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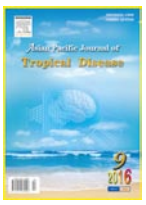

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Mathematical modeling of Zika virus

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ABSTRACT

Zika virus (ZIKV) mathematical model is formulated. Optimal control strategies are introduced into the model. The basic properties of the model without control strategies are determined including the reproduction number. Pontryagin's maximum principle is used to characterize the necessary conditions for optimal control of ZIKV. The preventive and treatment strategy without spraying the mosquitoes showed a great reduction in infected humans, however no significant reduction in the infected mosquitoes population. The use of preventive and insecticide techniques to minimize the spread of the virus showed a greater significance in the reduction of both infected humans and mosquitoes. The application of preventive, treatment and insecticide showed the best way of reducing the spread of ZIKV. The best strategy to minimize the spread of ZIKV is to use prevention, treatment and insecticide as control strategy at the same time.

1. Introduction

Zika virus (ZIKV) outbreak was initially recognized in Africa[1], which occurred in Yap during April[2]. This was then followed by another outbreak in French Polynesia for six months between October 2013 and April 2014[3], and took place in some Pacific countries[4,5]. In 2015, some cases of ZIKV were recorded among South American countries, which Brazil and Columbia were victim[6-8]. Specifically, ZIKV transmission is basically vector-borne, however, in some circumstances it can also be transmitted through sexual contact and blood transfusions process[4]. The *Aedes* species mosquito is the main agent of transmission of the virus[9], which is also at the same time the vector for dengue virus. ZIKV has been identified as able to sustain transmission in other tropical regions[10]. The symptoms of ZIKV include fever, rash, increased incidence of neurological sequelae[11,12] and microcephaly in infants born to mothers who contracted ZIKV in pregnancy period[13]. The recent ZIKV incidence in Brazil and French Polynesia possibly compels World Health Organization to declare a Public Health Emergency of International Concern in response to the clusters of microcephaly and other neurological disorders. Apart from the major outbreak in French Polynesia incident which saw 42 Guillain-Barre syndrome cases[11,14] between March 2014 and May 2015 in same region, 10 cases of Guillain-Barre syndrome with microcephaly and severe brain lesions were reported[12]. Globally ZIKV has the potential to spread across all continents, therefore, it is critical to characterize the transmission dynamics of the disease. Mathematical models have been recognized as essential tools for investigating the dynamics of the spread of infectious diseases. Mathematical models can help to determine a threshold called reproduction number which usually provides information on how infection will be sustained. Application of mathematical models to study mosquito related diseases have been studied by several researchers[15-19]. The potential factors for spreading ZIKV can be well appreciated via mathematical models. Control of infectious diseases is a key to World Health Organization and optimal time control is capable of providing useful theoretical information on both prevention and treatment of diseases. The information obtained from optimal control modeling can help decision makers to plan well and provide the best services to manage and cure diseases. Optimal time control has been employed to study many mosquito related diseases[15,18-22]. To the best of our knowledge there is no optimal control model

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on ZIKV. In this study we propose a new model with optimal control to examine the effect of mass treatment and insecticide. The purpose of this control is to minimize the number of Zika infected hosts and vectors with optimal cost of mass treatment and insecticide applying Pontryagin's maximum principle. The paper is arranged as follows; In Section 3, we apply Pontryagin's maximum principle to explore analysis of control strategies, and to determine the necessary conditions for the optimal control of the ZIKV model. In Sections 4, we present the simulation results to illustrate the population dynamics, with prevention and treatment as controls. In Section 5, conclusions are discussed and drawn.

2. Model formulation

There is evidence that *Aedes* species mosquito transmits both dengue fever and ZIKV and for the purpose of this study we explore susceptible-infected-recovered model to examine the dynamics of transmission of ZIKV to human[23]. The model sub-classifies the entire human population at time t, represented by N_H, into the following sub-divisions of susceptible individuals, $S_H(t)$ individuals with Zika symptoms and infectious $I_H(t)$, $R_H(t)$ individual recovered from Zika. Thus $N_H(t) = S_H(t) + I_H(t) + R_H(t)$. The overall vector (mosquito) population at time t, given by $N_V(t)$, is sub-classified into susceptible mosquitoes $S_V(t)$ and infectious mosquitoes $I_V(t)$. Therefore, $N_V(t) = S_V(t) + I_V(t) + R_V(t)$. β_H is the transmission rate from humans to mosquitoes. β_V is the transmission rate of ZIKV from the vector (mosquitoes) to humans. Natural death rate of host is denoted by μ_H. The recruitment rate into susceptible population is denoted by Λ_H. Natural death rate of vector is denoted by μ_V. η_H is the recovery rate from treatment. Here, Λ_V is the recruitment rate into susceptible mosquito population. While η_V is the vector death rate from insecticide. Also, $\frac{1}{\gamma}$ is the average infectious period for humans. We consider the prevention control μ_1, treatment control μ_2 and the insecticide control μ_3. These control functions μ_1, μ_2 and μ_3 are bounded and Lebesgue integrable. The Figure 1 depicts transmission dynamics of ZIKV between the host and the vector.

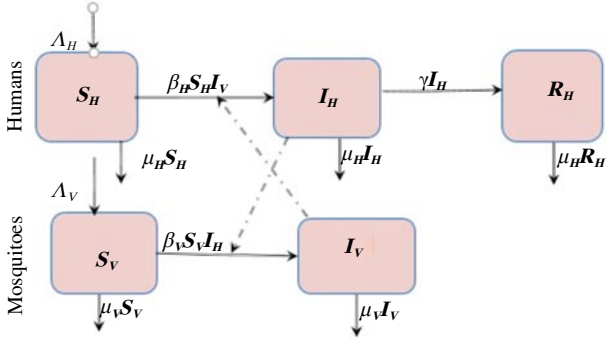

Figure 1. The model for transmission diagram.

The set of differential equations corresponding to the above transmission diagram:

$$\begin{aligned}
\frac{dS_H}{dt} &= \Lambda_H - (1-\mu_1)\beta_H S_H(I_V + \sigma I_H) - \mu_H S_H,\\
\frac{dI_H}{dt} &= (1-\mu_1)\beta_H S_H(I_V + \sigma I_H) - (\mu_H + \gamma + \eta_H\mu_2)I_H,\\
\frac{dR_H}{dt} &= (\gamma + \eta_H\mu_2)I_H - \mu_H R_H,\\
\frac{dS_V}{dt} &= \Lambda_V - (1-\mu_1)\beta_V S_V I_H - (\mu_V + \eta_V\mu_3)S_V,\\
\frac{dI_V}{dt} &= (1-\mu_1)\beta_V S_V I_H - (\mu_V + \eta_V\mu_3)I_V.
\end{aligned} \tag{1}$$

3. Model analysis

In this section, the basic properties and stability analysis of system 1 are carried out without time optimal controls incorporated.

