Deterministic Models in Dengue Transmission Dynamics

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Abstract

A deterministic model for monitoring the impact of treatment on the transmission dynamics of dengue in the human and vector populations is presented. In addition to having a locally-asymptotically stable disease-free equilibrium (DFE) whenever the basic *reproduction number* is less than unity, it is shown, using a Lyapunov function and LaSalle Invariance Principle that the DFE of both treatment-free and treatment model, in the absence of dengue-induced mortality, is globally-asymptotically stable whenever the *reproduction number* is less than unity. Each of the models has a unique endemic equilibrium whenever its reproduction number exceeds unity. Numerical simulations of the model show that for high treatment rates, the disease can be controled within a community.

Introduction

Dengue hemorrhagic fever (DHF) was first recognized in the Philippines in 1953, and in Thailand in 1955 (Esteva [12], Gubler [19], WHO [32]). It has become the most important arthropod-borne viral disease of humans that is endemic in many countries in Southeast Asia, the Americas, the Africa, the Eastern Mediterranean, and the Western Pacific (Chowell et. al[8], Shekhar [28]). Currently, the annual estimations of dengue fever range from 50 to 100 million cases yearly (Monath [27]), with approximately 20,000 deaths globally (Shekhar [28]). Figures from the World Health Organization show that hundreds of thousands of cases of DHF are recorded annually (Blaney [3,4], WHO [33]). Cases of dengue range from asymptomatic to clinically non-specific flu-like symptoms to dengue fever (DF) to dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS). DHF and DSS are the most severe form of dengue disease with an average case-fatality rate being approximately 17%. Many primary dengue infections are asymptomatic.

The disease is caused by any of four closely-related virus serotypes (DEN-1-4) of the genus *Flavivirus*, and is transmitted by its principle mosquito mainly Aedes aegypti. Aedes aegypti is a highly anthropophilic daytime feeder, living around densely populated human habitat (Chowell [8]). Susceptible female mosquitoes acquire the infection when feeding on infectious humans. Susceptible humans are infected when bitten by feeding infectious female (Yang [34]).

There is no specific treatment for dengue. Persons with dengue fever should rest and drink plenty of fluids. They should be kept away from mosquitoes for the protection of others. At present, the treatment strategy of dengue fever consists of the following: (i) The Hemopurifier, which has been designed to isolate and capture highly pathogenic viruses and emerging viral threats, it represents the only proposed treatment for DHF that simultaneously targets broad-strain clearance of dengue virus and also assists in the modulation of excessive cytokine activity. (ii) Antipyretics-aspirin and nonsteroidal anti-inflammatory drugs such as ibuprofen should be avoided so that platelet function will not be impaired. (iii) Monitoring of blood pressure, urine output, hematocrit, platelet count, and level of consciousness.

Several mathematical models have been developed in the literature to gain insights into the transmission dynamics of dengue in a community (see, for instance, Chowell et. al [8]. Coutinho [9], Derouich [10], Esteva [11,12,13 and 14] Feng [15], Ferguson et. al [16], Garba [17, 18], Struchiner et. al [29], Tewa et. al [30], Yang [34]). While Chowell et al. [8] estimated the basic reproduction number of dengue using spatial epidemic data. Tewa et al. [30] established global asymptotic stability of the equilibria of a single-strain dengue model. Garba et al. [17] investigate the qualitative dynamics of a single strain dengue model in the presence of an imperfect vaccine, the authors [18] also consider the effect of cross-immunity on the transmission dynamics of two

strains of dengue, and Struchiner et al. [29] gave a detailed discussion on current research issues in modelling mosquito-borne diseases.

This paper complement, and extends, the aforementioned studies by considering a new mathematical model which incorporates the dynamics of individuals and vectors who are asymptomatically infected to the disease (that is, individuals that are infected but not yet infectious are assumed capable of transmitting the disease).

Basic model

The basic dengue treatment model to be designed is based on subdividing the total human population at time t, denoted by $N_H(t)$, into a number of mutually-exclusive compartments namely, susceptible $(S_H(t))$, asymptomatically infected $(A_H(t))$, symptomatically infected $(I_H(t))$, treated individuals $(T_H(t))$ and individuals in whom treatment fails $(F_H(t))$, so that

$$N_H(t) = S_H(t) + A_H(t) + I_H(t) + T_H(t) + F_H(t).$$

Similarly, the total vector population at time t, denoted by $N_V(t)$, is split into susceptible $(S_V(t))$, exposed $(E_V(t))$ and infectious mosquitoes $(I_V(t))$, so that

$$NV(t) = S_V(t) + E_V(t) + I_V(t).$$

The susceptible human population is increased by the recruitment of individuals into the population at a rate Π_H. These individuals acquire infection, following contact with exposed or infectious vectors in the E_V and I_V classes, at a rate λ_H where

$$\lambda_H = C_{VH}(N_H, N_V) \frac{(\eta_V E_V + I_V)}{N_V}. \qquad (1)$$

The parameter C_{HV} is the effective contact rate between the susceptible humans and infectious mosquitoes, while η_V is the modification parameter $0 < \eta_V < 1$ accounts for the assumed reduction in transmissibility of exposed mosquitoes relative to infectious mosquitoes. Noting that for the number of bites to be conserved, the following equation must hold (Garba [17]),

$$C_{HV} N_V = C_{VH}(N_H, N_V) N_H, \qquad (2)$$

where C_{VH} is the effective contact rate between infectious humans and susceptible mosquitoes, so that,

