DYNAMICS AND MANAGEMENT OF VECTOR-BORNE VIRAL EPIDEMICS

by

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B.S., Chemical Engineering, Boğaziçi University, 2017

Submitted to the Institute for Graduate Studies in
Science and Engineering in partial fulfillment of
the requirements for the degree of
Master of Science

Graduate Program in Industrial Engineering

Boğaziçi University

2022

ACKNOWLEDGEMENTS

First and foremost, I would like to thank my supervisors Assoc. Prof. Hakan Yaşarcan and Prof. Yaman Barlas for their support, patience and invaluable guidance during this study. Their guidance and advice carried me through all the stages of my thesis.

I also want to thank to the members of my committee; Assist. Prof. Özge Karanfil and Assoc. Prof. Gönenç Yücel for their contributions to this thesis with their valuable feedbacks.

I am thankful to my family for their continuous support during this study. My husband Özgür Bulut Durak, my mother Öznur Kurtbay, my father Nuri Kurtbay, my mother-in-law Nazan Ersan, and my father-in-law Kenan Durak. I could not have completed this study without their understanding and their valuable support.

I want to thank to Assoc. Prof. Yeşim Tozan for taking the time to meet me and giving me guidance for my academic life.

I am thankful to the people in my workplace, SPRO SAP Consulting Company, for their understanding about my work hours during my thesis study.

Last but not least, I want to thank to my dear friend Bibiana Batista from Brazil for her support and friendship.

ABSTRACT

DYNAMICS AND MANAGEMENT OF VECTOR-BORNE VIRAL EPIDEMICS

In this thesis, we model the dynamics of vector-borne viral epidemics. We choose dengue fever as the specific viral epidemic for the study, which is a mosquito-borne viral infection caused by the dengue virus. Dengue virus relies on the human-vector interaction to spread; thus, we need to model a host-vector system. We use system dynamics methodology and construct a dynamic model. We choose Rio de Janeiro as the area. We obtain the average parameter values from the relevant literature or use our close estimations. We observe that the number of infectious human and infected vectors converge to zero in the model, which means the virus decays and eradicates. However, the viral epidemic of dengue is persistent in the region. We try to understand the reasons behind the persistent existence of this specific viral epidemic. We identify the leverage parameters, and calibrate them to obtain persistence in the epidemic. We compare the outputs with the data for validation to show that the model can reproduce the dynamics of the real system with its own internal causal feedback structure. The model we construct does not only aim to generate valid dynamics, but it also goes beyond the existing models in the sense that it serves as an experimental platform for scenario analyses to support the understanding and management of the disease. The second aim is to demonstrate at a conceptual level that the internal structure of our model makes scenario analyses possible. In scenario experiments, we try to eliminate the virus with two parameters related to the biting rates and vector births. Biting rates and vector births can be decreased by taking precautions such as wearing clothes with more skin coverage, using repellents, and cleaning the water storages regularly. We conclude that the virus can be eliminated if humans take precautions against the interaction with vectors or against vector breeding areas.

ÖZET

VEKTÖREL KAYNAKLI VİRAL SALGINLARIN DİNAMİKLERİ VE YÖNETİMİ

Bu tezde vektörel kaynaklı viral salgınları modelliyoruz. Bu çalışmada spesifik viral salgın olarak dang virusünün sebep olduğu sivrisinek kaynaklı dang humması seçiyoruz. Dang humması insan ve vektör ilişkisinden kaynaklandığı için bir konak-vektör sistemini, sistem dinamiği metodolojisini kullanarak modelliyoruz. Rio de Janeiro bölgesini seçiyoruz. Parametre değerleri için literatürdeki ortalamaları veya tahminlerimizi kullanıyoruz. Benzetim koşumu aldığımızda hastalığı taşıyan insan ve vektörlerin sayısının sıfıra yakınsadığını gözlemliyoruz ve bu, virüsün azalarak ortadan kalktığı anlamına geliyor. Bununla birlikte, dang humması viral salgınının bölgede devam ettiğini biliyoruz. Bu spesifik viral salgının kalıcı varlığının arkasındaki nedenleri anlamaya çalışıyoruz. Etkili parametreleri seçip kalibre ederek salgında kalıcılığı model koşumunda da elde ediyoruz. Geçerlilik testi amacıyla, ilgili verilerin dinamiklerini modelin kendi dahili nedensel geri bildirim yapısıyla yeniden üretebildiğini göstermek için, model çıktılarını gerçek hayattan alınmış verilerle karşılaştırıyoruz. Modelimiz sadece geçerli dinamikler üretmeyi amaçlamıyor, aynı zamanda hastalığın anlaşılmasını ve yönetimini desteklemek için senaryo analizlerine deneysel bir platform olarak da hizmet ediyor ve bu anlamda mevcut modellerin ötesine geçiyor. Bu çalışmadaki ikinci amaç modelimizin iç yapısının senaryo analizlerini mümkün kıldığını kavramsal düzeyde göstermektir. Senaryo denemelerinde, ısırılma oranları ve vektörlerin doğum oranları ile ilişkili parametreler ile virüsü ortadan kaldırıyoruz. Isırılma oranları ve vektörlerin doğum oranları, daha kapalı giysiler giymek, sivrisinek kovucuları kullanmak, ve su depolarını düzenli olarak temizlemek gibi önlemler alınarak azaltılabilir. İnsanlar, vektörlerle etkileşime ve vektör üreme alanlarına karşı önlem alırsa virüsün ortadan kaldırılabileceği sonucuna varıyoruz.

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DENV	Dengue Virus
Dmnl	Dimensionless
max	Maximum
PAHO	Pan American Health Organization
SD	System Dynamics
SEIR	Susceptible Exposed Infected Recovered
SIR	Susceptible Infected Recovered

1. INTRODUCTION

This thesis is about modelling the dynamics of viral epidemics by using system dynamics (SD) approach. Dengue fever is the specific viral epidemic chosen for the study, which is a mosquito-borne viral infection caused by the dengue virus. Rio de Janeiro in Brazil is the selected area for this thesis because the dengue epidemic is persistent in the region since the seventeenth century. Accordingly, a significant part of this study is to understand how the viral epidemic is sustained by the host-vector system so that it can completely be eradicated. SD is used as the modeling approach because of the complexities existent in the system such as feedback loops, non-linarites, accumulations, and delays [3].

Dengue virus is transmitted by vectors (i.e., female mosquitoes); mainly Aedes aegypti species of mosquitoes. There are four types of DENV serotypes which are DENV1, DENV2, DENV3 and DENV4. Getting infected with one of the four serotypes provides immunity for that serotype of dengue virus and partial temporary cross-immunity for other three dengue serotypes [4, 5]. Dengue fever can be subclinical or severe. Subclinical cases can be symptomatic or asymptomatic, while severe dengue is always symptomatic [5]. People who are infected with dengue virus and show symptoms are called as symptomatic infectious people. While asymptomatic infectious people show no symptoms but still spread the disease. Symptomatic infectious people can show symptoms for two to seven days after four to seven days of incubation period [5]. Headache, vomiting, pain behind the eyes, muscle and joint pains are some of the common symptoms of dengue [5]. An infected human can use pain killers or fever reducers to deal with the symptoms. Humans should avoid getting infected by a vector, because there is no medication that can kill the virus. Also, humans should be educated for vector breeding prevention methods. Insecticides can be applied to water storage containers. Humans should wear clothes that increases skin coverage and use sprays to avoid vector contact. [5].

Dengue virus can be transmitted from vectors to humans and from humans to vectors [5]. Also, vertical transmission of dengue virus from infected vectors to eggs is possible. The infected pupa evolves from infected eggs. And the pupa can evolve into an infectious adult vector [6–9].

Seasons have an effect on the vector population and also another effect on human-vector contact rates. December to March usually provides the optimal weather conditions needed for an outbreak to occur in Brazil [10–12]. Moreover, in warm weather, people tend to wear clothes that cover less body area that increases human-vector interaction, compared to cold weather. Reoccurring outbreaks can also be observed in an area, because there are four types of dengue, and a person cannot develop permanent immunity against all of them.

The first dengue epidemic is seen in the West Indies in 1635 [13]. The first case in Brazil is seen in 1685 [14]. "Dengue virus (DENV) was reintroduced into Brazil in 1981 and by 1995 it had spread throughout the country" [2]. In the web page of PAHO (Pan American Health Organization), data is available for many countries including Brazil for years between 1980 and 2020. PAHO declares in the website that the data can be changed at any time by PAHO. PAHO does not take any responsibility for the given data. The data used in this study is taken from PAHO in March 2020 and the data is assumed to be valid for that date [1]. For example, in 2018, 265,613 non-severe dengue cases, 321 severe dengue cases, total of 265,934 dengue cases and 155 deaths were recorded for Brazil. In 2019, these numbers were 2,118,792 non-severe dengue cases, 1,350 severe dengue cases, total of 2,120,142 dengue cases and 722 deaths for Brazil. The increase in the number of cases can be seen clearly. Brazil is the country with highest non-severe dengue and death numbers in 2019 [1]. Rio de Janeiro is the second largest city in Brazil with high number of dengue cases. We examined the number of dengue cases in Rio de Janeiro between 2000 and 2015. The dengue case numbers have a maximum value of 152,687 human in 2002, a minimum value of 2,606 human in 2004, and a mean value of 43,670 human between 2000 and 2015. Further data can be found at the Table 6 of the relevant literature [2]. As these summarized case numbers

indicate, dengue virus is sustained by the human-vector system for many years. We model and analyze this system to understand how the dengue virus is sustained in this area for centuries with human-vector interactions.

There are modelling studies on dengue aiming to analyze the effect of changes in specific parameters. A human-vector model in the literature, analyses the dengue cases with immunity and without immunity to see the difference. Two-dimensional delay differential equations are used for the no immunity scenario with incubation period delay. It is concluded that the results are similar for both cases [15]. In our model, we used temporal immunity for all dengue serotypes. For all the parameters of our model, the effect of changes can be examined for different scenario analyses.

The first aim of this thesis is to model the dynamics of dengue fever epidemic. The model outputs are compared with the data collected from relevant literature, aiming to show that the model can reproduce the observed epidemic dynamics with its own internal causal feedback structure. To serve this purpose, data from Rio de Janeiro is used to calibrate the model. As mentioned before, a significant part of this study is to understand how the viral epidemic is sustained by the host-vector system so that it can completely be eradicated. Therefore, before we generate the desired output, we determine leverage parameters that enable us to calibrate the model. The constructed model does not only aim to generate valid dynamics, but it also goes beyond the existing models in the sense that it serves as an experimental platform for scenario analyses to support the understanding and management of the disease. Consequently, the second objective is to investigate examples of prevention scenarios, eradication scenarios, and scenarios for several possible problematic cases. The aim is to demonstrate at a conceptual level that the internal structure of the model makes scenario analyses possible. Obtaining results for a specific region with high accuracy requires more time, effort, and detailed work, which is beyond the scope of this master's thesis. With further research, our model can be used to test possible strategies that aim for the elimination of the epidemic in the region. Also, our model can be used for other regions after calibration with the relevant regional data. We show example

scenario runs in Chapter 7.

In the following sections, we first provide a brief explanation on problem definition and research objectives. Then research methodology, overview of the model, the model description and validation are given. After these, model behavior and calibration with several runs, scenario analysis and their discussions are provided. Finally, the results and the conclusion are given.

2. PROBLEM DEFINITION AND RESEARCH OBJECTIVES

The dengue virus exists in Rio de Janeiro for many years and is persistent; the virus does not decay over time. The efforts aiming to fight the virus have not been successful in eliminating it. The first aim in this study is to understand how the virus continues to exist in the region considering that humans carry the virus for only one to two weeks and the lifetime of the vector is only three weeks. Furthermore, the vertical infection of vectors is quite low; it is at a negligible value according to the references from the relevant literature [7, 16]. The second aim is to promote the use of our model to determine possible strategies for the elimination of the epidemic in the region by running possible scenario analyses. We suggest the use of our model for other regions after necessary calibrations with the relevant regional data.

Accordingly, the research objectives in this thesis are (1) to construct an SD model; (2) to estimate the model parameters from the literature; (3) to determine leverage parameters; (4) to calibrate the model dynamics; (5) to run scenarios that can eliminate the epidemic.

3. RESEARCH METHODOLOGY

Our model is a host-vector model with internal causal feedback loops, accumulations, delays and nonlinearities. Because of the complexities in our problem, analytical methods cannot be employed. SD modelling approach is suitable to model and analyze these kinds of problems. The main focus of our model is the interaction between humans and vectors. Also, SD supports scenario analysis.

Causal loop diagrams can describe all the loops interacting in the system. They also help us to visualize the interactions between the variables. Qualitative relationships between variables can be given with causal loop diagrams. Causal loop diagrams are also called as conceptual models. We use the conceptual models to show the relations between humans and vectors in a simpler way. Our conceptual model is given in Chapter 4.

Stock flow diagrams are used to show the quantitative relations between variables. There are stock variables, flow variables and auxiliary variables (also known as converters) in a stock flow model. "Stocks are the memory variables both in models and in systems. Stocks are accumulations in time. Stocks have inertia, because they are the results of integrations. Their change is more gradual, and complex compared to the changes in their flows. Flows define the way the stocks change" [17]. In our model, human and vector stocks are used as memory variables. The inflows between human stocks and inflows between the vector stocks fill in and the outflows drain out these stocks according to their locations in our model. The stock flow diagrams are given in detail in Chapter 6. Also, a simplified stock flow diagram is given in Chapter 4.

4. OVERVIEW OF THE MODEL

In this chapter, we give a simplified stock flow diagram and a causal loop diagram of our model. In the simplified stock flow diagram, we give the stocks, flows and some relevant variables that effect these flows. We show the direct relations with solid line arrows, and indirect relations with dotted line arrows. Then we give the causal loop diagram with main positive and negative feedback loops. We aim to understand the main relations between variables by using these diagrams.

4.1. Simplified Stock Flow Diagram

We constructed a simple stock flow diagram of our model. In this stock flow diagram, we can see the relations between humans and vectors. *Infection flow of vector* is mainly affected from infectious human. *Infection flow of human* is mainly affected from *infected vector ratio* and *total vector*.

The simplified stock flow diagram of our model has five human stocks and two vector stocks. *Susceptible human* is the stock of human who never had dengue before or who recovered from a dengue serotype and became susceptible to dengue virus again. *Exposed human* is the stock of human who got bitten by an *infected vector* but are not infectious yet. *Symptomatic infectious human* is the stock of human who got bitten by an *infected vector* and became infectious with symptoms. *Asymptomatic infectious human* is the stock of human who got bitten by an *infected vector* and became infectious without symptoms. *Recovered human* is the stock of human who got recovered after the dengue infection. *Susceptible vector* is the stock of vectors that do not carry dengue virus. If a *susceptible vector* bites an infectious human, there is a probability of getting infected for the vector. *Infected vector* is the stock of vectors that got infected by feeding on an infectious human or is an offspring of an *infected vector*. The equations and explanations of these seven stocks are given in detail in Chapter 5.

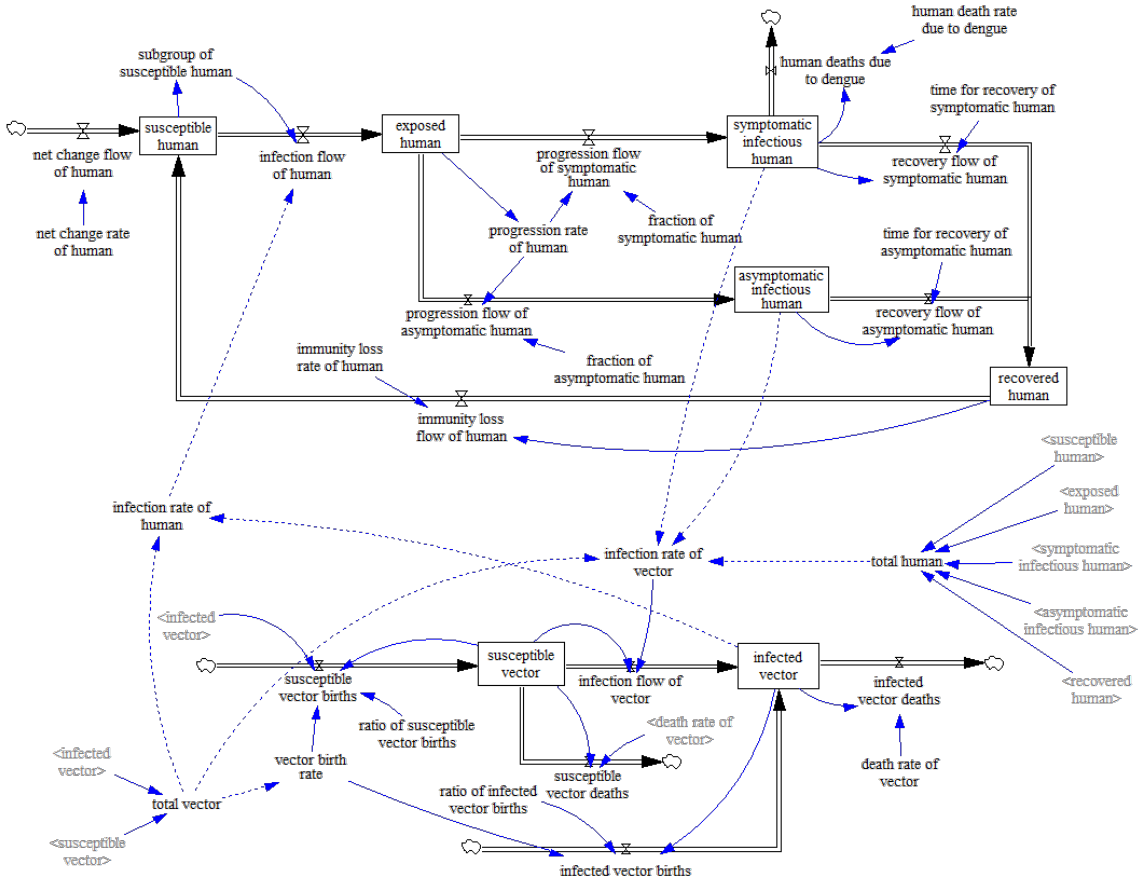


Figure 4.1. Simplified Stock Flow Diagram of Our Model.

As we can see from the Figure 4.1, *infection rate of vector* gets affected from *symptomatic infectious human*, *asymptomatic infectious human*, *total human*, and *total vector*. *Infection flow of vector* gets affected from *infection rate of vector* and *susceptible vector*. *Infection rate of human* gets affected from *infected vector* and *total vector*. *Infection flow of human* gets affected from a *subgroup of susceptible human* and *infection rate of human*.

4.2. Causal Loop Diagram

In this section, we present a causal loop diagram, which describes the loops interacting in the system. The human-vector interaction is the most important factor resulting in a vector-borne epidemic. Therefore, we focus on this interaction.

The causal loop diagram has positive and negative feedback loops. Feedback loops start with a variable and end with the same variable to complete the loop. We can call the positive feedback loops in our diagram as reinforcing loops "because they reinforce an increase or a decrease in a variable that is on the loop". We can call the negative feedback loops as counteracting loops "as they counteract to an increase or a decrease in a variable on the loop". "The arrows represent the directions of the relations" [17]. We provide the detailed explanations for the effects of '+' and '-' signs in the head of the arrows, below.

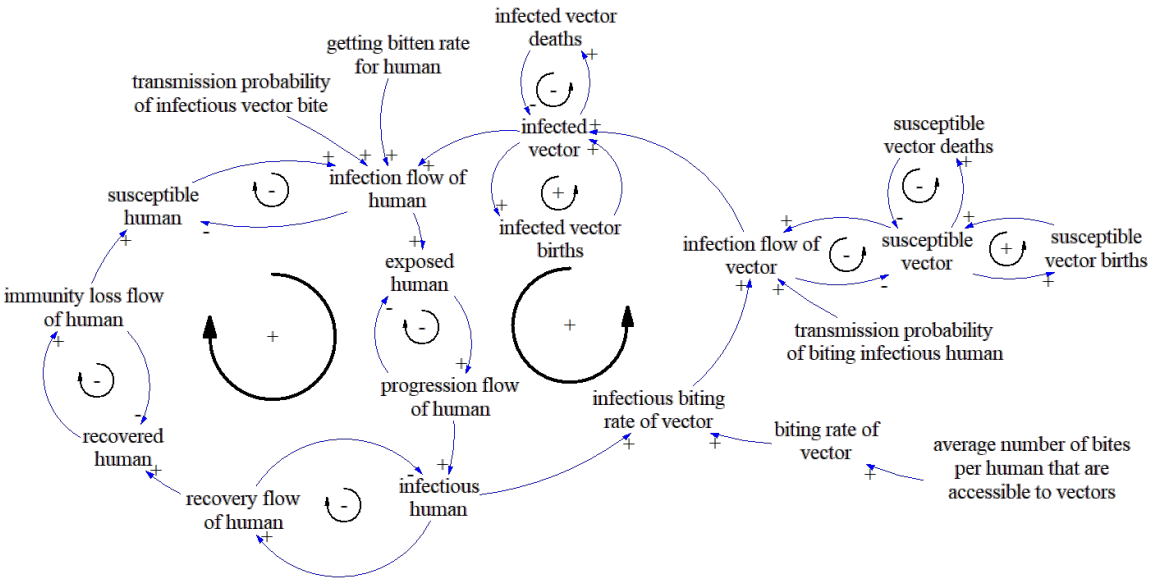


Figure 4.2. The Causal Loop Diagram of Our Model.

We give the main relations of the model with loops and their signs in the Figure 4.2. All the relations and loops are the same for *symptomatic infectious human* and *asymptomatic infectious human*. We simplify our causal loop diagram. Therefore, we combine the *symptomatic infectious human* and *asymptomatic infectious human* together and name their combined variable as *infectious human*. Thus, the *progression flow of human* and the *recovery flow of human* both include the *symptomatic infectious human* and *asymptomatic infectious human* together.

The big positive feedback loop for human part does not produce a growth with an unstable behavior. This positive loop supports the existence of the *susceptible human* so that the *susceptible human* does not decay to zero. This feedback loop starts with the *susceptible human* and ends with it. Increasing *susceptible human* values, increases the *infection flow of human*. The increase in *infection flow of human* increases *exposed human*. The increase in *exposed human* increases *progression flow of human*. The increase in *progression flow of human* increases *infectious human*. The increase in *infectious human* increases *recovery flow of human*. The increase in *recovery flow of human* increases *recovered human*. The increase in *recovered human* increases *immunity loss flow of human*. And the increase in *immunity loss flow of human* increases *susceptible human*. Finally, the positive feedback loop completes itself with the *susceptible human*. There are four negative feedback loops between the variables in this positive loop. As *susceptible human* increases the *infection flow of human*; *infection flow of human* decreases the *susceptible human*. This loop is a balancing loop with a convergent behavior. Similar to this loop, as *exposed human* increases the *progression flow of human*; *progression flow of human* decreases *exposed human*. As *infectious human* increases the *recovery flow of human*; *recovery flow of human* decreases the *infectious human*. And as *recovered human* increases the *immunity loss flow of human*; *immunity loss flow of human* decreases the *recovered human*. *Total human* population stays constant in our model. Therefore, the big positive human feedback loop cannot create a growth behavior. It only sustains *susceptible human*.

As we stated before, the human-vector interaction is the focus of this model. We give the relations between the related variables in the second big positive feedback loop of our causal loop diagram. This positive feedback loop is the loop of our model that keeps the virus persistent. We explain the interaction between *infectious human* and *infected vector* that spreads the virus with this positive loop. We can start the loop from *infectious human*. As *infectious human* increases, *infectious biting rate of vector* increases. Also increasing value of *average number of bites per human that are accessible to vectors* increases the *biting rate of vector*. And increasing value of *biting rate of vector* increases the *infectious biting rate of vector*. The increase in *infectious*

biting rate of vector increases the *infection flow of vector*. Also, the increase in the value of *transmission probability of biting infectious human* increases the *infection flow of vector*. As *infection flow of vector* increases, *infected vector* increases. As *infected vector* increases *infection flow of human* increases. Also increasing value of *getting bitten rate for human* increases *infection flow of human*. And increasing value of *transmission probability of infectious vector bite* increases *infection flow of human*. Then the increase in *infection flow of human* increases *exposed human*. The increase in *exposed human* increases *progression flow of human*. And the increase in *progression flow of human* increases *infectious human*. And the positive feedback loop of human-vector relations completes itself.

There is a negative feedback loop between *susceptible vector* and *infection flow of vector*. As *susceptible vector* increases, *infection flow of vector* increases, because there are more vectors to get infected. However, the increase in *infection flow of vector* decreases *susceptible vector*. This relation creates a balancing loop.

There are also two positive feedback loops for vector births and two negative feedback loops for vector deaths. As *infected vector* increases, *infected vector births* increase. And *infected vector births* increase the *infected vector*. Similarly, as *susceptible vector* increases, *susceptible vector births* increase. And *susceptible vector births* increase the *susceptible vector*. These two loops are positive feedback loops. When we consider the loops for vector deaths, as *infected vector* increases, *infected vector deaths* increase. However, *infected vector deaths* decrease the *infected vector*. Similarly, as *susceptible vector* increases, *susceptible vector deaths* increase. However, *susceptible vector deaths* decrease the *susceptible vector*. These two loops are negative feedback loops.

