Mosquito-borne Diseases and Control Strategies

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Graduate Modelling Camp Programme

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Sunday 19th January, 2025

Contents

Introduction

- In tropical parts of the world, malaria is a vector-borne illness that has a high rate of morbidity.
- It is a worldwide public health issue. Humans contract the disease when a female Anopheles mosquito bites them while they are consuming the blood meal required for egg formation. The disease is caused by multiple species of parasites of the Plasmodium genus type
- An estimated 228 million cases of malaria were reported globally in 2018, and an estimated 405,000 people died from malaria-related causes [WHO, 2018]
- Numerous mathematical models have been developed to understand the transmission dynamics of malaria and its control measures. [**et al R. Anguelo , 2013**]

Introduction

- Insecticide-treated nets (ITNs) are highly used in reducing human-mosquito interactions. However, the effectiveness of these nets has been inconsistent, as many people either neglect to repair holes, fail to use them regularly, or repurpose them for activities like fishing [**R. Short**, **R. Gurung et al**, **2018**].
- The use of insecticide-treated bednets can affect various factors such as the force of infection, the recruitment rate of new female mosquitoes, or the mosquito death rate. Additionally, the use of treated bednets can impact the rate at which immunity is lost.[**N. Chitnis**, **J. M. Hyman**, **and J. Cushing**, **2008**].

Figure: Mosquito bed net

Aims

- To use mathematical modelling to study the usefulness of bed nets for control of Malaria

Objectives

- To use mathematical modelling to study the usefulness of bed nets for control of Malaria.
- Investigate and Analyze the effectiveness of insecticide-treated bednets in reducing malaria transmission and mortality rates.

Defining Variables

Table: Variables of the model

Variable	Description
S_h	Number of susceptible humans within the population
E_h	Number of latent humans within the population
I_h	Number of infected humans within the population
S_v	Number of susceptible mosquitoes
I_v	Number of infectious mosquitoes

Model Formulation:

- The total human and mosquito population size at time t is denoted by $N_h(t)$ and $N_v(t)$ respectively, therefore we have:

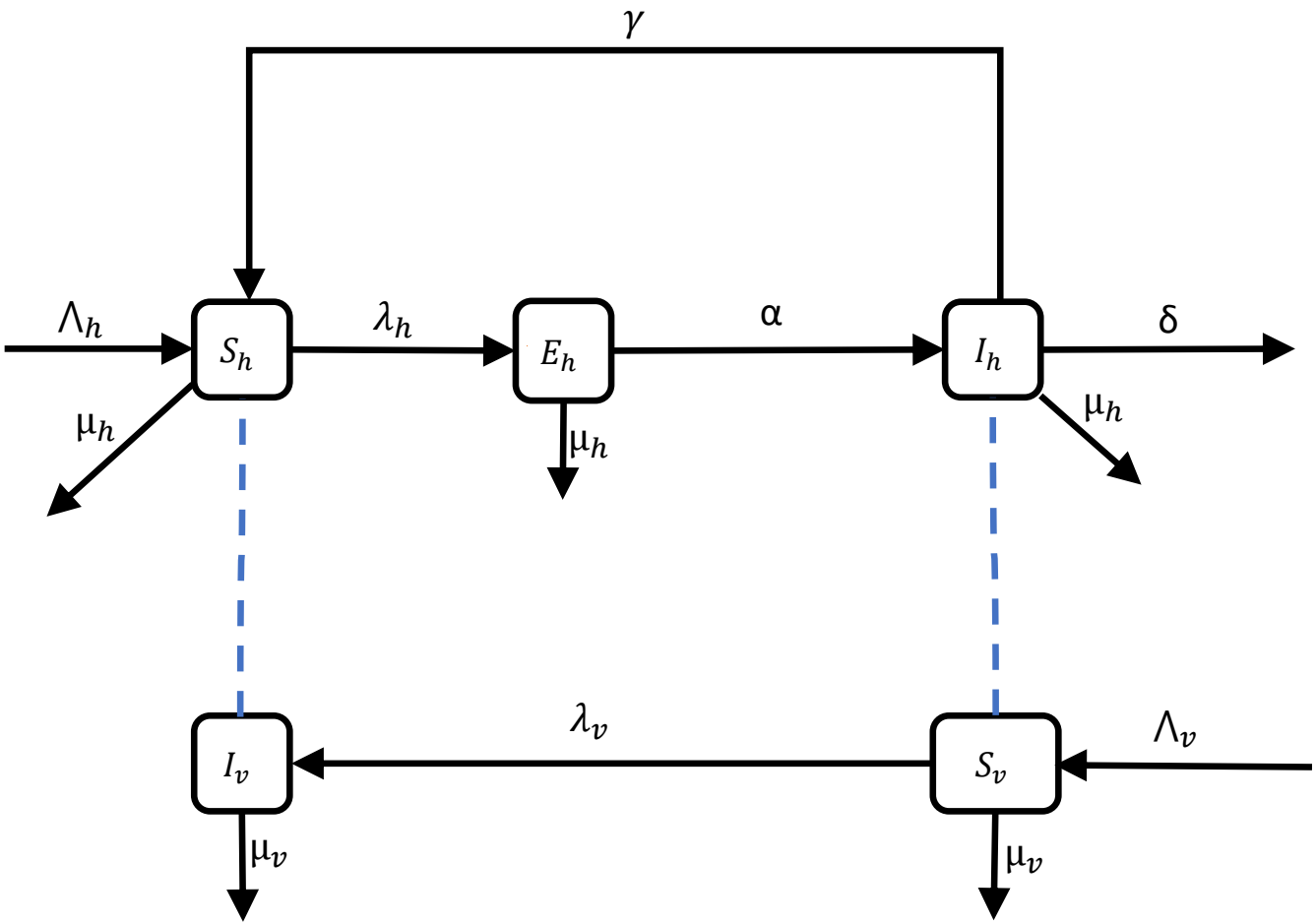
$$N_h(t) = S_h(t) + E_h(t) + I_h(t) \quad (1)$$
$$N_v(t) = S_v(t) + I_v(t). \quad (2)$$

