A novel way to consider uncertainty in epidemiological models based on ODEs: Considering actual data from two municipalities in Colombia affected by Dengue

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Abstract

Uncertainty is present in any measurement process and in modeling real phenomena. Frequently, available information is not 100% reliable or accurate. This work considers the modeling of uncertainty in epidemiological models based on systems of Ordinary Differential Equations (henceforth ODEs) where knowledge and available information on model parameters and initial conditions is limited. This is especially true for models that simulate the transmission of vector-borne diseases such as dengue, our study case. To achieve this goal, we model the uncertainty through interval analysis by representing the input parameters and initial conditions as closed real intervals. To find guaranteed enclosures on the solutions of such systems, we apply a method based on the use of Taylor series and Taylor models to represent dependence on uncertain param-

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eters or initial conditions; specifically, we use the VSPODE software (Verifying Solver for Parametric ODEs). To enhance the use of this numerical method, we perform structural identifiability and sensitivity analysis to determine which parameters and initial conditions should be considered uncertain. Finally, our results so obtained enable us to show the worst-case scenarios of an outbreak, according to uncertainties considered. This allows considering under-reporting in the modeling process and designing more effective control strategies.

Keywords: Ordinary Differential Equations; Uncertainty; Interval analysis; Epidemiological models.

1. Introduction

Uncertainty is present in any process of measuring and obtaining information that is required to explain a real phenomenon. One source of uncertainty may be the lack of knowledge about the study phenomenon, to determine which char-
5 acteristics will be considered and which to ignore within the modeling. Other sources include the impossibility of obtaining measurements of some relevant factors, collecting information over long time periods, etc. [1].

In the case of vector-borne diseases such as West Nile virus, Malaria, Zika, and Dengue, among others, there is uncertainty due to the inability to accurately
10 and reliably measure transmission rates, vector populations, and the recovery rate in humans. Usually, these characteristics are included in the modeling process as parameters or initial conditions. This information is necessary to build more reliable models that allow us to understand the dynamics of this type of disease and thus be able to propose appropriate control strategies. However, in
15 contrast to other sciences where it is possible to carry out several experiments to obtain information and test hypotheses, such experiments are often impossible, unethical or expensive when modeling the spread of infectious diseases in human populations [2].

For instance, when we perform experimental assays with vector populations,
20 these experiments involve imprecision, some degree of approximation, or uncer-

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tainty to various degrees, since it is not possible to include in the laboratory all external aspects involved in development process. As an example, consider an experiment where three replicas with vector population are carried out. Suppose that each experiment starts with 100 eggs, and we want to measure the percentage of eggs hatching for this vector population. This measure may be stated in different ways as follows: (a) between 86 and 92 percent, (b) about 89 percent, or (c) has a mean value of 89 and a standard deviation of 2 percent and follows a normal distribution. Depending on the nature of imprecision, the analysis of the system can be conducted using interval analysis, fuzzy theory, or a probabilistic approach [3]. For the interested reader, we suggest seeing [4].

According to the type of information obtained from experimental assays, we consider that, for transmission of vector-borne diseases, an efficient and reliable way to account for uncertainty is through interval analysis: unlike applications based on probability and fuzzy theory, interval analysis does not attempt to infer an uncertainty structure of the model-output based on an uncertainty structure assumed for model-input.

On the other hand, recently, there has recently been an increasing interest in understanding and identifying the main factors involved in transmission and spread of infectious diseases through different strategies, such as as the formulation of models based on ODEs, the construction of risk maps considering external factors (social and environmental) [5, 6, 7], the analysis of development features of vector population through experimental assays [8, 9], and the formulation of statistical models that consider information from social media [10], among others. All these approaches require information in order to obtain solutions, formulate control strategies, or make predictions about the spread of infectious diseases. However, as we have mentioned before, to obtain more reliable conclusions from models, special attention is required to support and validate them by data specific to the disease, and to include a realistic assessment of parameter uncertainty and variability [11].

Our focus here is on ODE models which are formulated as Initial Value

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Problems (IVPs). Usually, an analytical solution does not exist for these models, so we have to use numerical methods to obtain the model trajectories. To compute these solutions, it is necessary to define initial parameters and initial conditions taking into account the features of the phenomenon under study, and thereby obtain mathematically reliable solutions.

In summary, this study was designed to incorporate uncertainty in parameters and initial conditions of epidemiological models that simulate the transmission of vector-borne diseases through the application of interval analysis, where the available information is not accurate and sufficient because of the characteristics of these diseases. To this end, we will perform local sensitivity analysis and structural identifiability analysis to select the parameters and initial conditions, to which we will incorporate the uncertainty due to the lack of information and due to lack of measurement precision.

From the mathematical point of view, we will consider the initial value problem (IVP) in ODEs given by

$$\dot{x}(t) = f(x, \theta), \qquad\qquad x(t_0) = x_0, \qquad\qquad (1)$$

where $t \in [t_0, t_k]$, $t_k > t_0$, $\theta \in \Theta$ is the m-dimensional vector of parameters, x is the n-dimensional vector of state variables, and x_0 is the n-dimensional vector of initial conditions. Furthermore, Θ and x_0 are interval vectors that represent the enclosures of the uncertainties of parameters and initial conditions, respectively. The purpose here is to obtain mathematically and computationally guaranteed enclosures for the vector of state variables x at all times, i.e. from t_0 to t_m, and compare these enclosures with the behavior of real data. To do this, we will use the software VSPODE (Validating Solver for Parametric ODEs), which can produce guaranteed enclosures on models when initial states and parameters are given by intervals. Moreover, VSPODE has been applied to obtain rigorous enclosures for some psychology models, ecology models, and epidemiological models [12, 13, 14]. For a deeper discussion of different methodologies proposed to solve (1) and the main drawbacks (overestimation caused by the dependency

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problem and wrapping effect) that arise and how they have been solved, we refer the reader to [15, 16].

To illustrate the performance of this methodology, we formulate a model of seven state variables and nine parameters that simulates the transmission of dengue diseases. We chose this model based on the availability of information on new dengue reported cases per week and the results of experimental assays with the local population of mosquitoes, allowing us to establish the initial ranges for human initial conditions and parameters of development stages of the vector. Also, because of the high epidemiological, social, and economic impact of dengue transmission in tropical countries [17, 18], it is relevant to evaluate different levels of uncertainty in parameters and initial conditions that have the primary role in the production of new outbreaks.

The remainder of this paper is organized as follows. First, we provide background on interval analysis and a brief introduction to the use of Taylor models. Section 2 describes the problem we are addressing, the notation used, the model formulation, and methodology details for the sensitivity and structural identifiability analyses. After that, we present the results of several numerical experiments for two municipalities of Colombia. Finally, we draw our main conclusions and discuss some future work.

2. Background

2.1. Interval analysis

Interval-arithmetic is largely attributed to Ramon Moore in the 1960s; he developed it to rigorously account for rounding errors linked to mathematical calculations: The object on which this theory is constructed is the set of closed intervals in $\mathbb{R}$.

$$\mathcal{I} = \{\, X = [\,\underline{x}, \overline{x}\,] \mid \underline{x} \leq \overline{x} \,\wedge\, \underline{x}, \overline{x} \in \mathbb{R} \,\}.$$

This definition can be extended in a natural way to n-dimensional real interval vectors, $\mathcal{I}^n$ as $\mathbf{X} = [\,X_1, \ldots, X_n\,]^T$, where $X_i = [\,\underline{x_i}, \overline{x_i}\,]$ and $n \geq 1$. An n-dimensional interval vector can be interpreted geometrically as an n-dimensional

rectangle or box. For X and $Y \in \mathcal{I}$ is possible to define the basic arithmetic operations according to $X \circ Y = \{x \circ y \,|\, x \in X, y \in Y\}$, $\circ \in \{+, -, *, \div\}$, where we require $0 \notin Y$ for division[3]. Additionally, addition and multiplication in $\mathcal{I}$ are associative and commutative, but only subdistributive: $(X * (Y + Z) \subseteq (X * Y) + (X * Z))$. The interval $[0, 0]$ plays the role of neutral element in addition, while the interval $[1, 1]$ has the same role for multiplication. In general, for an arbitrary interval X there exists neither an additive nor multiplicative inverse, that is, $X - X = 0$ and $X * 1/X = 1$ are not satisfied. Furthermore, although interval evaluation of an expression always *contains* the set of all values of the expression as the arguments to the expression range over all values in the specified intervals, ways of rewriting the expression that are equivalent in real arithmetic are not equivalent in interval arithmetic; for example, matrix multiplication is not associative.

An interval-valued function F can be defined as an extension of a real valued function f, if for degenerate intervals, that is, intervals of the form $[a, a]$, $F([x, x]) = f(x)$. Moreover, for a real function $f : \mathbb{R}^n \to \mathbb{R}$ we can use interval arithmetic to bound the range of f over an interval X, replacing all the occurrences of x by X, to obtain $f(x) = \{f(x) \,|\, x \in X\} \subseteq f(X)$. A challenge in particular applications is to choose the form of the expressions or computation order for f to obtain the narrowest possible interval extension $f(X)$. For details, consult introductions to interval computations, such as [20] or [21, Section 1.3].

Finally, if we consider the metric

$$d_H(X, Y) = \max\{\,|\underline{x} - \underline{y}|, \, |\overline{x} - \overline{y}|\,\},\tag{2}$$

where $X = [\underline{x}, \overline{x}]$ and $Y = [\underline{y}, \overline{y}] \in \mathcal{I}$, it is possible to define all the elements of local analysis, such as limits, sequences, continuity, convergence, weak differentiablility, and integrability over $\mathcal{I}$. With this we have all the tools to formulate differential equations in $\mathcal{I}$ [20].

The main drawbacks when using interval analysis are the *dependency problem*

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[3]Division is extended in various ways to remove this restriction; see, for example [19].

and *the wrapping effect*. The dependency problem occurs when there is more than one occurrence of the same variable in the expression for a function. The wrapping effect appears when, in intermediate computation steps, the result is not an interval or box, and it is necessary to enclose the result in an interval or box.

2.2. Taylor models

Consider a function $f : D \subset \mathbb{R}^s \to \mathbb{R}$ that is $(n+1)$ times continuously partially differentiable. A *Taylor model* for a function f that is $(n+1)$ times continuously partially differentiable is given by $T = (P, e) = P + e$ where P denotes the n-th order Taylor polynomial of f around the expansion point $x_0 \in D$ and e is a small bounding set for the remainder of this approximation:

$$f(x) - P(x - x_0) \in e, \ \forall x \in D \text{ where } x_0 \in D. \tag{3}$$

3. Materials and methods

3.1. Solution procedure

In this work, as in [14] and [22], we consider systems of ordinary differential equations given by the following formulation:

$$\dot{x}(t) = f(x, \theta), \qquad\qquad x(t_0) = x_0, \tag{4}$$

where $t \in [t_0, t_k]$, $t_k > t_0$, and $\theta \in \Theta$ is the m-dimensional vector of parameters. The variables x and x_0 are n-dimensional vectors of state variables and initial conditions, respectively. In addition, Θ and X_0 are interval vectors that represent the enclosures of the uncertainties of parameters and initial conditions, respectively. Also, we assume that $f : \mathbb{R}^n \times \mathbb{R}^p \to \mathbb{R}^n$ is $k-1$ times continuously differentiable with respect to x and $q+1$ times continously differentiable with respect to θ.

To solve (4), we applied the method proposed in [22] which was implemented by the authors in the VSPODE software (Validated solutions of initial value

problems for parametric ODEs). We briefly describe the method here; for more detailed information, we refer to [22].

First, consider a sequence of values $t_0 < t_1 < \cdots < t_m$ with step size $h_j = t_{j+1} - t_j$ at the $(j+1)$-th integration step, $j = 0, 1, \ldots, m-1$. A solution to the IVP

$$\dot{x}(t) = f(x, \theta), \qquad\qquad x(t_j) = x_j$$

is given by

$$x(t; t_j, X_j, \Theta) = \{ \, x(t; t_j, x_j, \theta) \,|\, x_j \in X_j, \, \theta \in \Theta \, \}.$$

In algorithms to solve (4), each integration step is divided into two stages. The first stage consists of validating the existence and uniqueness of the solution, while the second stage consists of computing a tighter enclosure.

3.1.1. First stage

The goal in the first stage is to find a step size $h_j = t_{j+1} - t_j > 0$ and an a priori enclosure $\tilde{X}_j$ of the solution such that a unique solution $x(t; t_j, x_j, \theta)$ is guaranteed to exist for all $t \in [t_j, t_{j+1}]$, all $x_j \in X_j$ and all $\theta \in \Theta$. For this purpose, the algorithm uses Interval Taylor Series (ITS) with respect to time. The uniqueness of the solution $x(t; t_j, x_j, \theta)$ is proved by using the Picard-Lindelöf operator and the Banach fixed-point theorem [15].

To compute the enclosure $\tilde{X}_j$, VSPODE uses high-order enclosure methods based on using many terms in the Taylor series. In this way, it is possible to determine $h_j = t_{j+1} - t_j$ and $\tilde{X}_j$ such that

$$\tilde{X}_j = \sum_{i=0}^{k-1} [0, h_j]^i F^{[i]}(X_j, \Theta) + [0, h_j]^k F^{[k]}(\tilde{X}_j^0, \Theta) \subseteq \tilde{X}_j^0. \qquad (5)$$

where $(X_i)_j = F^{[i]}(X_j, \Theta)$ are the interval extensions of the Taylor coefficients[4] for $x_j \in X_j$ and $\theta \in \Theta$. One of the advantages of considering more terms in the Taylor series is that it is possible to consider larger step sizes, unlike first-order enclosure methods (constant enclosure methods).

