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# The impact of bed-net use on malaria prevalence

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## HIGHLIGHTS

- The existence of backward bifurcation is presented.
- Bed-net usage has a positive impact in reducing the reproduction number $\mathcal{R}$.
- Malaria could be eliminated if 75% of the population were to use bed-nets.

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## ABSTRACT

Malaria infection continues to be a major problem in many parts of the world including the Americas, Asia, and Africa. Insecticide-treated bed-nets have shown to reduce malaria cases by 50%; however, improper handling and human behavior can diminish their effectiveness. We formulate and analyze a mathematical model that considers the transmission dynamics of malaria infection in mosquito and human populations and investigate the impact of bed-nets on its control. The effective reproduction number is derived and existence of backward bifurcation is presented. The backward bifurcation implies that the reduction of $\mathcal{R}$ below unity alone is not enough to eradicate malaria, except when the initial cases of infection in both populations are small. Our analysis demonstrate that bed-net usage has a positive impact in reducing the reproduction number $\mathcal{R}$. The results show that if 75% of the population were to use bed-nets, malaria could be eliminated. We conclude that more data on the impact of human and mosquito behavior on malaria spread is needed to develop more realistic models and better predictions.

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## 1. Introduction

Malaria is a disease that can be transmitted to people through the bites of infected mosquitoes. It is one of the leading causes of morbidity and mortality in some of the poorest tropical and subtropical regions in the world including the Americas, Asia, and Africa. Malaria is particularly a major public health problem in Africa, where 20% of children under the age of 5 die as a result of infection. The World Health Organization (WHO) estimates that every year 250 million people become infected and nearly one million die.

Malaria was successfully eliminated from many parts of the world including Europe, North America, the Caribbean, and parts of Asia and South-Central America in the early 20th century. Dichlorodiphenyltrichloroethane (DDT) was one of the main intervention strategies used to eradicate malaria in these countries. However, these efforts were abandoned but have gradually been revived by different organizations including the WHO and the Bill & Melinda Gates Foundation. There are several new interventions that are currently being used in the fight against malaria including insecticide-treated bed-nets (ITNs).

ITNs are mosquito nets treated with insecticides that protect individuals by diverting mosquitos and killing those who come in contact with the net. A review of 22 randomized control trials of ITNs (Lengeler, 2004) found that they can reduce malaria cases by 50% and deaths in children by one-fifth. Although the cost-effectiveness

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of ITNs has been demonstrated in numerous studies (Goodman and Mills, 1999), there are many challenges due to improper handling and human behavior (e.g., lack of use due to hot weather). Moreover, insecticide on nets usually lasts between 3 and 5 years due to frequent washing, type of soap used, and exposure to direct sunlight, which can deteriorate the effectiveness of the insecticide sprayed on it.

Mathematical models of the transmission of infectious agents can be useful tools in understanding disease dynamics and assessing the effect of different interventions (Hethcote, 2000). Although several articles have investigated the impact of various intervention strategies including ITNs (Chitnis et al., 2010; Killeen and Smith, 2007; Smith et al., 2008; White et al., 2009), none of them have incorporated human behavior. Killeen and Smith (2007) used a deterministic model to investigate the impact of mosquito behavior in response to ITN usage. Smith et al. (2008) used an individual-based stochastic simulation of malaria to estimate the impacts of various intervention strategies including ITNs on the spread of malaria, response activities, and cost. White et al. (2009) used a simple deterministic model and compared it to more sophisticated models to evaluate the impact of different intervention strategies. They concluded that a combined intervention strategy could achieve elimination through a sustained control strategy. Chitnis et al. (2010) used a system of difference equations to analyze the impact of ITNs and indoor residual spraying (IRS) on malaria-control programs. They showed that people that use only ITNs are better protected than those with only IRS.

Therefore, understanding the impact of human behavior (Del Valle et al., 2005) can help us develop optimal intervention strategies and devise more realistic predictions to control malaria spread. In this paper, we identify a threshold needed to reduce malaria cases through the use of ITNs and the impact of human behavior on ITNs' effectiveness.

## 2. Model formulation

We formulate the basic model for the effects of bed-net on the transmission dynamics of malaria infection consisting of mosquito (also referred as vector) and human populations (also referred as host). The host population is grouped into two compartments, susceptible and infectious, which are denoted by $S_h$, $I_h$, respectively, with a total population given by $N_h = S_h + I_h$. The vector population is similarly grouped into two compartments, susceptible and infectious with sizes $S_v$, $I_v$, respectively, and the total population size is given by $N_v = S_v + I_v$. All newborn individuals are assumed to be susceptible and no infected individuals are assumed to come from outside of the community.

One of the basic forms of protections against the transmission of malaria is the usage of pesticide-treated bed-nets. According to reports (Kayedi et al., 2008; Vanlerberghe et al., 2010), the pesticide treatment on the bed-nets could fade out due to frequent washing with certain soap and exposure to direct sunlight. Despite these problems, bed-nets are among the most important and affordable means of defense against malaria transmissions. Accordingly, we assume that malaria transmission reduces as a function of bed-net usage. We denote the contact rate of mosquitoes and humans by $\beta(b)$. This rate is assumed to be the same for the human and mosquito populations. However, the probability of effective transmission from human to mosquito, which we denote by $p_1$, is different from the probability of effective transmission from mosquito to humans, denoted by $p_2$. Normally, the transmission rate is the product of the contact rate and the probability of passing infection. Following the general results obtained as a result of treated bed-net usage in reducing

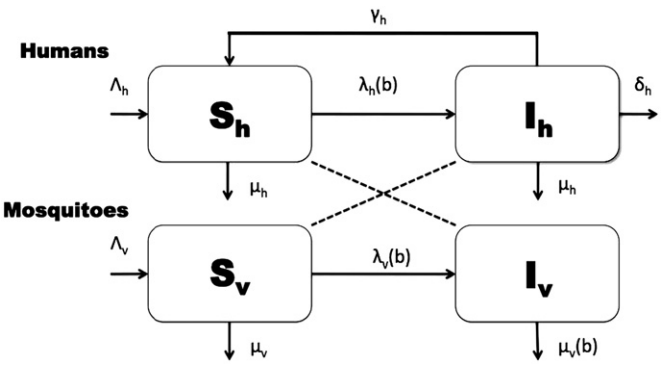


**Fig. 1.** Flow-chart showing movements of humans and mosquitoes between the susceptible and infectious compartments and the flow of the malaria disease from humans to mosquitoes and from mosquitoes to humans. At time, $t$, the total human population is $N_h(t) = S_h(t) + I_h(t)$ and the total mosquito population is $N_v(t) = S_v(t) + I_v(t)$.

malaria transmission, we model the average number of bites per mosquito per unit time (contact rate) by a linearly decreasing function of treated bed-net usage, $b$:

$$\beta(b) = \beta_{\max} - b(\beta_{\max} - \beta_{\min}), \quad 0 \le b \le 1. \tag{1}$$

Note that the parameters $\beta_{\max}$ and $\beta_{\min}$ are the maximum and the minimum transmission rates, respectively, and $b$ is the proportion of bed-net usage that could reduce the mosquito–human contact rate to a minimum level $\beta_{\min}$.

