



Research article

Using compartmental models and Particle Swarm Optimization to assess Dengue basic reproduction number R_0 for the Republic of Panama in the 1999-2022 period

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ABSTRACT

Nowadays, the ability to make data-driven decisions in public health is of utmost importance. To achieve this, it is necessary for modelers to comprehend the impact of models on the future state of healthcare systems. Compartmental models are a valuable tool for making informed epidemiological decisions, and the proper parameterization of these models is crucial for analyzing epidemiological events. This work evaluated the use of compartmental models in conjunction with Particle Swarm Optimization (PSO) to determine optimal solutions and understand the dynamics of Dengue epidemics. The focus was on calculating and evaluating the rate of case reproduction, R_0 , for the Republic of Panama. Three compartmental models were compared: Susceptible-Infected-Recovered (SIR), Susceptible-Exposed-Infected-Recovered (SEIR), and Susceptible-Infected-Recovered Human-Susceptible-Infected Vector (SIR Human-SI Vector, SIR-SI). The models were informed by demographic data and Dengue incidence in the Republic of Panama between 1999 and 2022, and the susceptible population was analyzed. The SIR, SEIR, and SIR-SI models successfully provided R_0 estimates ranging from 1.09 to 1.74. This study provides, to the best of our understanding, the first calculation of R_0 for Dengue outbreaks in the Republic of Panama.

1. Introduction

The current landscape of global events is characterized by its complexity and its interconnections, making it necessary to proactively anticipate and mitigate future challenges. In response to this, there has been a growing emphasis on approaching public health events, such as epidemic outbreaks, through a mathematical lens. Mathematical models provide a valuable tool in predicting the

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spread of diseases and determining effective strategies for intervention and control. This is supported by previous research that has shown the crucial role that mathematical models can play in understanding and addressing complex public health issues [1–8].

Dengue, a vector-borne disease, is one of the most significant health concerns globally. It is primarily transmitted by mosquitoes of the *Aedes* family [9], including *Aedes aegypti* in urban areas and *Aedes albopictus* in rural areas [10]. The elimination of mosquito breeding grounds represents the first and most effective barrier in preventing the spread of the disease. This simple yet crucial measure of primary hygiene serves as a foundation in controlling the transmission of Dengue and other vector-borne diseases [9–12]. The history of Dengue prevention and control is marked by an aggressive vector control campaign aimed at eliminating *Aedes aegypti* mosquitoes in the 1950s. However, the rise of insecticide resistance and decreased funding for vector eradication programs led to the reemergence of *Aedes* vectors and Dengue cases in the Americas.

Over the last few decades, the number of Dengue cases has risen dramatically, from 1.5 million over the 1980s to 16.2 million over the decade of 2010s, according to the World Health Organization (WHO) [13]. The prevalence of Dengue in the Americas is a persistent challenge for public health systems and individuals, with the circulation of four distinct serotypes (DENV-1, DENV-2, DENV-3, and DENV-4) [14]. In the Republic of Panama, the presence of Dengue virus has been recorded since 1993 [15]. To standardize the definitions and classifications of Dengue symptoms, the Republic of Panama has regulated its Dengue management in accordance with the WHO recommendations since 1993.

Humanity is facing the consequences of a rapid and unregulated industrial evolution, as indicated by various studies [16–18]. The accelerated anthropogenic impact on the climate, commonly referred to as climate change, has heightened the variability of various climate phenomena, a variety of climatic and environmental factors are considered in the spread and control of vector-borne diseases. With the arrival of climate change, there is a growing concern that we may see an increase in epidemic outbreaks. These scenarios, although seemingly exaggerated, represent a harsh reality that both public health systems and individuals must be prepared to face [19,20]. To meet these challenges and contribute to the global response, it is essential to have a well-coordinated and resilient approach. In this context, it has become increasingly important to analyze public health events from a mathematical point of view, with the aim of improving our understanding and ability to respond to future outbreaks.

The tropical regions, characterized by warm temperatures ranging from 20 °C to 35 °C, provide favorable conditions for the hatching of mosquito vectors of Dengue disease [21]. The high temperatures in these regions result in increased hatching rates of vector eggs. With the ongoing global warming trend [22], areas with the highest hatching rate of mosquito eggs are likely to shift, thereby requiring a shift in control efforts aimed at these vectors. In particular, the temperature shifts associated with El Niño-Southern Oscillation and La Niña can have a negative impact on the Central and South American regions, making it an important consideration in the study of vector-borne diseases and the development of effective control strategies [23]. These fluctuations in precipitation could result in a heightened number of Dengue cases during years of increased rainfall, and could also lead to Dengue outbreaks of unprecedented aggression [22,24]. Parameterizing an epidemiological model is a crucial step in understanding the spread of diseases, such as Dengue, within populations and the interactions that contribute to its transmission. This understanding is essential in developing a practical framework for measuring the severity of Dengue outbreaks and supporting decision-makers in implementing effective control strategies.

The evaluation of the dynamics of Dengue outbreaks in the Republic of Panama is a crucial step forward in the use of compartmental models for disease control, as it provides insights into the intricacies of the disease transmission process, which will aid in the formulation of evidence-based strategies to mitigate the impact of Dengue outbreaks. By accurately parameterizing an epidemiological model, decision-makers will be better equipped to respond to Dengue outbreaks in an informed and effective manner, ultimately reducing their negative impact on public health and society [23,24]. The objective of this study was to gain a thorough understanding of the dynamics of Dengue transmission in the Republic of Panama by utilizing compartmental models over the period of 1999 to 2022. Real-world data, including the population of the Republic of Panama and recorded Dengue cases from 1999 to 2022, was utilized for model parameterization. Based on these parameters, the reproductive number (R_0) was calculated, which represents the estimated number of secondary cases generated by each initial case [25,26]. Three models were compared in this study to explain the observed behavior of Dengue outbreaks: the SIR model [27], the SEIR model [28,29], and the SIR-SI model [30]. The ultimate goal of this study is to provide valuable insights into the dynamics of Dengue transmission, and support decision-makers in formulating effective control strategies to mitigate future Dengue outbreaks. The purpose of this study is to further investigate the utility of mathematical models in the analysis of public health events, specifically to measure the reproductive rate (R_0) for Dengue outbreaks.

2. Importance of R_0 estimation

The basic reproduction number R_0 or “the average number of secondary cases generated by a single infected individual in a completely susceptible population”, is crucial in the examination of the spread of infectious illnesses. Its estimation is crucial since it gives valuable insights into the communicability of the disease, the chances of an outbreak to expand, and the intensity of intervention necessary to regulate its spread.

By knowing R_0 and the susceptible population, one could predict the evolution of an epidemic, if less than one case is generated from a first infected the epidemic is extinguished. If more than one case is generated, it is important to know the value of R_0 , since from this parameter it is possible to know the speed of spread of the epidemic.

Knowing the value of R_0 has several important implications, including:

1. Understanding the transmission of the disease: R_0 provides a gauge of the transmissibility of the disease and the likelihood of an outbreak to spread, helping public health officials comprehend the underlying dynamics of disease transmission.

2. Formulating control strategies - By estimating R_0 , public health officials can determine the appropriate level of intervention needed to control the spread of the disease.
3. Assessing the impact of interventions - By monitoring changes in R_0 over time, public health officials can assess the effectiveness of various control measures and adjust their strategies as needed.
4. Forecasting the progression of an outbreak - By estimating R_0 and using epidemiological models, public health officials can make predictions about the future progression of an outbreak and prepare accordingly.

More importantly estimating R_0 is crucial to determine the intensity of intervention needed to regulate its transmission.

2.1. An R_0 for Dengue in the Republic of Panama

In the last 10 years the Republic of Panama, has seen the emergence, impact and global expansion, of vector-borne infectious diseases, such as: Chikungunya [31,32] and Zika, [33,34]. Diseases that are known to increase its prevalence and incidence due to the irruption of the environmental equilibrium, thus anthropogenic in nature [35]. For this reason, using mathematical approaches, that focus on multiple sources and their interactions, has become even more important in the context of public health.

Even though vector control, vaccines candidates and preventive health polices, can mitigate the burden of Dengue, it still is the most important vector-borne disease worldwide. In the Republic of Panama, an aggressive vector control politics almost eradicated *Aedes* and *Anopheles* mosquitoes in 1950's. Thus, for at least 30 years the report for Dengue and Malaria diseases, only accounted for imported cases. This was true, until the resurgence of *Aedes* vectors and Dengue diseases outbreaks in 1985 and 1993, respectively [15].

