = 0$$

$$\frac{d\lambda_3}{dt} = -\frac{\partial H}{\partial R_H}, \lambda_3(t) = 0$$

$$\frac{d\lambda_4}{dt} = -\frac{\partial H}{\partial S_V}, \lambda_4(t) = 0$$

$$\frac{d\lambda_5}{dt} = -\frac{\partial H}{\partial I_V}, \lambda_5(t) = 0$$

This, evaluated at the optimal control u_1^*, u_2^*, u_3^* and corresponding state, gives the results in (17).

Considering the optimality conditions,

$$\frac{\partial H}{\partial u_1} = 0, \frac{\partial H}{\partial u_2} = 0, \frac{\partial H}{\partial u_3} = 0$$

And solving for u_1^*, u_2^*, u_3^*, subject to the state variables, the characterization in equation (18) is obtained.

This end the proof.

6.0 Numerical Results

The optimality screening, prophylactic drugs and gametocytes destroying drugs strategy is obtained by solving the optimality system which is made up of the state and adjoint equations. The optimality system is solved using MATLAB with a Runge-Kutta fourth order scheme. The state system, with an initial condition, is solved forward in time, with a guess for the controls over the simulated time, while the adjoint system, with values at final time T, is solved backward in time using the current iteration solution of the state equations. The controls are updated by using a convex combination of the previous controls and the value from the characterization. We shall repeat this process and the iteration is stopped if the value of unknowns at the previous iteration are very close to the ones at the present iteration [15].

By varying the values of one parameter while keeping the others constant, we observe a corresponding change in the solution of the system of differential equations. This shows that the solution depends continuously on the parameter values. In this research, we experimented with two different values for some of the parameters. For instance, we had $\beta_h = 0.022$ adjusted

to $\beta_h = 0.00022$ and $\beta_m = 0.028$ adjusted to $\beta_m = 0.00028$ .The different solutions where shown and explained.

For the bounds on the control, we have that $0 \le \mu_1 \le 1$, $0 \le \mu_2 \le 1$ and $0 \le \mu_3 \le 1$.

We have assumed that the weight factors, C_2 and C_3 associated with controls u_2 and u_3 is greater than or equal to C_1 which is associated with control u_1. This is because the cost associated with u_1 is made up of screening and testing of immigrants, and most times, the immigrant may bear the cost; hence the policy makers as well as public health officials may have little to spend in this regards. The cost associated with u_2 will entail giving prophylactic drugs to susceptible humans, while the cost associated with u_3 will entails the distribution of gametocytes destroying drugs to infected humans.

6.1 Numerical Results of model (2)

We explore model (2) that includes immigration of infective with immigrant screening, the use of Prophylactic drugs and gametocytes destroying drugs, as control measures, to study the effects of control practices on the transmission of malaria. Parameters used for the simulation were obtained from [16]. See Table 1.

Table 1: Parameters, their Symbols and Values used in Simulating model 2.

Parameter	Description	Value
$\wedge_h$	Birth rate of humans	0.00011
P	Proportion of infective immigrants	0.7
A	Rate of Immigration	0.033
ρ_h	Rate of loss of immunity	0.000055
β_h	Rate of transmission of infection from infected mosquito to susceptible human	0.022
μ_h	Natural death rate for humans	0.000016
γ_h	Recovery rate of humans	0.0035
$\wedge_m$	Birth rate of mosquitoes	0.13
β_m	Rate of transmission of infection from infective human to susceptible mosquitoes	0.0028
μ_m	Natural death rate of mosquitoes	0.033

6.1.1 Results with A=0

In this section, the three controls are used for the simulations. For the numerical results presented here, we assumed that there are no immigrants coming into the target population