Bed-nets are typically used at night, thus, we assume that even if the entire host population used bed-nets ($b=1$), the transmission can only be reduced to a minimum value ($\beta_{\min}$). Similarly, if no one uses bed-nets ($b=0$), transmission would be at its maximum level ($\beta_{\max}$).

A drastic decline in relative exposure to mosquitoes as a result of ITN usage is observed in some parts of Africa (Govella et al., 2010). This leads to a significant reduction of disease transmission. This reduction could be well described by either exponentially decreasing or linearly decreasing function of ITN usage. To simplify the model, we choose the transmission to be a linearly decreasing function of $b$.

The model is constructed by making some basic assumptions: all new arrivals into the human population are susceptible with recruitment rates as $\Lambda_h$ and $\Lambda_v$ for human beings and mosquitoes respectively, the disease is fast progressing so that the exposed stage is minimal and is not considered, infectious humans could die from the disease or become susceptible after recovery, the mosquito population does not recover from infection, insecticide-treated bed-nets contribute to the mortality rate of mosquitoes.

Following the approaches in Blayneh et al. (2009), Bowman et al. (2005) and Teboh-Ewungkem et al. (2010) the value of $\beta(b)$ is the same for each population, so the average number of bites per human per unit time is $\beta(b)N_v/N_h$. Thus, the force of infection for susceptible humans is given by

$$\lambda_h(b) = p_1 \frac{\beta(b)N_v}{N_h}\frac{I_v}{N_v} = \frac{p_1\beta(b)I_v}{N_h},$$

where $p_1$ is the transmission probability per bite from infectious mosquitoes to humans. The force of infection for susceptible vectors is

$$\lambda_v(b) = \frac{p_2\beta(b)I_h}{N_h},$$

where $p_2$ is the transmission probability per bite from infectious humans to mosquitoes.

Due to insecticide treatment of bed-nets, female mosquitoes questing for blood meal could die when they become in contact

with a treated bed-net. Therefore, we have modeled the death rate of the mosquitoes as $\mu_v(b)=\mu_{v_1}+\mu_{\max}b$, $0\le b\le 1$, where $\mu_{v_1}$ is the natural death rate and $\mu_{\max}b$ is the death rate due to pesticide on treated bed-nets, taken as a linear function of $b$.

Thus, using the formulation provided above, the variables, and parameters' descriptions given in Table 1, we arrive at the following non-linear system of differential equations:

$$\begin{aligned}
\dot{S_h} &= \Lambda_h-\lambda_h(b)S_h+\gamma_h I_h-\mu_h S_h,\\
\dot{I_h} &= \lambda_h(b)S_h-(\mu_h+\gamma_h+\delta_h)I_h,\\
\dot{S_v} &= \Lambda_v-\lambda_v(b)S_v-\mu_v(b)S_v,\\
\dot{I_v} &= \lambda_v(b)S_v-\mu_v(b)I_v.
\end{aligned} \tag{2}$$

A schematic diagram of the model is depicted in Fig. 1

### 2.1. Basic quantitative properties

#### 2.1.1. Positivity and boundedness of solutions

Since the system of equations given in (2) represents human and mosquito populations, all parameters in the model are non-negative and it can be shown that the solutions of the system are non-negative, given non-negative initial values. In order to analyze this system, we split it into two parts, namely the human and mosquito populations. Consider the biologically feasible region consisting of

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

with

$$\Omega_h=\left\{(S_h(t),I_h(t))\in\mathbb{R}^2_+ : 0\le N_h(t)\le\frac{\Lambda_h}{\mu_h}\right\},$$

and

$$\Omega_v=\left\{(S_v(t),I_v(t))\in\mathbb{R}^2_+ : 0\le N_v(t)\le\frac{\Lambda_v}{\mu_v(b)}\right\}.$$

The following steps are followed to establish the positive invariance of $\Omega$ (i.e., solutions in $\Omega$ remain in $\Omega$ for all $t>0$). The rate of change of the total human and mosquito populations is obtained by adding the first two equations and the last two equations of the system (2) to give

$$\begin{aligned}
\frac{dN_h(t)}{dt} &= \Lambda_h-\mu_h N_h(t)-\delta_h I_h(t),\\
\frac{dN_v(t)}{dt} &= \Lambda_v-\mu_v(b)N_v(t).
\end{aligned} \tag{3}$$

Thus, it follows that

$$\begin{aligned}
\frac{dN_h(t)}{dt} &\le \Lambda_h-\mu_h N_h(t),\\
\frac{dN_v(t)}{dt} &= \Lambda_v-\mu_v N_v(t).
\end{aligned} \tag{4}$$

A standard comparison theorem Lakshmikantham et al. (1989) can then be used to show that $N_h(t)\le N_h(0)e^{-\mu_h t}+(\Lambda_h/\ \mu_h)(1-e^{-\mu_h t})$ and $N_v(t)=N_v(0)e^{-\mu_v(b)t}+(\Lambda_v/\mu_v(b))(1-e^{-\mu_v(b)t})$. In particular, $N_h(t)\le\Lambda_h/\mu_h$ and $N_v(t)\le\Lambda_v/\mu_v(b)$, if $N_h(0)\le\Lambda_h/\mu_h$, and $N_v(0)\le\Lambda_v/\mu_v(b)$, respectively. Thus, the region $\Omega$ is positively invariant. Hence, it is sufficient to consider the dynamics of the flow generated by (2) in $\Omega$. In this region, the model is epidemiologically and mathematically well-posed (Hethcote, 2000). Thus, every solution of the basic model (2) with initial conditions in $\Omega$ remains in $\Omega$ for all $t>0$. Therefore, the $\omega$-limit sets of the system (2) are contained in $\Omega$. This result is summarized below.

**Lemma 1.** *The region $\Omega=\Omega_h\times\Omega_v\subset\mathbb{R}^2_+\times\mathbb{R}^2_+$ is positively invariant for the basic model (2) with non-negative initial conditions in $\mathbb{R}^4_+$.*

Throughout this paper, we consider the system given by (2) with initial values in $\Omega$.

## 3. Model analysis

In this section, the conditions for the existence of the equilibria of the system (2) are explored.

