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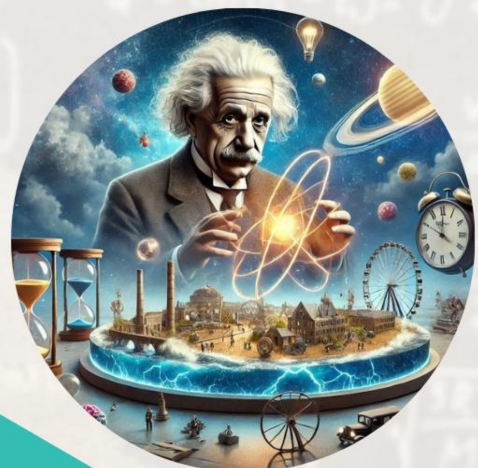

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An Optimal Saturated Incidence Model for Malaria Transmission Control

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Abstract: The transmission and control of malaria may be represented by a vector-host deterministic model, with treatment and prevention serving as the controls. A new preventive function, an essential tool in the battle against malaria, has been added to our model, bringing attention to the importance of prevention in lowering vector populations. An additional innovation is the use of a new treatment function. This reflects the reality that only a fraction of the infected population has access to treatment at any given moment. The key to successfully controlling malaria is increasing this fraction. Finding the right mix of preventive and treatment is essential for successfully reducing malaria transmission, and optimal control strategies help with that. By simulating the optimality system's solutions with different parameter values, we find that adjacent communities may greatly decrease the prevalence of malaria and, with the right measures taken, might even eliminate the disease entirely.

Keywords: Malaria Transmission Model, Saturated Incidence, Optimal Control Formulation, Pontryagin's Maximum Principle, Forward-Backward Sweep method

Introduction

Approximately 200 million people are always at risk of contracting malaria, making it a major cause of death and disability in tropical and subtropical areas worldwide. The disease has a disproportionately large effect on Africa. At least one million people die from malaria every year in Sub-Saharan Africa, according to the World Health Organization (WHO), and the number might rise sharply as a result of ongoing climate change. The illness is still going strong and is a major social and economic problem in poor nations.Plasmodium is a genus of protozoan parasites that may infect humans via mosquito bites. Human malaria is caused by the following species: The most common tropical parasite, Plasmodium falciparum, which is also the deadliest; There are two types of malaria parasites: Plasmodium vivax, which is the most frequent kind but seldom lethal, and Plasmodium malariae, which is uncommon but may cause low-grade parasitaemia that can persist for decades, especially in Africa. Although infections with other species may sometimes reveal Plasmodium ovale, which produces clinically relevant but not severe illness, it is not always the case.

The female anopheles mosquito is the vector for transmitting the Plasmodium parasite (Putri and Jaharuddin, 2014). When a vector bites a person with the virus, it becomes infected.Bite severity, when it occurs, the vector, the host, and environmental conditions are all influenced by the Plasmodium parasite, which may bite either people or animals (WHO, 2019a). Bite timing is also a role. Mosquitoes inflict malaria when they inject people with saliva that contains sporozoites. Within 30-60 minutes, these sporozoites are transported to the liver.After invading the liver hepatocytes, the worms proceed through an asexual reproduction phase, when they produce 8–6 merozoites, which then infiltrate the red blood cells.

This ongoing process is what really causes malaria infections. Malaria is characterized by a high temperature, chills, headache, vomiting, anemia, diarrhea, liver damage, and neurological symptoms (Adamu et al., 2017). The best way to prevent illnesses spread by mosquitoes is to take precautions on an individual level. Using insect repellents is one way to protect oneself. These are chemicals that may be applied to exposed skin or garments to repel mosquitoes. Using them won't really kill mosquitoes; they only keep them at bay. Indoor residual spraying and insecticide-treated bed nets are two other methods for personal protection. There is evidence that shows a decrease in malaria cases when persons use ITNs.

half the morbidity of malaria in children less than five years old and a 20-30% reduction in child mortality worldwide (Binka et al., 1996). Integrated pest management systems (ITMS) are seen as effective instruments for controlling malaria vectors when implemented on a grand scale. But the pesticides used to impregnate the nets have a limit: resistance. In certain West African nations, notably Ghana, the most significant malaria vector in Africa, Anopheles gambiae S.l., has already developed resistance to pyrethroid. Mass spraying of endemic regions is only one of several kinds of government action. The number of vectors is reduced as a result of several of these preventative measures. In order to better understand how infectious illnesses propagate, mathematical biologists and epidemiologists often use mathematical models. An early malaria researcher who used mathematical models to investigate the disease's transmission mechanisms (Ross, 1911). A differential equation model including standard incidence and some biological variables, such mosquito bite frequency, was the focus of his study. Inoculation of all mosquitoes is therefore unnecessary for the eradication of malaria. Researchers have created and examined many malaria models. Also, other researchers have looked at malaria epidemic models and used optimal control techniques to them in order to find ways to manage the disease via treatment and prevention. (Adamu et al., 2017; Bakare and Abolarin, 2018; Bala and Gimba, 2019; Blayneh et al., 2009; Nana-Kyere and Doe, 2017; Yusuf and Benyah, 2012) and others are notable within this group of works.

Formulation of the Model

We formulate an SEIRS-SI epidemic model for the spread of malaria in human and mosquito populations, respectively. The compartments in the human population consist of susceptible individuals S_h, exposed individuals E_h, infectious individuals I_h and recovered individuals R_h. The total human population $N_h(t)$, at time *t*, is given by

$$N_h(t) = S_h(t) + E_h(t) + I_h(t) + R_h(t)$$

Similarly, the compartments in the mosquito population are susceptible vectors S_v and infectious vectors I_v. The total vector population $N_v(t)$, at time t, is given by:

$$N_v(t) = S_v(t) + I_v(t)$$

Movement from the susceptible classes to either the exposed class for humans or the infectious class for the vector population depends on the biting rate b of the mosquitoes and their transmission probabilities β_h, β_v respectively. The biting rate b is defined as the averagenumber of bites per mosquito per day, while the transmission probabilities β_h, β_v, is the probability that an infectious bite produces a new case in a susceptible population only.

This model is related partly, to the one in Esteva and Vargas (1998), where they assumed that apart from humans, the mosquitoes have alternative hosts available as blood sources (Esteva and Vargas, 1998). Let m be the number of alternative sources for a blood meal. The probability that a mosquito chooses a human as a host over the other sources is given by $\frac{Nh}{N_h+m}$. The probability that an individual receives a bite from a mosquito per unit of time is given as $(\frac{bN_v}{N_h})(\frac{N_h}{N_h+m})$ and the rate at which a susceptible human is being infected is $(\frac{\beta_h b I_v}{N_h+m})$.

For the vector population, susceptible mosquitoes become infected when they bite an infected human. Once infected, they remain infected for life. The probability that a mosquito takes a human blood meal is $(\frac{bN_h}{N_h+m})$ per unit time and the rate at which a susceptible vector is being infected is $(\frac{\beta_v b I_h}{N_h+m})$.

In the absence of vaccination, the key intervention strategies for the effective control of malaria are prevention and treatment.

Prevention as a Means of Reducing Vector Populations

There is less chance of human interaction with mosquitoes when there are fewer of them, which is why several preventative strategies, such as Indoor Residual Spraying (IRS) and Insecticide Treated Bed-Nets (ITNs), work to reduce the mosquito population. Malaria can only remain if mosquito populations reach a certain level, according to research by Ross (1911) (Ross, 1911). The inclusion of a term that illustrates the role of preventative initiatives in decreasing mosquito populations is a significant novelty in our model. The fraction of the preventive effort that goes toward lowering the populations of vectors is represented by $c\alpha$, where $0 \leq c < 1$, with a prevention rate of α per unit time. If the vector's natural death rate per capita is μa, then the total per-capita death rate is defined as:

$$\mu_v + c\alpha \quad (1)$$

For instance, $c = 0$ corresponds to protection methods like mosquito repellents applied to exposed skin to prevent human-mosquito contact. These do not kill mosquitoes. However, the other values of $c, (0 < c \leq 1)$ corresponds to the use of prevention methods like IRS and ITNs, which kill the mosquitoes and thus, help to reduce their population.

A Novel Treatment Function

Effective treatment of malaria includes the use of appropriate medications, especially, those recommended by WHO (2019a). In all the models reviewed, the treatment (recovery) term is given as:

Table 1: Description of state variables

State variables	Explanation
$S_h(t)$	Susceptible humans at time *t*
$E_h(t)$	Exposed humans at the time *t*
$I_h(t)$	Infectious humans at time *t*
$R(t)$	Recovered humans at the time *t*
$\gamma I_h(2) S_v(t)$	Susceptible mosquitoes at time *t*
$I_v(t)$	Infectious mosquitoes at time *t*

where γ is the per-capita recovery rate and I_h is the total infective population. The treatment term given above, implicitly, assumes that treatment is readily available to all infected individuals. In fact, there are many instances in which those infected do not have ready access to healthcare facilities. Besides, there are individuals who cannot afford the cost of the medication. The reality of all of this is that, at any given time, only a proportion κ, of the infected get effective treatment. Another innovation in our model, is we replace Eq. (1) with the term:

$$\gamma(\kappa I_h) \quad (3)$$

to show that, at any given time, only a proportion of the infective population receives full treatment. Bearing in mind that, all untreated cases become reservoirs for mosquitoes to further transmit malaria to healthy individuals, part of our strategies for eliminating malaria in our communities, will be to ensure that treatment is readily available to all infectious individuals.

Taking into consideration the aforementioned, the description of the SEIRS-SI model is presented in Fig. 1. The resulting system of non-linear ordinary differential equations with saturation incidence is given as:

Table 2: Description of parameters used in the model in Eq. 4

Parameters	Detailed explanation
Λ_h	Recruitment rate for humans
Λ_v	Recruitment rates for mosquitoes
β_h	Transmission rate from infectious vector to a susceptible human
β_v	Transmission rate from infectious human to a susceptible vector
μ_h	Per-capita natural death rate for humans
δ	Disease-induced death rate
γ	Per-capita recovery rate
α	Prevention rate
$c\alpha$	Prevention efforts directed at reducing the mosquito population
μ_v	Natural per-capita death rate for mosquitoes
$(\mu_v + c\alpha)$	Total per-capita death rate for mosquitoes
μ_h	Per-capita natural death rate for humans
ω	Rate of loss of immunity for recovered individuals
b	Biting rate for the mosquitoes
m	Number of alternative hosts for a blood meal
ρ_h	Progression rate from the exposed state to the infectious state
	Latent period
c	A constant $0 \leq c \leq 1$
κ	A constant $0 \leq \kappa \leq 1$

The description of the state variables and parameters for the model are defined in Tables 1-2.
where:

$$N_h(t) = S_h(t) + E_h(t) + I_h(t) + R_h(t)$$
$$N_v(t) = S_v(t) + I_v(t)$$

Let:

$S = \Lambda - \frac{\beta_h b I_v S_h}{} + \alpha) S$

$+ \omega R q_1 = \mu_h + \alpha$ (5) $h \quad h_{h+m} \quad h \quad h \quad h \beta_h b I_h S_h q_2 = \mu_h + \rho_h E_h = {}_{N+m} - (\mu_h + \rho_h) E_h$

$I_h = \rho_h E_h - (\mu_h + \gamma\kappa + \delta) I_h$

$R_h = \gamma(\kappa I_h) + \alpha S_h - (\mu_h + \omega) R_h$

(4) $q_3 = \mu_h + \gamma\kappa + \delta$

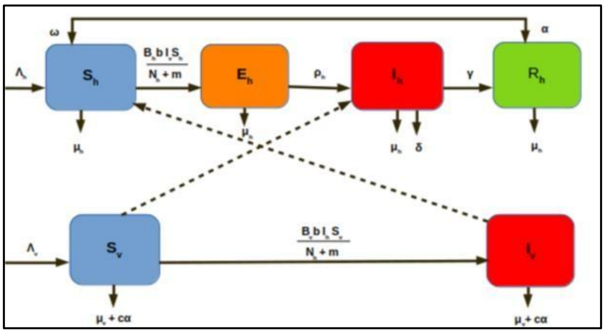
$q_4 = \mu_h + \omega$

$q_5 = \mu_v + c\alpha S_v = \Lambda_v - \frac{\beta_v b I_h S_v}{} - (\mu^{N_h+m} + c\alpha) S_v$ Then, Eq. (4) can be written as

$I = \frac{\beta_v b I_h S_v}{} - (\mu + c\alpha) I S = \Lambda - \frac{\beta_h b I_v S_h}{} - q\ S$

ωR

$\{ \quad vN_h+m \quad v \quad v \quad h \quad h N_h+m \quad 1 \ h \quad h$



$E_h = \frac{\beta_h b I_h S_h}{N_h+m} - q_2 E_h$

$I_h = \rho_h E_h - q_3 I_h$

$R_h = \gamma\kappa I_h + \alpha S_h - q_4 R_h$ (6)

$I = \frac{\beta_v b I_h S_v}{} - q\ I$

$S = \Lambda_v - \frac{\beta_v b I_h S_v}{vN_h+m} - q_5\ S$

$\{ \quad vN_h+m \quad v$

Fig. 1: Schematic diagram for the dynamics of the SEIRS-SI epidemic modelModel Analysis

In order for the model in Eq. (6) to be mathematically and epidemiologically meaningful, all the populations and subpopulations must be non-negative for $t > 0$. This can be achieved by determining an appropriate feasible region, for the model in Eq. (4).

ositivity of Solutions

The following proposition would be used to investigate

$S_h(t) \geq e^{-(\beta\ b I^{max} + (\mu_h + \alpha))t + k N_h + m}$ (11) $\quad \frac{h \quad v}{}$

the positivity of the solutions of state variables for t >0.