$$N_V = \frac{C_{VH}(N_H, N_V)}{C_{HV}} N_H. \qquad (3)$$

Thus, substituting (3) in (1), gives

$$\lambda_H = C_{HV} \frac{(\eta_V E_V + I_V)}{N_H} .$$

Similarly, it can be shown that the rate at which mosquitoes become infected denoted by λ_V is given by,

$$\lambda_V = C_{HV} \frac{(\eta_A A_H + I_H + \eta_F F_H)}{N_H} .$$

The parameter $0 \le \eta_A \le 1$ accounts for the assumed reduced infectiousness of asymptomatically infected individuals, while $\eta_F \ge 0$ is the relative risk of infectiousness of individuals who fail treatment. It is assumed that newly-infected individuals are asymptomatically infected before clinical symptoms, after which they become symptomatically infected (Yang [34]). It is worth stating that since the focus of the paper is to evaluate treatment strategies of dengue that target individuals who are symptomatically infected, transition to or from A_H to T_H is not incorporated; this is needed to help keep track of the infection and treatment stages. It is assumed that the population of asymptomatically infected humans is generated by the infection of susceptible humans (at the rate λ_H) and diminished by development of clinical symptoms (at a rate σ_H) and natural death (at a rate μ_H). Symptomatically infected individuals are generated via the development of symptoms by asymptomatically infected humans (at the rate σ_H), these population is reduced following treatment (at a rate τ_H) and moved to the treated class (T_H), while those who fail treatment move to the class (F_H) (at a rate γ_H). All human population suffer natural death (at the rate μ_H). Furthermore, infected individuals in the I_H and F_H class suffer an additional dengue disease-induced death (at a rate δ_H). It is assumed that treated individuals acquire lifelong immunity against re-infection (so that they do not acquire dengue infection again). Individuals in F_H class fail treatment for various reason including non-compliance to the treatment or development of resistance. In other words, individuals in F_H class may have (and can

transmit) dengue resistant strain. For mathematical convenience, we are not considering multiple strain dynamics.

The susceptible mosquitoes are generated by birth (at a rate Π_V) and diminished by infection, following effective contact with infectious human (at the rate λ_V), and due to natural death (at a rate μ_V). All vectors suffer natural death (at the rate μ_V), and infectious vector suffer additional dengue disease-induced death (at a rate δ_V). Finally, the insecticide to eliminate the adult mosquitoes, which is applied inside and surrounding houses (in severe epidemic situations heavy duty application of insecticide can be used), is assessed by the additional mortality rate to all vectors population (at a rate υ_V). The model is given by the following system of differential equations (see Figure 1 for a flow diagram)

$$\frac{dS_H}{dt} = \Pi_H - \lambda_H S_H - \mu_H S_H,$$

$$\frac{dA_H}{dt} = \lambda_H S_H - (\sigma_H + \mu_H) A_H,$$

$$\frac{dI_H}{dt} = \sigma_H A_H - (\tau_H + \mu_H + \delta_H) I_H,$$

$$\frac{dT_H}{dt} = \tau_H S_H - (\gamma_H + \mu_H) T_H,$$
$$\text{(4)}$$

$$\frac{dF_H}{dt} = \gamma_H T_H - (\mu_H + \delta_H) F_H,$$

$$\frac{dS_V}{dt} = \Pi_V - \lambda_V S_V - (\mu_V + \upsilon_V) S_V,$$

$$\frac{dE_V}{dt} = \lambda_V S_V - (\sigma_V + \mu_V + \upsilon_V) E_V,$$

$$\frac{dI_H}{dt} = \sigma_V E_V - (\mu_V + \upsilon_V + \delta_V) I_V.$$

It is assumed that all the parameters and stated variables of the model are non-negative (since the model monitors human and vector populations) for all $t \geq 0$.

Basic properties

In this section, the basic dynamical features of the model will be explored. We claim the following: The closed set

$$D = \left\{ \begin{array}{l} (S_H, A_H, I_H, T_H, F_H, S_V, E_V, I_V) \in \mathbb{R}_+^8 : \\ S_H + A_H + I_H + T_H + F_H \leq \dfrac{\Pi_H}{\mu_H}; S_V + E_V + I_V \leq \dfrac{\Pi_V}{\mu_V + \upsilon_V} \end{array} \right\}$$

is positively-invariant and attracting with respect to the basic model .

Thus, in D, the model is well-posed

epidemiologically and mathematically (Hethcote [20]). Hence, it is sufficient to study the dynamics of the basic model in D.

Treatment-free model

Before analyzing the full model, we first consider the treatment-free model, obtained by setting $\tau_H = \gamma_H = T_H = F_H = 0$ in (5). Further, since data suggest that the dengue-induced mortality in human is negligible (Kawaguchi [22]), we set the mortality parameter to zero (i.e., $\delta_H = 0$). Thus,

$$\frac{dN_H}{dt} = \Pi_H - \mu_H N_H,$$

so that the total human population is constant at steady-state give the following reduced model.

$$\frac{dS_H}{dt} = \Pi_H - \lambda_H S_H - \mu_H S_H,$$

$$\frac{dA_H}{dt} = \lambda_H S_H - (\sigma_H + \mu_H) A_H,$$

$$\frac{dI_H}{dt} = \sigma_H A_H - \mu_H I_H,$$
$$\text{(5)}$$

$$\frac{dS_V}{dt} = \Pi_V - \lambda_V S_V - (\mu_V + \upsilon_V) S_V,$$

$$\frac{dE_V}{dt} = \lambda_V S_V - (\sigma_V + \mu_V + \upsilon_V) E_V,$$

$$\frac{dI_H}{dt} = \sigma_V E_V - (\mu_V + \upsilon_V + \delta_V) I_V.$$

It can be shown that the biologically-relevant region

$$\Gamma = \left\{ \begin{array}{l} (S_H, A_H, I_H, S_V, E_V, I_V) \in \mathbb{R}_+^6 : \\ S_H + A_H + I_H \leq \dfrac{\Pi_H}{\mu_H}; SV + EV + IV \leq \dfrac{\Pi_V}{\mu_V + \upsilon_V} \end{array} \right\}$$

Is positively-invariant and attracting with respect to treatment-free model.