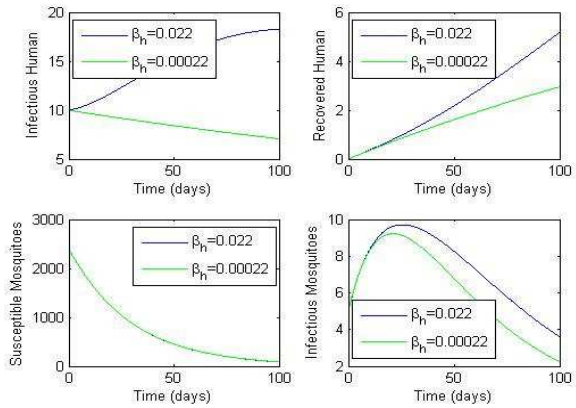

Fig 1. Optimal control strategy when A = 0, β_h varied, initial conditions $S_h(0) = 1000$, $I_h(0) = 10$, $R_h(0) = 0$, $S_v(0) = 2400$, $E_v(0) = 500$ and $I_v(0) = 5$. Other parameters are stated in Table 1

We use the three controls u_1, u_2 and u_3 to optimize the objective functional J. Figure 1 represent some of the epidemiological classes after the optimal strategy was implemented, with the rate of progression of humans from the susceptible state to the infectious state β_h, reduced from 0.022 to 0.00022.

Figure 2 shows the controls plotted as a function of time for both values of β_h. Observe in figure 10 that the control u_1 is zero, this is true since there are no infective immigrants coming into the population. To minimize the total number of infectious human, we observed in figure 9 that the control strategies resulted in a decrease in the numbers of infectious human. I_h and infectious mosquitoes I_m

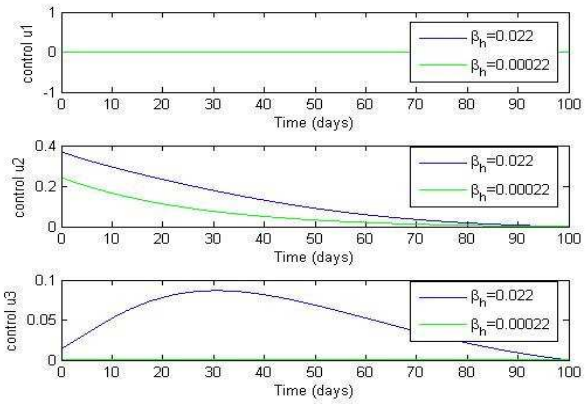

Fig.2: Control u_1, u_2 and u_3 when A = 0 and β_h varied.

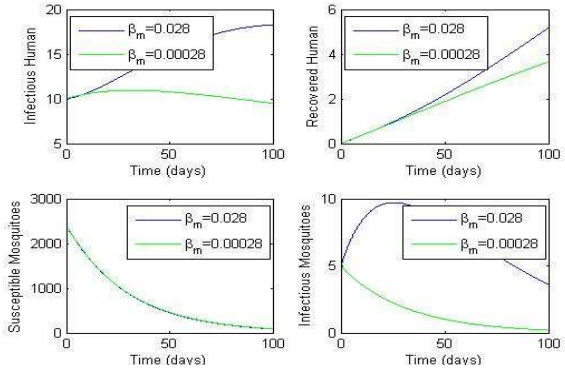

Fig 3: Optimal control strategy when A = 0, β_m varied, initial conditions $S_h(0) = 1000$, $I_h(0) = 10$, $R_h(0) = 0$, $S_v(0) = 2400$, $E_v(0) = 500$ and $I_v(0) = 5$. Other parameters are stated in Table 1.