Proposition 1 (positivity of solutions). Let:That is:

$\beta\ b I^{max}$

$\Omega := \Omega_h \times \Omega_v \subset \mathbb{R}^4 \times \mathbb{R}^2 S_h(t) \geq A e^{-(\frac{h \quad v}{} + (\mu_h + \alpha)) t N_h + m}$ (12)

where: $4 \underline{\Lambda_h}$ where, $A = e^k$. From the initial condition, we have h

$S_h(0) \geq$ A. This implies that: max

$\Omega_h = \{(S_h, E_h, I_h, R_h) \epsilon \mathbb{R}_+ : S_h + E_h + I_h + R_h \leq {}_\mu\ ,\}$

and: $S_h(t) \geq S_h(0) e^{-(\frac{\beta_h b I_v}{} + (\mu_h + \alpha)) t N_h + m}$ $h \geq 0$ (13)

$\leq \quad \} \Omega := \{(S, I) \epsilon \mathbb{R}^2 : S + I \underline{\Lambda_v}$

The time derivative of E_h satisfies:

$+ \quad v^v \mu_v + c\alpha \frac{dE_h}{} = \frac{\beta_h b I_v S_h}{} - (\mu + \rho) E \geq -(\mu + \rho) E$ (14) $dt N_h + m h \quad h\ hhh\ h$

Suppose that the initial conditions satisfy: It follows that:

$$\{S_h(0) > 0, E_h(0) \geq 0, I_h(0) \geq 0, R_h(0) \geq 0, S_v > 0, I_v(0)) \geq 0\} \in \Omega$$

$\frac{dE_h}{} \geq -(\mu_{th} + \rho_h) E_h$ (15)

Then the solution set:

$\{S_h(t),\ E_h(t),\ I_h(t),\ R_h(t),\ S_v(t),\ I_v(t)\}$ for Eq. (6) satisfy:Separating the variables gives:

$\{S\ (t) > 0, E\ (t) \geq 0, I\ (t) \geq 0, R\ (t) \geq 0, S\ (t) \geq \frac{dE_h}{} \geq -(\mu_{E_h} + \rho_h)dt$ h (16) h h h v
$0, I_v(t) \geq 0\}$ for all $t > 0$

Proof. From Eq. (4), the time derivative of S_h satisfies:Integrating gives:

$ln\, E_h \geq -(\mu_h + \rho_h)t + k$ (17)$\frac{dS_h}{dt} = \frac{\beta_h b I_v}{N_h + m} S - (\mu_h + \alpha)S_h + \omega R_h$ (7)Exponentiation gives:

$\geq -\frac{\beta_h b I_v}{N_h + m} S_h - (\mu_h + \alpha)S E_h(t) \geq e^{-(\mu_h+\rho_h)t+k}$ (18)

where, k is a constant. The expression can now be written as:
It follows that:

$E_h(t) \geq Be^{-(\mu_h+\rho_h)t}(19)\frac{dS_h}{} \geq -(\frac{\beta_h b}{} I + (\mu + \alpha))$
S(8)$t_{N_h+}$where, $B = e^k$. With the given initial condition and at $t =$

Separating the variables gives:0, we have $E_h(0) \geq B$.

Therefore:

$\frac{dS_h}{t} \geq -(\frac{\beta_h b}{N_h+m} I_v + (\mu + \alpha))\, dt \geq$ (9)

$E_h(t) \geq E_h(0)e^{-(\mu_h+\rho_h)t} \geq 0$ (20)

$-(\frac{\beta_h b}{N_h + m} I_v^{max} + (\mu_h + \alpha))\, dt$

Similarly, it can be shown that:
where, I_v^{max} is the maximum of I_v the interval $[0, T]$.

Integrating both sides gives: $I_h(t) \geq I_h(0)e^{-(\mu_h+\gamma\kappa)t} \geq 0$ (21)

$lnS_h \geq -(\frac{\beta_h b}{N_h+m}\int_0 I_v^{max} d\tau + (\mu + \alpha)t) + k \geq$ and:

$-(\frac{\beta_h b I_v^{max}}{N_h+m} t + (\mu_h + \alpha)t) + k$ (10)$R_h(t) \geq R_h(0)e^{-(\mu_h+\omega)t} \geq 0$ (22)

where, k is a constant of integration.

Exponentiation gives: $S_h(t) \geq S_h(0)e^{-(\frac{\beta_v b I_v^{max}}{N_h+m}+(\mu_h+\alpha c))t} \geq 0$ (23)

nd: $N_v(0) \leq \frac{\Lambda_v}{\mu_v + c\alpha} \Rightarrow N_v(t) \leq \frac{\Lambda_v}{\mu_v + c\alpha}, \forall t \geq 0$

$I_v(t) \geq I_v(0)e^{-(\mu_h+\alpha c)t} \geq 0$ (24)

Proposition 2 (invariant region). The region $\Omega = \Omega_h \times \Omega_v$ defined by:That is, if the initial vector $N_v(0)$, lies within the feasible region Ω_v, then $N_v(t)$ lies in the feasible region for the all-time $t > 0$:

$\Omega_h = \{(S_h, E_h, I_h, R_h) \epsilon \mathbb{R}_+^4 : S_h + E_h + I_h + R_h \leq \frac{\Lambda_h}{\mu_h}, S_h > 0, E_h > 0, I_h > 0, R_h > 0\}$

$\limsup_{h\to\infty} N_h(t) = \frac{\Lambda_h}{\mu_h + c\alpha}$

The vector population is bounded above by its carrying $K_v = \frac{\Lambda_v}{\mu_v + c\alpha}$ and:

$\Omega_v = \{(S_v, I_v) \epsilon \mathbb{R}_+^2 : S_v + I_v \leq \frac{\Lambda_v}{\mu_v + c\alpha}, S_v > 0, I_v > 0\}$ The region $\Omega = \Omega_h \times \Omega_v$ is, therefore, positively invariant. Hence, the model in Eq. (6) is mathematically and epidemiologically well-posed.

Is positively invariant under the flow given by the system in (6).
Proof. Using the expression for total human population:

$N_h = S_h + E_h + I_h + R_h$ we have:Equilibrium Points

Without loss of generality, we determine the equilibrium points of the system in Eq. (6), with $\kappa = 1$. The equilibrium points are the solutions of:
$N_h = S_h + E_h + I_h + R = \Lambda - \mu_h N_h - \delta I$(25) $S_h = E_h = I_h = R_h = S_v = I_v = 0$ (29)
From the last equation in Eq. (25), we obtain we obtain: $N_h + \mu_h N_h = \Lambda_h - \delta I_h$

$$N_h + \mu_h N_h \le \Lambda_h$$

(26)
The system has unique disease-free and endemic equilibrium points denoted respectively, by: $\Theta^0 = (S^0, E^0, I^0, R^0, S^0, I^0)$

Using integrating factor $e^{\mu_h t}$, the solution of the linear system in Eq. (26) gives:
and:

$N_h(t) \le \frac{\Lambda_h}{\mu_h} + k_1 e^{-\mu_h t}$ (27) $\Theta^* = (S^*_h, E^*_h, I^*_h, R^*_h, S^*_v, I^*_v)$

where, the constant $k_1 = N_h(0) - \frac{\Lambda_h}{\mu_h}$. Substituting into The *DFE* is given by:

(27) and re-arranging gives $\Theta^0 = \left(\frac{\Lambda_h(\mu_h+\omega)}{\mu_h(\alpha+\mu_h+\omega)}, 0, 0, \frac{\Lambda_h \alpha}{\mu_h(\alpha+\mu_h+\omega)}, \frac{\Lambda_v}{\alpha c+\mu_v}, 0\right)$ (30)

$N_h(t) + \left(\frac{\Lambda_h}{\mu_h} - N_h(0)\right) e^{-\mu_h t} \le \frac{\Lambda_h}{\mu_h}$ (28) The endemic equilibrium point is given by: $\Theta = (S^*_h, E^*_h, I^*_h, R^*_h, S^*_v, I^*_v)$

The inequality in (28), shows that:

$N_h(0) \le \frac{\Lambda_h}{\mu_h} \Rightarrow N(t) \le \frac{\Lambda_h}{\mu_h}, \forall t \ge 0$ where: $(K_h + m)^2 q_2 q_3 q_5^2 (q_2 q_3 q_4 - \gamma\kappa\omega\rho_h)$

$$S^*_h = \frac{+q_2 q_3 q_4 q_5 \Lambda_h b \beta_v (K_h + m)}{\Lambda_v b^2 \beta_h \beta_v \rho_h (q_2 q_3 q_4 - \gamma\kappa\omega\rho_h) + b\beta_v q_2 q_3 q_5 \rho_h (K_h + m)[q_1 q_4 - \alpha\omega]}$$

That is, if the initial population $N_h(0)$, lies within the feasible region Ω_h, then $N_h(t)$ lies in the feasible region for the all-time $t > 0$:

$$E^*_h = \frac{(q_3 q_5^2 (K_h + m)^2 (q_1 q_4 - \alpha\omega)) - \Lambda_h \Lambda_v b^2 \beta_h \beta_v \rho_h q_3 q_4}{\Lambda_v b^2 \beta_h \beta_v \rho_h (q_2 q_3 q_4 - \gamma\kappa\omega\rho_h) + b\beta_v q_2 q_3 q_5 \rho_h (K_h + m)[q_1 q_4 - \alpha\omega]}$$

$$\limsup_{t\to\infty} N_h(t) = \frac{\Lambda_h}{\mu_h}$$

The host population is bounded above by its carrying capacity $K_h = \frac{\Lambda_h}{\mu_h}$.

$$I^*_h = \frac{\left(q_2 q_3 q_5^2 (K_h + m)^2 (q_1 q_4 - \alpha\omega)\right) - \Lambda_h \Lambda_v b^2 \beta_h \beta_v \rho_h q_4}{\Lambda_v b^2 \beta_h \beta_v \rho_h \left(q_2 q_3 q_4 - \gamma\kappa\omega\rho_h\right) + b\beta_v q_2 q_3 q_5 \rho_h (K_h + m)\left[q_1 q_4 - \alpha\omega\right]}$$

Similarly, for the vector population, it can be shown that:

$$R^*_h = \frac{(K_h + m)^2 q_2 q_3 q_5^2 \left(\alpha q_3 - \gamma\kappa q_5\right) + \Lambda_h \Lambda_v b^2 \beta_h \beta_v \gamma\kappa\rho_h^2 + \Lambda_h \alpha b \beta_v \rho_h q_2 q_3 q_5 (K_h + m)}{\Lambda_v b^2 \beta_h \beta_v \rho_h \left(q_2 q_3 q_4 - \gamma\kappa\omega\rho_h\right) + b\beta_v q_2 q_3 q_5 \rho_h (K_h + m)\left[q_1 q_4 - \alpha\omega\right]}$$