Disease-free equilibrium (DFE)

The disease-free equilibrium (DFE) of treatment-free model (5) is given by

$$E_0 = (S_H, A_H, I_H, S_V, E_V, I_V) = \left(\frac{\Pi_H}{\mu_H}, 0, 0, \frac{\Pi_V}{\mu_V + \upsilon_V}, 0, 0 \right)$$

Following Vanden [31], the linear stability of E_0 can be established using the next generation operator method on system. The matrices, F_1 (for the new infection terms) and V_1 (of the transition terms) are given, respectively, by

$$F_1 = \begin{bmatrix} 0 & 0 & C_{HV}\eta_V & C_{HV} \\ 0 & 0 & 0 & 0 \\ \frac{\mu_H C_{HV}\eta_A S_V^*}{\Pi_H} & \frac{\mu_H C_{HV} S_V^*}{\Pi_H} & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix}$$

$$V_1 = \begin{bmatrix} T_1 & 0 & 0 & 0 \\ -\sigma_H & \mu_H & 0 & 0 \\ 0 & 0 & T_2 & 0 \\ 0 & 0 & -\sigma_V & T_3 \end{bmatrix}$$

where,

$T_1 = \sigma_H + \mu_H, \quad T_2 = \sigma_V + \mu_V + \upsilon_V$
and $T_3 = \mu_V + \upsilon_V + \delta_V$.

It then follow that the *basic reproduction number*, denoted by $\Re_0$, is given by

$$\Re_0 = \rho(F_1 V_1^{-1}) = \sqrt{\frac{C_{HV}^2 \Pi_V (\eta_A \mu_H + \sigma_H)(\eta_V T_3 + \sigma_V)}{\Pi_H (\mu_V + \upsilon_V) T_1 T_2 T_3}},$$

where ρ is the spectral radius (dominant eigenvalue in magnitude) of the next generation matrix $F_1 V_1^{-1}$. Hence, using Theorem 2 of Vanden [31], we have established the following result:

Lemma 2 The disease free equilibrium, E_0, of the model (5), is locally asymptotically stable (LAS) if $\Re_0 < 1$, and unstable if $\Re_0 > 1$.

The threshold quantity $\Re_0$, is the *basic reproduction number* of the disease (Anderson [1, 2] and Hethcote [21]). It represents the average number of secondary cases that one infected case can generate if introduced into a completely susceptible population. It can be interpreted as follows. Susceptible mosquitoes can acquire infection following effective contact with either an asymptomatically (A_H) or symptomatically infected human (I_H). The number of vector infections generated by an asymptomatically infectious human (near the DFE) is given by the product of the infection rate $C_{HV}\eta_A\mu_H/\Pi_H$ and the average duration in the A_H class $1/T_1$. Furthermore, the number of vector infections generated by an infectious human (near the DFE) is given by the product of the infection rate of infectious humans $C_{HV}\mu_H/\Pi_H$, the probability that an asymptomatically infectious human survives the asymptomatic stage and move to the symptomatic infectious stage σ_H/T_1 and the average duration in the infectious stage $(1/\mu_H)$. Thus, the average number of new mosquito infections generated by infected humans (asymptomatically or symptomatically) is given by (noting that $S_V = \Pi_V/(\mu_V + \upsilon_V)$

$$C_{HV} \frac{(\eta_A \mu_H + \sigma_H)\Pi_V}{\Pi_H T_1 (\mu_V + \upsilon_V)} \tag{6}$$

Similarly, susceptible humans acquire infection following effective contact with either an exposed (E_V) or infectious mosquito (I_V). The number of human infections generated by an exposed mosquito is the product of the infection rate of exposed mosquito $(C_{HV}\eta_V\mu_H/\Pi_H)$ and the average duration in the exposed class $(1/T_2)$. The number of human infections generated by an infectious mosquito is the product of the infection rate of infectious mosquitoes $C_{HV}\mu_H/\Pi_H$, the probability that an exposed mosquito survives the exposed class and move to the infectious stage σ_V/T_2 and the average duration in the infectious stage $(1/T_3)$. Thus, the average number of new human infections generated by an infected mosquito (exposed or infectious) is given by (noting that $S_H^* = \Pi_H/\mu_H$)

$$C_{HV} \frac{(\eta_A T_3 + \sigma_V)\Pi_V}{T_2 T_3}. \tag{7}$$

The geometric mean of (6) and (7) gives the basic reproduction number, $\Re_0$ (interpretation for $\Re_0$, for dengue disease is also given in Chowell [8], Esteva [11]).

The epidemiological implication of Lemma 2 is that, in general, when $\Re_0$ is less than unity, a small influx of infected mosquitoes into the community would not generate large outbreaks, and the disease dies out in time (since the DFE is LAS).

Global stability of disease-free equilibrium

Theorem 1

The disease-free equilibrium E_0 of the treatment-free model is globally asymptotically stable (GAS) if $\Re_0 < 1$.

