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TRANSMISSION DYNAMICS OF DENGUE IN COSTA RICA: THE ROLE OF HOSPITALIZATIONS

DINÁMICA DE LA TRANSMISIÓN DE DENGUE EN COSTA RICA: EL ROL DE LAS HOSPITALIZACIONES

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Abstract

For decades, dengue virus has caused major problems for public health officials in tropical and subtropical countries around the world. We construct a compartmental model that includes the role of hospitalized individuals in the transmission dynamics of dengue in Costa Rica. The *basic reproductive number*, $\mathcal{R}_0$, is computed, as well as a sensitivity analysis on $\mathcal{R}_0$ parameters. The global stability of the disease-free equilibrium is established. Numerical simulations under specific parameter scenarios are performed to determine optimal prevention/control strategies.

Keywords: dengue fever; mathematical modeling; epidemic model; vector-borne diseases.

Resumen

Durante décadas, el virus del dengue ha causado grandes problemas a los funcionarios de salud pública en países tropicales y subtropicales de todo el mundo. Construimos un modelo compartimental que incluye el papel de las personas hospitalizadas en la dinámica de transmisión del dengue en Costa Rica. Calculamos el *número básico reproductivo*, $\mathcal{R}_0$, así como un análisis de sensibilidad en los parámetros de $\mathcal{R}_0$ y discutimos la importancia de las políticas de salud pública. Se establece la estabilidad local y global del estado libre de enfermedad. Se hacen simulaciones numéricas bajo escenarios específicos para determinar estrategias óptimas de prevención y control.

Palabras clave: dengue; modelo matemático; modelo epidémico; enfermedades vectoriales.

Mathematics Subject Classification: 93A30, 92B99, 37N25.

1 Introduction

Dengue is a vector-borne viral infection that inflicts substantial health, economic, and social burden to more than 100 countries in tropical and subtropical regions around the world [5]. Globalization, climate change, unplanned urbanization, and insufficient mosquito control programs [17, 32], are among the complex factors that have contributed to the geographic expansion and rise in the global incidence of a disease, that is now causing an estimated 390 million infections annually, of which an approximated 96 million have clinical manifestations [4].

The highly anthropophilic *Aedes aegyti* mosquito, is the predominant vector [36] of the four dengue viruses (DENV-1, DENV-2, DENV-3, and DENV-4)

[18], while *Aedes albopictus* is considered a secondary and less efficient in urban settings [38]. Both mosquitoes have adapted to local human habitation with oviposition and larval habitats in natural and artificial collection [25]. Both species are also day-biting mosquitoes, exhibiting two main peaks of activity, one in the early morning and other in the late afternoon [44], with a flight range that is usually limited in or around the locations where they emerged as adults [20].

Under natural conditions, a susceptible mosquito can acquire the DENV after it has taken a blood meal from a viremic individual [8], making humans the main host of the DENV [53]. Within a day before or after the onset of symptoms most individuals become infectious, as levels of viremia are high enough to infect a mosquito [19], this period of infectivity lasts an average of 7-12 days [52]. After the incubation period (8-10 days), the infected *Aedes* mosquito can transmit the DENV to susceptible individuals for the remainder of its life [52]. In Figure 1, we present the DENV transmission cycle.

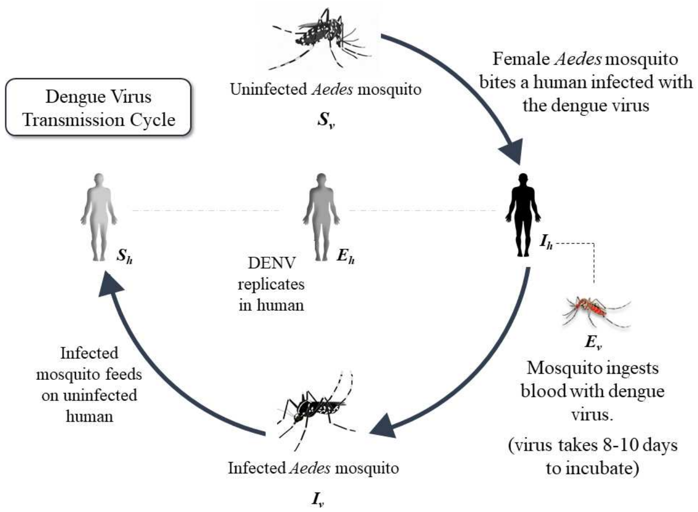


Figure 1: Dengue virus transmission cycle. The DENV transmission cycle involves mosquitoes and humans, with humans as the main carriers of the virus, serving as a source of the DENV for uninfected mosquitoes [52].

After the bite of an infected mosquito, the majority of individuals will be asymptomatic, and a silent reservoir of crucial importance in dengue dynamics [13]. In those individuals that do experience symptoms the most common outcome is a self-limiting febrile illness that does not progress to a more severe form, and do not need admission to a hospital. Those that evolve, and require hospitalization show a variety of warning signs such as constant and intense abdominal pain, persisting vomiting, ascitis, pleural o pericardial effusion, mucosal bleeding, lethargy, lipothymia, hepatomegaly, and progressive increase in the hematocrit [53]. The disease can also progress to hemorrhagic and shock complications that can lead to death of the patient [52]. It is estimated that each year, approximately 500,000 cases require hospital care [55].