Defining Parameters

Table: Parameters of the model

Parameters	Description
p_1	Probability of infected humans
p_2	Probability of mosquitoes to be infected
b	proportion of bed-nets being used
$\beta(b)$	biting rate dependent on b
$1/\alpha$	latent period
γ_h	recovery rate
μ_h	death rate of humans
$\mu_v(b)$	Mortality rate of mosquitoes, potentially dependent on b
δ	death rate due to malaria
β_M	Maximum transmission rate of Mosquitoes
β_m	Minimum transmission rate of Mosquitoes
μ_0	Natural death rate of mosquitoes
$b\mu_1$	Death rate due to insecticides on treated nets

Model Formulation $(S_h E_h I_h - S_v I_v)$



Model Formulation

$$S_h = \frac{\Lambda_h}{\mu_h + P_1\beta(b)\frac{I_v}{N_v}},$$

$$E_h = \frac{P_1\beta(b)\frac{S_h I_v}{N_v}}{\mu_h + \alpha},$$

$$I_h = \frac{\alpha E_h}{\mu_h + \gamma_h + \delta_h},$$

$$S_v = \frac{\Lambda_v}{\mu_v + P_2\beta(b)\frac{I_h}{N_h}},$$

$$I_v = \frac{P_2\beta(b)\frac{S_v I_h}{N_h}}{\mu_v}.$$

Subject to initial conditions:

$$S_h(0) = S_h^0 \geq 0, \qquad E_h(0) = E_h^0 \geq 0, \qquad I_h(0) = I_h^0 \geq 0,$$
$$S_v(0) = S_v^0 \geq 0, \qquad I_v(0) = I_v^0 \geq 0.$$

Well-posedness of the model

Theorem

The model is a dynamical system on the biologically feasible region Ω *defined as:*

$$\Omega = \Omega_h \times \Omega_v \subset \mathbb{R}^3_+ \times \mathbb{R}^2_+,$$

where:

$$\Omega_h = \{(S_h, E_h, I_h) \in \mathbb{R}^3_+ \mid N_h \leq \frac{\Lambda_h}{\mu_h}\},$$

$$\Omega_v = \{(S_v, I_v) \in \mathbb{R}^2_+ \mid N_v \leq \frac{\Lambda_v}{\mu_v}\}.$$

Proof

The existence of a unique local solution for the model follows directly from the **Cauchy–Lipschitz theorem**,[**et al Walter G**, **2010**] since the right-hand sides of the differential equations are continuously differentiable.

To ensure positivity of the variables, we use the **tangent condition**.

For this, we need to show that:

$$\langle n(x), g(x) \rangle \leq 0,$$

where:

- $n(x)$ is the outward normal vector to the hyperplane,
- $g(x)$ is the vector field defined by the right-hand side of the model.