Despite the fact that Dengue is endemic in Panama since 1993, there is no information about the real prevalence of the diseases in the country. The circulation of Zika and Punta Toro viruses, which antibody's cross reaction and has similar clinical presentation respectively to Dengue, could overshadow the real Dengue incidence in the country [33,36]. More important is to recognize that, none of the endemic (seasonal and regional) diseases before discussed, have an estimated R_0 for Panama. Thus the importance of this effort to gather 20+ years of Dengue incidence data, and to able to make the first estimate for the country.

3. Experimental methods

The experimental method section is organized as follows, first it starts with a brief summary of the parameterization process. The origin and format of the data used are then introduced. The models under examination, such as the SIR, SEIR, and SIR-SI, are then described in detail. This includes their parameters, underlying assumptions, and the calculation of R_0 . Finally, the optimization method applied to determine the optimal model parameters is explained. This includes the definition of the objective function, which combines the data and model results, and the criteria for the parameter search range.

Parameterizing a compartmental model to get an estimate of R_0 usually involves the following steps:

1. Collect data on the number of cases over time. This data may include the number of new cases, the number of cases accumulated and the number of deaths.
2. Determine the initial values of the model's parameters, such as the proportion of the population that is susceptible, infected, and recovered.
3. Use mathematical optimization techniques, to find the set of parameter values that best fit the data.
4. Use the parameterize model to estimate R_0 .
5. Compare the results with the observed data to check the validity of the model.

The process of parameterizing epidemic models is crucial in gaining insights into the dynamics of disease transmission. This includes determining the proportion of the population that is susceptible to infection, the rate at which susceptible individuals become infected, and the time required for recovery. These parameters are typically are taken from real epidemic data.

3.1. Data set

The quality and composition of data sets are paramount in epidemiological modeling, as they serve as the basis for accurate disease spread predictions. The utilization of robust and comprehensive data sets is crucial in ensuring the validity of the models and the subsequent effectiveness of disease control strategies derived from them.

As it is shown in Fig. 1, the dengue incidence for the Republic of Panama was analyzed in the 1999-2022 period. It can be noticed that there outbreak years with its incidence being prominent and shaded in green. These peaks found in this period could be of three types: outbreak in the whole year, outbreak in the first semester of the year (named *a*) and outbreak in the second semester of the year (named *b*). In this manner, outbreak can be found for the years: 1999, 2001-2002, 2005-2006*a*, 2006*b*-2007*a*, 2007*b*-2008*a*, 2008*b*-2009*a*, 2009*b*-2010*a*, 2010*b*, 2011-2012*a*, 2012*b*-2013*a*, 2013*b*-2014*a*, 2014*b*-2015*a*, 2015*b*-2016*a*, 2016*b*-2017*a*, 2017*b*-2018*a*, 2018*b*-2019*a*, 2019*b*-2020, 2021, 2022.

The data set employed in this study was collected by the Gorgas Memorial Institute for Health Studies (ICGES), the Ministry of Health (MINSAs), and the Pan American Health Organization (PAHO) of the WHO.

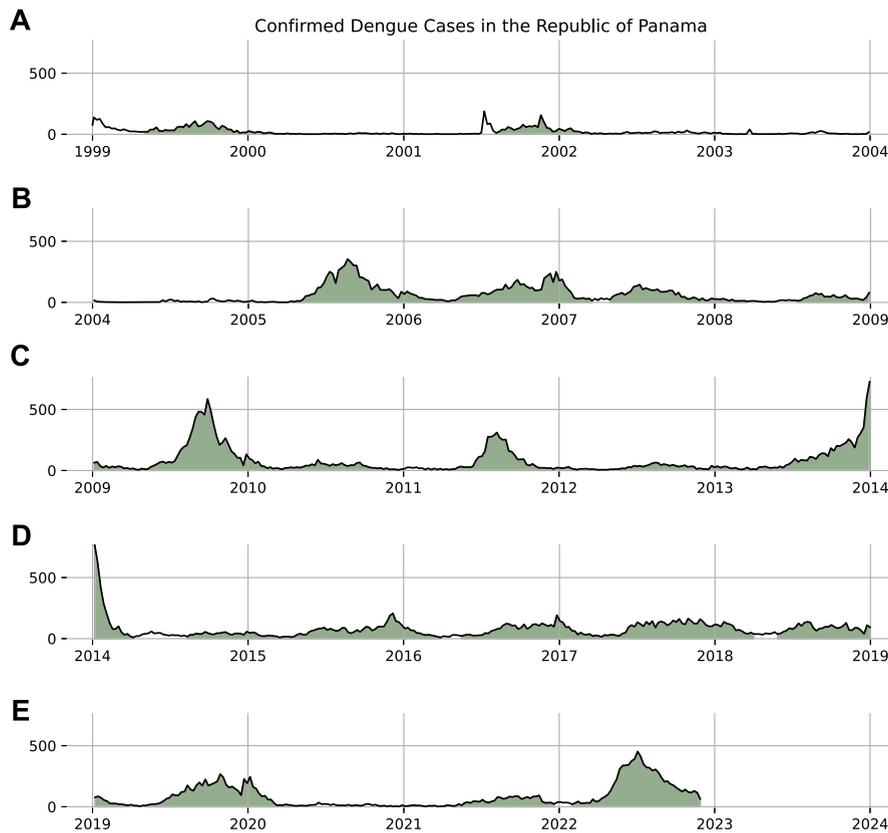


Fig. 1. Confirmed Dengue Cases. The Incidence of Confirmed Cases of Dengue in the Republic of Panama spanning from 1999 to 2022, divided into periods of 5 years: 1999-2004 (A), 2004-2009 (B), 2009-2014 (C), 2014-2019 (D) and 2019-2022 (E).

Dengue cases were grouped by epidemiological week and were represented as a time series of 24 years (1999-2022). It is important to note that this period has been well studied, with publications focusing on molecular aspects of the serotypes, studying the demographic groups it affects via statistical analysis and finally the relationship with incidence and climate variables [15,24]. The data set used in this study is similar to that used in these publications before mentioned, which is taking into account cases of Dengue confirmed by laboratory and with a known epidemiological link.

The parameterization was carried out in the intervals corresponding to Dengue outbreaks mentioned before, which are characterized by an abrupt increase in Dengue cases after a period with a low incidence of cases.

The demographic data was obtained from the National Institute of Statistics (INEC). The estimated population of the Republic of Panama during the study period (1999-2021) was obtained from the open data portal on the INEC website, while the population for 2022 was predicted based on previous data [37–40].

3.2. Compartmental models

Epidemiology plays a crucial role in understanding the spread and control of diseases, particularly in the context of pandemics. One of the most effective ways to study the spread of diseases is through mathematical models. In this field, several models have been developed, each with a specific focus on different aspects of disease transmission and control. These models provide a theoretical framework to understand the underlying mechanisms of disease spread, and to guide decision-making in the control and prevention of pandemics.

The use of systems of differential equations plays a crucial role in modeling the dynamics of various situations, including the study of pandemics such as COVID-19 [41] and the impact of deforestation on wildlife [42].

Investigative efforts in vector-borne pandemics have leveraged ordinary differential equations (ODEs) as a valuable tool to guide the development of effective control strategies. The SIR and SIR-SI models, for instance, have been widely employed to determine optimal vaccination schedules and assess the efficacy of various control methods, as demonstrated in several recent studies [43–45].

The utilization of SIR and SIR-SI models in epidemiology has been extensively studied, with a focus on the impact of incorporating periodic components in disease transmission models. Research has compared the advantages and disadvantages of incorporating such components, which can help to accurately capture the seasonal fluctuations in disease transmission [46,47].

The consideration of periodic components in models is crucial as it helps to better predict the spread of diseases, particularly those with seasonal patterns such as vector-borne diseases. This information can then inform the development of effective control and intervention strategies to prevent outbreaks and minimize the impact of pandemics.

In this study, the focus is placed on three models that have been widely used in epidemiology: the SIR, SEIR, and SIR-SI models. These models have been utilized to provide valuable insights into the dynamics of disease transmission, and to evaluate the effectiveness of various control and prevention strategies.

The SIR model considers the flow of individuals between susceptible, infected, and recovered compartments. The SEIR model extends the SIR model to account for the incubation period between exposure to the disease and symptom onset. Finally, the SIR-SI model extends the SIR model to account for additional sources of infection, such as the mosquito vector.

3.2.1. Model assumptions

The SIR, SEIR, and SIR-SI models might seem similar, but they differ in their complexity. Each additional compartment added to a model increases the number of equations that it represents, enabling the model to fit better increasingly complex data. Hence, a model with more compartments is anticipated to provide a superior fit to the data. These compartments models play a crucial role in capturing the dynamics of the spread of the disease in a population.