In Costa Rica, dengue has been a significant public health challenge since 1993, when autochthonous cases were reported on the Pacific coast [31]. Since then, and despite efforts made, dengue infections have been documented annually, with peaks of transmission observed seasonally (within the year) and cyclical every 2-5 years. A total of 376,158 clinically suspected and confirmed cases [30] have been reported to the Ministry of Health, of which more than 45,000 cases have required hospital care [30, 7]. DENV-1, DENV-2 and DENV-3 have circulated the country in different time periods and 1,196 of the total of cases, have been classified as severe dengue, which have lead to 23 deaths [30].

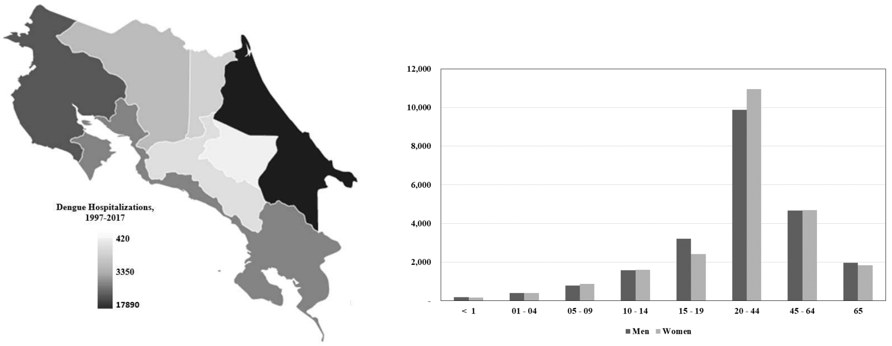
In order to better understand the interactions between the vector, the virus and the host, mathematical models play a significant role in understanding dengue dynamics. In this article we develop a compartmental model that analyzes the effect of discriminating the hospitalized infected individuals, therefore temporarily isolated, and its role on the overall behavior of dengue dynamics in Costa Rica, which can provide information for public health authorities to implement optimal prevention and control approaches. As previous studies have shown, the role of hospitalized patients could affect the transmission dynamics of dengue infections, as hospital admission could decrease the transmission rate of severely affected symptomatic individuals [33, 2].

The article is divided in the following sections. In Section 2, we introduce a compartmental model that describes the transmission dynamics of dengue fever; Section 3, presents the results of the model and numerical simulations; in Section 4, we give a discussion and concluding remarks.

2 Model

We introduce a model that describes the dynamics of dengue between hosts and mosquitoes in Costa Rica that includes the role of hospitalizations. According to data provided by the Costa Rican Social Security Fund (CCSS), during the last two decades, a total of 45,577 patients with DENV infections, have required hospital care services [7], which represents 13% of the total of reported confirmed and suspected cases reported during that same period. In Figure 2, we illustrate the concentration of hospitalizations due to the DENV in the country.

As seen in the map, the vast majority of hospitalized patients were reported from regions near the coasts, where climate conditions are ideal for mosquito prevalence and with circulation of the other two arboviruses, zika and chikungunya. Limón, a province located in the Caribbean coast, reported a total of 17,894 hospitalized cases, follow by Guanacaste with 12,233 cases and Puntarenas with 8,244 cases, both of them located in the Pacific coast. Patients in the age group of 20-44 represented 43.8% of the total of hospitalized patients and no significant difference between men and women was observed [7].



(a) Dengue hospitalizations by region, Costa Rica 1997-2017.

(b) Dengue hospitalizations by sex and age group, Costa Rica 1997-2017.

Figure 2: Hospitalizations by regions (a) and by sex (b) in Costa Rica. The vast majority of hospitalizations were reported in the coastal regions. These areas, are characterized by been highly infested by the *Aedes* mosquito and by having higher incidence of dengue cases throughout the year [7].

Throughout these 26 years, Costa Rica, has presented several epidemic peaks. The largest on record was reported in 2013, with almost 50,000 cases reported to the Ministry of Health, 6,530 of which require hospital care. Before 2013, there was a major outbreak in 2005, with 37,798 cases and 6,319 hospitalized patients [30, 7]. According to the dengue guidelines for Costa Rica, patients who meet the criteria for hospital management are, ideally, admitted in a dengue attention unit. This unit is provided with the necessary resources for dengue treatment, where doors and windows remain close and with sieves, to decrease the risk of further contact with *Aedes* mosquitoes [6].

Our model transitions (see Figure 3) represent the interactions between susceptible individuals (S_h) that can become infected by having contact with an infected mosquito (I_v/N_v), once the individual acquires the virus from the mosquito the individual becomes latent (E_h) and can transition to the infected class (I_h) or if the symptoms are strong enough, to the hospitalized class (H).