### 3.1. Local stability of the disease-free equilibrium (DFE)

The disease-free equilibrium of the system given by (2) is

$$\Sigma_0=\left(\frac{\Lambda_h}{\mu_h},0,\frac{\Lambda_v}{\mu_v(b)},0\right). \tag{5}$$

Using the next generation operator approach as presented in van den Driessche and Watmough (2002), we calculate the reproduction number $\mathcal{R}$ of the system (2). To do this, we define a vector valued function $\tilde{F}$ for rate of new infection cases in the infected and recovered groups of both populations, namely in $I_h$,$I_v$. $\tilde{F}=(\beta(b)p_1 I_v S_h/N_h,\ \beta(b)p_2 I_h S_v/N_h)$. And another function $\tilde{V}$ for the transmission terms between the disease infected compartments listed above and the exit terms (by mortality or emigration) $\tilde{V}=((\mu_h+\gamma_h+\delta_h)I_h,\ \mu_v(b)I_v)$. Next, we evaluate $F$ and $V$, which are the Jacobian matrices of $\tilde{F}$ and $\tilde{V}$, respectively, evaluated as functions of the vector $(I_h,I_v)$ at the disease-free equilibrium $\Sigma_0$ given by (5)

$$F=\begin{pmatrix} 0 & \beta(b)p_1\\ \frac{\beta(b)p_2\Lambda_v\mu_h}{\mu_v(b)\Lambda_h} & 0\end{pmatrix},\quad V=\begin{pmatrix} L & 0\\ 0 & \mu_v(b)\end{pmatrix},$$

where

$$L=\mu_h+\gamma_h+\delta_h.$$

The basic reproduction number $\mathcal{R}$ is defined as the spectral radius of

$$FV^{-1}=\begin{pmatrix} 0 & \frac{\beta(b)p_1}{\mu_v(b)}\\ \frac{\beta(b)p_2\Lambda_v\mu_h}{\Lambda_h\mu_v(b)L} & 0\end{pmatrix}.$$

**Table 1**
Description of the variables and parameters of the system (2).

| Variable | | Description |
|---|---|---|
| $S_h(t)$ | | Susceptible humans |
| $I_h(t)$ | | Infectious humans |
| $S_v(t)$ | | Susceptible vectors |
| $I_v(t)$ | | Infectious vectors |
| **Parameter** | **Description** | **Baseline value** |
| $\Lambda_h$ | Recruitment rate in humans | $10^3/(70\times365)$ |
| $\Lambda_v$ | Recruitment rate in mosquitoes | $10^4/21$ |
| $\mu_h$ | Natural mortality rate in humans | $1/(70\times365)$ |
| $\delta_h$ | Disease induced mortality rate in humans | $10^{-3}$ |
| $b$ | Proportion of treated net usage | |
| $\gamma_h$ | Recovery rate of infectious human to be susceptible | 1/4 |
| $\mu_{v_1}$ | Natural mortality rate of mosquitoes | 1/21 |
| $\mu_{\max}b$ | Mortality rate of mosquitoes due to treated net | |
| $\beta(b)$ | Mosquito–human contact rate | |
| | $\beta_{\max}$ | 0.1 |
| | $\beta_{\min}$ | 0 |
| $p_1$ | Probability of disease transmission from mosquito to human | 1 |
| $p_2$ | Probability of disease transmission from human to mosquito | 1 |

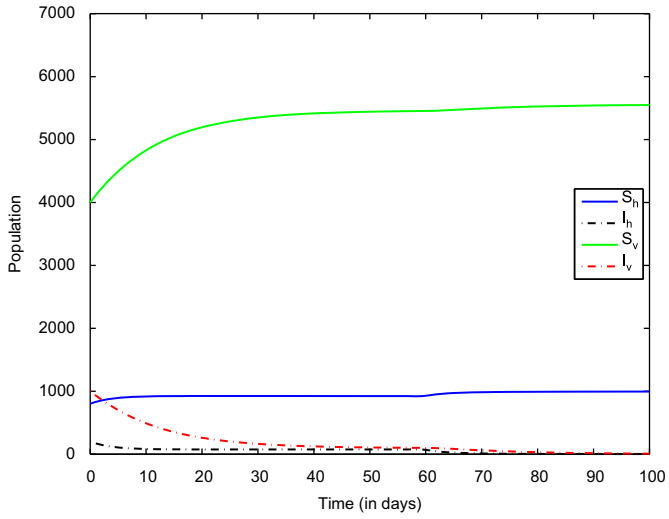


**Fig. 2.** Simulations of model (2) for the population level as a function of time for $\mathcal{R}<1$ using parameter values: $b=0.8$, $\delta_h=10^{-3}$, $\beta_{max}=0.1$, $\beta_{min}=0$, $\mu_{max}=1/21$, $\mu_h=1/(70\times 365)$, $\mu_{v1}=1/21$, $\mu_v(b)=\mu_{v1}+\mu_{max}b$, $\Lambda_h=1/(70\times 365)$, $\Lambda_v=10^4/21$, $\gamma_h=1/4$, and $\mathcal{R}=0.32$.

Accordingly, it is given by

$$\mathcal{R}=\frac{\beta(b)}{\mu_v(b)}\sqrt{\frac{p_1p_2\Lambda_v\mu_h}{L\Lambda_h}}. \tag{6}$$

This threshold represents the average number of infected mosquitoes and humans caused by a cross-infection of one human and one mosquito when the other population consists of only susceptibles. This is clear when $\mathcal{R}$ is rewritten as follows:

$$\mathcal{R}=\sqrt{\frac{\beta(b)p_2}{\mu_v(b)(\mu_h+\gamma_h+\delta_h)}\frac{\beta(b)p_1}{\Lambda_h}\frac{\Lambda_v}{\mu_v(b)\mu_h}}. \tag{7}$$

We now proceed to study the local stability of the disease-free equilibrium $\Sigma_0$. The Jacobian of system (2) at the disease-free equilibrium is given by

$$J=\begin{pmatrix}-\mu_h & \gamma_h & 0 & -\beta(b)p_1\\ 0 & -L & 0 & \beta(b)p_1\\ 0 & -K & -\mu_v(b) & 0\\ 0 & K & 0 & -\mu_v(b)\end{pmatrix},$$

where

$$K=\frac{p_2\beta(b)\mu_h\Lambda_v}{\Lambda_h\mu_v(b)}.$$

The eigenvalues of $J$ are $\lambda_1=-\mu_h$, $\lambda_2=-\mu_v(b)$ and the other two are solutions of

$$\lambda^2+(L+\mu_v(b))\lambda+L\mu_v(b)-p_1\beta(b)K=0.$$

Since $L\mu_v(b)-p_1\beta(b)K=L\mu_v(b)(1-\mathcal{R}^2)$, the quadratic equation has two negative real roots provided that $\mathcal{R}<1$. For $\mathcal{R}>1$, the quadratic has one positive solution, which makes $\Sigma_0$ unstable. Thus we have the following result.

**Theorem 1.** *The disease-free equilibrium point $\Sigma_0$, which is given by (5), is locally asymptotically stable (LAS) if $\mathcal{R}<1$ and it is unstable if $\mathcal{R}>1$.*

Fig. 2 shows numerical solutions for the host and vector populations for the DFE. The parameter regime $b=0.8$, $\delta_h=10^{-3}$, $\beta_{max}=0.1$, $\beta_{min}=0$, $\mu_{max}=1/21$, $\mu_h=1/(70\times 365)$, $\mu_{v1}=1/21$, $\mu_v=\mu_{v1}+\mu_{max}b$, $\Lambda_h=1/(70\times 365)$, $\Lambda_v=10^4/21$, and $\gamma_h=1/4$ is used to generate this figure and the basic reproduction number based on this parameter regime is $\mathcal{R}=0.61$. Note that although the initial infected populations ($I_h$ and $I_v$) were not zero, these populations die out asymptotically over time since $\mathcal{R}<1$.