3.1. Invariant region

Theorem 1: *If* $S_H(0)$; $I_H(0)$; $R_H(0)$; $S_V(0)$ and $I_V(0)$ are non-negative, then so are $S_H(t)$; $I_H(t)$; $R_H(t)$; $S_V(t)$ and $I_V(t)$ for all $t > 1$. Furthermore, $\limsup_{t\to\infty} N_H(t) \leqslant \frac{\Lambda_H}{\mu_H}$, $\limsup_{t\to\infty} N_V(t) \leqslant \frac{\Lambda_V}{\mu_V}$

Also, if in addition $N_H(0) \leqslant \frac{\Lambda_H}{\mu_H}$ (based on $N_V(0) \leqslant \frac{\Lambda_V}{\mu_V}$), then $N_H(t) \leqslant \frac{\Lambda_H}{\mu_H}$ (based on $N_V(t) \leqslant \frac{\Lambda_V}{\mu_V}$). In specific, the region $\Omega = \Omega_H \times \Omega_V$ with $\Omega_H = (S_H, I_H, R_H) \in R^3_+ : S_H + I_H + R_H \leqslant \frac{\Lambda_H}{\mu_H}$ and $\Omega_V = (S_V, I_V) \in R^2_+ : S_V + I_V \leqslant \frac{\Lambda_V}{\mu_V}$ is positively invariant.

Proof: $t_1 = \sup\{t > 1: S_H, I_H, R_H$ and I_H are positive on $[0,t]\}$. By the fact that $S_H(0) > 0$, $I_H(0) > 0$, $R_H(0) > 0$, $S_V(0) > 0$ and $I_V(0) > 0$ then $t_1 > 0$. If $t_1 < +\infty$, then employing the variation of constants formula to the initial equation of the system (1), we obtain: $S_H(t_1) > \phi(t_1, 0)S_H(0) + \int_0^{t_1}\phi\Psi(t_1, \tau)d\tau$, where $\phi(t_1, \tau) = \ell^{-\int_\tau^t(\beta_H + \mu_H)(s)ds}$.

Obviously, $S_H(t_1) > 0$, and it can be demonstrated in the same way that this is the case for the other variables. This contradicts the point that t_1 is the supremum since one of the variables must be equal to t_1. Thus, $t_1 = \infty$ which means that S_H, I_H, R_H, S_V and I_V are positive for all $t_1 > 0$. For the second aspect of the proof, we obtain it, by summing up the first three equations and the last three equations of the model (1), respectively.

$$\begin{aligned}
\frac{dH_H(t)}{dt} &= \Lambda_H - \mu_H N_H(t),\\
\frac{N_V(t)}{dt} &= \Lambda_V - \mu_V N_V(t).
\end{aligned} \tag{2}$$

As $0 < I_H(t) \leqslant N_H(t)$, $\Lambda_H - \mu_H N_H(t) \leqslant \frac{dN_H}{dt}(t) < \Lambda_H - \mu_H N_H(t)$. By applying standard comparison theorem[23], we have;

$$N_H(0)e^{-(\mu_H)t} + \frac{\Lambda_H}{\mu_H}(1 - e^{-(\mu_H)t}) \leqslant N_H(t) \leqslant N_H(0)e^{-(\mu_H)t} + \frac{\Lambda_H}{\mu_H}(1 - e^{-(\mu_H)t}) \tag{3}$$

$$N_V(t) = N_V(0)e^{-(\mu_V)t} + \frac{\Lambda_V}{\mu_V}(1 - e^{-(\mu_V)t})$$

Thus, if $N_H(0) \leqslant \frac{\Lambda_H}{\mu_H}$ (based on $N_V(0) \leqslant \frac{\Lambda_V}{\mu_V}$), then $N_H(t) \leqslant \frac{\Lambda_H}{\mu_H}$ (based on $N_V(t) \leqslant \frac{\Lambda_V}{\mu_V}$). Furthermore,

$$\frac{\Lambda_H}{\mu_H} \leqslant \liminf_{t\to\infty} N_H(t) \leqslant \limsup_{t\to\infty} N_H(t) \leqslant \frac{\Lambda_H}{\mu_H}, \tag{4}$$

$$\liminf_{t\to\infty} N_v(t) = \frac{\Lambda}{\mu_v}$$

This provides the invariance of as to be determined. We conclude from this this theorem that it is sufficient to deal with the dynamics of (1) in Ω. In this respect, the model can be assumed as being epidemiologically well-posed for mathematical analysis[24].

3.2. Positivity of solutions

We need to demonstrate by a way of proof that given any non-negative initial conditions of system (1), say, $S_H(0)$, $I_H(0)$, $R_H(0)$, $S_V(0)$, $I_V(0)$ the solutions continue to be non-negative for all $t\in[0, \infty)$. We show that the entire state variables stay non-negative. The solution of the zika model of system (1) having non-negative initial conditions will continue to be positive for all $t > 1$. We therefore state the following lemma.

Lemma 1: supposed that the initial conditions of system (2) are non-negative, the solutions: $S_H(t)$, $I_H(t)$, $R_H(t)$, $S_V(t)$ and $I_V(t)$ are positive for all $t > 0$

Proof: we assume that, $\hat{t} = \sup\{t > 1: S_H > 0, I_H > 0, R_H > 0, S_V > 0, I_V > 0\}\in[0, t]$. So $\hat{t} > 0$, and it can be seen straight from system (1) of equation 1 that; $\frac{dS_H}{dt} \leqslant (\mu_H)[(\mu_H + \lambda)]S_H$, where $\lambda = (\beta_H I_V + \sigma I_H) > 0$. We therefore obtain;

$$\frac{d}{dt}[S_H(t)\exp\{(\mu_H)t + \int_0^{\hat{t}}\lambda(s)ds\}] \leqslant (\mu_H)\exp[(\mu_H)t + \int_0^{t}\lambda(s)ds]$$