Also, individuals who are infected (I_h) can develop strong symptoms and transition to the hospitalized class (H). From the hospitalized and infected classes individuals recover (R_h). In the mosquito model: susceptible mosquitoes (S_v) can become latent (E_v) via feeding (biting a human) and after the latency period become infectious (I_v). It is important to note that mosquitoes can come in contact with infected humans (I_h), as well as hospitalized individuals ($(1-\eta)H$). The interaction between mosquitoes and hospitalized individuals has a reduction factor based on the hospitalization effectiveness. Model state variables are presented in Table 1. The following is the system of nonlinear differential equations:

$$\begin{array}{rcl} S_h' &=& \mu_h N_h - \beta_{hv} S_h \frac{I_v}{N_v} - \mu_h S_h, \\ E_h' &=& \beta_{hv} S_h \frac{I_v}{N_v} - (\mu_h + \alpha_h) E_h, \\ I_h' &=& (1-p)\alpha_h E_h - (\mu_h + \gamma + \delta) I_h, \\ H' &=& p\alpha_h E_h + \delta I_h - (\mu_h + \gamma) H, \\ R_h' &=& \gamma I_h + \gamma H - \mu_h R_h, \\ S_v' &=& \mu_v N_v - \beta_{vh} S_v \frac{(I_h + (1-\eta)H)}{N_h - \eta H} - \mu_v S_v, \\ E_v' &=& \beta_{vh} S_v \frac{(I_h + (1-\eta)H)}{N_h - \eta H} - (\mu_v + \alpha_v) E_v, \\ I_v' &=& \alpha_v E_v - \mu_v I_v, \end{array} \tag{1}$$

where $N_h = S_h + E_h + I_h + H + R_h$ and $N_v = S_v + E_v + I_v$ and each variable is described in Table 1 and their respective parameters in Table 2. The model diagram is presented in Figure 3.

Table 1: Model variables.

State Variable	Description
S_h	Susceptible individuals
E_h	Exposed individuals (infected but not infectious)
I_h	Infected individuals
H	Hospitalized individuals
R_h	Recovered individuals
S_v	Susceptible vectors
E_v	Exposed vectors (infected but not infectious)
I_v	Infected vectors

Table 2: Model parameters and description. All parameters are in days^{-1}, except for η and p that are dimensionless.

Parameter	Description
β_{hv}	Transmission rate (host-vector)
β_{vh}	Transmission rate (vector-host)
α_h	Per capita exposed rate of humans
α_v	Per capita exposed rate of vectors
δ	Per capita hospitalization rate after infection (undiagnosed)
γ	Per capita recovery rate of humans
p	Proportion of individuals being hospitalized (diagnosed)
η	Effectiveness of hospitalization (dimensionless)
μ_h	Per capita mortality rate of humans
μ_v	Per capita mortality rate of vectors

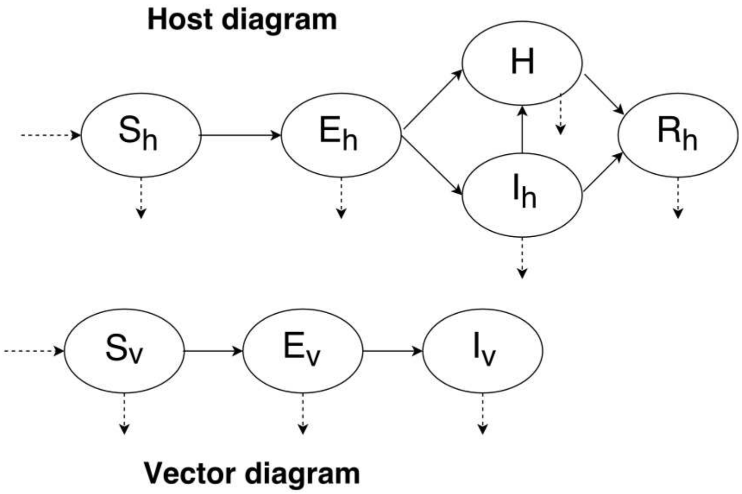


Figure 3: Model diagram.

We assume the host and mosquito populations remain constant in time, moreover we can have the following re-scaled variables, $s_h = \frac{S_h}{N_h}$, $e_h = \frac{E_h}{N_h}$, $i_h = \frac{I_h}{N_h}$, $\hbar = \frac{H}{N_h}$, $r_h = \frac{R_h}{N_h}$, $s_v = \frac{S_v}{N_v}$, $e_v = \frac{E_v}{N_v}$, $i_v = \frac{I_v}{N_v}$.

Hence, the re-scaled system becomes:

$$\begin{array}{rcl} s_h' &=& \mu_h - \beta_{hv} s_h i_v - \mu_h s_h, \\ e_h' &=& \beta_{hv} s_h i_v - (\mu_h + \alpha_h) e_h, \\ i_h' &=& (1-p)\alpha_h e_h - (\mu_h + \gamma + \delta) i_h, \\ \hbar' &=& p\alpha_h e_h + \delta i_h - (\mu_h + \gamma)\hbar, \\ r_h' &=& \gamma i_h + \gamma \hbar - \mu_h r_h, \\ s_v' &=& \mu_v - \beta_{vh} s_v \frac{(i_h + (1-\eta)\hbar)}{1-\eta\hbar} - \mu_v s_v, \\ e_v' &=& \beta_{vh} s_v \frac{(i_h + (1-\eta)\hbar)}{1-\eta\hbar} - (\mu_v + \alpha_v) e_v, \\ i_v' &=& \alpha_v e_v - \mu_v i_v, \end{array} \qquad (2)$$

where $s_h + e_h + i_h + \hbar + r_h = 1$ and $s_v + e_v + i_v = 1$.