It should be noted that both presented models have assumptions in order to simplify the number of compartments and the number of equations, as well as the amount of data needed to make the model. These assumptions include, but are not limited to:

- Population is assumed to be homogeneous in terms of susceptibility, transmission and recovery.
- Individuals are equally likely to mix with one another, regardless of their Dengue serotype.
- Transmission rate is assumed to be constant over the course of the outbreaks.
- Once an individual recovers from the disease, they develop immunity to it.
- Constant efforts to control Dengue spread impact the susceptible population.

Assumptions play a crucial role in epidemiology models as they provide a foundation for forecasting the spread of diseases. These assumptions, when correctly interpreted, can provide valuable insights into the behavior of the disease and inform decision-making for disease control measures.

However, it is important to be aware of the limitations of assumptions and to critically evaluate their validity in the context of a specific outbreak. A thorough understanding of the assumptions used in a model and how they impact the predictions is essential for the effective interpretation and use of epidemiology models in disease control and prevention.

These assumptions are important for building accurate and realistic models of Dengue transmission, but they are also limitations, and it is important to be aware of these limitations when interpreting model results. To solve the system of differential equations, 4th-order Runge-Kutta method (RK-4) [48–50], with a step size (or integration time step) of $h = 0.01$, representing time in weeks, was used.

3.2.2. SIR

The SIR model was originally formulated by Kermack et al. [5], later introduced, with a small aggregate representing the Demographic Data of Birth and Removal people [27].

In all the models used in this study, there are three compartments representing populations, which are the susceptible (S), infected (I), and recovered (R) compartments. The susceptible compartment represents the population that is susceptible to the disease. The infected compartment represents the population that is infected at a rate βI . The recovered compartment represents the population that has recovered from the disease at a rate γ .

Additionally, people are added to the susceptible compartment at a birth rate αN , and people are removed from all compartments at a mortality rate μ , where N represents the population at any time.

The differential equations of this model can be seen in Equation (1).

$$\begin{aligned}\frac{dS}{dt} &= \alpha N - \frac{\beta SI}{N} - \mu S \\ \frac{dI}{dt} &= \frac{\beta SI}{N} - (\gamma + \mu) I \\ \frac{dR}{dt} &= \gamma I - \mu R\end{aligned}\tag{1}$$

The SIR model, representation shown in Fig. 2, is a theoretical framework that is used to describe the spread of infectious diseases within a population. The model tracks the number of individuals in each compartment over time and seeks to explain the dynamics of disease transmission based on the movement of individuals between compartments. In order to solve the SIR model, initial conditions must be introduced. The main objective of the SIR model is to understand the spread of disease by accounting for the velocity at which individuals move through the different compartments.

3.2.3. SEIR

The SEIR model is a modified version of the SIR model that includes a compartment to represent individuals who have been infected with the disease, but have not yet become infectious. This compartment, referred to as “exposed” (E), represents individuals

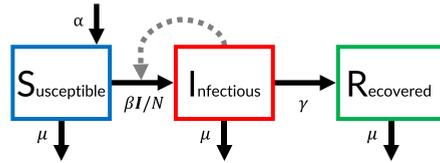


Fig. 2. SIR Model. Representation of compartments and input-output ratios of each compartment.

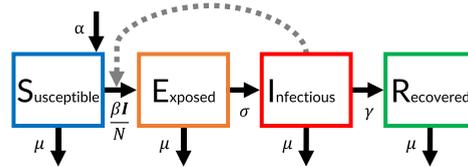


Fig. 3. SEIR Model. Representation of compartments and input-output ratios of each compartment.

who have been exposed to the virus, but have not yet developed symptoms or become contagious. This model is a local adaptation from the model presented by Yang et al. in [28].

The incubation rate, denoted by $\frac{1}{\sigma}$, reflects the length of the incubation period, the time between exposure and the onset of symptoms. By incorporating the exposed compartment, the SEIR model provides a more comprehensive understanding of the dynamics of disease transmission.

Equation (2) represents the mathematical formulation of the SEIR model.

$$\begin{aligned} \frac{dS}{dt} &= \alpha N - \frac{\beta SI}{N} - \mu S \\ \frac{dE}{dt} &= \frac{\beta SI}{N} - (\sigma + \mu) E \\ \frac{dI}{dt} &= \sigma E - (\gamma + \mu) I \\ \frac{dR}{dt} &= \gamma I - \mu R \end{aligned} \tag{2}$$

The SEIR model, representation shown in Fig. 3, considers the progression of individuals through different stages of a disease, beginning with exposure and ending with recovery or death. The model differentiates between individuals who have been exposed to the virus but have not yet developed symptoms (E), individuals who are infected and can spread the disease to others (I), and individuals who have recovered from the disease (R).

In the SEIR model, after contact with an infected individual, individuals progress from the susceptible compartment to the exposure compartment, where they remain for an incubation period before moving on to the infected compartment. This progression represents the host's response to a new virus, and the model provides insight into the spread of infectious diseases within a population.

3.2.4. SIR(h) - SI(v)

The third model employed in this study is the two-tier host-vector model SIR(h)-SI(v), which represents the interactions between the mosquito vector and the human host in Dengue epidemics. This model considers the dynamics of the spread of the Dengue virus between the human host and the mosquito vector, allowing for a more comprehensive understanding of the dynamics of the disease transmission process. This model is a local adaptation from the model presented by Nishura et al. in [29].

The differential equations of this model can be seen in Equation (3).

$$\begin{aligned} \frac{dS_h}{dt} &= \alpha_h N - \frac{C_{vh} I_v}{N_h} S_h - \mu_h S_h \\ \frac{dI_h}{dt} &= \frac{C_{vh} I_v}{N_h} S_h - (\gamma_h + \mu_h) I_h \\ \frac{dR_h}{dt} &= \gamma_h I_h - \mu_h R_h \\ \frac{dS_v}{dt} &= A_v - \frac{C_{hv} I_h}{N_h} S_v - \mu_v S_v \\ \frac{dI_v}{dt} &= \frac{C_{hv} I_h}{N_h} S_v - \mu_v I_v \end{aligned} \tag{3}$$

The SIR-SI model, representation shown in Fig. 4 captures complex interactions between host and vector and offers a more complete understanding of Dengue fever transmission dynamics. It considers both host and vector factors, providing a deeper insight into the virus, vector and host interplay.

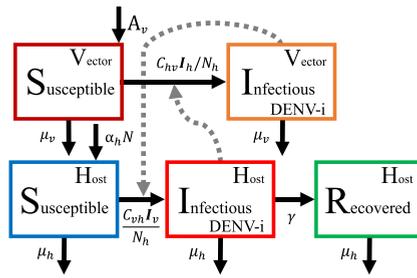


Fig. 4. SIR(h) - SI(v) Model. Representation of compartments and input-output ratios of each compartment in the SIR(h) - SI(v) model.

This model includes the interaction between mosquitoes and human hosts, both at the host and vector levels. Key parameters include: the likelihood of infection from mosquitoes to humans (p_{vh}), the likelihood of infection from humans to mosquitoes (p_{hv}), and the ratio of mosquito bites per unit time (b_i). These parameters are combined to create the host-vector ratios ($C_{hv} = p_{hv} * b_i$) and vector-host ratios ($C_{vh} = p_{vh} * b_i$), and take into account the demographics of both mosquito vectors and human hosts.

3.2.5. R_0 and the Next-Generation-Matrix Method

One of the ways that R_0 is determined is via the Next Generation Matrix Method (NGM), developed by Diekmann et al. [51–53]. The NGM technique involves constructing two matrices, the *Transmission* $F_i(x)$ and the *Transition* $V_i(x)$, consider *transmission* to the positive ratio that introduces new infected individuals and *transition* to the negative ratio that move individuals from infected states (other than susceptible and recovered).

Equation (4) provides a mathematical representation of the two matrices needed to calculate the NGM model. See Appendix A for the complete derivation procedure.

$$\begin{aligned}
 T &= J (F(x)_{@disease-free-point}) \\
 \Sigma &= J (V(x)_{@disease-free-point})
 \end{aligned}
 \tag{4}$$

Once the matrices T and Σ are obtained, next, the product of $-T \times \Sigma^{-1}$ is calculated and later their eigenvalues. The predominant eigenvalue (largest absolute value of its eigenvalues) or the spectral radius is the basic reproduction number R_0 .

In our case, each model used has a slightly different expression for R_0 but encapsulates the same meaning, compare the speed of add and remove individuals between the infected compartments.