The negative feedback loop between *infectious human* and *recovery flow of human* is very strong, because humans recover in around a week. Also, the negative feedback loop between *infected vector* and *infected vector deaths* is very strong, because lifetime of vector is only three weeks. Therefore, at the initial run, we are not able to sustain

infectious human and *infected vector* populations, which indicates that we are not able to keep the virus persistent in the model. We are trying to understand how the virus persists in real life. The human-vector interaction feedback loop sustains the virus. Also, the positive feedback loop of *infected vector births* has effect on the persistence. But it is not very strong according to the literature. Also, in human feedback loop, sustaining the *susceptible human* population effects the persistence of the virus. *Susceptible human* increases with *immunity loss flow of human*. Therefore, as *susceptible human* increases, *infection flow of human* increases.

5. MODEL DESCRIPTION AND VALIDATION

In this chapter we provide the simplifying assumptions of our model. We explain the model descriptions of the two main substructures for humans and vectors in detail. We provide the validation of the model within the explanations of the human and vector substructures, and in the validation section.

5.1. Simplifying Assumptions

- *Total human* population stays constant with time.
  - We neglect natural human births and deaths.
- Vectors cannot bite a given fraction of human population.
- We take the value of transmission probability from human to vector higher than the transmission probability from vector to human.
- We include the rate of vertical infection of vectors in our model.
  - Vertical infection is the transfer of dengue virus from vectors (i.e., infected female mosquitoes) to some portion of their off springs (i.e., eggs).
  - We consider vertical infection in our model as *ratio of infected vector births* from *infected vector*s.
- Humans stay immune to all dengue serotypes for five years.
  - Normally, people become immune to the dengue serotype that they got infected with. They also become partially immune to other three dengue serotypes temporarily. Four types of dengue virus are named as DENV1, DENV2, DENV3 and DENV4 serotypes. We simplify the real situation for our case.
- Seasonality affects *vector capacity*.
- Seasonality affects human-vector contact rate.
- Vector lifetime is shorter than the recovery time of *infected vector*s from the dengue virus.
- We neglect the probability of infected human births.

- We ignore the transmission probability of the virus from an infectious human to a *susceptible human* by blood transmission.

5.2. Description and Validation of the Model

This model has two main substructures: Human substructure and vector substructure.

5.2.1. Description of Human Substructure

In human substructure, there are five main stocks. And there are two more human stocks to calculate the cumulative sum of dengue cases and the cumulative sum of deaths due to dengue. We explain these two stocks later in this chapter.

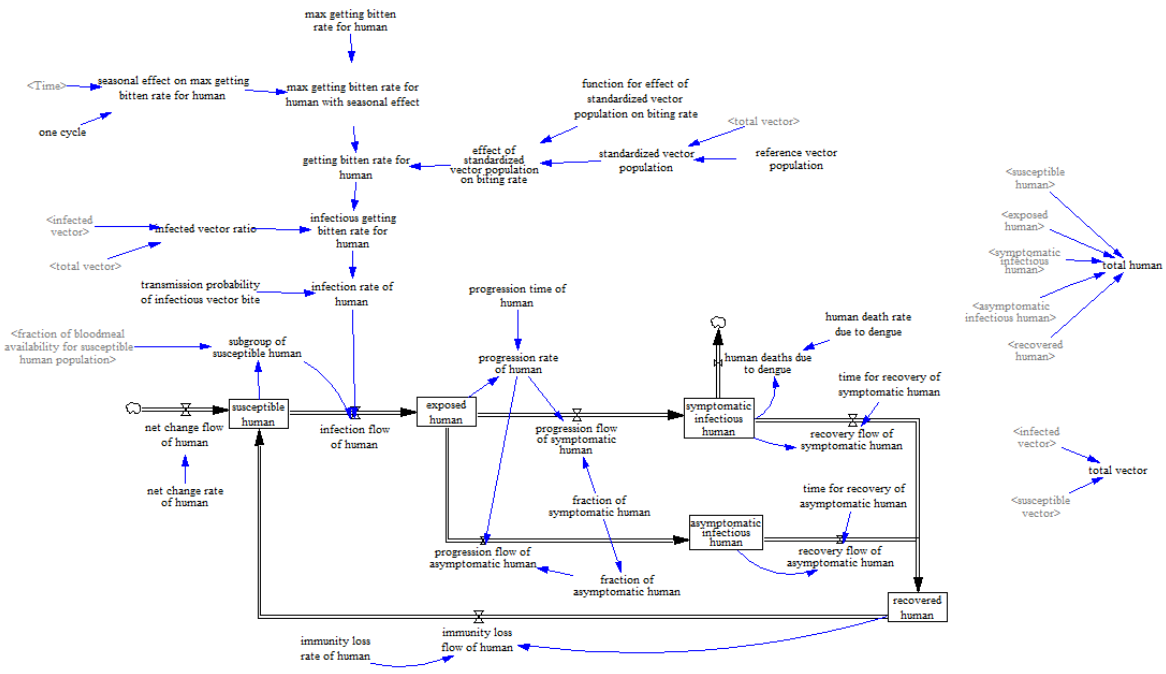


Figure 5.1. Human Substructure.

Susceptible human is the stock of human who never had dengue before and who recovered from a dengue serotype and became susceptible to dengue virus again after the partial-immunity period. Therefore, *susceptible human* is the stock of human who

have the possibility to get infected with a dengue serotype when got bitten by an *infected vector*, and the equation of *susceptible human* is

$$\begin{aligned}\frac{d(\text{susceptible human})}{dt} &= \text{net change flow of human} \\ &+ \text{immunity loss flow of human} \\ &- \text{infection flow of human.}\end{aligned} \tag{5.1}$$

Susceptible human has units of Human/Week.

Exposed human is the stock of human who got bitten by an *infected vector*. These human got exposed to the dengue virus from an infectious vector bite, but these human are not infectious yet. Equation of *exposed human* is

$$\begin{aligned}\frac{d(\text{exposed human})}{dt} &= \text{infection flow of human} \\ &- \text{progression flow of symptomatic human} \\ &- \text{progression flow of asymptomatic human.}\end{aligned} \tag{5.2}$$

Exposed human has units of Human/Week.

Symptomatic infectious human is the stock of human who got bitten by an *infected vector* and became infectious with symptoms. This is the stock of human that can be tracked and used for the calculations of reported dengue cases. These human can recover from the symptoms after the *time for recovery of symptomatic human*. With a very low probability, they can die due to dengue virus. Equation of *symptomatic infectious human* is

$$\begin{aligned}\frac{d(\text{symptomatic infectious human})}{dt} &= \text{progression flow of symptomatic human} \\ &- \text{recovery flow of symptomatic human} \\ &- \text{human deaths due to dengue.}\end{aligned} \tag{5.3}$$

Symptomatic infectious human has units of Human/Week.

Asymptomatic infectious human is the stock of human who got bitten by an *infected vector* and became infectious without symptoms. In real life people do not track this stock of human. These human can recover from dengue and become *recovered human* after the *time for recovery of asymptomatic human*. Equation of *asymptomatic infectious human* is

$$\begin{aligned}\frac{d(\text{asymptomatic infectious human})}{dt} &= \text{progression flow of asymptomatic human} \\ &\quad - \text{recovery flow of asymptomatic human.}\end{aligned} \tag{5.4}$$

Asymptomatic infectious human has units of Human/Week.

Recovered human is the stock of human who got recovered after the dengue infection. In the model, we assume that human lose their immunity for all dengue serotypes after five years on average. Equation of *recovered human* is

$$\begin{aligned}\frac{d(\text{recovered human})}{dt} &= \text{recovery flow of symptomatic human} \\ &\quad + \text{recovery flow of asymptomatic human} \\ &\quad - \text{immunity loss flow of human.}\end{aligned} \tag{5.5}$$

Recovered human has units of Human/Week.

These five human stocks have initial values different than zero. We know that the dengue virus is in the selected area (Rio de Janeiro) since 1986 [18]. The modelling time is starting from time zero, but the virus did not enter the selected area at the time zero, the virus already existed in the area. There are *recovered human*s at the time zero of the modelling time, because many human have recovered from the disease before the time zero. And these human gained temporal immunity for dengue virus. Therefore, we cannot take the initial values as zero at the time zero. With similar reasons, susceptible, exposed and infectious human stocks also have values higher than zero at the beginning of the modelling time. We take the initial values of *susceptible human*, *exposed human*, *symptomatic infectious human*, *asymptomatic infectious hu-*

man, *recovered human*, *susceptible vector* and *infected vector* different for each run. We provide the initial values under each run in Chapter 6.

We assume that the *total human* population is constant throughout the year. *Net change flow of human* is the inflow to the *susceptible human* stock. This inflow does not directly represent human birth. We add this inflow to our model to keep the *total human* population at a constant level as we assume. We do not explicitly consider natural births and deaths of humans in our system. We assume that the *total human* population is almost constant, because *human death rate due to dengue* is very low (0.1 percent) and has a negligible effect on the *total human* population. Therefore, we take the average value of *human deaths due to dengue*. We assign this value to the *net change rate of human* as a constant to keep the *total human* population at a constant level. Equation of net change flow of human is

$$\text{net change flow of human} = \text{net change rate of human}. \tag{5.6}$$

Net change flow of human has units of Human/Week.

We take the *net change rate of human* as a constant. The constant value is one human per week as a rough value, and the equation is

$$\text{net change rate of human} = 1\ [\frac{\text{Human}}{\text{Week}}]. \tag{5.7}$$

The *infection flow of human* is the flow from *susceptible human* stock to *exposed human* stock. This flow represents the number of *susceptible human* getting bitten by an *infected vector* and getting exposed to the dengue virus in a week, and the equation is

$$\begin{aligned}\text{infection flow of human} = {} & \text{infection rate of human} \\ & \times \text{subgroup of susceptible human}.\end{aligned} \tag{5.8}$$

Infection flow of human has units of Human/Week.

Many different variables have effect on *infection flow of human*. To explain the *infection flow of human*, we should explain the group of variables that affect this flow.

Subgroup of susceptible human is the number of human that are susceptible and accessible to the vectors, and the equation is

$$\begin{aligned}&\text{subgroup of susceptible human} = \\ &\text{fraction of bloodmeal availability for susceptible human population} \\ &\times \text{susceptible human.}\end{aligned} \tag{5.9}$$

Subgroup of susceptible human has units of Human.

Fraction of bloodmeal availability for susceptible human population is the fraction of *susceptible human* that have a possibility of contacting vectors. *Fraction of bloodmeal availability for susceptible human population* variable is given in Equation (5.65). The contacted vector can be susceptible or infected. We assume the *fraction of bloodmeal availability for susceptible human population* to be between zero and the *fraction of bloodmeal availability for total human population* value. We assume that the value of *fraction of bloodmeal availability for total human population* is 95 percent as a rough number. *Fraction of bloodmeal availability for total human population* variable is given in Equation (5.66). Further explanations on these variables will be given in vector substructure.

Max getting bitten rate for human is the maximum ratio of human that can get bitten by vectors in a given week. *Max getting bitten rate for human* is taken roughly as 1 per week, and the equation is

$$\text{max getting bitten rate for human} = 1\ [\frac{1}{\text{Week}}]. \tag{5.10}$$

We add *seasonal effect on max getting bitten rate for human* to the model to include the effect of seasonality on human-vector interaction. The seasonality has an effect on the skin coverage of the clothes that human wear during different seasons. In the beginning of the year, the weather is warmer, and people tend to wear clothes with less skin coverage, that increases the human-vector interaction rate, compared to cold weather. We add the *seasonal effect on max getting bitten rate for human* as a sinus function. The average value of sinus function is 0.75 throughout the year. Equation of *seasonal effect on max getting bitten rate for human* is

$$\begin{aligned} &\text{seasonal effect on max getting bitten rate for human} = \\ &0.75 + 0.25 \times \text{SIN}(\frac{2 \times 3.1416 \times \text{Time}}{\text{one cycle}} + 4 \times \frac{3.1416}{12}). \end{aligned} \tag{5.11}$$

Seasonal effect on max getting bitten rate for human is dimensionless.

One cycle is the time that the same pattern repeats itself. The same pattern repeats itself in every 52 weeks. Therefore 52 weeks is given as the cycle time, and the equation is

$$\text{one cycle} = 52 \text{ [Week]}. \tag{5.12}$$

Max getting bitten rate for human with seasonal effect is the ratio of human that can get bitten by vectors in a given week, considering the seasonal effect on human-vector interaction, and the equation is

$$\begin{aligned} &\text{max getting bitten rate for human with seasonal effect} = \\ &\text{seasonal effect on max getting bitten rate for human} \\ &\times \text{max getting bitten rate for human}. \end{aligned} \tag{5.13}$$

Max getting bitten rate for human with seasonal effect has units of 1/Week.

We assume that 75 percent of the *total human that vector can reach*, who are

accessible to the vectors, are getting bitten by the vectors on average, due to the seasonality effect. *Total human that vector can reach* variable is given in Equation (5.64). *Max getting bitten rate for human with seasonal effect* does not include the number of bites a human can get in a week. We assume that a human who gets bitten by a vector can be bitten once or many times during that week. Therefore, 25 percent of the population of *total human that vector can reach* do not get any bites from vectors in a week, while the other 75 percent can get bitten for several times throughout the same week. We assume that a person that gets bitten by a vector that week, gets bitten for twenty times on average. 75 percent and 25 percent are average values, these values change with time.

Getting bitten rate for human is a variable for human that gets bitten by any vector. The vector can be infected or susceptible. Equation of *getting bitten rate for human* is

$$\begin{aligned} &\text{getting bitten rate for human} = \\ &\text{max getting bitten rate for human with seasonal effect} \\ &\times \text{effect of standardized vector population on biting rate.} \end{aligned} \tag{5.14}$$

Getting bitten rate for human has units of 1/Week.

To understand the *getting bitten rate for human*, we must understand the previous variables in the model.

Standardized vector population is the ratio of *total vector* population to the *reference vector population*. We add this variable to our model to consider the effect of *total vector* population on biting rate. As the *standardized vector population* increases, the value of the *effect of standardized vector population on biting rate* also increases. The *effect of standardized vector population on biting rate* is given in the Figure 5.2.

Equation of *standardized vector population* is

$$\text{standardized vector population} = \frac{\text{total vector}}{\text{reference vector population}}. \tag{5.15}$$

Standardized vector population is dimensionless.

Total vector is the sum of *infected vector* and *susceptible vector*. The *total vector* has units of Vector. Equation of *total vector* is

$$\text{total vector} = \text{susceptible vector} + \text{infected vector}. \tag{5.16}$$

We assume that the *reference vector population* is 200 million vectors. This is the average of the initial values of *total vector* population and the *max vector capacity*. We assume that the initial value of *total vector* population is 150 million vector. *Max vector capacity* is given in Equation (5.43) as 250 million vector. Equation of *reference vector population* is

$$\text{reference vector population} = 2 \times 10^8 \text{ [Vector]}. \tag{5.17}$$

Function for effect of standardized vector population on biting rate, is a graphical function. Values of *function for effect of standardized vector population on biting rate* results in a linear function with a saturation point at *reference vector population*. The *effect of standardized vector population on biting rate* (Y-axis value) reaches the value of one, which is the upper limit of the graphical function, when the *standardized vector population* (X-axis value) is around one.

The purpose of this graph, given in Figure 5.2, is to show the increase in the biting rate when vector population increases. However, the increase in biting rate has a saturation point.

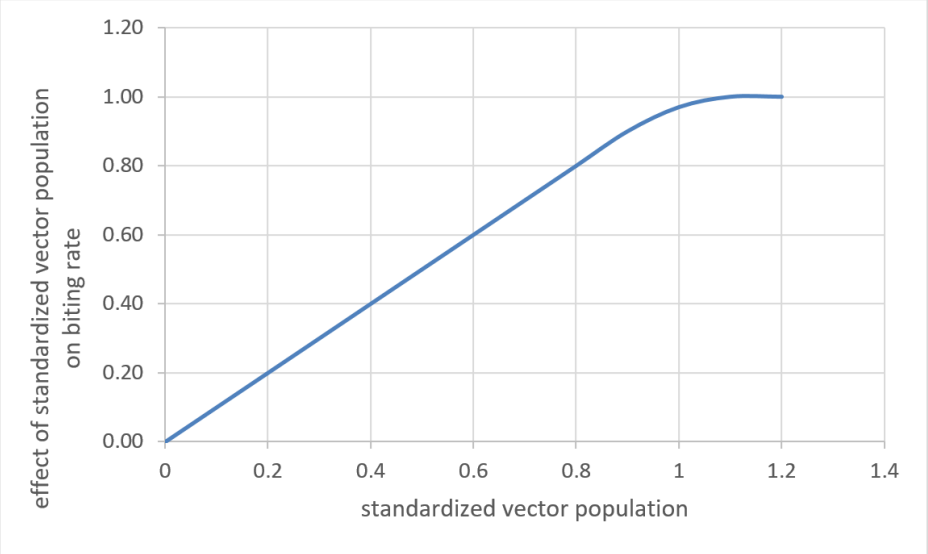


Figure 5.2. *Effect of Standardized Vector Population on Biting Rate* Graph.

At the *standardized vector population* value of 1.2, the *effect of standardized vector population on biting rate* value is one, which means the *getting bitten rate for human* is at its maximum possible value. When *standardized vector population* decreases to 0.5, the *effect of standardized vector population on biting rate* value is 0.5, which means we multiply the *getting bitten rate for human* value with 0.5 to decrease the number of bites when *total vector* population decreases. When *standardized vector population* is zero, the *effect of standardized vector population on biting rate* value is zero, which means we multiply the *getting bitten rate for human* value with zero and there are no bites in the model.

Infected vector ratio is the ratio of *infected vector* to *total vector* population, and the equation is

$$\text{infected vector ratio} = \frac{\text{infected vector}}{\text{total vector}}. \tag{5.18}$$

Infected vector ratio is dimensionless.

Infectious getting bitten rate for human is the rate of human that got bitten by an *infected vector*. The virus may or may not be transmitted to the human from the *infected vector*. Equation of *infectious getting bitten rate for human* is

$$\begin{aligned}\text{infectious getting bitten rate for human} &= \text{infected vector ratio} \\ &\quad \times \text{getting bitten rate for human.}\end{aligned} \tag{5.19}$$

Infectious getting bitten rate for human has units of 1/Week.

We note that *getting bitten rate for human* is a variable for the rate of human that got bitten by any vector. When we multiply this variable with *infected vector ratio*, we obtain *infectious getting bitten rate for human*. For a *susceptible human* to become an *exposed human*, the vector that bites the human should transmit the virus. The virus is not transmitted from *infected vector* to *susceptible human* with every infectious bite, there is a transmission probability.

Transmission probability of infectious vector bite is the probability of a *susceptible human* getting the virus after an infectious vector bite. We do not consider the number of infectious bites in the model explicitly; we consider it implicitly in the *transmission probability of infectious vector bite* variable. We take the probability as an average value, considering the possible number of bites within the average transmission probability. Equation of *transmission probability of infectious vector bite* is

$$\text{transmission probability of infectious vector bite} = 0.4 \text{ [Dimensionless]}. \tag{5.20}$$

We take the *transmission probability of infectious vector bite* value from the reference literature as 0.4 as a rough number [19]. This means that 40 percent of the human who got bitten by an *infected vector* gets infected with dengue virus.

Infection rate of human is the rate of human that gets bitten by an *infected vector* and get the virus after the bite, and the equation is

$$\begin{aligned}\text{infection rate of human } &= \text{infectious getting bitten rate for human} \\ &\times \text{transmission probability of infectious vector bite.}\end{aligned} \tag{5.21}$$

Infection rate of human has units of 1/Week.

Infection rate of human is the rate of a human getting infected from an infectious vector bite with a probability. We obtain this rate for one human. When we multiply the *infection rate of human* with *subgroup of susceptible human* population, we obtain the number of human getting infected per week; that is *infection flow of human*. *Infection flow of human* is given in Equation (5.8).

After human get exposed to the virus, they become infected with a delay. The delay is about a week. *Progression time of human* is the time that an *exposed human* becomes infected. The *progression time of human* is four to ten days and can be taken as seven days as an average value [5,20,21]. The equation of *progression time of human* is

$$\text{progression time of human} = 1 \text{ [Week]}. \tag{5.22}$$

Progression rate of human is the number of *exposed human* that becomes infectious in a week. When we divide *exposed human* population by *progression time of human*, we obtain *progression rate of human*, and the equation is

$$\text{progression rate of human} = \frac{\text{exposed human}}{\text{progression time of human}}. \tag{5.23}$$

Progression rate of human has units of Human/Week.

When a person gets infected, that person is also infectious for vectors. Infectious human may or may not show symptoms. *Fraction of symptomatic human* is the ratio of *exposed human* that shows symptoms when they become infectious [2], and the equation is

$$\text{fraction of symptomatic human} = 0.1 \text{ [Dimensionless]}. \tag{5.24}$$

Progression flow of symptomatic human is the number of human that becomes infectious with symptoms in a week, and the equation is

$$\begin{aligned}&\text{progression flow of symptomatic human } = \\ &\text{fraction of symptomatic human} \times \text{progression rate of human.}\end{aligned} \tag{5.25}$$

Progression flow of symptomatic human has units of Human/Week.

Fraction of asymptomatic human is the ratio of human that become infectious without symptoms [2], and the equation is

$$\text{fraction of asymptomatic human} = 1 - \text{fraction of symptomatic human.} \tag{5.26}$$

Fraction of asymptomatic human is dimensionless.

Progression flow of asymptomatic human is the number of humans that become infectious without symptoms in a week, and the equation is

$$\begin{aligned}&\text{progression flow of asymptomatic human } = \\ &\text{fraction of asymptomatic human} \times \text{progression rate of human.}\end{aligned} \tag{5.27}$$

Progression flow of asymptomatic human has units of Human/Week.

After a human becomes infectious, that human mostly recovers from dengue. However, some can die with a low probability. In our model *human deaths due to dengue* represents the number of deaths due to dengue per week. In our model, we only consider the death of *symptomatic infectious human*, and the equation is

$$\begin{aligned}&\text{human deaths due to dengue } =\\&\text{human death rate due to dengue} \times \text{symptomatic infectious human.}\end{aligned} \tag{5.28}$$

Human deaths due to dengue has units of Human/Week.

Human death rate due to dengue is the death rate of *symptomatic infectious human*. *Human death rate due to dengue* is very low. We take *human death rate due to dengue* as 0.001 in our model as a rough number, and the equation is

$$\text{human death rate due to dengue} = 0.001\ [\frac{1}{\text{Week}}]. \tag{5.29}$$

Recovery flow of symptomatic human is the number of *symptomatic infectious human* getting recovered from dengue virus in a week, and the equation is

$$\text{recovery flow of symptomatic human } = \frac{\text{symptomatic infectious human}}{\text{time for recovery of symptomatic human}}. \tag{5.30}$$

Recovery flow of symptomatic human has units of Human/Week.

Recovery flow of asymptomatic human is the number of *asymptomatic infectious human* who are recovered from dengue virus in a week, and the equation is

$$\text{recovery flow of asymptomatic human } = \frac{\text{asymptomatic infectious human}}{\text{time for recovery of asymptomatic human}}. \tag{5.31}$$

Recovery flow of asymptomatic human has units of Human/Week.

Since the *human death rate due to dengue* is very low, we consider *time for recovery of symptomatic human* and *time for recovery of asymptomatic human* in the model instead of recovery rate of human. Recovery rate of human is very close to one, thus we consider the delay between getting infectious and getting recovered. *Time for recovery of symptomatic human* and *time for recovery of asymptomatic human* can have individual values. We take both recovery times as one week as an average value [5], and the equations are

$$\text{time for recovery of symptomatic human} = 1 \text{ [Week]}, \tag{5.32}$$

and

$$\text{time for recovery of asymptomatic human} = 1 \text{ [Week]}. \tag{5.33}$$

We assume that *recovered human* stays immune to all serotypes of dengue for five years on average. *Immunity loss flow of human* is the number of humans losing their immunity in a week, and the equation is

$$\begin{aligned} \text{immunity loss flow of human} &= \text{immunity loss rate of human} \\ &\quad \times \text{recovered human}. \end{aligned} \tag{5.34}$$

Immunity loss flow of human has units of Human/Week.

A new serotype usually comes into an area with cycles of three to five years [22]. The average can be taken as four years. Since normally a person gains immunity for one of the four dengue serotypes, we should also consider this for *immunity loss rate of human* in our model. Therefore, we take the time roughly five years, as it is the upper bound. Then we calculate the *immunity loss rate of human* considering five years of immune time. After the loss of immunity, humans return to the *susceptible human* stock. Therefore, we take *immunity loss rate of human* as 0.00385 per week, and the

equation is

$$\text{immunity loss rate of human} = 0.00385\ [\frac{1}{\text{Week}}]. \tag{5.35}$$

In human substructure, we added two more stocks to obtain the *total symptomatic infected human* and *total human deaths* for the period of the modelling time.

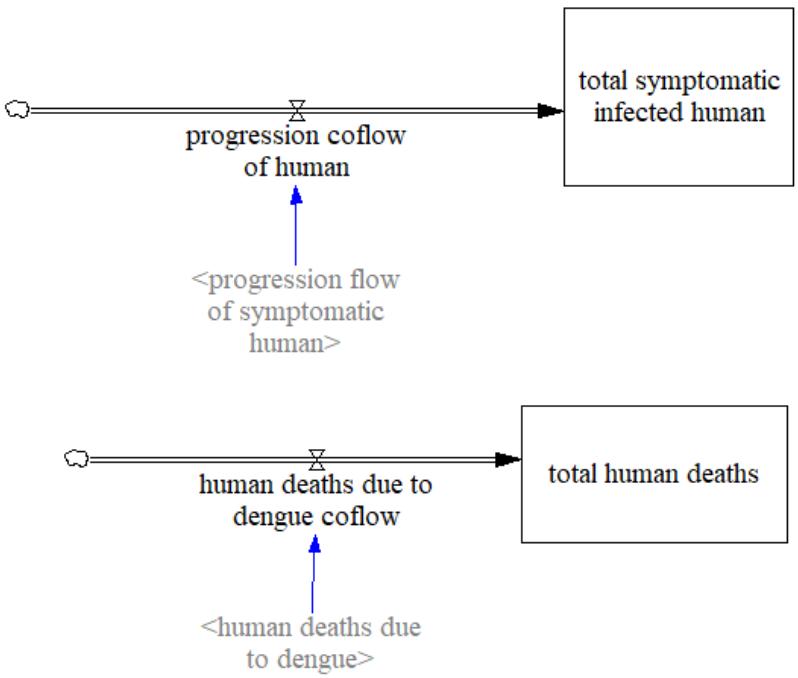


Figure 5.3. *Total Symptomatic Infected Human* and *Total Human Deaths.*

We need to calculate the total number of humans that got infected and the total number of humans that died due to dengue virus throughout the modelling time for the average case number comparison with the relevant data taken from literature [1,2].