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[4]The j-th Taylor coefficient evaluated at t_i is denoted by $(x_i)_j = \frac{x^{(j)}(t_i)}{j!}$

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3.1.2. Second stage

The goal in the second stage is to compute a tighter enclosure X_{j+1} such that $X_{j+1} \subseteq \tilde{X}_j$. In VSPODE this is done by using ITS to compute a Taylor model $T_{f^{[i]}} = f^{[i]}(T_{x_j}, T_\theta)$ which depends on the initial conditions (x_0) and parameters (θ). For the Taylor model computations, the interval initial states and parameters are represented by the Taylor models

$$x_{0_i} \in T_{x_{0_i}} = m(X_{0_i}) + (x_0 - m(X_{0_i})) + [0,0], \;\; i = 1, \ldots, n.$$

$$\theta_i \in T_{\theta_i} = m(\Theta_i) + (\theta_i - m(\Theta_i)) + [0,0], \;\; i = 1, \ldots, p.$$

Then, it is possible to determine Taylor models $T_{f^{[i]}}$ of the ITS coefficients $f^{[i]}(x_j, \theta)$ by using remainder differential algebra (RDA) [23] to compute $T_{f^{[i]}} = f^{[i]}(T_{x_j}, T_\theta)$. To reduce the overestimation produced due to interval dependency and the continuous growth of the remainder in each integration step, we use Taylor models $T_{f^{[i]}}$ and the mean value theorem to compute the enclosure for each coefficient $f^{[i]}(x_j, \theta)$ for the ITS of x_{i+j}. Thus, we obtain the Taylor model $T_{x_{j+1}}$ for x_{j+1} in terms of the uncertain quantities θ and x_0. Finally, to control the wrapping effect, the state enclosures are propagated using a new type of Taylor model. This new Taylor model consists of a polynomial and a remainder bound represented by an n-dimensional parallelepiped.

3.2. Mathematical model: Dengue transmission

The model developed here is based on the one given in [24], where the female mosquito population M is divided into three compartments: susceptible (M_s), exposed (M_e), and infected (M_i). Moreover, we allowed the size of the mosquito population to change in time. Also, we captured the behavior of the aquatic phase of the vector population in one parameter, Λ, which is interpreted as the recruitment rate. To establish an appropriate biological range for this parameter, we define $\Lambda = f\gamma_m A^*$ with $A^* = C\left(1 - \frac{1}{R_m}\right)$ and $R_m = \frac{\rho f \gamma_m}{\mu_m(\gamma_m + \mu_a)}$, where R_m is the number of secondary females produced by only one female (the offspring), and A^* is the equilibrium value of the aquatic phase in which mosquitoes are present. Thus, we take into account parameters that describe

the transition and mortality from the aquatic phase to the adult phase of the vector $(\rho, \gamma_m, \mu_a, \mu_m, f)$.

To define the biological ranges for these parameters, we used the results of life tables created from experiments performed in the BCEI laboratory (Grupo de Biología y Control de Enfermedades infecciosas de la Universidad de Antioquia) between 2017 and 2019, with mosquito populations of Itagüí and Neiva. For a deeper description of the experimental protocol, we refer the reader to [25]. Then, we applied interval arithmetic to compute the range of Λ. The biological interpretations of these parameters and their ranges for each municipality are summarized in Table 1.

The size of human population H is considered constant with respect to the per capita mortality rate (μ_h), and is divided into four compartments: susceptible (H_s), exposed (H_e), infected (H_i), and recovered (H_r).

In both populations, the flow from the susceptible to exposed compartment depends on the proportion of infected in each population $(\frac{H_i}{H}$ and $\frac{M_i}{M})$ and the transmission coefficients $(\beta_h$ and $\beta_m)$. Here, we assumed the transmission coefficients to be the product of the mosquito's biting rate and the transmission probabilities. Once extrinsic and intrinsic incubation periods are completed, the exposed mosquitoes and humans become infected at a rate of θ_m and θ_h, respectively. Finally, infected humans recover at a rate of γ_h, while mosquitoes remain infected for the rest of their lives [26].

Based on the above assumptions, the dynamics of dengue transmission is

given by the following system of differential equations:

$$\frac{dM_s}{dt} = \Lambda - \beta_m \frac{H_i}{H} M_s - \mu_m M_s$$

$$\frac{dM_e}{dt} = \beta_m \frac{H_i}{H} M_s - (\theta_m + \mu_m) M_e$$

$$\frac{dM_i}{dt} = \theta_m M_e - \mu_m M_i$$

$$\frac{dH_s}{dt} = \mu_h H - \beta_h \frac{M_i}{M} H_s - \mu_h H_s \qquad (6)$$

$$\frac{dH_e}{dt} = \beta_h \frac{M_i}{M} H_s - (\theta_h + \mu_h) H_e$$

$$\frac{dH_i}{dt} = \theta_h H_e - (\gamma_h + \mu_h) H_i$$

$$\frac{dH_r}{dt} = \gamma_h H_i - \mu_h H_r$$

3.3. Basic Reproductive Number

The Basic Reproductive Number (R_0), is defined as the expected number of new cases of an infection produced by a typical infected individual in a wholly susceptible population over the full course of the infectious period [27]. In mathematical epidemiology, this number is one of the most important concepts, since it is a threshold parameter that helps us to determine if the disease dies out ($R_0 < 1$) or if the disease persists ($R_0 > 1$).

Several strategies have been proposed to calculate R_0. However, for a fixed model, the R_0 values calculated with the different strategies may differ. This shows the difficulty in accurately calculating the number of secondary infections within an entirely susceptible population [28]. Here, to compute R_0, we applied the *Next Generation Matrix* (NGM) to model (6) around the disease-free equilibrium point. This approach gives us the geometric mean of the number of infections per generation [29]. From the mathematical point of view, according to [30], R_0 is given by the dominant eigenvalue of the matrix $\mathbf{K} = -T\Sigma^{-1}$, where the entries of the matrix T are the rates of appearance of new infections, and Σ is the transition matrix.

The disease-free equilibrium for model (6) is given as $P_0 = (M, 0, 0, H, 0, 0, 0)$, where the variables are arranged in the same way as the equations in the system.

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Computing the matrix $\mathbf{K}$ at the disease-free equilibrium gives

$$\mathbf{K} = \begin{pmatrix} 0 & 0 & \frac{\beta_m \theta_h}{(\theta_h + \mu_h)(\gamma_h + \mu_h)} \frac{M_s^*}{H} & \frac{\beta_m}{(\gamma_h + \mu_h)} \frac{M_s^*}{H} \\ 0 & 0 & 0 & 0 \\ \frac{\beta_h \theta_m}{\mu_m(\theta_m + \mu_m)} H_s^* & \frac{\beta_h}{\mu_m} \frac{H_s^*}{M} & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix}$$

where

$$T = \begin{pmatrix} 0 & 0 & 0 & \beta_m \frac{M_s^*}{H} \\ 0 & 0 & 0 & 0 \\ 0 & \beta_h \frac{H_s^*}{M} & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix},$$

$$\Sigma = \begin{pmatrix} -(\theta_m + \mu_m) & 0 & 0 & 0 \\ \theta_m & -\mu_m & 0 & 0 \\ 0 & 0 & (\theta_h + \mu_h) & 0 \\ 0 & 0 & \theta_h & -(\gamma_h + \mu_h) \end{pmatrix},$$

$H_s^* = H$, and $M_s^* = M$. Therefore, the basic reproductive number R_0 is given by:

$$R_0 = \sqrt{\frac{\beta_m \beta_h \theta_m \theta_h}{\mu_m(\theta_m + \mu_m)(\theta_h + \mu_h)(\gamma_h + \mu_h)}} \tag{7}$$

For more details about the calculation of R_0 for model (6) we refer the reader to [24].

3.4. Structural Identifiability Analysis

Structural identifiability analysis of a model can be interpreted as a way to determine if it is possible to uniquely recover the best model parameters if the data is assumed to be noise-free [31]. This analysis is only based on the model structure, and is independent of the accuracy of experimental data. When the identifiability issue is addressed by taking into account the type and quality of available data, we refer to practical (a posteriori) identifiability [32], but we do not consider this analysis here.

Formally, we say that a system (1) is *globally identifiable* if for any two parameter vectors θ_1 and θ_2 in the parameter space,

$$y(x(t), \theta_1) = y(x(t), \theta_2) \tag{8}$$

holds if and only if $\theta_1 = \theta_2$, where $y(x(t), \theta_1)$ and $y(x(t), \theta_2)$ are the trajectories solutions for θ_1 and θ_2, respectively. If the equation (8) is only satisfied for any θ_1 and θ_2 within an open neighborhood of some point θ^* in the parameter space, we say the system (1) is *locally identifiable* (definitions taken from [32]).

Different approaches have been proposed to test if a model is structurally identifiable; among these are the *direct test*, *differential algebra*, *Laplace transform*, *implicit function theorem*, the application of *Taylor series*, *profile likelihood*, and *output sensitivities*. We refer the reader to [33, 32] for a deeper discussion of these approaches.

In this study, we just can test locally structural identifiability analysis of the epidemiological model of dengue transmission (6). To achieve this goal, we use the *Identifiability Analysis* package in *Mathematica* software. This implementation is based on a probabilistic numerical method of computing the rank of the identifiability (Jacobian) matrix, where the matrix parameters and initial state variables are assigned random integers. Then, from the application of the inverse function theorem, it is possible to determine if parameters and initial conditions can be estimated uniquely if and only if the Jacobian matrix has full rank [34].

3.5. Data and Parameter values

In this study, we consider the data from the 2016 dengue outbreaks in the municipalities of Itagüí (Antioquia, Colombia) and Neiva (Huila-Colombia). The outbreak in Itagüí lasted 60 epidemiological weeks, beginning in epidemiological week 51 of 2015 (with 10 reported cases) and ending in epidemiological week 6 of 2016 (with 4 reported cases). The total number of dengue cases reported during this period was 2915.

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₂₅₅ Meanwhile, the outbreak in Neiva lasted 24 epidemiological weeks, beginning in the epidemiological week 38 of 2016 (with 16 reported cases) and ending in the epidemiological week 9 of 2017 (with 7 reported cases). The total number of dengue cases reported during this period was 687. The information of the reported dengue cases was obtained from the *National Public Health Surveil-*
₂₆₀ *lance System* (SIVIGILA by its Spanish initials) (`http://portalsivigila.ins.gov.co/sivigila/documentos/Docs_1.php`). The information about the size of human population for each municipality was taken from the National Administrative Department of Statistics (DANE by its Spanish initials).

Ranges for parameters and initial conditions for each municipality are sum-
₂₆₅ marized in Tables 2 and 3, respectively.

4. Results

4.1. Mathematical model: Dengue transmission

The model defined in (6) with some parameter and initial condition values taken from their biological ranges (see Tables 2 and 3) is capable of suc-
₂₇₀ cessfully simulating the dengue outbreak that occurred in Itagüí and Neiva in 2016 (see Fig 1).

4.2. Local sensitivity analysis of R_0

To investigate the local sensitivity of the basic reproductive number (R_0) to changes in the parameters, we calculate the derivative with respect to each one.

We observe from the expression (7) that:

$$\frac{\partial R_0}{\partial \beta_m} = \frac{1}{2\beta_m} R_0$$

$$\frac{\partial R_0}{\partial \beta_h} = \frac{1}{2\beta_h} R_0$$

$$\frac{\partial R_0}{\partial \theta_m} = \frac{\mu_m}{2\theta_m(\theta_m + \mu_m)} R_0$$

$$\frac{\partial R_0}{\partial \theta_h} = \frac{\mu_h}{2\theta_h(\theta_h + \mu_h)} R_0$$

$$\frac{\partial R_0}{\partial \mu_m} = -\frac{1}{2(\theta_m + \mu_m)}\left(2 + \frac{\theta_m}{\mu_m}\right) R_0$$

$$\frac{\partial R_0}{\partial \gamma_h} = -\frac{1}{2(\gamma_h + \mu_h)} R_0$$

Partial derivatives of parameters such as transmission rate from human to mosquito (β_m), transmission rate from mosquito to human (β_h), transition rate from exposed to infected mosquitoes (θ_m), and transition rate from exposed to infected humans (θ_h) always are positive, i.e. an increase in them increases the value of R_0. Meanwhile, for mortality rate in mosquitoes (μ_m) and recovery rate in humans (γ_h), partial derivatives always are negative, thus when values of these parameters decrease, the value of R_0 increases.

To determine which parameters have more influence in the occurrence of new dengue cases, we calculate the *elasticity* of R_0 with respect to each parameter θ. The elasticity is given by

$$\varepsilon_\theta^{R_0} = \frac{\partial R_0}{\partial \theta}\frac{\theta}{R_0} \approx \frac{\%\Delta R_0}{\%\Delta \theta}. \tag{9}$$

The elasticities give the percentage change in R_0 in response to 1% increase in the parameter θ. When $\varepsilon_\theta^{R_0} > 0$, that means that R_0 increases with θ; when $\varepsilon_\theta^{R_0} < 0$ that means that R_0 decreases when θ increases [35]. For instance, the fact that $\varepsilon_{\beta_m}^{R_0} = 0.5$ means that 1% increase in β_m will produce 0.5% increase in R_0. We summarize these results for each municipality in Table 4.