### 3.2. Existence of backward bifurcation

We have shown from Theorem 1 that the DFE of the model (2) is LAS if $\mathcal{R}<1$. However, this equilibrium may not be globally asymptotically stable in $\Omega$ for $\mathcal{R}<1$, owing to the possibility of backward bifurcation. A backward bifurcation is possible when the stable DFE co-exists with a stable endemic equilibrium for $\mathcal{R}<1$ (Agusto and Gumel, 2010; Dushoff et al., 1998; Milner and Zhao, 2010; Garba et al., 2008). The public health implication of backward bifurcation is that the classical requirement of having the reproduction number less than unity, although necessary, is no longer sufficient for disease control. This implies that effective disease control is dependent on the initial sizes of the sub-populations of the model. The possibility of the model (2) exhibiting backward bifurcation phenomenon is now investigated below.

The components of any endemic equilibrium $\Sigma_1=(S_h^*, I_h^*, S_v^*, I_v^*)$ of the system given by (2) satisfy the following equations:

$$S_h^*=\frac{L\Lambda_h}{L(\lambda_h^*(b)+\mu_h)-\gamma_h\lambda_h^*(b)},\quad I_h^*=\frac{\lambda_h^*(b)\Lambda_h}{L(\lambda_h^*(b)+\mu_h)-\gamma_h\lambda_h^*(b)},$$
$$S_v^*=\frac{\Lambda_v}{\lambda_v^*(b)+\mu_v(b)},\quad I_v^*=\frac{\lambda_v^*(b)\Lambda_v}{\mu_v(b)(\lambda_v^*(b)+\mu_v(b))}. \tag{8}$$

Fig. 3 shows numerical solutions for the endemic equilibrium for the parameter set $b=0.1$, $\delta_h=10^{-3}$, $\beta_{max}=0.1$, $\beta_{min}=0$, $\mu_{max}=1/21$, $\mu_h=1/(70\times 365)$, $\mu_{v1}=1/21$, $\mu_v=\mu_{v1}+\mu_{max}b$, $\Lambda_h=1/(70\times 365)$, $\Lambda_v=10^4/21$, $\gamma_h=1/4$. This parameter set yields $\mathcal{R}=2.83$. Note that $\mathcal{R}>1$ and that both infected populations co-exist and relax to their respective non-trivial equilibrium values as time progresses. This depicts the situation in which the malaria disease establishes itself in the population.

In terms of the force of infection

$$\lambda_h^*(b)=\frac{p_1\beta(b)I_v^*}{N_h^*},\quad \lambda_v^*(b)=\frac{p_2\beta(b)I_h^*}{N_h^*}.$$

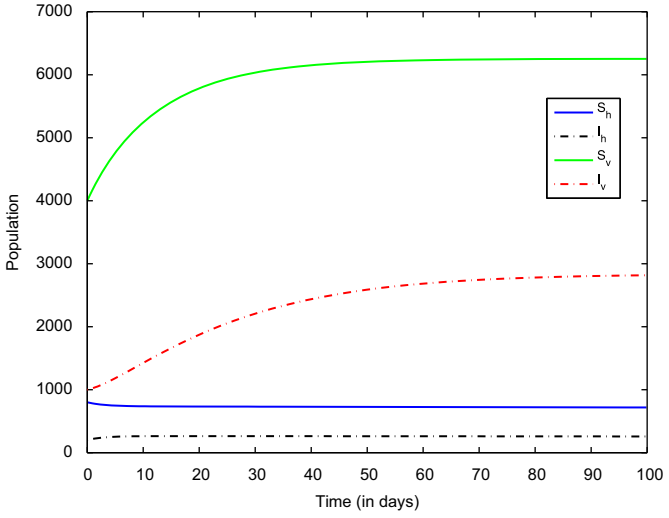


**Fig. 3.** Simulations of model (2) for the population level as a function of time for $\mathcal{R}>1$ using parameter values: $b=0.1$, $\delta_h=10^{-3}$, $\beta_{max}=0.1$, $\beta_{min}=0$, $\mu_{max}=1/21$, $\mu_h=1/(70\times 365)$, $\mu_{v1}=1/21$, $\mu_v(b)=\mu_{v1}+\mu_{max}b$, $\Lambda_h=1/(70\times 365)$, $\Lambda_v=10^4/21$, $\gamma_h=1/4$, and $\mathcal{R}=2.37$.

Since $I_h^*/N_h^* = \lambda_h^*(b)/(L+\lambda_h^*(b))$, $\lambda_h^*(b)$ and $\lambda_v^*(b)$ are related as follows:

$$\lambda_v^*(b) = \frac{p_2\beta(b)\lambda_h^*(b)}{L+\lambda_h^*(b)}$$

and

$$\lambda_h^*(b) = \frac{p_1\beta(b)\Lambda_v}{\mu_v(b)}\frac{L(\lambda_h^*(b)+\mu_h)-\lambda_h^*(b)\gamma_h}{\Lambda_h(L+\lambda_h^*(b))}\frac{\lambda_v^*(b)}{\lambda_v^*(b)+\mu_v(b)}.$$

We also have

$$\frac{\lambda_v^*(b)}{\lambda_v^*(b)+\mu_v(b)} = \frac{p_2\beta(b)\lambda_h^*(b)}{\lambda_h^*(b)A+\mu_v(b)L},$$

where $A = p_2\beta(b)+\mu_v(b)$.

This leads to

$$a_0[\lambda_h^*(b)]^2 + b_0\lambda_h^*(b) + c_0 = 0, \tag{9}$$

where

$$a_0 = \mu_v(b)\Lambda_h A,$$

$$b_0 = \mu_v(b)\Lambda_h L p_2\beta(b) + 2\mu_v^2(b)\Lambda_h L - p_1p_2\beta^2(b)\Lambda_v(\mu_h+\delta_h),$$

$$c_0 = (\mu_v(b)L)^2\Lambda_h(1-\mathcal{R}^2).$$

It should be noted that the coefficient $a_0$ of the quadratic (9) is always positive, however, the coefficient $c_0$ is positive or negative depending on the value of the reproduction number, $\mathcal{R}$. That is, if $\mathcal{R}$ is less than unity, $c_0$ is positive and if it is greater than unity, $c_0$ is negative. Thus, the following results have been established:

**Theorem 2.** *The model (2) has*

(i) *precisely one unique endemic equilibrium if* $c_0 < 0$ *or* $\mathcal{R} > 1$,
(ii) *precisely one unique endemic equilibrium if* $b_0 < 0$, *and either* $c_0 = 0$ *or* $b_0^2 - 4a_0c_0 = 0$,
(iii) *precisely two endemic equilibria if* $c_0 > 0, b_0 < 0$ *and* $b_0^2 - 4a_0c_0 > 0$,
(iv) *no endemic equilibrium otherwise.*

