# Modeling and control of malaria when mosquitoes are used as vaccinators 

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Dedicated to Mimmo Iannelli on the occasion of his 65th birthday


#### Abstract

From the idea of turning mosquitoes into vaccinators (D.S. Yamamoto, et al. 2010), a first model of the transmission of malaria uses standard incidence leads to express the basic reproduction number $R_{0}(\psi)$ and the effective reproduction number $\mathcal{R}(\psi)$. The disease-free equilibrium is locally asymptotically stable if $R_{0}(\psi)<1$. A necessary and sufficient condition for backward bifurcation is derived. A unique endemic equilibrium exists if $R_{0}(\psi)>1$. A second model, with mass action incidence, leads to express the basic reproduction number $R_{0}^{m}(\psi)$. The disease-free equilibrium is both locally asymptotically stable and globally


[^0]stable if $R_{0}^{m}(\psi)<1$. A unique endemic equilibrium exists if $R_{0}^{m}(\psi)>1$ and is locally asymptotically stable. Simulations help calibrate the theoretical results.

Keywords: malaria; vaccine; basic reproduction number; effective reproduction number; backward bifurcation

## 1 Introduction

Vector control and treatment are the main prophylactic measures against malaria. Indoor residual spraying and insecticide-treated nets contribute to vector control. Mosquitoes' resistance to DDT, pyrethroids, and other insecticides is growing. Improper use of antimalaria drugs and mutation have increased drug resistance in the parasite.

Targeting different stages in the plasmodium's life cycle, scientists have developed a series of candidate malaria vaccines, such as CSP, MSP1, pfs25, and SPf66 peptide malaria vaccine. (Yamamoto et al., 2010) has successfully turned mosquitoes into flying vaccinators in the lab. We shall model the potential effects of using mosquitoes for delivering human vaccines.

The strategy 'Flying vaccinator' consists in using genetically engineered hematophagous insects to deliver vaccines. Transgenic anopheline mosquitos can already express the Leishmania vaccine candidate, SP15, fused to monomeric red fluorescent protein (mDsRed) in mosquito's salivary glands. Mice bitten repeatedly by the transgenic mosquitoes raised anti-SP15 antibodies, indicating delivery of SP15 through blood feeding.

We shall formulate novel malaria transmission models using mosquitoes for human vaccine delivery either with standard or with mass action incidence (Teboh-Ewungkem et al., 2013).

## 2 Transmission of malaria with standard incidence

### 2.1 Model

The total human population $N_{h}(t)$ at time $t$ is divided into the susceptible $S_{h}(t)$, the infectious $I_{h}(t)$, the recovered $R_{h}(t)$, and the vaccinated $V_{h}(t)$. Due to the mosquito's short lifespan, we assume that a mosquito will never recover from infection. The total vector population $N_{v}(t)$ at time $t$ is split into susceptible $S_{v}(t)$, infectious $I_{v}(t)$, and vaccinated $M_{v}(t)$ :

$$
\begin{equation*}
N_{h}(t)=S_{h}(t)+I_{h}(t)+R_{h}(t)+V_{h}(t), \quad N_{v}(t)=S_{v}(t)+I_{v}(t)+M_{v}(t) . \tag{1}
\end{equation*}
$$

The human and the mosquito populations mix homogeneously, so that the average number of mosquito bites received by humans depends on the population sizes of mosquitoes and humans (Bowman et al, 2005). $C_{h v}\left(N_{h}, N_{v}\right)$ is the per head biting rate of a mosquito, constant, equal to $C_{h v} . C_{v h}\left(N_{h}, N_{v}\right)$ is the rate at which a single host per unit time is bitten. The total number of bites by mosquitoes equals the total number of bites on humans (conservation law):

$$
\begin{equation*}
C_{h v} N_{v}=C_{v h}\left(N_{h}, N_{v}\right) N_{h} . \tag{2}
\end{equation*}
$$

The transmission probability per contact from an infectious vector to a susceptible human is $\beta_{v}$, then $\beta_{v} C_{h v}$ is the effective contact rate between a susceptible human and an infectious vector. A susceptible human acquires infection, after effective contact with infectious vectors, at a rate $\lambda_{v}$ :

$$
\begin{equation*}
\lambda_{v}=\frac{\beta_{v} C_{v h}\left(N_{h}, N_{v}\right)}{N_{v}} I_{v}=\frac{\beta_{v} C_{h v}}{N_{h}} I_{v} . \tag{3}
\end{equation*}
$$

Similarly, the transmission probability $\beta_{m}$ per contact from a vaccinated vector to a susceptible human leads to an effective contact rate $\beta_{m} C_{h v}$ between a susceptible human and a vaccinated vector. A susceptible human becomes vaccinated, after effective
contact with vaccinated vectors, at a rate $\lambda_{m}$ :

$$
\begin{equation*}
\lambda_{m}=\frac{\beta_{m} C_{v h}\left(N_{h}, N_{v}\right)}{N_{v}} M_{v}=\frac{\beta_{m} C_{h v}}{N_{h}} M_{v} . \tag{4}
\end{equation*}
$$

The rate at which vectors acquire infection from infectious human hosts is:

$$
\begin{equation*}
\lambda_{h}=\frac{\beta_{h} C_{h v}}{N_{h}} I_{h} . \tag{5}
\end{equation*}
$$

Assumptions:
$\left(H_{1}\right)$ Recruitment for humans is $\Pi_{h}$, constant; recruitment for vectors is $\Pi_{v}$, constant. All recruited humans and vectors are susceptible.
$\left(H_{2}\right)$ The natural death rate is $\mu_{h}$ for humans and $\mu_{v}$ for mosquitoes. The diseaseinduced death rate for humans is $\varepsilon_{h}$, and the pesticide-induced death rate for mosquitoes is $\delta_{v}$.
$\left(H_{3}\right)$ Recovered humans may contract malaria again at a reduced infectious rate, but, we simplify to lifelong infection-acquired immunity.
$\left(H_{4}\right)$ The vaccination is perfect.
$\left(H_{5}\right)$ Susceptible mosquitoes acquire the disease only from infected humans, and susceptible humans acquire the disease only from infected mosquitoes.

Figure 1 shows the transmission process of malaria. The model is:

$$
\left\{\begin{array}{l}
S_{h}^{\prime}(t)=\Pi_{h}-\left(\lambda_{v}(t)+\lambda_{m}(t)+\mu_{h}\right) S_{h}(t)  \tag{6}\\
I_{h}^{\prime}(t)=\lambda_{v}(t) S_{h}(t)-\left(\mu_{h}+\varepsilon_{h}+\gamma_{h}\right) I_{h}(t) \\
R_{h}^{\prime}(t)=\gamma_{h} I_{h}(t)-\mu_{h} R_{h}(t) \\
V_{h}^{\prime}(t)=\lambda_{m}(t) S_{h}(t)-\mu_{h} V_{h}(t) \\
S_{v}^{\prime}(t)=\Pi_{v}-\lambda_{h}(t) S_{v}(t)-\left(\mu_{v}+\delta_{v}+\psi\right) S_{v}(t) \\
I_{v}^{\prime}(t)=\lambda_{h}(t) S_{v}(t)-\left(\mu_{v}+\delta_{v}\right) I_{v}(t) \\
M_{v}^{\prime}(t)=\psi S_{v}(t)-\left(\mu_{v}+\delta_{v}\right) M_{v}(t)
\end{array}\right.
$$

where

$$
\lambda_{v}(t)=\frac{\beta_{v} C_{h v}}{N_{h}} I_{v}(t), \quad \lambda_{m}(t)=\frac{\beta_{m} C_{h v}}{N_{h}} M_{v}(t), \quad \lambda_{h}(t)=\frac{\beta_{h} C_{h v}}{N_{h}} I_{h}(t) .
$$



Figure 1: Transmission of malaria between mosquitoes and humans

Table 1 lists the parameters.
Table 1: Description of parameters for model Eq. (6)

| Parameter | Description |
| :---: | :--- |
| $\Pi_{h}$ | Recruitment rate of humans |
| $\Pi_{v}$ | Recruitment rate of mosquitoes |
| $C_{h v}$ | Average biting rate of mosquitoes on a host |
| $\beta_{v}$ | Transmission probability from infectious mosquitoes to humans |
| $\beta_{m}$ | Transmission probability from vaccinated mosquitoes to humans |
| $\beta_{h}$ | Transmission probability from infectious humans to mosquitoes |
| $\mu_{h}$ | Natural death rate for humans |
| $\mu_{v}$ | Natural death rate for mosquitoes |
| $\varepsilon_{h}$ | Disease-induced death rate for humans |
| $\delta_{v}$ | Pesticide-induced death rate for mosquitoes |
| $\gamma_{h}$ | Recovery rate for humans |
| $\psi$ | Vaccination rate for mosquitoes |

Eq. (6), the total human population $N_{h}(t)$ and the total vector population $N_{v}(t)$ yield:

$$
\begin{equation*}
N_{h}^{\prime}(t)=\Pi_{h}-\mu_{h} N_{h}(t)-\varepsilon_{h} I_{h}(t), \quad N_{v}^{\prime}(t)=\Pi_{v}-\left(\mu_{v}+\delta_{v}\right) N_{v}(t) . \tag{7}
\end{equation*}
$$

Theorem 1. The closed set
$\mathcal{D}=\left\{\left(S_{h}, I_{h}, R_{h}, V_{h}, S_{v}, I_{v}, M_{v}\right) \in R_{7}^{+} \left\lvert\, S_{h}+I_{h}+R_{h}+V_{h} \leq \frac{\Pi_{h}}{\mu_{h}}\right. ; S_{v}+I_{v}+M_{v} \leq \frac{\Pi_{v}}{\mu_{v}+\delta_{v}}\right\}$
is positively invariant and attracting with respect to the solutions of Eq. (6).
Proof. As

$$
\begin{equation*}
N_{h}^{\prime}(t)=\Pi_{h}-\mu_{h} N_{h}(t)-\varepsilon_{h} I_{h}(t) \leq \Pi_{h}-\mu_{h} N_{h}(t) \tag{8}
\end{equation*}
$$

and

$$
\begin{equation*}
N_{v}^{\prime}(t) \leq \Pi_{v}-\left(\mu_{v}+\delta_{v}\right) N_{v}(t), \tag{9}
\end{equation*}
$$

$N_{h}^{\prime}(t) \leq 0$ if $N_{h}(t) \geq \frac{\Pi_{h}}{\mu_{h}}$ and $N_{v}^{\prime}(t) \leq 0$ if $N_{v}(t) \geq \frac{\Pi_{v}}{\mu_{v}+\delta_{v}}$. Comparison theorem (Lakshmikantham et al., 1989) shows that

$$
\begin{equation*}
N_{h}(t) \leq N_{h}(0) e^{-\mu_{h} t}+\frac{\Pi_{h}}{\mu_{h}}\left(1-e^{-\mu_{h} t}\right), \tag{10}
\end{equation*}
$$

and

$$
\begin{equation*}
N_{v}(t) \leq N_{v}(0) e^{-\left(\mu_{v}+\delta_{v}\right) t}+\frac{\Pi_{v}}{\mu_{v}+\delta_{v}}\left(1-e^{-\left(\mu_{v}+\delta_{v}\right) t}\right) . \tag{11}
\end{equation*}
$$

In particular, $N_{h}(t) \leq \frac{\Pi_{h}}{\mu_{h}}$ if $N_{h}(0) \leq \frac{\Pi_{h}}{\mu_{h}}$ and $N_{v}(t) \leq \frac{\Pi_{v}}{\mu_{v}+\delta_{v}}$ if $N_{v}(0) \leq \frac{\Pi_{v}}{\mu_{v}+\delta_{v}}$. The region $\mathcal{D}$ is positively invariant. If $N_{h}(0) \geq \frac{\Pi_{h}}{\mu_{h}}$ and $N_{v}(0) \geq \frac{\Pi_{v}}{\mu_{v}+\delta_{v}}$, then either the solution enters $\mathcal{D}$ in finite time, or $N_{h}(t)$ approaches $\frac{\Pi_{h}}{\mu_{h}}$ and $N_{v}(t)$ approaches $\frac{\Pi_{v}}{\mu_{v}+\delta_{v}}$ asymptotically. Hence, the region $\mathcal{D}$ attracts all solutions in $R_{7}^{+}$.