4.3. Structural Identifiability

We evaluated if model (6) is locally structurally identifiable from the weekly number of reported dengue cases when we fix: (1) the values of human mortality

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rate (μ_h), (2) the size of human population (H), (3) the initial condition of infected humans ($H_i(0)$ as the lower bound), and (4) the initial condition of recovered humans as $H_r(0) = H - H_s(0) - H_e(0) - H_i(0)$. Under these conditions, the parameter Λ and the initial conditions for susceptible, exposed and infected mosquitoes are not locally identifiable.

4.4. Numerical Simulations

In the formulation of model (6) we included nine parameters, seven state variables, and their respective initial conditions. Additionally, the vector function is a polynomial function in the model parameters and a rational function in the state variables. In this way, the function satisfies the condition of continuous differentiability with respect the state variables and model parameters necessary to apply the VSPODE algorithm.

We perform simulations for Itagüí and Neiva considering uncertainty in some parameters and initial conditions according to results obtained from local sensitivity analysis of R_0 and the locally structurally identifiability analysis of model (6). We applied VSPODE, with its default ITS (Interval Taylor Series) order $k = 17$ and a default Taylor model order $q = 5$, to determine a verified enclosure of all possible solutions for model (6) under several scenarios for each municipality. We defined the interval integration for each municipality according to the duration of the outbreak. For Itagüí the interval of integration was from $t = 0$ to $t = 60$ epidemiological weeks, while, for Neiva was from $t = 0$ to $t = 30$ epidemiological weeks. We consider only the scenarios below:

1. **Considering uncertainty in one parameter at a time.** In this scenario we considered uncertainty in transmission rates from human to mosquito and from mosquito to human (β_m and β_h respectively), mortality rate in mosquitoes (μ_m), recovery rate in humans (γ_h) and recruitment rate in mosquitoes (Λ). The first four parameters were included according to results obtained from local sensitivity analysis of R_0 (see Table 4). The recruitment rate (Λ) was included since it was the only parameter that is

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not locally structurally identifiable (see Section 4.3). Fig 2, 3, 4, and 5 show the guaranteed enclosures for the possible trajectories of infectious humans for Itagüí and Neiva.

2. **Considering uncertainty in several parameters at the same time.** In this scenario we obtained verified computational and mathematical enclosures when (a) uncertain values are assumed for β_m and β_h, (b) uncertain values are assumed for β_m, β_h, and μ_m, and (c) uncertain values are assumed for β_m, β_h, μ_m, and γ_h. Fig 6 and Fig 7 show mathematically and computationally guaranteed upper and lower bounds for the possible trajectories of infected humans for Itagüí and Neiva, respectively.

3. **Considering uncertainty in initial conditions only.** In this scenario we considered uncertainty in (a) the initial mosquito population ($M_s(0)$, $M_e(0)$ and $M_i(0)$), (b) initial human population ($H_s(0)$, $H_e(0)$, $H_i(0)$ and $H_r(0)$), and (c) all initial conditions of model (6). These scenarios make sense because it is not possible to determine exactly which is the number of susceptible, exposed, and infected mosquitoes in a specific region. Additionally, these initial conditions are not locally structurally identifiable (see Section 4.3). On the other hand, according to the World Health Organization (WHO), the number of reported dengue cases is not 100% reliable or accurate because of under-reporting concerns, which can affect up to 75% of the total number of cases occurring anywhere Dengue transmission is present [36]. Fig 8 and Fig 9 show mathematically and computationally guaranteed upper and lower bounds on the possible trajectories of infected humans for Itagüí and Neiva, respectively.

4. **Considering uncertainty in parameters and initial conditions at the same time.** In this scenario, we consider uncertainty in transition rate from exposed to infected mosquito (θ_m) and exposed and infected human initial conditions ($H_e(0)$ and $H_i(0)$ respectively). VSPODE breaks down at the second integration step for Itagüí when $H_e(0) \in [21, 61]$ and $H_i(0) \in [10, 30]$, and at $t = 18$ for Neiva, when $H_e(0) \in [27, 77]$ and $H_i(0) \in [16, 46]$, due to rapid growth of the enclosure. Thus, to obtain

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guaranteed enclosures, we split the intervals of $H_e(0)$ and $H_i(0)$ into 10 equal-sized sub-boxes for both municipalities, and then used VSPODE to determine the solution for each sub-box. The final solution enclosure is then the union of all the enclosures resulting from each sub-box. However, with the VSPODE specifications that we mention above the solutions for Itagüí always blow up in some integration point. For that reason, we consider (only for Itagüí and this scenario) ITS (Interval Taylor Series) order $k = 12$ and a default Taylor model order $q = 9$. Fig 10 and 11 show mathematically and computationally guaranteed upper and lower bounds on the possible trajectories of infected humans for Itagüí and Neiva, respectively.

Tables 5–6 show the interval enclosures and their widths at different times t (in epidemiological weeks), calculated with VSPODE for the first three scenarios.

5. Discussion

We present a novel strategy to include uncertainty in modeling based on ODEs, through the application of interval arithmetic, structural identifiability analysis, and local sensitivity analysis. Further, we take into account the available information, knowledge, and understanding of the phenomenon under study. **To the best of our knowledge,** this is the first study in which a strategy to select parameters and initial conditions that should be considered uncertain based on the results of structural identifiability analysis and local sensitivity analysis is introduced.

To illustrate the performance of these analyses jointly we considered as an example a model of seven state variables and nine model parameters that simulates the transmission of dengue diseases (see Eq (6)). In [24], we showed through several analyses **how reliable is this model to simulate dengue transmission.**

Previous studies have incorporated uncertainty in epidemiological models via fuzzy and stochastic modeling [37, 38, 39], and to a lesser extent through the

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application of interval analysis in [14]. However, few studies have assessed the relation between the available data and the model formulation to decide which is the best option to consider the uncertainty in the modeling process [4, 3]. In this work, we represented uncertain values by intervals, since available information is not enough to determine the probability distribution that measurement errors follow. Also, we do not have enough information to define an appropriate membership function for model parameters and initial conditions in the fuzzy context.

To define initial intervals for parameters and initial conditions for model (6) with biological meaning, we had (a) results from experimental assays with local mosquito populations for each municipality; (b) the average time for transition from exposed to infectious (mosquitoes and humans); (c) the average time of recovery rate in humans; official information of new dengue cases per week; and (d) the size of human population for each municipality (see Tables 2–3). Nevertheless, it is important to take into account that experimental assays under laboratory conditions did not consider the mortality rate due to external factors. In this way, these results do not always correspond to the life of the vector in the wild. For this reason, it is necessary to consider uncertainty in models that include the development features of the vector.

Here, we extended the range for mosquito mortality rate (μ_m) to include external causes that increase it (see Table 2). In addition, for *Ae. aegypti* populations from Itagüí and Neiva, we observed significant differences between values for mortality rate and recruitment rate in simulations. For Neiva, the values of these parameters were higher than for Itagüí. These results were consistent with climatic characteristics and control strategies used in each municipality [40].

We showed that model (6) can successfully simulate dengue outbreaks that occurred in Itagüí and Neiva during 2016, based on biologically significant parameters and initial conditions without considering uncertainty in them (see Figure 1). An important expression for outbreak characterization is R_0. This number gives us information about the average number of secondary cases that a single case can produce if it is introduced into a susceptible population and

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regarding whether an outbreak will occur [30].In this way, to determine which parameters have more influence in the output of epidemiological models we can

perform local sensitivity analysis on R_0 instead of the model. According to this, for model (6), we found that the occurrence of new dengue cases was more sensitive to transmission rate from human to mosquito (β_m), transmission rate from mosquito to human (β_h), the recovery rate in humans (γ_h), and mortality rate in mosquitoes (μ_m) (see Table 4). These results coincide with the results shown in [41]. It is worth pointing out that, as mentioned in [42], frequently, transmission rates determine the occurrence or not of an outbreak. However, for ethical reasons it is not possible to obtain measures for these parameters through experimental assays. In this manner, the parameter values of transmission rates contain a significant amount of uncertainty.

The results of locally structurally identifiability analysis for model (6) (see Section 4.3) suggest that is necessary to collect information about the mosquito population for the model (6) to be structurally identifiable. However, collecting this information for long periods can be expensive and unreliable.

This suggests that considering uncertainty in mosquito initial conditions through interval arithmetic is a good way to determine how an outbreak would be in the presence of larger populations (see Figs 8–9). Under this assumption, it is possible to define the frequency, the intensity, and the duration of more efficient and robust control strategies. This result is important since, at present, the only way to mitigate dengue outbreaks efficiently is by controlling the vector population [43]. Finally, we consider uncertain values in human initial conditions since according to [36], the number of reported new dengue cases per week does not correspond to the total number of cases that occurred in a period. For the above reasons, from the biological point of view it makes sense to consider the four scenarios described in Section 4.4. In these scenarios, we defined the uncertainty ranges for each parameter and initial condition in such a manner that the number of dengue cases will increase. Thus, we evaluated what could be the worst possible outbreak when parameters and initial conditions change. In this manner, it is possible to plan control strategies in consideration of under-

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reported cases.

In general, we considered wider intervals for Neiva than for Itagüí for all four scenarios (see Figures 2–11), because the interval of integration for Neiva was shorter than for Itagüí, i.e., the number of steps for error propagation was smaller for Neiva. We proceeded by cases. In the first scenario, we limit the level of uncertainty that can be considered for each parameter to avoid blow up of solutions. For both municipalities, we found that for β_h, it was possible to consider wider intervals than for the other parameters. Additionally, in Table 5 we can see that at the final step of integration when we considered uncertainty in recruitment rate (Λ) the solution started to blow up. This is an indicator that we will not obtain verified enclosures after this integration step. Possible solutions to this drawback are to split the range of uncertainty and then join the solutions (as we did in scenario four), to increase the order of Taylor Model or increase the order of ITS (Interval Taylor Series) or to split the integration range into smaller sub-boxes [44].

For the second scenario, we evaluated if it was possible considering at the same time all the most important parameters in the production of secondary cases. To achieve this goal we have to reduce the uncertainty considered in the first scenario for β_m, β_h and γ_h to obtain guaranteed enclosures and not change the specifications of VSPODE. This scenario allows us to work with different sources of uncertainty, and as we mentioned before, for the parameters considered here we did not have reliable measures.

In the third scenario, we evaluated how the output model changed when we considered uncertainty in initial conditions. Figures 8–9 show that the human initial conditions have more impact on the number of dengue cases per week than mosquito initial conditions. These results make sense since there exist cities with large mosquito population where the number of dengue cases is low and some cities with a significant number of dengue cases where the presence of mosquitoes is not significant [45]. This relation can be explained by vector capacity of the vector [46].

Finally, in the fourth scenario, we evaluated the performance of the method

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implemented in VSPODE when we considered uncertainty in parameters and initial conditions at the same time. However, we just can consider uncertainty in two human initial conditions ($H_e(0)$ and $H_i(0)$) and one parameter (θ_m) at the same time to have guaranteed enclosures of trajectories of the model (see Figures 10 and 11), even when we split the integration box into smaller sub-boxes to avoid blow up of the solution. In addition, we have to increase the order of Taylor Model for Itagüí. A possible explanation for this might be that VSPODE considers the Taylor model dependent on initial conditions and parameters at the same time.

In contrast to traditional numerical methods, the results obtained from interval numerical methods are guaranteed mathematically and computationally [15]. However, due to overestimation from the dependency problem, the wrapping effect and the curse of dimensionality, it was not possible to consider uncertainty in a larger number of parameters and initial conditions at the same time. For these reasons, it is important to consider alternative strategies to select the parameters and initial conditions that should be considered uncertain. In our case we considered the results of locally structural identifiability analysis, the results of local sensitivity analysis, the available information and the knowledge of study phenomenon. In this way, we can reduce the dimension of our problem and successfully apply interval methods to find guaranteed enclosures for all trajectories of the model.

However, it is worth noting that although the algorithm used in this paper attempts to manage overestimation and envelopment at each integration step, further research could explore a way to improve these techniques or formulate new strategies to manage these problems with integrating for longer time intervals without the solutions exploding. Furthermore, future studies should try to weaken the requirement for differentiability and continuity in the vector field to apply interval arithmetic algorithms to a larger number of systems.

A final aspect that should be mentioned is that the strategy presented here to select and subsequently incorporate uncertainty can be extrapolated to models that simulate other phenomena of different application areas, and models that

can incorporate uncertainty in other ways. In summary, the methodology raised in this work represents a pioneering effort (1) to select uncertain parameters and initial conditions with biological meaning and (2) to propagate uncertainty using interval arithmetic, taking into account the available information. In this way, we will have a broader picture, in which we consider the worst and the best cases of the studied phenomenon.

