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Sensitivity analysis of dengue model with vector control

Ronica M. de Leon

College of Arts and Sciences
Don Mariano Marcos Memorial State University
Bacnotan, La Union, Philippines

email: rmasangkay@dmmmsu.edu.ph

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Abstract

Dengue remains a threat to human health, and epidemics can still occur, especially in rainy seasons. Addressing the need to implement adequate preventive interventions requires a better understanding and assessment of the vector control strategies' impact on host and vector populations. In this study, the sensitivity of state variables of a dengue model with vector control strategy was analyzed. Using the model and estimated parameters from a data set on dengue cases, sensitivities of state variables were solved. Relative sensitivities revealed that application of chemical control has a greater impact on decreasing the number of dengue cases than the non-chemical control but using both types can help mitigate the increase of cases.

1 Introduction

Dengue, regarded as the most important mosquito-borne viral disease [1], poses an alarming threat to human health in tropical and subtropical regions [2] . The World Health Organization(WHO) records 100–400 million infections each year, making about half of the world's population at risk of

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dengue. In more than 100 countries, the disease is now endemic, with Asia being one of the most seriously affected region. The highest global incidence of dengue cases was recorded in 2019 [3].

Mathematical models have been a significant tool in understanding the dynamics of disease transmitted by mosquitoes. The result of the analysis of these models aids public health professionals in developing measures for prevention and eradication as well as evaluating its impact in the community [1]. Many have been developed and used to describe and understand the process of infection at the population level. Some are formulated with the goal of assessing the strategies that control the transmission. The effect of vaccination [4], pesticide [5], integrated vector control strategy [6], and combination of different control measures such as vaccination and insecticide [7], outdoor residual spraying, the placement of mosquito traps, and community engagement activities[8] were studied. However, the dengue model that includes both vector control and medical care has not yet been analyzed.

Since mitigation is reliant to vector control methods and access to proper medical care are necessary[3] [9],a model that incorporates both together with a set of data on dengue cases in an Asian country were utilized to explore transmission of dengue in human and mosquito populations. Specifically, influential parameters affecting model output were determined.

2 Model Formulation

The dengue model developed by de los Reyes and Escaner [10] which included healthcare-seeking class was extended by incorporating the integrated vector control strategies studied by Kasbawati et al. [6]. The variables studied are the host population and vector population. The human population is divided to four compartments, namely the population of susceptible host (S_h), population of unhospitalized or unmonitored infectious host (I_h), population of health-care seeking infected host (J_h) and the population of recovered individuals (R_h). Moreover, the mosquito population is divided to two compartments, namely the population of susceptible vector(S_v) and the population of infected vector (I_v).

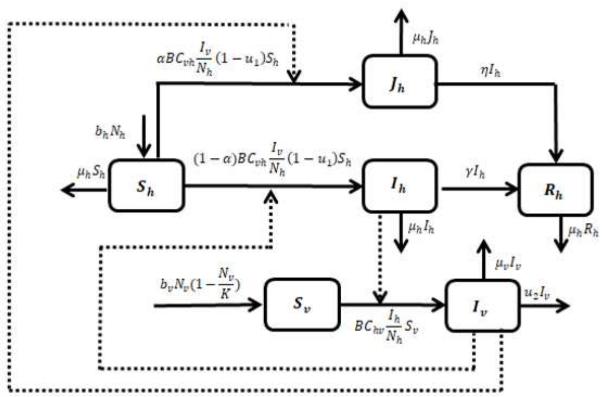

Figure 1: Schematic diagram of the model

$$
\begin{array}{rcl}
\dot{S}_h & = & b_h N_h - (BC_{vh}\frac{I_v}{N_h}(1-u_1) + \mu_h)S_h \\
\dot{I}_h & = & (1-\alpha)BC_{vh}\frac{I_v}{N_h}(1-u_1) - (\gamma + \mu_h)I_h \\
\dot{J}_h & = & \alpha BC_{vh}\frac{I_v}{N_h}(1-u_1) - (\eta + \mu_h)J_h \\
\dot{R}_h & = & \gamma I_h + \eta J_h - \mu_h R_h \\
\dot{S}_v & = & b_v N_v(1 - \frac{N_v}{K}) - (BC_{hv}\frac{I_h}{N_h} + \mu_v + u_2)S_v \\
\dot{I}_v & = & BC_{hv}S_v\frac{I_h}{N_h} - (\mu_v + u_2)I_v
\end{array}
\tag{2.1}
$$

Note that the total human and vector population is the defined by $N_h = S_h + I_h + J_h + R_h$ and $N_v = S_v + I_v$, respectively.

The number of susceptible host per time t increases due to birth rate b_h and decreases due to the death rate μ_h and transmission rate of the virus. The transmission is influenced by the vector biting rate B and probability of transmission $C_v h$ for every interaction of human and the mosquito which is described by the term $I_v S_h$. The number of infected host increases as the transmission of virus increases in the population. Some belongs to the class who did not seek medical care I_h and the other moves to class that received medical treatment J_h. Both number of infected host decrease due to natural mortality rate. The recovery rates of the classes are γ and η, respectively. The number of recovered individuals is increased by recovery rates and decreased by mortality rate.