### 2.2 Disease-free equilibrium and Reproduction numbers

Eq. (6) has always the disease-free equilibrium (DFE)

$$
\begin{equation*}
E_{0}\left(S_{h}^{0}, 0,0, V_{h}^{0}, S_{v}^{0}, 0, M_{v}^{0}\right) \tag{12}
\end{equation*}
$$

where

$$
\begin{array}{ll}
S_{v}^{0}=\frac{\Pi_{v}}{\mu_{v}+\delta_{v}+\psi}, & M_{v}^{0}=\frac{\psi}{\mu_{v}+\delta_{v}} S_{v}^{0}, \\
N_{h}^{0}=\frac{\Pi_{h}}{\mu_{h}}, & \lambda_{m}^{0}=\frac{\beta_{m} C_{h v}}{N_{h}^{0}} M_{v}^{0},  \tag{13}\\
S_{h}^{0}=\frac{\Pi_{h}}{\mu_{h}+\lambda_{m}^{0}}, & V_{h}^{0}=\frac{\lambda_{m}^{0} S_{h}^{0}}{\mu_{h}} .
\end{array}
$$

The existence and stability of non-trivial equilibria depend on several parameters, introduced below. Firstly, we define the basic reproduction number to represent the average total number of secondary infections in humans stemming from one infected human introduced into a completely uninfected population.

$$
\begin{equation*}
R_{0}(\psi)=\frac{\beta_{v} \beta_{h} C_{h v}^{2} \mu_{h} \Pi_{v}}{Q\left(\Pi_{h}\left(\mu_{v}+\delta_{v}\right)\left(\mu_{v}+\delta_{v}+\psi\right)+\beta_{m} C_{h v} \psi \Pi_{v}\right)}, \tag{14}
\end{equation*}
$$

where $Q=\mu_{h}+\varepsilon_{h}+\gamma_{h}$.
The total number of vectors corresponding to one person is $\frac{N_{v}}{N_{h}}$. A human receives $C_{h v} \frac{N_{v}}{N_{h}}$ bites per unit of time on average. The transmission probability from infectious humans to mosquitoes is $\beta_{h}$; the proportion of susceptible vectors in the total vector population is $\frac{S_{v}}{N_{v}}$; and the time spent in the class $I_{h}$ is $\frac{1}{Q}$. The total number of secondary infectious vectors one infectious human will produce in a completely uninfected vector population is then $\beta_{h} C_{h v} \frac{N_{v}}{N_{h}} \frac{S_{v}}{N_{v}} \frac{1}{Q}$. The effective contact rate between an infectious vector and a susceptible human is $\beta_{v} C_{h v}$, and the time spent in the class $I_{v}$ is $\frac{1}{\mu_{v}+\delta_{v}}$. The proportion of susceptible humans in the total human population is $\frac{S_{h}}{N_{h}}$. In the absence of disease, $S_{h}=S_{h}^{0}, N_{h}=N_{h}^{0}=\frac{\Pi_{h}}{\mu_{h}}$ and $S_{v}=S_{v}^{0}=\frac{\Pi_{v}}{\mu_{v}+\delta_{v}}$. Consequently,

$$
\begin{equation*}
\beta_{h} C_{h v} \frac{N_{v}^{0}}{N_{h}^{0}} \frac{S_{v}^{0}}{N_{v}^{0}} \frac{1}{Q} \beta_{v} C_{h v} \frac{S_{h}^{0}}{N_{h}^{0}} \frac{1}{\mu_{v}+\delta_{v}}=\frac{\beta_{v} \beta_{h} C_{h v}^{2} \mu_{h} \Pi_{v}}{Q\left[\Pi_{h}\left(\mu_{v}+\delta_{v}\right)\left(\mu_{v}+\delta_{v}+\psi\right)+\beta_{m} C_{h v} \psi \Pi_{v}\right]}, \tag{15}
\end{equation*}
$$

represents the average total number of secondary infections of humans stemming from one infected human introduced into a completely uninfected population.

The basic reproduction number $R_{0}(\psi)$ can also represent the average total number of secondary infections in mosquitoes stemming from one infected mosquitoes intro-
duced into a completely uninfected human population. Similarly, $\beta_{v} C_{h v} \frac{S_{h}^{0}}{N_{h}^{0}} \frac{1}{\mu_{v}+\delta_{v}}$ represents the total number of secondary infectious humans stemming from one infectious mosquitoes
a completely uninfected human population. A human receives on average $\beta_{h} C_{h v} \frac{N_{v}}{N_{h}}$ effective bites per unit of time, and the time spent in the class $I_{h}$ is $\frac{1}{Q}$. The proportion of susceptible mosquitoes in the total mosquitoes is $\frac{S_{v}}{N_{v}}$. In the absence of the disease,

$$
\begin{equation*}
\beta_{v} C_{h v} \frac{S_{h}^{0}}{N_{h}^{0}} \frac{1}{\mu_{v}+\delta_{v}} \beta_{h} C_{h v} \frac{N_{v}^{0}}{N_{h}^{0}} \frac{S_{v}^{0}}{N_{v}^{0}} \frac{1}{Q}=\frac{\beta_{v} \beta_{h} C_{h v}^{2} \mu_{h} \Pi_{v}}{Q\left[\Pi_{h}\left(\mu_{v}+\delta_{v}\right)\left(\mu_{v}+\delta_{v}+\psi\right)+\beta_{m} C_{h v} \psi \Pi_{v}\right]}, \tag{16}
\end{equation*}
$$

represents the average total number of secondary infections of mosquitoes stemming from one infected mosquito introduced into a completely uninfected mosquitoes population.

The next generation approach (Driessche and Watmough, 2002) gives the next generation matrix (Diekmann et al, 1990) for Eq. (6):

$$
F=\left(\begin{array}{cc}
0 & \frac{\beta_{v} C_{h v} v_{h}^{0}}{N_{h}^{0}}  \tag{17}\\
\frac{\beta_{h} C_{h v}}{N_{h}^{0}} & 0
\end{array}\right), \quad V=\left(\begin{array}{cc}
Q & 0 \\
0 & \mu_{v}+\delta_{v}
\end{array}\right)
$$

and another form of reproduction number $\widetilde{R}_{0}(\psi)$ for Eq. (6):

$$
\begin{equation*}
\widetilde{R}_{0}(\psi)=\rho\left(F V^{-1}\right)=\left(\frac{\beta_{v} \beta_{h} C_{h v}^{2} \mu_{h} \Pi_{v}}{Q\left(\Pi_{h}\left(\mu_{v}+\delta_{v}\right)\left(\mu_{v}+\delta_{v}+\psi\right)+\beta_{m} C_{h v} \psi \Pi_{v}\right)}\right)^{\frac{1}{2}}=R_{0}(\psi)^{\frac{1}{2}} \tag{18}
\end{equation*}
$$

where $\rho$ denotes the spectral radius. $\widetilde{R}_{0}(\psi)>1\left(\widetilde{R}_{0}(\psi)<1\right)$ if and only if $R_{0}(\psi)>1$ $\left(R_{0}(\psi)<1\right)$.
$R_{0}(\psi)$ in Eq. (14) (Anderson and May, 1991; Aron and May, 1982; Ngwa and Shu, 2000) approximates the number of secondary infections of humans caused by one infected human, while $\widetilde{R}_{0}(\psi)$ in Eq. (18) approximates the number of secondary infections (human or mosquito) due to one infected individual (human or mosquito) per generation. The infection takes two generations, from human to mosquito, and from the mosquito to another human, which leads to the square root. The two basic reproduction numbers give equivalent threshold conditions.

If $\psi=0$, the disease-free-equilibrium and the basic reproduction number become

$$
\begin{equation*}
\bar{E}_{0}\left(\bar{S}_{h}^{0}, 0,0,0, \bar{S}_{v}^{0}, 0,0\right) \tag{19}
\end{equation*}
$$

where

$$
\begin{equation*}
\bar{S}_{h}^{0}=\frac{\Pi_{h}}{\mu_{h}}, \quad \bar{S}_{v}^{0}=\frac{\Pi_{v}}{\mu_{v}+\delta_{v}}, \tag{20}
\end{equation*}
$$

and

$$
\begin{equation*}
R_{0}(0)=\frac{\beta_{v} \beta_{h} C_{h v}^{2} \mu_{h} \Pi_{v}}{Q \Pi_{h}\left(\mu_{v}+\delta_{v}\right)^{2}} . \tag{21}
\end{equation*}
$$

In analogy to $R_{0}(\psi)$, a vaccination reproduction number

$$
\begin{equation*}
R_{1}(\psi)=\frac{\psi \beta_{m} C_{h v} \Pi_{v}}{\Pi_{h}\left(\mu_{v}+\delta_{v}\right)^{2}}, \tag{22}
\end{equation*}
$$

gives the average total number of vaccinated humans stemming from entirely susceptible human population placed in a fully vaccinated mosquitoes population with vaccination rate of mosquitoes, $\psi$. To interpret the meaning of $R_{1}(\psi)$ more clearly, we rewrite it as

$$
\begin{equation*}
R_{1}(\psi)=\beta_{m} C_{h v} \frac{\psi \bar{S}_{v}^{0}}{\bar{N}_{h}^{0}} \frac{1}{\mu_{v}+\delta_{v}} \frac{\bar{S}_{h}^{0}}{\bar{N}_{h}^{0}} \frac{1}{\mu_{h}}, \tag{23}
\end{equation*}
$$

where $\bar{N}_{h}^{0}=\bar{S}_{h}^{0}=\frac{\Pi_{h}}{\mu_{h}}, \bar{S}_{v}^{0}=\frac{\Pi_{v}}{\mu_{v}+\delta_{v}}$.
Finally, we define the effective reproduction number

$$
\begin{equation*}
\mathcal{R}(\psi)=\frac{R_{0}(0)}{R_{1}(\psi)}=\frac{\beta_{v} \beta_{h} C_{h v} \mu_{h}}{\psi \beta_{m} Q}, \tag{24}
\end{equation*}
$$

which is a threshold for the existence of backward bifurcation.
Theorem 2. If $R_{0}(\psi)<1$, then DFE $E_{0}$ is locally asymptotically stable (LAS); if $R_{0}(\psi)>1$, then $E_{0}$ is unstable.