Theorem 1 *The closed set* $\Omega = \{(s_h, e_h, i_h, \hbar, r_h, s_v, e_v, i_v) \in \Re^8_+ : 0 < s_h + e_h + i_h + \hbar + r_h \leq 1,\ \ 0 < s_v + e_v + i_v \leq 1\}$ *is positively invariant for System 2 and if* y *is any variable of the model and it satisfies that* $y(0) < 0$*, then* $y \to 0$ *as* $t \to \infty$.

Proof.

Let $x_0 \in \Omega$ be the initial state of System 2. To prove this theorem we will show that if $y = 0$, then $y' \geq 0$, where y is any variable of the model.

Assume first that $y = 0$, then notice that, from the model we have that $y' = f(x) - yg(x)$, where x is the state of the system and f is a non-negative function, and g is a positive function. Then it happens that $y' = f(x) \geq 0$ if $y = 0$, therefore $y \geq 0$.

Now, since $s_h + e_h + i_h + \hbar + r_h = 1$ and $s_v + e_v + i_v = 1$ and from the previous step all variables are non-negative, then all variables y satisfy that $y \leq 1$.

Therefore Ω is a positively invariant set for the model. Following from this argument, if $y < 0$, then it happens that $y' = f(x) - yg(x) \geq -yg(x) > 0$ and thus $y \to 0$ as $t \to \infty$. ■

Theorem 2 *The System 2 has exactly one equilibrium point when there is no disease in* $\Omega \in \Re^8_+$.

Proof. The local equilibria $(s_h^*, e_h^*, i_h^*, \hbar^*, r_h^*, s_v^*, e_v^*, i_v^*)$ such that all of the derivatives in System 2 are equal to 0. Some simple algebra leads us to the following relation between exposed individuals on each population:

$$e_h^* = \frac{\beta_h \mu_h \alpha_v}{\mu_h + \alpha_h} \frac{e_v^*}{\mu_h \mu_v + \beta_h \alpha_v e_v^*},$$

where, if

$$\hat{H} = \frac{i_h^*(1-\eta)\hbar^*}{1-\eta\hbar^*},$$

then

$$\frac{e_v^*}{\mu_h\mu_v + \beta_h\alpha_v e_v^*} = \frac{\beta_v\mu_v}{\mu_v+\alpha}\frac{\hat{H}}{\mu_v + \hat{H}\beta_v}.$$

To turn this system into a single variable equation, notice that i_h^* and $\hbar^*$ satisfy the following relationships:

$$\begin{aligned}\hbar^* &= \frac{p\alpha_h e_h^* + \delta i_h^*}{\mu_h+\gamma},\\ i_h^* &= \frac{(1-p)\alpha_h e_h^*}{\mu_h+\gamma+\delta}.\end{aligned}$$

By making those substitutions on $\hat{H}$ and simplifying, we get that:

$$\frac{\hat{H}}{\mu_v+\hat{H}\beta_v} = \frac{e_h^*\Delta_i}{M + e_h^*(\Delta_i - \Delta_v)},$$

where:

$$\begin{aligned}\Delta_i &= (1-p)\alpha_h(\mu_h+\gamma) + (1-\eta)p\alpha_h(\mu_h+\gamma+\delta) + (1-\eta)\delta(1-p)\alpha_h,\\ \Delta_v &= \eta\mu_v\alpha_h(\mu_h+\gamma+\delta) + \eta\mu_v\delta(1-p)\alpha_h,\\ M &= \mu_v(\mu_h+\gamma)(\mu_h+\gamma+\delta).\end{aligned}$$

If we let

$$\begin{aligned}\Gamma_h &= \frac{\beta_h\mu_h\alpha_v}{\mu_h+\alpha_h},\\ \Gamma_v &= \frac{\beta_v\mu_v}{\mu_v+\alpha},\end{aligned}$$

then we get the following equation:

$$e_h^* = \frac{\Gamma_h\Gamma_v\Delta_i e_h^*}{M + e_h^*(\Delta_i - \Delta_v)},$$

which has the following two solutions:

$$\begin{aligned}e_h^* &= 0,\\ e_h^* &= \frac{\Gamma_h\Gamma_v\Delta_i - M}{\Delta_i - \Delta_v},\end{aligned} \tag{3}$$

which correspond to the disease-free and endemic equilibrium points, respectively. If we let e_h^* as any of those values, by simplifying the other equations we get that:

$$\begin{aligned}
s_h^* &= \frac{1}{k_s e_h^* + 1},\\
i_h^* &= k_i e_h^*,\\
\hbar^* &= k_\hbar e_h^*,\\
r_h^* &= k_r e_h^*,\\
s_v^* &= \frac{1}{1 + \kappa_s e_h^*},\\
e_v^* &= \kappa_e e_h^*,\\
i_v^* &= \kappa_i e_h^*,
\end{aligned}$$

where the k's and κ's are parameters. The case $e_h^* = 0$ shows the existence of the disease-free equilibrium point $(1, 0, 0, 0, 0, 1, 0, 0)$. ■

3 Model results

In this section we perform the following analyses for System 2: $\mathcal{R}_0$ calculation, global equilibria of disease free equilibrium, sensitivity analysis, and numerical simulations.

