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Development and Modeling of a Dengue Vaccine for Children Aged 10-14 in Rio de Janeiro, Brazil

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Abstract. This study introduces a model for developing a dengue vaccine program for children aged 10-14 in Rio de Janeiro, Brazil. We simulate dengue spread and vaccination impacts over three years, focusing on vaccine efficacies, timing, and stochastic rates within a SIRS-V framework. Our findings highlight the importance of vaccine efficacy and timing in reducing infections and managing outbreaks. Even with lower efficacy, early vaccination significantly reduces infection peaks and delays epidemic onset. While there are discrepancies with actual data, suggesting model refinement, our results emphasize the value of targeted vaccination strategies in controlling dengue. This research offers insights for policymakers on optimizing dengue control through timely and effective vaccination campaigns.

Keywords Dengue Vaccine Model, Vaccine Efficacy, Vaccination Rates

1 Introduction

Dengue virus (DENV) is primarily transmitted by *Aedes aegypti* mosquitoes in urban areas and *Aedes albopictus* in rural areas [4]. DENV has four strains, with people in endemic regions at risk of multiple infections over their lifetime [4, 5]. However, re-infection with a different DENV strain can lead to more severe clinical outcomes due to a phenomenon known as antibody-dependent enhancement (ADE) [4, 5]. The spread of dengue has become a major public health concern, and efforts to control the disease have focused on mosquito control, vaccine development, and improved clinical management. To control dengue disease, two vaccines have been approved: Dengvaxia (CYD-TDV) by Sanofi Pasteur and TAK-003 by Takeda. Dengvaxia, the first dengue vaccine to be licensed globally, was initially registered in Mexico in December 2015 [7]. It subsequently received approval in other countries, mainly in regions endemic for dengue such as parts of Latin America and Asia. Consequently, the World Health Organization (WHO) recommends that this vaccine be administered only to seropositive individuals (those previously exposed to the virus)[7]. It was observed that seronegative individuals (those who had not been previously infected) who received the vaccine developed severe dengue, an effect attributed to ADE [7]. In contrast, the Takeda vaccine (TAK-003) shows minimal potential impact from ADE [6]. Clinical trial data indicate

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that TAK-003 protects against dengue in both seropositive and seronegative individuals, with no significant increase in severe disease observed. This suggests that TAK-003 may not exacerbate dengue severity through ADE, offering a critical advantage by allowing safer vaccination without the need for prior serostatus screening [6]. The data from the Ministry of Health for the first 11 epidemiological weeks of 2024 show a significant increase in dengue cases in Brazil. Specifically, in the 8^{th} epidemiological week of 2024, there were 299,420 probable cases, a substantial rise from the 11,840 cases recorded during the same week in 2023 [3]. Rio de Janeiro has been facing the dengue epidemic in 2024, declaring a state of public health emergency, establishing the Emergency Operations Center (COE-Dengue), when 11 service centers for the disease were opened throughout the city (prepared for the diagnosis and treatment of people with dengue). Beds were dedicated for dengue patients in municipal hospitals; the use of fumigate cars in regions with the highest incidence of cases; and compulsory entry into closed and abandoned properties to search for and eliminate mosquito outbreaks. The observed improvement in epidemiological indicators in recent weeks may be associated with the dengue vaccination campaign. The dengue vaccine, provided by Takeda in collaboration with UFMS, targets municipalities in Brazil with high transmission rates over the past decade, including Rio de Janeiro. Starting in March 2024, the campaign focuses on vaccinating children and adolescents aged 10 to 14, who represent the highest hospitalization rates among non-elderly age groups. The vaccine regimen requires two doses spaced three months apart [1]. Figure 1 shows weekly dengue cases for the age group 10-14 years in Rio de Janeiro city from 2014–2024 [2].

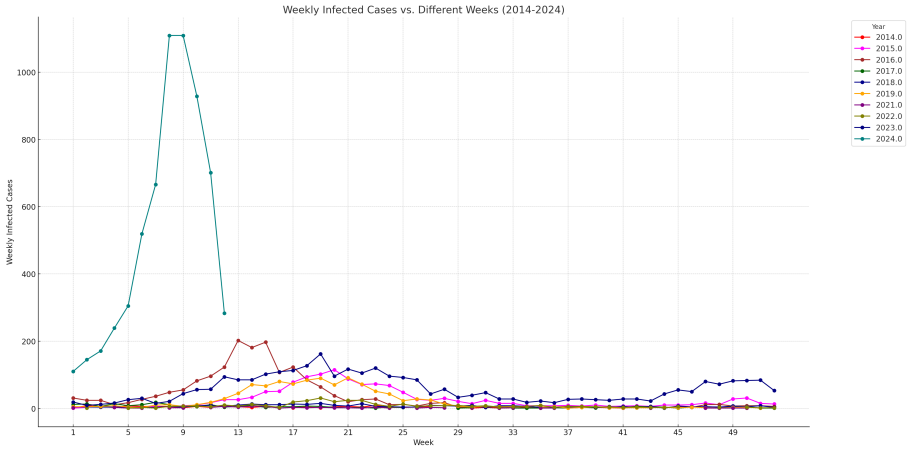

Figure 1: Weekly dengue cases for the age group 10-14 years in Rio de Janeiro city from 2014–2024 [2].