$G = FV^{-1}$ is called the next-generation matrix, (Diekmann *et al.*, 1990).

$$S^*_v = \frac{\Lambda_v b \beta_h (N_h + m)\left[q_2 q_3 q_4 - \gamma\kappa\omega\rho_h\right] + q_2 q_3 q_5 (K_h + m)^2 \left[q_1 q_4 - \alpha\omega\right]}{b\beta_h q_5 (K_h + m)\left[q_2 q_3 q_4 - \gamma\kappa\omega\rho_h\right] + \Lambda_h b^2 \beta_h \beta_v q_4 \rho_h}$$

The entries of the matrix give the rate at which infected individuals of state j generate new infections of type i. The basic reproduction number $\Re_0$, is the dominant eigenvalue of G denoted by $\rho(G)$. That is:

$\Re_0 = \rho(G) = \rho(FV^{-1})$ (32)

$$I^*_v = \frac{q_2 q_3 q_5^2 \left(K_h + m\right)^2 \left[q_1 q_4 - \alpha\omega\right] - \Lambda_h \Lambda_v b^2 \beta_h \beta_v q_4 \rho_h}{b\beta_h q_5 \left(K_h + m\right)\left[q_2 q_3 q_4 - \gamma\kappa\omega\rho_h\right] + \Lambda_h b^2 \beta_h \beta_v q_4 \rho_h}$$

One important aspect of the basic reproduction

The Basic Reproduction Number

In epidemiology, the next-generation matrix is a method used to derive the basic reproduction number, for a compartmental model of the spread of infectious diseases and the method is given by Van den Driessche andnumber is that; it determines whether a disease will persist or die out if there is an outbreak or there is a small perturbation of the system. Therefore, using the next- generation matrix approach (Diekmann *et al*., 1990) the appearance of new cases of infections F_i and the rate of transfer of infectious from one compartment to a different one in the systems V_i for Eq. (6) is given as:

$\beta_h b I_v s_h$

Watmough (2002); Diekmann *et al.* (1990). Many of$K + m(\rho_h - \mu_h)E_h$

today's most important emerging infectious diseases aremulti-host infections by their very nature. As a result, h

$F_i = |\ 0\ |$ and $V_i = [(\delta + \kappa\gamma + u_h)I_h]$

they require a slightly more complex formalism for investigating epidemic thresholds, etc. The basic tool for $|\beta_v b I_h S_v|$

$[K_h + m](u_v + c\alpha)I_v$

examining epidemic thresholds in complex, structured models is the so-called next-generation matrix. Consider a population of individuals (or species) subdivided intoThe corresponding Jacobian matrix F and V evaluated at the DFE respectively is given as:

$S_h b\beta_h$ n compartments, of which m are infected. Let x_i represent the proportion of the population in the i^{th} 0 $0F = K_h + m$

compartment and let the vector of the proportions in all the compartments be . 0 0 0 0

$S_v b\beta_{v}$ 0 x

In order to compute $\Re_0$, it is important to distinguish new infections from all other changes in the population.and:[

$K_h + m$]

Let: $\mu_h + \rho_h$ 0 0

- $F_i(x)$ the rate of appearance of new infections in$V = [-\rho_h$ $\delta + \kappa\gamma + \mu_h$ 0]

0 0 $\alpha c + \mu_v$

compartment iThe next generation matrix $G = FV^{-1}$ is given as:

- $V_i^{+}(x)$ is the rate of transfer of individuals into$(\Lambda\ \mu_h + \Lambda_h\ \omega)b\beta_h$ compartment I by all other means and 0 0_h $]\Psi_1$
- $V_i^{-}(x)$ is the rate of transfer of individuals out of$G = |$ 0 0 0 $|$ compartment i

It is assumed that each function is continuously differentiable at least twice in each variable. The disease

where:$|\Lambda_v b\beta_v \rho_h$

$[\ \ \Psi_2 \Lambda_v b\beta_v$ 0 $|$

Ψ_2]

transmission model consists of non-negative initial conditions together with the following system of equations:$\Psi_1 = (\alpha c + \mu_v)(\alpha\mu_h + \mu_h^2 + \mu_h\omega)(K_h + m)$

$\dot{x}_i = f_i(x) = F_i(x) - V_i(x), i = 1, \dots, n$ (31)$\Psi_2 = (\alpha c + \mu_v)(\delta + \kappa\gamma + \mu_h)(K_h + m)$

The eigenvalues obtained from G are:

where, $V_i = V_i^{-} - V_i^{+}$ We define the matrices: $_h\Lambda_v b^2 \beta_h \beta_v(\mu_h + \omega)\rho_h$

$\partial F \partial V \Re\ (\alpha) = +(\alpha + \mu\omega)(\delta + \kappa\gamma + \mu\ )(\mu + \rho\ )$ 1

$F = [\frac{i}{}(E^0)], V = [\frac{i}{}(E^0)]_h$ h h h

$\partial x_j 0$

∂x_j

$\Re(\alpha) = \mu_h(\alpha c + \mu_v)^2(K_h + m)^2$ $\frac{\Lambda_h \Lambda_v b^2 \beta_h \beta_v(\mu_h + \omega)\rho_h}{}$

(33)where, E

denotes the disease-free equilibrium and the $2\sqrt{(\alpha + \mu_h + \omega)(\delta + \kappa\gamma + \mu_h)(\mu_h + \rho_h)}$indices $i, j = 1, \cdots, m$. The matrix G, given by:

$\mu_h(\alpha c + \mu_v)^2(K_h + m)^2$

he spectral radius is the dominant eigenvalue obtained in Eq. (33). The basic reproduction number, with prevention at the rate α, denoted by $R_o(\alpha)$, is given by:

Theorem 1. The disease-free equilibrium point for the model in 4 is locally asymptotically stable in Ω if $\Re_o(0) < 1$ and unstable if $\Re_o(0) > 1$.

Proof. The Jacobian matrix J, for linearizing the

$\Re_0(\alpha) = \dfrac{\Lambda_h \Lambda_v b^2 \beta_h \beta_v (\mu_h + \omega)\rho_h}{\sqrt{\mu_h(\alpha c+\mu_v)(K_h+m)(\alpha+\mu_h+\omega)\ (\delta+k\gamma+\mu_h)(\mu_h+\rho_h)}}$ (34)

system of differential equation in Eq. 4 at the DFE, with $\alpha = 0$, is given by:

The corresponding basic reproduction number without prevention ($\alpha = 0$) is:

$$\Re_o(0) = \sqrt{\frac{\Lambda_h \Lambda_v b^2 \beta_h \beta_v \rho_h}{\mu_h(\mu_v)^2 (K_h + m)^2 (\delta + k\gamma + \mu_h)(\mu_h + \rho_h)}} \quad (35)$$

$$j = \begin{bmatrix} -\frac{1_v b\beta_h}{K_h+m} - \mu_h & 0 & 0 & \omega & 0 & -\frac{S_h b\beta_h}{K_h+m} \\ \frac{1_v b\beta_h}{K_h+m} & -q_2 & 0 & 0 & 0 & \frac{S_h b\beta_h}{K_h+m} \\ 0 & \rho_h & -q_3 & 0 & 0 & 0 \\ 0 & 0 & k\gamma & -q_4 & 0 & 0 \\ 0 & 0 & -\frac{S_v b\beta_v}{K_h+m} & 0 & -\frac{1_h b\beta_v}{K_h+m} - \mu_v & 0 \\ 0 & 0 & \frac{S_v b\beta_v}{K_h+m} & 0 & \frac{1_h b\beta_v}{K_h+m} & -\mu_v \end{bmatrix}$$

From Eqs. 34-35 it is easy to see that:

$$\Re_o(\alpha) \le \Re_o(0) \quad (36)$$

The inequality in indicates that it is easier to control the spread of an infectious disease when there is prevention than without prevention.

The Endemic Equilibrium Point Expressed in Terms of $\Re_0$

Evaluating J at DFE gives:

Using $\kappa = 1$, the endemic equilibrium is expressed in terms of the basic reproduction number as fellow:

$$J(\alpha_0) = \begin{bmatrix} -\mu_h & 0 & 0 & \omega & 0 & -\frac{\Lambda_h b\beta_h}{(K_h+m)\mu_h} \\ 0 & -q_2 & 0 & 0 & 0 & \frac{\Lambda_h b\beta_h}{(K_h+m)\mu_h} \\ 0 & \rho_h & -q_3 & 0 & 0 & 0 \\ 0 & 0 & \kappa\gamma & -q_4 & 0 & 0 \\ 0 & 0 & -\frac{\Lambda_v b\beta_v}{(K_h+m)\mu_v} & 0 & -\mu_v & 0 \\ 0 & 0 & \frac{\Lambda_v b\beta_v}{(K_h+m)\mu_h} & 0 & 0 & -\mu_v \end{bmatrix} \quad (38)$$

$$S_h^* = \frac{A(q_1 q_3 q_4 - \omega\rho_h) + Bq_4^2 \Re_o^2(\alpha)(q_1 q_4 - \gamma\omega)}{C\Re_o^2(\alpha)(q_1 q_4 - \gamma\omega)}$$

$$E_h^* = \frac{D(\Re_o^2(\alpha) - 1)}{C}$$

$$I_h^* = \frac{Dq_3(\Re_o^2(\alpha) - 1)}{C}$$

Three of the eigenvalues of $J(\theta_0)$ is given as:

$$R_h^* = \frac{A\rho_h(\alpha q_3 - \gamma\kappa q_1) + (A\rho_h + B)\Re_o^2(\alpha)(q_1 q_4 - \alpha\omega)}{C\Re_o^2(\alpha)(q_1 q_4 - \alpha\omega)}$$

$$\lambda_{1,2,3} = -\mu_v, -\mu_h, -(\mu_h + \omega) < 0 \quad (39)$$

Respectively we now use the corollary of gershgorin's circle theorem given in Appendix A, to establish the stability of the 3×3 sub-matrix $J_3(\alpha_0)$, given by:

$$S_v^* = \frac{q_5\Re_o^2(\alpha) + AqS_h^*}{Hq_4\Re_o^2(\alpha)}$$

$$I_v^* = \frac{D(\Re_o^2(\alpha) - 1)}{H}$$

$$J_3(\alpha_0) = \begin{bmatrix} -\rho - \mu_h & 0 & \frac{\Lambda_h b\beta_h}{\mu_h(K_h+m)} \\ \rho_h & -\delta - \kappa\gamma - \mu_h & 0 \\ 0 & \frac{\Lambda_v b\beta_v}{(K_h+m)\mu_v} & -\mu_v \end{bmatrix} \quad (40)$$

where: $A = \Lambda_v \Lambda_h b^2 \beta_h \beta_v \rho$

Applying the corollary of Gershgorin's circle theorem to the Jacobian matrix $J(\alpha)$ gives the inequalities.