3.1 Basic reproductive number

We compute the *basic reproductive number*, $\mathcal{R}_0$, using the next generation operator [12]. We compute the F matrix where the entries include the transmission terms for both, the host and vector populations,

$$F = \begin{bmatrix} 0 & 0 & 0 & 0 & \beta_{hv} \\ 0 & 0 & \beta_{vh} & \beta_{vh}(1-\eta) & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{bmatrix},$$

and the V matrix that includes the infectious periods of both, the host and vector populations.

$$V = \begin{bmatrix} (\mu_h+\alpha_h) & 0 & 0 & 0 & 0 \\ 0 & (\mu_v+\alpha_v) & 0 & 0 & 0 \\ -\alpha_h(1-p) & 0 & (\mu_h+\gamma+\delta) & 0 & 0 \\ -p\alpha_h & 0 & -\delta & (\mu_h+\gamma) & 0 \\ 0 & \alpha_v & 0 & 0 & \mu_v \end{bmatrix}.$$

We then find V^{-1} and compute $\rho = max\{FV^{-1}\}$, where ρ represents the dominant eigenvalue, and hence, the *basic reproductive number* is given by:

$$\mathcal{R}_0 = \sqrt{\frac{\beta_{hv}}{(\mu_h+\gamma+\delta)}\frac{\beta_{vh}}{\mu_v}\frac{\alpha_h}{(\mu_h+\alpha_h)}\frac{\alpha_v}{(\mu_v+\alpha_v)}\left[\frac{\delta(1-\eta)}{(\mu_h+\gamma)}+(1-\eta p)\right]}.$$

And can be broken down and interpreted as in Table 3.

Table 3: Basic reproductive number factors.

Number	Description
β_{hv}	Transmission rate (host-vector)
$\frac{\alpha_h}{\mu_h+\alpha_h}$	Probability an individual survives the exposed period
$\frac{1}{\mu_h+\gamma+\delta}$	Average human infectious period
β_{vh}	Transmission rate (vector-host)
$\frac{\alpha_v}{\mu_v+\alpha_v}$	Probability a vector survives the exposed period
$\frac{1}{\mu_v}$	Average vector infectious period

We define,

$$\mathcal{R}_u = \frac{\beta_{hv}}{(\mu_h+\gamma+\delta)}\frac{\beta_{vh}}{\mu_v}\frac{\alpha_h}{(\mu_h+\alpha_h)}\frac{\alpha_v}{(\mu_v+\alpha_v)}(1-\eta p),$$

as the contribution of individuals that are infected and undiagnosed. And

$$\mathcal{R}_d = \frac{\beta_{hv}}{(\mu_h+\gamma+\delta)}\frac{\beta_{vh}}{\mu_v}\frac{\alpha_h}{(\mu_h+\alpha_h)}\frac{\alpha_v}{(\mu_v+\alpha_v)}\frac{\delta(1-\eta)}{(\mu_h+\gamma)},$$

as the contributions of individuals that are hospitalized and therefore diagnosed by default.

Therefore, $\mathcal{R}_0$ can be represented by the contributions of individuals that are undiagnosed and hospitalized (diagnosed), respectively. Hence,

$$\mathcal{R}_0 = \sqrt{\mathcal{R}_u + \mathcal{R}_d}.$$

3.2 Global equilibria

In this section we establish the global stability of the disease-free equilibrium using the methods developed in [9].

Theorem 3 *The disease-free equilibrium of System 2 is globally asymptotically stable if* $\mathcal{R}_0 < 1$.

Proof. Let $X \in \mathbb{R}^n$ be the uninfected individuals and $Z \in \mathbb{R}^m$ the infected individuals in the system such that the System 2 is rewritten as:

$$\begin{aligned} \frac{dX}{dt} =& F(X, Z), \\ \frac{dZ}{dt} =& G(X, Z). \end{aligned} \tag{4}$$

Then, if the following conditions are met:

1. $\mathcal{R}_0 < 1$.
2. For $\frac{dX}{dt} = F(X, 0)$, the disease-free equilibrium X^* is globally asymptotically stable.
3. $G(X, Z) = AZ - \hat{G}(X, Z)$, where $A = G_Z(X^*, 0)$ and $\hat{G}(X, Z) \geq 0$ for all (X, Z) where the model makes sense.

Then the disease-free equilibrium is globally asymptotically stable.