Proof. Linearizing system Eq. (6) at the point $E_{0}$, we get the characteristic equation:

$$
\left|\begin{array}{ccccccc}
\lambda+\mu_{h}+K_{1} & -K_{2} & -K_{2} & -K_{2} & 0 & K_{3} & K_{4}  \tag{25}\\
0 & \lambda+Q & 0 & 0 & 0 & -K_{3} & 0 \\
0 & -\gamma_{h} & \lambda+\mu_{h} & 0 & 0 & 0 & 0 \\
-K_{1} & K_{2} & K_{2} & \lambda+\mu_{h}+K_{2} & 0 & 0 & -K_{4} \\
0 & K_{5} & 0 & 0 & \lambda+Q_{1} & 0 & 0 \\
0 & -K_{5} & 0 & 0 & 0 & \lambda+\mu_{v}+\delta_{v} & 0 \\
0 & 0 & 0 & 0 & -\psi & 0 & \lambda+\mu_{v}+\delta_{v}
\end{array}\right|=0,
$$

where $K_{1}=\lambda_{m}^{0}\left(1-\frac{S_{h}^{0}}{N_{h}^{0}}\right), K_{2}=\lambda_{m}^{0} \frac{S_{h}^{0}}{N_{h}^{0}}, K_{3}=\frac{\beta_{v} C_{h v} S_{h}^{0}}{N_{h}^{0}}, K_{4}=\frac{\beta_{m} C_{h v} S_{h}^{0}}{N_{h}^{0}}, K_{5}=\frac{\beta_{h} C_{h v} S_{v}^{0}}{N_{h}^{0}}$, and $Q_{1}=\mu_{v}+\delta_{v}+\psi$. Manipulating the determinant, we obtain the eigenvalues:

$$
\begin{equation*}
\lambda_{1}=-\left(\mu_{v}+\delta_{v}\right), \quad \lambda_{2}=-Q_{1}, \quad \lambda_{3}=\lambda_{4}=-\mu_{h}, \quad \lambda_{5}=-\left(\mu_{h}+\lambda_{m}^{0}\right) . \tag{26}
\end{equation*}
$$

The remaining two eigenvalues $\lambda_{6}$ and $\lambda_{7}$ satisfy

$$
\begin{equation*}
\lambda^{2}+\left(Q+\mu_{v}+\delta_{v}\right) \lambda+Q\left(\mu_{v}+\delta_{v}\right)-K_{3} K_{5}=0 \tag{27}
\end{equation*}
$$

Since $Q\left(\mu_{v}+\delta_{v}\right)-K_{3} K_{5}=Q\left(\mu_{v}+\delta_{v}\right)\left(1-R_{0}(\psi)\right)$, we have

$$
\begin{equation*}
\lambda_{6}+\lambda_{7}=-\left(Q+\mu_{v}+\delta_{v}\right), \quad \lambda_{6} \lambda_{7}=Q\left(\mu_{v}+\delta_{v}\right)\left(1-R_{0}(\psi)\right), \tag{28}
\end{equation*}
$$

if $R_{0}(\psi)<1$, both $\lambda_{6}$ and $\lambda_{7}$ have negative real parts, which implies $E_{0}$ is locally asymptotically stable; if $R_{0}(\psi)>1$, there is a positive eigenvalue, which indicates $E_{0}$ is unstable.

### 2.3 Endemic equilibria and existence of backward bifurcation

$E^{*}\left(S_{h}^{*}, S_{h}^{*}, I_{h}^{*}, R_{h}^{*}, V_{h}^{*}, S_{v}^{*}, I_{v}^{*}, M_{v}^{*}\right)$ represents any endemic equilibrium of Eq. (6). The algebraic equations below are solved with one of the non-zero infected components:

$$
\left\{\begin{array}{l}
\Pi_{h}-\lambda_{v}^{*} S_{h}^{*}-\lambda_{m}^{*} S_{h}^{*}-\mu_{h} S_{h}^{*}=0  \tag{29}\\
\lambda_{v}^{*} S_{h}^{*}-Q I_{h}^{*}=0 \\
\gamma_{h} I_{h}^{*}-\mu_{h} R_{h}^{*}=0 \\
\lambda_{m}^{*} S_{h}^{*}-\mu_{h} V_{h}^{*}=0 \\
\Pi_{v}-\lambda_{h}^{*} S_{v}^{*}-\left(\mu_{v}+\delta_{v}+\psi\right) S_{v}^{*}=0 \\
\lambda_{h}^{*} S_{v}^{*}-\left(\mu_{v}+\delta_{v}\right) I_{v}^{*}=0 \\
\psi S_{v}^{*}-\left(\mu_{v}+\delta_{v}\right) M_{v}^{*}=0
\end{array}\right.
$$

where

$$
\begin{equation*}
\lambda_{v}^{*}=\frac{\beta_{v} C_{h v} I_{v}^{*}}{N_{h}^{*}}, \quad \lambda_{m}^{*}=\frac{\beta_{m} C_{h v} M_{v}^{*}}{N_{h}^{*}}, \quad \lambda_{h}^{*}=\frac{\beta_{h} C_{h v} I_{h}^{*}}{N_{h}^{*}}, \tag{30}
\end{equation*}
$$

and

$$
\begin{equation*}
N_{h}^{*}=S_{h}^{*}+I_{h}^{*}+R_{h}^{*}+V_{h}^{*} . \tag{31}
\end{equation*}
$$

Eq. (29) and Eq. (30) imply

$$
\begin{align*}
\lambda_{m}^{*} & =\frac{\beta_{m} \psi}{\beta_{v} \lambda_{h}^{*}} \lambda_{v}^{*} \\
\lambda_{h}^{*} & =\frac{\beta_{h} C_{h v} \mu_{h} \lambda_{v}^{*}}{\mu_{h}\left(Q+\lambda_{v}^{*}\right)+\gamma_{h} \lambda_{v}^{*}+Q \lambda_{m}^{*}},  \tag{32}\\
\lambda_{v}^{*} & =\frac{\beta_{v} C_{h v} \mu_{h} \Pi_{v} Q \lambda_{h}^{*}\left(\mu_{h}+\lambda_{v}^{*}+\lambda_{m}^{*}\right)}{\Pi_{h}\left(\mu_{v}+\delta_{v}\right)\left(\mu_{v}+\delta_{v}+\psi+\lambda_{h}^{*}\right)\left(\mu_{h}\left(Q+\lambda_{v}^{*}\right)+\gamma_{h} \lambda_{v}^{*}+Q \lambda_{m}^{*}\right)} .
\end{align*}
$$

Substituting the fist term of Eq. (32) into the second term, we get

$$
\begin{equation*}
\lambda_{h}^{*}=\frac{\psi \beta_{m} Q \lambda_{v}^{*}(\mathcal{R}(\psi)-1)}{\beta_{v}\left(\mu_{h}\left(Q+\lambda_{v}^{*}\right)+\gamma_{h} \lambda_{v}^{*}\right)} . \tag{33}
\end{equation*}
$$

Substituting Eq. (33) into the first term of Eq. (32), we have

$$
\begin{equation*}
\lambda_{m}^{*}=\frac{\psi \beta_{m}\left(\mu_{h}\left(Q+\lambda_{v}^{*}\right)+\gamma_{h} \lambda_{v}^{*}\right)}{\psi \beta_{m} Q(\mathcal{R}(\psi)-1)} \tag{34}
\end{equation*}
$$

$\mathcal{R}(\psi)>1$ is a necessary condition for $\lambda_{v}^{*}, \lambda_{h}^{*}$ and $\lambda_{m}^{*}$ to be simultaneously positive. The two Theorems below follow:

Theorem 3. If $\mathcal{R}(\psi) \leq 1$, there are no endemic equilibria.
Eq. (33) and Eq. (34) are substituted into the third term of Eq. (32) to show that the non-zero equilibria of the model satisfy a quadratic equation in terms of $\lambda_{v}^{*}$ :

$$
\begin{equation*}
a_{0}\left(\lambda_{v}^{*}\right)^{2}+b_{0} \lambda_{v}^{*}+c_{0}=0, \tag{35}
\end{equation*}
$$

where

$$
\begin{align*}
a_{0}= & \beta_{v} \beta_{h} C_{h v} \mu_{h} \Pi_{h}\left(\mu_{v}+\delta_{v}\right)\left(\mu_{h}+\gamma_{h}\right)\left(\psi \beta_{m} Q(\mathcal{R}(\psi)-1)+\beta_{v}\left(\mu_{v}+\delta_{v}+\psi\right)\left(\mu_{h}+\gamma_{h}\right)\right), \\
b_{0}= & \beta_{v} \beta_{h} C_{h v} \mu_{h}^{2} \Pi_{h} Q\left(\mu_{v}+\delta_{v}\right)\left(\psi \beta_{m} Q(\mathcal{R}(\psi)-1)+2 \beta_{v}\left(\mu_{v}+\delta_{v}+\psi\right)\left(\mu_{h}+\gamma_{h}\right)\right) \\
& -C_{h v} \Pi_{v} Q^{2} \mu_{h} \beta_{v} \psi \beta_{m}(\mathcal{R}(\psi)-1)\left(\psi \beta_{m} Q(\mathcal{R}(\psi)-1)+\psi \beta_{m} Q \mu_{h}\right), \\
c_{0}= & \beta_{v}^{3} \beta_{h}^{2} C_{h v}^{3} \mu_{h}^{4} Q \Pi_{v}\left(\frac{1}{R_{0}(\psi)}-1\right) . \tag{36}
\end{align*}
$$

Solving Eq. (35) for $\lambda_{v}^{*}$ and substituting positive values of $\lambda_{v}^{*}$ into Eq. (29) and Eq.(30) we obtain equilibria of system Eq. (6). There is no endemic equilibrium if $\mathcal{R}(\psi) \leq 1$.

Endemic equilibria exist if $\mathcal{R}(\psi)>1$. In this case, the coefficient $a_{0}$, of Eq. (35), is always positive, and $c_{0}$ is positive if $R_{0}(\psi)<1$ and negative if $R_{0}(\psi)>1 . \mathcal{R}(\psi)>$ $R_{0}(\psi)$ implies $R_{0}(\psi) \geq 1 \Rightarrow \mathcal{R}(\psi)>1$. The following result is established.

Theorem 4. (1) If $R_{0}(\psi)>1$, then there is a unique endemic equilibrium;
(2) If $R_{0}(\psi)=1$, then there is an unique endemic equilibrium where $\lambda_{v}^{*}=-\frac{b_{0}}{a_{0}}$ if $b_{0}<0$;
(3) If $R_{0}(\psi)<1$ and $\mathcal{R}(\psi)>1$, then there are two endemic equilibria where

$$
\begin{equation*}
\lambda_{v 1}^{*}=\frac{-b_{0}-\left(b_{0}^{2}-4 a_{0} c_{0}\right)^{1 / 2}}{2 a_{0}}, \quad \lambda_{v 2}^{*}=\frac{-b_{0}+\left(b_{0}^{2}-4 a_{0} c_{0}\right)^{1 / 2}}{2 a_{0}}, \tag{37}
\end{equation*}
$$

if $b_{0}^{2}-4 a_{0} c_{0}>0$ and $b_{0}<0$;
(4) There are no endemic equilibria otherwise.