Thus, $S_H(\hat{t})\exp[(\mu_H)t + \int_0^{\hat{t}}\lambda(s)ds] - S(0) \leqslant \int_0^{t}(\mu_H)\exp[(\mu_H)\hat{t}\int_0^{\hat{t}}\lambda(\omega)d\omega]dt$. So that,

$$S_H(\hat{t}) \leqslant S_H(0)\exp[-(\mu_H)t + \int_0^{\hat{t}}\lambda(s)ds] + \exp\{-[(\mu_H)\hat{t}\int_0^{\hat{t}}\lambda(s)ds]\}\{\int_0^{t}(\mu_H)\exp[(\mu_H)t + \int_0^{\hat{t}}\lambda(\omega)d\omega]d\hat{t}\} \quad (5)$$

The right hand side of (5) is obviously positive. Hence, the solution $S_H(t)$ will thus be continuously positive. The second equation of system (1) we thus have,

$$\frac{dI_H}{dt} \geqslant -(\mu_H + \gamma)I_H$$
$$I_H \geqslant I_H(0)\exp-(\mu_H + \gamma)t > 0$$

Likewise, it can be demonstrated that $R_H > 0$, $S_V > 0$ and $I_V > 0$ for all $t > 0$, and this therefore completes the proof.

3.3. Steady states and the model reproductive number

In this subsection, we determine the steady states solution by putting the right hand side of system (1) to be equal to zero. This direct computation indicates that system (1) consequently has a disease free equilibrium point $E_0 = (\frac{\Lambda_H}{\mu_H}, 0, 0, \frac{\Lambda_V}{\mu_V}, 0$ and endemic equilibrium point is $E_1=(S_H^*, I_H^*, R_H^*, S_V^*, I_V^*)$ in Ω where,

$$\begin{aligned}
S_H^* &= \frac{-\gamma\beta_V\Lambda_V - \beta_V\Lambda_V\mu_H + \beta_V\Lambda_H\mu_V + \gamma\mu_V^2 + \mu_H\mu_V^2}{\beta_V\mu_H\mu_V},\\
I_H^* &= \frac{\beta_V\Lambda_V - \mu_V^2}{\beta_V\mu_V},\\
R_H^* &= \frac{\gamma(\beta_V\Lambda_V - \mu_V^2)}{\beta_V\mu_H\mu_V},\\
S_V^* &= \frac{\mu_V}{\beta_V},\\
I_H^* &= \frac{\mu_H(\gamma+\mu_H)(\beta_V\Lambda_V - \mu_V^2)}{\beta_H(\gamma\beta_V\Lambda_V + \beta_V\Lambda_V\mu_H - \beta_V\Lambda_H\mu_V - \gamma\mu_V^2 - \mu_H\mu_V^2}
\end{aligned} \quad (6)$$

3.4. The reproduction number of model

It is worthy to note that R_0 represents the reproduction number of model. A reproduction number, often expressed as the average number of human infected by an index case, is a vital threshold parameter that determines whether a disease persists and becomes extinct in a population. By employing the next-generation operator approach of Okosun and Makinde to determine the reproduction number[18,19], F and V correspondingly stand for matrices for the new infections generated and the transition terms, then we thus have

$$F = \begin{bmatrix} \frac{\sigma\beta_H\Lambda_H}{\mu_H} & \frac{\beta_H\Lambda_H}{\mu_H} \\ \frac{\beta_V\Lambda_V}{\mu_V} & 0 \end{bmatrix} \text{ and } V = \begin{bmatrix} \gamma+\mu_H & 0 \\ 0 & \mu_V \end{bmatrix}$$

The basic reproduction number R_0 is expressed as the spectral radius of the matrix FV^{-1} and thus

$$R_0 = \rho(FV^{-1}) = \frac{\sqrt{\beta_H\Lambda_H(4\gamma\mu_H\beta_V\Lambda_V + \sigma^2\beta_H\Lambda_H\mu_V^2 + 4\mu_H^2\beta_V\Lambda_V)} + \sigma^2\beta_H\Lambda_H\mu_V}{2\mu_H\mu_V(\gamma+\mu_H)} \quad (7)$$

It is remarkable to note that R_0 depends on infection rate of human and vector populations and also is driven by the respective recruitment rate. The reduction of ZIKV is driven by recovery rate and natural mortality of human and vector population.

3.5. Stability of the disease-free equilibrium

Theorem 2: the disease-free equilibrium E_0 whenever it exists, is locally asymptotically stable if $R_0 < 1$ and unstable otherwise.

Proof: the Jacobian matrix of system (1) at the equilibrium point E_0 is obtained as

$$J_{E_0} = \begin{bmatrix} -\mu_H & -\frac{\sigma\beta_H\Lambda_H}{\mu_H} & 0 & 0 & -\frac{\beta_H\Lambda_H}{\mu_H} \\ 0 & -\gamma-\mu_H+\frac{\sigma\beta_H\Lambda_H}{\mu_H} & 0 & 0 & \frac{\beta_H\Lambda_H}{\mu_H} \\ 0 & \gamma & -\mu_H & 0 & 0 \\ 0 & -\frac{\beta_V\Lambda_V}{\mu_V} & 0 & -\mu_V & 0 \\ 0 & \frac{\beta_V\Lambda_V}{\mu_V} & 0 & 0 & -\mu_V \end{bmatrix}$$

It can be observed that the eigenvalues of J_{E_0} are $-\mu_H$, $-\mu_H$, $-\mu_V$ and the solution of the characteristic polynomial is

$$P(x) = x^2 + \eta_1 x + \eta_0 = 0 \quad (8)$$

where

$$\eta_1 = -\sigma\beta_H\Lambda_H + \gamma\mu_H + \mu_H^2$$
$$\eta_0 = \frac{(1-R_0)\beta_H\Lambda_H(\beta_V\Lambda_V + \sigma\mu_V^2)}{\mu_H\mu_V} + \mu_V(-\gamma-\mu_H)$$

The solution of P(x) = 0 have negative real parts only if $R_0 < 1$. The thus concluded that the disease free equilibrium is locally asymptotically stable whenever $R_0 < 1$.

Theorem 3: the disease free equilibrium point E_0whenever it exists, is globally asymptotically stable if $R_0 < 1$ when all solutions of system (1) in R^5 are bounded.