For x on the hyperplane $S_h = 0$, we have:

$$n_{S_h} = (-1, 0, 0, 0, 0),$$

and:

$$\langle n_{S_h}, g(x) \rangle = -(\mu_h + \gamma_h I_h) \leq 0.$$

Thus, the tangent condition is satisfied, ensuring $S_h \geq 0$ for all $t \geq 0$.
The positivity of the other variables (E_h, I_h, S_v, I_v) can be shown similarly by applying the tangent condition to their respective hyperplanes.
For the Boundedness of Solutions the total human population N_h satisfies:

$$\frac{dN_h}{dt} = \Lambda_h - \mu_h N_h - \delta I_h \leq \Lambda_h - \mu_h N_h.$$

Using the integrating factor method, we find that:

$$N_h(0) \leq \frac{\Lambda_h}{\mu_h}$$

ensuring that N_h is bounded for $t \geq 0$. Similarly, for the mosquito population N_v:

$$N_v(t) \leq \frac{\Lambda_v}{\mu_v}.$$

Therefore, the solution is biologically feasible, since all variables remain non-negative and bounded in the region Ω.

Existence of Disease Free Equilibrium (DFE)

For the DFE, we let $I_h(t) = I_v(t) = 0$
Thus there exists a Disease Free Equilibrium for equation denoted by

$$E_0 = (S_h^0, 0, 0, S_v^0, 0) = (\frac{\Lambda_h}{\mu_h}, 0, 0, \frac{\Lambda_v}{\mu_v}, 0)$$

Stability of the Disease Free Equilibrium

The DFE represents a state where no individuals in the population are infected by the disease occurs when $I_h = I_v = 0$, with the susceptible individuals in both host populations given by:

$$S_h^* = \frac{\Lambda_h}{\mu_h}, \quad E_h^* = 0, \quad I_h^* = 0, \quad S_v^* = \frac{\Lambda_v}{\mu_v}, \quad I_v^* = 0$$

Endemic Equilibrium

The endemic equilibrium is a solution to the system of differential equations:

$$S_h^* = \frac{A_h + \delta_h I_h^*}{\lambda_h + \mu_h}, \quad E_h^* = \frac{\lambda_h S_h^*}{\mu_h + \alpha}, \quad I_h^* = \frac{\alpha E_h}{\lambda_h + \gamma_h + \mu_h},$$

$$S_v^* = \frac{A_v}{\lambda_v + \mu_v}, \quad I_v^* = \frac{A_v \lambda_v}{\mu_v(\lambda_v + \mu_v)}$$

R_0 is a threshold parameter that helps determine whether an infectious disease will spread in a population or die out. The endemic equilibrium exists only if the basic reproduction number $R_0 > 1$.This means that, on average, each infected individual causes more than one new infection, allowing the disease to persist in the population.

The basic reproduction number R_0 and Local stability of the Disease Free Equilibrium

Theorem (Van den Driessche, P. and Watmough, J., 2002[134])

The disease free-equillibrium is locally asymptotically stable when the basic reproduction number $R_0 < 1$, and unstable for $R_0 > 1$.

The basic reproduction numberR_0 is given by:

$$R_0 = \frac{p_1\beta(b)p_2\beta(b)}{(\mu_h+\alpha)(\mu_h+\delta_h+\gamma_h)\mu_v}$$

- When $R_0 > 1$ there exist a unique endemic equilibrium

Global Stability for DFE

The global asymptotic stability (GAS) of the disease-free state of the model is investigated using the theorem by Castillo-Chavez et.al(2002).

- While local stability focuses on the system's behavior near the disease-free equilibrium (DFE), global stability determines whether the system will return to the DFE regardless of the initial conditions. This ensures that the disease dies out completely for any starting state, as long as certain parameters (e.g., basic reproduction number R_0) satisfy specific conditions.
- Let $X = (S_h, S_v)$ and $Z = (E_h, I_h, I_v)$.
- We rewrite the model as

$$\frac{dX}{dt} = F(X, 0), \qquad \frac{dZ}{dt} = G(X, Z),$$

where $F(X,0)$ is the right-hand side of $\frac{dS_h}{dt}$ and $\frac{dS_v}{dt}$ with $I_h = 0 = I_v$ and $G(X,Z)$ is the right-hand side of $\frac{dI_h}{dt}$ and $\frac{dI_v}{dt}$.
Now we have

$$\dot{X} = \begin{pmatrix} S_h' \\ S_v' \end{pmatrix} = \begin{pmatrix} \Lambda_h - \mu_h S_h \\ \Lambda_v - \mu_v S_v \end{pmatrix}.$$

The disease-free equilibrium is now denoted as

$$E^0 = (X^*, 0) \qquad \text{where} \quad (X^*, 0) = \left(\frac{\Lambda_h}{\mu_h}, \frac{\Lambda_v}{\mu_v} \right)$$

The condition $\hat{G}(X, Z) \geq 0$ in Ω where Ω is the region where the model makes biological sense, must be met to guarantee a local asymptotic stability.
Define:

$$\hat{G}(X, Z) = D_Z G(X^*, 0)Z - G(X, Z),$$

where

$$(X^*, 0) = \begin{pmatrix} S_h^*, & S_v^* \end{pmatrix}, \quad Z = \begin{pmatrix} I_h \\ I_v \end{pmatrix}.$$

Here, $D_Z G(X^*, 0)$ is the Jacobian matrix of $G(X, Z)$ evaluated at $(X^*, 0)$, which is an M-matrix (its diagonal entries are negative).