Theorem 4 includes Theorem 3. From Theorem 4 (Case 1) it follows that the model has a unique endemic equilibrium whenever $R_{0}(\psi)>1$. Case 3 suggests that model Eq. (6) may have backward bifurcation. Backward bifurcation has been previously found in a number of models (Arion et al, 2003; Brauer, 2004; Castillo-Chavez and Song, 2004; Elbasha and Gumel, 2006; Sharomi et al, 2007; Kribs-Zaleta and Martcheva, 2002). To check for backward bifurcation, we set $b_{0}^{2}-4 a_{0} c_{0}=0$ and solve for the critical value of $R_{0}(\psi), R_{c}(\psi)$. The critical value is given by

$$
\begin{equation*}
R_{c}(\psi)=\frac{1}{\frac{b_{0}^{2}}{4 a_{0} \beta_{v}^{3} \beta_{h}^{2} C_{h v}^{3} \mu_{h}^{4} Q \Pi_{v}}+1}=\frac{\beta_{v} \beta_{h} C_{h v}^{2} \mu_{h} \Pi_{v}}{Q \Pi_{h}\left(\mu_{v}+\delta_{v}\right)\left(\mu_{v}+\delta_{v}+\psi\right)+\beta_{v} \beta_{h} C_{h v}^{2} \mu_{h} \Pi_{v}} \tag{38}
\end{equation*}
$$

Simple calculations give the following results:
Theorem 5. (1) $\mathcal{R}(\psi)<1$ if and only if $R_{0}(\psi)<R_{c}(\psi)$;
(2) $\mathcal{R}(\psi)>1$ if and only if $R_{0}(\psi)>R_{c}(\psi)$;
(3) $\mathcal{R}(\psi)=1$ if and only if $R_{0}(\psi)=R_{c}(\psi)$.
$\mathcal{R}(\psi)>1$ is equivalent to $R_{0}(\psi)>R_{c}(\psi)$ which is equivalent to $b_{0}^{2}-4 a_{0} c_{0}>0$, and the conditions of case 3 in Theorem 4 can be simplified. From Theorem 4 and Theorem

5 , backward bifurcation may occur under certain conditions for $R_{0}(\psi)$. In particular, we must have $R_{c}(\psi)<R_{0}(\psi)<1$, or if $R_{0}(\psi)<1$ and $\mathcal{R}(\psi)>1$. From the expression of $\mathcal{R}(\psi)$ we know that if vaccination is high enough, there is no backward bifurcation. The presence of backward bifurcation indicates that the classical requirement of $\boldsymbol{R}_{0}(\psi)<1$ although necessary, is not sufficient for disease elimination.

The Center Manifold theory will be used to improve the conditions on existence of backward bifurcation. To apply this method, the following simplification and change of variables are made: $S_{h}=x_{1}, I_{h}=x_{2}, R_{h}=x_{3}, V_{h}=x_{4}, S_{v}=x_{5}, I_{v}=x_{6}$, $M_{v}=x_{7} . N_{h}=x_{1}+x_{2}+x_{3}+x_{4}$ and $N_{v}=x_{5}+x_{6}+x_{7}$. By using the vector notation $X=\left(x_{1}, x_{2}, \cdots, x_{7}\right)^{T}$, the model Eq. (6) can be written in the form $d X / d t=F(X)$, with $F=\left(f_{1}, f_{2}, \cdots, f_{7}\right)^{T}$, as follows:

$$
\left\{\begin{align*}
x_{1}^{\prime}(t) & =f_{1}=\Pi_{h}-\lambda_{v}(t) x_{1}(t)-\lambda_{m}(t) x_{1}(t)-\mu_{h} x_{1}(t)  \tag{39}\\
x_{2}^{\prime}(t) & =f_{2}=\lambda_{v} x_{1}(t)-\left(\mu_{h}+\varepsilon_{h}+\gamma_{h}\right) x_{2}(t) \\
x_{3}^{\prime}(t) & =f_{3}=\gamma_{h} x_{2}(t)-\mu_{h} x_{3}(t) \\
x_{4}^{\prime}(t) & =f_{4}=\lambda_{m} x_{1}(t)-\mu_{h} x_{4}(t) \\
x_{5}^{\prime}(t) & =f_{5}=\Pi_{v}-\lambda_{h}(t) x_{5}(t)-\left(\mu_{v}+\delta_{v}+\psi\right) x_{5}(t), \\
x_{6}^{\prime}(t) & =f_{6}=\lambda_{h} x_{5}(t)-\left(\mu_{v}+\delta_{v}\right) x_{6}(t), \\
x_{7}^{\prime}(t) & =f_{7}=\psi x_{5}(t)-\left(\mu_{v}+\delta_{v}\right) x_{7}(t),
\end{align*}\right.
$$

with the forces of infection given by

$$
\begin{align*}
& \lambda_{v}(t)=\frac{\beta_{v} C_{h v} x_{6}(t)}{x_{1}(t)+x_{2}(t)+x_{3}(t)+x_{4}(t)}, \\
& \lambda_{m}(t)=\frac{\beta_{m} C_{h v} x_{7}(t)}{x_{1}(t)+x_{2}(t)+x_{3}(t)+x_{4}(t)},  \tag{40}\\
& \lambda_{h}(t)=\frac{\beta_{h} C_{h v} x_{2}(t)}{x_{1}(t)+x_{2}(t)+x_{3}(t)+x_{4}(t)} .
\end{align*}
$$

Solving for $\beta_{v}$ from $R_{0}(\psi)=1$, gives

$$
\begin{equation*}
\beta_{v}=\beta_{v}^{*}=\frac{Q\left(\Pi_{h}\left(\mu_{v}+\delta_{v}\right)\left(\mu_{v}+\delta_{v}+\psi\right)+\beta_{m} C_{h v} \psi \Pi_{v}\right)}{\beta_{h} C_{h v}^{2} \mu_{h} \Pi_{v}} . \tag{41}
\end{equation*}
$$

The Jacobian of the system Eq. (6), evaluated at the DFE $E_{0}$ with $\beta_{v}=\beta_{v}^{*}$ (denoted
by $\left.J^{*}\right)$, is
$J^{*}=\left|\begin{array}{ccccccc}-\left(\mu_{h}+K_{1}\right) & K_{2} & K_{2} & K_{2} & 0 & -K_{3} & -K_{4} \\ 0 & -Q & 0 & 0 & 0 & K_{3} & 0 \\ 0 & \gamma_{h} & -\mu_{h} & 0 & 0 & 0 & 0 \\ K_{1} & -K_{2} & -K_{2} & -\left(\mu_{h}+K_{2}\right) & 0 & 0 & K_{4} \\ 0 & -K_{5} & 0 & 0 & -\left(\mu_{v}+\delta_{v}+\psi\right) & 0 & 0 \\ 0 & K_{5} & 0 & 0 & 0 & -\left(\mu_{v}+\delta_{v}\right) & 0 \\ 0 & 0 & 0 & 0 & \psi & 0 & -\left(\mu_{v}+\delta_{v}\right)\end{array}\right|$,
where $K_{1}=\lambda_{m}^{0}\left(1-\frac{S_{h}^{0}}{N_{h}^{0}}\right), K_{2}=\lambda_{m}^{0} \frac{S_{h}^{0}}{N_{h}^{0}}, K_{3}=\frac{\beta_{v}^{*} C_{h v} S_{h}^{0}}{N_{h}^{0}}, K_{4}=\frac{\beta_{m} C_{h} S_{h}^{0}}{N_{h}^{0}}$, and $K_{5}=\frac{\beta_{h} C_{h v} S_{v}^{0}}{N_{h}^{0}}$.
It can be shown that if $R_{0}(\psi)=1$, the Jacobian $J^{*}$ has a simple zero eigenvalue with all other eigenvalues having negative real part. The Center Manifold Theory (Castillo-Chavez and Song, 2004; Carr, 1981) can be used to analyze the dynamics of the system Eq. (6). In particular, a theorem in (Castillo-Chavez and Song, 2004), will be applied.

Theorem 6. (Castillo-Chavez and Song, 2004) Consider the following general system of ordinary differential equations with a parameter $\phi$

$$
\begin{equation*}
\frac{d x}{d t}=f(x, \phi), \quad f: R^{n} \times R \rightarrow R, \quad \text { and } \quad f \in C^{2}\left(R^{n} \times R\right) \tag{43}
\end{equation*}
$$

Without loss of generality, it is assumed that 0 is an equilibrium for system Eq.(43) for all values of the parameter $\phi$, (that is $f(0, \phi) \equiv 0$ ). Assume

A1: $A=D_{x} f(0,0)=\left(\frac{\partial f_{i}}{\partial x_{j}}, 0,0\right)$ is the linearized matrix of system Eq.(43) around the equilibrium 0 with $\phi$ evaluated at 0 . Zero is a simple eigenvalue of $A$ and all other eigenvalues of $A$ have negative real parts;

A2: Matrix A has a nonnegative right eigenvector $w$ and a left eigenvector $v$ corresponding to the zero eigenvalue. Let $f_{k}$ be the $k$-th component of $f$ and

$$
\begin{align*}
a & =\sum_{k, i, j=1}^{n} v_{k} w_{i} w_{j} \frac{\partial^{2} f_{k}}{\partial x_{i} \partial x_{j}}(0,0) \\
b & =\sum_{k, j=1}^{n} v_{k} w_{i} \frac{\partial^{2} f_{k}}{\partial x_{i} \partial \phi}(0,0) \tag{44}
\end{align*}
$$

The local dynamics of system Eq. (43) around 0 are totally determined by $a$ and $b$.
(i) $a>0, b>0$. When $\phi<0$ with $|\phi| \ll 1,0$ is locally asymptotically stable and there exists a positive unstable equilibrium; when $0<\phi \ll 1,0$ is unstable and there exists a negative and locally asymptotically stable equilibrium.
(ii) $a<0, b<0$. When $\phi<0$ with $|\phi| \ll 1,0$ is unstable; when $0<\phi \ll 1,0$ is locally asymptotically stable, and there exists a positive unstable equilibrium;
(iii) $a>0, b<0$. When $\phi<0$ with $|\phi| \ll 1,0$ is unstable, and there exists $a$ locally asymptotically stable negative equilibrium; when $0<\phi \ll 1,0$ is stable, and a positive unstable equilibrium appears;
(iv) $a<0, b>0$. When $\phi$ changes from negative to positive, 0 changes its stability from stable to unstable. Correspondingly a negative unstable equilibrium becomes positive and locally asymptotically stable. Particularly, if $a>0$ and $b>0$, then a backward bifurcation occurs at $\phi=0$.
$J^{*}$ has a right eigenvector (corresponding to the zero eigenvalue), given by $w=$ $\left(w_{1}, w_{2}, \cdots, w_{7}\right)^{T}$, where,

$$
\begin{align*}
& w_{1}=\frac{K_{2}\left(w_{2}+w_{3}\right)-\left(\mu_{h}+K_{2}\right) w_{6}-K_{4} w_{7}}{\mu_{h}+K_{1}+K_{2}}, \quad w_{2}=w_{2}>0, \\
& w_{3}=\frac{\gamma_{h}}{\mu_{h}} w_{2}, \quad w_{4}=-\frac{K_{3}}{\mu_{h}} w_{6}-w_{1}, \quad w_{5}=\frac{-K_{5}}{\mu_{v}+\delta_{v}+\psi} w_{2},  \tag{45}\\
& w_{6}=\frac{K_{5}}{\mu_{v}+\delta_{v}} w_{2}, \quad w_{7}=\frac{\psi}{\mu_{v}+\delta_{v}} w_{5} .
\end{align*}
$$

Similarly, $J^{*}$ has a left eigenvector (corresponding to the zero eigenvalue), given by $v=\left(v_{1}, v_{2}, \cdots, v_{7}\right)^{T}$, where,

$$
\begin{array}{ll}
v_{1}=0, & v_{2}=v_{2}>0, \quad v_{3}=0, \quad v_{4}=0, \\
v_{5}=0, & v_{6}=\frac{Q}{K_{5}} v_{2}, \quad v_{7}=0 . \tag{46}
\end{array}
$$