By hypothesis, condition (1) is met. In this section we will prove that conditions (2) and (3) are met by our model. First, consider that $X = (s_h, r_h, s_v)$ and $Z = (e_h, i_h, \hbar, e_v, i_v)$, then:

$$F(X, Z) = \begin{pmatrix} \mu_h - \beta_{hv} s_h i_v - \mu_h s_h \\ \gamma i_h + \gamma \hbar - \mu_h r_h \\ \mu_v - \beta_{vh} s_v \frac{i_h + (1-\eta)\hbar}{1 - \eta\hbar} - \mu_v s_v \end{pmatrix},$$

$$G(X, Z) = \begin{pmatrix} \beta_{hv} s_h i_v - (\mu_h + \alpha_h) e_h \\ (1-p)\alpha_h e_h - (\mu_h + \gamma + \delta) i_h \\ p\alpha_h e_h + \delta i_h - (\mu_h + \gamma)\hbar \\ \beta_{vh} s_v \frac{i_h + (1-\eta)\hbar}{1 - \eta\hbar} - (\mu_v + \alpha_v) e_v \\ \alpha_v e_v - \mu_v i_v \end{pmatrix}.$$

For verifying condition (2), note that:

$$F(X,0) = \begin{pmatrix} \mu_h - \mu_h s_h \\ -\mu_h r_h \\ \mu_v - \mu_v s_v \end{pmatrix}.$$

In this case, the equation:

$$\frac{dX}{dt} = F(X,0).$$

Has the solution:

$$X(t) = \begin{pmatrix} 1 + e^{-\mu_h} \\ e^{-\mu_h} \\ 1 + e^{-\mu_v} \end{pmatrix},$$

which satisfies that

$$\lim_{t \to \infty} X(t) = (1,0,1) = X^*.$$

Therefore the disease-free equilibrium X^* is globally asymptotically stable and condition (2) holds. For condition (3), consider the following matrix:

$$A = \begin{pmatrix} -(\mu_h + \alpha_h) & 0 & 0 & 0 & \beta_{hv} \\ (1-p)\alpha_h & -(\mu_h + \gamma + \delta) & 0 & 0 & 0 \\ p\alpha_h & \delta & -(\mu_h + \gamma) & 0 & 0 \\ 0 & \beta_{vh} & \beta_{vh}(1-\eta) & -(\mu_v + \alpha_v) & 0 \\ 0 & 0 & 0 & \alpha_v & -\mu_v \end{pmatrix}.$$

Let:

$$\hat{G}(X,Z) = \begin{pmatrix} \beta_{hv} i_v - \beta_{hv} s_h i_v \\ 0 \\ 0 \\ \beta_{vh}(i_h + (1-\eta)\hbar) - \beta_{vh} s_v \frac{i_h + (1-\eta)\hbar}{1-\eta\hbar} \\ 0 \end{pmatrix}.$$

Note that $s_h \leq 1$ and $\frac{s_h}{1-\eta\hbar} \leq 1$, then $\hat{G}(X,Z) \geq 0$ for all $(X,Z) \in \Omega$, where Ω is given in Theorem (1). Then $G(X,Z) = AZ - \hat{G}(X,Z)$ and condition (3) follows. ■

3.3 Sensitivity analysis

For analyzing the sensitivity of our model, we compute the sensitivity indices of the parameters with respect to $\mathcal{R}_0$ as described in [11]. These indices correspond to the partial derivatives of $\mathcal{R}_0$ with respect to each parameter evaluated on the baseline values found in Table 4. Further discussion with respect to η (effectiveness of hospitalization) and p (proportion of individuals with strong symptoms) is presented in 3.4.

Table 4: Parameters for dengue with baseline values, range and references. Unit of time is days.

Parameter	Baseline	Range	Reference
β_{hv}	0.33	$0.10 - 0.75$	[28]
β_{vh}	0.33	$0.10 - 0.75$	[28]
$1/\alpha_h$	5	$4 - 7$	[28]
$1/\alpha_v$	10	$7 - 14$	[28]
δ	0.20	$0.10 - 5$	[41]
$1/\gamma$	6	$4 - 12$	[28]
p	0.20	$0 - 1$	estimated
η	0.80	$0 - 1$	estimated
$1/\mu_h$	70	$68 - 76$	[11]
$1/\mu_v$	14	$8 - 42$	[28]

Table 5: Sensitivity indices for $\mathcal{R}_0$.

Parameter	Sensitivity index
α_h	$+0.2534$
α_v	$+3.1677$
β_{hv}	$+2.3038$
β_{vh}	$+2.3038$
δ	-1.2037
η	-0.9352
γ	-2.8710
μ_h	-6.4188
μ_v	-15.0783
p	-0.5732

These indices give us an insight on which parameters affect in a more significant manner the value of $\mathcal{R}_0$. Notice the high negative value of the sensitivity index of the mortality rate of the vector μ_v, which is biologically explained by the fact that as the rate in which infected vectors are replaced by susceptible vectors grows, then the incidence of infected hosts is reduced since there are less infected vectors.

Another tool to understand the sensibility of the $\mathcal{R}_0$ value is through the global uncertainty quantification described in [28]. This quantification consists in developing an empirical probability distribution for the $\mathcal{R}_0$ value by assuming the parameters follow a uniform distribution in their ranges displayed in Table 4 and then performing random sampling of those parameters and plugging them in the value of $\mathcal{R}_0$. The probability distribution of $\mathcal{R}_0$ obtained after $100,000$ samples is displayed in Figure 4.