Proof: in order to show this result, we construct the following Lyapunov function:

$$L(t) = \mu_V\left\{S_H - S_H^0 - S_H^0\log\frac{S_H}{S_H^0}\right\} + \mu_V I_H + \frac{\beta_H\Lambda_H}{\mu_H}\left\{S_V - S_V^0 - S_V^0\log\frac{S_V}{S_V^0}\right\} + \frac{\beta_H\Lambda_H}{\mu_H}I_V \quad (9)$$

Taking the time derivative of (9) along the solutions of system (9), we obtain

$$L^1(t) = \mu_V\left\{\frac{S_H - S_H^0}{S_H}\right\}[\Lambda_H - \beta_H S_H(I_V + \sigma I_H) - \mu_H S_H] + \mu_V[\beta_H S_H(I_V + \sigma I_H) - (\mu_H+\gamma)I_H]$$
$$+ \frac{\beta_H\Lambda_H}{\mu_H}\left\{\frac{S_H - S_H^0}{S_H}\right\}[\Lambda_V - \beta_V S_V I_H - \mu_V S_V] + \frac{\beta_H\Lambda_H}{\mu_H}[\beta_V S_V I_H - \mu_V I_V] \quad (10)$$

Making use of $S_H^0 = \frac{\Lambda_H}{\mu_H}$ and $S_V^0 = \frac{\Lambda_V}{\mu_V}$ in equation (10), and taking some arrangements, we get

$$L^1(t) = -\mu_V\mu_H\frac{(S_H - S_H^0)^2}{S_H} - \mu_V\frac{\beta_H\Lambda_H}{\mu_H}\frac{(S_V - S_V^0)^2}{S_V} - \mu_V\mu_H I_H^2 - \mu_V\frac{\beta_H\Lambda_H}{\mu_H}I_V^2 - I_H(\mu_H+\gamma)\mu_V(1-R_0)$$

$L^1(t)$ is negative if $R_0 < 1$ and $L^1(t) = 0$ if $S_H = S_H^0$, $S_V = S_V^0$, $I_H = I_V = 0$. Hence, the largest compact invariant set $(S_H, I_H, R_H, S_V, I_V) \in \Omega : L^1(t) = 0$ is the singleton set E_0, where E_0 is the disease free equilibrium. Thus, by principle[25], E_0, is globally asymptotically stable in π.

3.6. Stability of the endemic equilibrium

Theorem 4: if $R_0 > 1$, the endemic equilibrium point of system (1), is locally asymptotically stable.

Proof: the Jacobian matrix of system (1) at endemic equilibrium is determined so that

$$J_{E_1} = \begin{bmatrix} -\sigma I_H^*\beta_H - I_V^*\beta_H - \mu_H & -\sigma S_H\beta_H & 0 & 0 & -\beta_H S_H^* \\ \sigma I_H^*\beta_H + I_V^*\beta_H & -\gamma - \mu_H + \sigma S_H^*\beta_H & 0 & 0 & \beta_H S_H^* \\ 0 & \gamma & -\mu_H & 0 & 0 \\ 0 & -\beta_V S_V^* & 0 & -\mu_V - I_H^*\beta_V & 0 \\ 0 & \beta_V S_V^* & 0 & I_H^*\beta_V & -\mu_V \end{bmatrix}$$

The characteristics equation to the Jacobian matrix J_{E1} is followed as

$$q(x) = (x-\mu_H)(x^4 + \eta_3 x^3 + \eta_2 x^2 + \eta_1 x + \eta_0) = 0 \quad (11)$$

It is obvious that μ_H is negative and the other four eigenvalues of the E_1 can be obtained from the characteristic equation where,

$\eta_3 = \gamma + (\sigma I_H + I_V - \sigma S_H)\beta_H + I_H\beta_V + 2\mu_H + 2\mu_V$,

$\eta_2 = k_1 + k_2 + k_3$

$k_1 = \sigma I_H^{*2}\beta_H\beta_V - S_H^* S_V^*\beta_H\beta_V + \gamma\mu_H - \sigma S_H^*\beta_H\mu_H + \mu_H^2$,

$k_2 = 2(\gamma - \sigma S_H^*\beta_H + 2\mu_H) + \mu_V^2 + I_V^*\beta_H(\gamma + \mu_H + 2\mu_V)$,

$k_3 = I_H^*\{\beta_V(\gamma + 2\mu_H + \mu_V) + \beta_H[I_V^*\beta_H + \sigma(\gamma - S_H^*\beta_V + \mu_H + 2\mu_V)]\}$.

$\eta_1 = \sigma I_H^{*2}\beta_H\beta_V + m_1 - S_H^*[S_V^*\beta_H(\mu_H + \mu_V) + \sigma\mu_V(2\mu_H + \mu_V)] + m_2 + m_3$,

where

$m_1 = \mu_V[2(\gamma + \mu_H)(I_V^*\beta_H + \mu_H) + (\gamma + I_V^*\beta_H + 2\mu_H)\mu_V]$,

$m_2 = I_H^*\{I_V^*\beta_H\beta_V(\gamma + \mu_H + \mu_V) + \sigma\beta_H\mu_V[2(\gamma + \mu_H) + \mu_V + \mu_H](\gamma + I_V^*\beta_H + \mu_V)$,

$m_3 = \beta_V[\mu_H(\gamma - \sigma S_H^*\beta_H + \mu_H) + (\gamma - \sigma S_H^*\beta_H + 2\mu_H)\mu_V]$.

Owing to the mathematical complexity of the computation encompassed in an attempt to show the Routh-Hurwitz conditions for the stability of E_1, we just present the criterion under which endemic is said to be locally asymptotically stable at endemic equilibrium point. If $\eta_3 > 0$, $\eta_3\eta_2 - \eta_1 > 0, [\eta_3\eta_2 - \eta_1] - \eta_3^2\eta_0 > 0$, then the polynomial of endemic equilibrium E_1 has roots with negative real parts. Thus theorem (2) depicts that the disease free equilibrium whenever it exists, is locally asymptotically stable if $R_0 < 1$ and unstable otherwise

Theorem 5: the endemic equilibrium point whenever it exists, is globally asymptotically stable if $R_0 > 1$ when all solutions of system (1) in R^5 are bounded.