The susceptible mosquito population increases due to oviposition but limited by the carrying capacity K. It is decreased by vector mortality and the movement of mosquitoes from the susceptible class to infected class. The population of infected mosquitoes increases due to interaction of susceptible vectors and infected hosts and decreases due to natural mortality.

The integrated strategy is classified to non-chemical control strategy and chemical control strategy. Controlling transmission through environmental management is included in the non-chemical control strategy while preventing transmission like using insecticides is considered a chemical control strategy. Assuming that the strategies work successfully, then there exist u_1 percent of individuals who will be free from infection and parameter u_2 suppresses the growth of the vector population. The movement and interaction of host and vectors from and to the compartments of the model is represented through a schematic diagram. The solid arrows represent the movement while the broken arrows represent interaction.

3 Parameter Estimation

The model that was used to describe the dynamics of transmission is a system of ordinary differential equations of the form

$$\dot{x}(t) = G(t, x(t), \theta), x(0) = 0, t \geq 0, \theta A \tag{3.2}$$

where t denotes time, $x(t)$ is the vector of state variables, θ is the vector of parameters, A is the set of admissible parameter vectors, x_0 is the vector of initial conditions and G assumed to be sufficiently smooth function. To determine the parameter vector $\hat{\theta}$ that would minimize the cost function

$$J(\theta) = \frac{1}{2}\Sigma_{i=1}^{N}(y(t_i) - f(t_i, \theta))^2 \tag{3.3}$$

the vector should satisfy the equation

$$\hat{\theta} = \arg\min_{\theta \in A} J(\theta) \tag{3.4}$$

Note that N denotes the number of measurable outputs of the system. The function $fminsearch$ in Matlab employed Nelder-Mead Simplex algorithm to determine parameter estimates.

All parameters are positive and assumed to be constant. The parameters were estimated from the reported dengue cases in a province in the Philippines from 27th week to 52nd week of 2019 where peak of morbidity occurred and the year where there was a dengue epidemic in the country. The province was part of the region that exceeded the alert threshold [11]. The values obtained are shown in Table 1 and were used in the simulation.

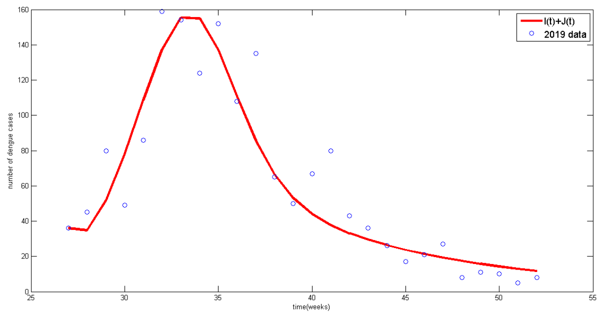

Figure 2: Model output and scatter plot of data

model parameter	value
b_h	0.00043
μ_h	0.00025
B	0.8964
C_{hv}	0.0098
C_{vh}	0.19999
γ	0.1035
η	1
b_v	79.73
μ_v	0.093
K	2992059
α	0.9
u_1	0.1293
u_2	0.1903

Table 1: Model parameters and values

Figure 2 shows the sum of the model output for the infected compartment together with the scatter plot of the available data. The infected is composed of the population who seek and did not seek medical care. It was observed that the concentration of cases is between weeks 30 to 40, this period falls within the country's rainy season.

4 Sensitivity Analysis

In modeling, it is necessary to determine the relative importance of the parameters. Sensitivity analysis can aid in identifying influential model parameters. It is an ensemble of technique that is used to understand the influence of change in parameter to the change in the model output [12] [13]. In order to compute the sensitivities of each state variable with respect to each parameter, the extended system was solved.

$$\begin{aligned} \dot{x}(t) &= G(t, x(t), \theta), t \geq 0, \theta \in A \\ \dot{w}(t) &= B(t, \theta)w(t) + g_k(t, \theta) \\ x(0) &= x_0 \\ w(0) &= 0 \end{aligned} \tag{4.5}$$

where

$$B = \frac{\partial G}{\partial x}, w = \frac{\partial x}{\partial \theta_k}, g_k = \frac{\partial G}{\partial \theta_k}$$

From the system, the relative sensitivities were computed as presented in the papers of Banks et al. [12] and Olufsen and Ottesen [14].