Proof: the proof is based on using the following Lyapunov function.

$$f = g_1 A_H + g_2 I_H + g_3 E_V + g_4 I_V$$

Where,

$$g_1 = C_{HV} \Pi_V T_3 (\eta_V T_3 + \sigma_v)(\eta_H \mu_H + \sigma_H),$$
$$g_2 = C_{HV} \Pi_V T_1 T_3 (\eta_V T_3 + \sigma_v),$$
$$g_3 = \Pi_H \mu_V T_1 T_3 \Re_0 (\eta_V T_3 + \sigma_v),$$
$$g_4 = \Pi_H \mu_V T_1 T_2 T_3 \Re_0.$$

The Lyapunov derivatives is given by (where a dot represent differentiation with respect to t)

$$\dot{f} = g_1 \dot{A}_H + g_2 \dot{I}_H + g_3 \dot{E}_V + g_4 \dot{I}_V,$$

$$\dot{f} = T_1 T_2 \left[\frac{C_{HV} \Pi_V \mu_H (\eta_V T_3 + \sigma_v)(\eta_A A_H + I_H)+}{\Pi_H \mu_V T_2 T_3 \Re_0 (\eta_V E_V + I_V)} \right] (\Re_0 - 1).$$

Thus $\dot{f} \le 0$ if $\Re_0 \le 1$ with $\dot{f} = 0$ if and only if $A_H = I_H = E_V = I_V = 0$. Further, the largest compact invariant set in $\{ (S_H, A_H, I_H, S_V, E_V, I_V) \in \Gamma : \dot{f} = 0 \}$ is the singleton $\{E_0\}$. It follows from LaSalle Invariance Principle that every solution to equation (5) with initial condition in Γ converges to DFE E_0 as $t \to \infty$. That is, $(A_H(t), I_H(t), E_V(t), I_V(T)) \to (0,0,0,0)$ as $t \to \infty$. Substituting $A_H = I_H = E_V = I_V = 0$ into the first and the fourth equations of the treatment-free model (5) gives $S_H(t) \to S_H^*$ and $S_v(t) \to S_V^*$ as $t \to \infty$. Thus:

$$(S_H(t), A_H(t), I_H(t), S_V(t), E_V(t), I_V(T)) \to (S_H^*, 0, 0 S_V^*, 0, 0)$$

as $t \to \infty$ for $\Re_0 < 1$, so that E_0 is GAS in Γ^* if $\Re_0 \le 1$.

The above result show that, for the model, dengue disease can be eliminated from the community if the associated threshold quantity, $\Re_0$, can be brought to a value less than unity. It also shows that, for the dengue treatment-free model the classical epidemiological requirement of $\Re_0 < 1$ is both necessary and sufficient for dengue elimination from the community.

Endemic equilibrium

The non-trivial equilibria of the model, where at least one of the infected variables is non-zero, can be obtained by solving the equations in at steady state. Let $E_0^* = \left(S_H^{**}, A_H^{**}, I_H^{**}, S_V^{**}, E_V^{**}, I_V^{**} \right)$ represents any arbitrary endemic equilibrium of the model. Further, let

$$\lambda_H^{**} = C_{HV} \frac{\mu_H (\eta_V E_V^{**} + I_H^{**})}{\Pi_H} \quad \text{and}$$

$$\lambda_V^{**} = C_{HV} \frac{\mu_H (\eta_A A_H^{**} + I_H^{**})}{\Pi_H} \tag{8}$$

be the forces of infection in humans and vectors at steady state, respectively. Solving the equations of the model at steady state gives

$$S_H^{**} = \frac{\Pi_H}{\lambda_H^{**} + \mu_H}, \quad A_H^{**} = \frac{\lambda_H^{**} \Pi_H}{T_1 (\lambda_H^{**} + \mu_H)},$$

$$I_H^{**} = \frac{\sigma_H \lambda_H^{**} \Pi_H}{\mu_H T_1 (\lambda_H^{**} + \mu_H)}, \quad S_V^{**} = \frac{\Pi_V}{\lambda_V^{**} + \mu_V + \upsilon_V}, \tag{9}$$

$$E_V^{**} = \frac{\lambda_V^{**} \Pi_V}{T_2 (\lambda_V^{**} + \mu_V + \upsilon_V)}, \quad I_V^{**} = \frac{\sigma_V \lambda_V^{**} \Pi_V}{T_2 T_3 (\lambda_V^{**} + \mu_V + \upsilon_V)}.$$

Non-existence of endemic equilibria for $\Re_0 \le 1$

In this section, the non-existence of endemic equilibria of the model when $\Re_0 \le 1$, will be explored. We claim the following:

Theorem 2 The dengue treatment-free model, given by (5), has no endemic equilibrium when $\Re_0 \le 1$, and has a unique endemic equilibrium otherwise.

Proof Using (9) in the expression for λ_H^{**} and λ_V^{**} in (8) and simplifying shows that the non zero (endemic) equilibria of the model satisfy the following linear equation

$$a_{11} \lambda_H^{**} + b_{11} = 0,$$

where

$$a_{11} = \Pi_H \mu_H T_2 T_3 \left[C_{HV} (\eta_A \mu_H + \sigma_H) + T_1 (\mu_V + \upsilon_V) \right],$$
$$and \ b_{11} = \Pi_H \mu_H^2 T_1 T_2 T_3 (1 - \Re_0^2)$$

It is clear that $a_{11} > 0$, and $b_{11} < 0$ whenever $\Re_0 > 1$. Thus, the basic linear system has a unique positive solution, given by $\lambda_H^{**} = b_{11}/a_{11}$ whenever $\Re_0 > 1$. Therefore the treatment-free model, has a unique positive endemic equilibrium whenever $\Re_0 > 1$. and no positive endemic equilibrium whenever $\Re_0 \le 1$.