$B =$ $\beta_v\rho_h(q_2q_3q_4 - \gamma\omega\rho_h)3$ 0($\Lambda\ b\beta$) $-(\delta + k\gamma + \mu_{h h})$

$\Lambda_h b\beta_v$ $+b^2\beta_v\rho_h q_2q_3q_5(K_h + m)(q_1q_4 - \gamma\omega)-(\rho+\mu_h) < (K+$ (41)^2 *(43)*$(K_h$

$\rho_h q_2q_3$ $m)\mu$ $) < -\rho_h$ $+m)\mu_v$

$q_5(K_h$ $D = q_2q_3q_5(K_h + m)\ (q_1q_4 - \alpha\omega)$ (42)

$+ m)$ $G = \Lambda_v b\beta_h(K_h + m)(q_2q_3q_4 - \gamma\omega\rho_h)$ *Local*

$C =$ $H = \Lambda_h b^2\beta_h\beta_v\rho_h q_4 + b\beta_h q_5(K_h + m)(q_2q_3q_4 -$ *Stability Analysis*$-\mu_v - (\frac{\Lambda_v b\beta_v}{\ })$

$\Lambda_v b^2\beta_h$ $\gamma\omega\rho_h)(37)$

Stability Analysis of the Disease-Free Equilibrium Point

The following theorem establishes the local stability of the disease-free equilibrium point.The above inequalities can be rewritten respectively, as:

$1 > (\frac{\Lambda_h b\beta_h}{\ })(44)(K_h+m)(\rho_h+\mu_h)\mu_h$

$1 > (\frac{\rho_h\quad v}{\ })(45)(\delta + \kappa\gamma + \mu_h)1 > (\frac{\Lambda_v b\beta_v}{\ })(46)(K_h+m)\mu^2$

$-\ q\ + Z\ < -\frac{(GR^2(\alpha)q\ + Aq\ )R^2(\alpha)b\beta\ q}{H(K_h+m)}(54)$ $(\ _5\quad _3)$ $\ _o\quad _5\quad _4\quad _o\quad _v\ _5$

Multiplying the inequalities 44-46 gives:

$-q_5 < -\frac{(GR^2(\alpha)q\ + Aq\ )R^2(\alpha)b\beta\ q}{\ } - Z_3 H(K_h+m)$ $H(K_3+m$ $\ _o\quad _5\quad _4\quad _o\quad _v\ _5$(55)

$1 > \frac{\Lambda_h\Lambda_v b^2\beta_h\beta_v\rho_h}{2\quad 2} = \Re^2_o(0)(47)\mu_h\mu\ (K_h+m)$The inequalities in Eqs. 51-55 can be rewritten respectively, as:

This implies that:$(q + Z\ ) - (\omega + \frac{\tau_1}{\ }) > 0$ (56)

1 1

$\Re^2_o(0) < 1(48)C(K_h+m)$

This shows that all the eigenvalues of the 3×3 sub-$q_2 - (Z_1 + \frac{\tau_1}{C(K_h+m)}) > 0$ (57)

matrix in (40) are negative, or have negative real parts. Therefore, DFE is locally asymptomatically stable.$q_3 - \rho_h > 0$ (58)

Local Stability of Endemic Equilibrium Point$q_4 - (\alpha + \kappa\gamma) > 0$ *(59)*

The following theorem establishes the local stability of the EE, with $\kappa = 1$. $(q\ + Z\ - (\frac{(GR^2(\alpha)q\ + Aq\ )R^2(\alpha)b\beta\ q}{H(K_h+m)}) > 0$ $\ _o\quad _5\quad _4\quad _o\quad _v\ _5$ (60)

Theorem 2. The endemic equilibrium is locally asymptotically stable in Ω if $\Re_o(\alpha) > 1$ and unstable if $\Re(\alpha) < 1$. 5 3

$\frac{(GR^2(\alpha)q\ + Aq\ )R^2(\alpha)b\beta\ q}{H(K_h+m)}q\ - (\ + Z\ ) > 0$ 5 $\ _o\quad _5\quad _4\quad _o\quad _v\ _5$ 3 (61)

Proof. The Jacobian matrix evaluated at the EE θ_* is:Adding the inequalities in Eqs. 56-61 gives:

$$J(\theta_*) = \begin{bmatrix} -q_1 & 0 & 0 & \omega & 0 & -\frac{\tau_1}{C(K_h+m)} \\ Z_1 & -q_2 & 0 & 0 & 0 & \frac{\tau_1}{C(K_h+m)} \\ 0 & \rho_h & -q_3 & 0 & 0 & 0 \\ 0 & 0 & \kappa\gamma & -q & 0 & 0 \\ 0 & 0 & -Z_2 & 0 & -Z_3 - q_5 & 0 \\ 0 & 0 & Z_2 & 0 & Z_3 & -q_5 \end{bmatrix}$$

(49)where:

$2\frac{\ _o\quad _v\ _3}{\ } + 2\frac{oh}{\ } + Z_4 > 0$ (62)$-Z - q\frac{\tau_1}{\ }$ $\frac{(R^2(\alpha)-1)Db\beta\ q}{C(K_h+m)H(K_h+m)}$ $(R^2(\alpha)-1)Db\beta$

$Z_4 = q_1 + q_2 + q_3 + q_4 + 2q_5 + \omega + \rho_h + (\alpha + \omega)$ (63)$+2(\omega + \frac{\tau_1}{C(K_h+m)}) + 2(\frac{(GR^2(\alpha)q\ + Aq\ )R^2(\alpha)b\beta\ q}{H(K_h+m)})$ 54 v 5

The inequality in (64) can be rewritten as:

where:

$(\Re^2(\alpha) - 1)(2\frac{Db\beta_v q_3}{\ } + 2\frac{Db\beta_h}{\ }) + Z$ 4

> 0 (64)$\tau = ((q\,q\ - \alpha\omega)BR^2(\alpha)q\ + (q\,q\,q\ - k\gamma\omega\rho\ )A)(q\,q\ - \alpha\omega)R^2(\alpha)b\beta C(K_h+m)H(K_h+m)$

$(R^2(\alpha) - 1)Db\beta_h$ Since $Z_4 > 0$, then the inequality in (64) is satisfied

$$z_1 = 0 \; \overline{} \; H\left(K_h + m\right)$$

provided:

$$\theta_2 \quad \frac{\left(GR_0^2(\alpha)q_5 + Aq_4\right)R_0^2(\alpha)b\beta v q_5}{C(K_h + m)H(K_h + m)} \qquad (\Re^2(\alpha) - 1)\left(2\frac{Db\beta_v q_3}{} + 2\frac{Db\beta_h}{}\right) > 0 \quad (65)$$

$$\frac{}{H\left(K_h + m\right)}$$

$= \frac{\left(R_0^2(\alpha)-1\right) Db\beta vq_3^{z_3}}{h} \quad C(K+m)$

Using the corollary of Gershgorin's circle theorem in Appendix A, we have:

$-(q_1+Z_1) < -(\omega + \frac{\tau_1}{C(K_h+m)\tau})$ (50) Again, the inequality in (66) is positive if:

$(\Re^2_o(\alpha) - 1) > 0$ (66)

That is:

$\Re^2_o(\alpha) > 1$ (67)

Or equivalently:

$\Re_o(\alpha) > 1$ (68)

Hence, the endemic equilibrium is locally asymptotically

$-q_2 < -(Z_1 + \frac{1}{C(K_h+m)})$ (51)

$-q_3 < -\rho_h$ (52)

$-q_4 < -(\alpha + \kappa\gamma)$ (53) stable provided $\Re_o(\alpha) > 1$ and unstable otherwise.

Global Stability of Disease-Free Equilibrium Point

In order to ensure that DFE is independent of the initial size of the sub-population of the model, it is necessary to show that the DFE is globally asymptotically stable. One of the approaches to studying the global

$= \frac{c_0 c_2 \mu_h(\mu_h + \alpha\omega)(\mu_v + c\alpha)(K_h + m)}{\beta_h b\Lambda_h(\mu_h + \omega)}$

asymptotic stability of DFE is to construct an appropriate Lyapunov function (Lazarus, 2018). The following $c_1 = \frac{c_0(\mu_h + \rho_h)}{\rho_h}$

theorem describes the global stability.

Theorem 3. The DFE is globally asymptotically stable $c_2 = \frac{c_1(\mu_h + \delta + \gamma\kappa)(\mu_v + c\alpha)(K_h + m)}{\beta_v b\Lambda_v}$

in Ω if $\Re_o \leq 1$.

Proof. Consider a Lyapunov function:

Substituting c_0, c_1 and c_2 into Eq. (73) gives:

$V = c_0E_h + c_1I_h + c_2I_v$ $V = c_0(\mu_h + \rho_h)[\frac{c_0(\mu_h+\rho_h)\rho_h}{c_0\rho_h(\mu_h+\rho_h)} - 1]E_h$

where: $c_0 > 0, c_1 > 0, c_2 > 0$ $+ c_1(\mu_h + \delta + \gamma\kappa)[\frac{(K_h+m)\beta_v b\Lambda_v}{2(K_h+m)\beta_v b\Lambda_v} \cdot \frac{c_1(\mu_h + \delta + \gamma\kappa)(\mu_v + c\alpha)}{c_1(\mu_h+\delta+\gamma\kappa)(\mu_v+c\alpha)} - 1] I_h$ (74)

The time derivative of the Lyapunov function V gives the following expression: $c_0\beta_v\beta_h b^2\Lambda_v\Lambda_h(\mu_h + \omega)\rho_h$ $+ c_2(\mu_v + \alpha c)[c_1(\mu_h + \delta + \gamma\kappa)(\mu_v + \alpha c)^2] I_v.$

$\dot{V} = c_0\dot{E}_h + c_1\dot{I}_h + c_2\dot{I}_v$ $\mu_h(\mu_h + \alpha + \omega)(K_h + m)^2$

Substituting $\dot{E}_h, \dot{I}_h$ and $\dot{I}_v$ into the equation above gives us: Simplifying Eq. (74) gives:

$\dot{V} = c_0[\frac{\beta_h bI_vS_h}{K_h+m} - (\mu_h + \rho_h)E_h]$ (69) $c_0\beta_v\beta_h b^2\Lambda_v\Lambda_h(\mu_h+\omega)\rho_h$

$+ c_1[\rho_hE_h - (\mu_h + \gamma\kappa + \delta)I_h]$ $V = c_2(\mu_v + \alpha c)[c_1(\mu_h + \delta + \gamma\kappa)(\mu_v + \alpha c)^2] I_v$ (75)

Note that: $+c_2[\beta_v b I_h S_v - (\mu$

$K_h + m^v + c\alpha) I_v] \mu_h(\mu_h + \alpha + \omega)(K_h + m)^2$

Again, substituting c_1 and q_5 from Eq. (77) and Eq. gives:

$S_h \beta \neq b^2 \rho \Lambda \Lambda (\mu + \omega)$ and $S = \frac{\Lambda_v}{}$ (70)

$\frac{\Lambda_h(\mu_h+\omega)}{\mu_h(\mu_h+\alpha+\omega)^v}$ $\mu_v + \alpha c$ $V = c_2(q_5)[$

$- 1 c_0(\mu_h+\rho_h)(\mu_h+\delta+\gamma\kappa)] I_v$, (76)

Substituting Eq. (70) into Eq. (69) gives: $(q_5)^2 \mu_h(\mu_h + \alpha + \omega)(K_h + m)^2$

$V = c$

$[\frac{\beta_h b I_v \Lambda_h(\mu_h+\omega)}{\mu_h(\mu_h+\alpha+\omega)(K_h+m)} - (\mu_h + \rho_h) E_h]$ (71) Which can be expressed in terms of R^2_o as:

$+c_1[\rho_h E_h - (\mu_h + \gamma\kappa + \delta)] I_h$

$+c2\left[\frac{\beta_v b I_h \Lambda_v}{(\mu_v + \alpha c)(K_h + m)} - (\mu_v + \alpha c) I_v\right]$

$V = c_2(\mu_v + \alpha c)[\Re^2_o(\alpha) - 1] I_v$ (77)

Grouping Eq. (71) into E_h, I_h and I_v gives:

$V = [c_1\rho_h - c_0(\mu_h + \rho_h)] E_h$ (72) Therefore:

$V = 0$ if $\Re^2 = 1$

$+\left[c2\frac{\beta_v b \Lambda_v}{} - c1(\mu_h + \gamma k + \delta)\right] I_h$ $\dot{V} < 0$ if $\Re^2 < 1$ (78)

$+ [c(\mu_v + \alpha c)(K_h + m)$

$\frac{\beta_h b \Lambda_h(\mu_h + \omega)}{} - c(\mu$

$+ c\alpha)] I_o$

Hence, the DFE is globally asymptotically stable in Ω

$\mu_h(\mu_h + \alpha + \omega)(K_h + m)$

if $\Re^2$.

Further simplification gives: $_o \leq 1$

Global Stability of the Endemic Equilibrium

The following theorem will be used to prove for global stability of the EE.