6. Conclusions

We present a methodology to consider uncertainty through interval analysis in models based on ODEs that simulate real phenomena, such as the transmission of infectious diseases. We include the uncertainty in a way that is consistent with the type of information that is usually available on the biological parameters and initial conditions of the study phenomenon. We use the interval method developed in [22] to compute mathematically and computationally guaranteed enclosures for trajectories of state variables . We achieved a better computational performance by applying a methodology based on sensitivity analysis, structural identifiability analysis, available information, and the parameters' biological meanings. The results of these analyses allowed us to choose which parameters and initial conditions should be considered as uncertain values. Finally, to illustrate the performance of this methodology, we have formulated a dengue transmission model (Eq (6)) and apply the aforementioned analysis to several scenarios. Additionally, we contrast the results obtained from the model with actual dengue case data for the Colombian cities of Itagüí and Neiva.

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[1] W. Maziak, Is uncertainty in complex disease epidemiology resolvable?, Emerging Themes in Epidemiology 12 (1) (2015) 7. doi:https://doi.org/10.1186/s12982-015-0028-5.

[2] H. W. Hethcote, The basic epidemiology models: models, expressions for R_0, parameter estimation, and applications, in: Mathematical understanding of infectious disease dynamics, 2009, pp. 1–61. doi:https://doi.org/10.1142/9789812834836_0001.

[3] H.-J. Zimmermann, An application-oriented view of modeling uncertainty, European Journal of Operational Research 122 (2) (2000) 190 – 198. doi:https://doi.org/10.1016/S0377-2217(99)00228-3.

[4] J. Helton, J. Johnson, W. Oberkampf, An exploration of alternative approaches to the representation of uncertainty in model predictions, Reliability Engineering & System Safety 85 (1) (2004) 39 – 71. doi:https://doi.org/10.1016/j.ress.2004.03.025.

[5] T.-H. Wen, N. H. Lin, C.-H. Lin, C.-C. King, M.-D. Su, Spatial mapping of temporal risk characteristics to improve environmental health risk identification: A case study of a dengue epidemic in Taiwan, Science of the Total Environment 367 (2) (2006) 631 – 640. doi:https://doi.org/10.1016/j.scitotenv.2006.02.009.

[6] A. M. Stewart-Ibarra, Á. G. Muñoz, S. J. Ryan, E. B. Ayala, M. J. Borbor-Cordova, J. L. Finkelstein, R. Mejía, T. Ordoñez, G. C. Recalde-Coronel, K. Rivero, Spatiotemporal clustering, climate periodicity, and social-ecological risk factors for dengue during an outbreak in Machala, Ecuador, in 2010, BMC Infectious Diseases 14 (1) (2014) 610. doi:https://doi.org/10.1186/s12879-014-0610-4.

[7] M. E. Parra-Amaya, M. E. Puerta-Yepes, D. P. Lizarralde-Bejarano, S. Arboleda-Sánchez, Early detection for dengue using Local Indicator of Spatial Association (LISA) analysis, Diseases 4 (2) (2016) 16. doi:https://doi.org/10.3390/diseases4020016.

[8] V. H. Peña-García, O. Triana-Chávez, S. Arboleda-Sánchez, Estimating Effects of Temperature on Dengue Transmission in Colombian cities, An-nals of Global Health 83 (3) (2017) 509 – 518, current Topics in Global Health. doi:https://doi.org/10.1016/j.aogh.2017.10.011.

[9] O. J. Brady, M. A. Johansson, C. A. Guerra, S. Bhatt, N. Golding, D. M. Pigott, H. Delatte, M. G. Grech, P. T. Leisnham, R. Maciel-De-Freitas, L. M. Styer, D. L. Smith, T. W. Scott, P. W. Gething, S. I. Hay, Modelling adult *Aedes aegypti* and *Aedes albopictus* survival at different temperatures in laboratory and field settings, Parasites and Vectors 6 (1). doi:https://doi.org/10.1186/1756-3305-6-351.

[10] C. d. A. Marques-Toledo, C. M. Degener, L. Vinhal, G. Coelho, W. Meira, C. T. Codeo, M. M. Teixeira, Dengue prediction by the web: Tweets are a useful tool for estimating and forecasting dengue at country and city level, PLOS Neglected Tropical Diseases 11 (7) (2017) 1–20. doi:https://doi.org/10.1371/journal.pntd.0005729.

[11] C. B. Beard, R. J. Eisen, C. M. Barker, J. F. Garofalo, M. Hahn, M. Hay-den, A. J. Monaghan, N. H. Ogden, P. J. Schramm, Ch. 5: Vector borne Diseases in: The Impacts of Climate Change on Human Health in the United States: A Scientific Assessment, U.S. Global Change Research Pro-gram, Washington, DC, 2016. doi:https://doi.org/10.7930/J0765C7V.

[12] J. A. Enszer, M. A. Stadtherr, Verified solution and propagation of uncer-tainty in physiological models, Reliable Computing 15 (3) (2011) 168–178.

[13] J. A. Enszer, D. A. Mces, M. A. Stadtherr, Probability bounds analysis for nonlinear population ecology models, Mathematical Biosciences 267 (2015) 97 – 108. doi:https://doi.org/10.1016/j.mbs.2015.06.012.

[14] J. Enszer, M. Stadtherr, Verified solution method for population epidemi-ology models with uncertainty, International Journal of Applied Math-ematics and Computer Science 19 (3) (2009) 501 – 512. doi:https://doi.org/10.2478/v10006-009-0040-4.

[15] N. Nedialkov, K. Jackson, G. Corliss, Validated solutions of initial value problems for ordinary differential equations, Applied Mathematics and Computation 105 (1) (1999) 21 – 68. `doi:https://doi.org/10.1016/S0096-3003(98)10083-8`.

[16] M. Neher, K. R. Jackson, N. S. Nedialkov, On Taylor model based integration of ODEs, SIAM Journal on Numerical Analysis 45 (1) (2007) 236–262. `doi:https://doi.org/10.1137/050638448`.

[17] D. Gulber, Epidemic dengue/dengue hemorrhagic fever as a public health, social and economic problem in the 21st century, Trends in Microbiology 10 (2) (2002) 100–103. `doi:https://doi.org/10.1016/S0966-842X(01)02288-0`.

[18] R. C. Rodríguez, G. Carrasquilla, A. Porras, K. Galera-Gelvez, J. G. L. Yescas, J. A. Rueda-Gallardo, The burden of dengue and the financial cost to Colombia, 2010-2012, American Journal of Tropical Medicine and Hygiene 94 (5) (2016) 1065–1072. `doi:https://doi.org/10.4269/ajtmh.15-0280`.

[19] IEEE Standard for Interval Arithmetic (June 2015). `doi:https://doi.org/10.1109/IEEESTD.2015.7140721`.

[20] R. E. Moore, R. B. Kearfott, M. J. Cloud, Introduction to Interval Analysis, SIAM, 2009.

[21] A. S. Ackleh, E. J. Allen, R. B. Kearfott, P. Seshaiyer, Classical and Modern Numerical Analysis. Theory, methods and practice, Chapman & Hall/CRC Numerical Analysis and Scientific Computing, 2010.

[22] Y. Lin, M. A. Stadtherr, Validated solutions of initial value problems for parametric ODEs, Applied Numerical Mathematics 57 (10) (2007) 1145 – 1162. `doi:https://doi.org/10.1016/j.apnum.2006.10.006`.

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[23] K. Makino, M. Berz, Remainder differential algebras and their applications, Computational Differentiation: Techniques, Applications and Tools (1996) 63–74.

[24] D. P. Lizarralde-Bejarano, D. Rojas-Díaz, S. Arboleda-Sánchez, M. E. Puerta-Yepes, Sensitivity, uncertainty and identifiability analyses to define a dengue transmission model with real data of an endemic municipality of Colombia, PLoS ONE 15 (3) (2020) e0229668. `doi:https://doi.org/10.1371/journal.pone.0229668`.

[25] D. P. Lizarralde-Bejarano, S. Arboleda-Sánchez, M. E. Puerta-Yepes, Understanding epidemics from mathematical models: Details of the 2010 dengue epidemic in Bello (Antioquia, Colombia), Applied Mathematical Modelling 43 (2017) 566 – 578. `doi:https://doi.org/10.1016/j.apm.2016.11.022`.

[26] L. Esteva, C. Vargas, A model for dengue disease with variable human population, Journal of Mathematical Biology 38 (3) (1999) 220–240. `doi:https://doi.org/10.1007/s002850050147`.

[27] F. Brauer, Mathematical epidemiology: Past, present, and future, Infectious Disease Modelling 2 (2) (2017) 113 – 127. `doi:https://doi.org/10.1016/j.idm.2017.02.001`.

[28] R. J. Smith, J. Li, D. Blakeley, The failure of R_0, Computational and Mathematical Methods in Medicine 2011. `doi:https://doi.org/10.1155/2011/527610`.

[29] J. A. P. Heesterbeek, A brief history of R_0 and a recipe for its calculation, Acta Biotheoretica 50 (3) (2002) 189–204. `doi:https://doi.org/10.1023/A:1016599411804`.

[30] O. Diekmann, J. A. Heesterbeek, J. A. Metz, On the definition and the computation of the basic reproduction ratio R_0 in models for infectious

diseases in heterogeneous populations, Journal of Mathematical Biology 28 (4) (1990) 365–382. `doi:https://doi.org/10.1007/BF00178324`.

[31] M. P. Saccomani, Structural vs Practical Identifiability in System Biology, IWBBIO 2013 Proceedings (2013) 305–313.

[32] H. Miao, X. Xia, A. S. Perelson, H. Wu, On identifiability of nonlinear ODE models and applications in viral dynamics, SIAM review 53 (1) (2011) 3–39. `doi:https://doi.org/10.1137/090757009`.

[33] O.-T. Chis, J. R. Banga, E. Balsa-Canto, Structural Identifiability of systems biology models: A critical comparison of methods, PLoS ONE 6 (11) (2011) e27755. `doi:https://doi.org/10.1371/journal.pone.0027755`.

[34] J. Karlsson, M. Anguelova, M. Jirstrand, An efficient method for structural identifiability analysis of large dynamic systems. 16th IFAC Symposium on System Identification, IFAC Proceedings Volumes 45 (16) (2012) 941 – 946. `doi:https://doi.org/10.3182/20120711-3-BE-2027.00381`.

[35] M. Martcheva, Ch. 6: Fitting Models to Data in: An Introduction to Mathematical Epidemiology, Springer US, 2015. `doi:https://doi.org/10.1007/978-1-4899-7612-3_6`.

[36] S. Bhatt, P. W. Gething, O. J. Brady, J. P. Messina, A. W. Farlow, C. L. Moyes, J. M. Drake, J. S. Brownstein, A. G. Hoen, O. Sankoh, M. F. Myers, D. B. George, T. Jaenisch, G. R. W. Wint, C. P. Simmons, T. W. Scott, J. J. Farrar, S. I. Hay, The global distribution and burden of dengue, Nature 496 (7446) (2013) 504–507. `doi:https://doi.org/10.1038/nature12060`.

[37] L. C. Barros, R. C. Bassanezi, R. Z. G. Oliveira, M. B. F. Leite, A disease evolution model with uncertain parameters, in: Proceedings Joint 9th IFSA World Congress and 20th NAFIPS International Conference (Cat. No. 01TH8569), Vol. 3, 2001, pp. 1626–1630. `doi:https://doi.org/10.1109/NAFIPS.2001.943794`.

[38] L. Barros, M. Leite, R. Bassanezi, The SI epidemiological models with a fuzzy transmission parameter, Computers & Mathematics with Applications 45 (10) (2003) 1619 – 1628. doi:https://doi.org/10.1016/S0898-1221(03)00141-X.

[39] T. Britton, D. Lindenstrand, Epidemic modelling: Aspects where stochasticity matters, Mathematical Biosciences 222 (2) (2009) 109 – 116. doi:https://doi.org/10.1016/j.mbs.2009.10.001.

[40] J. C. Padilla, D. P. Rojas, R. S. Gómez, Dengue en Colombia: epidemiología de la reemergencia a la hiperendemia, Guías de Impresión Ltda., 2012.

[41] L. Esteva, H. M. Yang, Assessing the effects of temperature and dengue virus load on dengue transmission, Journal of Biological Systems 23 (04) (2015) 1550027. doi:https://doi.org/10.1142/S0218339015500278.

[42] R. M. Christley, M. Mort, B. Wynne, J. M. Wastling, A. L. Heathwaite, R. Pickup, Z. Austin, S. M. Latham, "Wrong, but Useful": Negotiating Uncertainty in Infectious Disease Modelling, PLoS ONE 8 (10) (2013) e76277. doi:https://doi.org/10.1371/journal.pone.0076277.

[43] I. A. Rather, H. A. Parray, J. B. Lone, W. K. Paek, J. Lim, V. K. Bajpai, Y.-H. Park, Prevention and control strategies to counter Dengue virus infection, Frontiers in Cellular and Infection Microbiology 7 (2017) 336. doi:https://doi.org/10.3389/fcimb.2017.00336.

[44] K. Makino, M. Berz, Verified computations using taylor models and their applications, in: A. Abate, S. Boldo (Eds.), Numerical Software Verification, Springer International Publishing, Cham, 2017, pp. 3–13. doi:https://doi.org/10.1007/978-3-319-63501-9_1.

[45] V. H. Peña-García, O. Triana-Chávez, A. M. Mejía-Jaramillo, F. J. Díaz, A. Gómez-Palacio, S. Arboleda-Sánchez, Infection rates by dengue virus

695   in mosquitoes and the influence of temperature may be related to different endemicity patterns in three Colombian cities, International Journal of Environmental Research and Public Health 13 (7) (2016) 734. doi:https://doi.org/10.3390/ijerph13070734.