For the SIR Model, it is calculated via Equation (5):

$$R_0 = \frac{\alpha\beta}{\mu(\gamma + \mu)}
 \tag{5}$$

For the SEIR Model, it is calculated via Equation (6):

$$R_0 = \frac{\alpha\beta\sigma}{\mu(\gamma + \mu)(\sigma + \mu)}
 \tag{6}$$

For the SIR-SI Model, it is calculated via Equation (7):

$$R_0 = \sqrt{\frac{C_{hv}C_{vh}}{\mu_v(\gamma_h + \mu_h)} \frac{N_v}{N_h}}
 \tag{7}$$

After introducing the models used and the relevant expressions in this study, the following explanation is provided for determining the parameters of a system of differential equations using the PSO meta-heuristics method.

3.3. Particle Swarm Optimization meta-heuristics

PSO is a computational method for solving optimization problems, utilizing a meta-heuristic approach inspired by the collective behavior of swarms in nature such as hives, flocks, or schools of fish. It was first introduced by Kennedy and Eberhart in 1995 [54].

In PSO, particles or agents represent the coordinates of different points in the solution space at each iteration. Guided by their own best evaluations and the global best, they navigate the search space.

This algorithm has the potential to explore the entire function surface and find either a local or global solution, depending on the configuration and computational resources available.

When searching for a solution to a system of equations, it is crucial to have a structured method for solving the problem. There are various types of problems, such as scheduling problems, space allocation problems, clustering problems, classification problems, and in our case, we can define our problem as a standard weighted least-squares optimization problem.

In this problem, the algorithm searches for the best parameters that fit the in-silico simulation with real data. Each type of problem has a preferred method of solution, and multiple methods can be used to solve the same problem. For example, the standard weighted least-squares optimization problem can be solved using PSO [55] or genetic algorithms [56].

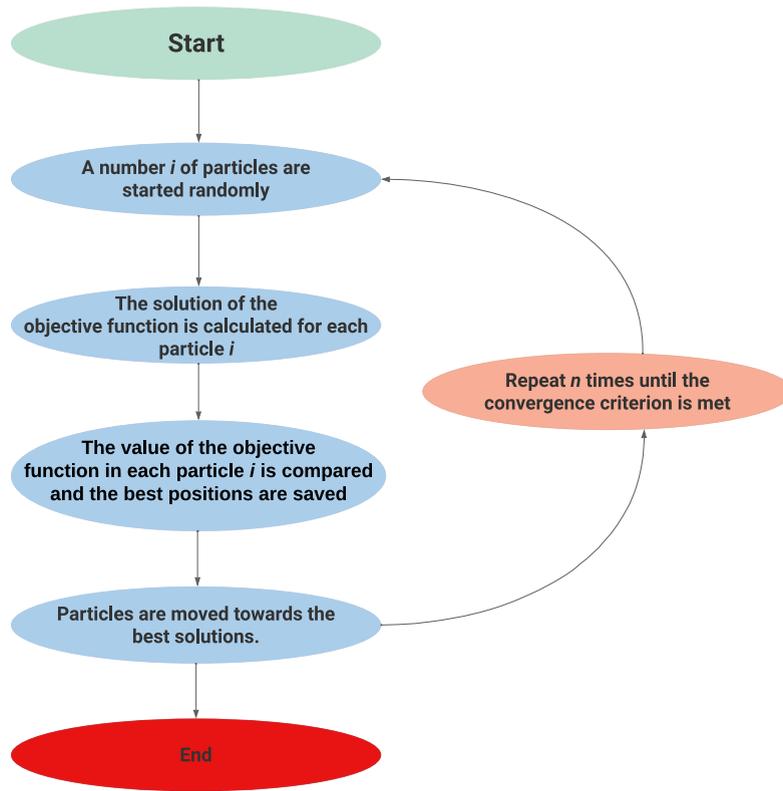


Fig. 5. PSO Algorithm. Diagrammatic representation of the PSO Meta-Heuristic method.

In our case an optimal solution, will be one that best fits a system of differential equations (SIR, SEIR and SIR-SI models) to a set of demographic data, Dengue data and subject to initial conditions. It is considered a solution when the parameters that best describe the spread of a disease in a population are determined, thus providing valuable information on the spread of the disease and assisting in decision making for the control measure.

In general, a swarm can be defined as shown in the following Equation (8):

$$\text{Swarm} = \{x_1, x_2, \dots, x_i | x_i \in (I_1, I_2, \dots, I_n)\} \tag{8}$$

where, particles x_i that compose the swarm, take values within the range defined by the limits I_1, I_2, \dots, I_n , particles move in search of solution parameters that minimize the objective function (OF). The initial distribution of particles is usually random over the solution space, but depending on the requirements of the model, an ordered initial distribution can sometimes yield better results.

The OF is first resolved for each particle, then the solutions are compared and the best ones are identified as a guide for the swarm. The process is repeated until the convergence criteria are met. Fig. 5 provides a diagrammatic representation of the functioning of the Particle Swarm Optimization (PSO) method.

Once the best solutions have been found, the particles move towards them. The velocity vector for each particle is calculated using the equation (9) that updates the speed of the swarm. The velocity vector includes three components: an inertia component c_0 that maintains the forward movement of the particles, a learning component c_1 with a random contribution r_i^1 that moves the particle towards its personal best position x_i^{pbest} , and a global learning component c_2 with its corresponding random contribution r_i^2 that moves the particle towards the best solution found by the entire swarm x^{gbest} .

$$v_i(t+1) = c_0 v_i(t) + c_1 r_i^1 (x_i^{pbest} - x_i(t)) + c_2 r_i^2 (x^{gbest} - x_i(t)) \tag{9}$$

When all the velocities at which the particles move have been calculated, the next step is to move the swarm. This happens by updating the position of each particle by adding its respective velocity using the following equation (10).

$$x_i(t+1) = x_i(t) + v_i(t+1) \tag{10}$$

In our case, this meta-heuristic method will be used to fit and optimize the parameters for each compartmental model. It allows the exploration of the entire solution surface space of the objective function (OF) within a given search interval. Finally, providing a local solution or even a global solution to the problem of adjusting an epidemiological model to real data.

Table 1
Range for parameter search: The parameters employed in the SIR, SEIR, and SIR-SI models, along with the intervals for their search.

Parameters	Meaning	Interval	Units
α	Birth rate	$[\frac{7}{29,200}, \frac{7}{27,375}]$	$week^{-1}$
β	Infectious rate	$[\frac{7}{28}, \frac{7}{4}]$	$week^{-1}$
C_{hv}	Host-vector infectious rate	[0, 2]	$week^{-1}$
C_{vh}	Vector-host infectious rate	[0, 2]	$week^{-1}$
γ	Recovery rate	$[\frac{7}{28}, \frac{7}{4}]$	$week^{-1}$
σ	Latent rate	$[\frac{7}{28}, \frac{7}{4}]$	$week^{-1}$
μ	Removal rate	$[\frac{7}{29,200}, \frac{7}{23,725}]$	$week^{-1}$
μ_v	Removal vector rate	$[\frac{7}{15}, \frac{7}{13}]$	$week^{-1}$

The Particle Swarm Optimization was carried out using the PySwarms package for Python [57] and accelerated using the CuPy package [58].

3.3.1. Objective function

The iterative method operated by resolving a system where the number of unknowns exceeded the number of variables, typically through a process of trial and error. Each iterative method had an adjustment equation or objective that was refined in each iteration round. This equation was commonly referred to as the objective function, which evaluated the solution at each epoch and the meta-heuristic searched across the search interval to find the best fit.

The goal was to fit a model to a set of Dengue epidemic data in order to estimate the evolution of outbreaks. To achieve this, the accumulated percentage difference between the *in-silico* results and real data was calculated, as well as the difference between the total simulated cases and actual cases. These metrics guided the search for the optimal parameters.

The objective function, shown in equation (11), was calculated based on the percentage difference between the predicted weekly cases from the simulation and the actual cases, as well as the percentage difference between the total simulated recoveries and the actual recoveries.

$$OF = \frac{1}{n} \sum_{i=1}^n \frac{|I_i^{in-silico} - I_i^{real}|}{|I_i^{real}|} + \frac{|R^{in-silico} - R^{real}|}{|R^{real}|} \tag{11}$$

3.3.2. Search interval

Determining the parameters to use was the central focus of the optimization algorithm. Its purpose was to calibrate the models to the given data, specifically to adjust epidemiological data to compartmental models in order to determine the reproductive rate of secondary cases at the onset of each annual outbreak. To facilitate the search, search intervals for each parameter were defined and listed in Table 1.

The interval for the demographic parameters was derived from the average life expectancy in Panama [59], while the average duration of the disease was estimated to be 21 days [15]. The average removal rate for vector was taken from previous studies in Panama [60].

3.4. Hardware specifications

All models were calculated using a Desktop PC with a Intel 11th Processor, 64 GB RAM and accelerated via GPU using an NVIDIA Ampere card.