Analysis of the treatment model

Consider, now, the full treatment model, given by with similar assumption of dengue-induced mortality rate negligible $(\delta_H = 0)$. Setting $N_H = \Pi_H / \mu_H$ and $\delta_H = 0$ in model (4) gives the following reduced model:

$$\frac{dS_H}{dt} = \Pi_H - \lambda_H S_H - \mu_H S_H,$$

$$\frac{dA_H}{dt} = \lambda_H S_H - (\sigma_H + \mu_H)A_H,$$

$$\frac{dI_H}{dt} = \sigma_H A_H - (\tau_H + \mu_H + \delta_H)I_H,$$

$$\frac{dT_H}{dt} = \tau_H S_H - (\gamma_H + \mu_H)T_H,$$

$$\frac{dF_H}{dt} = \gamma_H T_H - (\mu_H + \delta_H)F_H, \qquad (10)$$

$$\frac{dS_V}{dt} = \Pi_V - \lambda_V S_V - (\mu_V + \upsilon_V)S_V,$$

$$\frac{dE_V}{dt} = \lambda_V S_V - (\sigma_V + \mu_V + \upsilon_V)E_V,$$

$$\frac{dI_H}{dt} = \sigma_V E_V - (\mu_V + \upsilon_V + \delta_V)I_V.$$

Existence and stability of equilibria disease-free equilibrium (DFE)

The model has a DFE given by,

$$E_T = (S_H, A_H, I_H, T_H, F_H, S_V, E_V, I_V) = \left(\frac{\Pi_H}{\mu_H}, 0, 0, 0, 0, \frac{\Pi_V}{\mu_V + \upsilon_V}, 0, 0\right),$$

and the associated next generation matrices are given by

$$F_T = \begin{bmatrix} 0 & 0 & 0 & 0 & C_{HV}\eta_V & C_{HV} \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ \frac{\mu_H C_{HV}\eta_A S_V^*}{\Pi_H} & \frac{\mu_H C_{HV} S_V^*}{\Pi_H} & 0 & \frac{\mu_H C_{HV}\eta_F S_V^*}{\Pi_H} & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \end{bmatrix}$$

$$V_T = \begin{bmatrix} P_1 & 0 & 0 & 0 & 0 & 0 \\ -\sigma_H & P_2 & 0 & 0 & 0 & 0 \\ 0 & -\tau_H & P_3 & 0 & 0 & 0 \\ 0 & 0 & -\gamma_H & \mu_H & 0 & 0 \\ 0 & 0 & 0 & 0 & P_4 & 0 \\ 0 & 0 & 0 & 0 & -\sigma_V & P_5 \end{bmatrix},$$

where,

$$P_1 = \sigma_H + \mu_H, \ P_2 = \mu_H + \tau_H, P_3 = \gamma_H + \mu_H,$$

$$P_4 = \sigma_V + \mu_V + \upsilon_V \text{ and } P_5 = \mu_V + \upsilon_V + \delta_V.$$

It follows then that the basic reproduction number, denoted by $\Re_T$, is given by

$$\Re_T = \sqrt{\frac{C_{HV}^2 \Pi_V (\eta_V P_5 + \sigma_V)[\mu_H P_3(\eta_A P_2 + \sigma_H) + \eta_F \gamma_F \tau_H \sigma_H]}{\Pi_H(\mu_V + \upsilon_V)P_1 P_2 P_3 P_4 P_5}},$$

Hence, using Theorem 2 of Vanden [31], we have established the following result:

Lemma 3 The disease free equilibrium, E_T, of the model is locally asymptotically stable (LAS) if $\Re_T < 1$, and unstable if $\Re_T > 1$.

Global Stability of disease-free equilibrium

The disease-free equilibrium, E_T, of the treatment model, is globally asymptotically stable (GAS) in D if $\Re_T \leq 1$.

The proof is based on using a comparison theorem. Notice, first of all, that the equations for the infected components in can be written in terms of FV^{-1} matrix.

Endemic equilibrium

In order to find endemic equilibria of the treatment model (that is, equilibria where at least one of the infected components of the model is non-zero), the following steps are taken. Let

$$E_T^* = \left(S_H^{**}, A_H^{**}, I_H^{**}, T_H^{**}, F_H^{**}, S_V^{**}, E_V^{**}, I_V^{**}\right)$$

represents any arbitrary endemic equilibrium of the model . Further, let

$$\lambda_H^{**} = C_{HV}\frac{\mu_H(\eta_V E_V^{**} + I_H^{**})}{\Pi_H} \text{ and }$$

$$\lambda_V^{**} = C_{HV}\frac{\mu_H(\eta_A A_H^{**} + I_H^{**} + \eta_F F_H^{**})}{\Pi_H} \qquad (11)$$

be the forces of infection of humans and vectors at steady state, respectively. Solving the equations in (10) at steady state gives

$$S_H^{**} = \frac{\Pi_H}{\lambda_H^{**} + \mu_H}, \quad A_H^{**} = \frac{\lambda_H^{**}\Pi_H}{P_1(\lambda_H^{**} + \mu_H)},$$

$$I_H^{**} = \frac{\sigma_H \lambda_H^{**}\Pi_H}{P_1 P_2(\lambda_H^{**} + \mu_H)}, \quad T_H^{**} = \frac{\tau_H \sigma_H \lambda_H^{**}\Pi_H}{P_1 P_2 P_3(\lambda_H^{**} + \mu_H)},$$

$$F_H^{**} = \frac{\gamma_H \tau_H \sigma_H \lambda_H^{**}\Pi_H}{P_1 P_2 P_3 \mu_H(\lambda_H^{**} + \mu_H)}, \quad S_V^{**} = \frac{\Pi_V}{\lambda_V^{**} + \mu_V + \upsilon_V}, \qquad (12)$$

$$E_V^{**} = \frac{\lambda_V^{**}\Pi_V}{P_4(\lambda_V^{**} + \mu_V + \upsilon_V)}, \quad I_V^{**} = \frac{\sigma_V \lambda_V^{**}\Pi_V}{\lambda_V^{**} + \mu_V + \upsilon_V}.$$