For *total symptomatic infected human* calculation, we give the value of the *progression flow of symptomatic human* to the *progression coflow of human*. *Progression coflow of human* is the inflow to the *total symptomatic infected human*. Equation of

total symptomatic infected human is

$$\frac{d(\text{total symptomatic infected human})}{dt} = \text{progression coflow of human.} \tag{5.36}$$

Total symptomatic infected human has units of Human and the initial value is zero.

We give the value of the *progression flow of symptomatic human* to the *progression coflow of human*, and the equation of the *progression coflow of human* is

$$\text{progression coflow of human} = \text{progression flow of symptomatic human.} \tag{5.37}$$

Progression coflow of human has units of Human/Week.

In *total human deaths* calculation, we give the value of the human deaths due dengue to the *human deaths due to dengue coflow*. *Human deaths due to dengue coflow* is the inflow to the *total human deaths*, and the equation is

$$\frac{d(\text{total human deaths})}{dt} = \text{human deaths due to dengue coflow.} \tag{5.38}$$

Total human deaths have units of Human and the initial value is zero. Equation of *human deaths due to dengue coflow* is

$$\text{human deaths due to dengue coflow} = \text{human deaths due to dengue.} \tag{5.39}$$

Human deaths due to dengue coflow has units of Human/Week.

We take the initial values of these stocks as zero at time zero. Therefore, the cumulative sum of these two flows is calculated separately for the model run time.

5.2.2. Description of Vector Substructure

We explain the human substructure in Chapter 5.2.1, and now we will explain the vector substructure of our model.

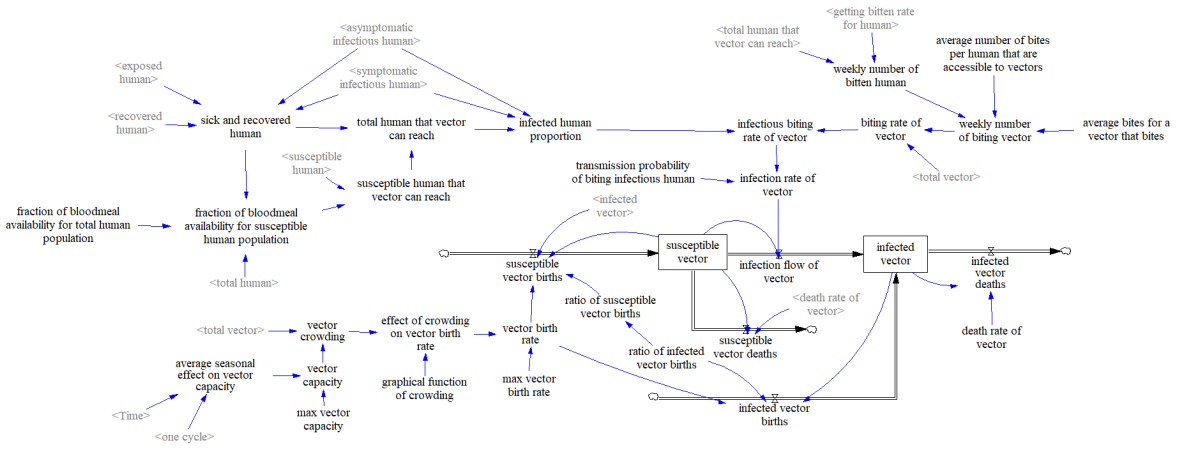


Figure 5.4. Vector Substructure.

In vector substructure, there are two stocks: *susceptible vector* and *infected vector*.

Susceptible vector is the stock of vectors that do not carry dengue virus. If a *susceptible vector* bites an infectious human, there is a probability of getting infected. Equation of *susceptible vector* is

$$\begin{aligned}\frac{d(\text{susceptible vector})}{dt} &= \text{susceptible vector births} \\ &\quad - \text{infection flow of vector} \\ &\quad - \text{susceptible vector deaths.}\end{aligned} \tag{5.40}$$

Susceptible vector has units of Vector.

Infected vector is the stock of vectors that got infected by feeding on an infectious human or is an offspring of an *infected vector*, and the equation is

$$\begin{aligned}\frac{d(\text{infected vector})}{dt} &= \text{infected vector births} \\ &+ \text{infection flow of vector} \\ &- \text{infected vector deaths.}\end{aligned} \tag{5.41}$$

Infected vector has units of Vector.

We take the ratio of *infected vector* to *total vector* around four percent in the model [23–25].

We do not consider exposed and recovered vectors in our model. We can neglect these because the lifetime of a vector is very short. We take vectors lifetime as three weeks on average [13]. Lifetime of a vector is shorter than the recovery time from dengue virus. Therefore, the vector dies before getting recovered.

Seasonal changes have effect on the vector births throughout the year. We assume that the same pattern of the seasonality repeats itself each year. We use a sinus function for simplicity. We take *one cycle* as 52 Weeks. We assume that the average value of seasonal effect on *vector capacity* is 0.6. The equation of *average seasonal effect on vector capacity* is

$$\begin{aligned}&\text{average seasonal effect on vector capacity} = \\ &0.6 + 0.16 \times \text{SIN}(\frac{2 \times 3.1416 \times \text{Time}}{\text{one cycle}} + 4 \times \frac{3.1416}{12}).\end{aligned} \tag{5.42}$$

Average seasonal effect on vector capacity is dimensionless.

There is a limit that vector population cannot exceed, that is *max vector capacity*.

Rain, temperature, and human population are three important factors that affect

the capacity of vector population. For maximum *vector capacity*, we assume that temperature and rain are at optimal levels of seasonality. Even though the environment has the optimum rain and temperature conditions, female vectors need human blood to lay eggs, and there are not infinite number of humans to feed on. Thus, number of human that vector can reach is a limit to *max vector capacity*. We assume that the *max vector capacity* is 250 million vectors [26], and the equation is

$$\text{max vector capacity} = 2.5 \times 10^8 \text{ [Vector]}. \tag{5.43}$$

Seasonality has effect on *vector capacity*. In this model, we consider rain and temperature effect implicitly in the seasonality effect. The rain and temperature should be at optimum conditions for vector population increase. However, weather conditions change throughout the year due to seasonality and the optimum conditions may not always be achieved. The vectors need water to lay eggs on, and the water level should rise over the eggs to hatch them. The temperature is important for eggs to evolve into vectors. Equation of *vector capacity* is

$$\begin{aligned} \text{vector capacity } &= \text{average seasonal effect on vector capacity} \\ &\times \text{max vector capacity}. \end{aligned} \tag{5.44}$$

Vector capacity has units of Vector.

Total vector population is the number of vectors at any given time. *Total vector* variable is given in Equation (5.16). *Total vector* population should not exceed the *vector capacity*. Therefore, we add a variable named as *vector crowding* to the model to set an upper limit in extreme conditions. We calculate *vector crowding* by dividing the *total vector* population to *vector capacity*, and the equation is

$$\text{vector crowding} = \frac{\text{total vector}}{\text{vector capacity}}. \tag{5.45}$$

Vector crowding is dimensionless.

We add the *effect of crowding on vector birth rate* to the model by using a simple graphical function. When the *total vector* is much lower than the *vector capacity*, we obtain higher birth rates. As *total vector* value gets closer to the *vector capacity*, the birth rate decreases. When the *total vector* number reaches the value of the *vector capacity*, the crowding value equals to one. At this point, births should be equal to deaths so that the vector population does not exceed the *vector capacity*. We use a graphical function in the model to include this behavior. This graphical function is given in Figure 5.5.

Graphical function of crowding:

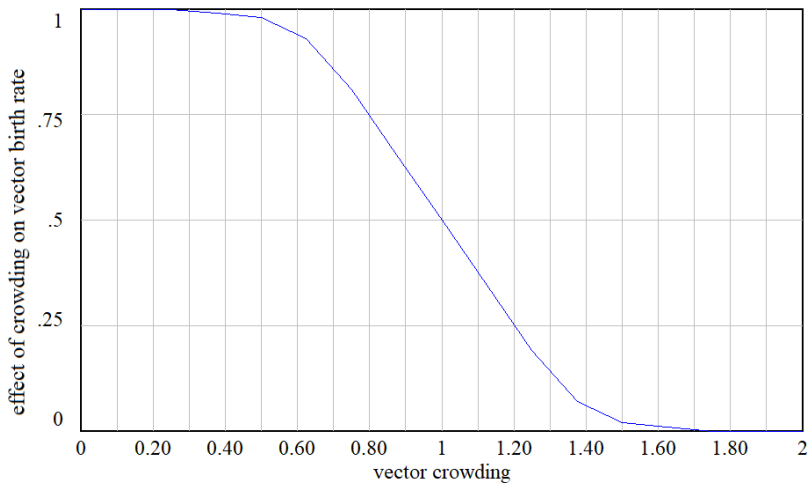


Figure 5.5. *Graphical Function of Crowding.*

In this model, we take *death rate of vector* as 0.33 per week, and *max vector birth rate* as 0.66 per week. In Figure 5.5, at (1, 0.5) point, the *total vector* equals to the *vector capacity* and the *vector birth rate* is half of the *max vector birth rate* (i.e., *vector birth rate* $= 0.66 \times 0.5 = 0.33$). After this critical value, as crowding exceeds the value of 1, we multiply the *max vector birth rate* with values lower than 0.5, so that the deaths are more than the births of the vectors. Thus, the *total vector* population decreases back to the value of *vector capacity*. First, we construct the graph as a linear graph starting from one and ending at zero, then we smooth it on the edges. Granted that the (1, 0.5) point is included, slope of the graph may be altered.

We obtain the values of *effect of crowding on vector birth rate* from the *graphical function of crowding*. We obtain *vector birth rate* by multiplying the values of *effect of crowding on vector birth rate* and the *max vector birth rate*, and the equation is

$$\begin{aligned} \text{vector birth rate } &= \text{effect of crowding on vector birth rate} \\ &\times \text{max vector birth rate.} \end{aligned} \tag{5.46}$$

Vector birth rate has units of 1/Week. We take *max vector birth rate* as 0.66 per week, and the equation is

$$\text{max vector birth rate} = 0.66\ [\frac{1}{\text{Week}}]. \tag{5.47}$$

For vector population not to extinct, *max vector birth rate* should exceed the death rate. Therefore, we assume that the *max vector birth rate* is two times of the death rate. Birth rate of vectors depend on temperature, rainfall and finding enough human to feed on. In the *max vector birth rate* scenario, we assume the optimum conditions of temperature and rainfall.

For the calculation of *susceptible vector births*, we consider vector birth from *susceptible vector* and from *infected vector*. We multiply the *vector birth rate* with the number of vectors that can lay susceptible eggs to evolve into *susceptible vector*s. All the eggs of the *susceptible vector* are also susceptible. Therefore, we consider all the *susceptible vector*s in the *susceptible vector births* calculation. Most of the *infected vector* eggs grow into *susceptible vector*s. To calculate the number of *infected vector*s that create *susceptible vector*s, we multiply *infected vector* value with the ratio of *infected vector*s that create *susceptible vector*s. We sum up *susceptible vector* and number of *infected vector*s that create *susceptible vector*s first, then multiply it with the *vector birth rate* to calculate the value of *susceptible vector births*.

The equation of *susceptible vector births* is

$$\begin{aligned}&\text{susceptible vector births} = \text{vector birth rate}\\&\times (\text{susceptible vector} + \text{ratio of susceptible vector births} \times \text{infected vector}).\end{aligned} \tag{5.48}$$

Susceptible vector births have units of Vector/Week.

Ratio of susceptible vector births is the ratio of eggs of an *infected vector* evolving into susceptible adult vectors. We calculate the *ratio of susceptible vector births* by subtracting the *ratio of infected vector births* from unity, and the equation is

$$\text{ratio of susceptible vector births} = 1 - \text{ratio of infected vector births}. \tag{5.49}$$

Ratio of susceptible vector births is dimensionless.

Ratio of infected vector births is the ratio of eggs of an *infected vector* evolving into infected adult vectors. *Infected vector* eggs can restart the virus if it is over, because the eggs can stay unhatched for months [9]. We assume that the *ratio of infected vector births* is 0.003 in our model [16], and the equation is

$$\text{ratio of infected vector births} = 0.003\ [\text{Dimensionless}]. \tag{5.50}$$

Detailed explanation about *susceptible vector births* and what effects these births are given above. *Infected vector births* have a similar structure. All the factors included in *susceptible vector births* are also valid for *infected vector births*. We use the same *vector birth rate* variable in *infected vector births* calculations. The only difference between *susceptible vector births* and *infected vector births* is that *infected vector*s can only be evolved from the eggs of *infected vector*s. None of the *susceptible vector* eggs evolve into an *infected vector*, because the blood of a susceptible female vector that lays the eggs does not have the dengue virus. Therefore, we multiply the *vector birth rate* with *ratio of infected vector births* and only the *infected vector* population.

The equation of *infected vector births* is

$$\begin{aligned}\text{infected vector births} &= (\text{ratio of infected vector births} \times \text{vector birth rate}) \\ &\quad \times \text{infected vector.}\end{aligned} \tag{5.51}$$

Infected vector births have units of Vector/Week.

Vector births for *susceptible vector*s and *infected vector*s are explained above. Now a *susceptible vector* becoming an *infected vector* by biting an infectious human will be explained.

Infection flow of vector represents the number of vectors getting infected in a week. When a *susceptible vector* feeds on an infectious human, that vector can become infected with a possibility. Further explanations will be given under each relevant variable in this substructure. Equation of *infection flow of vector* is

$$\text{infection flow of vector} = \text{infection rate of vector} \times \text{susceptible vector.} \tag{5.52}$$

Infection flow of vector has units of Vector/Week.

Infection rate of vector is the rate of vectors that get infected in a week, after biting infectious human. A *susceptible vector* does not always become infected after biting an infectious human, there is a transmission probability. In our model we take the *transmission probability of biting infectious human* as an average value. We do not show the effect of biting one human or multiple humans explicitly in our model, but we consider the effect implicitly in the *transmission probability of biting infectious human.* The equation of *infection rate of vector* is

$$\begin{aligned}\text{infection rate of vector} &= \text{infectious biting rate of vector} \\ &\quad \times \text{transmission probability of biting infectious human.}\end{aligned} \tag{5.53}$$

Infection rate of vector has units of 1/Week.

We take the *transmission probability of biting infectious human* from the reference literature as 0.7 as a rough number [27], and the equation is

$$\text{transmission probability of biting infectious human} = 0.7 \text{ [Dimensionless]}. \quad (5.54)$$

The transmission probability from human to vector is higher than the transmission probability from vector to human. This makes us think that, because vectors are very small and the blood taken from the infectious human is a big portion of the vector body, the vector should be highly affected by the infected blood.

Infectious biting rate of vector is a variable that denotes the rate of bites that are infectious to vectors. When a *susceptible vector* bites an infectious human, this is an infectious bite regardless of the results. The *susceptible vector* may get infected or not. We calculate this variable by the multiplication of *biting rate of vector* and *infected human proportion*, and the equation is

$$\begin{aligned} \text{infectious biting rate of vector} &= \text{infected human proportion} \\ &\quad \times \text{biting rate of vector}. \end{aligned} \quad (5.55)$$

Infectious biting rate of vector has units of 1/Week.

Biting rate of vector is the probability of a vector biting a human in a week. We calculate the *biting rate of vector* from the *getting bitten rate for human* and other related variables. The explanations will be given below with related order.

First of all, we calculate the *weekly number of bitten human*. *Weekly number of bitten human* is the number of human that get bitten in a week. In human substructure, we state that *getting bitten rate for human* is the probability of an accessible human getting bitten by a vector that week. *Getting bitten rate for human* variable is

given in Equation (5.14). We use the *total human that vector can reach* parameter as the accessible human population for vector bites. *Total human that vector can reach* variable is given in Equation (5.64). To calculate the number of human that get bitten in a week, we multiply the *getting bitten rate for human* and *total human that vector can reach*. Equation of *weekly number of bitten human* is

$$\begin{aligned}\text{weekly number of bitten human} = \text{getting bitten rate for human} \\ \times \text{ total human that vector can reach.}\end{aligned} \tag{5.56}$$

Weekly number of bitten human has units of Human/Week.

Average number of bites per human that are accessible to vectors is the number of bites that a human gets on average in a week, for the human population that gets bitten that week. We assume that the *average number of bites per human that are accessible to vectors* is 20 bites per human per week, and the equation is

$$\begin{aligned}&\text{average number of bites per human that are accessible to vectors} = \\ &20\ [\frac{\text{Bites}}{\text{Human} \times \text{Week}}].\end{aligned} \tag{5.57}$$

Weekly number of biting vector is the number of vectors that bite humans in a week. Vectors being infected or not, have no effect on this variable. We consider *total vector* population. When we multiply the *average number of bites per human that are accessible to vectors* and *weekly number of bitten human*, then divide this value to the average number of bites of a vector that bites that week, we obtain *weekly number of biting vector*, and the equation is

$$\begin{aligned}&\text{weekly number of biting vector} = \\ &\text{average number of bites per human that are accessible to vectors} \\ &\times \frac{\text{weekly number of bitten human}}{\text{average bites for a vector that bites}}.\end{aligned} \tag{5.58}$$

Weekly number of biting vector has units of Vector/Week.

Average bites for a vector that bites is the average number of bites per vector per week for the vector population that bites that week. Vectors being infected or not have no effect on this parameter. We do not consider the vectors that did not bite human that week. We assume that the *average bites for a vector that bites* is 1 bites per vector per week on average for the vectors that bite human in a given week, and the equation is

$$\text{average bites for a vector that bites} = 1\ [\frac{\text{Bites}}{\text{Vector} \times \text{Week}}]. \tag{5.59}$$

We note that, *biting rate of vector* is the rate of the vectors that bite human in a week. We calculate *biting rate of vector* by dividing the number of vectors that bite that week to the *total vector* population, and the equation is

$$\text{biting rate of vector} = \frac{\text{weekly number of biting vector}}{\text{total vector}}. \tag{5.60}$$

Biting rate of vector has units of 1/Week.

Biting rate of vector and *infected human proportion* are the two variables that have an effect on *infectious biting rate of vector*. *Infectious biting rate of vector* variable is given in Equation (5.55). *Infected human proportion* and the previous variables that affect *infected human proportion* are given below.

Infected human proportion is the ratio of total infected human to the *total human that vector can reach*. By infected human, we refer to the sum of *symptomatic infectious human* and *asymptomatic infectious human*, because for a human to be infectious, that human should get infected with dengue virus. We assume that vectors do not reach to all the human population. Technically vectors can contact any human in their flight area. However, in practice this does not apply. Therefore, we set a limit to the fraction of human that vectors can reach. As this fraction increases, number of human

considered increases. The equation of *infected human proportion* is

$$\text{infected human proportion} = \frac{\text{symptomatic infectious human} + \text{asymptomatic infectious human}}{\text{total human that vector can reach}}. \tag{5.61}$$

Infected human proportion is dimensionless.

The *total human* population in our model is six million. Humans at susceptible stage have a lower probability of contacting with vectors compared to the humans at the other stages. We assume that maximum 95 percent of the *total human* can contact vectors. Since exposed, infected, and *recovered human* contacted a vector before for sure, they have a higher possibility of contacting a vector again. We take the sum of exposed, infected, and *recovered human* populations and track this summation with the *sick and recovered human* population variable. The equation of *sick and recovered human* is

$$\begin{aligned}\text{sick and recovered human} &= \text{exposed human} + \text{symptomatic infectious human} \\ &\quad + \text{asymptomatic infectious human} + \text{recovered human}.\end{aligned} \tag{5.62}$$

Sick and recovered human has units of Human.

Susceptible human might have contacted with vectors before and did not get infected, but this cannot be tracked. Moreover, there can be some population in *susceptible human* stock that got recovered from a dengue serotype and lost the temporal immunity for all serotypes after immunity loss time. Contacted before or not, *susceptible human* can contact vectors, but the possibility is lower compared to the *sick and recovered human*. Therefore, we multiply the *susceptible human* with a fraction to decrease the number of human that vector can contact. We name this as *fraction of bloodmeal availability for susceptible human population* and we do not allow this fraction to exceed 95 percent.

The equation of *susceptible human that vector can reach* is

$$\begin{aligned}&\text{susceptible human that vector can reach } =\\&\text{fraction of bloodmeal availability for susceptible human population}\\&\times \text{ susceptible human.}\end{aligned} \tag{5.63}$$

Susceptible human that vector can reach has units of Human. The equation of *total human that vector can reach* is

$$\begin{aligned}&\text{total human that vector can reach } =\\&\text{susceptible human that vector can reach + sick and recovered human.}\end{aligned} \tag{5.64}$$

Total human that vector can reach has units of Human.

We add the *sick and recovered human* population directly to the *total human that vector can reach*. We multiply the *susceptible human* population with a fraction that only goes up to 95 percent. We cannot directly multiply *susceptible human* population with 95 percent. In calculation of *fraction of bloodmeal availability for susceptible human population*, we subtract the ratio of *sick and recovered human* to *total human* from the 95 percent. This subtraction prevents the risk of having a value higher than 1 for *infected human proportion*, when total infected human population exceeds the value of *total human that vector can reach*. Ratio of *sick and recovered human* to *total human* also cannot exceed 95 percent, because we assume that only 95 percent of human can contact vectors.

For extreme conditions, we add a max (0, rate) function to prevent having negative numbers on the *fraction of bloodmeal availability for susceptible human population*, and the equation is

$$\begin{aligned}\text{fraction of bloodmeal availability for susceptible human population} \; = \\ \text{If rate} \leq 0,\ 0 \\ \text{If rate} > 0,\ \text{rate} \qquad (5.65)\end{aligned}$$

$$\text{where, rate} = \text{fraction of bloodmeal availability for total human population} - \frac{\text{sick and recovered human}}{\text{total human}}.$$

Fraction of bloodmeal availability for susceptible human population is dimensionless.

Fraction of bloodmeal availability for total human population is the maximum fraction of human that is accessible to vector population. We assume that *fraction of bloodmeal availability for total human population* is 95 percent, and the equation is

$$\text{fraction of bloodmeal availability for total human population} = 0.95\ [\text{Dimensionless}]. \qquad (5.66)$$

Sick and recovered human have already contacted with vectors before. Since we assume maximum contact rate as 95 percent, if *sick and recovered human* has already reached the value of 95 percent, no more human can contact a vector. Therefore, the *fraction of bloodmeal availability for susceptible human population* will be zero in this case.

Total human is the sum of all the stocks of human populations, and the equation is

$$\begin{aligned}\text{total human} \; = \; & \text{susceptible human} + \text{exposed human} \\ & + \text{symptomatic infectious human} \\ & + \text{asymptomatic infectious human} + \text{recovered human}.\end{aligned} \qquad (5.67)$$

Total human has units of Human.

We keep vector death calculation very simple in the model. Infected or not, vectors die with natural causes after their lifetime. We assume that vectors lifetime is three weeks on average [13]. We assume the *death rate of vector* as 0.33 per week. We use the same *death rate of vector* for susceptible and *infected vector*s and multiply this rate with relevant populations to calculate vector deaths per week. The equation of *death rate of vector* is

$$\text{death rate of vector} = 0.33\ [\frac{1}{\text{Week}}]. \tag{5.68}$$

For *susceptible vector deaths*, we multiply *susceptible vector* with the *death rate of vector* to reflect the delay of three weeks before death and to calculate the number of *susceptible vector deaths* in a week, and the equation is

$$\text{susceptible vector deaths} = \text{susceptible vector} \times \text{death rate of vector}. \tag{5.69}$$

Susceptible vector deaths have units of Vector/Week.

For *infected vector deaths*, we multiply *infected vector* with the *death rate of vector* to reflect the delay of three weeks before death. We calculate the number of *infected vector deaths* in a week, and the equation is

$$\text{infected vector deaths} = \text{infected vector} \times \text{death rate of vector}. \tag{5.70}$$

Infected vector deaths have units of Vector/Week.

We do not calculate the cumulative sum of deaths due to dengue in our model for vectors, because the recovery time for vectors is longer than their lifetime. Therefore, we assume that *infected vector*s die with natural causes, before getting recovered from dengue.

5.2.3. Validation of the Model

We constructed a structurally valid model that originates from the literature. The SIR models in the literature have three state variables: susceptible human, infected human, and recovered human stocks [28–30]. Our model also has susceptible, infected, and recovered human stocks similar to the literature. The SEIR models have exposed human stock in addition to the susceptible, infected, and recovered human stocks [31]. Our model also has exposed human stock. In literature, some models have two infectious human stocks; asymptomatic and symptomatic [2]. We also have the two infectious human stocks in our model. In the real system, it is relatively easier to track symptomatic humans. However, asymptomatic humans also have an important effect on the persistence of the virus. If a human is symptomatic, that person can take precautions against interaction with the vector. However, an asymptomatic human is unaware of the infection and may spread the virus unknowingly. Accordingly, we cannot ignore the effect of asymptomatic infectious human population.