From the control profiles shown in Figure 2, the results suggest that using this strategy, the control u_1 and u_2 were at its lowest bound. This means that, in the absence of infective immigrants coming into the population, a strict on the use of prophylactic drugs and gametes destroying drugs can drastically reduce the spread of malaria in the target population. Figure 3, shows the optimal control strategy when the rate of progression of mosquitoes from the susceptible state to the infection state, β_m, is reduced from 0.028 to 0.00028. This strategy resulted in decrease in the number of infectious mosquitoes. From the control profile in Figure 4, we observe that the control u_2 was at its lowest bound while control u_3 decreases from 0.1 to its lowest at time t = 90. This suggests that without the influx of infective immigrants into the target population, a reduction in the value of β_m can drastically reduce infectious mosquitoes

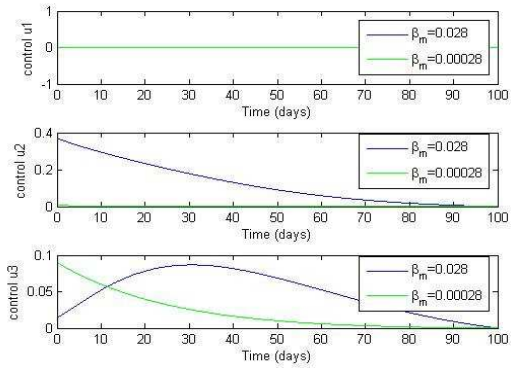

Fig.4: Control u_1, u_2 and u_3 when A = 0 and β_m varied.

6.1.2 Results with A>0.

In this section, the three controls are used for the simulations. For the numerical results presented here, we assumed that there is a constant influx of immigrants coming into the population.

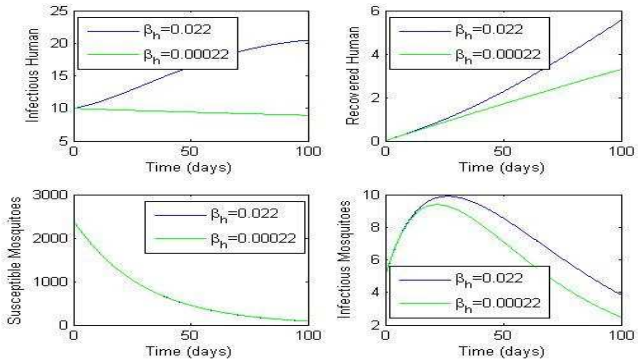

Fig 5: Optimal control strategy when A > 0, β_h varied, initial conditions $S_h(0) = 1000$, $I_h(0) = 10$, $R_h(0) = 0$, $S_v(0) = 2400$, $E_v(0) = 500$ and $I_v(0) = 5$. Other parameters are stated in Table 1

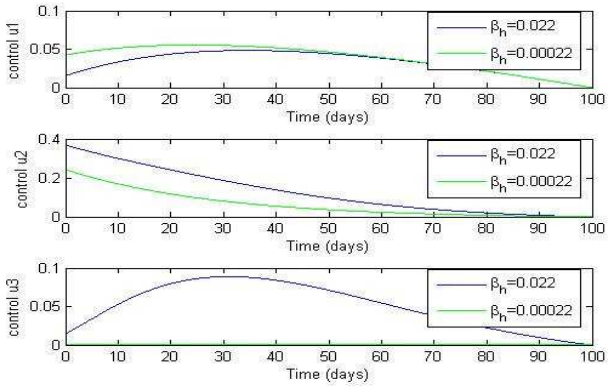

Fig.6: Control u_1, u_2 and u_3 when A > 0 and β_h varied.

We use all the controls u_1, u_2 and u_3 to optimize the objective functions. Figure 5, shows the epidemiological classes with infective immigrant after the optimal strategy was implemented with β_h reduced from 0.022 to 0.00022. We observe that in figure 5, even when β_h was reduced, the infectious human class still has a constant supply of infective humans, this is attributed to the influx of infective immigrants. Figure 6, shows the control profile plotted, that is, controls plotted as a function of time. The results suggest that using this strategy, the control efforts u_1 decreases from 0.05 till t = 100, while $u_2$decrease from 0.25 till t = 90 and u_3 were at its lowest bound when $\beta_h$is varied. The same result was also obtained when β_m was varied.