Substituting the expressions in (12) into (11), and simplifying, it follows that the non-zero equilibria

of the treatment model satisfy the quadratic

$$\lambda_H^{**}\left(a_{22}\lambda_H^{**}+b_{22}\right)=0,\qquad(13)$$

where,

$$a_{22}=\Pi_H P_4 P_5\left[\begin{array}{l}C_{HV}P_3\mu_H\left(\eta_{AP2}+\sigma_H\right)+\\P_1 P_2 P_3\left(\mu_V+\upsilon_V\right)+C_{HV}\eta_F\gamma_H\tau_H\sigma_H\end{array}\right]$$

and

$$b_{22}=\Pi_H\mu_H P_1 P_2 P_3 P_4 P\left(\mu_V+\upsilon_V\right)\left(1-\Re_T^2\right).$$

The positive endemic equilibrium of the model can be obtained by solving for $\hat{\lambda}_H^{**}$ in (13) and substituting the result into (12). Clearly, $\hat{\lambda}_H^{**}=0$ is a fixed point of (13) which corresponds to the DFE, E_T. For $\hat{\lambda}_H^{**}\neq 0$ equation can be reduced to

$$a_{22}\lambda_H^{**}+b_{22}=0.$$

Since all the model parameters are assumed to be non-negative, it follows that $a_{22}>0$ and $b_{22}<0$ whenever $\Re_T>1$. Thus, the linear equation has a unique positive solution, given by $\lambda_H^{**}=b_{22}/a_{22}$, whenever $\Re_T>1$, and no positive solution when $\Re_T<1$. This solution is summarized below.

Lemma 4 The model has a unique positive endemic equilibrium whenever $\Re_T>1$.

It can be shown, using the same approach as in the proof of Theorem 3, that the unique endemic equilibrium, E_T, is LAS whenever $\Re_T>1$.
In summary, it is clear that the treatment model has the same dynamical features as the treatment-free model (i.e., both models have globally-asymptotically stable DFE whenever the associated reproduction number is less than unity; and unique locally-asymptotically stable endemic equilibrium whenever the reproduction number exceeds unity). Thus, adding treatment to the model does not alter its dynamical features.

Numerical simulations

Since both models have been shown to exhibit similar qualitative dynamical features. Consequently, numerical simulations will be carried out on the treatment model. With the set of parameters in Table 2, the basic reproduction numbers $\Re_T=0.0547$ so that $\Re_T<1$). Thus by Theorem 5, the DFE is GAS Figure 2 depicts

simulation of this model when $\Re_T<1$. This result also holds for $\Re_T=1$, confirming the global asymptotic stability property of the DFE whenever $\Re_T\leq 1$.

It is also shown that, with the set of parameters in Table 2, and $\tau_H=0.1$, the prevalence of the infected individual is lower when an effective treatment strategy is applied (i.e, $\tau_H=0.99$), compared with less effective treatment method (i.e., $\tau_H=0.1$) as depicted in Figure 3A. Similarly, the number of treated individual is higher when $\tau_H=0.99$ and lower when $\tau_H=0.1$, as shown in Figure 3B, confirming the positive epidemiological impact of dengue treatment in the community (by reducing disease burden). Using the set of parameter in Table 2 and different values of (υ_V), it is shown that with a higher and effective mosquito control strategy, the population of susceptible and exposed mosquitoes is lower $(\upsilon_V=5)$, compared with less effective mosquito control strategy $(\upsilon_V=0.5)$ as shown in Figure 4A-B.

Conclusions

This paper presents a deterministic model for the transmission dynamics of a single strain of dengue disease. The model, which allows dengue transmission by exposed vectors, was extended to include treatment for dengue. The two models were rigorously analysed to gain insights into their qualitative dynamics. The following results were obtained:

i. The basic (treatment-free) model has a locally stable disease-free equilibrium whenever the *associated reproduction number* is less than unity.

ii. The treatment model, like the treatment-free model, has a globally-stable DFE whenever their associated reproduction number is less than unity.

iii. Each of the models has a unique endemic equilibrium whenever their associated reproduction number exceeds unity.

iv. Dengue treatment would always have positive epidemiological impact in the community (by reducing disease burden), or even disease elimination in the community.

v. Simulation of the treatment model shows that the use of vector control strategies can result in the effective control of dengue in a community by reducing the population

of susceptible and exposed mosquitoes.

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Table 1: Description of variables and parameters of the models