Jacobian Matrix:

$$D_Z G = \begin{pmatrix} \frac{\partial}{\partial E_h}\left(E_h'\right) & \frac{\partial}{\partial I_h}\left(E_h'\right) & \frac{\partial}{\partial I_v}\left(E_h'\right) \\ \frac{\partial}{\partial E_h}\left(I_h'\right) & \frac{\partial}{\partial I_h}\left(I_h'\right) & \frac{\partial}{\partial I_v}\left(I_h'\right) \\ \frac{\partial}{\partial E_h}\left(I_v'\right) & \frac{\partial}{\partial I_h}\left(I_v'\right) & \frac{\partial}{\partial I_v}\left(I_v'\right) \end{pmatrix}.$$

Evaluating $D_Z G$ at $(X^*, 0)$:

$$D_Z G(X^*, 0) = \begin{pmatrix} -(\mu_h + \nu) & 0 & P_1 \beta(b) \frac{\Lambda_h \mu_v}{\mu_h \Lambda_v} \\ \alpha & -(\mu_h + \delta_h + \gamma_h) & 0 \\ 0 & P_2 \beta(b) \frac{\Lambda_h \mu_v}{\mu_h \Lambda_v} & -\mu_v \end{pmatrix}.$$

Now,

$$\hat{G}(X,Z) = \begin{pmatrix} \frac{P_1\beta(b)I_v\mu_v}{\Lambda_v}\left(\frac{\Lambda_h}{\mu_h} - S_h\right) \\ 0 \\ P_2\beta(b)I_h\left(\frac{\Lambda_v\mu_h}{\mu_v\Lambda_h} - \frac{S_v}{N_h}\right) \end{pmatrix} \geq 0.$$

Hence the DFE is globally asymptotically stable provided that $\frac{S_v}{N_h} \leq \frac{S_v^*}{S_h^*}$.

Analysis of bed-net usage b

Taking the derivative of the reproduction number R with respect to the bed-net usage parameter b yields

$$\frac{dR_0}{db} < 0$$

It can be seen from the above that bed-net usage has a positive impact in reducing the reproduction number R_0 and therefore the disease burden.