For the model Eq. (6), the associated non-zero partial derivatives of the right-hand
side functions, $f_{i}, i=1,2, \cdots, 7$, are given by

$$
\begin{align*}
& \frac{\partial^{2} f_{2}}{\partial x_{1} \partial x_{6}}=2\left(\frac{\beta_{v}^{*} C_{h v} \mu_{h}}{\Pi_{h}}-\frac{\beta_{v}^{*} C_{h v} \mu_{h}^{2} S_{h}^{0}}{\Pi_{h}^{2}}\right), \\
& \frac{\partial^{2} f_{2}}{\partial x_{2} \partial x_{6}}=\frac{\partial^{2} f_{2}}{\partial x_{3} \partial x_{6}}=\frac{\partial^{2} f_{2}}{\partial x_{4} \partial x_{6}}=-2 \frac{\beta_{v}^{*} C_{h v} \mu_{h}^{2} S_{h}^{0}}{\Pi_{h}^{2}}, \\
& \frac{\partial^{2} f_{6}}{\partial x_{1} \partial x_{2}}=\frac{\partial^{2} f_{6}}{\partial x_{2} \partial x_{3}}=\frac{\partial^{2} f_{6}}{\partial x_{2} \partial x_{4}}=-2 \frac{\beta_{h} C_{h v} \mu_{h}^{2} S_{v}^{0}}{\Pi_{h}^{2}},  \tag{47}\\
& \frac{\partial^{2} f_{6}}{\partial x_{2}^{2}}=-2 \frac{\beta_{h} C_{h v} \mu_{h}^{2} S_{v}^{0}}{\Pi_{h}^{2}}, \quad \frac{\partial^{2} f_{2}}{\partial x_{2} \partial x_{5}}=2 \frac{\beta_{h} C_{h v} \mu_{h}}{\Pi_{h}}, \\
& \frac{\partial^{2} f_{2}}{\partial x_{6} \partial \beta_{v}^{*}}=\frac{C_{h v} \mu_{h} S_{h}^{0}}{\Pi_{h}} .
\end{align*}
$$

Substituting Eq. (45)-Eq. (47) into Eq. (44), it follows that

$$
\begin{align*}
a= & 2 v_{2} w_{2} Q\left[\frac{1}{S_{h}^{0}} w_{1}+\frac{1}{S_{v}^{0}} w_{5}-\frac{2 \mu_{h}}{\Pi_{h}}\left(w_{1}+w_{2}+w_{3}+w_{4}\right)\right] \\
= & \frac{2 Q v_{2} w_{2}^{2}}{\Pi_{h}}\left[\left(K_{2}-2 \mu_{h}\right)\left(1+\frac{\gamma_{h}}{\mu_{h}}\right)+\frac{K_{5}}{\mu_{v}+\delta_{v}}\left(2 K_{3}-\mu_{h}-K_{2}\right)\right.  \tag{48}\\
& \left.+\frac{\psi K_{4} K_{5}}{\left(\mu_{v}+\delta_{v}\right)\left(\mu_{v}+\delta_{v}+\psi\right)}-\frac{\Pi_{h} K_{5}}{\Pi_{v}}\right],
\end{align*}
$$

and

$$
\begin{equation*}
b=v_{2} w_{2} \frac{K_{5}}{\mu_{v}+\delta_{v}} \frac{C_{h v} \mu_{h} S_{h}^{0}}{\Pi_{h}}>0 . \tag{49}
\end{equation*}
$$

The coefficient $b$ is always positive. Theorem 6 implies that the model Eq. (6) will undergo backward bifurcation at $R_{0}(\psi)=1$ if $a>0$.

In order to reveal the mechanism of backward bifurcation more clearly, we further analyze the condition $a>0$. From the expression of $a, K_{2}, K_{3}, K_{4}$ it follows that

$$
\begin{align*}
& K_{2}-2 \mu=\frac{\mu_{h}}{\mu_{h}+\lambda_{m}^{0}}\left[-\lambda_{m}^{0}-2 \mu\right], \\
& 2 K_{3}-\mu_{h}-K_{2}=\frac{\mu_{h}}{\mu_{h}+\lambda_{m}^{0}}\left[2 \beta_{v}^{*} C_{h v}-2 \lambda_{m}^{0}-\mu_{h}\right],  \tag{50}\\
& \quad \frac{\psi K_{4}}{\left(\mu_{v}+\delta_{v}\right)\left(\mu_{v}+\delta_{v}+\psi\right)}-\frac{\Pi_{h}}{\Pi_{v}}=-\frac{\Pi_{h}}{\Pi_{v}} \cdot \frac{\mu_{h}}{\mu_{h}+\lambda_{m}^{0}} .
\end{align*}
$$

$a>0$ implies that

$$
\begin{equation*}
-\left(\lambda_{m}^{0}+2 \mu_{h}\right) \frac{\mu_{h}+\gamma_{h}}{\mu_{h}}+\frac{K_{5}}{\mu_{v}+\delta_{v}}\left(2 C_{h v} \beta_{v}^{*}-2 \lambda_{m}^{0}-\mu_{h}\right)-\frac{\Pi_{h}}{\Pi_{v}} K_{5}>0 . \tag{51}
\end{equation*}
$$

$\beta_{v}^{*}$ can be rewritten as

$$
\begin{equation*}
\beta_{v}^{*}=\frac{Q\left(\mu_{v}+\delta_{v}\right)}{K_{5} C_{h v}}+\frac{Q \lambda_{m}^{0}\left(\mu_{v}+\delta_{v}\right)}{K_{5} \mu_{h} C_{h v}}, \tag{52}
\end{equation*}
$$

Substituting Eq. (52) into Eq. (51), backward bifurcation occurs if and only if:

$$
\begin{equation*}
\frac{\mu_{h}+\gamma_{h}}{\mu_{h}} \lambda_{m}^{0}+\frac{2 \varepsilon_{h}}{\mu_{h}} \lambda_{m}^{0}+2 \varepsilon_{h}-\left(\frac{\mu_{h}}{\mu_{v}+\delta_{v}}+\frac{\Pi_{h}}{\Pi_{v}}+\frac{2 \lambda_{m}^{0}}{\mu_{v}+\delta_{v}}\right) K_{5}>0 . \tag{53}
\end{equation*}
$$

If $K_{5}$ is small enough, the above inequality will hold. The expression of $K_{5}$ shows that $K_{5}$ is small if $\beta_{h}$ is small. Since $\beta_{h}$ is not a part of the first three terms in Eq. (53), making $\beta_{h}$ small enough will allow for Eq. (53) to hold. Backward bifurcation will occur if the probability of transmission from infected human to mosquitoes is sufficiently small. Eq. (53) also reveals other mechanisms necessary for backward bifurcation. In particular, vaccine delivery from the flying vaccinators $\lambda_{m}^{0}>0$ (or $\beta_{m}>0$ ) and disease-induced mortality $\varepsilon_{h}>0$ are each necessary for backward bifurcation.

## 3 Model with mass action incidence

In this section we introduce a variant of model Eq. (6) with mass action incidence. The model with mass action incidence does not exhibit backward bifurcation.

### 3.1 Model formulation and existence of steady states

The standard incidence in Eq. (6) is replaced with mass action incidence. The associated forces of infection, $\lambda_{v}, \lambda_{m}, \lambda_{h}$, in Eq. (3), Eq. (4) and Eq. (5) respectively, become

$$
\begin{equation*}
\lambda_{v}(t)=\beta_{v} C_{h v} I_{v}(t), \quad \lambda_{m}(t)=\beta_{m} C_{h v} M_{v}(t), \quad \lambda_{h}(t)=\beta_{h} C_{h v} I_{h}(t) . \tag{56}
\end{equation*}
$$

We consider the model

$$
\left\{\begin{array}{l}
S_{h}^{\prime}(t)=\Pi_{h}-\left(\lambda_{v}(t)+\lambda_{m}(t)+\mu_{h}\right) S_{h}(t)  \tag{55}\\
I_{h}^{\prime}(t)=\lambda_{v}(t) S_{h}(t)-\left(\mu_{h}+\varepsilon_{h}+\gamma_{h}\right) I_{h}(t) \\
R_{h}^{\prime}(t)=\gamma_{h} I_{h}(t)-\mu_{h} R_{h}(t) \\
V_{h}^{\prime}(t)=\lambda_{m}(t) S_{h}(t)-\mu_{h} V_{h}(t) \\
S_{v}^{\prime}(t)=\Pi_{v}-\lambda_{h}(t) S_{v}(t)-\left(\mu_{v}+\delta_{v}+\psi\right) S_{v}(t) \\
I_{v}^{\prime}(t)=\lambda_{h}(t) S_{v}(t)-\left(\mu_{v}+\delta_{v}\right) I_{v}(t) \\
M_{v}^{\prime}(t)=\psi S_{v}(t)-\left(\mu_{v}+\delta_{v}\right) M_{v}(t)
\end{array}\right.
$$

with the forces of infection given by Eq. (56) Similarly to Theorem 1, we can prove that the closed set
$\mathcal{D}=\left\{\left(S_{h}, I_{h}, R_{h}, V_{h}, S_{v}, I_{v}, M_{v}\right) \in R_{7}^{+} \left\lvert\, S_{h}+I_{h}+R_{h}+V_{h} \leq \frac{\Pi_{h}}{\mu_{h}}\right. ; S_{v}+I_{v}+M_{v} \leq \frac{\Pi_{v}}{\mu_{v}+\delta_{v}}\right\}$, is positively invariant and attracting with respect to the model Eq. (55). We restrict the analysis of system Eq. (55) to the region $\mathcal{D}$.