4. Results

The accumulation of Dengue cases was documented over a period of 24 years, starting from 1999 to 2022, and was organized according to the epidemiological week. The yearly population data and the number of Dengue cases were carefully collected and recorded. Subsequently, the epidemic outbreaks were analyzed and classified with the objective of determining the reproductive number R_0 and the susceptible population.

The susceptible segment of the population represented areas where the epidemic control measures failed to achieve the desired outcomes. It signified the fraction of the effective population that was vulnerable to Dengue infection. For each outbreak, the reproductive rate and the size of the effective susceptible population were calculated. The estimation of these parameters was performed through the utilization of the PSO algorithm in 100 simulation runs.

The results of these simulations were used to derive the lower and upper confidence intervals, which are listed in Table 2, with the first row providing the value for the SIR model, the second row provides the value for the SEIR model and the third and last one provides the estimate for the SIR-SI mode. It should be noted that the PSO algorithm was applied to minimize the OF, and 100,000 particles were utilized over a span of 50 iteration epochs in each simulation run.

Table 2
 R_0 and susceptible population, for each model and for each outbreak (based on 100 simulation runs).

Year	Population	Confirmed Dengue Cases	Estimated R_0	Susceptible Population
				SIR SEIR SIR-SI
1999	2,980,355	1,928	1.20 ± 0.05	6,399 ± 23
			1.44 ± 0.11	3,519 ± 502
			1.29 ± 0.015	2,859 ± 35
2001-2002	3,040,701	1,482	1.28 ± 0.04	4,031 ± 41
			1.31 ± 0.03	3,230 ± 61
			1.28 ± 0.027	2,123 ± 44
2005-2006a	3,102,268	6,117	1.37 ± 0.05	15,115 ± 1063
			1.40 ± 0.09	12,472 ± 3691
			1.31 ± 0.015	9,550 ± 225
2006a-2007a	3,164,354	4,782	1.18 ± 0.05	16,008 ± 234
			1.21 ± 0.03	12,776 ± 481
			1.20 ± 0.008	8,012 ± 123
2007b-2008a	3,226,535	2,704	1.27 ± 0.05	7,674 ± 106
			1.26 ± 0.03	6,487 ± 199
			1.17 ± 0.023	5,432 ± 135
2008b-2009a	3,288,733	1,561	1.18 ± 0.04	6,753 ± 197
			1.16 ± 0.02	5,944 ± 237
			1.09 ± 0.014	4,344 ± 386
2009b-2010a	3,351,007	7,551	1.28 ± 0.04	19,785 ± 177
			1.74 ± 0.25	11,074 ± 1,980
			1.40 ± 0.017	9,733 ± 152
2010b	3,413,399	1380	1.18 ± 0.04	5,091 ± 23
			1.28 ± 0.05	3,065 ± 285
			1.24 ± 0.016	2,265 ± 38
2011-2012a	3,475,741	3,748	1.41 ± 0.05	7,733 ± 70
			1.62 ± 0.08	5,467 ± 287
			1.50 ± 0.027	4,355 ± 51
2012b-2013a	3,537,986	1,359	1.17 ± 0.05	6,173 ± 853
			1.16 ± 0.04	4,983 ± 717
			1.13 ± 0.020	3,243 ± 179
2013b-2014a	3,600,000	8,629	1.21 ± 0.05	24,166 ± 1,182
			1.24 ± 0.04	18,154 ± 1,573
			1.21 ± 0.005	12,836 ± 209
2014b-2015a	3,661,835	1,151	1.19 ± 0.05	4,884 ± 129
			1.18 ± 0.02	3,807 ± 115
			1.12 ± 0.019	2,925 ± 257
2015b-2016a	3,723,821	3,656	1.16 ± 0.04	15,254 ± 76
			1.18 ± 0.03	11,005 ± 573
			1.17 ± 0.005	7,422 ± 116
2016b-2017a	3,787,511	3,565	1.17 ± 0.04	1,3917 ± 143
			1.27 ± 0.04	8,478 ± 711
			1.22 ± 0.012	6,092 ± 116
2017b-2018a	3,850,735	5,062	1.15 ± 0.04	25,453 ± 691
			1.23 ± 0.04	14,873 ± 1,419
			1.18 ± 0.007	10,853 ± 203
2018b-2019a	3,913,275	3,315	1.17 ± 0.04	13,695 ± 231
			1.16 ± 0.02	10,890 ± 445
			1.17 ± 0.014	6,436 ± 114
2019b-2020	3,975,404	5,693	1.26 ± 0.04	15,879 ± 373
			1.32 ± 0.03	12,020 ± 151
			1.28 ± 0.009	8,065 ± 163
2021	4,037,043	1,834	1.26 ± 0.04	5,824 ± 239
			1.31 ± 0.03	4,104 ± 153
			1.26 ± 0.013	3,017 ± 49
2022	4,098,135	8,098	1.23 ± 0.04	26,080 ± 635
			1.62 ± 0.21	12,467 ± 1,996
			1.33 ± 0.014	11,460 ± 186

Table 3
Mosquito population and number of mosquitoes per capita for each outbreak.

Year	Susceptible Population Vector	Mosquito density (per person)
1999	26,632 ± 13,087	9.3 ± 4.6
2001-2002	21,354 ± 11,247	10.0 ± 5.3
2005-2006a	25,770 ± 10,598	2.7 ± 1.1
2006b-2007a	27,614 ± 10,762	3.4 ± 1.3
2007b-2008a	20,228 ± 10,302	3.7 ± 1.9
2008b-2009a	19,449 ± 11,770	4.6 ± 2.7
2009b-2010a	26,311 ± 10,055	2.7 ± 1.0
2010b	23,279 ± 11,692	10.3 ± 5.2
2011-2012a	23,462 ± 11,512	5.4 ± 2.7
2012b-2013a	24,076 ± 10,969	7.4 ± 3.3
2013b-2014a	34,074 ± 9,944	2.7 ± 0.8
2014b-2015a	19,653 ± 11,979	6.8 ± 4.2
2015b-2016a	26,082 ± 10,538	3.5 ± 1.4
2016b-2017a	26,523 ± 12,255	4.4 ± 2.0
2017b-2018a	29,751 ± 10,029	2.7 ± 0.9
2018b-2019a	25,658 ± 10,818	4.0 ± 1.7
2019b-2020	28,551 ± 12,541	3.5 ± 1.6
2021	26,069 ± 12,670	8.7 ± 4.2
2022	27,116 ± 9,117	2.4 ± 0.8

The outcomes of the simulation revealed that a segment of the population was prone to participating in Dengue outbreaks, in which they were exposed to the risk of infection from a contaminated vector. This segment of the population grew as the density of mosquitoes per capita or the number of infected individuals heightened.

The vulnerability of the population to Dengue was greatly affected by the education programs on the disease and the tireless efforts of the units tasked with controlling its spread. These units, responsible for maintaining the well-being of the public, regularly conducted fumigations in areas with a history of Dengue cases or a high risk of outbreaks, as a precautionary measure to mitigate the risk of further transmission. Through these proactive measures, the spread of Dengue was effectively managed and contained, reducing its impact on the vulnerable population.

Having analyzed the results and estimated the parameters, it was observed that the values of the susceptible population oscillated within comparable intervals for the three models. However, during epidemic outbreaks with a significant number of cases, the SIR model tended to estimate a comparatively higher effective susceptible population, whereas the SIR-SI model estimated a comparatively lower population, and the SEIR model estimated a population that was positioned somewhere between the values of the SIR and SIR-SI models.

As for the estimation of the reproductive ratio of cases, the SEIR model generally tended to estimate a higher value due to its lower fraction of effective susceptible cases compared to the SIR and SIR-SI model, which had a higher fraction of effective susceptible cases and a lower reproductive ratio. Nonetheless, the three models replicated the number of secondary cases with a similar performance metric.

The models demonstrated the ability to estimate the case curve and the number of recoveries during the end of the epidemic. Among the models, the SIR-SI model stood out for its ability to provide a more thorough analysis of parameters related to epidemic outbreaks, such as the density of mosquitoes per person.

4.1. Outbreak analysis

The process of parameterizing each individual outbreak year for Dengue was deemed highly important as it allowed for a more accurate estimation of the reproductive rate of secondary cases during the start of each annual outbreak. By tailoring the parameters to fit the specific circumstances of each year, the models used to analyze the outbreaks could be analyzed, leading to a better understanding of the spread and evolution of the disease. To further understand the impact of dengue outbreaks, each outbreak period was analyzed separately, results in terms of susceptible population is shown in Table 3. Also, mosquito density for each model is presented.