| Parameter	Interpretation	Nominal vaue
S_H	Susceptible humans	variable
A_H	Asymptomatically infected humans	variable
I_H	Symptomatically infected humans	variable
T_H	individuals in treatment class	variable
F_H	individuals in whom treatment fails	variable
S_H	Susceptible mosquitoes	variable
E_H	Exposed mosquitoes	variable
A_H	Infectious mosquitoes	variable
b_I	Biting rate of infectious mosquitoes	5 /day
b_S	Biting rate of susceptible mosquitoes	5/day
ρ_{VH}	Transmission probability from mosquitoes to humans	0.5
ρ_{HV}	Transmission probability from humans to mosquitoes	0.5
c_{VH}	Infection rate of humans	3.6/day
c_{HV}	Infection rate of mosquitoes	3.6 /day
Π_H	Recruitment rate of humans	50000/day
Π_V	Recruitment rate of mosquitoes	400000/ day
$\frac{1}{\phi_H}$	Average lifespan of humans	67 years
$\frac{1}{\phi_V}$	Average lifespan of mosquitoes	14 days
σ_H	Progression rate from A_H to I_H class	0.0548/ day
σ_V	Progression rate from E_V to I_V class	0.0384 /day
δ_H	Disease-induced death rate for humans	0.0005/ day
δ_V	Disease-induced death rate for mosquitoes	0.6 /day
τ_H	Treatment rate for humans	0.99/ day
γ_H	Failed treatment rate for humans	0.5 /day
υ_v	Vector control induced death for mosquitoes	0.5/ day
η_A, η_V	Modification parameters	
η_F	Relative risk of infectiousness of individuals in whom treatment fails	0.6 /day
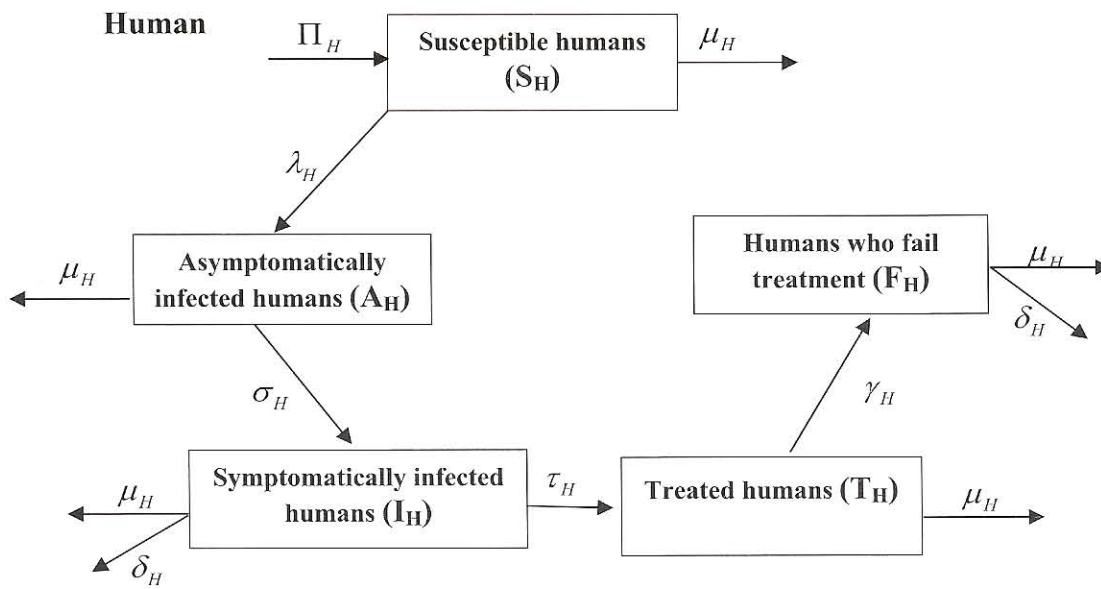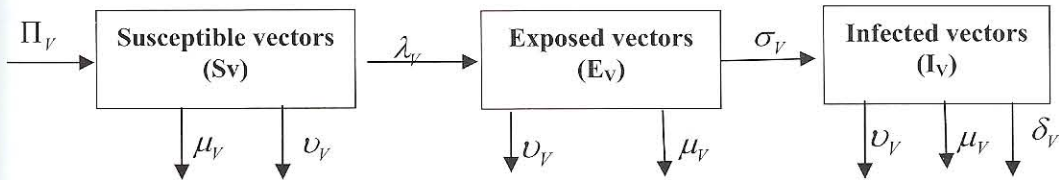
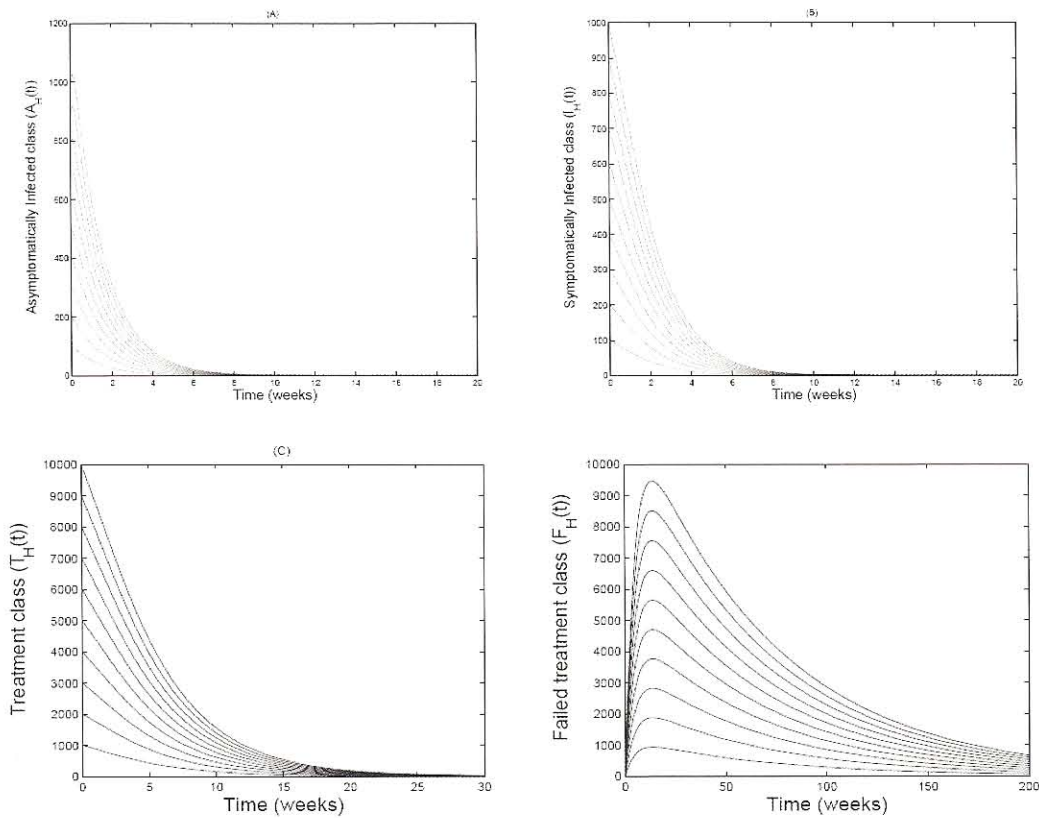**Figure 1:** Schematic diagram of the model