Proof: we consider the non-linear Lyapunov function below to establish the global stability of the model.

$$\dot{V} = S_H - \dot{S}_H - \dot{S}_H\ln\frac{S_H}{S_H^*} + \alpha_1\left\{I_H - I_H^* - I_H^*\ln\frac{I_H}{I_H^*}\right\} + \alpha_2\left\{R_H - R_H^* - R_H^*\ln\frac{R_H}{R_H^*}\right\} + \alpha_3\left\{S_V - S_V^* - S_V^*\ln\frac{S_V}{S_V^*}\right\} + \alpha_4\left\{I_V - I_V^* - I_V^*\ln\frac{I_V}{I_V^*}\right\} \quad (12)$$

Differentiating the above equation (12) with some algebraic simplifications and $a_1 = a_2 = a_3 = a_4 = 1$, we have:

$$\dot{V} = \left\{1 - \frac{S_H^*}{S_H}\right\}\dot{S}_H^* + \alpha_1\left\{1 - \frac{I_H^*}{I_H}\right\}\dot{I}_H^* + \alpha_2\left\{1 - \frac{R_H^*}{R_H}\right\}\dot{R}_H^* + \alpha_3\left\{1 - \frac{S_V^*}{S_V}\right\}\dot{S}_V^* + \alpha_4\left\{1 - \frac{I_V^*}{I_V}\right\}\dot{I}_V^*$$

$$\dot{V} = -\mu_H S_H^*\frac{(1-v)^2}{v} - \mu_V S_V^*\frac{(1-y)^2}{y} + H(v,w,x,y,z)$$

$$\alpha_1\beta_H S_H^* I_V^*\left\{1 - w - \frac{vz}{w} + vz\right\} \leqslant 0;\ \alpha_1\sigma\beta_H S_H^* I_H^*(1 - v - w + vw) \leqslant 0$$

$$\alpha_2\gamma I_H^*\left\{1 - \frac{w}{x} - x + w\right\} \leqslant 0;\ \alpha_3\beta_V S_V^* I_V^*\left\{1 - \frac{1}{y} - yw + w\right\} \leqslant 0;$$

$$\alpha_4\left\{1 - \frac{yw}{z} - z + yw\right\} \leqslant 0 \quad (13)$$

Since all the model parameters are non-negative, it follows that $\dot{V} \leqslant 0$ for $R_0 > 1$. Hence, by LaSalle's invariance principle[25], every solution of the equation in the model approaches the endemic equilibrium point as $t \to 0$ whenever $R_0 > 1$.

4. Analysis of optimal control

In this section, Pontryagin's maximum principle was used to determine the necessary conditions for the optimal control of the disease. We desire to minimize the number of ZIKV infected human host and the cost which involves using mass treatment and insecticide controls. We thus, examine an optimal control problem having the objective function and given by

$$J(u_1, u_2) = \int_0^{t_F}(AI_H + BI_V + \frac{d_1}{2}u_1^2 + \frac{d_2}{2}u_2^2 + \frac{d_3}{2}u_3^2)dt \quad (14)$$

where d_1, d_2 and d_3 denote the weighting constants for prevention, treatment and insecticide efforts, respectively. The costs of the prevention, treatment and insecticide turn to be nonlinear and assume quadratic function. We seek an optimal control u^*_1, u^*_2 and u^*_3 such that, $J(u_1^*, u_2^*, u_3^*) = \min J(u_1, u_2, u_3)$,

$\Gamma = \{(u_1, u_2, u_3) | 0 \leqslant \mu_i \leqslant 1, i = 1,2\}$.

$$\begin{cases} \frac{dS_H}{dt} = \Lambda_H - (1-u_1)\beta_H S_H(I_V + \sigma I_H) - \mu_H S_H, \\ \frac{dI_H}{dt} = (1-u_1)\beta_H S_H(I_V + \sigma I_H) - (\mu_H + \gamma + \eta_H u_2)I_H, \\ \frac{dR_H}{dt} = (\gamma + \eta_H u_2)I_H - \mu_H R_H, \\ \frac{dS_V}{dt} = \Lambda_V - (1-u_1)\beta_V S_V I_H - (u_V + \eta_H u_3)S_V, \\ \frac{dI_V}{dt} = (1-u_1)\beta_V S_V I_H - (u_V + \eta_H u_3)I_V. \end{cases} \quad (15)$$

The necessary conditions that an optimal solution must satisfy come from the maximum principle of Pontryagin *et al*.[26]. This principle converts (14)–(15) into a problem of minimizing pointwise a Hamiltonian H, with respect to u_1 and u_2.

$$H = AI_H + BI_V + d_1\mu_1^2 + d_2\mu_2^2 + d_3\mu_3^2 \quad (16)$$
$$+ \lambda_{S_H}\{\Lambda_H - (1-u_1)\beta_H S_H(I_V + \sigma I_H) - \mu_H S_H\}$$
$$+ \lambda_{I_H}\{(1-u_1)\beta_H S_H(I_V + \sigma I_H) - (\mu_H + \gamma + \eta_H u_2)I_H\}$$
$$+ \lambda_{R_H}\{(\gamma + \eta_H u_2)I_H - \mu_H R_H\} + \lambda_{S_V}\{\Lambda_V - (1-u_1)\beta_V S_V I_H - (\mu_V + \eta_V u_3)S_V\}$$
$$+ \lambda_{I_V}\{(1-u_1)\beta_V S_V I_H - (\mu_V + \eta_V u_3)I_V\}$$

where λ_{S_H}, λ_{I_H}, λ_{R_H}, λ_{S_V} and λ_{I_V} are the adjoint variables or co-state variables. The system of equations is found by taking the appropriate partial derivatives of the Hamiltonian (8) with respect to the associated state variable.

Theorem 6: given optimal controls μ_1^*, μ_2^*, μ_3^* and solutions S_H, I_H, R_H, S_V, I_V of the corresponding state system (14)–(15) that minimize $J(\mu_1,\mu_2, \mu_3)$ over U. Then there exists adjoint variables λ_{S_H}, λ_{I_H}, λ_{R_H}, λ_{S_V}, λ_{I_V} satisfying.

$$\frac{-d\lambda_i}{dt} = \frac{\partial H}{\partial_i} \tag{17}$$

where S_H, I_H, R_H, S_V, I_V and with transversality conditions

$$\lambda_{S_H}(t_f) = \lambda_{I_H}(t_f) = \lambda_{R_H}(t_f) = \lambda_{S_V}(t_f) = \lambda_{I_V}(t_f) = 0 \tag{18}$$

$$\mu_1^* = \min\left\{1,\max\left[0,\frac{S_H\beta_H I_V(\lambda_{I_H}-\lambda_{S_H}) + S_V\beta_V I_H(\lambda_{I_V}-\lambda_{S_V})}{d_1}\right]\right\} \tag{19}$$

$$\mu_2^* = \min\left\{1,\max\left[0,\frac{\eta_H I_H(\lambda_{I_H}-\lambda_{R_H})}{d_2}\right]\right\} \tag{20}$$

$$\mu_3^* = \min\left\{1,\max\left[0,\frac{\eta_V S_V\lambda_{SV} + \eta_V I_V\lambda_{I_V}}{d_3}\right]\right\} \tag{21}$$

Proof: corollary 4.1 of [27] gives the existence of an optimal control due to the convexity of the integrand of J with respect to μ_1, μ_2 and μ_3 a priori boundedness of the state solutions, and the Lipschitz property of the state system with respect to the state variables. The differential equations governing the adjoint variables are obtained by differentiation of the Hamiltonian function, evaluated at the optimal control.