Case (iii) indicates the possibility of backward bifurcation in the model (2) when $\mathcal{R} < 1$. To find the backward bifurcation when $\mathcal{R} < 1$, we set the discriminant $b_0^2 - 4a_0c_0$ to zero and solve for the critical value of $\mathcal{R}$ denoted by

$$\mathcal{R}_c = \sqrt{1 - \frac{[\mu_v(b)\Lambda_h L p_2\beta(b) + 2\mu_v^2(b)\Lambda_h L - p_1p_2\beta^2(b)\Lambda_v(\mu_h+\delta_h)]^2}{4A\mu_v^3(b)L^2\Lambda_h^2}}.$$

Thus, backward bifurcation will occur for values $\mathcal{R}_c$ such that $\mathcal{R} < 1$. This is illustrated by Figs. 4 and 5 using the following set of parameter values: $\beta_{\max} = 0.1$, $\beta_{\min} = 0$, $\mu_{\max} = 1/21$, $\mu_h = 1/(70\times 365)$, $\mu_{v1} = 1/21$, $\mu_v(b) = \mu_{v1} + \mu_{\max}b$, $\Lambda_h = 1000/(70 \times 365)$, $\Lambda_v = (10^4)/15$, $\gamma_h = 1/4$, and $0 \le \mathcal{R} \le 1$, $\delta_h = 10^{-3}$.

The above result is summarized below.

**Theorem 3.** *The model (2) undergoes a backward bifurcation when Case (iii) of Theorem (2) holds and* $\mathcal{R}_c < \mathcal{R} < 1$.

We would like to remark that condition (iii) of Theorem 2 is not possible for a mild disease-induced death rate, by this we mean, $0 \le \delta_h < \mu_h$. This case is relevant when the disease induced death rate is less than death rate in humans due to all cases not related to malaria. The bottom line is condition (iii) is possible for $(\delta_h : \mathcal{R}_c < \mathcal{R} < 1)$. In the following section we address the importance of disease-induced death rate $\delta_h$ on the direction of bifurcation. The numerical results in Figs. 6 and 7 also agree with our results, that is, $\delta_h = 10^{-5} < 1/(70 \times 365) = \mu_h$, whereas in Figs. 4 and 5, $\delta_h = 10^{-3} > \mu_h$.

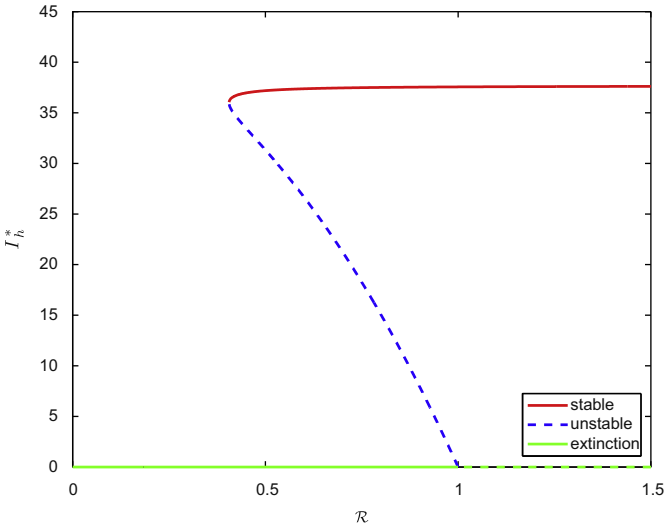


**Fig. 4.** Backward bifurcation diagram for the infectious host population for the following set of parameter values: $\delta_h = 10^{-3}$, $\beta_{\max} = 0.1$, $\beta_{\min} = 0$, $\mu_{\max} = 1/21$, $\mu_h = 1/(70 \times 365)$, $\mu_{v1} = 1/21$, $\mu_v(b) = \mu_{v1} + \mu_{\max}b$, $\Lambda_h = 1/(70 \times 365)$, $\Lambda_v = 10^4/21$, $\gamma_h = 1/4$.

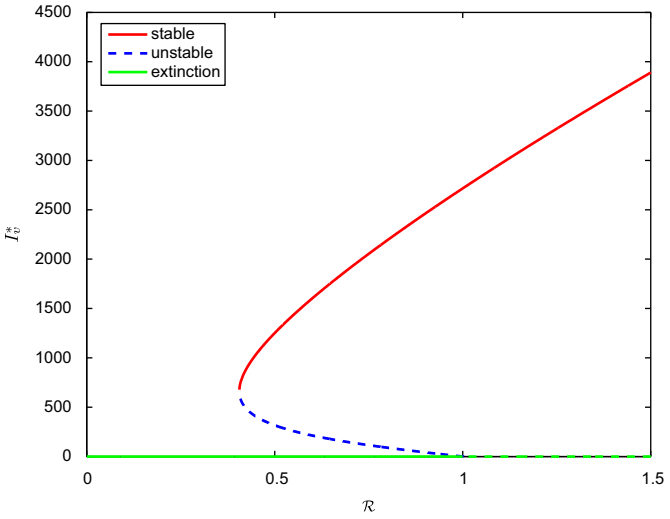


**Fig. 5.** Backward bifurcation diagram for the infectious vector population for the following set of parameter values: $\delta_h = 10^{-3}$, $\beta_{\max} = 0.1$, $\beta_{\min} = 0$, $\mu_{\max} = 1/21$, $\mu_h = 1/(70 \times 365)$, $\mu_{v1} = 1/21$, $\mu_v(b) = \mu_{v1} + \mu_{\max}b$, $\Lambda_h = 1/(70 \times 365)$, $\Lambda_v = 10^4/21$, $\gamma_h = 1/4$.

### 3.3. Analysis of the model for a special case

Next, we consider the case when the disease-induced mortality rate is ignored. It is known that some strains of the malaria disease are not deadly, for example *Plasmodium vivax* and *Plasmodium ovale* (Pertmann and Troy-Blomber, 2000). In this case, we can either ignore the disease-induced death rate ($\delta_h = 0$) or assume a very small value compared to the natural death rate, $\mu_h$. Thus, we consider $\delta_h = 0$ to study the global stability of the disease-free equilibrium and $\delta_h < \mu_h$ to establish a forward (e.g., transcritical) bifurcation at the critical value $\mathcal{R} = 1$.

#### 3.3.1. Global stability of DFE for a special case

One of the sufficient conditions for the global asymptotic stability (GAS) of the disease-free equilibrium (DFE) is a constant population level (see for example Blayneh et al., 2009; Garba et al., 2008; Teboh-Ewungkem et al., 2010). This is typically the

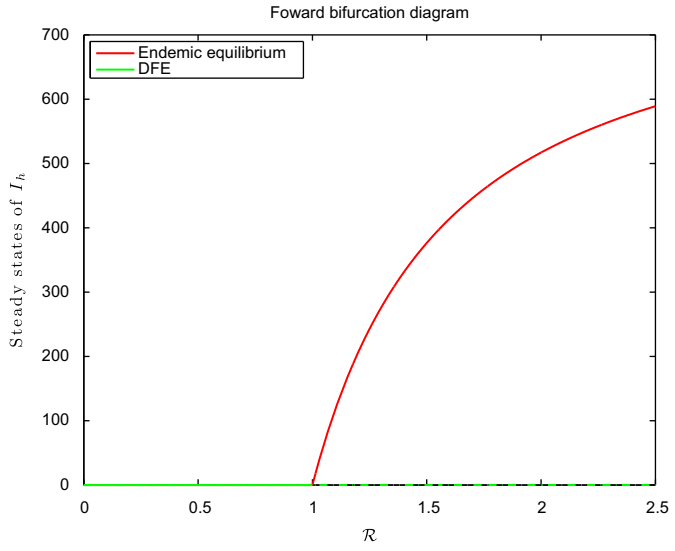


**Fig. 6.** Forward bifurcation diagram for the infectious host population for the following set of parameter values: $\delta_h = 10^{-5}$, $\beta_{max} = 0.1$, $\beta_{min} = 0$, $\mu_{max} = 1/21$, $\mu_h = 1/(70 \times 365)$, $\mu_{v1} = 1/21$, $\mu_v(b) = \mu_{v1} + \mu_{max} b$, $\Lambda_h = 1/(70 \times 365)$, $\Lambda_v = 10^4/21$, $\gamma_h = 1/4$.