[46] A. Catano-Lopez, D. Rojas-Diaz, H. Laniado, S. Arboleda-Sánchez, M. E.
700   Puerta-Yepes, D. P. Lizarralde-Bejarano, An alternative model to explain the vectorial capacity using as example *Aedes aegypti* case in dengue transmission, Heliyon 5 (10) (2019) e02577. doi:https://doi.org/10.1016/j.heliyon.2019.e02577.

Table 1: **Parameters used to define the recruitment rate** (Λ) **range.** We extend intervals for mortality rate (μ_m) since these ranges were calculated under experimental conditions and did not consider external factors (as fumigation) that can increase it.

Param.	Meaning	Itagüí		Neiva	
		Rang./day	**Rang./week**	**Rang./day**	**Rang./week**
ρ	Effective per capita oviposition rate	$[12, 60]$	$[12, 240]$	$[14, 29]$	$[14, 128]$
C	Carrying capacity of the environment	$[6400, 95000]$	$[6400, 95000]$	$[6400, 95000]$	$[6400, 95000]$
γ_m	Transition rate from the aquatic phase to the adult phase	$[0.11, 0.13]$	$[0.77, 0.88]$	$[0.11, 0.13]$	$[0.77, 0.88]$
μ_a	Mortality rate in the aquatic phase	$[0.001, 0.027]$	$[0.008, 0.19]$	$[0.015, 0.028]$	$[0.11, 0.19]$
f	Fraction of female mosquitoes hatched from all eggs	$[0.39, 0.51]$	$[0.39, 0.51]$	$[0.32, 0.45]$	$[0.32, 0.45]$
μ_m	Mortality rate in the adult phase	$[0.011, 0.016]$	$[0.008, 0.25]$	$[0.02, 0.027]$	$[0.14, 0.45]$
Λ	Recruitment rate	$[273, 6297]$	$[1779, 42612]$	$[223, 5550]$	$[1454, 37529]$

Table 2: **Parameters used in the simulations of model** (6) **for Itagüí and Neiva, their biological descriptions, and their values range.**

Param.	Meaning	Itagüí		Neiva	
		Rang./day	**Rang./week**	**Rang./day**	**Rang./week**
Λ	Recruitment rate	$[273, 6297]$	$[1779, 42612]$	$[223, 5550]$	$[1454, 37529]$
H	Size of human population	248036	248036	324466	324466
μ_m	Mortality rate in the adult phase	$[0.011, 0.016]$	$[0.008, 0.25]$	$[0.02, 0.027]$	$[0.14, 0.45]$
μ_h	Birth and death rate of the human population	0.000032	0.00023	0.000015	0.00011
β_m	Transmission rate from human to mosquito	$[0, 4]$	$[0, 4]$	$[0, 4]$	$[0, 4]$
β_h	Transmission rate from mosquito to human	$[0, 4]$	$[0, 4]$	$[0, 4]$	$[0, 4]$
θ_m	Transition rate from exposed to infected mosquito	$[0.08, 0.13]$	$[0.58, 0.88]$	$[0.08, 0.13]$	$[0.58, 0.88]$
θ_h	Transition rate from exposed to infected human	$[0.1, 0.25]$	$[0.7, 1.75]$	$[0.1, 0.25]$	$[0.7, 1.75]$
γ_h	Recovery rate	$[0.07, 0.25]$	$[0.5, 1.75]$	$[0.07, 0.25]$	$[0.5, 1.75]$

Table 3: **Initial conditions used in the simulations of model** (6) **for Neiva and Itagüí, their biological descriptions, and their values ranges.**

Initial condition	Meaning	Itagüí	Neiva
$M_s(0)$	For susceptible mosquitoes	$[0, 5000000]$	$[0, 5000000]$
$M_e(0)$	For exposed mosquitoes	$[0, 200]$	$[0, 200]$
$M_i(0)$	For infectious mosquitoes	$[0, 200]$	$[0, 200]$
$H_s(0)$	For susceptible humans	$[198429, 247912]$	$[259573, 324294]$
$H_e(0)$	For exposed humans	$[21, 84]$	$[27, 108]$
$H_i(0)$	For infectious humans	$[10, 40]$	$[16, 64]$
$H_r(0)$	For recovered humans	$[0, 49576]$	$[0, 64850]$

Table 4: **Elasticity of** R_0 **for Neiva and Itagüí taking parameter values from Fig 1.**

Elasticity	Itagüí	Neiva
$\varepsilon^{R_0}_{\beta_m}$	0.5	0.5
$\varepsilon^{R_0}_{\beta_h}$	0.5	0.5
$\varepsilon^{R_0}_{\theta_m}$	0.134	0.167
$\varepsilon^{R_0}_{\theta_h}$	8.8×10^{-5}	4.2×10^{-5}
$\varepsilon^{R_0}_{\mu_m}$	-0.634	-0.667
$\varepsilon^{R_0}_{\gamma_h}$	-0.5	-0.5

Table 5: **Results on model** (6)**, showing upper bound, lower bound, and width of these enclosures at different times for scenarios** 1, 2, **and** 3 **for Itagüí municipality.**

	Uncertain values		Epidemiological weeks t						
			1	10	20	30	40	50	60
Scenario 1	β_m	Sup	11.761	38.548	115.888	165.067	112.207	62.855	34.315
		Inf	11.749	32.979	80.647	93.126	50.953	22.914	9.966
		Width	0.012	5.569	35.241	71.941	61.254	39.941	24.348
	β_h	Sup	11.991	36.057	92.789	112.843	65.175	31.018	14.447
		Inf	11.7492	32.9785	80.6475	93.1356	50.9797	22.9754	10.0339
		Width	0.2414	3.079	12.142	19.707	14.195	8.043	4.414
	μ_m	Sup	11.749	32.994	81.409	97.631	55.520	25.73	11.595
		Inf	11.749	32.979	80.648	93.135	50.980	22.980	10.098
		Width	0.0	0.016	0.762	4.496	4.540	2.750	1.497
	γ_h	Sup	12.032	34.452	86.341	102.432	57.705	26.778	12.113
		Inf	11.749	32.979	80.648	93.136	50.980	22.981	10.098
		Width	0.283	1.473	5.693	9.296	6.725	3.797	2.014
	Λ	Sup	11.749	33.046	81.980	97.931	54.384	24.651	13.281
		Inf	11.749	32.979	80.648	93.136	50.980	22.879	7.598
		Width	0.0	0.067	1.332	4.795	3.404	1.772	5.683
Scenario 2	β_m, β_h	Sup	11.914	36.972	100.601	129.509	79.466	40.931	27.182
		Inf	11.749	32.901	79.978	91.469	49.227	20.929	1.846
		Width	0.165	4.071	20.623	38.040	30.239	20.002	25.336
	β_m, β_h, μ_m	Sup	11.832	34.937	90.925	115.121	69.343	34.570	18.846
		Inf	11.749	32.959	80.444	92.350	49.972	21.687	6.991
		Width	0.083	1.978	10.481	22.771	19.371	12.883	11.855
	$\beta_m, \beta_h, \mu_m, \gamma_h$	Sup	11.888	35.244	92.181	117.345	71.051	35.451	19.166
		Inf	11.749	32.948	80.361	92.109	49.753	21.674	7.144
		Width	0.139	2.296	11.820	25.236	21.298	13.777	12.022
Scenario 3	Mosquito initial conditions	Sup	13.652	45.921	112.037	129.164	71.357	32.909	15.351
		Inf	11.244	29.458	73.881	89.996	49.399	21.384	8.411
		Width	2.408	16.463	38.156	39.168	21.958	11.525	6.940
	Human initial conditions	Sup	35.308	49.040	125.575	151.516	86.668	41.208	23.689
		Inf	11.745	32.472	78.516	89.978	48.351	21.071	4.317
		Width	23.563	16.568	47.059	61.538	38.317	20.137	19.372
	All initial conditions	Sup	20.759	47.320	121.232	146.477	83.930	39.592	18.213
		Inf	11.596	31.624	76.988	89.637	48.535	21.589	9.325
		Width	9.163	15.696	44.244	56.840	35.395	18.003	8.888

Table 6: **Results on model** (6)**, showing upper bound, lower bound, and width of these enclosures at different times for scenarios** 1**,** 2**, and** 3 **for Neiva municipality.**

	Uncertain values		Epidemiological weeks t						
			1	5	10	15	20	25	30
Scenario 1	β_m	Sup	16.174	33.859	64.821	65.392	38.764	19.893	9.984
		Inf	16.122	29.811	46.241	37.155	17.144	6.774	2.604
		Width	0.051	4.048	18.581	28.236	21.620	13.120	7.380
	β_h	Sup	17.187	36.948	63.395	56.895	29.674	13.339	5.917
		Inf	16.122	29.811	46.241	37.157	17.150	6.783	2.561
		Width	1.064	7.138	17.155	19.739	12.524	6.556	3.356
	μ_m	Sup	16.123	29.874	47.833	42.820	22.232	9.789	4.380
		Inf	16.122	29.811	46.239	37.125	17.040	6.564	2.249
		Width	0.001	0.064	1.594	5.695	5.191	3.225	2.131
	γ_h	Sup	17.839	34.433	57.253	50.074	25.434	11.158	5.073
		Inf	16.122	29.810	46.238	37.149	17.128	6.716	2.273
		Width	1.717	4.623	11.016	12.926	8.306	4.441	2.800
	Λ	Sup	16.124	29.979	47.927	40.654	19.219	7.663	3.209
		Inf	16.122	29.810	46.241	37.157	17.148	6.760	2.365
		Width	0.002	0.169	1.686	3.497	2.071	0.903	0.844
Scenario 2	β_m, β_h	Sup	16.683	35.665	65.361	62.949	35.481	17.324	8.442
		Inf	16.121	29.642	45.166	35.128	15.290	5.442	1.588
		Width	0.562	6.023	20.196	27.821	20.192	11.881	6.854
	β_m, β_h, μ_m	Sup	16.567	34.159	60.618	58.464	32.888	16.055	8.746
		Inf	16.122	29.720	45.569	35.489	15.408	5.235	0.434
		Width	0.445	4.439	15.049	22.975	17.480	10.820	8.313
	$\beta_m, \beta_h, \mu_m, \gamma_h$	Sup	17.176	34.286	59.366	55.984	30.771	14.565	7.516
		Inf	16.119	29.698	45.586	35.629	15.581	5.498	0.963
		Width	1.057	4.588	13.781	20.355	15.190	9.067	6.553
Scenario 3	Mosquito initial conditions	Sup	20.406	47.292	73.043	58.646	27.042	10.690	4.125
		Inf	15.036	24.960	40.620	35.347	16.876	6.718	2.598
		Width	5.370	22.332	32.423	23.299	10.167	3.971	1.527
	Human initial conditions	Sup	49.036	44.165	70.251	57.261	26.852	10.803	4.244
		Inf	16.118	29.626	45.794	36.658	16.846	6.635	2.551
		Width	32.918	14.538	24.457	20.604	10.005	4.168	1.693
	All initial conditions	Sup	53.435	62.252	98.763	81.077	38.464	15.589	6.171
		Inf	14.960	24.416	39.385	34.003	15.743	6.079	2.269
		Width	38.476	37.836	59.378	47.075	22.721	9.510	3.902
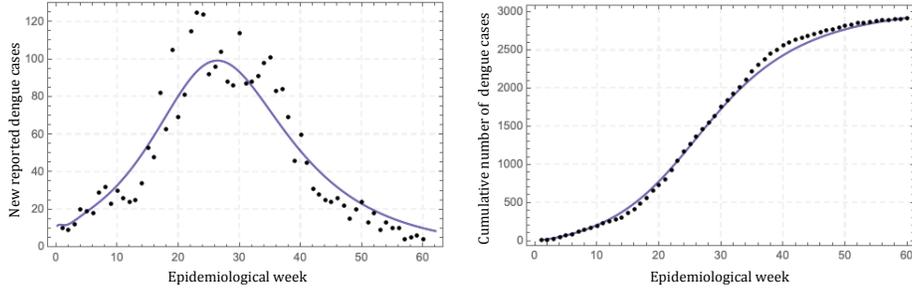
(a) Model fitted to real biological data of Itagüí
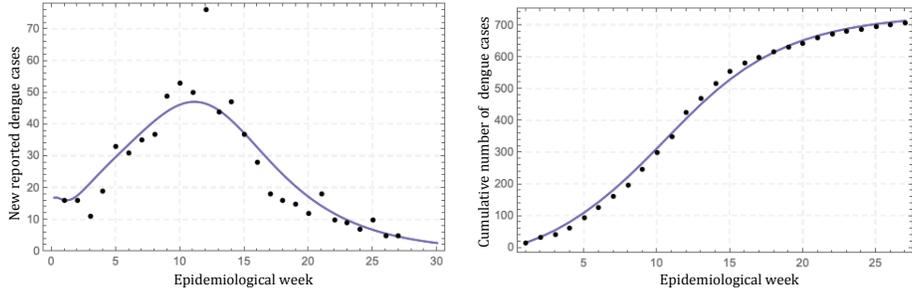
(b) Model fitted to real biological data of Neiva