Then the adjoint equations can be written as[27]:

$$\begin{aligned}
-\frac{d\lambda_{S_H}}{dt} &= \mu_H\lambda_{S_H} + (1-\mu_1)\beta_H(\lambda_{S_H}-\lambda_{I_H})(I_V+\bar{o}I_H)\\
-\frac{d\lambda_{I_H}}{dt} &= -A + (\mu_2\eta_H+\mu_H+\gamma)\lambda_{I_H} - (\gamma+\mu_2\eta_H)\lambda_{R_H}\\
&\quad + \bar{o}(1-\mu_1)\beta_H S_H(\lambda_{S_H}-\lambda_{I_H}) + (1-\mu_1)\beta_V S_V(\lambda_{S_V}-\lambda_{I_V})\\
-\frac{d\lambda_{R_H}}{dt} &= \varepsilon(\lambda_{R_H}-\lambda_{S_H}) + \mu_H\lambda_{R_H}\\
-\frac{d\lambda_{S_V}}{dt} &= (1-\mu_1)\beta_V I_H(\lambda_{S_V}-\lambda_{I_V}) - (\mu_V+\eta_V\mu_3)\lambda_{S_V}\\
-\frac{d\lambda_{I_V}}{dt} &= -B + (1-\mu_1)\beta_H S_H(\lambda_{S_H}-\lambda_{I_H}) + (\mu_V+\eta_V\mu_3)\lambda_{I_V}
\end{aligned} \tag{22}$$

5. Numerical simulations

In order to illustrate the results of the foregoing analysis, numerical simulations of the model are carried out, using parameter values given in Table 1. For the purpose of illustration, some parameter values are assumed. Find below in Table 1 the parameter descriptions and values used in the numerical simulation of the model.

Table 1
Description of variables and parameters of the model.

Parameter	Description	Value	Ref
β_H	Probability of individual getting infected	0.2/day	[28]
β_V	Probability of mosquitoes getting infected	0.09	[18,19]
μ_H	Natural death rate in humans	1/(365 × 60)/day	[14]
μ_V	Natural death rate in mosquito	1/14	[28,29]
η_H	Recovery rate from treatment	0.01	[28]
η_V	Death due to insecticides	0.001	Assumed
Λ_H	Recruitment rate of humans	100/day	Assumed
Λ_V	Mosquito recruitment rate	1 000/day	Assumed

5.1. Prevention (u_1) and treatment (u_2) control only

The Zika prevention control u_1 and the treatment control μ_2 are used to optimize the objective function J while we set the insecticide control (u_3) to zero. We observed in Figure 2a a significant difference in the number of infected humans I_H under control and those without control. The result in the depicted Figure 2b clearly suggests that this strategy is not very efficient and effective in the control of the number of infected mosquitoes I_V.

5.2. Prevention (u_1) and insecticide control (u_3) only

The prevention control μ_1 and the insecticide control μ_3 are used to optimize the objective function J while we set the treatment control (u_2) to zero. We observed in Figure 3a a significant difference in the number of infected humans I_H in the controlled cases and the cases without control. The result also depicted in Figure 3b suggests that this strategy is very efficient and effective in the control of the number of infected mosquitoes I_V.

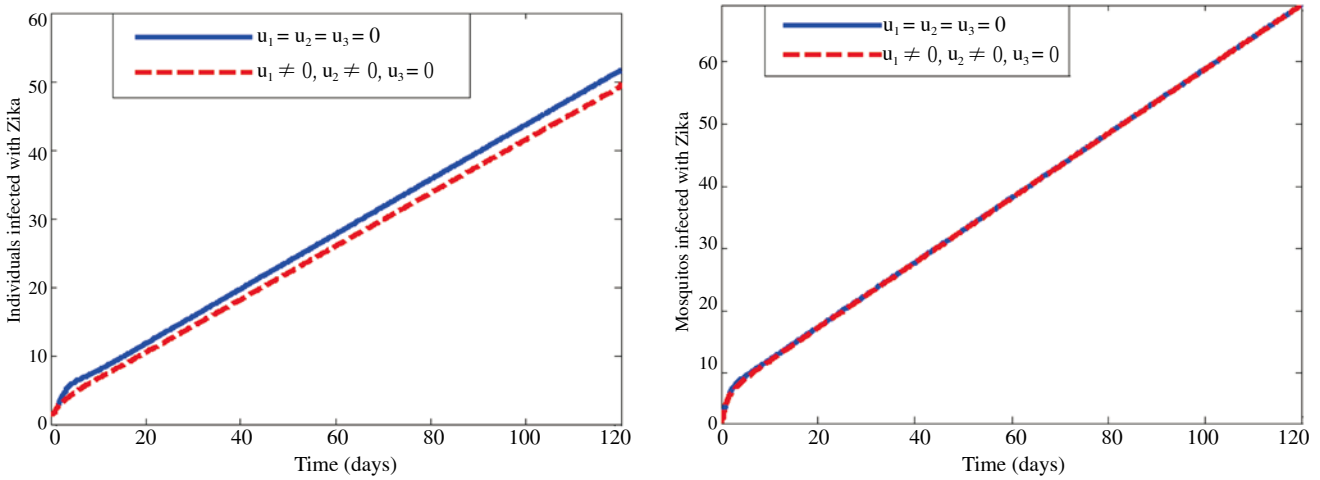

Figure 2. Simulations of the model showing the effect of Zika prevention and treatment only on transmission.