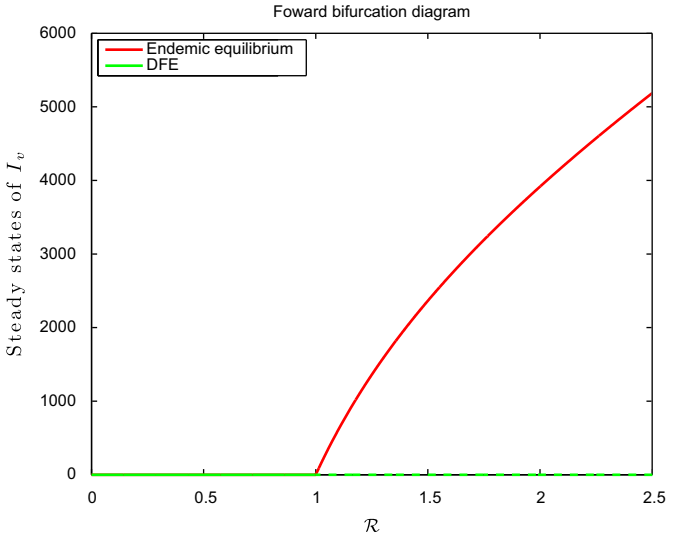


**Fig. 7.** Forward bifurcation diagram for the infectious vector population for the following set of parameter values: $\delta_h = 10^{-5}$, $\beta_{max} = 0.1$, $\beta_{min} = 0$, $\mu_{max} = 1/21$, $\mu_h = 1/(70 \times 365)$, $\mu_{v1} = 1/21$, $\mu_v(b) = \mu_{v1} + \mu_{max} b$, $\Lambda_h = 1/(70 \times 365)$, $\Lambda_v = 10^4/21$, $\gamma_h = 1/4$.

case when the disease-induced death rate is either ignored ($\delta_h = 0$) or assumed to be mild. In this case the GAS result could be established using the second generation approach given in Castillo-Chavez et al. (2002). This approach has been applied to models of vector-borne disease (Blayneh et al., 2009) and also to models of HIV/AIDS diseases (Bhunu and Mukandavire, 2009). Other approaches have considered building a Lyapunov function (Garba et al., 2008; Teboh-Ewungkem et al., 2010).

We let $X = (S_h, S_v)$ and $Z = (I_h, I_v)$ and group the system given by (2) into

$$\dot{X} = F(X,0),$$

$$\dot{Z} = G(X,Z), \tag{10}$$

where $F(X,0)$ is the right-hand side of $\dot{S_h}$ and $\dot{S_v}$ with $I_h = 0 = I_v$ and $G(X,Z)$ the right-hand side of $\dot{I_h}$ and $\dot{I_v}$. Define $\widehat{G}(X,Z) = D_Z G(X^*,0)Z - G(X,Z)$, where $(X^*,0) = (\Lambda_h/\mu_h, \Lambda_v/\mu_v(b), 0, 0)$ and $D_Z G(X^*,0)$ is the Jacobian of $G(X,Z)$ taken in $(I_h, I_v)$ and evaluated at $(X^*,0)$, which is an $M$-matrix (off diagonal elements are nonnegative). Based on what is given in Castillo-Chavez et al. (2002), the conditions for global stability of $\Sigma_0$ are

(i) local stability of $\Sigma_0$ (this is the case with our model for $\mathcal{R} < 1$),
(ii) global stability of $(X^*,0)$ under the sub system $\dot{X} = F(X,0)$, which is obvious,
(iii) $\widehat{G}(X,Z) \geq 0$ in $\Omega$. We look at some conditions which lead to this.

But first, the components of $\widehat{G}(X,Z)$, are

$$\widehat{G}_1(X,Z) = p_1\beta(b)I_v\left(1 - \frac{S_h}{N_h}\right) \quad \text{and} \quad \widehat{G}_2(X,Z) = p_2\beta(b)I_h\frac{S_v^*}{N_h^*}\left(1 - \frac{S_v N_h^*}{N_h S_v^*}\right),$$

where $N_h^* = \Lambda_h/\mu_h$ and $S_v^* = \Lambda_v/\mu_v(b)$. Clearly $\widehat{G}_1(X,Z) \geq 0$ because, $N_h = S_h + I_h \Rightarrow S_h \leq N_h$ and also in $\Omega$, $S_v \leq \Lambda_v/\mu_v(b) = S_v^*$. However, to have $\widehat{G}_2(X,Z) \geq 0$ some conditions are required. For example, we could let the human population be at equilibrium level. This ensures that $1 - S_v N_h^*/N_h S_v^* > 0$. Therefore, by the theorem in (Castillo-Chavez et al., 2002, p. 246), the disease-free equilibrium is globally asymptotically stable if we assume that the human population is at equilibrium. The foregoing discussion could be summarized in the following theorem.

**Theorem 4.** *Suppose that in system (2) the human population is at equilibrium. If $\mathcal{R} < 1$, then the disease-free equilibrium is globally asymptotically stable.*

In any case, it should be noted that the condition for the global stability of the DFE given in Castillo-Chavez et al. (2002) is a sufficient condition, which means that there is a possibility to come up with other conditions leading to the GAS of the DFE.

The following lemma establishes results for a less severe case of malaria disease. The condition on the disease-induced death rate, $\delta_h$, could indicate whether the system given by (2) has endemic equilibrium points for $\mathcal{R} < 1$ or not.