In some instances, the data sets incorporated epidemic weeks from two consecutive years due to the extended duration of specific outbreaks. During less severe dengue outbreaks, it can be assumed that high populations of mosquitoes per capita were present in a particular epidemic location. However, as the outbreak progresses, the number of mosquitoes per capita gradually decreases. The purpose of this parameterization was to optimize the estimates for each individual year of outbreak, in order to achieve a more accurate representation of the spread and evolution of the disease.

The magnitude of Dengue outbreaks has been found to be linked to the abundance of mosquitoes in a given area. Outbreaks of small scale often indicate the presence of a high concentration of mosquitoes in the susceptible population. However, more severe outbreaks do not necessarily imply a high density of mosquitoes, but instead point to the alongside presence of the vector in the vulnerable segment of the population.

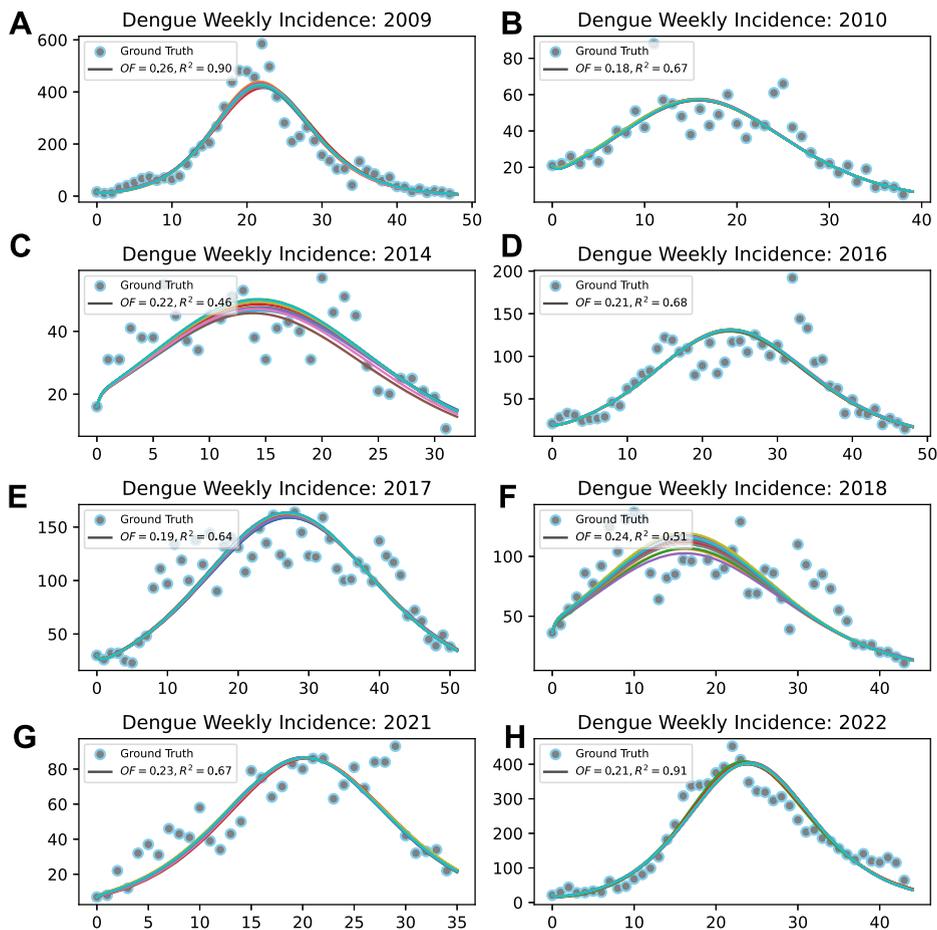


Fig. 6. SIR Fit. Optimized SIR Model Outcomes for Dengue Incidence for outbreak years: 2009 (A), 2010 (B), 2014 (C), 2016 (D), 2017 (E), 2018 (F), 2021 (G) and 2022 (H).

Moreover, Fig. 6, Fig. 7 and Fig. 8 illustrate the fitting capability of the (SIR, SEIR and SIR-SI) models. Each panel in Figs. 6-8, represents an outbreak year, starting from 2009 (A), 2010 (B), 2014 (C), 2016 (D), 2017 (E), 2018 (F), 2021 (G) and 2022 (H). In these Figures, the real incidence of the epidemiological outbreaks is indicated in circular gray with sky-blue edge color, while the fitted curve for each outbreak was depicted in colored curves. These figures provide a visual representation of the ability of each model to estimate the case curve. Also, the obtained OF value and R^2 are shown.

5. Discussion

The Republic of Panama, situated within the tropical region, experiences favorable climate conditions, particularly with regards to rainfall, that facilitate the propagation of the mosquito vector responsible for the transmission of Dengue. An analysis conducted by Díaz et al. [15] has confirmed the presence of all four serotypes of Dengue in the Republic of Panama since 1993. Compartmental models are a widely recognized tool in epidemiology, employed to comprehend the dynamics of an epidemic and, more significantly, to determine the rate of transmission, R_0 [61,62]. The purpose of this study was to determine the reproductive ratio in Dengue outbreaks through the use of actual data. Our findings revealed that the R_0 value can be effectively estimated with this method. Furthermore, our examination of years with documented outbreaks indicated a correlation between the number of mosquitoes per capita in the susceptible population and the likelihood of a Dengue epidemic.

Using the proposed methodology, it is noted that in all analyzed outbreaks, the mosquito density per person Table 3, starting from an average density of (2.4 ± 0.8) mosquitoes per person (as seen for the year 2022), plays an important role in the development of Dengue epidemics. To determine the role of mosquito density in R_0 estimation, a model akin to the one developed by Griffin for Malaria [63], should be studied. The Griffin model, uses parameters such as: biting rate on humans, expected duration of infectiousness of an infected mosquito, the probability of infection if bitten by an infected mosquito and human infectiousness to mosquitoes (if the human host is infected). These parameters to the best of our knowledge, have not been characterized for the Republic of Panama. Thus, the interpretation of results should be made in the direction that if at least one mosquito, with the ability to transmit the disease, is present in the presence of a susceptible person, there would be a possibility of transmission. Basically, while

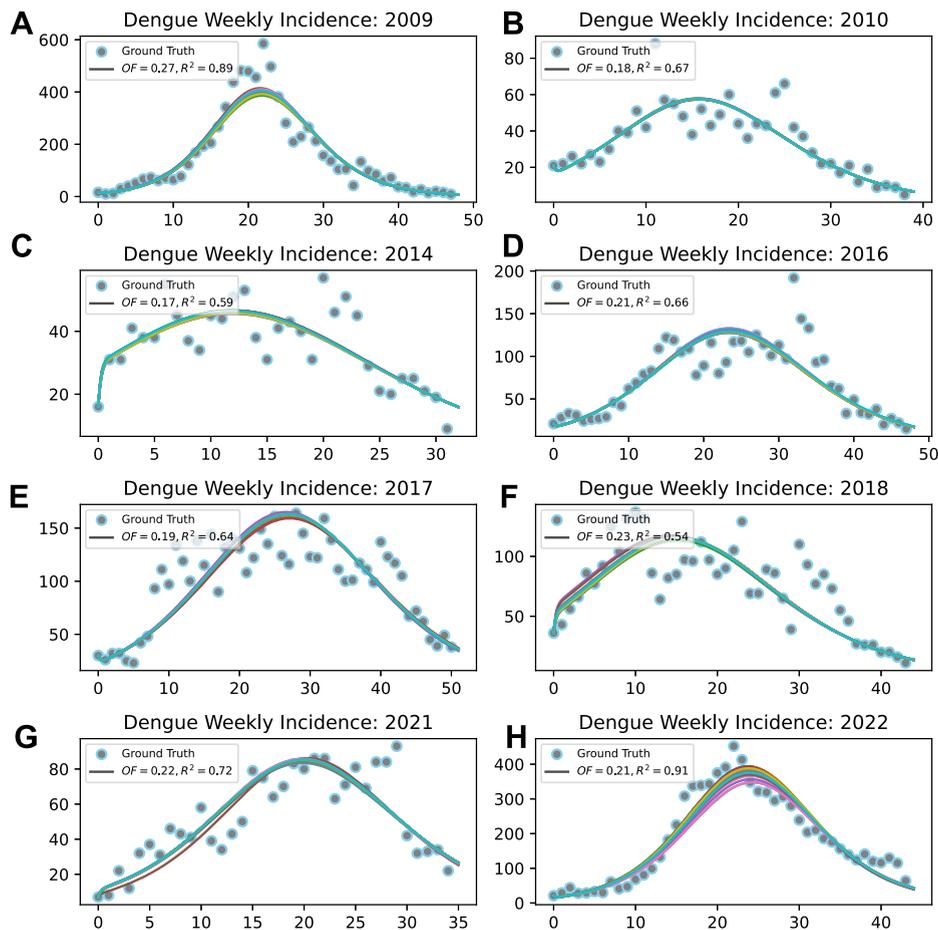


Fig. 7. SEIR Fit. Optimized SEIR Model Outcomes for Dengue Incidence for outbreak years: 2009 (A), 2010 (B), 2014 (C), 2016 (D), 2017 (E), 2018 (F), 2021 (G) and 2022 (H).

there could be other factors that contribute to the development of Dengue outbreaks, for our models, having mosquitoes capable of transmitting the disease is a crucial one.