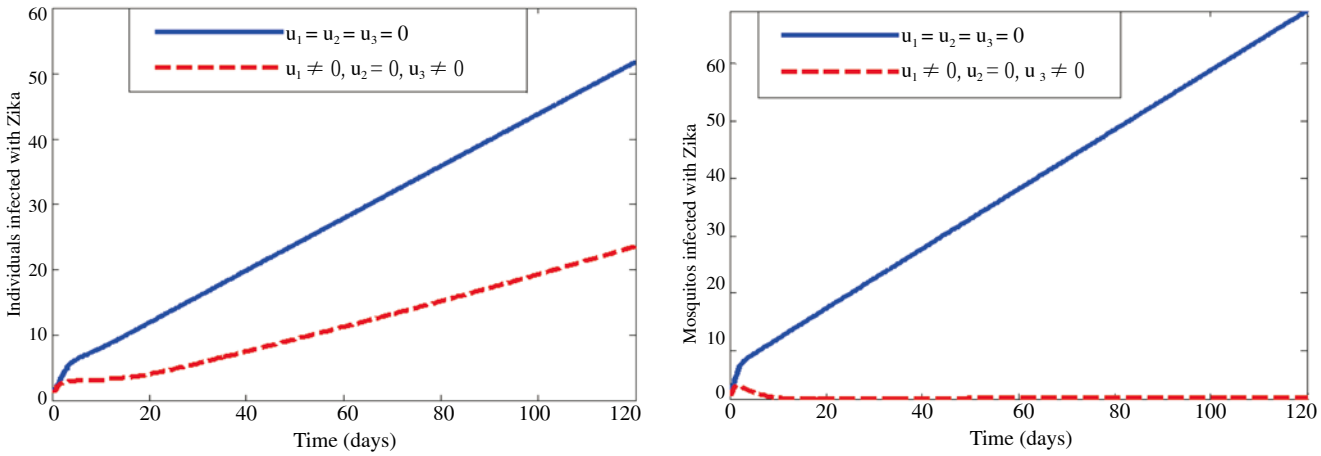

Figure 3. Simulations of the model showing the effect of prevention and insecticide only on transmission.

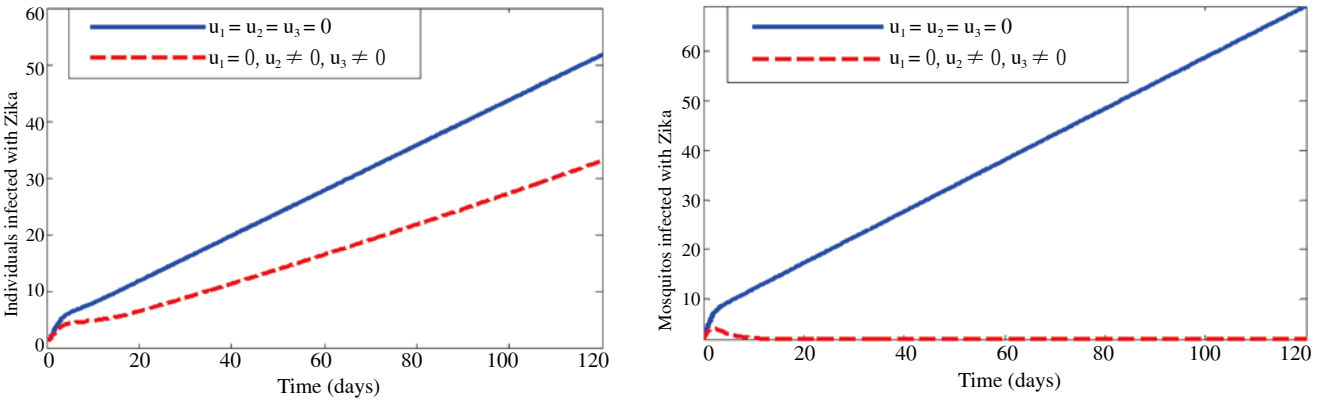

Figure 4. Simulations of the model showing the effect of treatment and insecticide only on transmission.

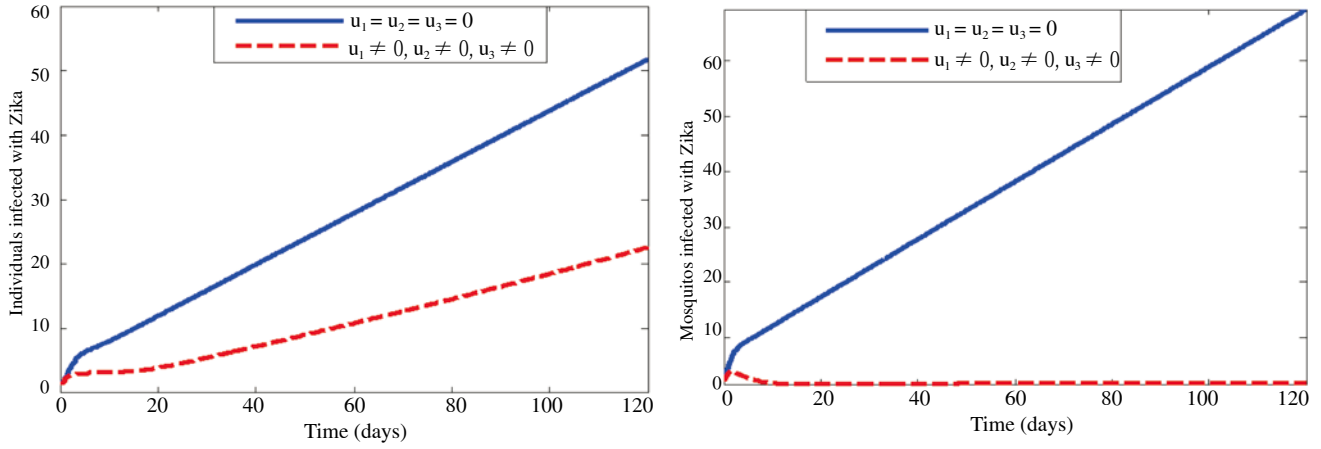

Figure 5. Simulations of the model showing the effect of all controls on transmission.

5.3. Treatment (u_2) and insecticide (u_3) only

The treatment control u_2 and the insecticide control u_3 are used to optimize the objective function J while we set the prevention control (u_1) to zero. That is, preventions only mechanisms are optimized without treatments. We observed in Figure 4a a significant difference in the number of infected humans I_H in the controlled cases and the cases without control. The result also depicted in Figure 4b suggests that this strategy is very efficient and effective in the control of the number of infected mosquitoes I_V.

5.4. Prevention, treatment and insecticide (u_1, u_2, u_3)

In this strategy all the control mechanism (u_1, u_2, u_3) are used to optimize the objective function J. That is, all the prevention, treatment and use of insecticide are optimized. A significant difference in the number of infected humans I_H in the controlled cases and the cases without control was observed in Figure 5a. The result depicted in Figure 5b suggests that this strategy is very efficient and effective in the control of the number of infected mosquitoes I_V.