In vector substructure of our model, we have susceptible and infected vector stocks similar to the models in the literature. In literature, there are many examples of models that have susceptible and infected vector stocks [28–31]. We use average values from the relevant literature. For example, transmission probability from human to vector is taken as a higher value from the transmission probability from vector to human in our model. The same variable could be used for both of the transmission probabilities. However, after literature review, different average values are assigned to them [19, 27]. As vectors are very small and the blood taken from the infectious human is quite high compared to the size of the vector, the vector is highly affected by the infected blood. However, when the infected vector bites, the transmitted blood is relatively small compared to the size of a human. This has a structural effect on the model, one single variable cannot explain the transmission of the disease from human to vector and from vector to human. This difference is considered in our model. Thus, we take the *transmission probability of infectious vector bite* value as 0.4 and the *transmission probability of biting infectious human* as 0.7 [19, 27].

The *progression time of human* is four to ten days in literature, and we take seven days as an average value [5, 20, 21]. *Time for recovery of symptomatic human* is taken as one week from relevant literature [5]. A new serotype usually comes into an area with cycles of three to five years. We take five years as an upper bound and calculate the immunity loss rate accordingly [22]. We take vectors lifetime as three weeks on average from the relevant literature [13]. We assume that the *max vector capacity* is 250 million vectors considering relevant literature [26]. Also, *infected vector births* is considered in our model [6–9].

We also performed several validation tests on the model as given below.

- We performed numerical confirmation tests. We constructed our model with average parameter values from the relevant literature and our close estimations. We explain the values in detail in Chapter 5.2.1 and in Chapter 5.2.2.
- We performed structural confirmation tests. All the equations in our model reflect the causal relationships of the real system and there are no dummy variables. All variables have meaningful counterparts.
- For dimensional consistency test, we performed the unit's check for the model, all units matched.
- We carried out output behavior tests with the data taken from relevant literature for the validation of our model [1, 2].
  - We calibrate the initial values of the human and vector stocks with the data taken from Rio de Janeiro. We take the initial value of *total human* as six million and the initial value of *total vector* as 150 million. We start with an equilibrium run while calibrating the initial values of all human and vector stocks. We take close rough numbers from the equilibrium values for the runs given in this study. Then we compare the results with the data of Rio de Janeiro for validation [2].
- We performed extreme condition tests and behavioral sensitivity tests on our model. We applied these tests to each equation in isolation. We performed the tests successfully.

6. MODEL BEHAVIOR AND MODEL CALIBRATION PROCESS

The viral epidemic of dengue is persistent in the selected region. To understand the viral epidemic, we need to analyze how the dengue virus is sustained in an area with human-vector interactions. Normally, dengue virus is sustained mostly with human and vector interactions. If the virus is eliminated for a while, vertical infection of vectors restarts the dengue virus. The parameters that we use in our model are mainly the average parameters that we take from the relevant literature for dengue virus in Rio de Janeiro. We name our model with these parameters as Run 0 in this study. In Run 0, the number of infectious human and *infected vector* converge to zero. This means the virus decays and eradicates when we use the average parameter values. And this behavior does not match with the data taken from the relevant literature [1]. Therefore, we try to understand the reasons behind the persistent existence of the virus in the region. We try to calibrate the parameters of our model to obtain persistence in the epidemic as it is in the real system. To have a wide perspective for scenario analyses, we examine the relevant literature of different countries and viruses [32, 33].

We perform sensitivity analysis on the model to discover the leverage parameters. For sensitivity analysis, we choose all the parameters one by one. We only change one parameter at a time, while all the other parameters stay the same. We assign different values to the parameters within their acceptable boundaries. And we observe the effect of these parameters on the resulting dynamics. We obtain three leverage parameters with these sensitivity analyses as; *time for recovery of asymptomatic human*, *ratio of infected vector births* and *average number of bites per human that are accessible to vectors*. To obtain a behavior similar to the relevant data, we try to calibrate the values of these three parameters. We carry out the first three runs by keeping the two of the parameters constant and interchanging only one parameter. In the first run, we only increase the value of *time for recovery of asymptomatic human* in the model. In the second run, we only increase the value of *ratio of infected vector births*. In the

third run, we only increase the value of *average number of bites per human that are accessible to vectors*. However, we have to increase the parameters to extreme values in these three runs. Therefore, in the fourth run, we try to obtain a combination of these three parameters with more moderate values, to get similar behavior with the relevant data.

We take the data from Rio de Janeiro for numerical results and behavioral results. We examine the yearly number of dengue cases in Rio de Janeiro between 2000 and 2015. The dengue cases numbers have a maximum value of 152,687 humans in 2002, a minimum value of 2,606 humans in 2004, and a mean value of 43,670 humans between 2000 and 2015. Further data can be found at the Table 6 in the relevant literature [2]. For the behavioral results, we examine the weekly number of dengue cases in Brazil between 2014 and 2019. We take the weekly data in Brazil in 2015 and modify it with the data of Rio de Janeiro between 2000 and 2015. The behavioral results are very similar to each other between 2014 and 2019, except 2018. All the years except 2018, have a peak between the fifth and the twentieth week, with similar behavior. We choose the weekly data of 2015 as an example, and we plot the data in Excel. We show the plotted data in the Figure 6.1 [1]. Then, we multiply the weekly dengue cases with the ratio of average infected human of Rio de Janeiro between 2000 and 2015 to infected human population of Brazil in 2015. Then we plot the data in Excel. We show the plotted data in the Figure 6.2 [1, 2]. We took the data used in this study from PAHO in March 2020 and the data is assumed to be valid for that date [1]. PAHO declares in the website that the data can be changed at any time by PAHO. PAHO does not take any responsibility for the given data.

In the Figure 6.1, we give the dengue case numbers of Brazil in 2015. We use this data by multiplying it with a ratio to modify it for Rio de Janeiro population. We perform numerical and behavioral result comparison with the derived data that is given in Figure 6.2.

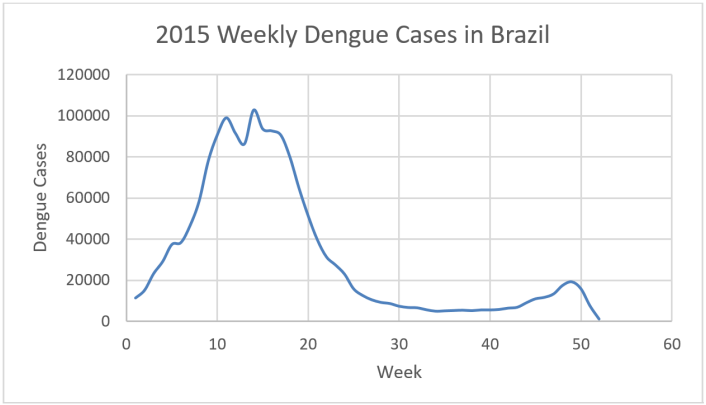


Figure 6.1. Weekly Dengue Cases in Brazil in 2015 [1].

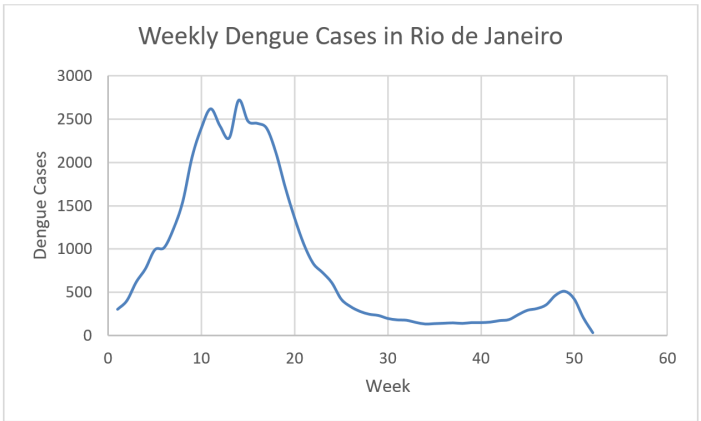


Figure 6.2. Weekly Dengue Cases in Rio de Janeiro [1, 2].

In the Figure 6.2, we use the dengue case numbers of Brazil and multiply them with a ratio. We use the ratio of total infected human population for a year in Rio de Janeiro on average between 2000 and 2015, to the data of total infected human population of Brazil in 2015 [1]. We take the average value between 2000 and 2015 in Rio de Janeiro as 43,670 humans and the value in Brazil in 2015 as 1,649,008 humans for the calculation of the ratio for total infected human populations. Using this ratio, we obtain the numerical values for Figure 6.2 from the numerical values of Figure 6.1. Later, we perform the behavioral result comparison with the derived data presented in Figure 6.2 because we do not have the weekly number of dengue cases for Rio de Janeiro [2].

We compare the model outputs of four runs with the estimated weekly dengue cases of Rio de Janeiro, aiming to show that the model can reproduce the observed epidemic dynamics with its own internal causal feedback structure. The behaviors of each of the four runs roughly approximate the derived data of Rio de Janeiro. We obtain similar values of dengue case numbers for one year for all of the following four runs by changing the values of the leverage parameters. The resulting values of four runs are between the mean value of 43,670 humans and maximum value of 152,687 humans [2]. Thus, our four runs roughly approximate the data and capture the essence of the dynamics of the viral epidemics. Note that, in the following sections, we simply refer to derived-data as data.

6.1. RUN 0

First, we construct the model with the average parameter values from the relevant literature and our close estimations. We take the values of *time for recovery of asymptomatic human*, *ratio of infected vector births* and *average number of bites per human that are accessible to vectors* as close estimations. In this run, the number of infectious human and *infected vector* converge to zero. This means the virus decays and eradicates when we use the average parameter values. However, the viral epidemic of dengue is persistent in the region. The resulting behavior is not similar to the actual case.

Leverage parameter values and initial values of the stocks are given in Table 6.1 and Table 6.2 respectively. We assume that the ratio of *asymptomatic infectious human* to *symptomatic infectious human* is nine [2]. Therefore, we assume that the ratio of *fraction of asymptomatic human* to *fraction of symptomatic human* is nine. Actual values of the *fraction of asymptomatic human* or *time for recovery of asymptomatic human* are unknown and we use our close estimations in our model. We assume that the *time for recovery of asymptomatic human* is one week to obtain numerically the one over nine ratio for symptomatic to asymptomatic human when *fraction of symptomatic human* is 0.1. We take the initial values of *symptomatic infectious human*

and *asymptomatic infectious human* as 1200 humans and 10800 humans as given in Table 6.2. The ratio of initial values of *asymptomatic infectious human* to *symptomatic infectious human* results as nine. We take the *ratio of infected vector births* as 0.003 in our model [16]. And we take the *average number of bites per human that are accessible to vectors* as 20 bites per human per week as a close estimation.

Table 6.1. Leverage Parameter Values for Run 0.

	Value	**Unit**
time for recovery of asymptomatic human	1	Week
ratio of infected vector births	0.003	Dimensionless
average number of bites per human	20	$\frac{\text{Bites}}{\text{Human} \times \text{Week}}$

The *average number of bites per human* denotes the *average number of bites per human that are accessible to vectors* in the Table 6.1.

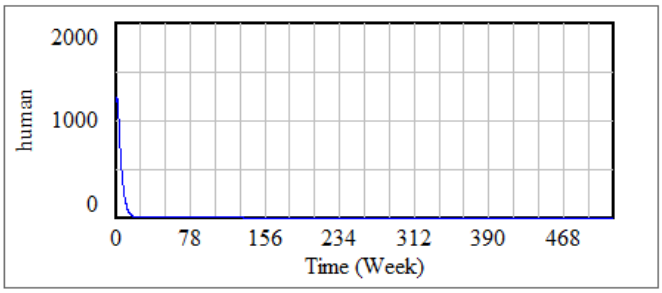
Table 6.2. Initial Values of Stocks for Run 0.

	Initial Value	**Unit**
susceptible human	2966000	Human
exposed human	12000	Human
symptomatic infectious human	1200	Human
asymptomatic infectious human	10800	Human
recovered human	3010000	Human
susceptible vector	144000000	Vector
infected vector	6000000	Vector

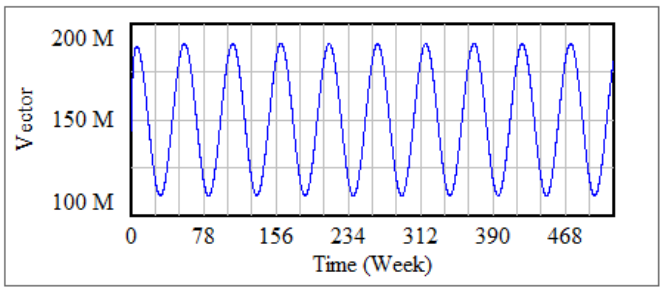
We give the run results for 520 weeks to observe the repeating pattern each year.

We can see in the Figure 6.3 that the values of *symptomatic infectious human* and *infected vector* approach to zero in the first year, which implies that virus does

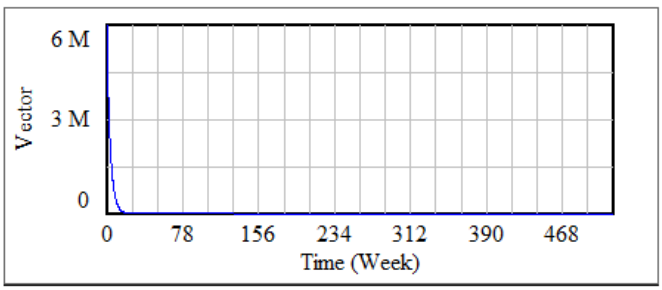
not persist in our model with the current set of parameter values. *Susceptible vector* pattern repeats itself each year.



(a) Symptomatic Infectious Human.



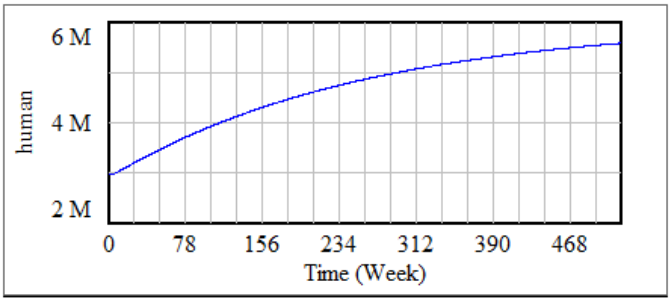
(b) Susceptible Vector.



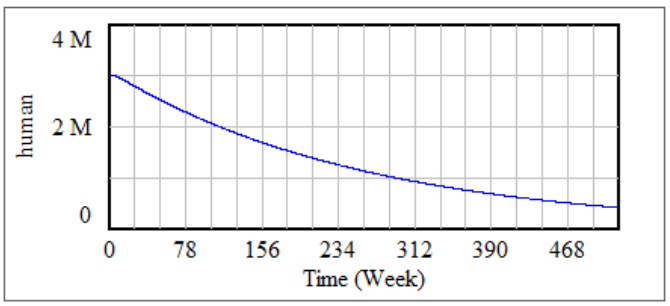
(c) Infected Vector.

Figure 6.3. Run 0 Results for *Symptomatic Infectious Human*, *Susceptible Vector*, and *Infected Vector* for Ten Years.

We can see in the Figure 6.4 that *susceptible human* increases as *recovered human* decreases, and this implies that virus does not persist in our model with the current set of parameter values.



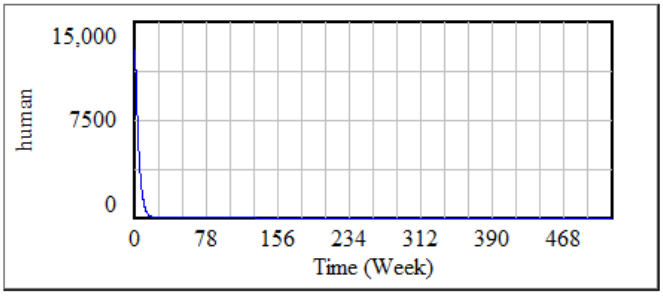
(a) Susceptible Human.



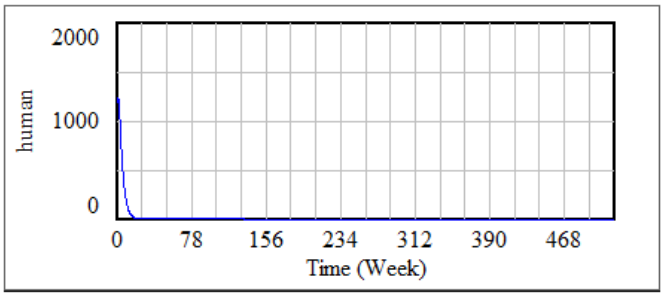
(b) Recovered Human.

Figure 6.4. Run 0 Results for *Susceptible Human* and *Recovered Human* for Ten Years.

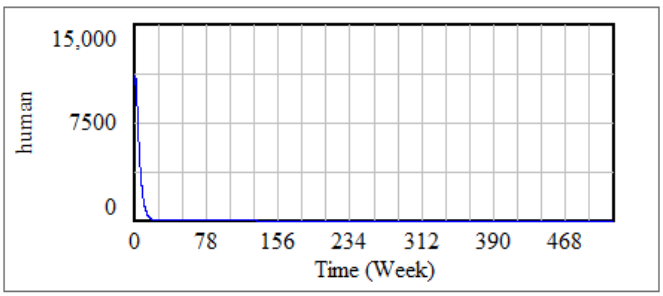
We can see in the Figure 6.5 that *exposed human*, *symptomatic infectious human*, and *asymptomatic infectious human* approach to zero, this implies that virus does not persist in our model with the current set of parameter values.



(a) Exposed Human.



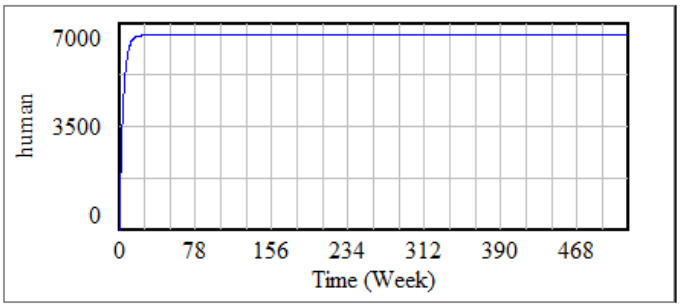
(b) Symptomatic Infectious Human.



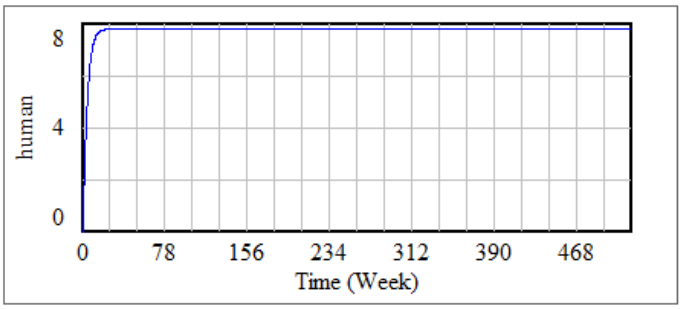
(c) Asymptomatic Infectious Human.

Figure 6.5. Run 0 Results for *Exposed Human*, *Symptomatic Infectious Human*, and *Asymptomatic Infectious Human* for Ten Years.

We can see in the Figure 6.6 that *total symptomatic infected human* and *total human deaths* are very low, because infectious human and *infected vector* values are approaching to zero in the first year.



(a) Total Symptomatic Infected Human.

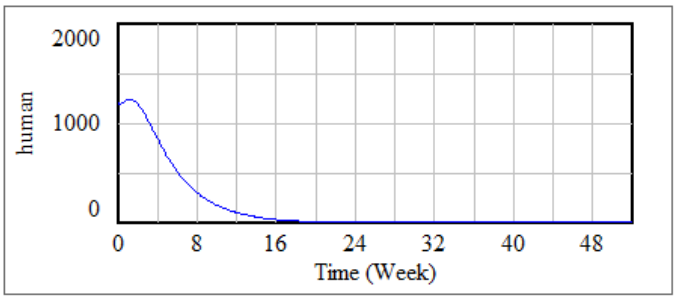


(b) Total Human Deaths

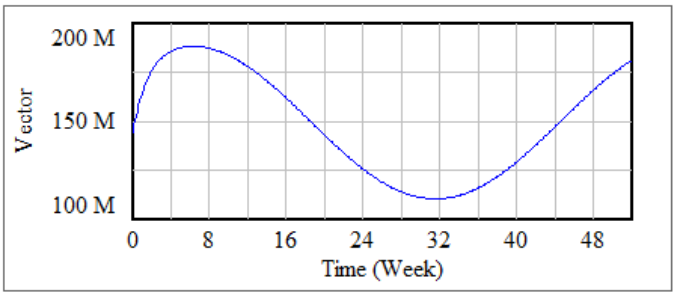
Figure 6.6. Run 0 Results for *Total Symptomatic Infected Human* and *Total Human Deaths* for Ten Years.

We give the run results for 52 weeks to observe the pattern in detail for a year.

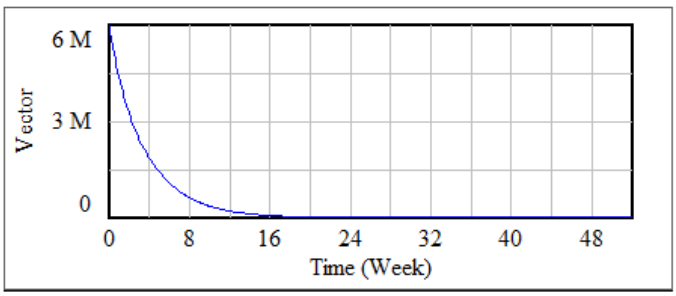
We can see in the Figure 6.7 that the *symptomatic infectious human* and *infected vector* values converge to zero in the first year and this implies that the virus does not persist in our model with the current set of parameter values. We can see that the model we construct with moderate literature parameter values results in unreasonable behavior.



(a) Symptomatic Infectious Human.



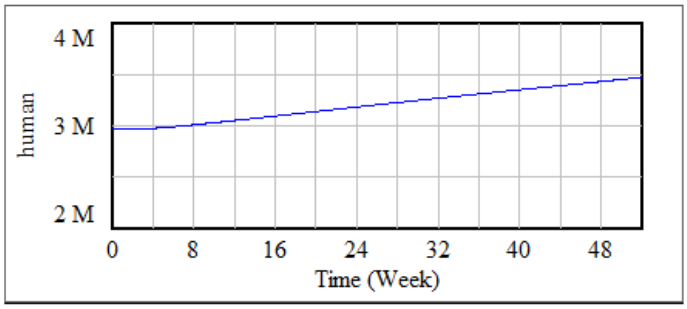
(b) Susceptible Vector.



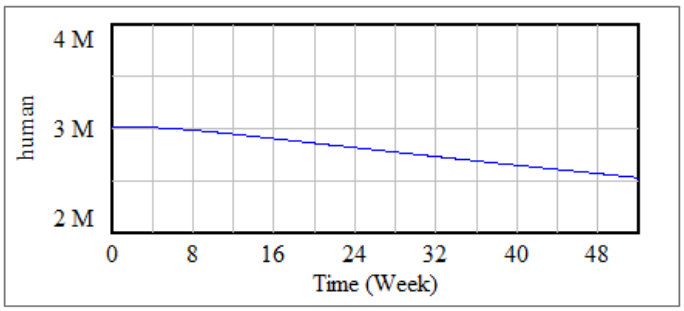
(c) Infected Vector.

Figure 6.7. Run 0 Results for *Symptomatic Infectious Human*, *Susceptible Vector*, and *Infected Vector* for One Year.

We can see in the Figure 6.8 that *susceptible human* increases as *recovered human* decreases, this implies that virus does not persist in our model with the current set of parameter values.



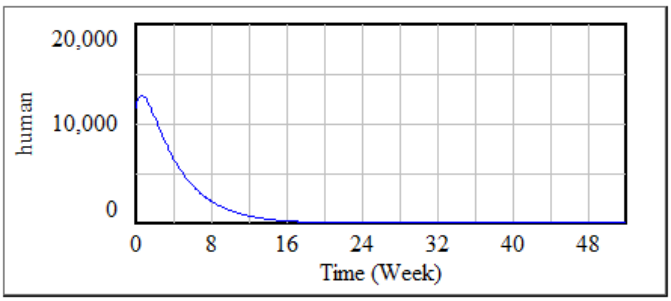
(a) Susceptible Human.



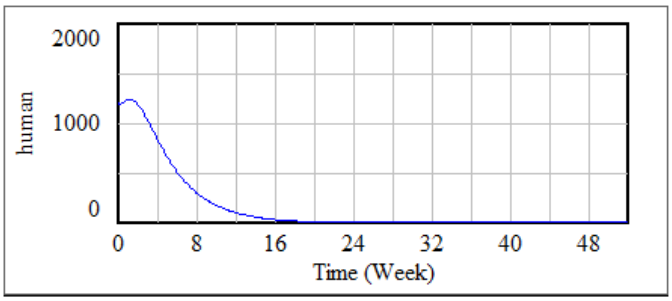
(b) Recovered Human.

Figure 6.8. Run 0 Results for *Susceptible Human* and *Recovered Human* for One Year.