$= c_0(\mu_h + \rho_h)[\frac{c_1\rho_h}{} - 1] E$

$+c_1(\mu_h + \delta + \gamma)\kappa [c_0(\mu_h+\rho_h)^h 2\beta_v b \Lambda_v c_1(\mu_h + \delta + \gamma\kappa)$

$] I_h$ (73)

Theorem 4. The EE is globally asymptotically stable in Ω if $\Re_o(\alpha) > 1$.

$(\mu_v + c\alpha)(K_h + m)$ Proof. We define the following candidate logarithmic Lyapunov function as:

$+c_2(\mu_v + \alpha c)[\frac{c_0\beta_h b \Lambda_h(\mu_h+\omega)}{c_2(\mu_v+\alpha c)\mu_h(\mu_h + +)(K_h+m)} - 1] I_v$

Considering the coefficient of I in Eq. (72), we

$V = c(S - S^* - S^* \log\frac{S_h}{S}) +$

choose the constant c_0, c_1, c_2 respectively as: $(S - S^*)\beta_v b I_h S_v$ $(E - E^* - E^* \log\frac{h}{E^*}) + c_4 |$ $| [-(\mu_v + \alpha c) S_v]$

$K_h + m (I - I^*) \beta b I S$ $+c_5 |$

$[\_^{v} \ \underline{h\ v} - (\mu_v + \alpha c)I_v]$

$c_3\,(I_h - I_h - I_h \log \frac{}{I^*}) + (I_v) K_h + m$

$c_4\,(S_v - S^* - S^* \log \underline{S_v}$ +Factorizing like terms gives:

$S_*\,(S - S^*)\ \ (\beta\, bI^*\, S\ \ \ \beta\, bI\, S\ )$

$V = c_1 |\ \underline{h\ \ h}\ |\ [\ |\ \underline{h\ \ v\ h}\ \underline{I_v}\ \ \underline{h\ \ v\ h}\ S_h)\ |\ ](82)\ K_h + m\ \ \ K_h + m\ )$

$c_5\,(I_v - I_v - I_v \log \quad)$ I^*

$(S - S^*) - c|\ \underline{h\ \ h}\ |\ [(\mu + \alpha)(S - S^*) - \omega(R - R^*)\ ]$

where, $(c_1, c_2, c_3, c_4, c_5) > 0$, are to be determined. Note that $V = 0$ when $(S_h, Eh, Ih, Sv, I_v) = 1\ (S$ $(E - E^*)[\ \beta_h bI_v S$ $(S^*, E^*, I^*, R^*, S^*, I^*)$ and $V > 0$, otherwise. Hence, V is radially unbounded. We need to show that the derivative $V > 0$. The time derivative of V is given by:

$c_2 |\ \underline{h\ \ E\ h}\ \|\ \underline{h\ \ v\ h}\ K + m - (\mu + \rho h)E_h\ |$

$+c_3 \left(\frac{I_h - I_h^*}{} \right) [\rho_h E_h - (\mu_h + \gamma\kappa + \delta)I_h]$

I_h

$c(1 - \ \ \ S$

E

$) Ec(79) + c(S - S^*)\ \ |\ [\ bI^*\ S^*$

$-\ \beta_v bI_h S_v\ ]$

$1\ \ S_h\ \ h\ \ 2E_h\ h\ \ \ 3\ 4(\ \ S\ \ )K_h + m + m*\ \ \ I^*\ \ S - S^* \mu + \alpha$

$(1 -$

$I_h)\ I_h + c_4(1 - S_v)\ S_v + c_5(1 - I_v)\ I_v c_4 - ((\ c)(S_v - S_v))$

S

$+c_5\,(\frac{I - I^*}{v\ \ \ v})\,[\_^{v}\ \underline{h\ v} - (\mu_v + \alpha c)I_v]$ $\beta\, bI\, S$

Substitute S_h, E_h, I_h, S_v, I_v into Eq. (79) gives: I_v $K_h + m$

$V = c_1 \left(\frac{S_h - S_h^*}{S_h} \right) [\Lambda_h - \underline{h\ \ v\ h} - (\mu_h + \alpha)S_h + \omega R_h] + c_2$ Multiplying out all of Eq. (82) is given as:

$K_h + m$ V

$c\ \beta\ bI^* S^*\ \ \ c\ \beta\ bI^* S^{*2} c_1 \beta_h bI_v S_h c\ \beta\ bI^* S^{*2}$

$E_h\ \ E_h$ $\beta_h bI_v S_h$

$I_h - I_h$ $mK_h + m$ $= \ \ \underline{1\ \ h\ \ v\ \ h} - \underline{1\ \ h\ \ v\ \ h} - + \underline{1\ \ h\ \ v\ \ h}\ \ E$

$|\ [\ K + m - (\mu_h + \rho_h)E_h] + c_3 |$ 2 $I\ \rho_h E_h K_h + m(K_h\ \ m)S_h K_h +$

$(\mu_h + \alpha)(S - S^*) + c_1\omega(R - R^*)\ (S - S^*)$

$+\gamma\kappa + \delta)I\ ] + c(\underline{S_v - S_v})$ $\beta_v bI_h S_v$ $[\Lambda$ $- (\mu\ +$

S_v $K_h + m^{v} - S_h$

$c\ \beta\ bS\ I\ - c_2 \beta_h bS_h I_v E_h^*$

$\alpha c)S_v] + c$

$(I_v - I_v)$ $[\beta_v bI_h S_v - (\mu + \alpha c)I\ ]$ (80) $\underline{2\ \ h\ \ \ h\ v}$ $- c\ (\mu$

$\rho\ )E$ 5 v

$K + m$ $K\ m)(Km)E_h$ I_v

$c_3 \rho_h E_h\ I^*$

$+ c\ (\mu\ + \rho\ )\ E^* + c\ \rho\ E\ -$

Replacing Λ_h and Λ_v with the corresponding values at the endemic equilibrium points gives: $h\ h\ \ c\ \beta\ b\ I^*\ S^*$

$- c\ (\mu\ + \gamma k + \delta)I + c\ (\mu + \gamma k + \delta)\ I^*\ + v$

$K_h + m$

$V = c$

$\frac{S_h - S_h}{S_h} \left[\frac{\beta_h bI_v S_h}{K_h + m} - (\mu\ \ \alpha)S^* - \omega R^*\ \right]$

81) $c\ \beta\ b\ I^*\ S^2 c\ \beta\ bI\ \ S^*$

$- \underline{4\ v}\ \ \underline{h\ v} = c_4 \beta_v bI_h S_v +$

$(S - S^*)\ [\beta\ bI\ S\ \ \ \ ]$

$K_h + m)S_v K_h + m \quad 2K_h + m$

$+\alpha)S^* - \omega R^*$ $c_4(\mu_v + c\alpha)(S_v - S) + c\ \beta\ bI\ Sc_5\beta_v bI_h S_v\ IK + m$ $S_v K_h + m)I_v$

$E - E^*$ $\beta\ bI\ S$ c_2 E_h

$-c_5(\mu_v + \alpha c)(I_v - I^*)$ (83) ρ E_h $K_h + m$

t is clearly seen that when $c = c, -\frac{c_1\beta_h bI_v S_h}{K_h+m}$ cancels

$c_3 \left(\frac{I_h - I_h^*}{I_h} \right) [\rho_h E_h - (\mu_h + \gamma\kappa + \delta)I_h] c_2\beta\ bI_v S\ c_4\beta_v bI\ S_v c_5\beta_v bI\ S_v$

$hK_h + m$

h; when $c_4 = c_5, -h$

$K_h + m$

cancels h

$K_h + m$ and $S - S^*$ $\beta\ bI\ S$ when $c = \frac{c_2(\mu_h+\rho_h)}{\rho_h}$, $c\ \rho\ E$ ancels $-c\rho)E$ $+c_4$ $- (\mu = \alpha c)S^*$

S_v

$K_h + m$ Equation (83) now simplifies to:

$$V = -\frac{c_2(\mu_h+\alpha)(S_h - S_h^*)^2}{S_h} + \frac{c_2\beta_h bI_v^* S_h^*}{K_h+m} - \frac{c_2\beta_h bI_v^* S_h^{*2}}{(K_h+m)S_h} - c_2(\mu_h+\alpha)(S_h - S_h) + c_2\beta_h b\ I_v\ S_h$$

$$\frac{c\beta\ bI\ S^*\ I^*}{K_h+m} \quad c\ \omega(R - R^*)(S - S^*) \quad c\beta\ bS^* I^* = S_h$$

$$\frac{S^* E^* I + S_h^* E_h}{K + m\ \ I^*} - \frac{}{S(K+m)}.$$

S_h $E_h I^* S^*$

I E

$E_h S_h I_v$ $+ c_2(\mu_h + \rho_h)E_h - c_3(\mu_h + \gamma k + \delta)I_h + c\ \beta\ b\ I\ S^* \omega(R_h - R^*)(S - S^*)S_h I_v$ I^* (84)

$K_h + m$ S_h

$c_3(\mu_h + \gamma k + \delta)I_h - c_3\rho_h E_h \frac{I}{I\ E^*} + c_3(\mu_h + \gamma k + \gamma)I_h - c_3(\mu_h + \gamma k + \delta)I_h$

$$-\frac{c_4(\mu_v + c\alpha)(S_v - S_v^*)^2}{S_v} + \frac{c_4\beta_v bI_h^* S_v^*}{(K_h+m)S_v} + c_4(\mu_v + c\alpha)(S - S^*) + c\ \beta\ b\ I^*\ S^*$$

S_v $K_h + m$ $\beta\ bI\ S^*$ $c\ \beta\ bI^* S^*\ I^* I^* S$

$$\frac{}{K_h+m} I_v - \frac{}{(K_h+m)} I_h S_v + c_2\beta_h b\ I_h\ S_v\ I^* I^* S^* [2 - \quad -$$

S_v I I^* S^*

$K_h + m$

From the Equilibrium points in Eq. (80), we obtain the following: $-c_4(\mu_v + \alpha c)(I_v - I^*)$ (87)

Again, suppose we have the relation $c_2 =$

$(\mu + \rho)E^* = \beta_h b S_h I_v$

$\frac{c_4(\mu_v+c\alpha)(K_h+m)}{}$, then Eq. (87) and $c = \frac{c_4\beta_v b\ S^*}{K_h + m}$

$c(\mu + \gamma k + \delta)I^* = c(\mu + \rho)E^* \beta_h b\ S^*$

becomes: $\frac{}{(\mu_h+\gamma\kappa+\delta)(K_h+m)}$

$$c\ \beta\ bS^* I^* \quad I^* E$$

$$c\ \rho\ E^* \frac{c_2\beta_h bS_h^* I_v^*}{} = c(\mu + \rho)(85)$$

$$-c_2(\mu_h+\alpha)(S_h - S_h^*) + c_2\beta_h b I_v S_h \ldots \frac{K_h+m}{} \ldots c\,\beta\, bS^* I^* I^* E$$

$$E_h \ldots I_v S_h I_h E_h + c(\mu + c\alpha)(K+m) \ldots \beta_h b S^* \quad (88)$$

Now, we have:

$$\beta\, bI\, S^* + c_1\omega\,(R_h - R^*)(S - S^*)$$

$$-c_2(\mu_h+\alpha)(S_h - S^*)$$

$$\dot{V} = \ldots - c\,\beta\, b \ldots + I_v S_h^2 \ldots I_v \ldots + {}_4 S_v(\mu_h+\gamma\kappa+\delta) I_h$$

$$\mu_h+\gamma\kappa+\delta\,(K_h+m)$$

$$c_2\beta_h b I_v S_h I_v + c_2\omega(R_h - R_h)(S_h - S_h)$$

$$c_2\beta_h b S_h I_v$$

$$+c\alpha)(S - S^*) c\,\beta_v b I_h S_v \ldots (K_h+m) I_h^* \ldots K_h+m$$

$$+c_2\beta_h b S_h I_v c_2\beta_h b S_h I_v$$

$$c_2\beta_h b S_h I_v$$

$$K+m\,K+m+ \ldots K+m^* \quad c\,\beta\, bI^* S^*$$

$$S_h S_h^* I^* I_v I_h S_v \ldots E_v \,[2 - \ldots] - c(\mu + c\alpha)(S - S^*) \ldots S_v\, I$$

$$I^* S^* K_h + m_4 \ldots + c_4\beta_v b I_h S_v$$

$$c_3(\mu_h+\gamma k+\delta) I_h - \ldots$$

$$-K_h+m$$

$$-c_4(\mu_v+\alpha c) I^*$$

$$c_4\beta_v b I S^2$$

$$c\,\beta\, bI\, S^* I^* - c\,\beta\, b I^* S^*$$

$$-c_4(\mu_v +$$

This simplifies to:

$\alpha c)\,(I_v - I_v^*)$ (86)
$-c_2(\mu_h + \alpha)(S_h - S^*)c\,\beta\, bI^*\, S^*$

This implies that: $V = h2\ h\ v\ h + S_h \quad K_h + m$

$[3 - \frac{S_h^*}{S_h} - \frac{E_h^*\, I_v\, S_h}{E_h\, I_v^*\, S_h^*} - \frac{I_h E_h^*}{I_h^* E_h}] + \frac{c_2\omega(R_h - R^*)(S - S^*)}{S_h}$ Hence, the estimated daily natural death μ_h rate is given as:

$c_4(\mu_v + c\alpha)(S_v S_v^*)^2 c_4 \beta_v b\, I^*\, S^*\, S^* \quad I^*\, I_h\, S$

$\mu_h = \frac{1}{64 \times 365} = 0.000042808219$

$\frac{}{S_v} + \frac{h\ v}{K_h + m}[2 - \frac{v}{S_v} - \frac{v\ v}{I_v I_h^*\, S_v^*}]$

$c_4(\mu_v \quad v$

$+\alpha c)\,(I^*)$ (89) We assume that the $birthrate = deathrate = \mu_h$.