6. Conclusion

In this paper, we explored and analyzed a ZIKV model which is deterministic. For the model without optimal control, we derived basic properties of the model. The basic reproduction number of the model is determined and steady states are investigated. The global stability of disease-free equilibrium is found to be asymptotically stable. Optimal control strategies of prevention, treatment and insecticide are incorporated into the model. The Pontryagin's maximum principle is used to characterize the conditions for existence of optimal control. The control strategy of prevention and treatment of infected mosquito ZIKV would not minimize the spread of the disease as depicted in the numerical simulation. The numerical analysis of the optimal control indicates that the best strategy is to combine all controls that is preventive, treatment and insecticides in order to control the disease.

Conflict of interest statement

We declare that we have no conflict of interest.

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References

[1] Hayes EB. Zika virus outside Africa. *Emerg Infect Dis* 2009; **15**(9): 1347-50.

[2] Duffy MR , Chen TH, Hancock WT, Powers AM, Kool JL, Lanciotti RS, et al. Zika virus outbreak on Yap Island, Federated States of Micronesia. *N Engl J Med* 2009; **360**: 2536-43.

[3] Cao-Lormeau VM, Roche C, Teissier A, Robin E, Berry AL, Mallet HP, et al. Zika virus, French polynesia, South pacific, 2013. *Emerg Infect Dis* 2014; **20**(6):1085-6.

[4] Musso D, Cao-Lormeau VM, Gubler DJ. Zika virus: following the path of dengue and chikungunya. *Lancet* 2015; **386**(9990): 243-4.

[5] Roth A, Mercier A, Lepers C, Hoy D, Duituturaga S, Benyon E, et al. Concurrent outbreaks of dengue, chikungunya and Zika virus infections - an unprecedented epidemic wave of mosquito-borne viruses in the Pacific 2012-2014. *Euro Surveill* 2014; doi: 10.2807/1560-7917.ES2014.19.41.20929.

[6] Campos GS, Bandeira AC, Sardi SI. Zika virus outbreak, Bahia, Brazil. *Emerg Infect Dis* 2015; **21**(10): 1885-6.

[7] Musso D. Zika virus transmission from French Polynesia to Brazil. *Emerg Infect Dis* 2015; **21**(10): 1887.

[8] Camacho E, Paternina-Gomez M, Blanco PJ, Osorio JE, Aliota MT. Detection of autochthonous Zika virus transmission in Sincelejo, Colombia. *Emerg Infect Dis* 2016; **22**(5): 927-9.

[9] Musso D, Nilles EJ, Cao-Lormeau VM. Rapid spread of emerging Zika virus in the Pacific area. *Clin Microbiol Infect* 2014; **20**(10): O595-6.

[10] Bogoch II, Brady OJ, Kraemer MU, German M, Creatore MI, Kulkarni MA, et al. Anticipating the international spread of Zika virus from Brazil. *Lancet* 2016; **387**(10016): 335-6.

[11] Oehler E, Watrin L, Larre P, Leparc-Goffart I, Lastere S, Valour F, et al. Zika virus infection complicated by Guillain-Barre syndrome – case report, French Polynesia, December 2013. *Euro Surveill* 2014; doi: 10.2807/1560-7917.ES2014.19.9.20720.

[12] Oehler E, Fournier E, Leparc-Goffart I, Larre P, Cubizolle S, Sookhareea C, et al. Increase in cases of Guillain-Barré syndrome during a chikungunya outbreak, French Polynesia, 2014 to 2015. *Euro Surveill* 2015; **20**(48): 30079.

[13] Schuler-Faccini L, Ribeiro EM, Feitosa IML, Horovitz DDG, Cavalcanti DP, Pessoa A, et al. Possible association between Zika virus infection and microcephaly – Brazil, 2015. *MMWR Morb Mortal Wkly Rep* 2016; **65**: 59-62.

[14] Nishiura H, Kinoshita R, Mizumoto K, Yasuda Y, Nah K. Transmission potential of Zika virus infection in the South Pacific. *Int J Infect Dis* 2016; **45**: 95-7.

[15] Blayneh K, Cao YZ, Kwon HD. Optimal control of vector-borne diseases: treatment and prevention. *Discrete Continuous Dyn Syst Ser B* 2009; **11**: 587-611.

[16] Boni MF, Smith DL, Laxminarayan R. Benefits of using multiple first-line therapies against malaria. *Proc Natl Acad Sci U S A* 2008; **105**: 14216-21.

[17] Koella JC, Antia R. Epidemiological models for the spread of anti-malarial resistance. *Malar J* 2003; doi: 10.1186/1475-2875-2-3.

[18] Okosun KO, Makinde OD. Modelling the impact of drug resistance in malaria transmission and its optimal control analysis. *Int J Phys Sci* 2011; **6**: 6479-87.

[19] Makinde OD, Okosun KO. Impact of chemo-therapy on optimal control of malaria disease with infected immigrants. *Biosystems* 2011; **104**: 32-41.

[20] Rafikov L, Bevilacqua L, Wyse AP. Optimal control strategy of malaria vector using genetically modified mosquitoes. *J Theor Biol* 2009; **258**: 418-25.

[21] Okosun K. Mathematical epidemiology of malaria disease transmission and its optimal control analyses [dissertation]. Western Cape: University of the Western Cape; 2010.

[22] Okosun KO, Ouifki R, Marcus N. Optimal control analysis of a malaria disease transmission model that includes treatment and vaccination with waning immunity. *Biosystems* 2011; **106**(2-3): 136-45.

[23] Duong V, Lambrechts L, Paul RE, Ly S, Lay RS, Long KC, et al. Asymptomatic humans transmit dengue virus to mosquitoes. *Proc Natl Acad Sci U S A* 2015; **112**(47): 14688-93.

[24] Hethcote HW. The mathematics of infectious diseases. *SIAM Rev* 2000; **42**(4): 599-653.

[25] La Salle JP. *The stability of dynamical systems*. Philadelphia: Society for Industrial and Applied Mathematics; 1976.

[26] Pontryagin LS, Boltyanskii VG, Gamkrelidze RV, Mishchenko EF. *The mathematical theory of optimal processes*. Bucks: Interscience; 1962.

[27] Fleming WH, Rishel RW. *Deterministic and stochastic optimal control*. New York: Springer Verlag; 1975.

[28] Mojumder MS, Cohn E, Fish D, Brownstein JS. Estimating a feasible serial interval range for Zika fever. Geneva: Bulletin of the World Health Organization; 2006. [Online] Available from: http://www.who.int/bulletin/online_first/16-171009.pdf [Accessed on 10th May, 2016]

[29] Centre for Disease Control and Prevention. Zika virus. Atlanta: Centre for Disease Control and Prevention; 2006. [Online] Available from: http://www.cdc.gov/zika/index.html [Accessed on 10th May, 2016]

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