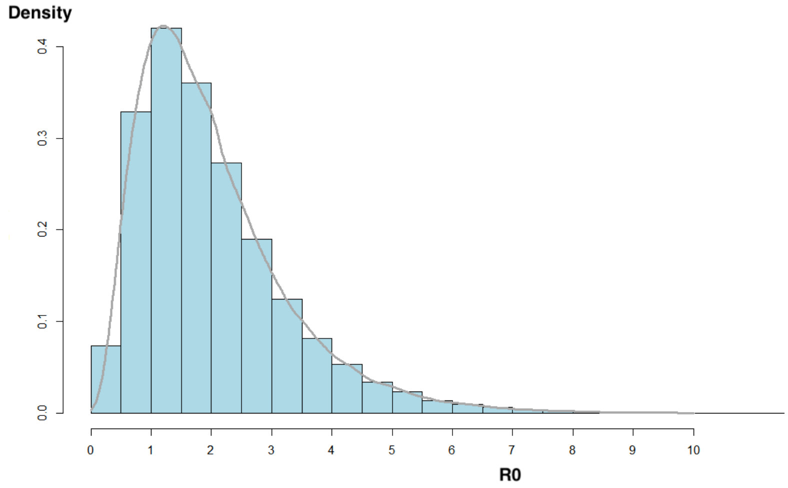


Figure 4: Probability distribution of $\mathcal{R}_0$ after 100,000 samples.

As suggested by Figure 4, the most possible range for the $\mathcal{R}_0$ value lies between 0.5 and 2, which implies that in the case of $\mathcal{R}_0 > 1$, it is likely that by performing tweaks in the parameters (in a real context, that is promoting policies that alter in a real population the values of the parameters of the model) we could reduce the value of $\mathcal{R}_0$ closer to 1 and thus significantly reduce the incidence of dengue in a human population.

3.4 Numerical scenarios for η and p

We explored numerical experiments in attempting to find the optimal effectiveness of hospitalization of individuals. However, this is highly correlated with the number of individuals who are hospitalized due to more acute symptoms and therefore diagnosed. We can assume that the hospitalization of individuals is for the most part effective. More specifically, in Costa Rica most hospitals have the adequate equipment and staff to attend these cases.

In Costa Rica, depending on the clinical manifestations and different social determinants, patients are usually sent home with basic clinical symptomatic care, recommendations, and schedule appointments in their local health care establishments to monitor how the disease evolves. Patients can also be referred for in-hospital management if severe dengue is diagnosed [6, 53]. The average hospital stays among those that do require so ranges between 3 and 4 days [27], with more severe forms requiring longer stays.

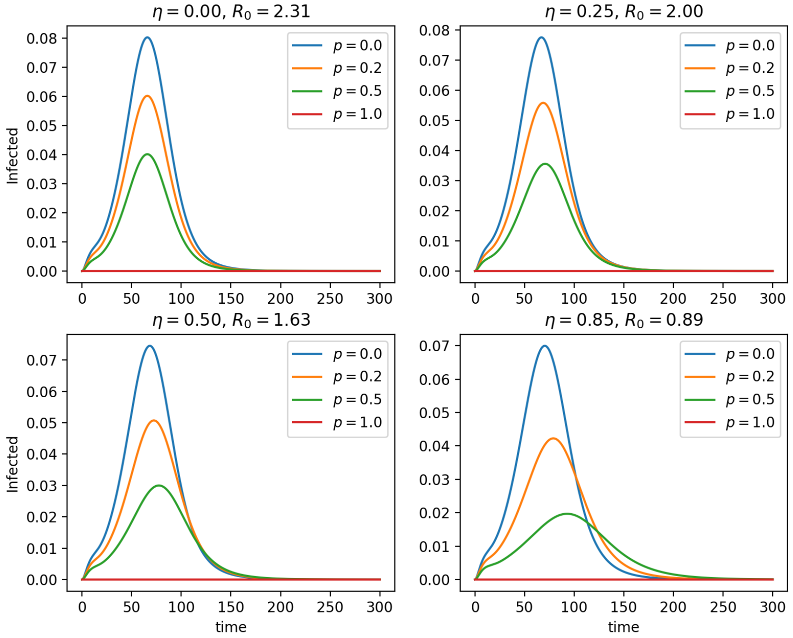


Figure 5: Time series solutions of infectious (undiagnosed) individuals, i_h.