Figure 1: Enclosures computed using VSPODE to solve model (6) for the number of new dengue cases per week (figures on the left) and for the cumulative number of dengue cases (figures on the right) without considering uncertainty. The black points are the reported dengue cases and the purple line is the model fit to real data: (a) Parameter and initial condition values for Itagüí: $H = 248036$, $\mu_h = 0.00023$, $\theta_m = 0.6$, $\theta_h = 1.3$, $\Lambda = 2000$, $\gamma_h = 1.75$, $\mu_m = 0.22$, $\beta_h = 2.5$, $\beta_m = 0.12$, $M_s(0) = 1800000$, $M_e(0) = 50$, $M_i(0) = 40$ $H_s(0) = 223000$, $H_e(0) = 21$, $H_i(0) = 10$ and $H_r(0) = 25005$. (b) Parameter and initial condition values for Neiva: $H = 324466$, $\mu_h = 0.00011$, $\theta_m = 0.8$, $\theta_h = 1.3$, $\Lambda = 15000$, $\gamma_h = 1.7$, $\mu_m = 0.4$, $\beta_h = 2.5$, $\beta_m = 0.14$, $M_s(0) = 3000000$, $M_e(0) = 100$, $M_i(0) = 50$ $H_s(0) = 315952$, $H_e(0) = 27$, $H_i(0) = 16$, and $H_r(0) = 8471$.
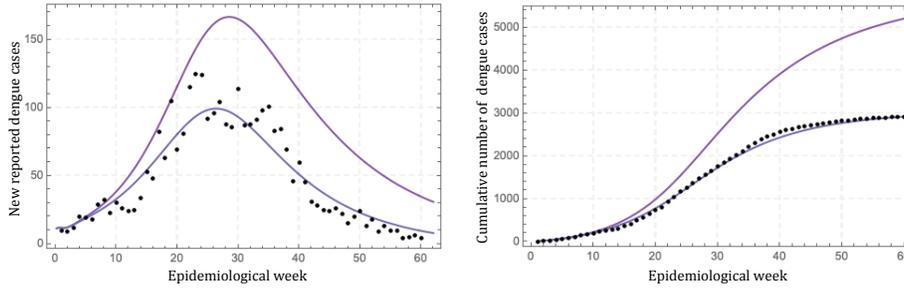
(a) Considering uncertainty in $\beta_m \in [0.12, 0.15]$
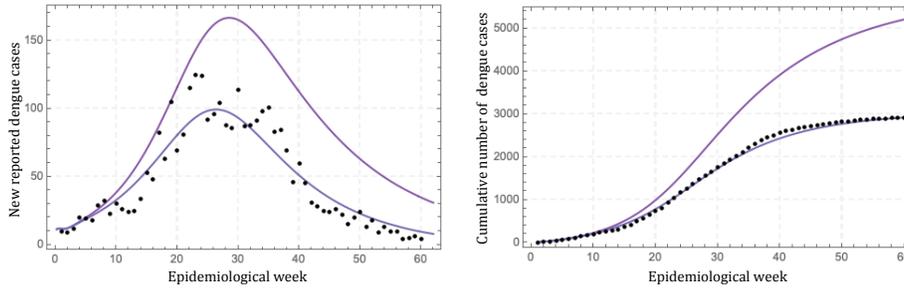
(b) Considering uncertainty in $\beta_h \in [2.5, 2.65]$
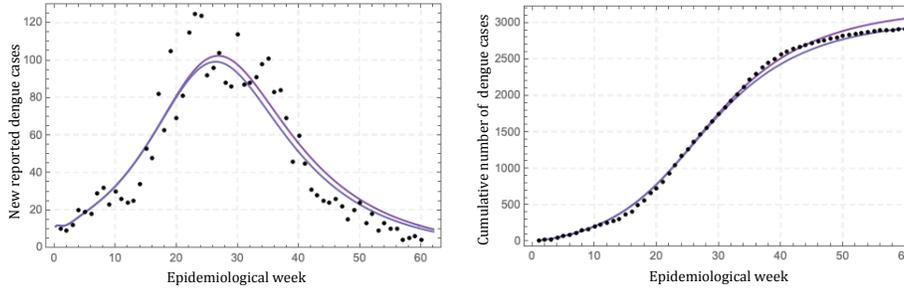
(c) Considering uncertainty in $\mu_m \in [0.217, 0.22]$

Figure 2: Enclosures computed using VSPODE to solve the system (6) for the number of new dengue cases per week (figures on the left) and for the cumulative number of dengue cases (figures on the right) considering uncertainty in different parameters for Itagüí municipality. Initial conditions values used to obtain these enclosures: $M_s(0) = 1800000$, $M_e(0) = 50$, $M_i(0) = 40$, $H_s(0) = 223000$, $H_e(0) = 21$, $H_i(0) = 10$, and $H_r(0) = 25005$. Parameter values used to obtain these enclosures: (a) $H = 248036$, $\mu_h = 0.00023$, $\theta_m = 0.6$, $\theta_h = 1.3$, $\Lambda = 2000$, $\gamma_h = 1.75$, $\mu_m = 0.22$, $\beta_h = 2.5$, and $\beta_m \in [0.12, 0.15]$. (b) $H = 248036$, $\mu_h = 0.00023$, $\theta_m = 0.6$, $\theta_h = 1.3$, $\Lambda = 2000$, $\gamma_h = 1.75$, $\mu_m = 0.22$, $\beta_m = 0.12$, and $\beta_h \in [2.5, 2.65]$. (c) $H = 248036$, $\mu_h = 0.00023$, $\theta_m = 0.6$, $\theta_h = 1.3$, $\Lambda = 2000$, $\gamma_h = 1.75$, $\beta_m = 0.12$, $\beta_h = 2.5$, and $\mu_m \in [0.217, 0.22]$.
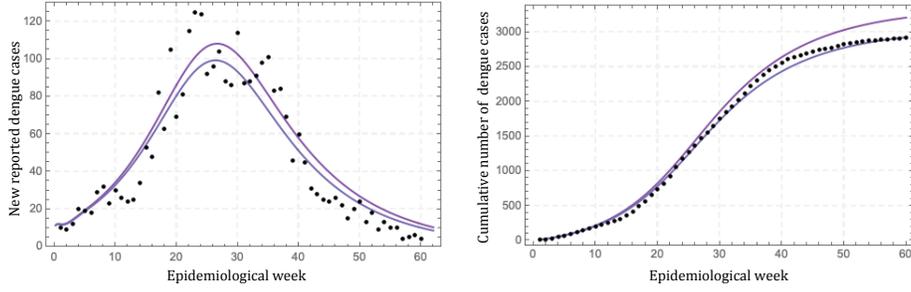
(a) Considering uncertainty in $\gamma_h \in [1.7, 1.75]$
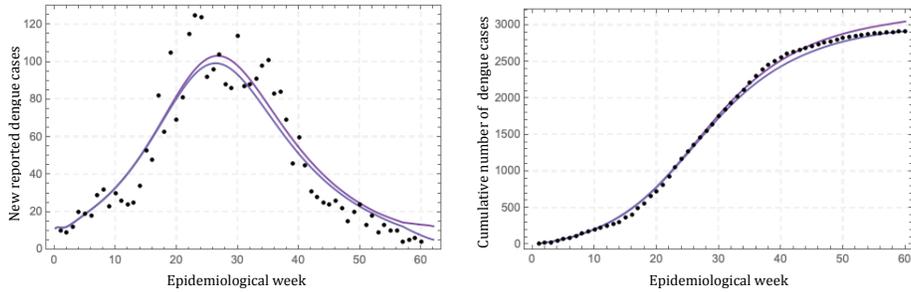
(b) Considering uncertainty in $\Lambda \in [1850, 2000]$

Figure 3: Enclosures computed using VSPODE to solve the system (6) for the number of new dengue cases per week (figures on the left) and for the cumulative number of dengue cases (figures on the right) considering uncertainty in different parameters for Itagüí municipality. Initial conditions values used to obtain these enclosures: $M_s(0) = 1800000$, $M_e(0) = 50$, $M_i(0) = 40$, $H_s(0) = 223000$, $H_e(0) = 21$, $H_i(0) = 10$, and $H_r(0) = 25005$. Parameter values used to obtain these enclosures: (a) $H = 248036$, $\mu_h = 0.00023$, $\theta_m = 0.6$, $\theta_h = 1.3$, $\mu_m = 0.22$, $\beta_m = 0.12$, $\beta_h = 2.5$, $\Lambda = 2000$, and $\gamma_h \in [1.7, 1.75]$. (b) $H = 248036$, $\mu_h = 0.00023$, $\theta_m = 0.6$, $\theta_h = 1.3$, $\mu_m = 0.22$, $\beta_m = 0.12$, $\beta_h = 2.5$, $\gamma_h = 1.75$, and $\Lambda \in [1850, 2000]$.
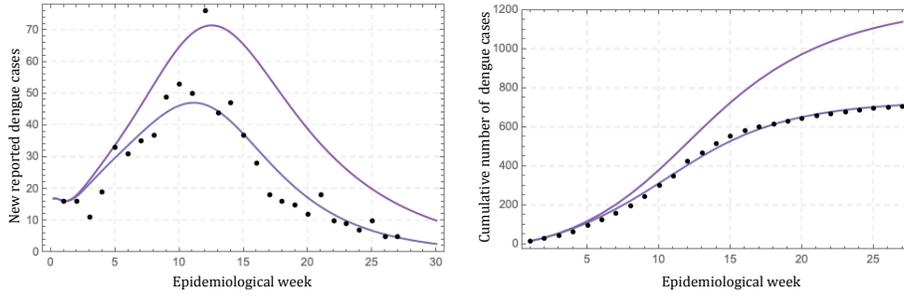
(a) Considering uncertainty in $\beta_m \in [0.14, 0.2]$.
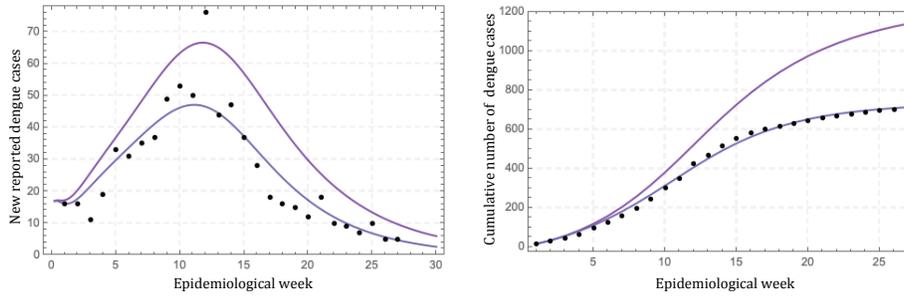
(b) Considering uncertainty in $\beta_h \in [2.5, 3.0]$.
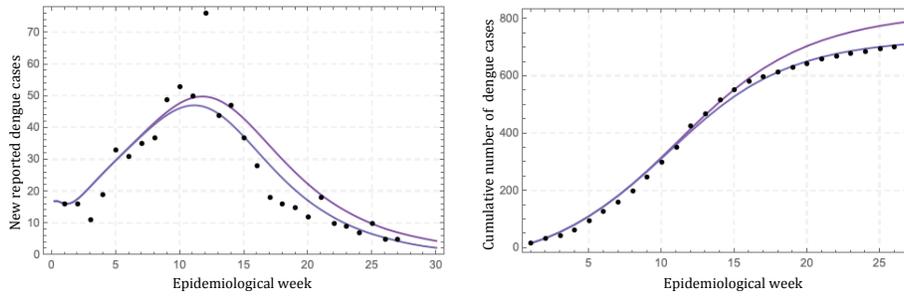
(c) Considering uncertainty in $\mu_m \in [0.38, 0.4]$.

Figure 4: Enclosures computed using VSPODE to solve the system (6) for the number of new dengue cases per week (figures on the left) and for the cumulative number of dengue cases (figures on the right) considering uncertainty in different parameters for Neiva municipality. Initial conditions values used to obtain these enclosures: $M_s(0) = 3000000$, $M_e(0) = 100$, $M_i(0) = 50$, $H_s(0) = 315952$, $H_e(0) = 27$, $H_i(0) = 16$, and $H_r(0) = 8471$. Parameter values used to obtain these enclosures: (a) $H = 324466$, $\mu_h = 0.00011$, $\theta_m = 0.8$, $\theta_h = 1.3$, $\Lambda = 15000$, $\gamma_h = 1.7$, $\mu_m = 0.4$, $\beta_h = 2.5$, and $\beta_m \in [0.14, 0.2]$. (b) $H = 324466$, $\mu_h = 0.00011$, $\theta_m = 0.8$, $\theta_h = 1.3$, $\Lambda = 15000$, $\gamma_h = 1.7$, $\mu_m = 0.4$, $\beta_m = 0.14$, and $\beta_h \in [2.5, 3.0]$. (c) $H = 324466$, $\mu_h = 0.00011$, $\theta_m = 0.8$, $\theta_h = 1.3$, $\Lambda = 15000$, $\gamma_h = 1.7$, $\beta_h = 2.5$, $\beta_m = 0.14$, and $\mu_m \in [0.38, 0.4]$.
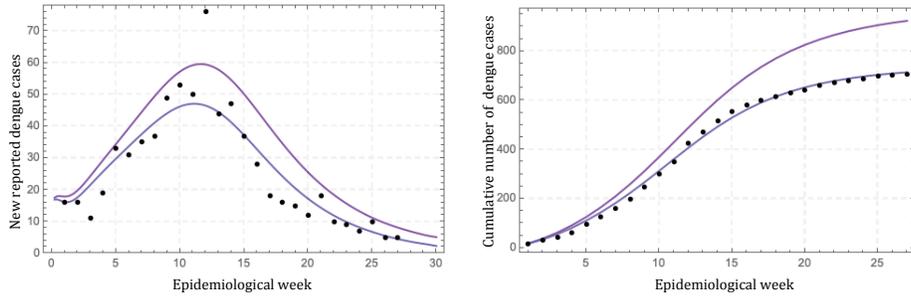
(a) Considering uncertainty in $\gamma_h \in [1.5, 1.7]$.
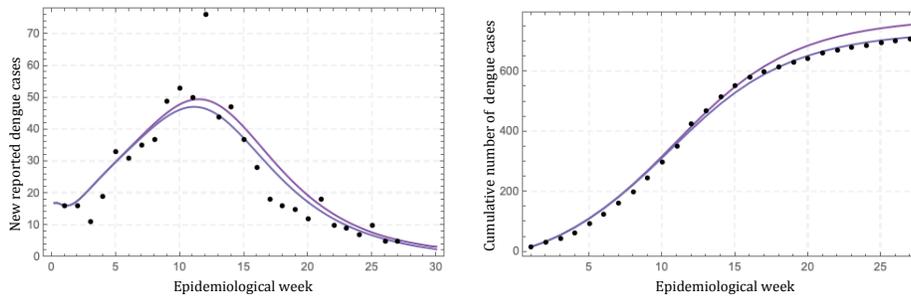
(b) Considering uncertainty in $\Lambda \in [13000, 15000]$.