Eq. (55) has always the DFE

$$
\begin{equation*}
E_{0}^{m}\left(\widehat{S}_{h}^{0}, 0,0, \widehat{V}_{h}^{0}, \widehat{S}_{v}^{0}, 0, \widehat{M}_{v}^{0}\right) \tag{56}
\end{equation*}
$$

where

$$
\begin{align*}
& \widehat{S}_{v}^{0}=\frac{\Pi_{v}}{\mu_{v}+\delta_{v}+\psi}, \quad \widehat{M}_{v}^{0}=\frac{\psi}{\mu_{v}+\delta_{v}} \widehat{S}_{v}^{0}, \\
& \widehat{\lambda}_{m}^{0}=\beta_{m} C_{h v} \widehat{M}_{v}^{0}, \quad \widehat{S}_{h}^{0}=\frac{\Pi_{h}}{\mu_{h}+\widehat{\lambda}_{m}^{0}}, \quad \widehat{V}_{h}^{0}=\frac{\widehat{\lambda}_{m}^{0} \widehat{S}_{h}^{0}}{\mu_{h}} . \tag{57}
\end{align*}
$$

Now we use the next generation approach to calculate the basic reproduction number:

$$
F_{m}=\left(\begin{array}{cc}
0 & \beta_{v} C_{h v} \widehat{S}_{h}^{0}  \tag{58}\\
\beta_{h} C_{h v} \widehat{S}_{v}^{0} & 0
\end{array}\right), \quad V_{m}=\left(\begin{array}{cc}
Q & 0 \\
0 & \mu_{v}+\delta_{v}
\end{array}\right),
$$

where $Q=\mu_{h}+\varepsilon_{h}+\gamma_{h}$. The basic reproduction number for model Eq. (55) is

$$
\begin{equation*}
\widetilde{R}_{0}^{m}(\psi)=\rho\left(F_{m} V_{m}^{-1}\right)=\left(\frac{\beta_{v} \beta_{h} C_{h v}^{2} \Pi_{h} \Pi_{v}}{Q\left(\mu_{h}\left(\mu_{v}+\delta_{v}\right)\left(\mu_{v}+\delta_{v}+\psi\right)+\beta_{m} C_{h v} \psi \Pi_{v}\right)}\right)^{\frac{1}{2}} \tag{59}
\end{equation*}
$$

where $\rho$ denotes the spectral radius. To be consistent with the model in section 2 , we redefine the basic reproduction number

$$
\begin{equation*}
R_{0}^{m}(\psi)=\left(\widetilde{R}_{0}^{m}(\psi)\right)^{2}=\frac{\beta_{v} \beta_{h} C_{h v}^{2} \Pi_{h} \Pi_{v}}{Q\left(\mu_{h}\left(\mu_{v}+\delta_{v}\right)\left(\mu_{v}+\delta_{v}+\psi\right)+\beta_{m} C_{h v} \psi \Pi_{v}\right)} . \tag{60}
\end{equation*}
$$

Endemic equilibria of the model Eq. (55), are obtained by assuming one of the infected components of the model is non-zero. $\widehat{E}^{*}\left(\widehat{S}_{h}^{*}, \widehat{I}_{h}^{*}, \widehat{R}_{h}^{*}, \widehat{V}_{h}^{*}, \widehat{S}_{v}^{*}, \widehat{I}_{v}^{*}, \widehat{M}_{v}^{*}\right)$ represents any endemic equilibrium of the model Eq. (55). Solving the resulting algebraic equations, we have

$$
\begin{align*}
& \widehat{S}_{h}^{*}=\frac{\Pi_{h}}{\mu_{h}+\widehat{\lambda}_{v}^{*}+\widehat{\lambda}_{m}^{*}}, \\
& \widehat{I}_{h}^{*}=\frac{\widehat{\lambda}_{v}^{*} \widehat{S}_{h}^{*}}{Q}=\frac{\widehat{\lambda}_{v}^{*} \Pi_{h}}{Q\left(\mu_{h}+\widehat{\lambda}_{v}^{*}+\widehat{\lambda}_{m}^{*}\right)}, \\
& \widehat{R}_{h}^{*}=\frac{\gamma_{h} \widehat{I}_{h}^{*}}{\mu_{h}}=\frac{\gamma_{h} \widehat{\lambda}_{v}^{*} \Pi_{h}}{\mu_{h} Q\left(\mu_{h}+\widehat{\lambda}_{v}^{*}+\widehat{\lambda}_{m}^{*}\right)}, \\
& \widehat{V}_{h}^{*}=\frac{\widehat{\lambda}_{m}^{*} \widehat{S}_{h}^{*}}{\mu_{h}}=\frac{\widehat{\lambda}_{m}^{*} \Pi_{h}}{\mu_{h}\left(\mu_{h}+\widehat{\lambda}_{v}^{*}+\widehat{\lambda}_{m}^{*}\right)},  \tag{61}\\
& \widehat{S}_{v}^{*}=\frac{\Pi_{v}}{\mu_{v}+\delta_{v}+\psi+\widehat{\lambda}_{h}^{*}}, \quad \\
& \widehat{I}_{v}^{*}=\frac{\widehat{\lambda}_{h}^{*} \widehat{S}_{v}^{*}}{\mu_{v}+\delta_{v}}=\frac{\widehat{\lambda}_{h}^{*} \Pi_{v}}{\left(\mu_{v}+\delta_{v}\right)\left(\mu_{v}+\delta_{v}+\psi+\widehat{\lambda}_{h}^{*}\right)}, \\
& \widehat{M}_{v}^{*}=\frac{\psi \widehat{S}_{v}^{*}}{\mu_{v}+\delta_{v}}=\frac{\psi \Pi_{v}}{\left(\mu_{v}+\delta_{v}\right)\left(\mu_{v}+\delta_{v}+\psi+\widehat{\lambda}_{h}^{*}\right)},
\end{align*}
$$

where

$$
\begin{equation*}
\widehat{\lambda}_{v}^{*}=\beta_{v} C_{h v} \widehat{I}_{v}^{*}, \quad \widehat{\lambda}_{m}^{*}=\beta_{m} C_{h v} \widehat{M}_{v}^{*}, \quad \widehat{\lambda}_{h}^{*}=\beta_{h} C_{h v} \widehat{I}_{h}^{*} . \tag{62}
\end{equation*}
$$

Substituting Eq. (61) into Eq. (62), and simplifying:

$$
\begin{align*}
& \widehat{\lambda}_{m}^{*}=\frac{\beta_{m} \psi}{\beta_{v} \widehat{\lambda}_{h}^{*}} \widehat{\lambda}_{v}^{*} \\
& \widehat{\lambda}_{h}^{*}=\frac{\beta_{h} C_{h v} \Pi_{h} \widehat{\lambda}_{v}^{*}}{Q\left(\mu_{h}+\widehat{\lambda}_{v}^{*}+\widehat{\lambda}_{m}^{*}\right)}  \tag{63}\\
& \widehat{\lambda}_{v}^{*}=\frac{\beta_{v} C_{h v} \Pi_{v} \widehat{\lambda}_{h}^{*}}{\left(\mu_{v}+\delta_{v}\right)\left(\mu_{v}+\delta_{v}+\psi+\widehat{\lambda}_{h}^{*}\right)} .
\end{align*}
$$

Plugging the fist term of Eq. (63) into the second term, we get

$$
\begin{equation*}
\widehat{\lambda}_{h}^{*}=\frac{\psi \beta_{m} Q \widehat{\lambda}_{v}^{*}\left(\mathcal{R}_{m}(\psi)-1\right)}{\beta_{v} Q\left(\mu_{h}+\lambda_{v}^{*}\right)} \tag{64}
\end{equation*}
$$

where $\mathcal{R}_{m}(\psi)=\frac{\beta_{v} \beta_{h} C_{h} \Pi_{h}}{\beta_{m} \psi Q} . \mathcal{R}_{m}(\psi)>1$ is a necessary condition for $\widehat{\lambda}_{v}^{*}$ and $\widehat{\lambda}_{h}^{*}$ to be simultaneously positive.

By substituting Eq. (64) into the third term of Eq. (63), it can be shown that the non-zero equilibria of the model Eq. (55) satisfy the following equation (in terms of $\left.\lambda_{v}^{*}\right)$

$$
\begin{equation*}
b_{1} \widehat{\lambda}_{v}^{*}+c_{1}=0, \tag{65}
\end{equation*}
$$

where

$$
\begin{align*}
& b_{1}=Q\left(\mu_{v}+\delta_{v}\right)\left[\beta_{m} \psi\left(\mathcal{R}_{m}(\psi)-1\right)+\beta_{v}\left(\mu_{v}+\delta_{v}+\psi\right)\right], \\
& c_{1}=\beta_{v} Q\left[\mu_{h}\left(\mu_{v}+\delta_{v}\right)\left(\mu_{v}+\delta_{v}+\psi\right)+\beta_{m} \psi C_{h v} \Pi_{v}\right]\left(1-R_{0}^{m}(\psi)\right) . \tag{66}
\end{align*}
$$

Positive endemic equilibria of the model Eq. (55) are obtained by solving for $\lambda_{v}^{*}$ equation Eq. (65) and substituting the positive values of $\lambda_{v}^{*}$ into the expressions Eq. (61) and Eq. (62). There is no endemic equilibrium if $\mathcal{R}_{m}(\psi) \leq 1$. If $\mathcal{R}_{m}(\psi)>1$, the coefficient $b_{1}$, of Eq. (65), is always positive, and $c_{1}$ is positive if $R_{0}^{m}(\psi)<1$ and negative if $R_{0}^{m}(\psi)>1$. In addition, $\mathcal{R}_{m}(\psi)>R_{0}^{m}(\psi) . R_{0}^{m}(\psi) \geq 1 \Rightarrow \mathcal{R}_{m}(\psi)>1$. The following result is established.

Theorem 7. (1) If $R_{0}^{m}(\psi)>1$, then there is a unique endemic equilibrium;
(2) If $R_{0}^{m}(\psi) \leq 1$, then there are no endemic equilibria.

### 3.2 Stability analysis

We consider the disease-free equilibrium.
Theorem 8. If $R_{0}^{m}(\psi)<1$, then the DFE $\widehat{E}_{0}$ is locally asymptotically stable (LAS); if $R_{0}^{m}(\psi)>1$, then $\widehat{E}_{0}$ is unstable.
Proof. Linearizing system Eq. (55) at the point $\widehat{E}_{0}$, we obtain the following charac-
teristic equation

$$
\left|\begin{array}{ccccccc}
\lambda+\mu_{h}+\widehat{\lambda}_{m}^{0} & 0 & 0 & 0 & 0 & \beta_{v} C_{h} \widehat{S}_{h}^{0} & \beta_{m} C_{h v} \widehat{S}_{h}^{0}  \tag{67}\\
0 & \lambda+Q & 0 & 0 & 0 & -\beta_{v} C_{h v} \widehat{S}_{h}^{0} & 0 \\
0 & -\gamma_{h} & \lambda+\mu_{h} & 0 & 0 & 0 & 0 \\
-\widehat{\lambda}_{m}^{0} & 0 & 0 & \lambda+\mu_{h} & 0 & 0 & -\beta_{m} C_{h v} \widehat{S}_{h}^{0} \\
0 & \beta_{h} C_{h v} \widehat{S}_{v}^{0} & 0 & 0 & \lambda+Q_{1} & 0 & 0 \\
0 & -\beta_{h} C_{h} \widehat{S}_{v}^{0} & 0 & 0 & 0 & \lambda+\mu_{v}+\delta_{v} & 0 \\
0 & 0 & 0 & 0 & -\psi & 0 & \lambda+\mu_{v}+\delta_{v}
\end{array}\right|=0,
$$

where $Q_{1}=\mu_{v}+\delta_{v}+\psi$. Manipulating the determinant, we obtain the following eigenvalues:

$$
\begin{equation*}
\lambda_{1}=\lambda_{2}=-\mu_{h}, \quad \lambda_{3}=-\left(\mu_{h}+\widehat{\lambda}_{m}^{0}\right), \quad \lambda_{4}=-\left(\mu_{v}+\delta_{v}\right), \quad \lambda_{5}=-Q_{1} . \tag{68}
\end{equation*}
$$

The remaining two eigenvalues $\lambda_{6}$ and $\lambda_{7}$ satisfy:

$$
\begin{equation*}
\lambda^{2}+\left(Q+\mu_{v}+\delta_{v}\right) \lambda+Q\left(\mu_{v}+\delta_{v}\right)-\beta_{v} C_{h v} \widehat{S}_{h}^{0} \beta_{h} C_{h v} \widehat{S}_{v}^{0}=0 . \tag{69}
\end{equation*}
$$

Since $Q\left(\mu_{v}+\delta_{v}\right)-\beta_{v} C_{h v} \widehat{S}_{h}^{0} \beta_{h} C_{h v} \widehat{S}_{v}^{0}=Q\left(\mu_{v}+\delta_{v}\right)\left(1-R_{0}^{m}(\psi)\right)$, we have

$$
\begin{equation*}
\lambda_{6}+\lambda_{7}=-\left(Q+\mu_{v}+\delta_{v}\right), \quad \lambda_{6} \lambda_{7}=Q\left(\mu_{v}+\delta_{v}\right)\left(1-R_{0}^{m}(\psi)\right) . \tag{70}
\end{equation*}
$$

If $R_{0}^{m}(\psi)<1$, both $\lambda_{6}$ and $\lambda_{7}$ have negative real parts, which implies that $\widehat{E}_{0}$ is locally asymptotically stable; if $R_{0}^{m}(\psi)>1$, there is a positive eigenvalue, which indicates that $\widehat{E}_{0}$ is unstable.