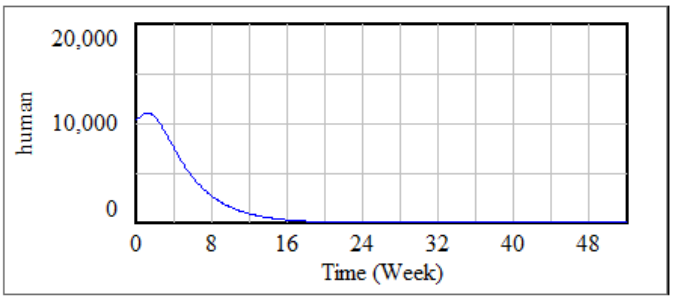
We can see in the Figure 6.9 that *exposed human*, *symptomatic infectious human*, and *asymptomatic infectious human* approach to zero, this implies that virus does not persist in our model with the current set of parameter values.



(a) Exposed Human.



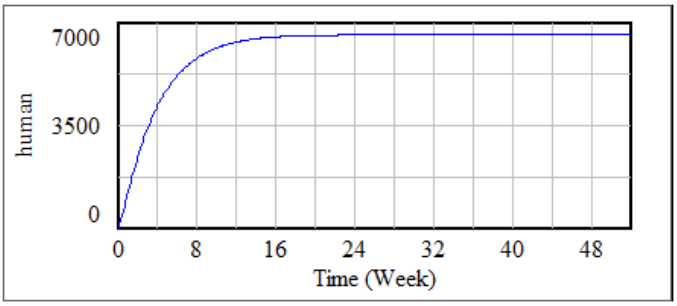
(b) Symptomatic Infectious Human.



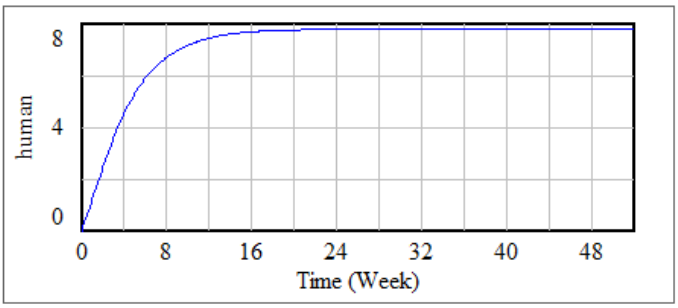
(c) Asymptomatic Infectious Human.

Figure 6.9. Run 0 Results for *Exposed Human*, *Symptomatic Infectious Human*, and *Asymptomatic Infectious Human* for One Year.

We can see in the Figure 6.10 that *total symptomatic infected human* and *total human deaths* are very low, because infectious human and *infected vector* values are approaching to zero in the first year.



(a) Total Symptomatic Infected Human.



(b) Total Human Deaths

Figure 6.10. Run 0 Results for *Total Symptomatic Infected Human* and *Total Human Deaths* for One Year.

6.2. RUN 1

In the first run, we construct the model with average parameter values from the relevant literature and our close estimations. We only change the value of *time for recovery of asymptomatic human* and take it as 26 weeks. We take the initial values of this run as the values of the model after the transition dynamic period is over. Infectious human and *infected vector* populations do not decay to zero, which indicates that the virus is persistent in this run. The number of total symptomatic dengue cases in a year is similar to the dengue cases taken from the relevant literature [2]. The resulting behavior also roughly approximates the behavior of the data [1, 2].

We give the leverage parameter values and initial values of the stocks in Table 6.3 and Table 6.4 respectively.

Table 6.3. Leverage Parameter Values for Run 1.

	Value	**Unit**
time for recovery of asymptomatic human	26	Week
ratio of infected vector births	0.003	Dimensionless
average number of bites per human	20	$\frac{\text{Bites}}{\text{Human} \times \text{Week}}$

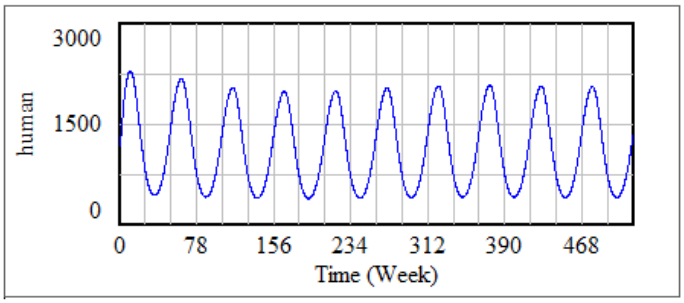
The *average number of bites per human* denotes the *average number of bites per human that are accessible to vectors* in the Table 6.3.

Table 6.4. Initial Values of Stocks for Run 1.

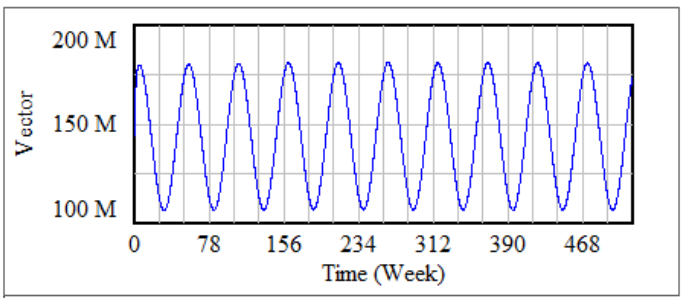
	Initial Value	**Unit**
susceptible human	2875200	Human
exposed human	11000	Human
symptomatic infectious human	1200	Human
asymptomatic infectious human	257500	Human
recovered human	2855100	Human
susceptible vector	144000000	Vector
infected vector	6000000	Vector

We give the run results for 520 weeks to observe the repeating pattern each year.

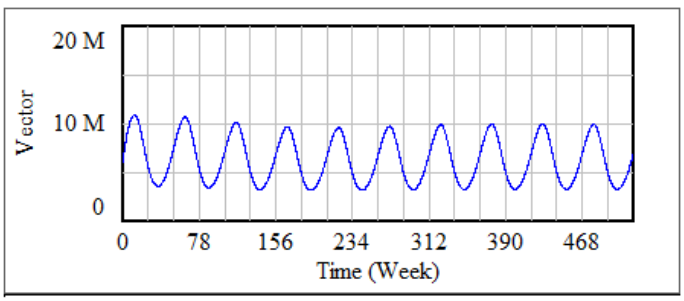
We can see in the Figure 6.11 that the pattern of the first year repeats itself for ten years for *symptomatic infectious human*, *susceptible vector*, and *infected vector*. The behavior we obtain for ten years is similar to the data. We take the initial values of this run as the values of the model after the transition dynamic period is over, therefore the amplitudes of the oscillations are similar each year for the same variable.



(a) Symptomatic Infectious Human.



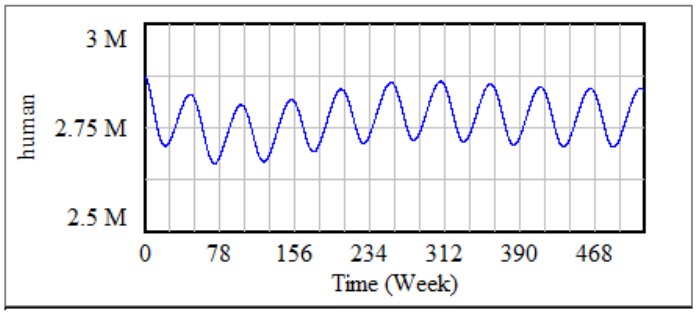
(b) Susceptible Vector.



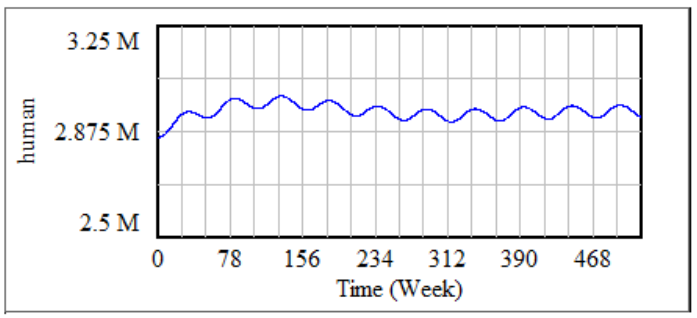
(c) Infected Vector.

Figure 6.11. Run 1 Results for *Symptomatic Infectious Human*, *Susceptible Vector*, and *Infected Vector* for Ten Years.

We can see in the Figure 6.12 that the pattern of the first year repeats itself for ten years for *susceptible human* and *recovered human*.



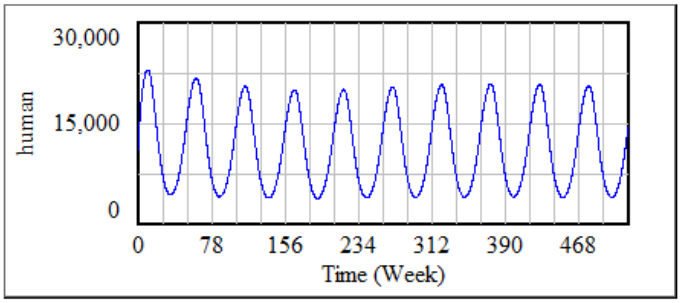
(a) Susceptible Human.



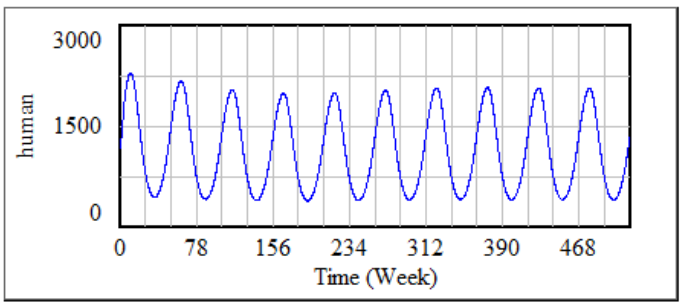
(b) Recovered Human.

Figure 6.12. Run 1 Results for *Susceptible Human* and *Recovered Human* for Ten Years.

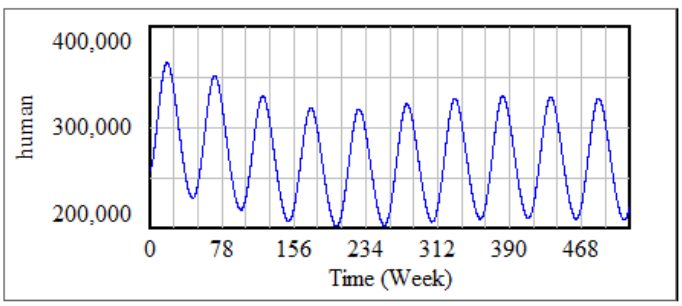
We can see in the Figure 6.13 that the pattern of the first year repeats itself for ten years for *exposed human*, *symptomatic infectious human*, and *asymptomatic infectious human*. The behavior we obtain for ten years is similar to the data. The amplitudes of the oscillations are similar each year for a variable, but the amplitudes of *exposed human*, *symptomatic infectious human*, and *asymptomatic infectious human* are different from each other.



(a) Exposed Human.



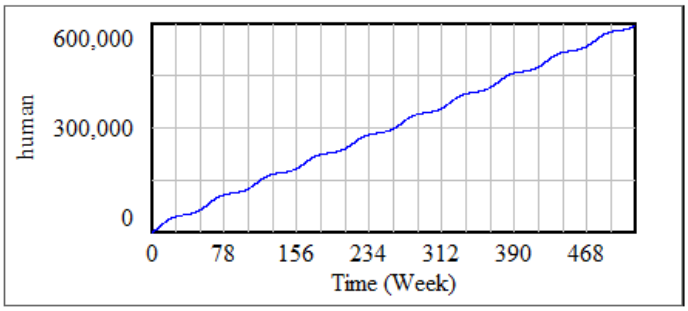
(b) Symptomatic Infectious Human.



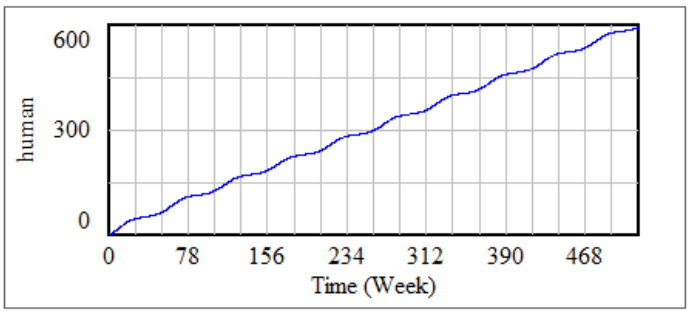
(c) Asymptomatic Infectious Human.

Figure 6.13. Run 1 Results for *Exposed Human*, *Symptomatic Infectious Human*, and *Asymptomatic Infectious Human* for Ten Years.

We can see in the Figure 6.14 that *total symptomatic infected human* and *total human deaths* have increasing patterns.



(a) Total Symptomatic Infected Human.

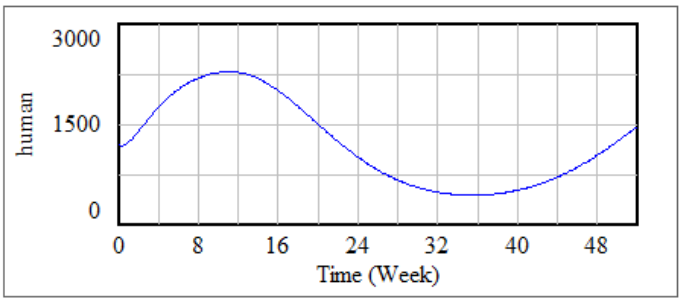


(b) Total Human Deaths

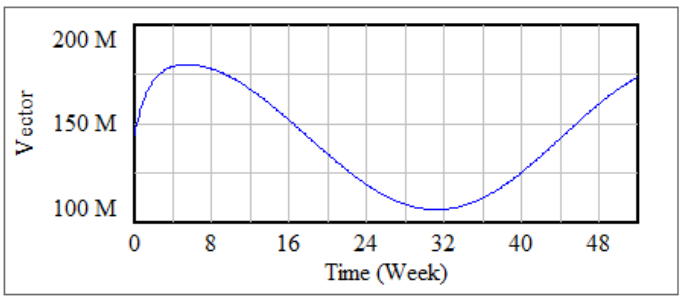
Figure 6.14. Run 1 Results for *Total Symptomatic Infected Human* and *Total Human Deaths* for Ten Years.

We give the run results for 52 weeks to observe the pattern in detail for a year.

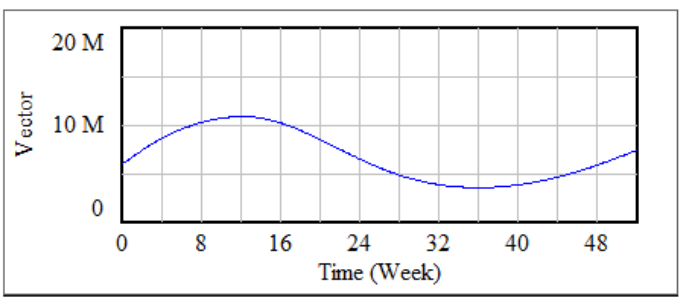
In the Figure 6.15 we can see that the *susceptible vector* makes a peak first, then it is followed by the *symptomatic infectious human* and *infected vector* peaks. *Susceptible vector* and *infected vector* behaviors are similar to sinus function as we expect. The behavior of *symptomatic infectious human* roughly approximates the derived data that is obtained from Brazil in 2015 and modified with the average data from Rio de Janeiro between 2000 and 2015 [1, 2]. The behavior of the data is given in Figure 6.2.



(a) Symptomatic Infectious Human.



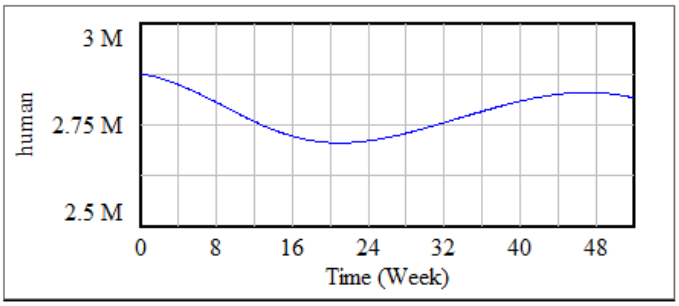
(b) Susceptible Vector.



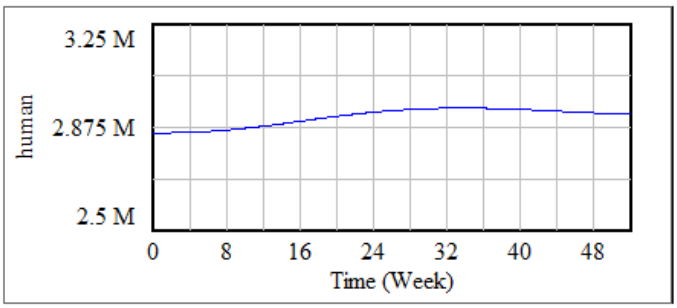
(c) Infected Vector.

Figure 6.15. Run 1 Results for *Symptomatic Infectious Human*, *Susceptible Vector*, and *Infected Vector* for One Year.

We can see in the Figure 6.16 that the change in the *recovered human* is more gradual than the *susceptible human*.



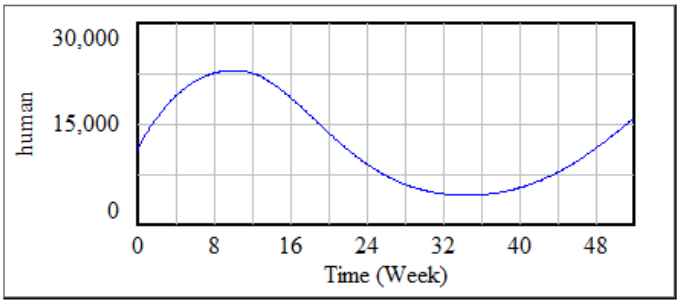
(a) Susceptible Human.



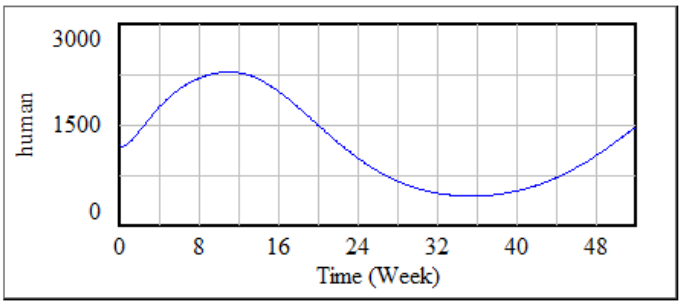
(b) Recovered Human.

Figure 6.16. Run 1 Results for *Susceptible Human* and *Recovered Human* for One Year.

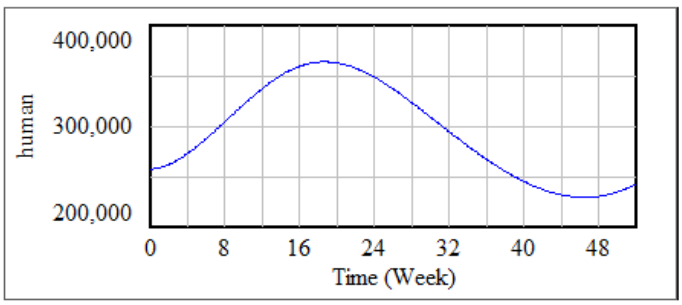
We can see in the Figure 6.17 that the amplitudes of *exposed human*, *symptomatic infectious human*, and *asymptomatic infectious human* are very different from each other. And the peaks of *exposed human* and *symptomatic infectious human* are close to each other. Then the peak of *asymptomatic infectious human* follows them with a delay.



(a) Exposed Human.

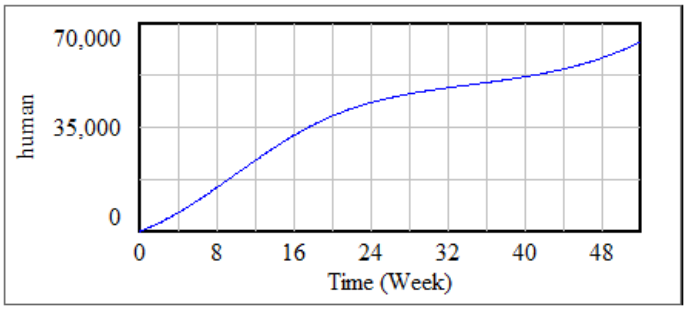


(b) Symptomatic Infectious Human.

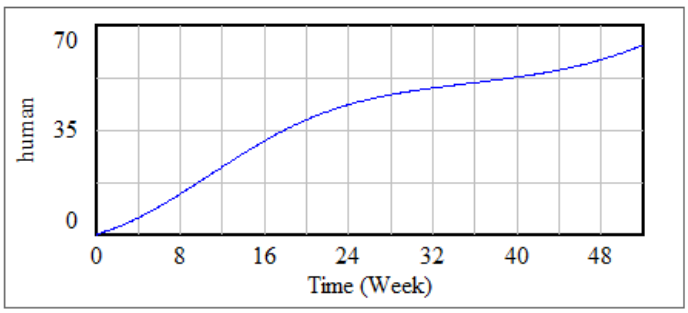


(c) Asymptomatic Infectious Human.

Figure 6.17. Run 1 Results for *Exposed Human*, *Symptomatic Infectious Human*, and *Asymptomatic Infectious Human* for One Year.



(a) Total Symptomatic Infected Human.



(b) Total Human Deaths

Figure 6.18. Run 1 Results for *Total Symptomatic Infected Human* and *Total Human Deaths* for One Year.

We obtain *total symptomatic infected human* for one year as 63,732 humans. This resulting value is within the range of mean value of 43,670 humans and maximum value of 152,687 humans for Rio de Janeiro [2].

We obtain the *total human deaths* for one year as 63.403 humans. Therefore, we can take 63 human deaths as a rough figure. And *total human deaths* value is around 0.1 percent of *total symptomatic infected human* as we expect.

6.3. RUN 2

In the second run, we construct the model with average parameter values from the relevant literature and our close estimations. We only change the value of *ratio*

of infected vector births and take it as 95.5 percent. We take the initial values of this run as the values of the model after the transition dynamic period is over. Infectious human and *infected vector* populations do not decay to zero, which indicates that the virus is persistent in this run. The number of total symptomatic dengue cases in a year is similar to the dengue cases taken from the relevant literature [2]. The resulting behavior also roughly approximates the behavior of the data [1, 2].

We give the leverage parameter values and initial values of the stocks in Table 6.5 and Table 6.6 respectively.

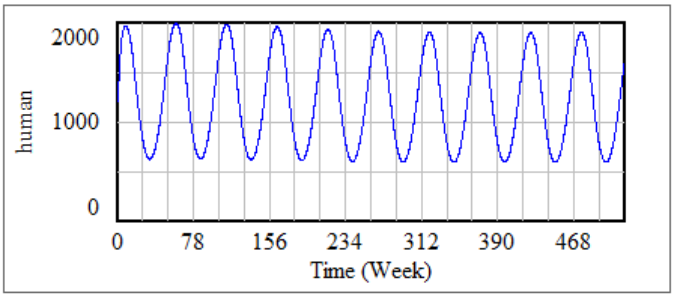
Table 6.5. Leverage Parameter Values for Run 2.

	Value	**Unit**
time for recovery of asymptomatic human	1	Week
ratio of infected vector births	0.955	Dimensionless
average number of bites per human	20	$\frac{\text{Bites}}{\text{Human} \times \text{Week}}$

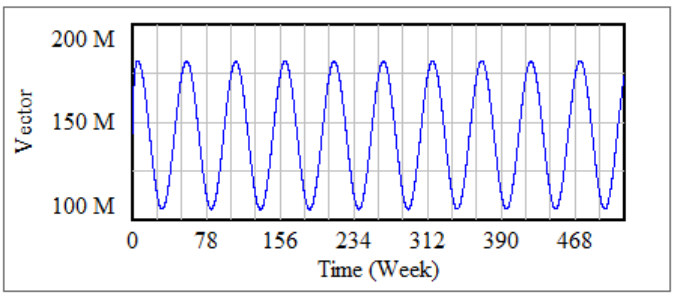
The *average number of bites per human* denotes the *average number of bites per human that are accessible to vectors* in the Table 6.5.

Table 6.6. Initial Values of Stocks for Run 2.

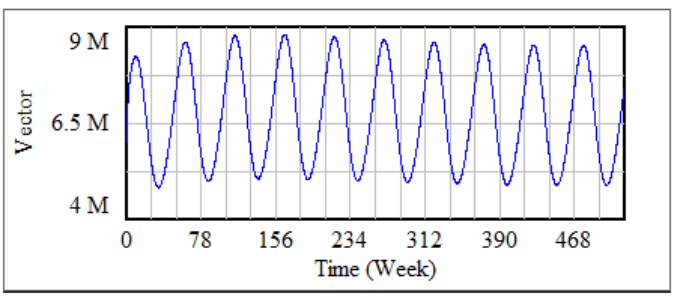
	Initial Value	**Unit**
susceptible human	2956500	Human
exposed human	11800	Human
symptomatic infectious human	1200	Human
asymptomatic infectious human	10500	Human
recovered human	3020000	Human
susceptible vector	144000000	Vector
infected vector	6000000	Vector



(a) Symptomatic Infectious Human.



(b) Susceptible Vector.

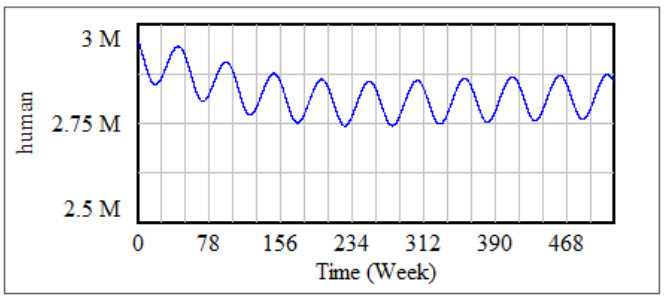


(c) Infected Vector.