The carrying capacity for humans K_h is given as

Substituting I_v^* into Eq. (89) gives: $K_h = \frac{\Lambda_h}{\mu_h}$

$-c_2(\mu_h + \alpha)(S_h - S^*) + c\,\beta\, b\ {}^*\ {}^*\ {}^*$

$V_h = [3 - \frac{2\ h I_v\ S_h}{S_h} - \frac{S_h}{K_h + m}\ S_h$ So the recruitment rate is given by:

$\frac{E_h\, I_v\, S_h}{E_h^*\, I_v^*\, S_h^*} - \frac{I_h E_h}{\Gamma E_h^*}] + \frac{c_2\omega(R_h - R^*)(S - S^*)}{S_h}$ $\Lambda_h = K_h \times \mu_h$

$c_4(\mu_v + c\alpha)(S - S^*)^2$

$c\,\beta\, b\ {}^*\ {}^*$

Therefore, the estimated daily recruitment rate for humans is computed as:

$\frac{}{S_v S_v^*} I^*\, I_h\, S[2 - \frac{I_h\, S_v}{} -] - S^* \quad K_h + m$ $\Lambda_h = K_h \times \mu_h = 28000000 \times 0.000042808219. \approx 1200$

The life expectancy for mosquitoes to live is 30 days (WHO, 2018). Hence, the estimated death rate for mosquitoes was given as:

$\frac{c_4(\mu_h+\rho_h)(\mu_h+\gamma\kappa+\delta)K^2}{v\ I_v\ I_h\ S_v}\left(\frac{(\mu_h(\mu_h+\alpha+\omega))[R^2(\alpha)-1]}{b\beta_h K\mu_h(\mu_h+\gamma\kappa+\delta)(\mu_h+\omega)+\omega\rho_h(\mu_h+\delta)]+\Lambda_h b^2\beta_h\beta_v(\mu_h+\omega)\rho_h}\right)$ (90)

$\mu_v = \frac{1}{30} = 0.03$

where, $K = (\mu_v + c\alpha)(K_h + m)$.

$c_1\omega(R_h - R^*)(S - S^*)$

The remaining parameters $\Lambda_v, b, \beta_h, \beta_v, \gamma, \alpha, \omega, \delta$ and m were obtained by fitting the model solution to the observed infection data.

The term $\frac{h\quad h}{S_h}$ is non-positive because S_h decreases monotonically S_h^* and R_h increases monotonically to R_h^*. The expression in Eq is, therefore, negative if $\Re^2(\alpha) > 1$.

Hence, the endemic equilibrium is globally asymptotically stable in Ω, if $\Re_o^2(\alpha) > 1$.

Parameter Estimation

The main tool for estimating the parameters of the model given in Eq. (91), is the use of demographic estimates and implementation of the least-square method approach in Python, using the daily confirmed cases in Ghana, obtained from WHO from 2004-2017.

Demographic Estimates

Here, pre-estimating some demographic parameters such as Λ_h and μ_h using information obtained from (FactBook, 2019; WHO, 2019b).

The total population of Ghana as of 2016 was given as 28,207,000 and the life expectancy at birth was given as 64 years (WHO, 2019b).Ghana Malaria Infection Data Sets and the Curve Fitting Process

The data for confirmed cases of malaria from Ghana obtained from WHO ranges from the year 2004 to the year 2017 and is shown in Table 3.

The data points in Table 3 is graphically represented in Fig. 2.

Table 3: Yearly Confirmed cases of malaria in Ghana from 2004-17

Years	Confirmed cases
2004	475441
2005	655093
2006	472255
2007	476484
2008	1094483
2009	1104370
2010	1071637
2011	1041260
2012	3755166
2013	1639451
2014	3415912
2015	4319919
2016	4535167
2017	4348694

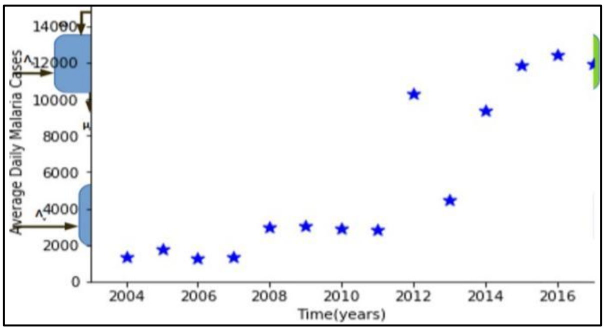


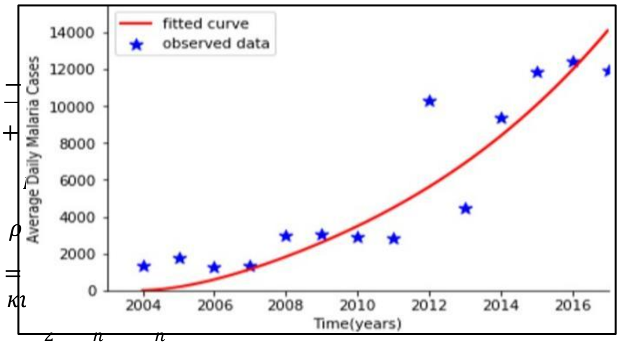
Fig. 2: Plot of average daily cases of malaria from the world health organization

Optimal Control Formulation

In this section, we formulate the strategy for effective control of malaria transmission as an optimal control problem. We then use pontryagin's maximum principle to determine an optimal combination of the prevention and treatment efforts needed to reduce the transmission. Numerical simulations will then be performed to determine the evolution of the disease, over a finite time horizon.

Let $u_1(t)$ represent the rate of prevention and $u_2(t)$ the rate at which infected individuals get treatment.

Replacing α and γ in the model Eq. (4) with the *controls* $u_1(t)$ and $u_2(t)$ respectively, gives:



$S = \Lambda$

h h

$E = \frac{\beta_h b I_v S_h}{K_h+mh} - (\mu$

h h

h h h h h

$R_h = \kappa u_2(t) I_h - \mu_h R_h - \omega R_h + u_1(t) S_h$ (91)

$S_v = \Lambda_v$

$\frac{\beta_v b I_h S_v}{K_h+m_v} - (\mu + u_1(t)c)S_v$ $I = \frac{\beta_v b I_h S_v}{K_h+m} - (\mu + u_1(t)c)I$

v v 1 v

We define our objective functional as

Fig. 3: Model in Eq. (4) fitted to the data in Table 1 $J(u_1, u_2) = I_h(T) + I_v(T) + \frac{1}{2}\int_0^T (B_1 u_1^2 + B_2 u_2^2)\, dt$ (92)

Table 4: Parameters obtained from the best fit and demographics

Parameters	Units (day⁻¹)	Values	Sources
Λ_h	day⁻¹	2367	(WHO)
Λ_v	day⁻¹	11007.6970	Estimated from data
β_h	day⁻¹	0.61844195	Estimated from data
β_v	day⁻¹	0.62695935	Estimated from data
μ_h	day⁻¹	$\frac{1}{(64\times365)}$	(fact book) and (WHO)
δ	day⁻¹	0.00900000	Estimated from data
γ	day⁻¹	[0.1, 0.2]	Per-capita treatment rate
α	day⁻¹	[0.05, 0.8]	Per-capita prevention rate
μ_v	day⁻¹	0.03	Estimated from data
ω	day⁻¹	0.00100000	Estimated from data
b	day⁻¹	0.79276092	Estimated from data
c	day⁻¹	[0,1]	Constant of proportionality
m	day⁻¹	3	Assumed

With $u_1, u_2 \in U$, the set of admissible controls of the Lebesgue measure is defined as:

$U = \{u_1(t), u_2(t) \in L'(0,T) \vee 0 \le u_i \le 1\}$

The terms $\frac{1}{2}B_1 u_1^2$ and $\frac{1}{2}B_2 u_2^2$, $(B_1, B_2 > 0)$

ρ_h	day^{-1}	0.07142857	Estimated from data

Figure 2 the blue stars represent the data points. The least square best fit is shown in Fig. 3.

A plot of the daily infection is shown with a representation of the data in Fig. 2 fit for the model is done using an implementation of the least square's curve fit approach in Python to estimate a new set of values of parameters at a given bound. The estimated values of parameters obtained from the demographic point of view were maintained. The best-fit diagram is given in Fig. 3.

Figure 3 The blue star represents the data while the red solid colored curve represents the curve of best fit to the data.

The parameters obtained from the best fit and the demographics are given in Table 4.gives the cost associated with implementing prevention and treatment. The choice of the quadratic cost for the controls indicates that the cost of applying the controls is nonlinear. The interval $[0, T]$ is the time horizon and T is the terminal time.

Also, $I_h(T)$ and $I_v(T)$represent the number of infected humans and vectors respectively, at the end of the terminal time.

The maximum values for u_1 and u_2 are denoted by $u_{1\max}$ and $u_{2\max}$ respectively.