Theorem 9. If $R_{0}^{m}(0)<1$, the DFE $\widehat{E}_{0}$ is globally asymptotically stable (GAS).
Proof. Since

$$
\begin{equation*}
\frac{d S_{v}(t)}{d t}=\Pi_{v}-\lambda_{h} S_{v}-\left(\mu_{v}+\delta_{v}+\psi\right) S_{v} \leq \Pi_{v}-\left(\mu_{v}+\delta_{v}+\psi\right) S_{v} \tag{71}
\end{equation*}
$$

Hence, $S_{v}(t) \leq \frac{\Pi_{v}}{\mu_{v}+\delta_{v}+\psi}=\widehat{S}_{v}^{0}$. Similarly,

$$
\begin{equation*}
\frac{d S_{h}(t)}{d t}=\Pi_{h}-\lambda_{v} S_{h}-\lambda_{m} S_{h}-\mu_{h} S_{h} \leq \Pi_{h}-\mu_{h} S_{h} \tag{72}
\end{equation*}
$$

Hence, $S_{h}(t) \leq \frac{\Pi_{h}}{\mu_{h}}$.
We choose a Lyapunov function

$$
\begin{equation*}
L=\left(\mu_{v}+\delta_{v}\right) I_{h}+\beta_{v} C_{h v} \frac{\Pi_{h}}{\mu_{h}} I_{v} . \tag{73}
\end{equation*}
$$

Differentiating the Lyapunov function with respect to $t$, we obtain:

$$
\begin{align*}
L^{\prime} & =\left(\mu_{v}+\delta_{v}\right) I_{h}^{\prime}+\beta_{v} C_{h v} \frac{\Pi_{h}}{\mu_{h}} I_{v}^{\prime} \\
& =\left(\mu_{v}+\delta_{v}\right)\left(\lambda_{v} S_{h}-Q I_{h}\right)+\frac{\Pi_{h}}{\mu_{h}}\left[\lambda_{h} S_{v}-\left(\mu_{v}+\delta_{v}\right) I_{v}\right]  \tag{74}\\
& \leq\left[\beta_{h} \beta_{v} C_{h v}^{2} \frac{\Pi_{h}}{\mu_{h}} \widehat{S}_{v}^{0}-\left(\mu_{v}+\delta_{v}\right) Q\right] I_{h} \\
& =\left(\mu_{v}+\delta_{v}\right) Q\left(R_{0}^{m}(0)-1\right) I_{h} .
\end{align*}
$$

$L^{\prime} \leq 0$ if $R_{0}^{m}(0)<1$. $L^{\prime}=0$ if and only if $I_{h}=0$. So the DFE $\widehat{E}_{0}$ is globally attracting if $R_{0}^{m}(\psi)<1$. Together with Theorem 7, we can conclude that the DFE $\widehat{E}_{0}$ is globally asymptotically stable if $R_{0}^{m}(\psi)<1$.

Theorem 10. If $R_{0}^{m}(\psi)>1$, then the endemic equilibrium is locally asymptotically stable (LAS).

Proof. Linearizing system Eq. (55) at the point $\widehat{E}^{*}$, we get the characteristic equation

$$
\left|\begin{array}{ccccccc}
\lambda+Q_{2} & 0 & 0 & 0 & 0 & \beta_{v} C_{h v} \widehat{S}_{h}^{*} & \beta_{m} C_{h v} \widehat{S}_{h}^{*}  \tag{75}\\
-\widehat{\lambda}_{v}^{*} & \lambda+Q & 0 & 0 & 0 & -\beta_{v} C_{h v} \widehat{S}_{h}^{*} & 0 \\
0 & -\gamma_{h} & \lambda+\mu_{h} & 0 & 0 & 0 & 0 \\
-\widehat{\lambda}_{m}^{*} & 0 & 0 & \lambda+\mu_{h} & 0 & 0 & -\beta_{m} C_{h v} \widehat{S}_{h}^{*} \\
0 & \beta_{h} C_{h v} \widehat{S}_{v}^{*} & 0 & 0 & \lambda+Q_{3} & 0 & 0 \\
0 & -\beta_{h} C_{h v} \widehat{S}_{v}^{*} & 0 & 0 & \widehat{\lambda}_{h}^{*} & \lambda+\mu_{v}+\delta_{v} & 0 \\
0 & 0 & 0 & 0 & -\psi & 0 & \lambda+\mu_{v}+\delta_{v}
\end{array}\right|=0
$$

where $Q_{2}=\mu_{h}+\widehat{\lambda}_{v}^{*}+\widehat{\lambda}_{m}^{*}$ and $Q_{3}=\mu_{v}+\delta_{v}+\psi+\widehat{\lambda}_{h}^{*}$. Manipulating the determinant, we obtain the following eigenvalues:

$$
\begin{equation*}
\lambda_{1}=\lambda_{2}=-\mu_{h}, \quad \lambda_{3}=-\left(\mu_{v}+\delta_{v}\right) . \tag{76}
\end{equation*}
$$

The remaining eigenvalues satisfy

$$
\begin{equation*}
\left(\lambda+Q_{2}\right)\left(\lambda+\mu_{v}+\delta_{v}\right)\left(\lambda+Q_{3}\right)(\lambda+Q)-\beta_{m} \beta_{h} \psi C_{h v}^{2} \widehat{S}_{h}^{*} \widehat{S}_{v}^{*} \widehat{\lambda}_{v}^{*}=0 \tag{77}
\end{equation*}
$$

Let

$$
\begin{align*}
& A=Q_{2}=\mu_{h}+\widehat{\lambda}_{v}^{*}+\widehat{\lambda}_{m}^{*}, \quad B=\mu_{v}+\delta_{v}, \quad C=Q_{3}=\mu_{v}+\delta_{v}+\psi+\widehat{\lambda}_{h}^{*}, \\
& D=Q, \quad E=\beta_{m} \beta_{h} \psi C_{h v}^{2} \widehat{S}_{h}^{*} \widehat{S}_{v}^{*} \widehat{\lambda}_{v}^{*}=\widehat{\lambda}_{m}^{*} \widehat{\lambda}_{h}^{*} Q\left(\mu_{v}+\delta_{v}\right) . \tag{78}
\end{align*}
$$

Eq. (77) can be rewritten as

$$
\begin{equation*}
\left(\lambda+Q_{2}\right)\left(\lambda+\mu_{v}+\delta_{v}\right)\left(\lambda+Q_{3}\right)(\lambda+Q)=\beta_{m} \beta_{h} \psi C_{h v}^{2} \widehat{S}_{h}^{*} \widehat{S}_{v}^{*} \widehat{\lambda}_{v}^{*} . \tag{79}
\end{equation*}
$$

Taking absolute value of both sides of the above equation, for $\lambda$ with $\Re \lambda \geq 0$ we have

$$
\begin{align*}
& \left|\left(\lambda+Q_{2}\right)\left(\lambda+\mu_{v}+\delta_{v}\right)\left(\lambda+Q_{3}\right)(\lambda+Q)\right| \\
& =\left|\left(\lambda+Q_{2}\right)\right|\left|\left(\lambda+\mu_{v}+\delta_{v}\right)\right|\left|\left(\lambda+Q_{3}\right)\right||(\lambda+Q)| \\
& >Q_{2}\left(\mu_{v}+\delta_{v}\right) Q_{3} Q \geq \widehat{\lambda}_{v}^{*} \widehat{\lambda}_{h}^{*} Q\left(\mu_{v}+\delta_{v}\right)  \tag{80}\\
& =\beta_{m} \beta_{h} \psi C_{h v}^{2} \widehat{S}_{h}^{*} \widehat{S}_{v}^{*} \widehat{\lambda}_{v}^{*} .
\end{align*}
$$

We conclude that equation Eq. (77) cannot have roots with non-negative real parts. The endemic equilibrium is locally asymptotically stable if $R_{0}^{m}(\psi)>1$.

## 4 Numerical simulations

In this section, numerical simulations are used to explore the behavior of the system Eq. (6) and the impact of different measures. The time unit is year ${ }^{-1}$. The average lifespan of human is assumed to be 70 years. The natural death rate of human is $\mu_{h}=\frac{1}{70} \approx 0.015$. The lifespan of a female mosquito is assumed to be three to 100 days. We take it as 60 days (that is, $\frac{1}{\mu_{v}}=\frac{1}{6}$ ). Non-treated malaria sufferers recover after 8 months, $\frac{1}{\gamma_{h}}=\frac{2}{3}$. In our numerical explorations we use $\beta_{h}=0.75, \beta_{m}=0.6, \beta_{v}=0.6$, disease-induced death rate for humans $\varepsilon_{h}=0.2$, and recruitment rate of mosquitoes $\Pi_{v}=100000$. Significant differences between the birth rate and immigration rate in different regions suggest a range of $\Pi_{h}$ between 50 and 1200 . Due to the differences in the kind and the dosage of pesticides, we assume $\delta_{v}$ varies between 5 to $100 . C_{h v}$ is also assumed to vary between 10 to 800 . The variability of $C_{h v}$ results from the different climates in different areas and the difference in the use of mosquito nets. In addition we take the vaccination rate for mosquitoes $\psi$ to vary between 0 and 1 .

In the first simulation we take $\Pi_{h}=100, \delta_{v}=10, C_{h v}=100, \psi=0.85$. That gives a value of $R_{0}$ of $R_{0} \approx 0.8965<1$, and $\mathcal{R} \approx 0.9004<1$. In this case only the disease-free equilibrium exists and it is stable. In Fig. 2 and Fig. 3 we can see that both $I_{h}$ and $I_{v}$ tend to 0 under different initial conditions

In the next simulation we take $\Pi_{h}=1000, \delta_{v}=10, C_{h v}=100, \psi=0.3$, and compute the expression of $R_{0}$. We have $R_{0} \approx 2.228>1$. So there exists a unique endemic equilibrium. In Fig. 4 and Fig. 5 we can see that both $I_{h}$ and $I_{v}$ tend to a constant and that this unique endemic equilibrium is stable.

Next, we explore the impact of different measures on the transmission and control of malaria. $i_{h}=\frac{I_{h}}{N_{h}}, v_{h}=\frac{V_{h}}{N_{h}}$, that is, $i_{h}$ and $v_{h}$ are the proportion of infected human individuals and vaccinated human individuals in the total population. We set the initial conditions as $S_{h}(0)=4000, I_{h}(0)=3000, R_{h}(0)=1000, V_{h}(0)=2000, S_{v}(0)=4600$, $I_{v}(0)=1200, M_{v}(0)=2500, i_{h}(0)=0.3, v_{h}(0)=0.2$. Firstly we study the impact on $i_{h}$ and $v_{h}$ of different vaccination rates $\psi$. Figure 6 shows that in the next 25 years, $v_{h}$ increases with the increase of $\psi$, namely, the larger the vaccination rate of mosquitoes, the bigger the proportion of vaccinated individuals in total human population. Figure 7 shows that $i_{h}$ decreases with the increase of $\psi$, namely, the larger the vaccination rate of mosquitoes, the smaller the proportion of infected individuals in total human population.