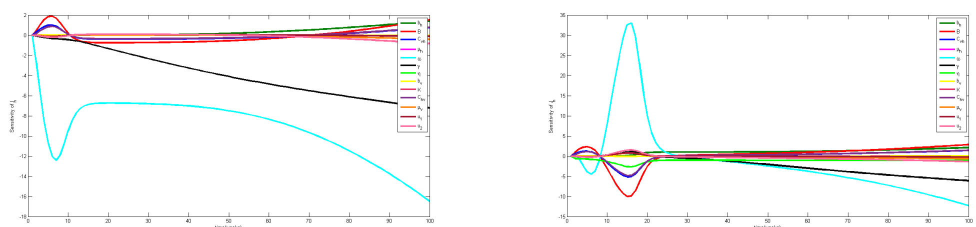

Figure 3: Sensitivity plot of I_h and J_h with respect to all parameters

The plots in Figure 3 present the sensitivities of each infected compartment with respect to each parameter. The greater the magnitude of the sensitivity means the model output is highly sensitive to small perturbations on the parameter. Based on the result, parameters α, B, C_{vh} and C_{hv} are the most influential for the state variables I_h and J_h. The same parameters, transition rate from infected to hospitalized humans, vector biting rate, transmission probability from vector to human, and vice versa, were identified in [10] as factors affecting the transmission of the disease.

Among the four parameters, transition rate from infected to hospitalized humans α is the most influential. People should therefore be encouraged to be monitored to prevent further increase in number of cases. The host that seeks medical care is isolated from a vector-borne disease endemic area which in turn can reduce the total number of infective [15]. On the other hand, the effect of the vector biting rate B and probabilities of transmission C_{vh} and C_{hv} can be lessened if the number of interaction between infected and susceptible is also decreased. Hence, we consider the parameters that allow human intervention, namely, u_1 and u_2. By performing numerical simulations, it is seen in Figure 4 that increasing the values of both parameters can decrease dengue cases.

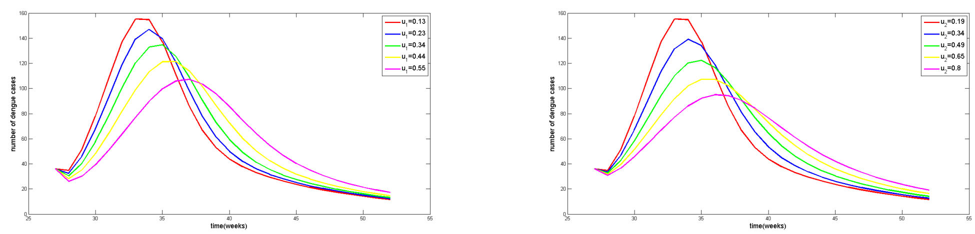

Figure 4: Plot of $I_h + J_h$ with varying u_1 and u_2

In Figure 5, the plot of the sensitivity of state variables with respect to u_1 and u_2 are compared. Based on the graph, u_2 is more influential than u_1. This implies that changing the value of u_2 could give a greater change in the dynamics of the system than changing the value of u_1. Hence, application of chemical control has greater impact to the decrease of the number of dengue cases than using the non-chemical control.

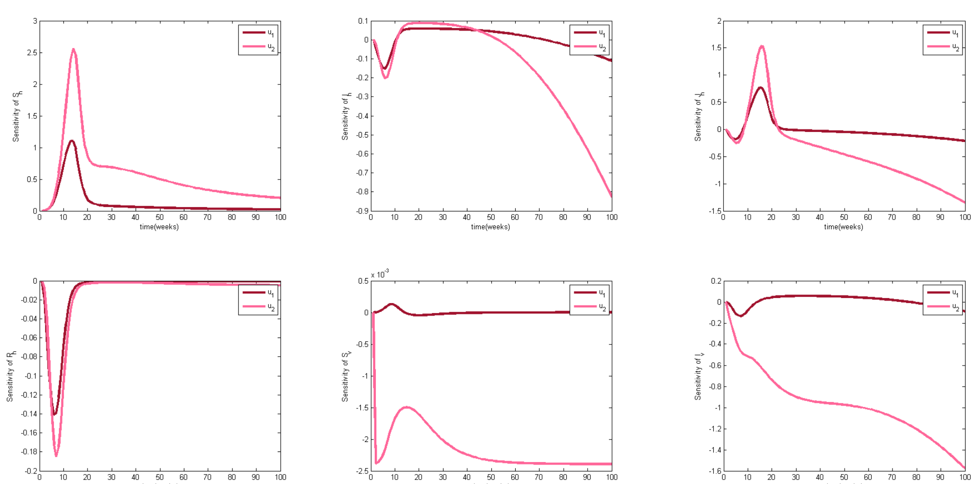

Figure 5: Sensitivity plot of state variables with respect to u_1 and u_2

5 Conclusion

In this study, the analysis of a dengue model provided a broader understanding of the impact of common strategies used to control infection in a population. The most influential parameters are the transition rate from infected to hospitalized humans, vector biting rate, and transmission probability from human to vector and vector to human. This indicates that obtaining medical attention is crucial, and that vector control methods, chemical and nonchemical, are required to lessen the transmission. Sensitivity analysis revealed that chemical control strategy has a greater contribution in lessening the disease burden. However, implementation of both approaches to mitigate the spread of dengue is essential. Hence, it is recommended that integrated prevention methods should be sustained during rainy seasons and infected individuals are encouraged to seek medical care.

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