The optimal control pair $\mu^* \mu^*$ is given by: 1 2

$J(\mu^* \mu^*) = min\{J(u_1, u_2): (u_1, u_2) \in U\}$ (93)$_{u_1,u_2}$ 1 2

Existence of the Optimal Control Pair

The necessary condition for the existence of the optimal control pair proposed by Fleming and Rishel (2012); Panetta and Fister (2000); Yusuf and Benyah (2012) is established in this section. According to Fleming and Rishel (2012), the xistence of an optimal control pair $(\mu^* \mu^*)$ is guaranteed

$d\lambda_1 = \beta_h bI_v - u\ (t))\,\lambda$

$+ \beta_h bI_v\lambda_2 + u\ (t)\lambda\ ],$

1 2

by the compactness of the states and the convexity of the problem. Therefore, the essential requirement cited in $= -[($

$K_h + m$ 1 dt

$\frac{d\lambda_2}{} = -[-(\mu\ \rho\ )\lambda$

1 $K_h + m$ 1 4

$+\rho\ \lambda\ ]$

Yusuf and Benyah (2012) is given by:dt h 2 h 3

$\frac{d\lambda_3}{} = -\frac{d\lambda_4}{} = -[\omega\lambda - (\omega + \mu\ )\lambda\ ]$

1. The set of all solutions to system (91) with corresponding admissible control functions in U is non-empty $\frac{d\lambda_5}{dt} = -[(\frac{-\beta_v^h bI_h^4}{K_h + m_{v1}{}^5} - (\mu + u\ (t)c))\,\lambda + \frac{\beta_v bI_h\lambda_6}{K_h + m}]$
2. he state system can be written as a linear function of the control variables $u_i''s$, with coefficients depending on time and the state variables $\frac{d\lambda_6}{dt} = -[\frac{-\beta_h bS_h\lambda_1}{K_h+m} + \frac{\beta_h bS_h\lambda_2}{K_h+m} - (\mu + u\ (t)c)\lambda\ ]$ (95) v 1 6
3. The integrand of $J(u_1, u_2)$ is convex on U and is bounded above by:

$B\ \|(u\ , u\ )\|^2 - B$With the transversality condition:

$\lambda_1(T) = {}_2(T) = {}_4(T) \quad \lambda_5(T) = 0,$ and

(96)

where: 1 1 2 $2\lambda_3(T) \quad \lambda_6(T) = 1,$

$B_1, B_2 > 0$

First Order Necessary Condition

In this section, we establish conditions that wouldOptimality conditions:

$\frac{\partial H}{\partial u} = B\ u\ + (\lambda\ - \lambda\ )S\ - (\lambda\ S\ + \lambda\ I\ )c = 0$ 1 1 4 1 h 5 v 6 v

∂H

(97)

help us solve our objective function. Using Pontryagin's Maximum Principles, the necessary

∂u_2

$= B_2 u_2 + (\lambda_4 - \lambda_3) I_h = 0$

conditions are derived using the following theorem by Panetta and Fister (2000).

where, H is the Hamiltonian of the system given by:

Theorem 5. Suppose (μ^*, μ^*_2) is an optimal control pair, with corresponding optimal states, $S^* E^* I^* R^* S^* I^*$ that

$H = \frac{1}{2}(B_1 u^2 + B_2 u^2) + \lambda_1 [\Lambda_h - \frac{\beta_h b I_v S_h}{K_h + m} - \mu_h S_h - u_1(t) S_h +$

$\omega R\ ] + \lambda_2 [\frac{\beta_h b I_v S_h}{K_h+m} - (\mu\ \rho\ )E\ ] + \lambda\ [\rho\ E - \mu\ I\ -$

minimizes the objective functional in Eq. 92, then there exists a co-state variables $\lambda^*, \ldots, \lambda^*_6$ such that the following necessary conditions are satisfied.

$u_2(t) I_h - \delta I_h] + \lambda_4 [u_2(t) I_h - \mu_h R_h - \omega R_h + u_1(t) S_h] +$

$\lambda_5 [\Lambda - \frac{\beta_v b I_h S_v}{K_h + mv} - (\mu_{1v} + u_1(t) c) S\ ] + \lambda_6 [\frac{\beta_v b I_h S_v}{K_h+m} - (\mu_v + u_1(t) c) I_v]$

State equations:

$$\frac{dS_h}{dt} = \frac{\partial H}{\partial \lambda_1}, \cdots, \frac{dI_v}{dt} = \frac{\partial H}{\partial \lambda_6}$$

Solving Eqs. 95-97 and for u_1 and u_2 gives

where:

respectively, the optimal controls:

$\frac{dS_h}{dt} = \Lambda_h - \frac{\beta_h b I_v S_h}{K_h + m} - \mu_h S_h - u_1(t) S_h + \omega R_h$

$\frac{dE_h}{dt} = \frac{\beta_h b I_v S_h}{K_h + m} - (\mu_h + \rho_h) E_h$

$$\mu_1^* = \frac{(\lambda_1 - \lambda_4) S_h + (\lambda_5 S_v + \lambda_6 I_v) c}{B_1}, \quad \mu_2^* = \frac{(\lambda_3 - \lambda_4) I_h}{B_2} \quad (98)$$

$\frac{dI_h}{dt} = \rho_h E_h - \mu_h I_h - \kappa u_2(t) I_h - \delta I_h$

$\frac{dR_h}{dt} = \kappa u_2(t) I_h - \mu_h R_h - \omega R_h + u_1(t) S_h$

$\frac{dS_v}{dt} = \Lambda_v - \frac{\beta_v b I_h S_v}{K_h + m} - (\mu_{v1} + u_1(t) c) S_v$

$\frac{dI_v}{dt} = \frac{\beta_v b I_h S_v}{K_h + m} - (\mu_{v1} + u_1(t) c) I_v \quad (94)$

Since the controls are bounded, that is, $0 \le \mu_1 \le \mu_{1max}, 0 \le \mu_2 \le \mu_{2max}$ the optimal controls in (98) are

With initial conditions:

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

replaced by:

1

$\overline{I^*}\lambda\,)\,c\,)\,S^* + (\lambda^*\,S^* + \lambda$

Co-state equations:

$max\{0,$ $\frac{d\lambda_1}{} = \frac{-\partial H}{}, \cdots, \frac{d\lambda_6}{} = -\partial H \mu^* = min_1$

$\{_4 \quad h \quad 5 \quad v \quad 6 \quad v\}$

B_1

$\}$

2

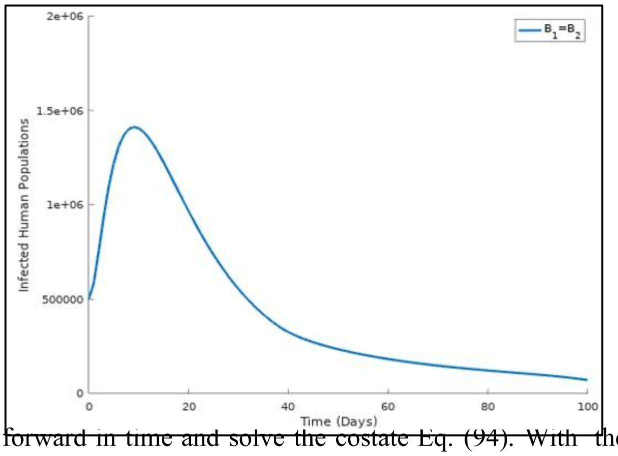
Given by:dt
$\partial S_h dt$
∂I_v

μ

$^{*} = min\{max\{0,(\lambda_3 - \lambda_4)\ I^{*}$ h (99)
$\}\}$

B_2

Numerical Solution of the Optimality System



The two-point boundary-value problem given in Eqs. (94-97), was solved using the forward-backward sweep method, developed by (Lenhart and Workman, 2007).

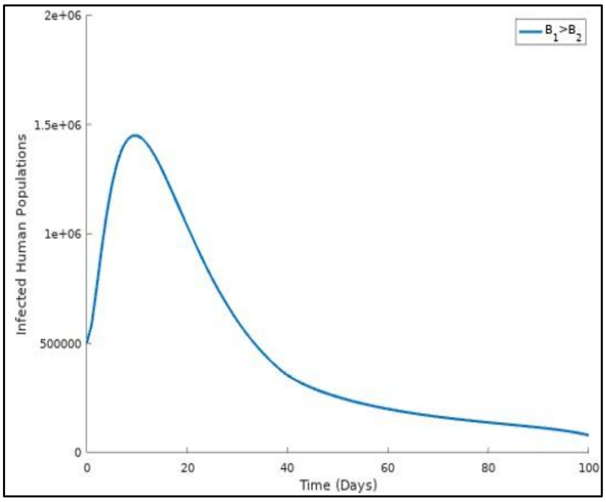
The values of the constants B_1, $B_2 > 0$ in the integrand are chosen first, to balance the units in the objective functional. Secondly, varying the constants during numerical simulations, show the effects of emphasizing one control over the other.

The procedure outlined below was implemented in Octave, a MATLAB-like public domain software. Choose an initial guess for μ_1^* μ_2^* and.

Solve the state Eq. (94), with the given initial conditions forward in time and solve the costate Eq. (94). With the given transversality conditions backward in

(b)

time. Update the expression for μ_1^* μ_2^* and in Eq. (99).

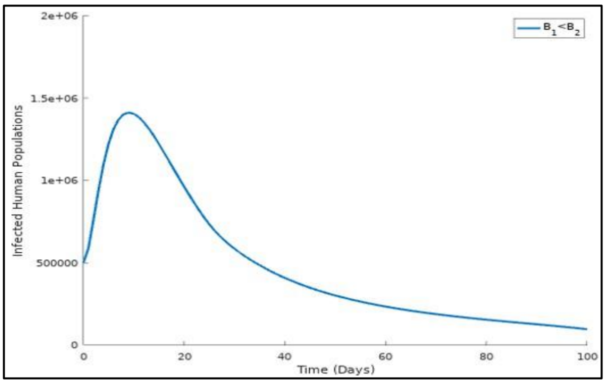


with the new values of the state and the costate variables. Repeat steps (2-4) until convergence criteria are met.

Simulations on the Effect of Weight B_1, B_2 on Infected Human Populations

We investigate how different weight combinations affect the infected human populations.
We consider three cases: (a) $B_1 < B_2$, (b) $B_1 = B_2$ and (c) $B_1 > B_2$.

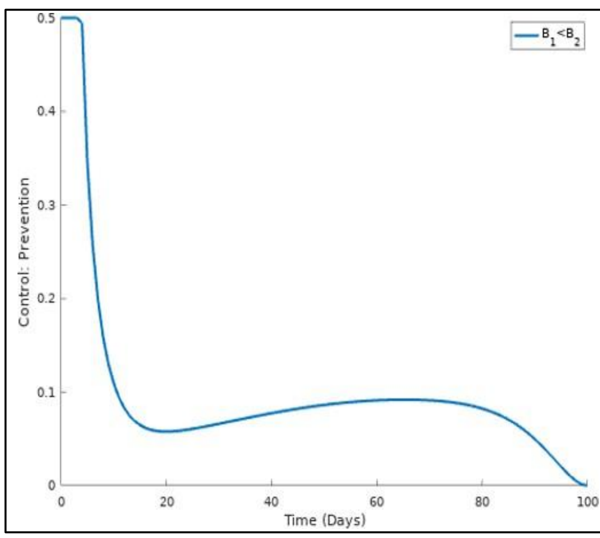
The numerical values of B_1 and B_2 used in our simulations were selected from the set $\{400000, 800000\}$. These values were chosen first, to balance the units in the objective function and secondly, to investigate the effects on the infected human populations, by putting different weights on each control.
The plots in Figs. 4a-c, show the infected human populations, when (Figs. 4a-c) respectively.
Figure 4, different combination of the weights reduces the human population respectively.
The plots in Fig. (5a-c) shows prevention functions, when; (Figs. 5a-c) respectively.

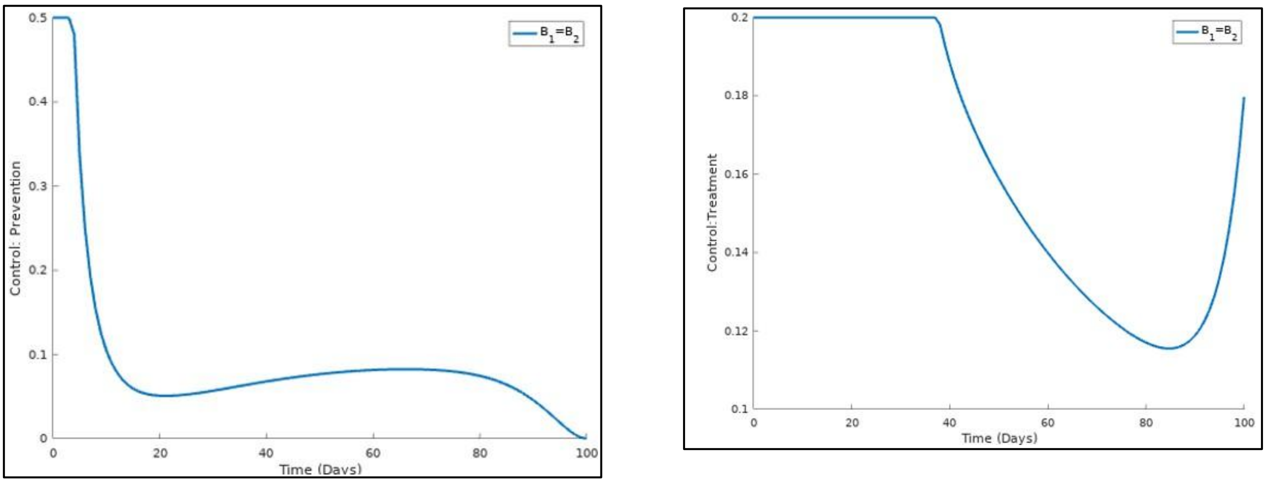


(a)