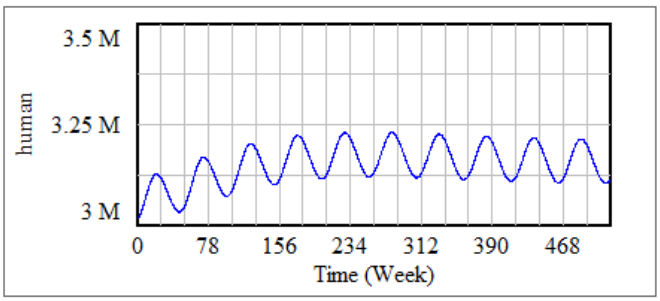
Figure 6.19. Run 2 Results for *Symptomatic Infectious Human*, *Susceptible Vector*, and *Infected Vector* for Ten Years.

We can see in the Figure 6.19 that the pattern of the first year repeats itself for ten years for *symptomatic infectious human*, *susceptible vector*, and *infected vector*. The behavior we obtain for ten years is similar to the data. We take the initial values of this model as the values of the model after the transition dynamic period is over, therefore the amplitudes of the oscillations are similar each year for the same variable.

We can see in the Figure 6.20 that the pattern of the first year repeats itself for ten years for *susceptible human* and *recovered human*.



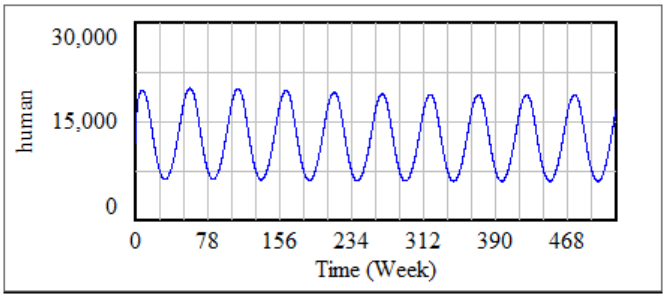
(a) Susceptible Human.



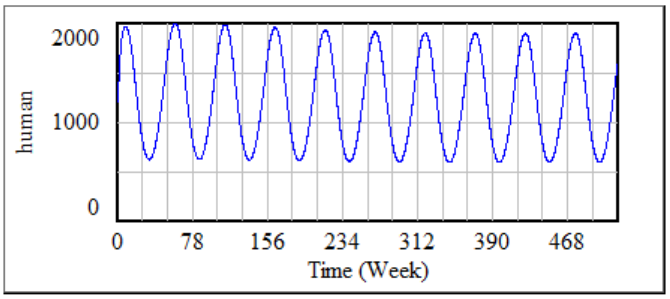
(b) Recovered Human.

Figure 6.20. Run 2 Results for *Susceptible Human* and *Recovered Human* for Ten Years.

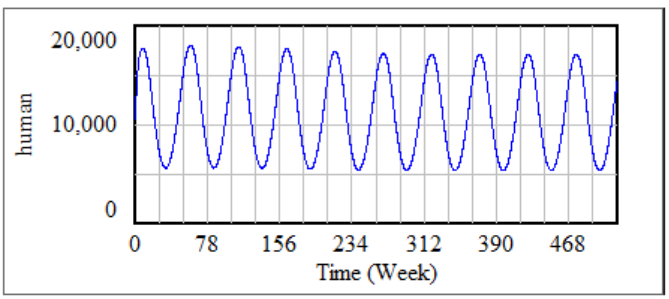
We can see in the Figure 6.21 that the pattern of the first year repeats itself for ten years for *exposed human*, *symptomatic infectious human*, and *asymptomatic infectious human*. The behavior we obtain for ten years is similar to the data. The amplitudes of the oscillations are similar to each other for each year. The amplitude of *exposed human* is slightly higher than the amplitude of *asymptomatic infectious human*. And the amplitude of *asymptomatic infectious human* is higher than the amplitude of *symptomatic infectious human*.



(a) Exposed Human.



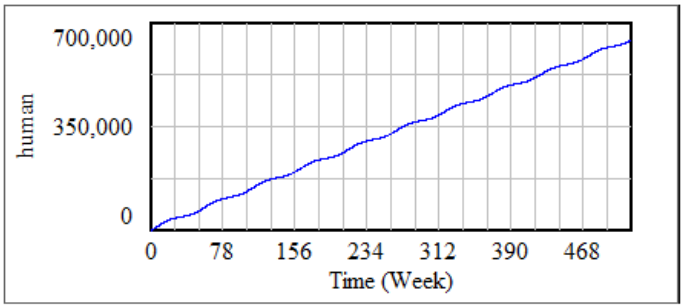
(b) Symptomatic Infectious Human.



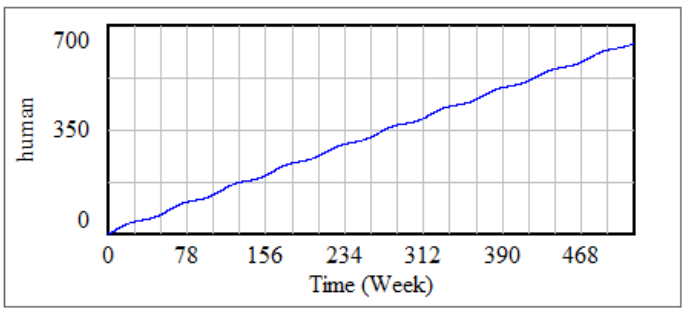
(c) Asymptomatic Infectious Human.

Figure 6.21. Run 2 Results for *Exposed Human*, *Symptomatic Infectious Human*, and *Asymptomatic Infectious Human* for Ten Years.

We can see in the Figure 6.22 that *total symptomatic infected human* and *total human deaths* have increasing patterns.



(a) Total Symptomatic Infected Human.

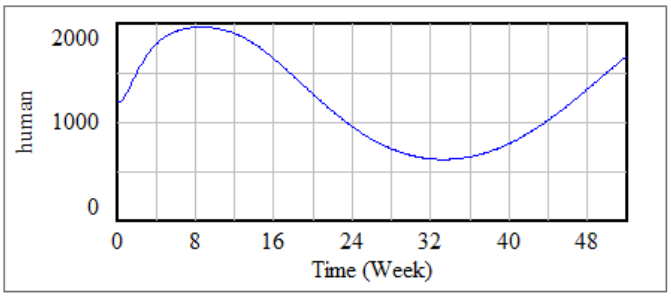


(b) Total Human Deaths

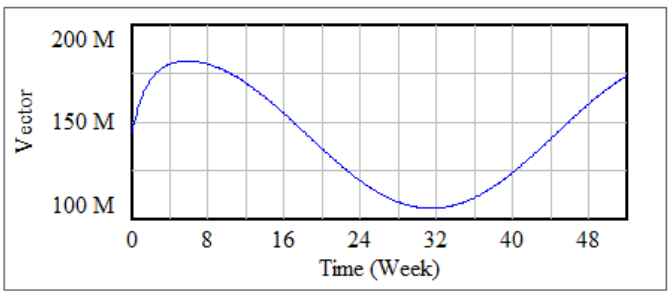
Figure 6.22. Run 2 Results for *Total Symptomatic Infected Human* and *Total Human Deaths* for Ten Years.

We give the run results for 52 weeks to observe the pattern in detail for a year.

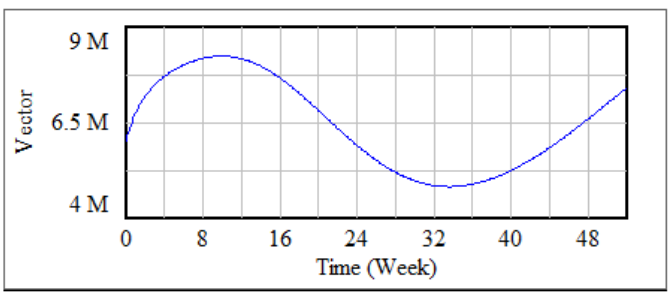
In the Figure 6.23 we can see that the *susceptible vector* makes a peak first, then it is followed by the *symptomatic infectious human* and *infected vector* peaks. *Susceptible vector* and *infected vector* behaviors are similar to sinus function as we expect. The behavior of *symptomatic infectious human* roughly approximates the behavior of the data of Rio de Janeiro that is given in Figure 6.2 [1, 2].



(a) Symptomatic Infectious Human.



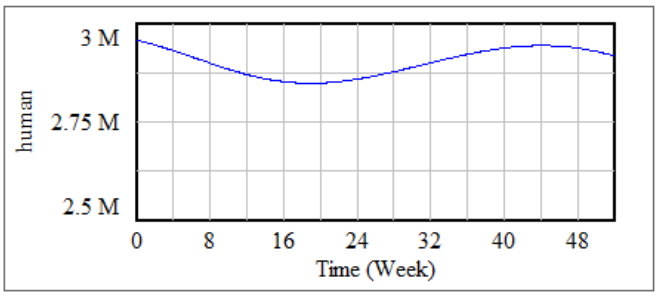
(b) Susceptible Vector.



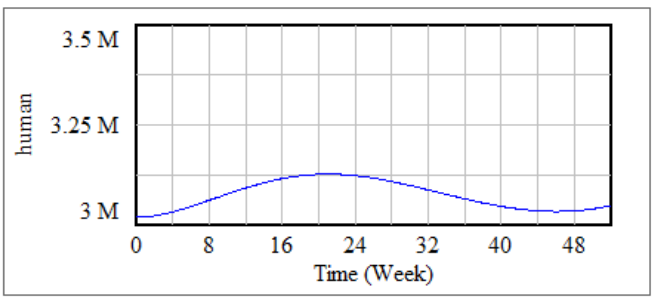
(c) Infected Vector.

Figure 6.23. Run 2 Results for *Symptomatic Infectious Human*, *Susceptible Vector*, and *Infected Vector* for One Year.

We can see in the Figure 6.24 that the *susceptible human* and *recovered human* have similar amplitudes.



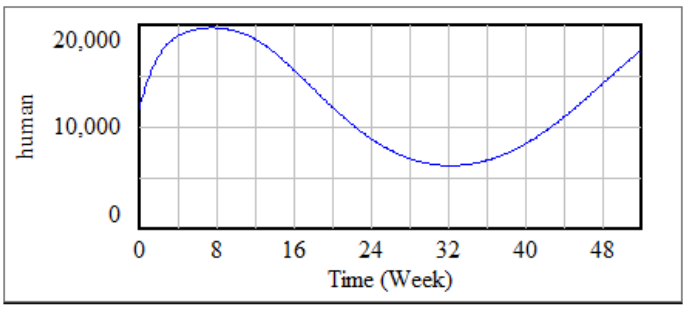
(a) Susceptible Human.



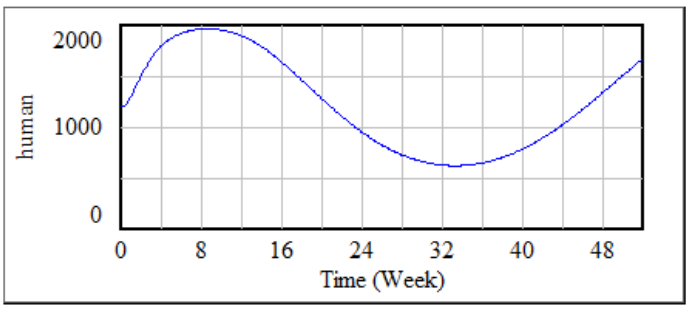
(b) Recovered Human.

Figure 6.24. Run 2 Results for *Susceptible Human* and *Recovered Human* for One Year.

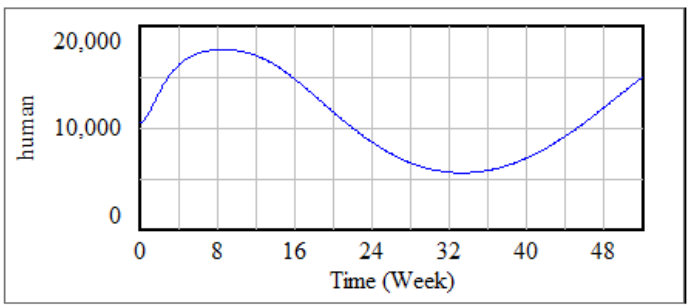
We can see in the Figure 6.25 that the amplitudes of *exposed human* and *asymptomatic infectious human* are similar to each other. The amplitude of *symptomatic infectious human* is lower. And the peaks of *exposed human*, *symptomatic infectious human* and *asymptomatic infectious human* are all close to each other.



(a) Exposed Human.

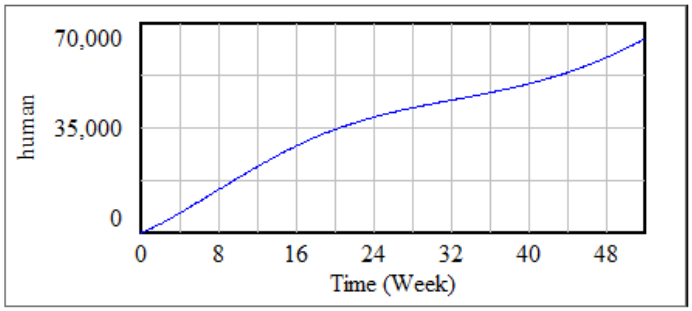


(b) Symptomatic Infectious Human.

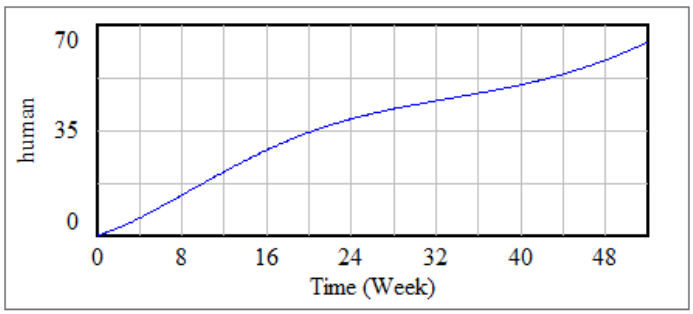


(c) Asymptomatic Infectious Human.

Figure 6.25. Run 2 Results for *Exposed Human*, *Symptomatic Infectious Human*, and *Asymptomatic Infectious Human* for One Year.



(a) Total Symptomatic Infected Human.



(b) Total Human Deaths

Figure 6.26. Run 2 Results for *Total Symptomatic Infected Human* and *Total Human Deaths* for One Year.

We obtain *total symptomatic infected human* for one year as 64,832 humans. This resulting value is within the range of mean value of 43,670 humans and maximum value of 152,687 humans for Rio de Janeiro [2].

We obtain the *total human deaths* for one year as 64.3013 humans. Therefore, we can take 64 human deaths as a rough figure. And *total human deaths* value is around 0.1 percent of *total symptomatic infected human* as we expect.

6.4. RUN 3

In the third run, we construct the model with average parameter values from the relevant literature and our close estimations. We only change the value of *average number of bites per human that are accessible to vectors* and take it as 380 bites per

human per week. We take the initial values of this run as the values of the model after the transition dynamic period is over. Infectious human and *infected vector* populations do not decay to zero, which indicates that the virus is persistent in this run. The number of total symptomatic dengue cases in a year is similar to the dengue cases taken from the relevant literature [2]. The resulting behavior also roughly approximates the behavior of the data [1, 2].

We give the leverage parameter values and initial values of the stocks in Table 6.7 and Table 6.8 respectively.

Table 6.7. Leverage Parameter Values for Run 3.

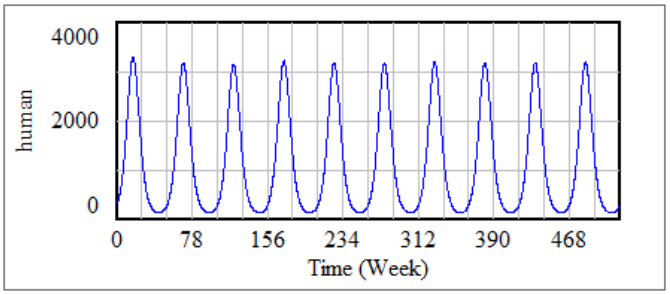
	Value	**Unit**
time for recovery of asymptomatic human	1	Week
ratio of infected vector births	0.003	Dimensionless
average number of bites per human	380	$\frac{\text{Bites}}{\text{Human} \times \text{Week}}$

The *average number of bites per human* denotes the *average number of bites per human that are accessible to vectors* in the Table 6.7.

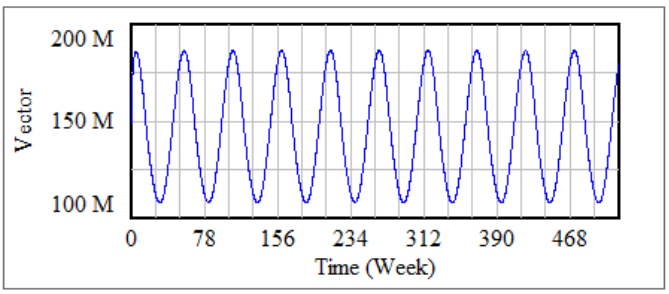
Table 6.8. Initial Values of Stocks for Run 3.

	Initial Value	**Unit**
susceptible human	3245960	Human
exposed human	3780	Human
symptomatic infectious human	320	Human
asymptomatic infectious human	2870	Human
recovered human	2747070	Human
susceptible vector	148810900	Vector
infected vector	1189100	Vector

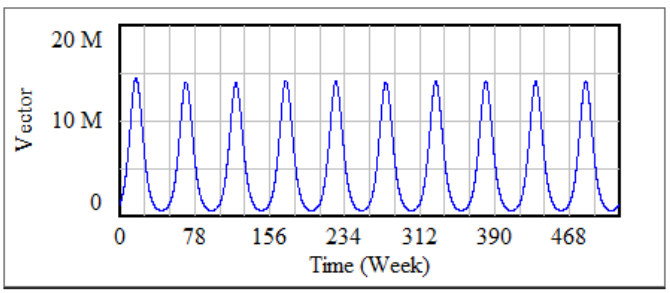
We give run results for 520 weeks to observe the repeating pattern each year.



(a) Symptomatic Infectious Human.



(b) Susceptible Vector.

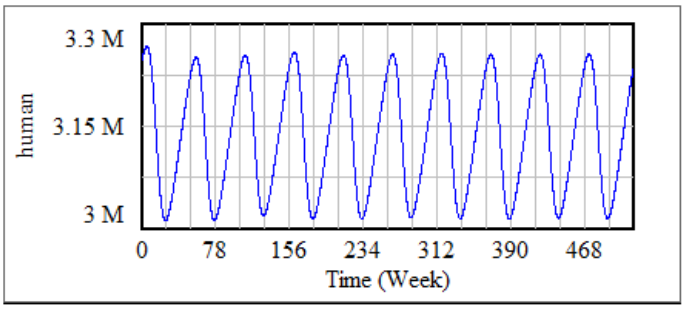


(c) Infected Vector.

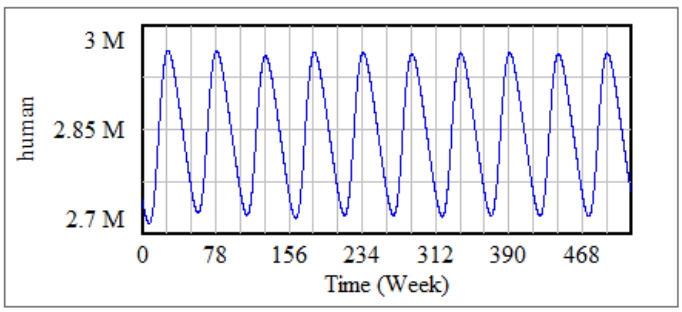
Figure 6.27. Run 3 Results for *Symptomatic Infectious Human*, *Susceptible Vector*, and *Infected Vector* for Ten Years.

We can see in the Figure 6.27 that the pattern of the first year repeats itself for ten years for *symptomatic infectious human*, *susceptible vector*, and *infected vector*. The behavior obtained for ten years is similar to the data. We take the initial values of this run as the values of the model after the transition dynamic period is over, therefore the amplitudes of the oscillations are similar each year for the same variable.

We can see in the Figure 6.28 that the pattern of the first year repeats itself for ten years for *susceptible human* and *recovered human*.



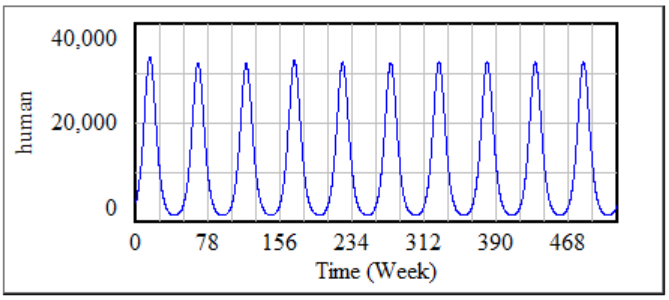
(a) Susceptible Human.



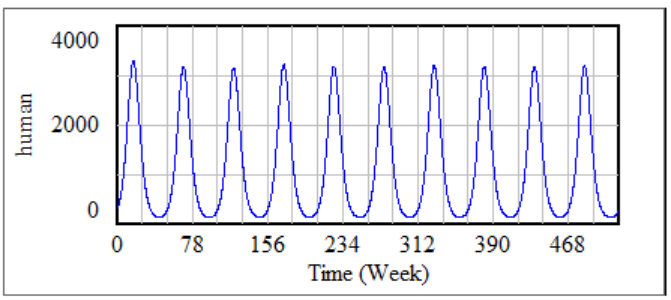
(b) Recovered Human.

Figure 6.28. Run 3 Results for *Susceptible Human* and *Recovered Human* for Ten Years.

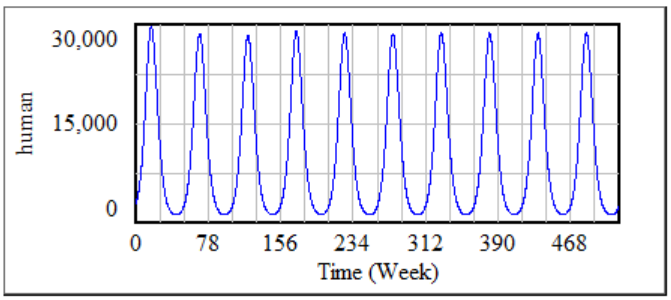
We can see in the Figure 6.29 that the pattern of the first year repeats itself for ten years for *exposed human*, *symptomatic infectious human*, and *asymptomatic infectious human*. The behavior we obtain for ten years is similar to the data. The amplitudes of the oscillations are similar each year for a variable, but the amplitudes of *exposed human*, *symptomatic infectious human*, and *asymptomatic infectious human* are different from each other. The sum of the amplitudes of the *symptomatic infectious human* and *asymptomatic infectious human* is similar to amplitude of the *exposed human* as we expect.



(a) Exposed Human.



(b) Symptomatic Infectious Human.



(c) Asymptomatic Infectious Human.

Figure 6.29. Run 3 Results for *Exposed Human*, *Symptomatic Infectious Human*, and *Asymptomatic Infectious Human* for Ten Years.

We can see in the Figure 6.30 that the *infected vector ratio* has a mean value around four percent as we expect.

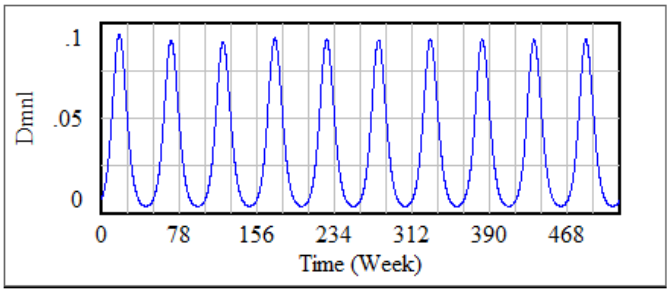
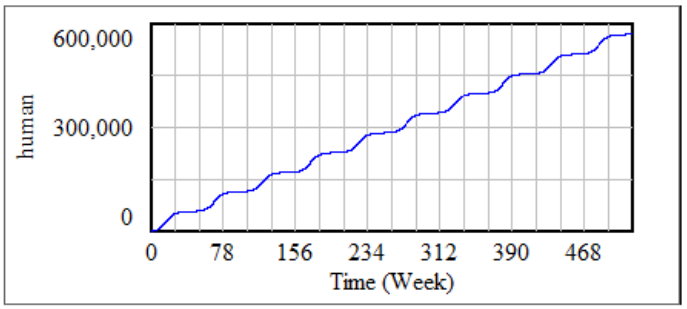
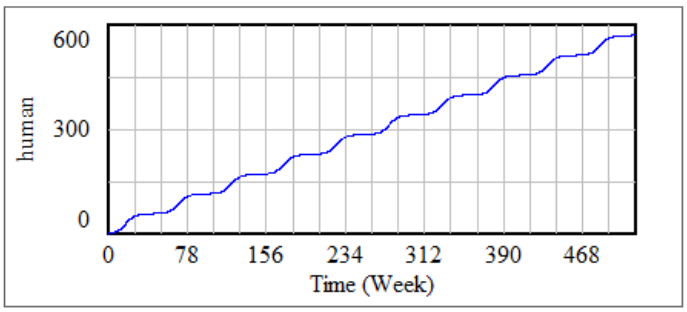


Figure 6.30. Run 3 Results for *Infected Vector Ratio* for Ten Years.

We can see in the Figure 6.31 that *total symptomatic infected human* and *total human deaths* have increasing patterns.



(a) Total Symptomatic Infected Human.