Comparing the resulting reproductive number across different countries in various latitudes can greatly aid in our understanding of the severity of Dengue outbreaks. By identifying similarities and differences in the ratios found, we can gain a deeper understanding of the results of the models used to estimate the reproductive number, which ultimately provides a foundation for developing effective strategies for controlling and mitigating the spread of the virus.

Studies on the reproductive ratio of Dengue in the city of Kupan, Indonesia, showed a value that is comparable to the reproductive ratio found in our study, with a range of 1.30 to 2.02 [44]. In contrast, a study conducted in Colombia found a reproductive ratio that oscillated between 1.01 and 1.11, which is in agreement with the range found in our study [64].

Studies conducted in Central and South America have estimated the reproductive ratio of Dengue fever between the years 1999 and 2010 in a number of countries. The results showed varying values for the reproductive ratio, with Brazil having a ratio of 2.75, Colombia with a ratio of 3.075, Honduras with a ratio of 2.7, Mexico with a ratio of 1.975, and Puerto Rico with a ratio of 2.15 [65,66]. These findings highlight the importance of examining the reproductive ratio on a country-by-country basis as it provides valuable insights into the transmission dynamics and potential severity of the epidemic in a specific region.

In this study, a SIR-SI model was introduced to address issues of mosquito disease control. This consideration can be further extended utilizing a granular approach by analyzing vector populations at the district or *corregimiento* levels in order to enhance the application of control strategies [67–70]. In this matter, works by Loaiza et al. can become very useful, as they have provided a first measure of mosquito larvae (both for *Aedes aegypti* and *Aedes albopictus*) first in the Azuero region [10] and then associated with specific Dengue cases countrywide [11].

Part of the challenge of adding this vector-host model can be to sort out a biological niche phenomenon, basically saying which species can be dominant in a specific region. For instance, it has been noted in the literature that there is ecological competition between *Aedes aegypti* and *Aedes albopictus* in parts of the country [71,72]. Moreover, as is known the same mosquito is responsible for Zika and Chikungunya on top of Dengue, which can alter the number of Dengue cases [34,15,31,73].

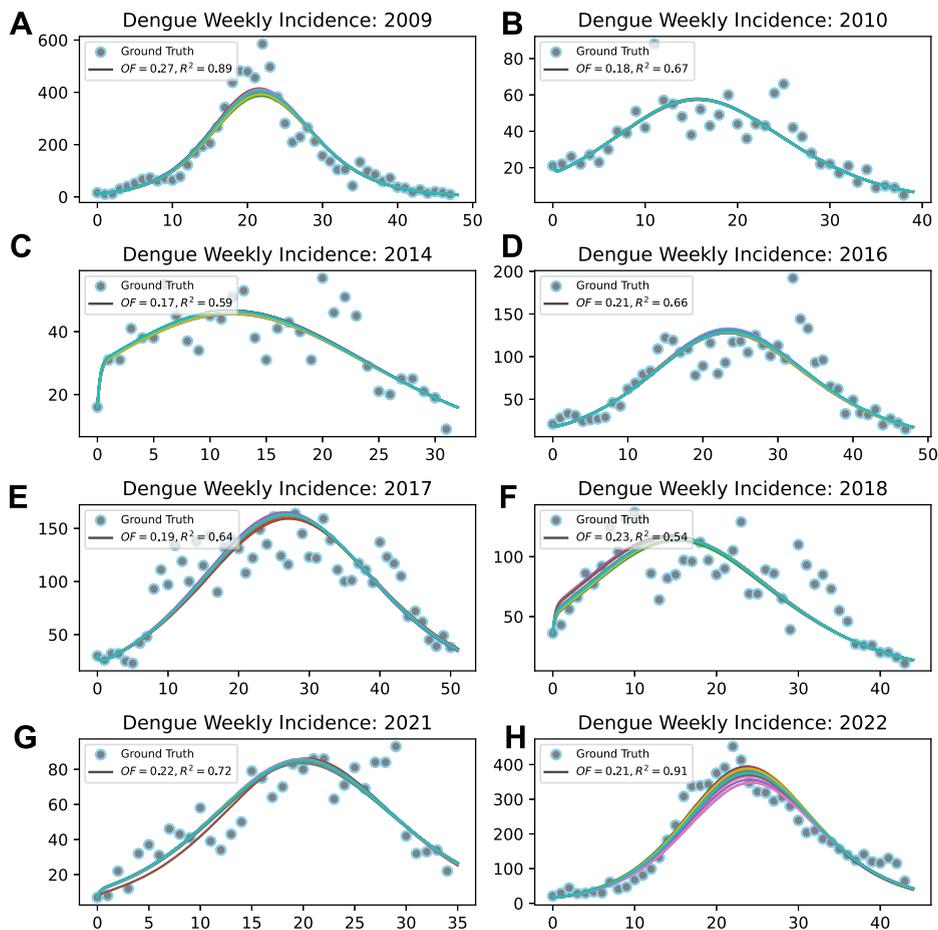


Fig. 8. SIR-SI Fit. Optimized SIR-SI Model Outcomes for Dengue Incidence for outbreak years: 2009 (A), 2010 (B), 2014 (C), 2016 (D), 2017 (E), 2018 (F), 2021 (G) and 2022 (H).

One of the limitations of this study was its reliance on certain assumptions, for instance, one of them is the notion of lifelong immunity following a primary Dengue infection. However, it is well established that this is not the case for Dengue, as subsequent infections can have different effects. As a result, the models may only reflect an approximation of the true dynamics of the disease.

Also, some of the limitations of this study are that the models were made to work under assumptions. For instance the assumption of life long immunity after a primary Dengue infection, that in case of Dengue is different due to the well-studied effect for subsequent Dengue infection, Antibody-dependent enhancement (ADE) effects and cross immunity for other flaviviruses [74].

Public health is always a priority, even more nowadays, in the lights of a global pandemic, such as the one caused by SARS-CoV-2 virus. Even though Dengue has 30 years of endemic circulation in Panama, this is the first time that R_0 have been calculated for these diseases in the country. Because subsequent Dengue infections the R_0 calculation will provide a better understanding of possible Dengue outbreak, since these have been related with the introduction of a different serotype or genotype of the virus and immunity to the serotype (s) that have been in previous circulation [15,75].

In future work, it would be valuable to explore the potential of other differential equation-based compartmental models that take into account vector-host-mitigation strategies (vaccination or Wolbachia bacterium inoculation) as interactions [44,45,43]. Such models have been used in the past to evaluate the impact of local vector eradication and control efforts carried out by Health authorities [76–78]. These models offer the potential to gain a deeper understanding of the dynamics of vector-host interactions, thereby facilitating the development of more effective control strategies.

6. Conclusions

The outcome of these findings underscores the ongoing necessity for effective vector control within communities, proper disposal of waste that could facilitate the spread of other viruses, and educational programs for the public regarding hygiene measures to prevent proliferation and infection from diseases similar to or including Dengue. It is crucial to address these issues in order to minimize the severity of future outbreaks.

Designing an effective dengue vaccination strategy requires the use of epidemiological modeling to understand the spread of the disease, the potential impact of the intervention, and inform resource allocation. Epidemiological models incorporate data, transmission dynamics, population demographics, and the impact of interventions such as inoculation to guide effective and efficient disease reduction strategies, highlighting the importance of applying models to assist decision makers.

Since Dengue is endemic and its circulation still causes severe cases and deaths each year, the R_0 calculation could be used as a tool of prevention for health authorities in the Republic of Panama. Regular collection and analysis of incidence data enables public health organizations to keep abreast of disease outbreaks and implement proactive interventions. Thus, the significance of high-quality data sets and consistent incidence reporting cannot be underestimated in the pursuit of successful epidemic control and prevention.

Taken as a whole, our results emphasize the significance of implementing measures to control the mosquito population, including using insecticides, mosquito nets, and other preventative methods to reduce their numbers and prevent the spread of Dengue. Moreover, it highlights the importance of continuous mosquito control efforts, proper waste management to prevent the spread of other viruses, and educational programs for the public on maintaining proper hygiene to prevent the proliferation of diseases such as Dengue.