**Lemma 2.** *Consider the quadratic equation (9) and $\mathcal{R}$ given by (6). If $\mathcal{R} \leq 1$, (9) has no positive root when $\delta_h < \mu_h$.*

**Proof.** The parameter $b_0$ in (9) can be expressed as

$$b_0 = \Lambda_h\mu_v(b)L\left[p_2\beta(b) + 2\mu_v(b) - \frac{\mu_v(b)\mathcal{R}^2(\mu_h + \delta_h)}{\mu_h}\right].$$

Observe that if $\delta_h < \mu_h$, in other words, if the natural death rate of humans is assumed to be larger than the disease-induced death rate, we get

$$p_2\beta(b) + 2\mu_v(b) - \frac{\mu_v(b)\mathcal{R}^2(\mu_h + \delta_h)}{\mu_h} \geq p_2\beta(b) + 2\mu_v(b) - \frac{2\mu_v(b)\mathcal{R}^2\mu_h}{\mu_h} = p_2\beta(b) + 2\mu_v(b)(1 - \mathcal{R}^2) > 0$$

for $\mathcal{R} \leq 1$, thus, $b_0 > 0$. Clearly, from (9) $c_0 \geq 0$ for $\mathcal{R} \leq 1$ and $a_0 > 0$. Therefore, the quadratic (9) has no positive root as $(\lambda_h(b))^* = -(b_0 \pm \sqrt{b_0^2 - 4a_0c_0})/2a_0 < 0$ for $\mathcal{R} \leq 1$. □

The following theorem follows from Lemma 2. It establishes the fact that there is a forward bifurcating branch of equilibrium points as $\mathcal{R}$ passes through 1. This is illustrated by Figs. 6 and 7.

**Theorem 5.** *The system given by (2) has no endemic equilibrium for $\mathcal{R} \leq 1$ as long as $\delta_h < \mu_h$.*

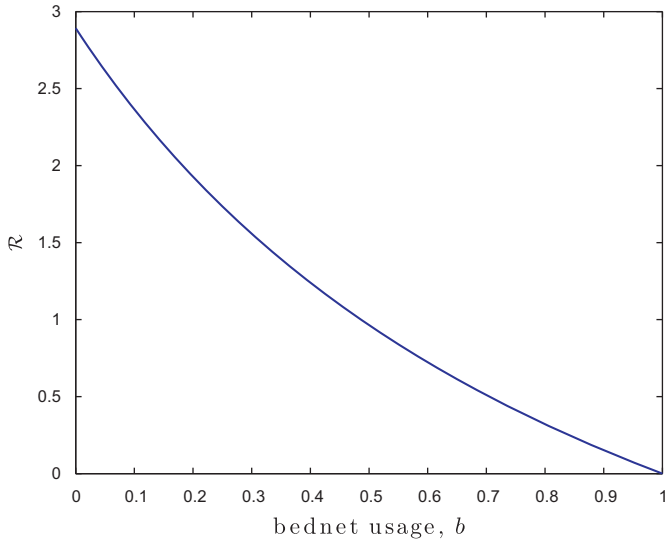


**Fig. 8.** Relationship between $\mathcal{R}$ and bed-net usage parameter $b$ for the parameter regime $\delta_h = 10^{-3}$, $\beta_{\max} = 0.1$, $\beta_{\min} = 0$, $\mu_{\max} = 1/21$, $\mu_h = 1/(70 \times 365)$, $\mu_{v1} = 1/21$, $\mu_v = \mu_{v1} + \mu_{\max} b$, $\Lambda_h = 10^3/(70 \times 365)$, $\Lambda_v = 10^4/21$, $\gamma_h = 1/4$, and $0 \le b \le 1$. Note that as the net usage decreases, $\mathcal{R}$ increases and vice versa.

## 4. Analysis of bed-net usage—*b*

In this section, we determine the critical value for the usage of bed-nets, but first, we determine the impact of ITNs in reducing the disease burden.

Taking the derivative of the reproduction number $\mathcal{R}$ with respect to bed-net usage parameter $b$ yields

$$\frac{d\mathcal{R}}{db} = -\frac{[\beta_{\max}\mu_{\max} + \mu_{v1}(\beta_{\max} - \beta_{\min})]}{(\mu_{v1} + \mu_{\max})^2} \sqrt{\frac{p_1 p_2 \Lambda_v \mu_h}{\Lambda_h(\gamma_h + \delta_h + \mu_h)}}. \tag{11}$$

As expected, it can be seen from the above that bed-net usage has a positive impact in reducing the reproduction number $\mathcal{R}$ and thus the disease burden.

Next, we determine the critical value $b_c$ for the use of bed-net. To determine the critical value $b_c$ for the use of bed-net, we consider two cases. In the first case, we assume that the bifurcation is supercritical (forward) and in the second, we consider a backward bifurcation. Considering the first case, when $\mathcal{R} < 1$, there is no endemic equilibrium point. If the contact rate

$$\beta(b) < \mu_v(b) \sqrt{\frac{L\Lambda_h}{\Lambda_v \mu_h p_1 p_2}} = \beta_c,$$

then $\mathcal{R} < 1$. Furthermore, recalling the model used for the contact rate $\beta(b) = \beta_{\max} - b(\beta_{\max} - \beta_{\min})$ and $\mu_v(b) = \mu_{v1} + \mu_{v2}(b)$, with $\mu_{v2}(b) = \mu_{\max} b$ for mortality rate of mosquitoes, it is possible to see that the condition

$$b > \frac{\beta_{\max} - \mu_{v1} Q}{\beta_{\max} - \beta_{\min} + \mu_{\max} Q} = b_c, \tag{12}$$

where $Q = \sqrt{L\Lambda_h/\Lambda_v \mu_h p_1 p_2}$, is required for the inequality $\mathcal{R} < 1$ to hold. This highlights a critical value, $b_c$, of treated bed-nets usage that is required to lower the value of $\mathcal{R}$. However, in general the reduction of $\mathcal{R}$ below unity alone is not enough to eradicate the diseases, except when initial cases of infection in each population are small. A good example is the emergence of a backward bifurcation at the critical value $\mathcal{R} = 1$. This phenomenon is observed in dengue fever and West Nile viruses, which are vector-borne diseases (Blayneh et al., 2010; Garba et al., 2008).

When there is a backward bifurcation, there is no endemic equilibrium for $\mathcal{R} < \mathcal{R}_c < 1$. Following the same approach we express $b_c$ in terms of $\mathcal{R}_c$ that is, for $b > (\beta_{\max} - \mu_{v1} Q \mathcal{R}_c)/(\beta_{\max} - \beta_{\min} + Q\mathcal{R}_c \mu_{\max}) = b_c$, where $Q$ is the same constant as in Eq. (12).

Next, we estimate numerically the threshold required to bring malaria to extinction through bed-net usage. Fig. 8 shows a schematic relationship between $\mathcal{R}$ and bed-net usage parameter $b$. Note that as net usage increases, $\mathcal{R}$ decreases and as net usage decreases, $\mathcal{R}$ increases. Our analyses on the existence of a backward bifurcation suggested that $\mathcal{R}$ had to be less than 0.4 in order to have extinction, which corresponds to net usage of 0.8.

## 5. Discussion and conclusion

One of the standard interventions for malaria-control is insecticide-treated bed nets (ITNs); however, improper handling and human behavior such as lack of usage can affect the effectiveness of nets on malaria transmission. We used a mathematical model to examine the effects of ITNs and human behavior on the spread of malaria. Although, bed-net usage is not a perfect mitigation, we demonstrated that bed-net usage has a positive impact in reducing the reproduction number and thus, disease burden.