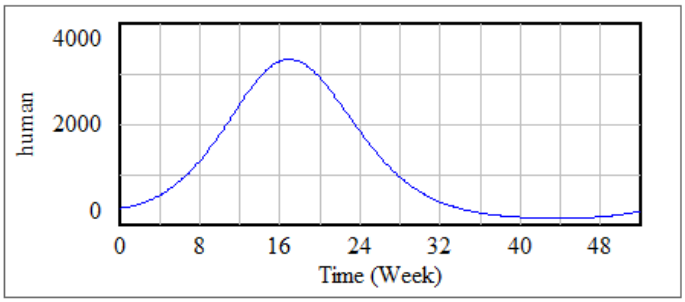


(b) Total Human Deaths

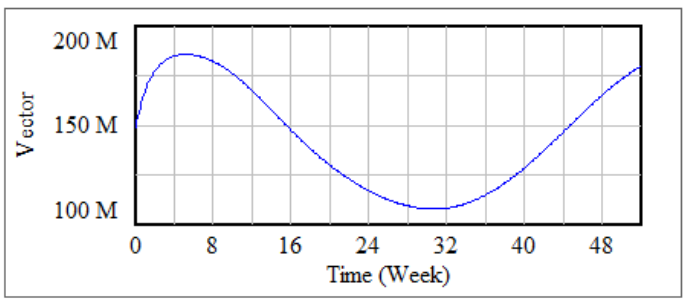
Figure 6.31. Run 3 Results for *Total Symptomatic Infected Human* and *Total Human Deaths* for Ten Years.

We give the run results for 52 weeks to observe the pattern in detail for a year.

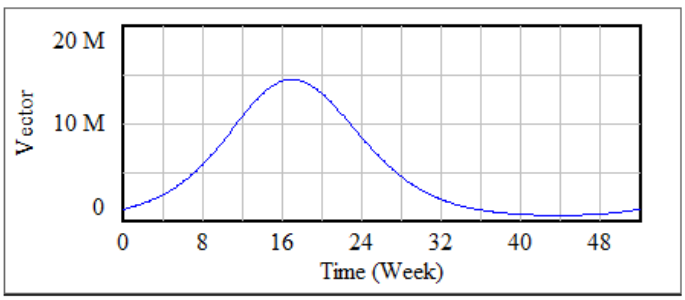
In the Figure 6.32 we can see that the *susceptible vector* makes a peak first, then it is followed by the *symptomatic infectious human* and *infected vector* peaks. *Susceptible vector* behavior is similar to sinus function as we expect. The behavior of *symptomatic infectious human* roughly approximates the behavior of the data of Rio de Janeiro that is given in Figure 6.2 [1, 2].



(a) Symptomatic Infectious Human.



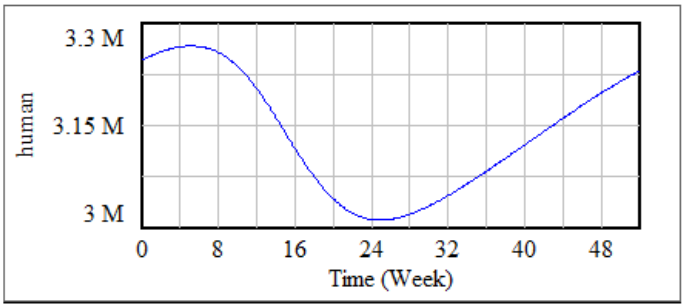
(b) Susceptible Vector.



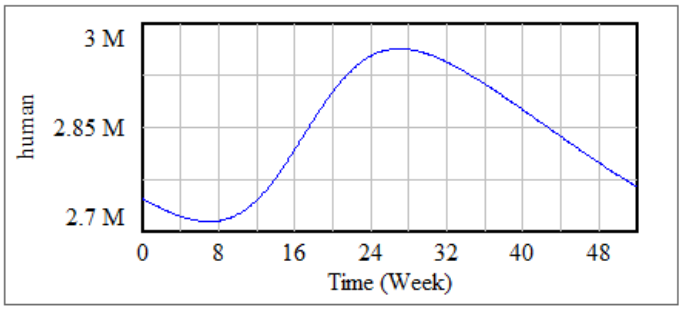
(c) Infected Vector.

Figure 6.32. Run 3 Results for *Symptomatic Infectious Human*, *Susceptible Vector*, and *Infected Vector* for One Year.

We can see in the Figure 6.33 that the amplitudes of the *susceptible human* and *recovered human* are similar to each other.



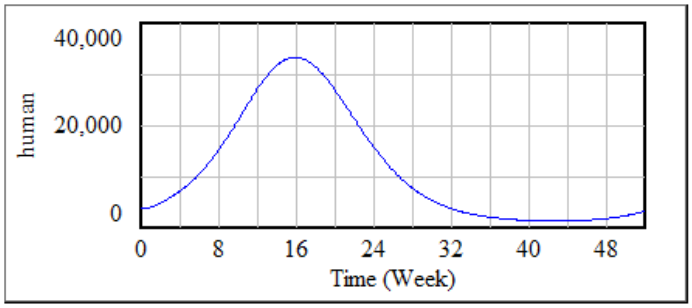
(a) Susceptible Human.



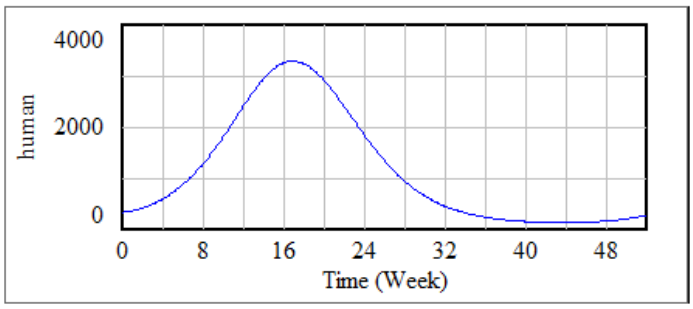
(b) Recovered Human.

Figure 6.33. Run 3 Results for *Susceptible Human* and *Recovered Human* for One Year.

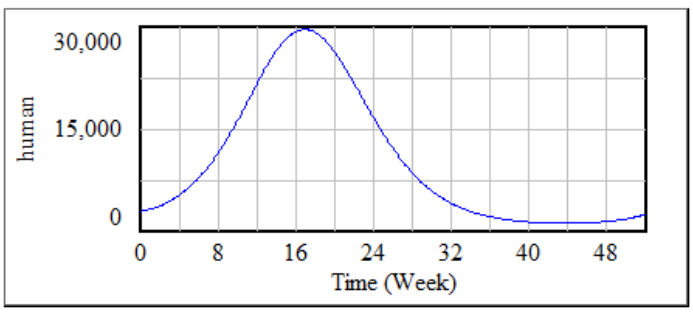
We can see in the Figure 6.34 that the amplitudes of *exposed human*, *symptomatic infectious human*, and *asymptomatic infectious human* are different from each other. And the peaks of *exposed human*, *symptomatic infectious human* and *asymptomatic infectious human* are all close to each other.



(a) Exposed Human.

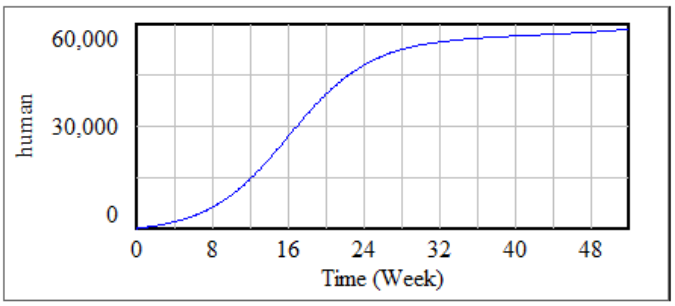


(b) Symptomatic Infectious Human.

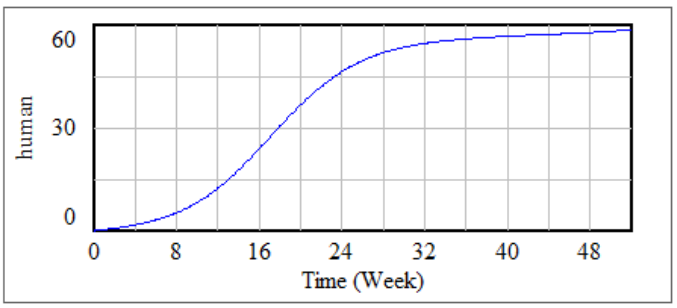


(c) Asymptomatic Infectious Human.

Figure 6.34. Run 3 Results for *Exposed Human*, *Symptomatic Infectious Human*, and *Asymptomatic Infectious Human* for One Year.



(a) Total Symptomatic Infected Human.



(b) Total Human Deaths

Figure 6.35. Run 3 Results for *Total Symptomatic Infected Human* and *Total Human Deaths* for One Year.

We obtain the *total symptomatic infected human* for one year as 58,582 humans. This resulting value is within the range of mean value of 43,670 humans and maximum value of 152,687 humans for Rio de Janeiro [2].

We obtain the *total human deaths* for one year as 58.569 humans. Therefore, we can take 59 human deaths as a rough figure. And *total human deaths* value is around 0.1 percent of *total symptomatic infected human* as we expect.

6.5. RUN 4

In the fourth run, we construct the model with average parameter values from the relevant literature and our close estimations. We change the values of the three leverage parameters. We take 20 percent as the *ratio of infected vector births*, because in the literature it is stated that 20 percent vertical infection of dengue virus is observed in the larvae of the vectors in India [33]. We take 25 bites per human per week as *average number of bites per human that are accessible to vectors* as a close estimation. And we take 16 weeks for the *time for recovery of asymptomatic human*. The asymptomatic to symptomatic human ratio is given in the literature for the foreign visitors. We can suspect and assume that this ratio may be higher for the local human in Rio de Janeiro. We take the initial values of this run as the values of the model after the transition dynamic period is over [2]. Infectious human and *infected vector* populations do not decay to zero, which indicates that the virus is persistent in this run. The number of total symptomatic dengue cases in a year is similar to the dengue cases taken from the relevant literature [2]. The resulting behavior also roughly approximates the behavior of the data [1, 2].

We give the leverage parameter values and initial values of the stocks in Table 6.9 and Table 6.10 respectively.

Table 6.9. Leverage Parameter Values for Run 4.

	Value	**Unit**
time for recovery of asymptomatic human	16	Week
ratio of infected vector births	0.2	Dimensionless
average number of bites per human	25	$\frac{\text{Bites}}{\text{Human} \times \text{Week}}$

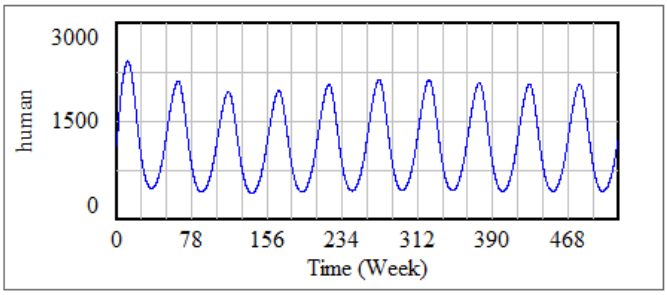
The *average number of bites per human* denotes the *average number of bites per human that are accessible to vectors* in the Table 6.9.

Table 6.10. Initial Values of Stocks for Run 4.

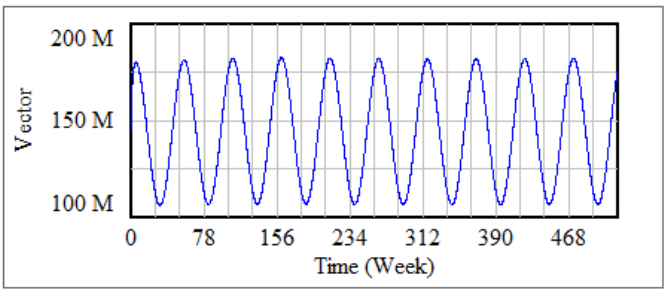
	Initial Value	**Unit**
susceptible human	2928360	Human
exposed human	11160	Human
symptomatic infectious human	1120	Human
asymptomatic infectious human	160710	Human
recovered human	2898650	Human
susceptible vector	144000000	Vector
infected vector	6000000	Vector

We give the run results for 520 weeks to observe the repeating pattern each year.

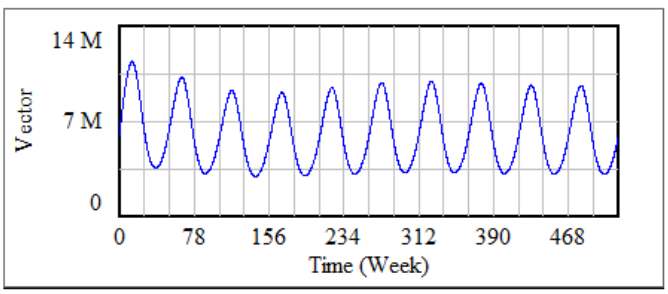
We can see in the Figure 6.36 that the pattern of the first year repeats itself for ten years for *symptomatic infectious human*, *susceptible vector*, and *infected vector*. The behavior we obtain for ten years is similar to the data. We take the initial values of this model as the values of the model after the transition dynamic period is over, therefore the amplitudes of the oscillations are similar each year for the same variable.



(a) Symptomatic Infectious Human.

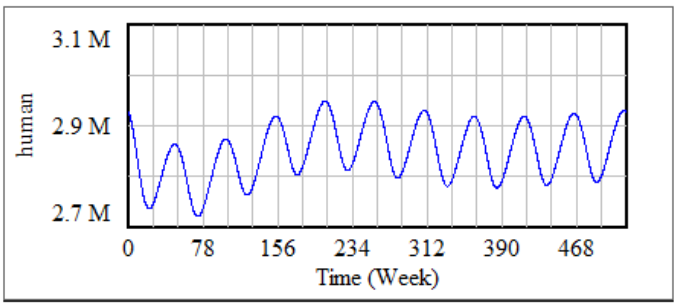


(b) Susceptible Vector.

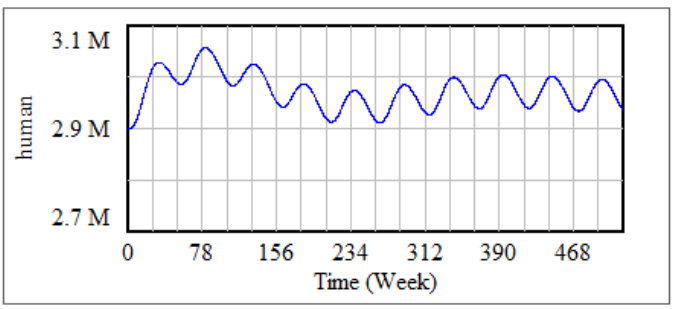


(c) Infected Vector.

Figure 6.36. Run 4 Results for *Symptomatic Infectious Human*, *Susceptible Vector*, and *Infected Vector* for Ten Years.



(a) Susceptible Human.

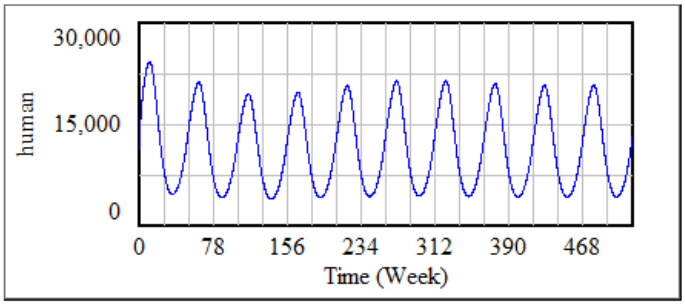


(b) Recovered Human.

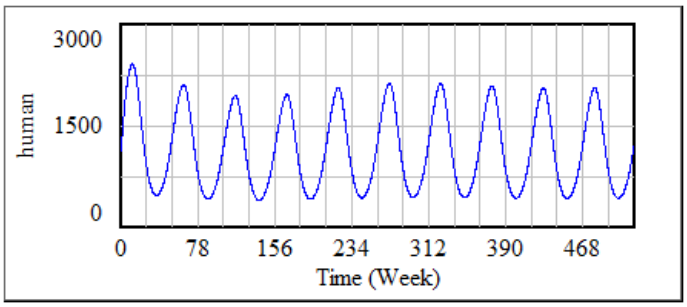
Figure 6.37. Run 4 Results for *Susceptible Human* and *Recovered Human* for Ten Years.

We can see in the Figure 6.37 that the pattern of the first year repeats itself for ten years for *susceptible human* and *recovered human*.

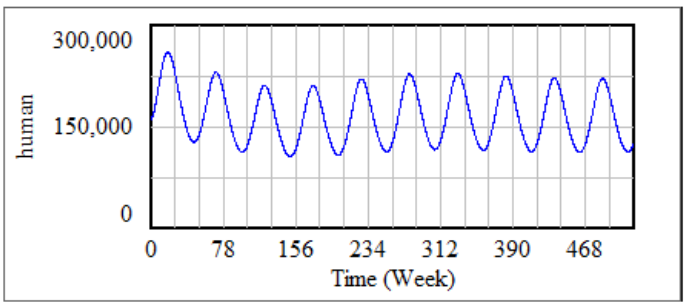
We can see in the Figure 6.38 that the pattern of the first year repeats itself for ten years for *exposed human*, *symptomatic infectious human*, and *asymptomatic infectious human*. The behavior we obtain for ten years is similar to the data. The amplitudes of the oscillations are similar each year for a variable, but the amplitudes of *exposed human*, *symptomatic infectious human*, and *asymptomatic infectious human* are different from each other as we expect.



(a) Exposed Human.



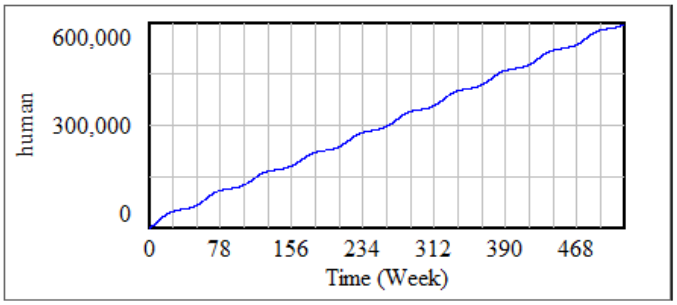
(b) Symptomatic Infectious Human.



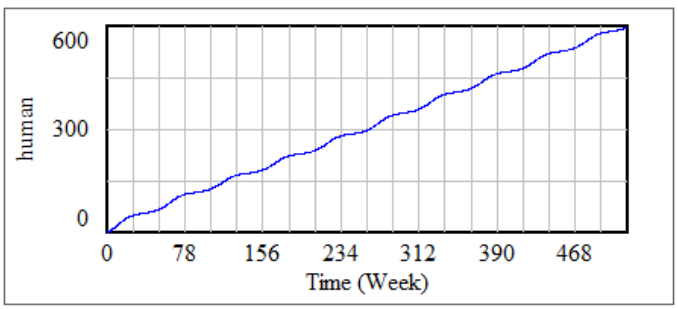
(c) Asymptomatic Infectious Human.

Figure 6.38. Run 4 Results for *Exposed Human*, *Symptomatic Infectious Human*, and *Asymptomatic Infectious Human* for Ten Years.

We can see in the Figure 6.39 that *total symptomatic infected human* and *total human deaths* have increasing patterns.



(a) Total Symptomatic Infected Human.

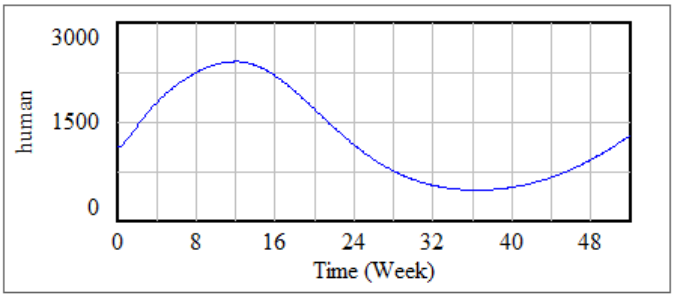


(b) Total Human Deaths

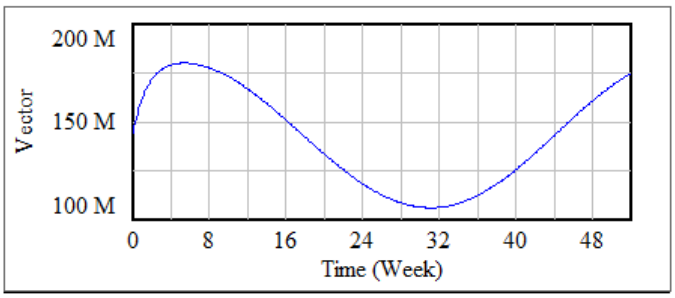
Figure 6.39. Run 4 Results for *Total Symptomatic Infected Human* and *Total Human Deaths* for Ten Years.

We give the run results for 52 weeks to observe the pattern in detail for a year.

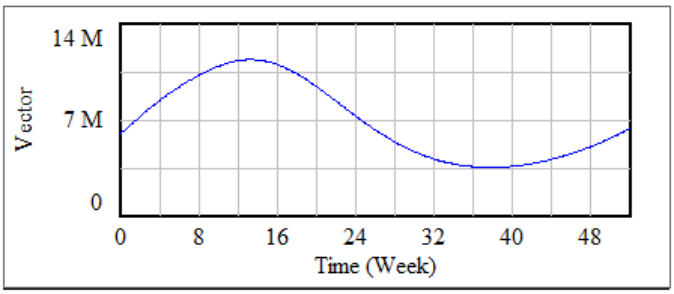
In the Figure 6.40 we can see that the *susceptible vector* makes a peak first, then it is followed by the *symptomatic infectious human* and *infected vector* peaks. *Susceptible vector* and *infected vector* behaviors are similar to sinus function as we expect. The behavior of *symptomatic infectious human* roughly approximates the behavior of the data of Rio de Janeiro that is given in Figure 6.2 and Figure 6.40.d [1, 2].



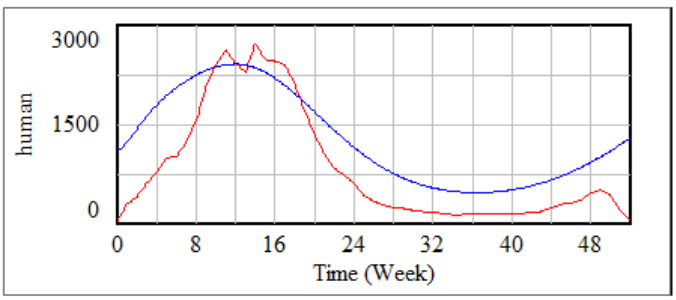
(a) Symptomatic Infectious Human.



(b) Susceptible Vector.



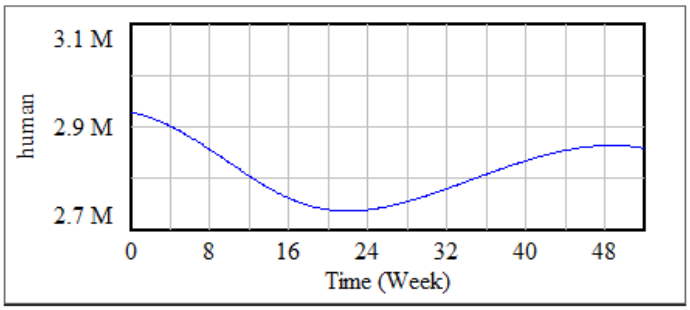
(c) Infected Vector.



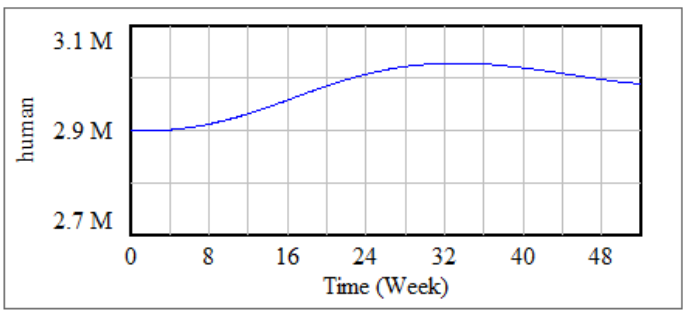
(d) Comparison of Run 4 and Data

Figure 6.40. Run 4 Results for *Symptomatic Infectious Human*, *Susceptible Vector*, *Infected Vector* and Comparison of Data and Run 4 *Symptomatic Infectious Human* for One Year.

We can see in the Figure 6.41 that the amplitudes of *susceptible human* and *recovered human* are similar to each other.



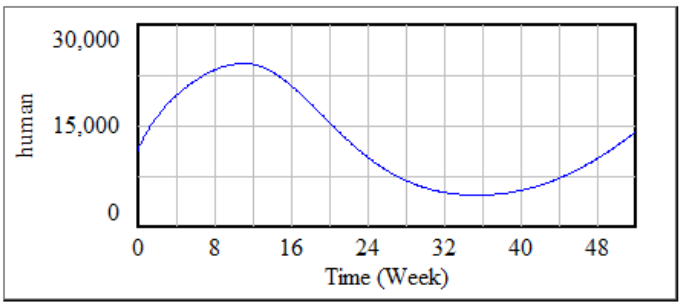
(a) Susceptible Human.



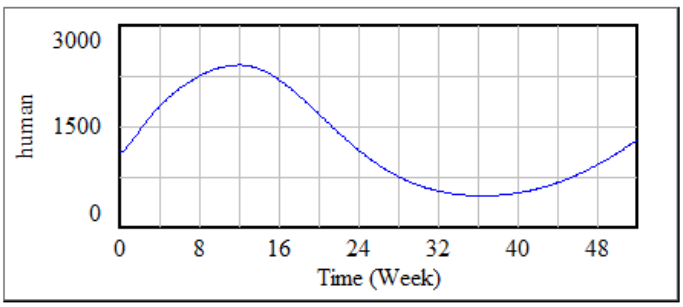
(b) Recovered Human.