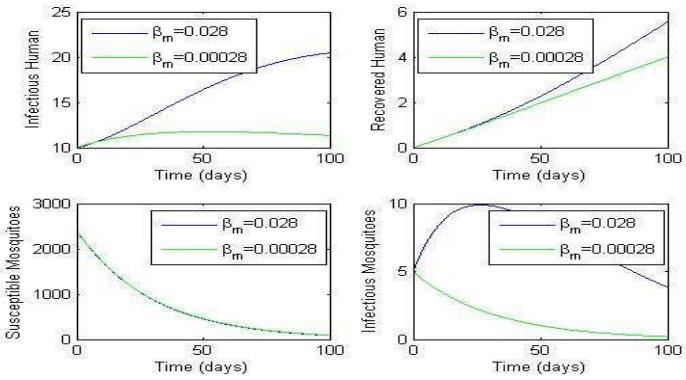

Fig.7: Optimal control strategy when A > 0, β_m varied, initial conditions $S_h(0) = 1000$, $I_h(0) = 10$, $R_h(0) = 0$, $S_v(0) = 2400$, $E_v(0) = 500$ and $I_v(0) = 5$. Other parameters are stated in Table 1

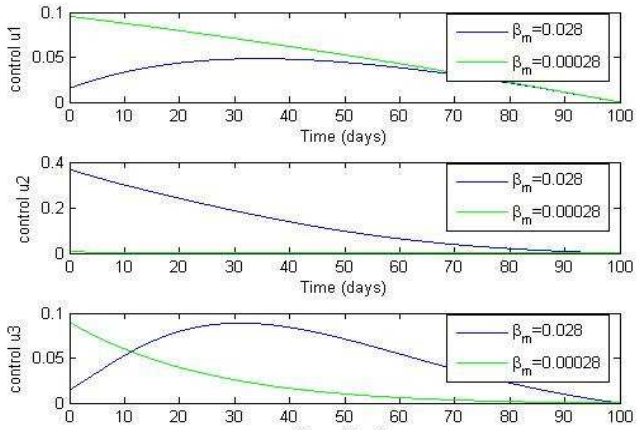

Fig.8: Control u_1, u_2 and u_3 when A > 0 and β_m varied.

7.0 Conclusion

In this work, we apply Optimal Control theory to a model that includes a constant influx of immigrants into the Susceptible class, out of which a proportion of the immigrant is considered infective. The model is analysed for the existence of disease-free and endemic equilibrium points. It was found that if there is an influx of infective immigrants into the population, a steady state with a positive fraction of infective always exists. This means that the model does not have disease-free equilibrium point and has only the endemic disease equilibrium point in which the disease persist in the population. According to [7], human migration plays an important role in the transmission and spread of malaria. It contributes to the transmission and spread of malaria infection and exposes the non-immune to the risk of infection and complicates the control measures. It was also found out that the influx of infective immigrants into the population does not alter the value of the basic reproduction number, R_0 . That is, R_0 is irrelevant and has limited application in the eradication of malaria when there is an influx of infective immigrant into the population.The model was extended to assess the impact of the anti-malaria control measures (immigrant screening, use of Prophylactic drugs and gametocytes destroying drugs) by reformulating the model as an optimal control problem. Using analytical method, the existence of an optimal control and the optimality of the system was proved. The simulation of the optimal control model was done using MATLAB. Numerical results agree with our analytical result that if there is a constant influx of infected immigrant, the model does not have disease-free equilibrium It was also found that infected immigrant may not have strong impact in the spread of malaria if there is a strict policy on the use of prophylactic drugs and gametocytes destroying drugs. However, the combination of the three controls, that is, screening/medical testing of immigrants, the use of prophylactic drugs and gametocytes destroying drugs, gave a better and efficient result in controlling the spread of malaria. This means that control programmes that use these three strategies can effectively reduce the spread of malaria in the target community.

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