The model considered malaria transmission in mosquito and human populations. The expression in Eq. (7) for the effective reproduction number $\mathcal{R}$ showed its explicit dependence on the cross-infection of mosquitoes and humans and bed-nets. The derivative of $\mathcal{R}$ with respect to bed-net usage demonstrated a positive impact in reducing the reproduction number.

Our analysis revealed the existence of a backward bifurcation for certain parameter values which implies that the reduction of $\mathcal{R}$ below unity alone is not enough to eradicate malaria. Therefore, additional mitigation strategies such as indoor residual spraying and treatment might be necessary to reduce malaria burden and eradication.

The numerical simulation results for the parameters $\delta_h = 10^{-3}$, $\beta_{\max} = 0.1$, $\beta_{\min} = 0$, $\mu_{\max} = 1/21$, $\mu_h = 1/(70 \times 365)$, $\mu_{v1} = 1/21$, $\mu_v = \mu_{v1} + \mu_{\max} b$, $\Lambda_h = 1/(70 \times 365)$, $\Lambda_v = 10^4/21$, $\gamma_h = 1/4$ suggested that $\mathcal{R}$ should be less than 0.4 in order to have extinction, which corresponded to bed-net usage of 75%. Therefore, educational campaigns must continue encouraging the population to use bed-nets because they will be playing an important role in eradication activities for malaria.

We conclude that models must include human behavior in order to provide realistic estimates of malaria dynamics. Improper handling and lack of use will affect the effectiveness of bed-net activities. Therefore, more data on human behavior is needed to validate models, especially if the model predictions are being used to guide public health policy. We recognize that the dynamics of bed-net usage may be more complex and could include the emergence of insecticide resistance and changes on human immunity; however, as a first approximation, we used a simple model. Even this simple model displays rich dynamics, including the occurrence of a backward or subcritical bifurcation, which is essential for disease control. The effects of nonlinear bed-net usage and other aspects of human behavior on the dynamics of malaria are currently under study and these shall constitute the basis for a separate paper.

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## References

Agusto, F.B., Gumel, A.B., 2010. Theoretical assessment of avian influenza vaccine. DCDS Ser. B 13 (1), 1–25.

Blayneh, K.W., Cao, Y., Kwon, H.-D., 2009. Optimal control of vector-borne diseases: treatment and prevention. DCDS Ser. B 11 (3), 587–611.

Blayneh, K.W., Gumel, A.B., Lenhart, S., Clayton, T., 2010. Backward bifurcation and optimal control in transmission dynamics of West Nile virus. Bull. Math. Biol. 72 (4), 1006–1028.

Bowman, C., Gumel, A.B., van den Driessche, P., Wu, J., Zhu, H., 2005. A mathematical model for assessing control strategies against West Nile virus. Bull. Math. Biol. 67, 1107–1133.

Bhunu, C.P., Mukandavire, W.G., 2009. Modeling HIV/AIDS and tuberculosis coinfection. Bull. Math. Biol. 71, 1745–1780.

Castillo-Chavez, C., Blower, S., van den Driessche, P., Kirschner, D., Yakubu, A.-A., 2002. Mathematical Approaches for Emerging and Reemerging Infectious Diseases. Springer-Verlag, New York.

Chitnis, N., Schapira, A., Smith, T., Steketee, R., 2010. Comparing the effectiveness of malaria vector–control interventions through a mathematical model. Am. J. Trop. Med. Hyg. 83 (2), 230–240.

Del Valle, S., Hethcote, H., Hyman, J.M., Castillo-Chavez, C., 2005. Effects of behavioral changes in a smallpox attack model. Math. Biosci. 195, 228–251.

Dushoff, J., Huang, W., Castillo-Chavez, C., 1998. Backwards bifurcations and catastrophe in simple models of fatal diseases. J. Math. Biol. 36, 227–248.

Govella, Nicodem J., Okumu, Fredros O., Killeen, Gerry F., 2010. Insecticide-treated nets can reduce malaria transmission by mosquitoes which feed outdoors. Am J. Trop. Med. Hyg. 82 (3), 415–419, http://dx.doi.org/10.4269/ajtmh.2010.09-0579.

Garba, S.M., Gumel, A.B., Abu Bakar, M.R., 2008. Backward bifurcations in dengue transmission dynamics. Math. Biosci. 215 (1), 11–25.

Goodman, C.A., Mills, A.J., 1999. The evidence base on the cost-effectiveness of malaria control measures in Africa. Health Policy Plann. 14 (4), 301–312.

Hethcote, H.W., 2000. The mathematics of infectious diseases. SIAM Rev. 42 (4), 599–653.

Kayedi, M.H., Lines, J.D., Haghdoost, A.A., Vatandoost, M.H., Rassi, Y., Khamisabady, K., 2008. Evaluation of the effects of repeated hand washing, sunlight, smoke and dirt on the persistence of deltamethrin on insecticide-treated nets. Trans. R. Soc. Trop. Med. Hyg. 10 (2), 811–816.

Killeen, G.F., Smith, T.A., 2007. Exploring the contributions of bed nets, cattle, insecticides and excitorepellency to malaria control: a deterministic model of mosquito host-seeking behaviour and mortality. Trans. R. Soc. Trop. Med. Hyg. 101 (9), 867–880.

Lakshmikantham, V., Leela, S., Martynyuk, A.A., 1989. Stability Analysis of Nonlinear Systems. Marcel Dekker, Inc., New York and Basel.

Lengeler, C., 2004. Insecticide-treated bed nets and curtains for preventing malaria. Cochrane Database Syst. Rev. Art. No.: CD000363.

Milner, F.A., Zhao, R., 2010. A new mathematical model of syphilis. Math. Model. Nat. Phenom. 5 (6), 96–108.

Pertmann, P., Troy-Blomber, M., 2000. Malaria blood-stage infection and its control by the immune system. Folia Biol. 46 (6), 210–218, PMID 11140853.

Smith, L., Maire, N., Ross, A., Penny, M., Chitnis, N., Schapira, A., Studer, A., Genton, B., Lengeler, C., Tediosi, F., De Savigny, D., Tanner, M., 2008. Towards a comprehensive simulation model of malaria epidemiology and control. Parasitology 135, 1507–1516.

Teboh-Ewungkem, M.I., Podder, C.N., Gumel, A.B., 2010. Mathematical study of the role of gametocytes and an imperfect vaccine on malaria transmission dynamics. Bull. Math. Biol. 72, 63–93.

van den Driessche, P., Watmough, J., 2002. Reproduction numbers and subthreshold endemic equilibria for compartmental models of disease transmission. Math. Biosci. 180, 29–48.

Vanlerberghe, V., Trongtokit, Y., Cremonini, L., Jirarojwatana, S., Apiwathnasorn, C., Van der Stuyft, P., 2010. Residual insecticidal activity of long-lasting deltamethrin-treated curtains after 1 year of household use for dengue control. Trop. Med. Int. Health 15 (9), 1067–1071.

White, L.J., Maude, R.J., Pongtavornpinyo, W., Saralamba, S., Aguas, R., Van Effelterre, T., Day, N.P.J., White, N.J., 2009. The role of simple mathematical models in malaria elimination strategy design. Malaria J. 8, 212.