Figure 5: Enclosures computed using VSPODE to solve the system (6) for the number of new dengue cases per week (figures on the left) and for the cumulative number of dengue cases (figures on the right) considering uncertainty in different parameters for Neiva municipality. Initial conditions values used to obtain these enclosures: $M_s(0) = 3000000$, $M_e(0) = 100$, $M_i(0) = 50$, $H_s(0) = 315952$, $H_e(0) = 27$, $H_i(0) = 16$, and $H_r(0) = 8471$. Parameter values used to obtain these enclosures: (a) $H = 324466$, $\mu_h = 0.00011$, $\theta_m = 0.8$, $\theta_h = 1.3$, $\mu_m = 0.4$, $\beta_h = 2.5$, $\beta_m = 0.14$, $\Lambda = 15000$, and $\gamma_h \in [1.5, 1.7]$. (b) $H = 324466$, $\mu_h = 0.00011$, $\theta_m = 0.8$, $\theta_h = 1.3$, $\mu_m = 0.4$, $\beta_h = 2.5$, $\beta_m = 0.14$, $\gamma_h = 1.7$, and $\Lambda \in [13000, 15000]$.
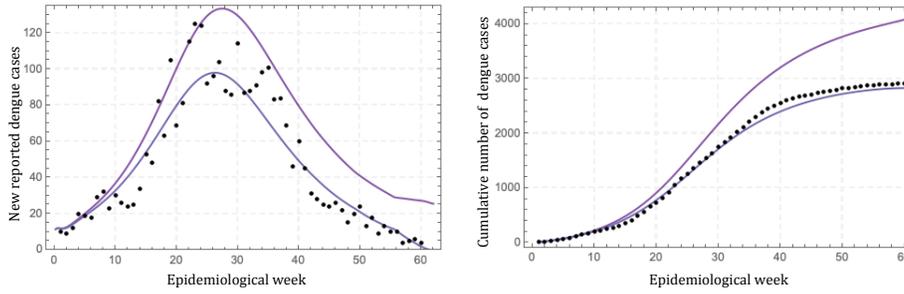
(a) Considering uncertainty in β_m and β_h.
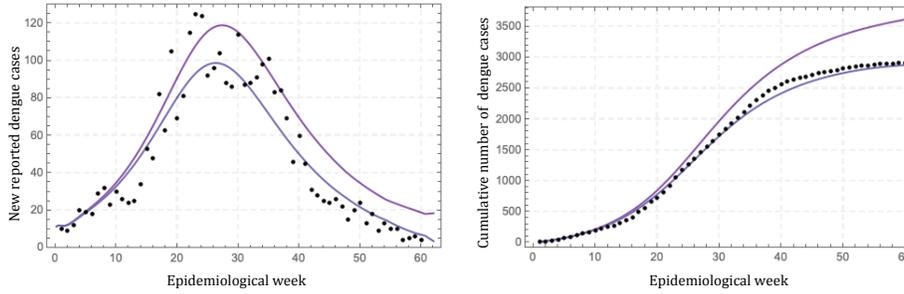
(b) Considering uncertainty in β_m, β_h, and μ_m.
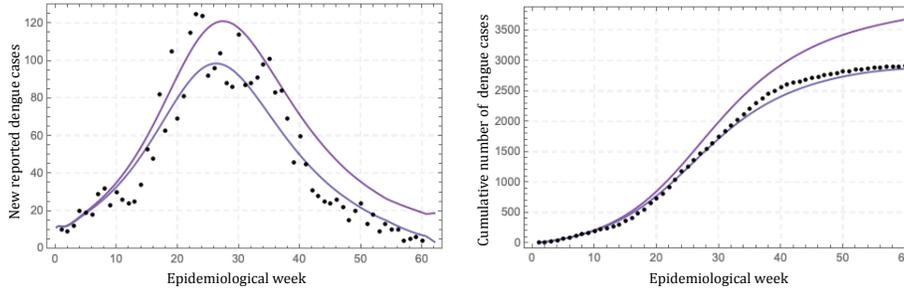
(c) Considering uncertainty in β_m, β_h, μ_m, and γ_h.

Figure 6: Enclosures computed using VSPODE to solve the system (6) for the number of new dengue cases per week (figures on the left) and for the cumulative number of dengue cases (figures on the right) considering uncertainty in different parameters for Itagüí municipality. Initial conditions values used to obtain these enclosures: $M_s(0) = 1800000$, $M_e(0) = 50$, $M_i(0) = 40$, $H_s(0) = 223000$, $H_e(0) = 21$, $H_i(0) = 10$, and $H_r(0) = 25005$. Parameter values used to obtain these enclosures: (a) $H = 248036$, $\mu_h = 0.00023$, $\theta_m = 0.6$, $\theta_h = 1.3$, $\Lambda = 2000$, $\gamma_h = 1.75$, $\mu_m = 0.22$, $\beta_m \in [0.12, 0.13]$, and $\beta_h \in [2.5, 2.6]$. (b) $H = 248036$, $\mu_h = 0.00023$, $\theta_m = 0.6$, $\theta_h = 1.3$, $\Lambda = 2000$, $\gamma_h = 1.75$, $\beta_m \in [0.12, 0.125]$, $\beta_h \in [2.5, 2.55]$, and $\mu_m \in [0.217, 0.22]$. (c) $H = 248036$, $\mu_h = 0.00023$, $\theta_m = 0.6$, $\theta_h = 1.3$, $\Lambda = 2000$, $\gamma_h = 1.75$, $\beta_m \in [0.12, 0.125]$, $\beta_h \in [2.5, 2.55]$, $\mu_m \in [0.217, 0.22]$, and $\gamma_h \in [1.74, 1.75]$.
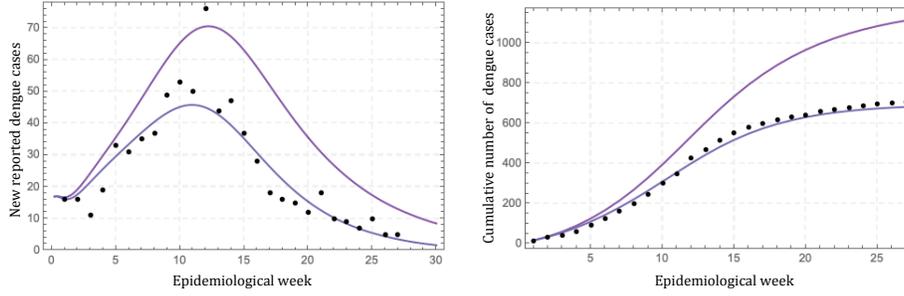
(a) Considering uncertainty in β_m, β_h.
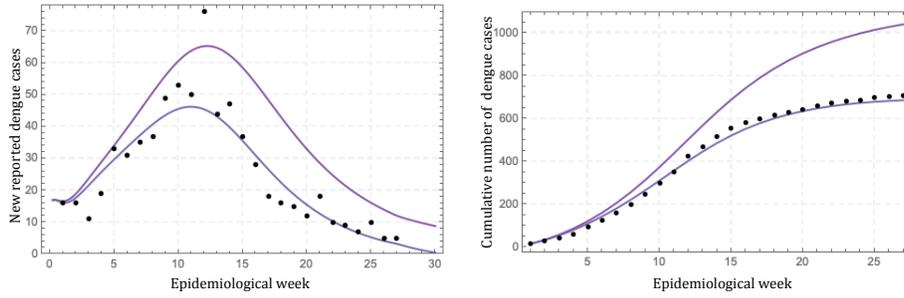
(b) Considering uncertainty in β_m, β_h and μ_m.
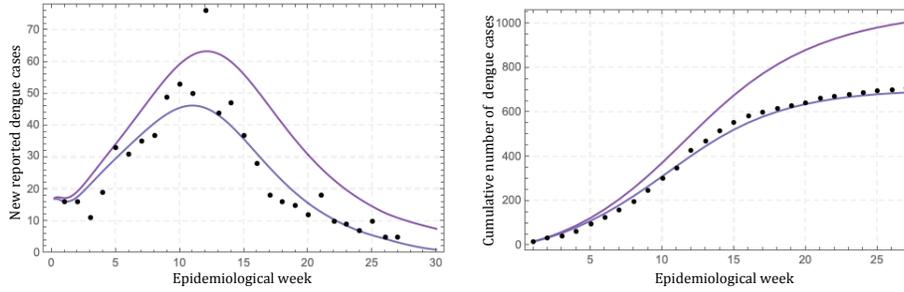
(c) Considering uncertainty in β_m, β_h, μ_m and γ_h.

Figure 7: Enclosures computed using VSPODE to solve the system (6) for the number of new dengue cases per week (figures on the left) and for the cumulative number of dengue cases (figures on the right) considering uncertainty in different parameters for Neiva municipality. Initial conditions values used to obtain these enclosures: $M_s(0) = 3000000$, $M_e(0) = 100$, $M_i(0) = 50$, $H_s(0) = 315952$, $H_e(0) = 27$, $H_i(0) = 16$, and $H_r(0) = 8471$. Parameter values used to obtain these enclosures: (a) $H = 324466$, $\mu_h = 0.00011$, $\theta_m = 0.8$, $\theta_h = 1.3$, $\Lambda = 15000$, $\gamma_h = 1.7$, $\mu_m = 0.4$, $\beta_m \in [0.14, 0.17]$, and $\beta_h \in [2.5, 2.75]$. (b) $H = 324466$, $\mu_h = 0.00011$, $\theta_m = 0.8$, $\theta_h = 1.3$, $\Lambda = 15000$, $\gamma_h = 1.7$, $\beta_m \in [0.14, 0.16]$, $\beta_h \in [2.5, 2.7]$, and $\mu_m \in [0.39, 0.4]$. (c) $H = 324466$, $\mu_h = 0.00011$, $\theta_m = 0.8$, $\theta_h = 1.3$, $\Lambda = 15000$, $\beta_m \in [0.14, 0.16]$, $\beta_h \in [2.5, 2.7]$, $\mu_m \in [0.39, 0.4]$, and $\gamma_h \in [1.6, 1.7]$.
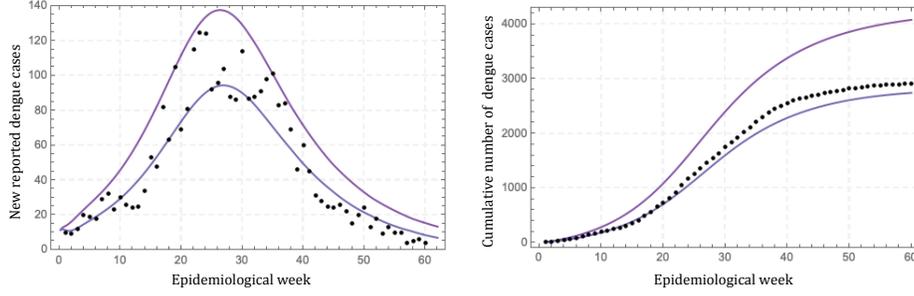
(a) Considering uncertainty in mosquito initial conditions: $M_s(0), M_e(0)$, and $M_i(0)$.
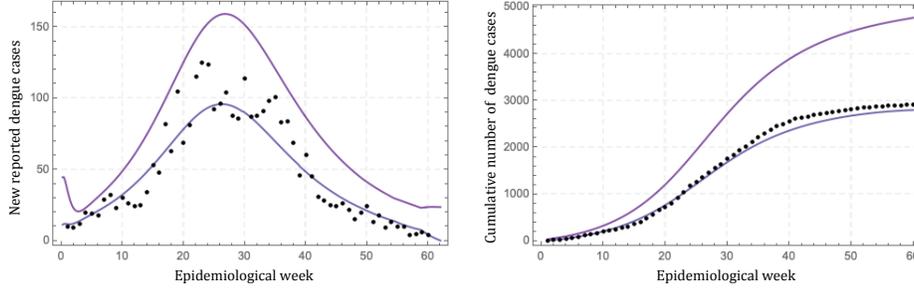
(b) Considering uncertainty in human initial conditions: $H_s(0), H_e(0), H_i(0)$ and $H_r(0)$.
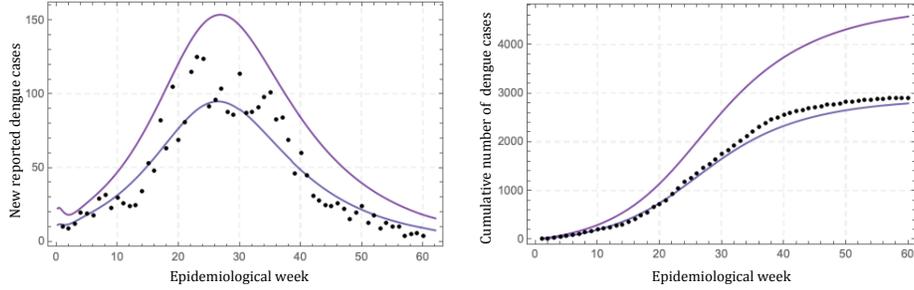
(c) Considering uncertainty in all initial conditions of model (6).