Relevance of bed-nets for the control of malaria

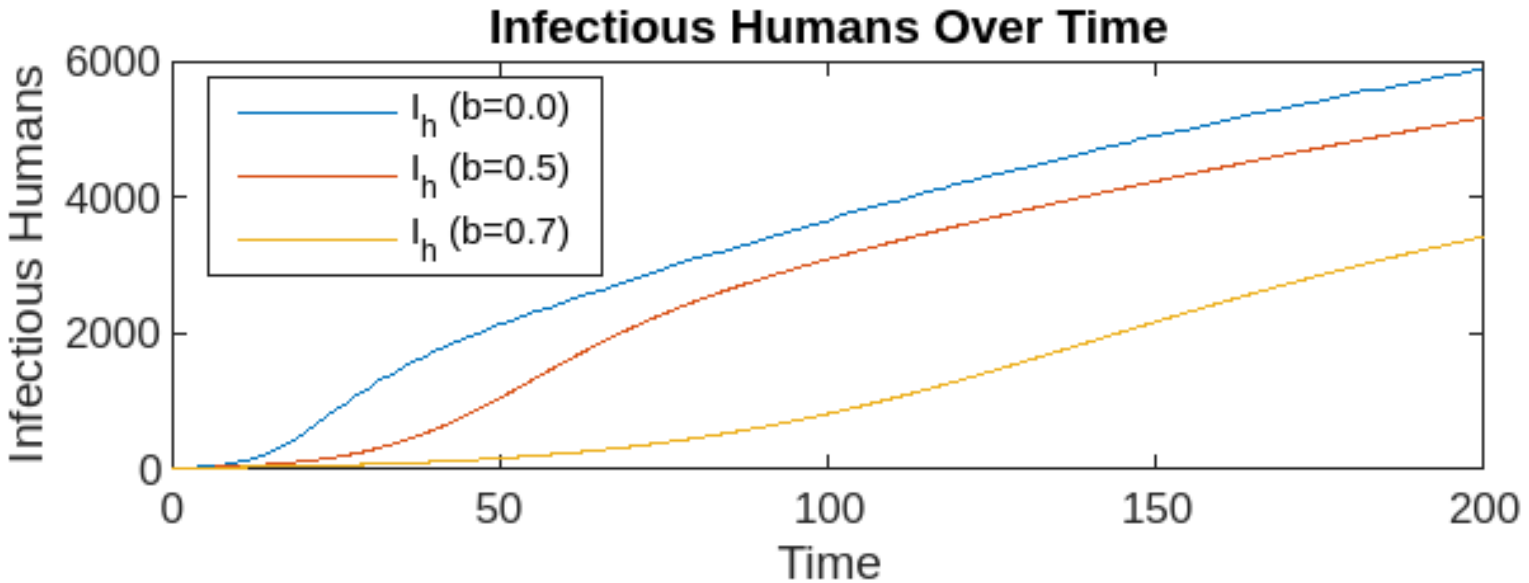


Figure: Comparative Analysis of Bed-nets (with and without intervention)

Relevance of bed-nets for the control of malaria

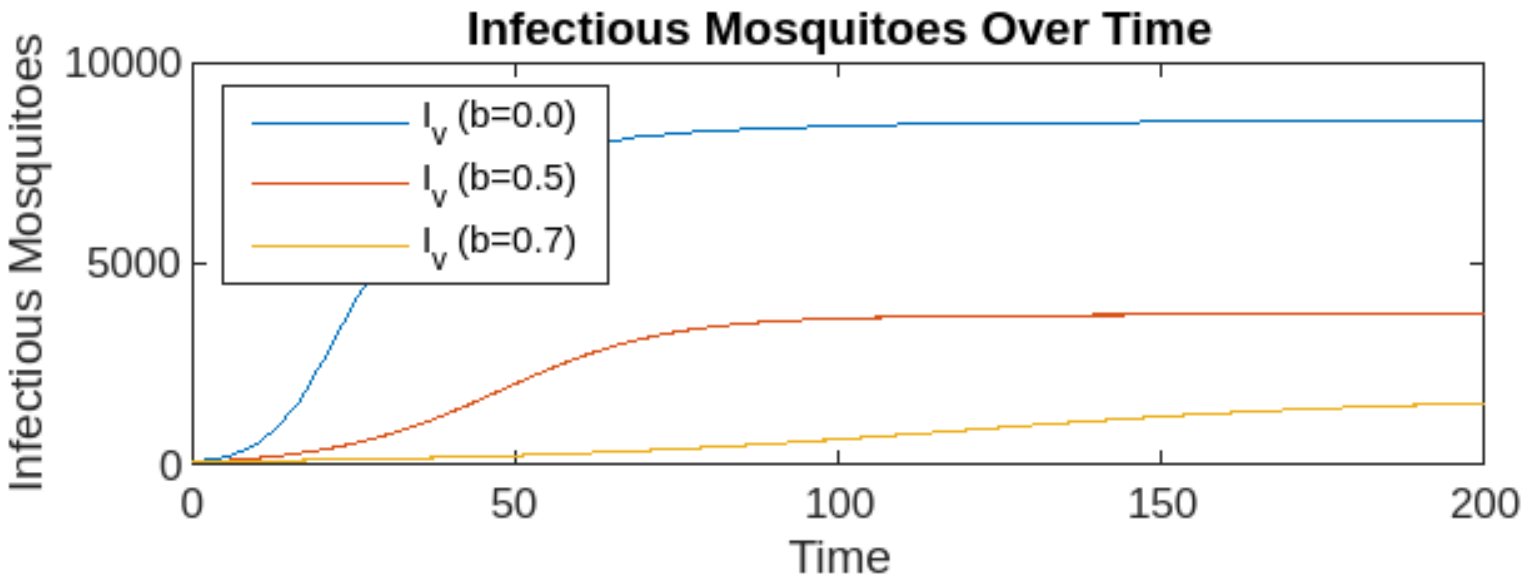


Figure: Comparative Analysis of Bed-nets (with and without intervention)

Conclusion

- The greatest reductions in I_v are observed when both bed net usage and mosquito mortality are high, emphasizing the importance of integrated vector control strategies.
- These findings suggest that public health interventions should prioritize either improving bed net coverage or increasing mosquito mortality through insecticides or other measures or both, to achieve maximum impact on reducing disease transmission.

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Acknowledgement