We consider the impact of mosquito nets use on $i_{h}$ and $v_{h}$. The use of nets corresponds to reduction of the per capita biting rate of mosquitoes on a host $C_{h v}$. Figure 8 shows that, increasing the biting rate initially, increases the proportion of the vaccinated individuals for small period of time, however, it seems that this positive effect of vaccination does not persist long-term. The interesting behavior occurs since all the three forces of infection $\lambda_{v}, \lambda_{m}, \lambda_{h}$ are nonlinear functions with respect to the biting rate $C_{h v}$. Figure 9 indicates that $i_{h}$ initially increases with the increase of $C_{h v}$ but in the long run $i_{h}$ tends to a stable state which is lower with the increase of $C_{h v}$.

Finally, we analyze the impact of pesticide use on $i_{h}$ and $v_{h}$. The pesticide use impacts the mosquito pesticide-induced death rate $\delta_{v}$. Figure 10 shows that in the next 15 years, $v_{h}$ decreases with the increase of the use of pesticides. For the values of $\delta_{v}$ investigated, $v_{h}$ decreases in the early years, and increases in the later years. Figure 11 shows that $i_{h}$ decreases with the increase of $\delta_{v}$.

The variation of $R_{0}$ and $\mathcal{R}$ in terms of some parameters are represented in Figure 12 to Figure 14. These figures show that the impact on $R_{0}$ and $\mathcal{R}$ is different for the different parameters. In particular, $R_{0}$ and $\mathcal{R}$ increase with the increase of $C_{h v}$, and with the decrease of $\psi, \beta_{m}, \delta_{v}$ or $\Pi_{h}$. The impact by $\psi$ is most notable which may suggest that vaccination is the most effective measure.

## 5 Conclusion

We investigate two transmission models of malaria with mosquitoes used to deliver the human vaccine. The two models differ in their incidence rates: one uses standard incidence and the other uses mass action incidence. The model with standard incidence exhibits backward bifurcation if and only if $a>0$ which leads to an explicit necessary and sufficient condition on the parameters. The model with mass action incidence does not have backward bifurcation.

Backward bifurcation has significant consequences for the persistence or elimination of the disease when the reproduction number of the model is less than one. As a result many authors have tried to identify the epidemiological mechanisms that can induce this phenomenon in various disease transmission models. It has been shown (see KribsZaleta and Martcheva, 2002; Kribs-Zaleta and Velasco-Hernandez, 2000; Gumel, 2012) that backward bifurcation could arise due to mechanisms such as: (1) vaccination (imperfect vaccines; vaccine-derived immunity wanes at a slower rate than natural immunity; vaccine failure duration exceeds a certain critical value); (2) re-infection; (3) hosts disease-induced mortality; (4) differential susceptibility.

The cause of backward bifurcation in our model is vaccination coupled with standard incidence. Vaccination, just like re-infection, creates two classes with different susceptibilities to the disease, which in turn, may lead to backward bifurcation. We identify the small transmission probability from infected human to mosquitoes as a specific mechanism of the backward bifurcation in our model.

Backward bifurcation occurs in the model with standard incidence and not in the model with mass action incidence because in mass action incidence, the force of infection $\lambda_{v}$ of humans increases with the force of infection of mosquitoes. In standard incidence, however, the force of infection $\lambda_{v}$ of humans has a complicated feedback dependence on itself as well as on the force of infection of mosquitoes.

The necessary and sufficient condition for backward bifurcation suggests that the main mechanisms of backward bifurcation are the delivery of the vaccine from the flying vaccinators to the humans and the disease-induced mortality. Given that these two mechanisms are in place, then backward bifurcation occurs if the transmission of the pathogen from infected human to mosquito is sufficiently small.

Finally we investigate the impact of a number of control measures on the proportion of infected and vaccinated humans. We observe that the vaccination rate $\psi$ increases the proportion of vaccinated individuals and decreases the proportion of infected individuals. More surprising is the impact of the biting rate $C_{h v}$. Decreasing the biting rate, potentially through the use of bed nets, initially decreases the proportion of vaccinated individuals but long-term it results in an increased proportion of vaccinated individuals. At equilibrium, decreasing the biting rate results in higher proportion of infected individuals. This observation is rather counterintuitive. It may be due to a very non-linear dependence of the forces of infection on the biting rate.

## References

Anderson, R. M. and May, R. M. (1991). Infectious Diseases of Humans: Dynamics and Control. Oxford University Press, Oxford, UK.

Arino, J., McCluskey, C.C., van den Driessche, P. (2003). Global results for an epidemic model with vaccination that exhibits backward bifurcation. SIAM Journal on Applied Mathematics, 64: 260-274.

Aron, J. L., May, R. M. (1982). The population dynamics of malaria, in The Population Dynamics of Infectious Disease: Theory and Applications. R. M. Anderson, ed., Chapman and Hall, London: 139-179.

Bowman, C., Gumel, A. B., van den Driessche P., et al. (2005). A mathematical model for assessing control strategies against West Nile virus. Bulletin of Mathematical Biology, 67: 1107-1133.

Brauer, F. (2004). Backward bifurcation in simple vaccination models. Journal of Mathematical Analysis and Application, 298(2): 418-431.

Carr, J. (1981). Applications of Centre Manifold Theory, Springer-Verlag, New York.
Castillo-Chavez, C., Song, B. (2004). Dynamical model of tuberclosis and their applications Mathematical Biosciences and Engineering, 1(2): 361-404.

Diekmann, O., Heesterbeek, J. A. P., Metz J. A. J. (1990). On the definition and the computation of the basic reproduction ratio R 0 in models for infectious diseases in heterogeneous populations. Journal of Mathematical Biology, 28: 365-382.
van den Driessche P., Watmough, J. (2002). Reproduction numbers and sub-threshold endemic equilibria for compartmental models of disease transmission. Mathematical Biosciences, 180: 29-48.

Elbasha, E.H., Gumel, A.B. (2006). Theoretical assessment of public health impact of imperfect prophylactic HIV-1 vaccines with therapeutic benefits. Bulletin of Mathematical Biology, 68: 577-614.

Gumel,A.B. (2012). Causes of backward bifurcations in some epidemiological models. Journal of Mathematical Analysis Applications, 395: 355-365.

Kribs-Zaleta, C., Martcheva, M. (2002) . Vaccination strategies and backward bifurcation in an age-since-infection structured model. Mathematical Biosciences, 177/178: 317-332.

Kribs-Zaleta, C., Velasco-Hernandez, J. X. (2000). A simple vaccination model with multiple endemic states. Mathematical Biosciences, 164: 183-201.

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

Ngwa G. A., Shu, W. S. (2000). A mathematical model for endemic malaria with variable human and mosquito populations. Mathematics and Computer Modelling, 32: 747-763.

Sharomi, O., Podder,C.N., Gumel,A.B., Elbasha,E.H., Watmough, J. (2007). Role of incidence function in vaccine-induced backward bifurcation in some HIV models. Mathematical Biosciences, 210: 436-463.

Teboh-Ewungkem, M.I., Ngwa, G.A., and Ngonghala, C. N. (2013). Models and proposals for malaria: a review, Math. Pop. Studies 20 (2): 57-81.
Yamamoto, D. S., Nagumo, H., Yoshida, S. (2010). Flying vaccinator: a transgenic mosquito delivers a Leishmania vaccine via blood feeding. Insect Molecular Biology, 19: 391-398.


Figure 2: Stable disease-free equilibrium: $C_{h v}=100, \Pi_{h}=100, \Pi_{v}=100000, \beta_{h}=$ $0.75, \beta_{m}=0.6, \beta_{v}=0.6, \delta_{v}=10, \gamma_{h}=1.5, \mu_{h}=0.015, \mu_{v}=6, \psi=0.85, \varepsilon_{h}=0.2$. $R_{0} \approx 0.8965<1, \mathcal{R} \approx 0.9004<1$.


Figure 3: Stable disease-free equilibrium: $C_{h v}=100, \Pi_{h}=100, \Pi_{v}=100000, \beta_{h}=$ $0.75, \beta_{m}=0.6, \beta_{v}=0.6, \delta_{v}=10, \gamma_{h}=1.5, \mu_{h}=0.015, \mu_{v}=6, \psi=0.85, \varepsilon_{h}=0.2$. $R_{0} \approx 0.8965<1, \mathcal{R} \approx 0.9004<1$.


Figure 4: Stable endemic equilibrium: $C_{h v}=100, \Pi_{h}=1000, \Pi_{v}=100000, \beta_{h}=0.75$, $\beta_{m}=0.6, \beta_{v}=0.6, \delta_{v}=10, \gamma_{h}=1.5, \mu_{h}=0.015, \mu_{v}=6, \psi=0.3, \varepsilon_{h}=0.2$. $R_{0} \approx 2.228>1$.


Figure 5: Stable endemic equilibrium: $C_{h v}=100, \Pi_{h}=1000, \Pi_{v}=100000, \beta_{h}=0.75$, $\beta_{m}=0.6, \beta_{v}=0.6, \delta_{v}=10, \gamma_{h}=1.5, \mu_{h}=0.015, \mu_{v}=6, \psi=0.3, \varepsilon_{h}=0.2$. $R_{0} \approx 2.228>1$.


Figure 6: $v_{h}: \psi=0,0.1,0.2,0.3,0.4,0.5,0.6,0.7,0.8,0.9$ corresponding to I-XI respectively; values of other parameters are same as Fig. 4.


Figure 7: $i_{h}: \psi=0,0.45,0.85$ corresponding to I-III respectively; values of other parameters are same as Fig. 4.


Figure 8: $v_{h}(\psi=0.85): C_{h v}=30,50,75,100,150,250,800$ corresponding to I-VII respectively; values of other parameters are same as Fig. 4.


Figure 9: $i_{h}(\psi=0.3): C_{h v}=10,30,300$ corresponding to I-III respectively; values of other parameters are same as Fig. 4.


Figure 10: $v_{h}(\psi=0.85): \delta_{v}=5,20,30,40,60,80$ corresponding to I-VI respectively; values of other parameters are same as Fig. 4.


Figure 11: $i_{h}(\psi=0.3): \delta_{v}=10,50,100$ corresponding to I-III respectively; values of other parameters are same as Fig. 4.



Figure 12: $C_{h v}=100, \Pi_{h}=100, \Pi_{v}=100000, \beta_{h}=0.75, \beta_{v}=0.6, \delta_{v}=10, \gamma_{h}=1.5$, $\mu_{h}=0.015, \mu_{v}=6, \varepsilon_{h}=0.2$.


Figure 13: $\Pi_{h}=100, \Pi_{v}=100000, \beta_{h}=0.75, \beta_{m}=0.6, \beta_{v}=0.6, \delta_{v}=10, \gamma_{h}=1.5$, $\mu_{h}=0.015, \mu_{v}=6, \varepsilon_{h}=0.2$.


Figure 14: $C_{h v}=100, \Pi_{v}=100000, \beta_{h}=0.75, \beta_{m}=0.6, \beta_{v}=0.6, \gamma_{h}=1.5$, $\mu_{h}=0.015, \mu_{v}=6, \varepsilon_{h}=0.2, \Pi_{h}=1000, \delta_{v}=10$.


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