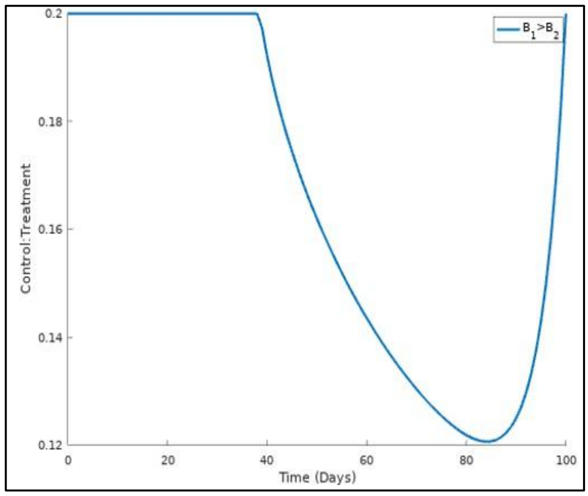
(c)

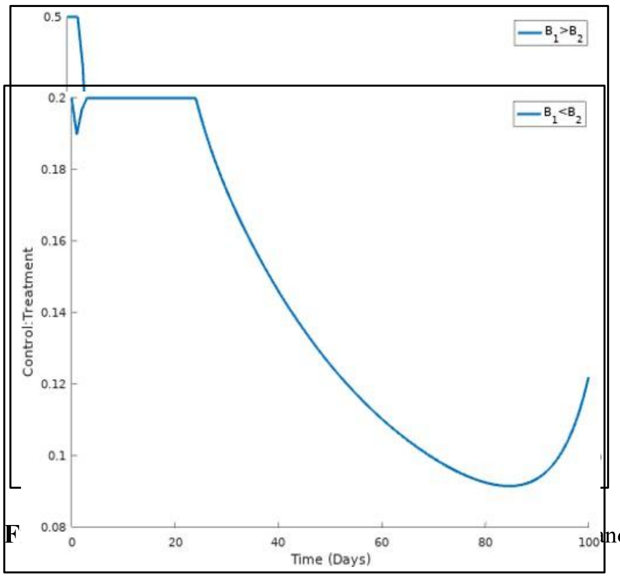
Fig. 4: Infected human populations when; (a) $B_1 < B_2$; (b) $B_1 = B_2$; (c) $B_1 > B_2$




Control: Prevention
Time (Days)
$B_1=B_2$
Control:Treatment
Time (Days)
$B_1=B_2$

(b)





(c)

F nd (c) $B_1 > B_2$

(a)(b)(c)

Fig. 6: Treatment functions when (6a) $B_1 < B_2$, (6b) $B_1 < B_2$ and (6c) $B_1 < B_2$

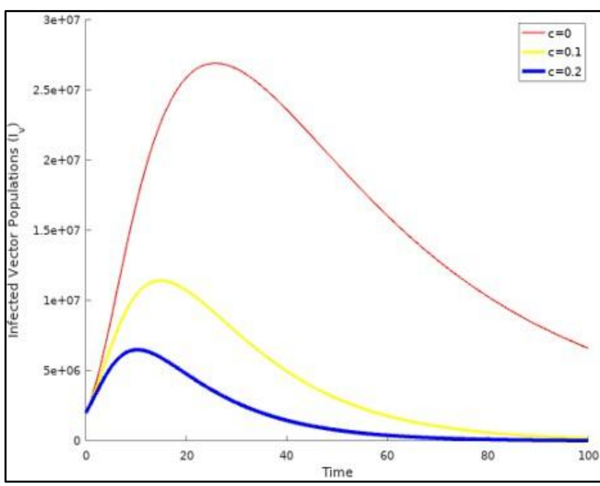


Fig. 7: Infected vector populations with $u_{1max} = 0.5, u_{2max} = 0.2$

Figure 5 giving equal weights, $B_1 = - B_2$ reduces the vector population than giving different combination of the weights.

The plots in Figs. 6a-c shows treatment functions, when respectively.

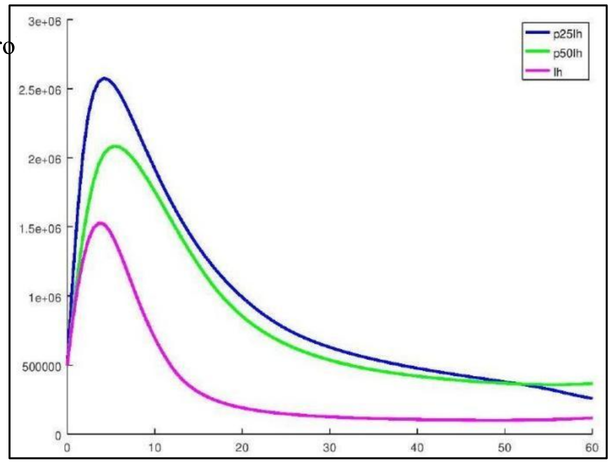
Figure 6, giving more weights to B_1 reduces the treatment function than giving equal or more weight to B_2.

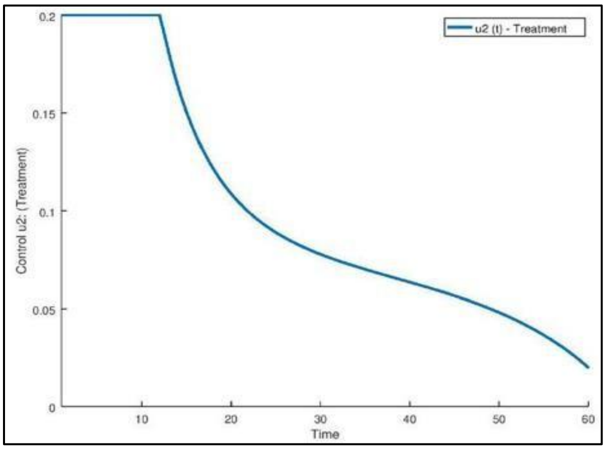
Materials and Methods

In order to get a least-squares estimate of the model parameters, we utilized the WHO-provided annual malaria transmission data for Ghana from 2004 to 2017. We developed an optimum control problem to find the best course of action in terms of both prevention and therapy. The first-order required conditions were obtained by using Pontryagin's maximal principle. The optimality system was subsequently solved using a forward-backward sweep approach.

Numerical Simulations

The following simulations were performed using optimal contro





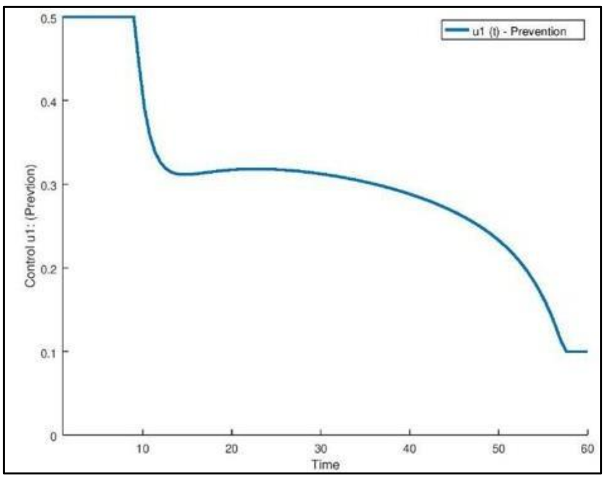
(b)

Fig. 8: Optimal Function with $u_{1max} = 0.5, u_{2max} = 0.2$; (a) Optimal control function $u_1(t)$; (b) Optimal control function $u_2(t)$

$u_{1max} = 0.5$, so that $u_{1max} S_h$ represents a maximum of 50% of the susceptible population using adequate prevention methods. $u_2max = 0.2$, corresponds to a treatment period of about $1/0.2 = 5$ days and weights $B_1 = B_2 = 400000$.

Simulations on the Effect of c on Infected Vector Population

We investigate the effect of the parameter c on the vector population using increasing values of $c = 0.0, 0.1, 0.2$, with the following fixed values of u_{1max}, u_{2max} and κ.



(a)

ig. 9: Infected human populations with differential treatment regimes

$u_{1max} = 0.5$, so that $u_{1max} S_h$ represents a maximum of 50% the susceptible population using adequate prevention methods.

Let $\kappa = 1$, so that $\gamma \times (\kappa I_h) = \gamma I_h$, gives the best scenario for treatment availability.

Figure 7 shows a plot of the infected vector populations, with $c = 0.0, 0.10, 0.20$ respectively.

Figure 7, we notice a dramatic reduction in the infected vector population, with increasing values of c.

The corresponding optimal control functions are displayed in Fig. 8a-b.

The control functions prevention $\mu_1$and treatment μ_2 in Fig. 8 starts from maximum 0.5 and 0.2 respectively and decreases gradually as infected population also decreases in Fig. 7.

Simulations with Differential Treatment $\gamma(\kappa I_h)$ Regimes

We investigate the effects on the total infected human populations when effective treatment is only available to a proportion $0 \leq \kappa \leq 1$ of the infected population in Fig. 9. This scenario happens for a variety of reasons including, lack of medical facilities in some communities, as well as affordability for the cost of treatment. The labels "$p25I_h$", "$p50I_h$" and "pI_h" in Fig. 9 represents respectively, the effect on the total infected human populations, when 25, 20 and 100% of the infected population receive treatment.

Figure 9 shows that the total infected human populations decrease faster, when treatment is accessible to a greater proportion of those infected.

Results and Discussion

One important tactic in malaria management, the impact of prevention on lowering the vector population by raising their mortality rate Eq. (1), is a distinctive and new aspect of our model. Increasing the vector mortality rate is the goal of a percentage $c\alpha$ of the preventative effort α, where c ranges from 0 to 1. The results of our simulations demonstrate unequivocally that lowering the parameter c decreases the population of vectors. The sensitive human population is reduced and the vector mortality rate is increased even higher when the preventive rate is increased (= $\mu 1$). Our treatment function Eq. (2), which accounts for the fact that only a fraction κ of the afflicted population has access to efficient therapy, is another distinctive aspect of our model. By raising the parameter κ, our simulations demonstrate that more detected patients will have access to treatment, resulting in a lower total human infection population. The lower the number of affected individuals, the slower the rate of transmission. Actually, mosquitoes may spread malaria from one untreated patient to another.

Conclusion

Prevention and quick, efficient treatment for malaria patients are the two most important factors in limiting the disease's spread. The lower the number of affected individuals, the slower the rate of transmission. The ultimate goal of malaria eradication must be the implementation of effective preventative measures in neighboring communities, which may serve as a vaccine. The models demonstrate that a significant decrease in transmission may be achieved if half or more of the vulnerable population adheres to the recommended preventative measures. By ensuring that everyone affected has access to treatment, we can quickly reduce the infected population via efficient means. We derived the following suggestions from our simulation findings and the maxim that the

Quickly reducing the vulnerable population via adequate preventative measures and rapidly reducing the sick population through effective treatment are the two most important factors in efficiently managing any infectious illness. Strategies for preventing the spread of vectors include:

1. Indoor spraying with residual insecticides. This is when the inside of house structures is prayed once or twice a year with insecticide spray. This activity should be regularly done since it reduces the proportion of the resident mosquitoes whether susceptible or infectious
2. The use of insecticide-treated mosquito Nets (ITN). This reduces the contact rates
3. Larval control. This activity may be implemented through environmental modification such as draining and killing or the use of larvacides

Treatment strategies must include:

1. Early diagnosis and effective treatment. Each untreated case becomes a reservoir for mosquitoes to further transmit to other susceptible

2. The use of WHO-approved Anti-malarial medications including Coartem 80/480, Hydroxyl-Chloroquine and Fansidar (Sulfadoxine and Pyrimethamine)

In order to eradicate malaria, especially in developing countries, where most people cannot afford the cost of treatment:

- Malaria medication must be free, or at least, highly subsidized in order to ensure a rapid reduction in the infected population
- The prevention methods listed above must be enforced in all contiguous neighborhoods

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