Figure 8: Enclosures computed using VSPODE to solve the system (6) for the number of new dengue cases per week (figures on the left) and for the cumulative number of dengue cases (figures on the right) considering uncertainty in different parameters for Itagüí municipality. Parameter values used to obtain these enclosures: $H = 248036$, $\mu_h = 0.00023$, $\theta_m = 0.6$, $\theta_h = 1.3$, $\Lambda = 2000$, $\gamma_h = 1.75$, $\mu_m = 0.22$, $\beta_m = 0.12$, and $\beta_h = 2.5$. Initial conditions used to obtain these enclosures: (a) $M_s(0) \in [1800000, 2000000]$, $M_e(0) \in [50, 70]$, $M_i(0) \in [40, 60]$, $H_s(0) = 223000$, $H_e(0) = 21$, $H_i(0) = 10$, and $H_r(0) = 25005$. (b) $M_s(0) = 1800000$, $M_e(0) = 50$, $M_i(0) = 40$, $H_s(0) \in [223000, 235634]$, $H_e(0) \in [21, 84]$, $H_i(0) \in [10, 40]$, and $H_r(0) \in [12340, 25005]$. (c) $M_s(0) \in [1800000, 1850000]$, $M_e(0) \in [50, 60]$, $M_i(0) \in [40, 50]$, $H_s(0) \in [223000, 235634]$, $H_e(0) \in [21, 42]$, $H_i(0) \in [10, 20]$, and $H_r(0) \in [12340, 25005]$.
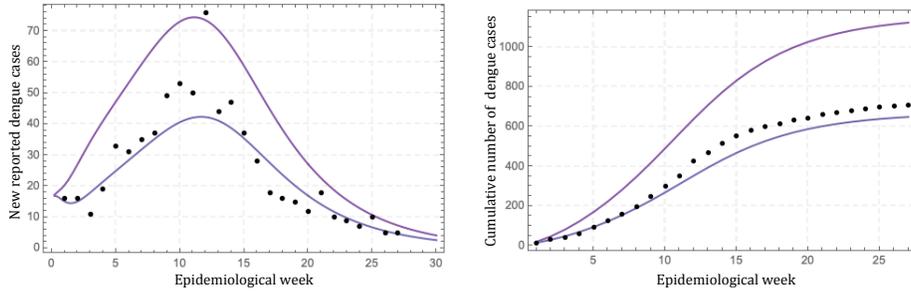
(a) Uncertainty in mosquito initial conditions.
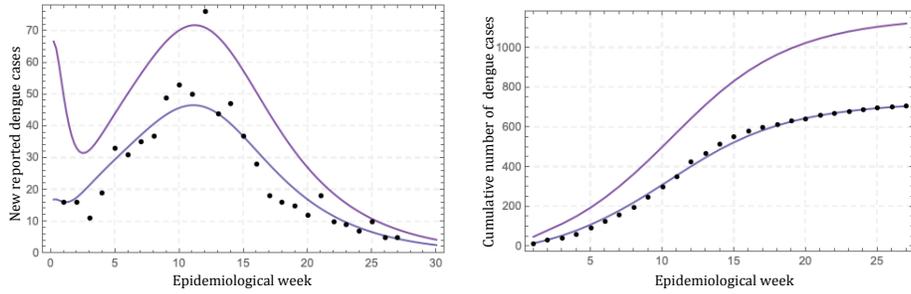
(b) Uncertainty in human initial conditions.
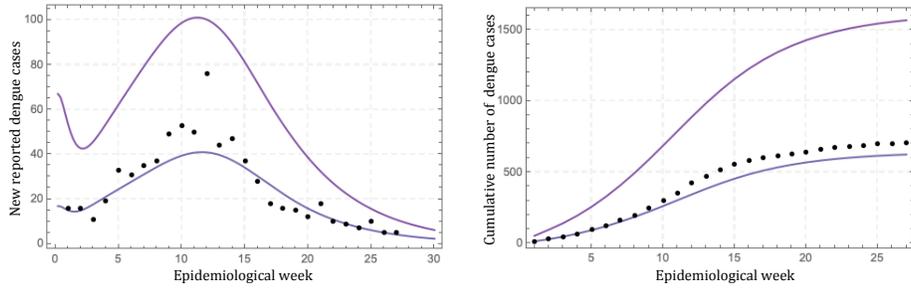
(c) Uncertainty in all initial conditions.

Figure 9: Enclosures computed using VSPODE to solve the system (6) for the number of new dengue cases per week (figures on the left) and for the cumulative number of dengue cases (figures on the right) considering uncertainty in different parameters for Neiva municipality. Parameter values used to obtain these enclosures: $H = 324466$, $\mu_h = 0.00011$, $\theta_m = 0.8$, $\theta_h = 1.3$, $\Lambda = 15000$, $\gamma_h = 1.7$, $\mu_m = 0.4$, $\beta_h = 2.5$, and $\beta_m = 0.14$. Initial conditions used to obtain these enclosures: (a) $M_s(0) \in [3000000, 3500000]$, $M_e(0) \in [100, 150]$, $M_i(0) \in [50, 100]$, $H_s(0) = 315952$, $H_e(0) = 27$, $H_i(0) = 16$, and $H_r(0) = 8471$. (b) $M_s(0) = 3000000$, $M_e(0) = 100$, $M_i(0) = 50$, $H_s(0) \in [315952, 324294]$, $H_e(0) \in [27, 108]$, $H_i(0) \in [16, 64]$, and $H_r(0) \in [0, 8471]$. (c) $M_s(0) \in [3000000, 3500000]$, $M_e(0) \in [100, 150]$, $M_i(0) \in [50, 100]$, $H_s(0) \in [315952, 324294]$, $H_e(0) \in [27, 108]$, $H_i(0) \in [16, 64]$, and $H_r(0) \in [0, 8471]$.
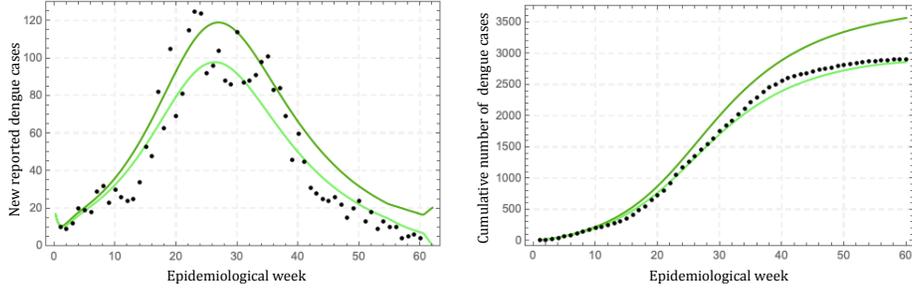
(a) Considering uncertainty in $\theta_m \in [0.58, 0.88]$.
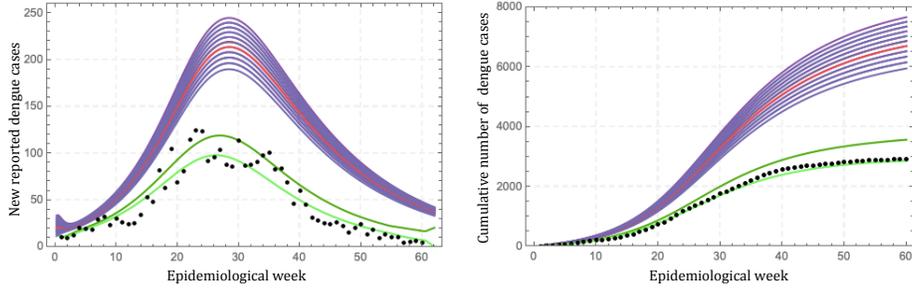
(b) Considering uncertainty in θ_m, $H_e(0)$, and $H_i(0)$.

Figure 10: Enclosures computed using VSPODE to solve the system (6) for the number of new dengue cases per week (figures on the left) and for the cumulative number of dengue cases (figures on the right) considering uncertainty in different parameters for Itagüí municipality. Parameter values used to obtain these enclosures: $H = 248036$, $\mu_h = 0.00023$, $\theta_h = 1.3$, $\Lambda = 2000$, $\gamma_h = 1.75$, $\mu_m = 0.22$, $\beta_m = 0.12$, and $\beta_h = 2.5$. Initial conditions used to obtain these enclosures: $M_s(0) = 1800000$, $M_e(0) = 50$, $M_i(0) = 40$, $H_s(0) = 223000$, and $H_r(0) = 25005$. In (a) we consider $H_e(0) = 21$, $H_i(0) = 10$ and uncertainty in $\theta_m \in [0.58, 0.88]$. In (b) we consider uncertainty in $\theta_m \in [0.58, 0.88]$, $H_e(0) \in [21, 61]$, and $H_i(0) \in [10, 30]$. The curves shown in this figure are upper and lower bounds, obtained by dividing into sub-intervals of four and two width $[21, 61]$ and $[10, 30]$ respectively, to guarantee verified solutions.
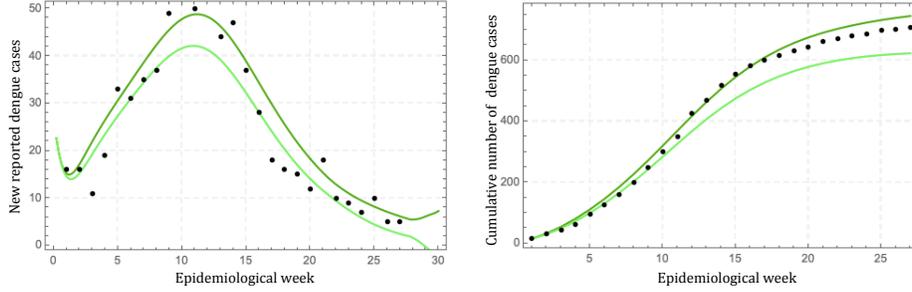
(a) Uncertainty in θ_m.
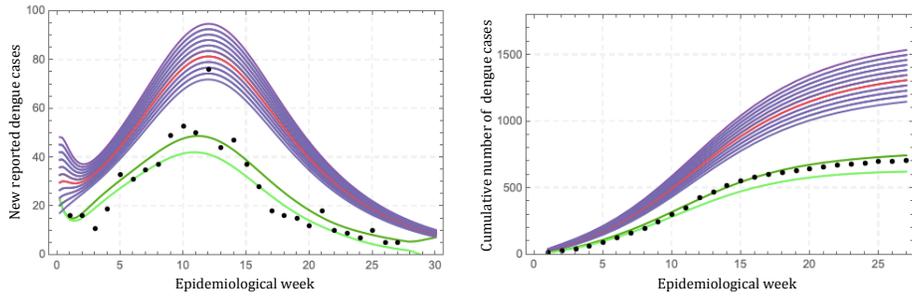
(b) Uncertainty in θ_m, $H_e(0)$, and $H_i(0)$.

Figure 11: Enclosures computed using VSPODE to solve the model (6) for the number of new dengue cases per week (figures on the left) and for the cumulative number of dengue cases (figures on the right) considering uncertainty in different parameters for Neiva municipality. Parameter values used to obtain these enclosures: $H = 324466$, $\mu_h = 0.00011$, $\theta_m = 0.8$, $\theta_h = 1.3$, $\Lambda = 15000$, $\gamma_h = 1.7$, $\mu_m = 0.4$, $\beta_h = 2.5$, and $\beta_m = 0.14$. Initial conditions used to obtain these enclosures: $M_s(0) = 3000000$, $M_e(0) = 100$, $M_i(0) = 50$ $H_s(0) = 315952$, and $H_r(0) = 8471$. In (a) we consider $He(0) = 21$, $Hi(0) = 10$ and uncertainty in $\theta_m \in [0.58, 0.88]$. In (b) we consider uncertainty in $\theta_m \in [0.58, 0.88]$, $H_e(0) \in [32, 82]$, and $H_i(0) \in [16, 49]$. The curves shown in these figures are upper and lower bounds, obtained by dividing into sub-intervals of three ($[32, 82]$) and five ($[16, 49]$) width respectively, to guarantee verified solutions.