Figure 6.41. Run 4 Results for *Susceptible Human* and *Recovered Human* for One Year.

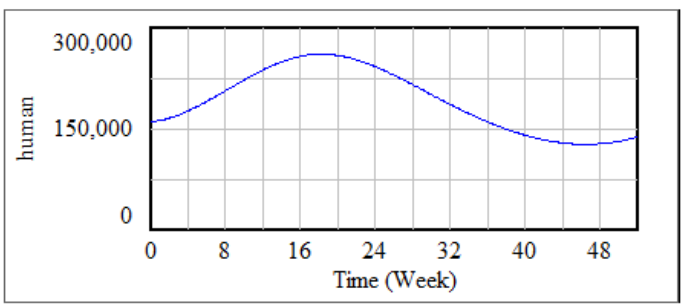
We can see in the Figure 6.42 that the amplitudes of *exposed human*, *symptomatic infectious human*, and *asymptomatic infectious human* are different from each other. And the peaks of *exposed human* and *symptomatic infectious human* are close to each other. Then the peak of *asymptomatic infectious human* follows them with a delay.



(a) Exposed Human.

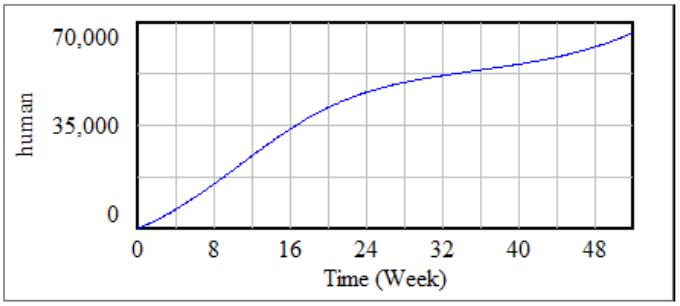


(b) Symptomatic Infectious Human.

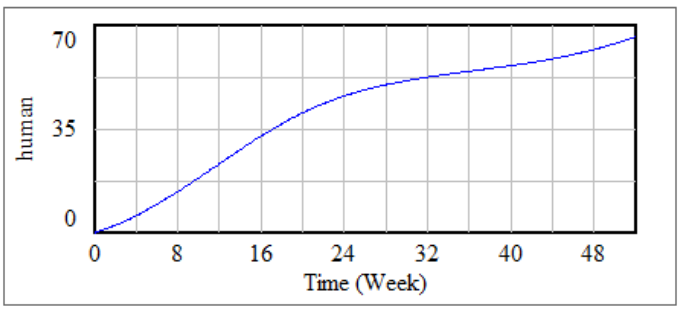


(c) Asymptomatic Infectious Human.

Figure 6.42. Run 4 Results for *Exposed Human*, *Symptomatic Infectious Human*, and *Asymptomatic Infectious Human* for One Year.



(a) Total Symptomatic Infected Human.



(b) Total Human Deaths

Figure 6.43. Run 4 Results for *Total Symptomatic Infected Human* and *Total Human Deaths* for One Year.

We obtain the *total symptomatic infected human* for one year as 66,375 humans. This resulting value is within the range of mean value of 43,670 humans and maximum value of 152,687 humans for Rio de Janeiro [2].

We obtain the *total human deaths* for one year as 66.1336 humans. Therefore, we can take 66 human deaths as a rough figure. And *total human deaths* value is around 0.1 percent of *total symptomatic infected human* as we expect.

We cannot use Run 0 in scenario analysis, because infectious human and *infected vector* populations decay to zero in this run. This implies that the virus does not persist with the parameter values that produce Run 0. However, the virus persists in the real system according to the relevant data. Therefore, we calibrate the leverage parameters so that the output behavior matches the relevant data taken from the literature. After

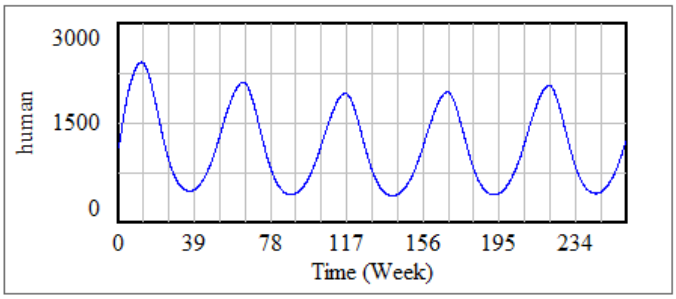
calibration, infectious human and *infected vector* populations do not decay to zero. We obtain similar behavior for all of the four runs. We have more moderate parameter values in Run 4 compared to the first three runs. Thus, we select Run 4 as the base run and use Run 4 in scenario analysis too. However, there is arbitrariness in our procedure because we do not know the exact values of these parameters; we assigned somewhat reasonable values to them. This arbitrariness will not affect the results of this thesis because the exactness of the parameter values would not change the behavior. However, we still suggest that further research must be carried out in Rio de Janeiro on these parameter values.

In Run 0, *time for recovery of asymptomatic human* is given as one week to be the same with the symptomatic human recovery time. In Run 1, we calibrate the *time for recovery of asymptomatic human*. We suspect and assume that recovery time of asymptomatic human is longer than recovery time of symptomatic human, therefore, we increased the value of this parameter. In Run 2, we calibrate the *ratio of infected vector births*. Vertical infection rate values are low in literature. However, we suspect and assume that this rate should be higher than the literature values for the persistence of the virus. We suggest that further research is carried out to find more accurate values of vertical infection. In Run 3, we calibrate the *average number of bites per human that are accessible to vectors*. We do not know the *average number of bites per human that are accessible to vectors*. We use our best estimations. In Run 4, we calibrate the three leverage parameter (*time for recovery of asymptomatic human*, the *ratio of infected vector births*, and the *average number of bites per human that are accessible to vectors*) values simultaneously. The suggested change in the *average number of bites per human that are accessible to vectors* is minimal, compared to the changes in the *time for recovery of asymptomatic human* and the *ratio of infected vector births*.

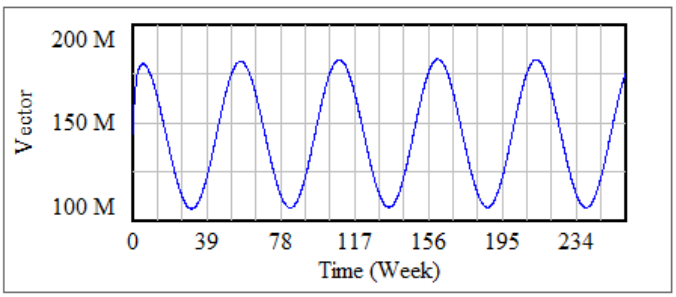
7. SCENARIO ANALYSIS

There may be several ways to decrease or eliminate the case numbers due to dengue virus. Two of the examples are decreasing the number of vectors and decreasing the human-vector interaction. To decrease the interaction between human and vector, we can decrease *seasonal effect on max getting bitten rate for human*. And to decrease the vector population, we can decrease *max vector birth rate*. Humans can take precautions against the interactions with vectors by protecting their body and the buildings they live in or work in. Window screens can be used in buildings. Repellents can be used on the open body areas. Clothes with more body coverage can be preferred as much as possible. The community can be educated to take precautions against the virus. Humans can take precautions against the vectors breeding areas by cleaning and drying water storages regularly. Insecticides can be used in vector breeding areas.

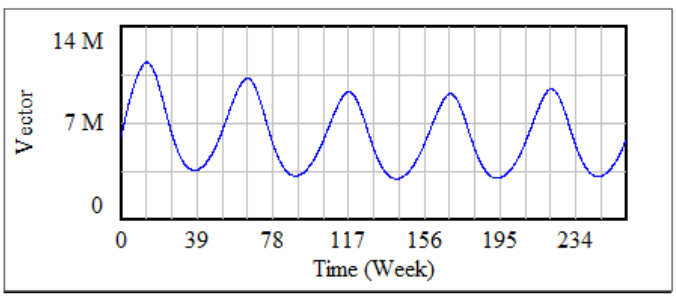
We use Run 4 for the scenario analyses. We obtain the scenario analyses results for 5 years (260 weeks). The behavior of *symptomatic infectious human*, *susceptible vector*, and *infected vector* for five years for Run 4 is given in the Figure 7.1.



(a) Symptomatic Infectious Human.



(b) Susceptible Vector.



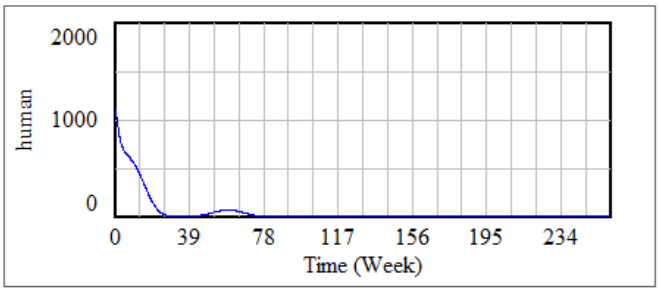
(c) Infected Vector.

Figure 7.1. Run 4 Results for *Symptomatic Infectious Human*, *Susceptible Vector*, and *Infected Vector* for Five Years.

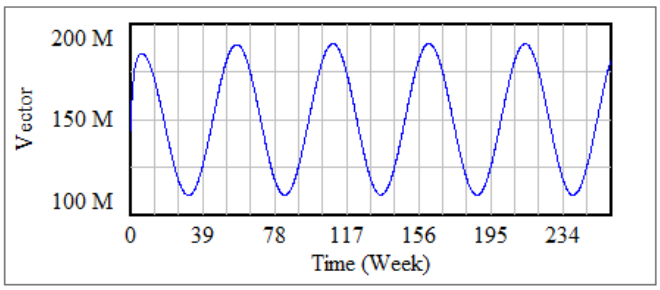
7.1. Scenario Analysis 1

We assume that humans wear clothes with more skin coverage at all seasons and take precautions against human-vector contact. However, we do not change the behavior of the seasonal effect, we only decrease the average value. We take the constant part of the *seasonal effect on max getting bitten rate for human* as 0.25 instead of 0.75.

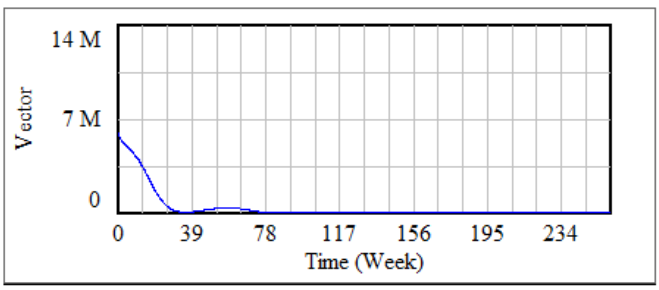
We give the resulting behavior in the Figure 7.2. We can see that *symptomatic infectious human* population and *infected vector* population approach to zero, which indicates that the virus is eliminated within two years. Note that, the dynamics of *asymptomatic infectious human* in this run is very similar to the dynamics of *symptomatic infectious human* population. Accordingly, *asymptomatic infectious human* also approaches to zero. Thus, we do not include its figure in this chapter. There are still *susceptible vector*s, however, they do not carry the dengue virus, and this implies that the virus is eliminated.



(a) Symptomatic Infectious Human.



(b) Susceptible Vector.



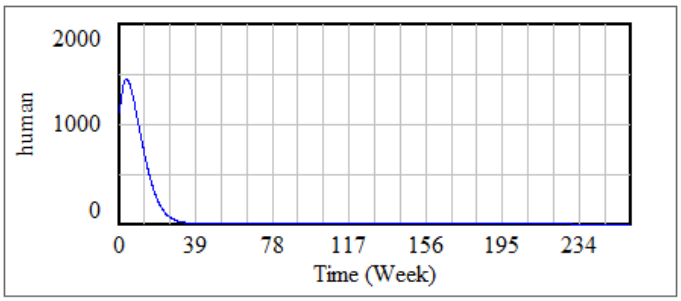
(c) Infected Vector.

Figure 7.2. Scenario Analysis Run 1 Results for *Symptomatic Infectious Human*, *Susceptible Vector*, and *Infected Vector* for Five Years.

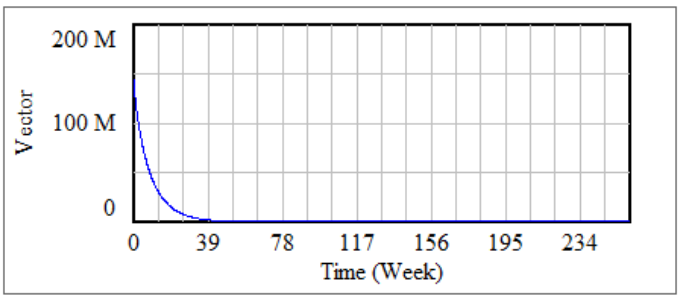
7.2. Scenario Analysis 2

We assume that humans take precautions against vector breeding areas. For example, by drying water storage tanks, humans eliminate the breeding areas for vectors. Vector births decrease as humans eliminate the breeding areas. We take the value of the *max vector birth rate* as 0.22 per week instead of 0.66 per week.

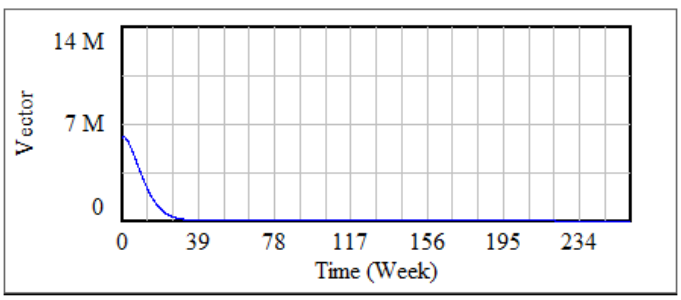
We give the resulting behavior in the Figure 7.3. We can see that the *symptomatic infectious human* and *infected vector* populations approach to zero, thus virus is eliminated within a year. Even the *susceptible vector* population is eliminated in this scenario, because the vector breeding areas are taken under control and all the vectors are eliminated with this precaution.



(a) Symptomatic Infectious Human.



(b) Susceptible Vector.



(c) Infected Vector.

Figure 7.3. Scenario Analysis Run 2 Results for *Symptomatic Infectious Human*, *Susceptible Vector*, and *Infected Vector* for Five Years.

8. RESULTS

The viral epidemic of dengue is a result of human-vector interactions. The parameters we use in our model are mainly the average parameters taken from the literature reported for the dengue epidemic in Rio de Janeiro. Also, we examine the literature of different countries and viruses to be inspired by the characteristics of the diseases to have a wide perspective for scenario analyses [32, 33]. We observe that the number of infectious human and *infected vector* converge to zero indicating that the virus disappears in time. However, this contradicts with the fact that virus is persistent in the region. Initially, we failed to generate the dengue dynamics reported by PAHO [1]. We name this run as run zero. We try to understand the reasons behind the actual behavior and try to estimate the parameters that can reflect the persistent nature of the epidemic. We obtain two main leverage parameters; *time for recovery of asymptomatic human* and *ratio of infected vector births*. We also obtain another leverage parameter as *average number of bites per human that are accessible to vectors*. Values of these parameters for run zero are 0.3 percent for *ratio of infected vector births*, 1 week for the *time for recovery of asymptomatic human* and 20 bites per human per week for *average number of bites per human that are accessible to vectors*. To obtain behavior similar to the dynamics reported by PAHO [1], we increase the values of these three parameters. First, we try to increase only one parameter while keeping the other two constant. However, we have to increase the parameters to extreme and probably unrealistic values. Therefore, after these trials, we try to obtain a combination of these three parameters with moderately increased values. The behavioral and numerical results we obtain roughly approximates the relevant data [1, 2].

We perform two scenario analyses. In the first analysis, we decrease the average value of the *seasonal effect on max getting bitten rate for human*. And the virus is eliminated in two years as a result. In the second analysis, we decrease the value of the *max vector birth rate*. And the virus is eliminated in a year as a result.

9. CONCLUSION

We constructed an SD model in order to represent the dynamics of dengue fever epidemic and to understand how the virus is sustained by a human-vector system. First, we used average parameter values from the relevant literature and our close estimations in our model. We observed that, the number of infectious human and infected vector converge to zero in the model when the average parameter values are used, thus the virus decays and eradicates. The run that eradicates the virus in this thesis is referred as run zero. However, the dengue epidemic is persistent in Rio de Janeiro for many years. Therefore, we tried to understand the reasons behind the actual behavior. We calibrated the parameters of our model to obtain persistence in the epidemic as it is in the real system. After these trials, we concluded that the values of parameters related to recovery time of infectious human and vertical infection of the vector may be higher than the values given in the relevant literature. We suggest that more research and experiments are carried out to obtain more accurate values for these parameters.

The constructed model does not only aim to generate the observed dynamics, but it also goes beyond the existing models in the sense that it serves as an experimental platform for scenario analyses to understand the dynamics of the disease and to support its management. The fourth run is used for further scenario analyses, because the leverage parameters related to recovery time of infectious human and vertical infection of the vector have more moderate values compared to the first three runs. We are able to keep the virus persistent in our model with higher values of the parameters related with recovery time of infectious human or vertical infection of the vector.

In the scenario analyses, we decided to use two parameters related to biting rates and vector births to eliminate the virus. We chose these two parameters on purpose because they are related with the precautions taken by the human against the virus. We decreased these two parameters one by one, to see the effects on the results. We conclude that the virus can be eliminated if humans take precautions against the

interactions with vectors and fight against vector breeding areas continuously. Humans can wear clothes with more skin coverage, use repellents and use window screens to decrease the interaction with vectors, and clean water storages regularly to decrease the vector births. One can calibrate and use our model for other regions too.

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APPENDIX A:

MODEL EQUATIONS

(01) asymptomatic infectious human= INTEG (progression flow of asymptomatic human-recovery flow of asymptomatic human , 160710) Units: human

(02) average bites for a vector that bites= 1 Units: Bites/(Vector*Week)

(03) average number of bites per human that are accessible to vectors= 25 Units: Bites/(human*Week)

(04) average seasonal effect on vector capacity = 0.6 + 0.16 * SIN(2 * 3.1416 * Time/one cycle + 4 * 3.1416/12) Units: Dmnl 3.1416 = PI

(05) biting rate of vector= weekly number of biting vector/total vector Units: 1/Week

(06) death rate of vector= 0.33 Units: 1/Week

(07) effect of crowding on vector birth rate= LOOKUP EXTRAPOLATE (graphical function of crowding, vector crowding) Units: Dmnl

(08) effect of standardized vector population on biting rate= LOOKUP EXTRAPOLATE(function for effect of standardized vector population on biting rate , standardized vector population) Units: Dmnl

(09) exposed human= INTEG (infection flow of human-progression flow of symptomatic human-progression flow of asymptomatic human , 11160) Units: human

(10) FINAL TIME = 52 Units: Week The final time for the simulation.

(11) fraction of asymptomatic human= 1-fraction of symptomatic human Units: Dmnl

(12) fraction of bloodmeal availability for susceptible human population = MAX (0,fraction of bloodmeal availability for total human population-sick and recovered human /total human) Units: Dmnl

(13) fraction of bloodmeal availability for total human population= 0.95 Units: Dmnl

(14) fraction of symptomatic human= 0.1 Units: Dmnl

(15) function for effect of standardized vector population on biting rate ([(0,0)-(1.2,1)],(0,0),(0.1,0.1), (0.2,0.2),(0.3,0.3),(0.4,0.4),(0.5,0.5), (0.6,0.6),(0.7,0.7),(0.8,0.8), (0.9,0.9), (1,0.951),(1.1,1),(1.2,1)) Units: Dmnl

(16) getting bitten rate for human= effect of standardized vector population on biting rate*max getting bitten rate for human with seasonal effect Units: 1/Week

(17) graphical function of crowding ([(0,0)-(2,1)], (0,1), (0.25,1), (0.5,0.98), (0.6,0.95), (0.7,0.87), (1,0.5), (1.3,0.13), (1.4,0.05), (1.5,0.02), (1.75,0),(2,0)) Units: Dmnl

(18) human death rate due to dengue= 0.001 Units: 1/Week

(19) human deaths due to dengue= human death rate due to dengue*symptomatic infectious human Units: human/Week

(20) human deaths due to dengue coflow= human deaths due to dengue Units:

human/Week

(21) immunity loss flow of human= immunity loss rate of human*recovered human Units: human/Week

(22) immunity loss rate of human= 0.00385 Units: 1/Week 1/(5years)

(23) infected human proportion= (symptomatic infectious human+asymptomatic infectious human)/total human that vector can reach Units: Dmnl

(24) infected vector= INTEG (infected vector births+infection flow of vector-infected vector deaths, 6e+06) Units: Vector

(25) infected vector births = (ratio of infected vector births * vector birth rate) * infected vector Units: Vector/Week

(26) infected vector deaths= infected vector*death rate of vector Units: Vector/Week

(27) infected vector ratio= infected vector/total vector Units: Dmnl

(28) infection flow of human= infection rate of human*subgroup of susceptible human Units: human/Week

(29) infection flow of vector= infection rate of vector*susceptible vector Units: Vector/Week

(30) infection rate of human= infectious getting bitten rate for human * transmission probability of infectious vector bite Units: 1/Week

(31) infection rate of vector= infectious biting rate of vector * transmission prob-

ability of biting infectious human Units: 1/Week

(32) infectious biting rate of vector= infected human proportion*biting rate of vector Units: 1/Week

(33) infectious getting bitten rate for human= infected vector ratio*getting bitten rate for human Units: 1/Week

(34) INITIAL TIME = 0 Units: Week The initial time for the simulation.

(35) max getting bitten rate for human= 1 Units: 1/Week

(36) max getting bitten rate for human with seasonal effect= seasonal effect on max getting bitten rate for human*max getting bitten rate for human Units: 1/Week

(37) max vector birth rate= 0.66 Units: 1/Week

(38) max vector capacity= 2.5e+08 Units: Vector

(39) net change flow of human= net change rate of human Units: human/Week Assumption: Total human population is constant through the year.

(40) net change rate of human= 1 Units: human/Week

(41) one cycle= 52 Units: Week

(42) progression coflow of human= progression flow of symptomatic human Units: human/Week

(43) progression flow of asymptomatic human= fraction of asymptomatic human*progression rate of human Units: human/Week

(44) progression flow of symptomatic human = fraction of symptomatic human * progression rate of human Units: human/Week

(45) progression rate of human= exposed human/progression time of human Units: human/Week

(46) progression time of human= 1 Units: Week

(47) ratio of infected vector births= 0.2 Units: Dmnl

(48) ratio of susceptible vector births= 1-ratio of infected vector births Units: Dmnl

(49) recovered human= INTEG (recovery flow of symptomatic human+recovery flow of asymptomatic human-immunity loss flow of human , 2.89865e+06) Units: human

(50) recovery flow of asymptomatic human= asymptomatic infectious human / time for recovery of asymptomatic human Units: human/Week

(51) recovery flow of symptomatic human= symptomatic infectious human/time for recovery of symptomatic human Units: human/Week

(52) reference vector population= 2e+08 Units: Vector

(53) SAVEPER = TIME STEP Units: Week [0,?] The frequency with which output is stored.

(54) seasonal effect on max getting bitten rate for human= 0.75 + 0.25*SIN (2*3.1416*Time/one cycle+4*3.1416/12) Units: Dmnl 3.1416 = PI

(55) sick and recovered human= exposed human+symptomatic infectious human+asymptomatic infectious human+ recovered human Units: human

(56) standardized vector population= total vector/reference vector population Units: Dmnl

(57) subgroup of susceptible human= fraction of bloodmeal availability for susceptible human population*susceptible human Units: human

(58) susceptible human= INTEG (net change flow of human+immunity loss flow of human-infection flow of human , 2.92836e+06) Units: human

(59) susceptible human that vector can reach= fraction of bloodmeal availability for susceptible human population*susceptible human Units: human

(60) susceptible vector= INTEG (susceptible vector births-infection flow of vector-susceptible vector deaths , 1.44e+08) Units: Vector

(61) susceptible vector births= vector birth rate*(susceptible vector+ratio of susceptible vector births* infected vector) Units: Vector/Week

(62) susceptible vector deaths= susceptible vector*death rate of vector Units: Vector/Week

(63) symptomatic infectious human= INTEG (progression flow of symptomatic human-recovery flow of symptomatic human- human deaths due to dengue, 1120) Units: human

(64) time for recovery of asymptomatic human= 16 Units: Week

(65) time for recovery of symptomatic human= 1 Units: Week

(66) TIME STEP = 0.125 Units: Week [0,?] The time step for the simulation.

(67) total human= susceptible human+exposed human+symptomatic infectious human+asymptomatic infectious human +recovered human Units: human

(68) total human deaths= INTEG (human deaths due to dengue coflow, 0) Units: human

(69) total human that vector can reach= susceptible human that vector can reach+sick and recovered human Units: human

(70) total symptomatic infected human= INTEG (progression coflow of human, 0) Units: human

(71) total vector= susceptible vector + infected vector Units: Vector

(72) transmission probability of biting infectious human= 0.7 Units: Dmnl

(73) transmission probability of infectious vector bite= 0.4 Units: Dmnl

(74) vector birth rate= effect of crowding on vector birth rate*max vector birth rate Units: 1/Week

(75) vector capacity= average seasonal effect on vector capacity * max vector capacity Units: Vector

(76) vector crowding= total vector/vector capacity Units: Dmnl

(77) weekly number of biting vector= average number of bites per human that are accessible to vectors*weekly number of bitten human /average bites for a vector that bites Units: Vector/Week

(78) weekly number of bitten human= getting bitten rate for human*total human that vector can reach Units: human/Week