As final words, it is imperative that public health be given priority, especially in the midst of a global pandemic such as that caused by the SARS-CoV-2 virus. The significance of this study lies in the fact that it provides, to the best of our knowledge, the first ever calculation of the reproductive ratio R_0 for Dengue outbreaks in the Republic of Panama during the period from 1999 to 2022. Despite being endemic, Dengue continues to cause severe cases each year, emphasizing the importance of understanding its dynamics.

Ethics approval and consent to participate

Not applicable. The original study from which the data in this article was generated was approved by the Institutional Research Bioethics Committee for the Gorgas Memorial Institute for Health Studies approved under approval code 019/CBI/ICGES/18 on January 11th 2018.

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Consent for publication

All authors have read and agreed to the published version of the manuscript.

CRediT authorship contribution statement

Conceptualization, V.N., Y.D., M.F.B., J.M.P. and J.E.S.-G.; methodology, V.N. and J.E.S.-G.; software, V.N. and J.E.S.-G.; validation, V.N., Y.D., M.F.B., J.M.P. and J.E.S.-G.; resources, M.F.B., Y.D., J.M.P. and J.E.S.-G.; writing—original draft preparation, V.N. and J.E.S.-G.; writing—review and editing, V.N., Y.D., M.F.B., J.M.P. and J.E.S.-G.; visualization, V.N. and J.E.S.-G.; supervision of students, J.E.S.-G.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data regarding the incidence of Dengue cases is of public domain, and is compiled yearly by MINSA and published in the Health Statistical Yearbook <http://minsa.gob.pa/informacion-salud/anuarios-estadisticos>, last accessed in May 25th, 2022. Demographic is compiled by the Instituto Nacional de Estadística y Censo and published in “Panama en Cifras” yearbook <https://inec.gob.pa/publicaciones/Default.aspx>, last accessed in May 25th, 2022.

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Appendix A. Instructions for using the Next Generation Matrix method (NGM)

First is to write the SIR, SEIR and SIR-SI equations for the *Transmission* $F_i(x)$ state and the *Transition* $V_i(x)$ state.

For the SIR:

$$\frac{dI}{dt} = \overbrace{\frac{\beta SI}{N}}^{\text{Transmission}} - \overbrace{(\gamma + \mu) I}^{\text{Transition}} \tag{A.1}$$

$$F_{SIR} = [F_1] = \left[\frac{\beta SI}{N} \right] \tag{A.2}$$

$$V_{SIR} = [V_1] = [(\gamma + \mu) I]$$

For the SEIR:

$$\frac{dE}{dt} = \overbrace{\frac{\beta SI}{N}}^{\text{Transmission}} - \overbrace{(\sigma + \mu) E}^{\text{Transition}} \tag{A.3}$$

$$\frac{dI}{dt} = \overbrace{\sigma E}^{\text{Transition}} - \overbrace{(\gamma + \mu) I}^{\text{Transition}}$$

$$F_{SEIR} = \begin{bmatrix} F_1 \\ F_2 \end{bmatrix} = \begin{bmatrix} \frac{\beta SI}{N} \\ 0 \end{bmatrix} \tag{A.4}$$

$$V_{SEIR} = \begin{bmatrix} V_1 \\ V_2 \end{bmatrix} = \begin{bmatrix} (\sigma + \mu) E \\ (\gamma + \mu) I - \sigma E \end{bmatrix}$$

For the SIR-SI:

$$\frac{dI_h}{dt} = \overbrace{\frac{C_{vh} I_v}{N_h} S_h}_{\text{Transmission}} - \overbrace{(\gamma_h + \mu_h) I_h}_{\text{Transition}} \tag{A.5}$$

$$\frac{dI_v}{dt} = \overbrace{\frac{C_{hv} I_h}{N_h} S_v}_{\text{Transmission}} - \overbrace{\mu_v I_v}_{\text{Transition}}$$

$$F_{SEIR} = \begin{bmatrix} F_1 \\ F_2 \end{bmatrix} = \begin{bmatrix} \frac{C_{vh} I_v}{N_h} S_h \\ \frac{C_{hv} I_h}{N_h} S_v \end{bmatrix} \tag{A.6}$$

$$V_{SEIR} = \begin{bmatrix} V_1 \\ V_2 \end{bmatrix} = \begin{bmatrix} (\gamma_h + \mu_h) I_h \\ \mu_v I_v \end{bmatrix}$$

The next step is to assemble the matrices T and Σ , incorporating the Jacobian, and then substitute in the values at the disease-free equilibrium point (DFP).

For SIR, DFP ($S = \frac{\alpha N}{\mu}, I = 0, R = 0$):

$$T = \mathbb{J}(F_{SIR})_{@DFP} = \alpha\beta/\mu \tag{A.7}$$

$$\Sigma = \mathbb{J}(V_{SIR})_{@DFP} = \gamma + \mu \tag{A.8}$$

For SEIR, DFP ($S = \frac{\alpha N}{\mu}, E = 0, I = 0, R = 0$):

$$T = \mathbb{J}(F_{SEIR})_{@DFP} = \begin{bmatrix} 0 & \alpha\beta/\mu \\ 0 & 0 \end{bmatrix} \tag{A.9}$$

$$\Sigma = \mathbb{J}(V_{SEIR})_{@DFP} = \begin{bmatrix} \sigma + \mu & 0 \\ -\sigma & \gamma + \mu \end{bmatrix} \tag{A.10}$$

For SIR-SI, DFP ($S_h = \frac{\alpha_h N}{\mu_h}, I_h = 0, R_h = 0, S_v = A_v/\mu_v, I_v = 0$):

$$T = \mathbb{J}(F_{SEIR})_{@DFP} = \begin{bmatrix} 0 & C_{vh} \\ \frac{A_v C_{hv}}{N_h \mu_v} & 0 \end{bmatrix} \tag{A.11}$$

$$\Sigma = \mathbb{J}(V_{SEIR})_{@DFP} = \begin{bmatrix} (\gamma_h + \mu_h) & 0 \\ 0 & \mu_v \end{bmatrix} \tag{A.12}$$

The next step is to compute the product of $-T\Sigma^{-1}$ and find the supremum absolute value of its eigenvalues.

For SIR:

$$-T\Sigma^{-1} = -\frac{\alpha\beta}{\mu} * \frac{1}{(\gamma + \mu)} = -\frac{\alpha\beta}{\mu(\gamma + \mu)} \quad (\text{A.13})$$

$$R_0 = \sup \left| -\frac{\alpha\beta}{\mu(\gamma + \mu)} \right| = \frac{\alpha\beta}{\mu(\gamma + \mu)}$$

For SEIR:

$$-T\Sigma^{-1} = -\begin{bmatrix} 0 & \alpha\beta/\mu \\ 0 & 0 \end{bmatrix} * \begin{bmatrix} \frac{1}{\sigma} & 0 \\ \frac{1}{(\gamma+\mu)(\sigma+\mu)} & \frac{1}{\gamma+\mu} \end{bmatrix} = \begin{bmatrix} \frac{-\alpha\beta\sigma}{\mu(\gamma+\mu)(\sigma+\mu)} & \frac{-\alpha\beta}{\mu(\gamma+\mu)} \\ 0 & 0 \end{bmatrix} \quad (\text{A.14})$$

$$R_0 = \sup \left| \det \left(\begin{bmatrix} \frac{-\alpha\beta\sigma}{\mu(\gamma+\mu)(\sigma+\mu)} & \frac{-\alpha\beta}{\mu(\gamma+\mu)} \\ 0 & 0 \end{bmatrix} - \lambda I \right) \right| = \frac{\alpha\beta\sigma}{\mu(\gamma + \mu)(\sigma + \mu)}$$

For SIR-SI:

$$-T\Sigma^{-1} = -\begin{bmatrix} 0 & C_{vh} \\ \frac{A_v C_{hv}}{N_h \mu_v} & 0 \end{bmatrix} * \begin{bmatrix} \frac{1}{(\gamma_h + \mu_h)} & 0 \\ 0 & \frac{1}{\mu_v} \end{bmatrix} = \begin{bmatrix} 0 & \frac{-C_{vh}}{\mu_v} \\ \frac{-A_v C_{hv}}{N_h \mu_v (\gamma_h + \mu_h)} & 0 \end{bmatrix} \quad (\text{A.15})$$

$$R_0 = \sup \left| \det \left(\begin{bmatrix} 0 & \frac{-C_{vh}}{\mu_v} \\ \frac{-A_v C_{hv}}{N_h \mu_v (\gamma_h + \mu_h)} & 0 \end{bmatrix} - \lambda I \right) \right| = \sqrt{\frac{C_{hv} C_{vh}}{\mu_v (\gamma_h + \mu_h)} \frac{N_v}{N_h}}$$

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