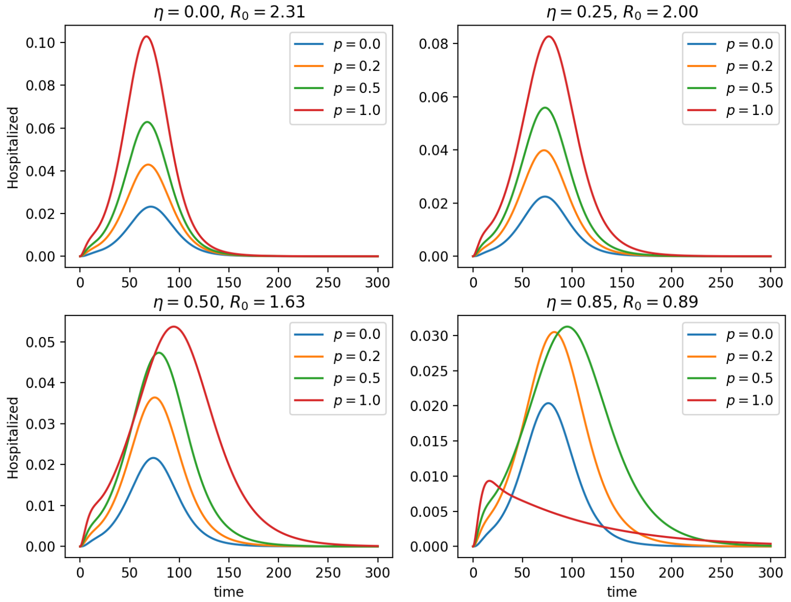
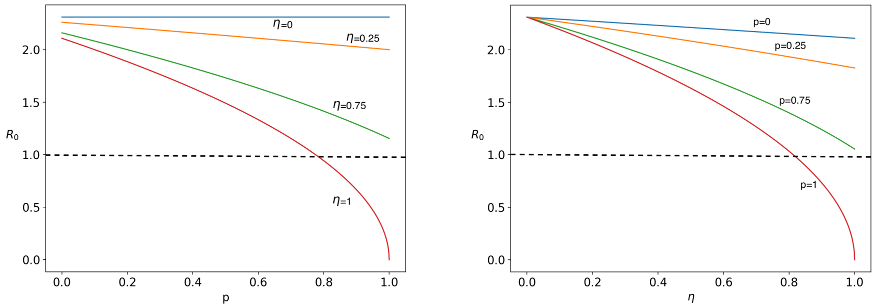


Figure 6: Time series solutions of hospitalized (diagnosed) individuals, $\hbar$.

Figure 5 shows the evolution of infectious individuals. Here, changes in p, probability of developing strong symptoms and being hospitalized, illustrate a reduction in the proportion of infectious individuals. This is directly related to a more precise diagnosis, and more opportunities for public health officials to further improve control measures. Figure 7 shows how the $\mathcal{R}_0$ value behaves as p and η changes, leaving all the other parameters with their baseline values found on Table 4. Notice that numerical estimations hint us that fixing the value of p and increasing the value of η lowers the $\mathcal{R}_0$ value in a faster rate than by fixing the value of η and increasing the value of p. This finding relates to the difference in the sensitivity indexes found in Table 5 and suggests that, based on this model, increasing the effectiveness in hospitalization along with educating patients on preventing methods to minimize infecting others can potentially reduce dengue incidence. Effective isolation, in this case hospitalization, reduces $\mathcal{R}_0$ more effectively than better diagnosing individuals. This is not surprising. However, an opportunity for improved public health policies potentially relies on symptomatic individuals. When individuals are diagnosed and present strong symptoms, the next step is typically a visit to a health facility where treatment is limited. In the majority of cases, those individuals are sent home where the potential for further infections is high. This is where better control policies could play an important role in reducing dengue incidence during an outbreak. Individuals that are sent home after presenting strong symptoms need to be well educated on how to prevent further infections.



(a) $\mathcal{R}_0$ versus p. **(b)** $\mathcal{R}_0$ versus η.

Figure 7: $\mathcal{R}_0$ versus the probability of presenting strong symptoms and effectiveness of hospitalization.

4 Discussion

In Costa Rica, as in most of the endemic countries, prevention and control strategies have focused on vector control mainly through insecticides targeting at larval or adult mosquitoes [29, 45]. The country, also follows the recommendations made by the World Health Organization, to promote an strategic approach known as Integrated Vector Management [54]. However, despite these efforts its proper implementation has been difficult to achieve and dengue continues to represent a mayor burden to the health care system.

Based on the results of our model, timely and context-specific dengue contingency plans that involve providing a safer environment for those patients that stay home during their treatments, hence preventing them from propagating the virus, should be one of the priorities among public health officials. Year-round routine activities that involve more active participation from members of the community is one of the strategies that are increasingly being thought to be relevant for a successful control program [48, 3, 35]. Continuous capacity building in the communities will allow to reinforce local ownership, and create awareness of their role as main multipliers of the virus when infected. Therefore, programs adapted to the specific social, economic, environmental and geographic characteristics are a priority [47]. These strategies need to go in hand with better coordination and communication among institutions so that successful activities of one sector will no be weakened by the lack of commitment from another. Also, because the clinical symptoms of dengue are so diverse and the recent emergence of other two arboviruses, each one with similar symptoms but different clinical outcomes, accurate clinical diagnosis is challenging. As such, training of health professional in diagnosis and management in conjunction with laboratory and epidemiological surveillance, is essential [40]. Early accurate notifications of DENV infections will allow health officials to initialized promptly and targeted responses, and continues to highlight the importance and urgent need for the development of specific and sensitive point-of-care test for DENV infections [24].

The intricacies involved in the transmission dynamics of vector-borne viruses, such as the dengue virus, makes interdisciplinary collaboration essential to successfully achieve more efficient prevention and control strategies. As dengue virus continues to spread worldwide, the ever increasing need to develop and apply cost-effective, evidence-based approaches to identify and respond to potential outbreaks, has been one of the central topics from many points of view, including mathematics and medical scientists. As part of this collaboration, mathematical models have proven to be an increasingly valuable tool for the decision making process of public health authorities [22].

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