Figure 2: Time series plots for the model (16). (A) Asymptomatically infected individuals (A_H); (B) Symptomatically infected individuals (I_H); (C) Treated individuals (T_H); and (D) Individuals in whom treatment fails (F_H). Parameter values used are as in Table 2 with $\sigma_2 = 0.09$ (so that $\Re_T = 0.0547 < 1$)
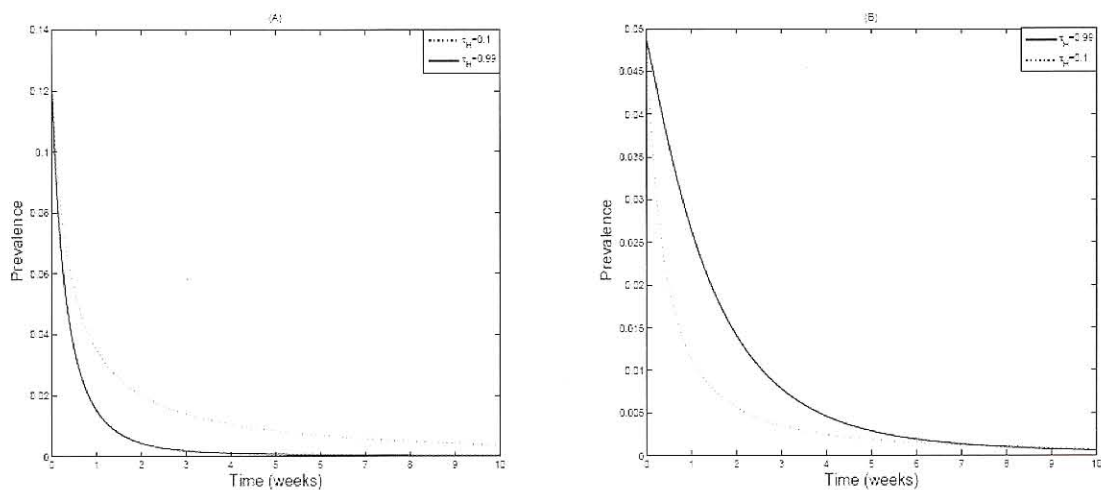

Figure 3: Prevalence as a function of time for the treatment model (16). (A) Symptomatically infected individuals (I_H); (B) Treated individuals (T_H); using various values of treatment rate ($\tau_H = 0.10$ (dotted line) and $\tau_H = 0.99$ (solid line)). Other parameter values used are as in Table 2.
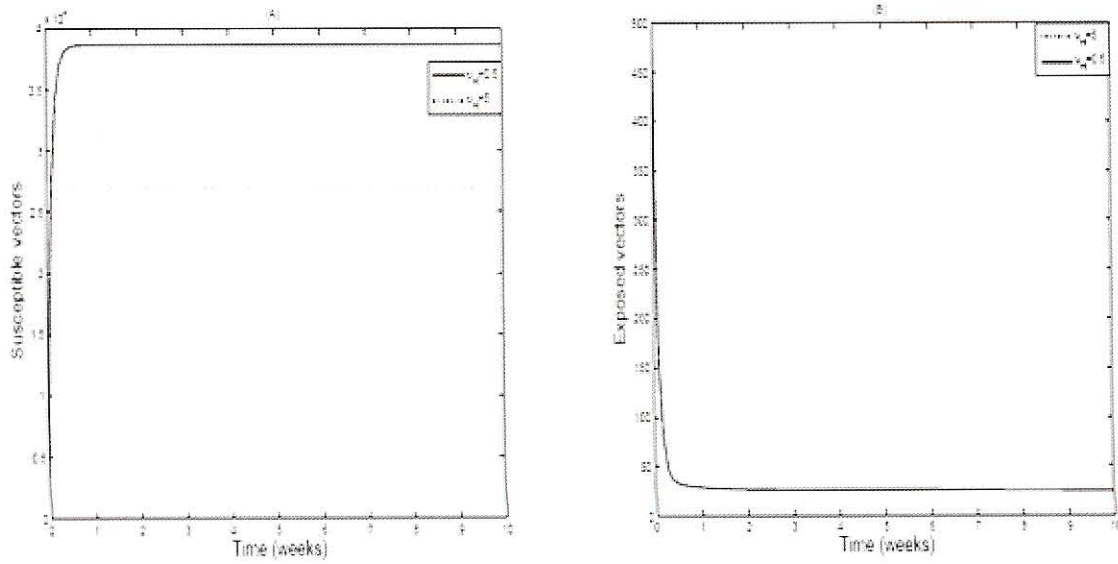
Figure 4: Graph that show the dynamics of (A) Susceptible mosquitoes (B) exposed mosquitoes using different mosquitoes control strategies for the treatment model (16). $v_H = 0.5$ (solid line). Other parameter values used are as in Table 2.