This study proposes a dengue vaccine model for 10–14-year-olds in Rio de Janeiro, assessing vaccination impacts on the epidemic for three years. It examines the effects of seasonal transmission, varying vaccination rates, and efficacy, highlighting the relationship between vaccination rates and infection peaks, with a focus on stochastic efficacy outcomes.

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2 Mathematical Model

2.1 Model Overview

We propose a compartmental deterministic model within the SIRS-V framework for modeling the dengue vaccines in the city of Rio de Janeiro, specifically targeting children aged 10-14 years. The population is divided into four compartments: Susceptible (S), Infected (I), Recovered (R), and Vaccinated (V). We have assumed the population of the age group 10-14 years old is homogenous. The model is governed by the following system of differential equations:

$$\frac{dS}{dt} = \mu N - \beta(t)\frac{SI}{N} - (\psi + \mu)S + \gamma R, \tag{1}$$

$$\frac{dI}{dt} = \beta(t)\frac{SI}{N} + (1 - V_e)\beta(t)\frac{VI}{N} - (\mu + \alpha)I, \tag{2}$$

$$\frac{dR}{dt} = \alpha I - (\mu + \gamma)R, \tag{3}$$

$$\frac{dV}{dt} = \psi S - (1 - V_e)\beta(t)\frac{VI}{N} - \mu V, \tag{4}$$

$$\tag{5}$$

where, N represents the total population, μ the natural death rate, γ the reinfection rate, α the recovery rate. The time-dependent transmission rate, $\beta(t)$, is modeled using a cosine function to capture seasonal variations in dengue disease transmission dynamics :

$$\beta(t) = \beta_0 \left(1 + \epsilon \left[\cos(n\omega t + \phi)\right]\right), \tag{6}$$

where β_0 is the base transmission rate, $\omega = \frac{2\pi}{52}$ represents the fundamental frequency of seasonal variation with a period one year (52 weeks), ϵ is the degree of periodic forcing, $0 < \epsilon < 1$, ϕ is the phase constant, ψ is the vaccination rate, V_e is the vaccine efficacy.

3 Results and Discusssion

The data from the Public Health System (SUS) reveals that less than 2% of children in a specific age group are affected by dengue, leading us to estimate that about 1% of children aged $10 - 14$ years might be susceptible to the disease. Our initial conditions for the simulation are: $I(0) = 110$ (infected), $R(0) = 1$ (recovered), $V(0) = 0$ (vaccinated), and $S(0)$ calculated from the total population, $N = 0.01 \times 354,000$, representing 5.7% of Rio de Janeiro's population (6.2 million). We used parameters: $\beta_0 = 1.4$ (base transmission rate), $\psi = 0.12$ (vaccination rate), $V_e = 0.7$ (vaccine efficacy), and $\gamma = \frac{1}{12}$ week^{-1}. The effect of stochasticity has been modeled considering a Gaussian distribution of vaccination rate, $\psi \sim \mathcal{N}(0.08, 0.001^2)$. The simulations have been carried out using the programming language Python. Figure 2 shows a comparison between actual reported dengue cases in children aged 10-14 years and the forecasted cases derived from our model, under scenarios with and without the implementation of a vaccination program across a 12-week timeline. The model captures the overall trend of the dengue outbreak, demonstrating a reduction in the number of cases and a delay in the epidemic peak as a result of vaccination. This attenuation and temporal shift suggest that vaccinations are not only instrumental in decreasing incidence rates but may also provide valuable time for the deployment of additional public health measures. However, the model predictions and the real infection data do not perfectly align, indicating potential areas for refinement in the model's parameters or assumptions. Such discrepancies

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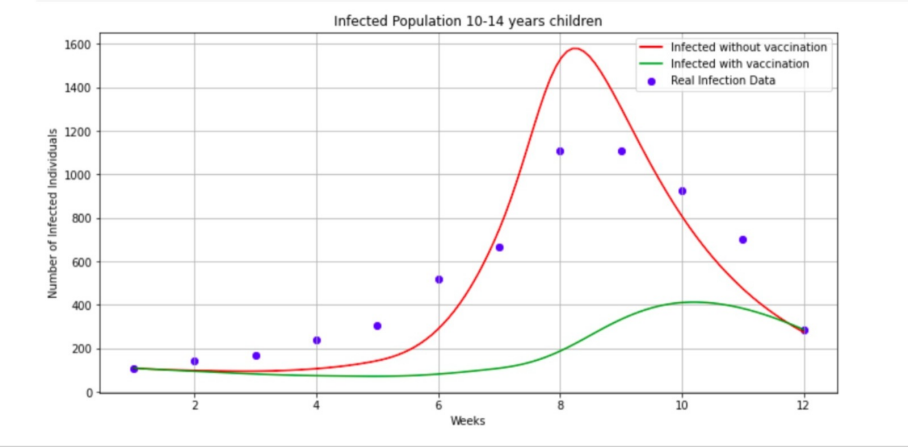

Figure 2: Short-term infection dynamics without vaccination and with vaccination.

underscore the complexity of infectious disease modeling and the need for continuous calibration against real-world data.

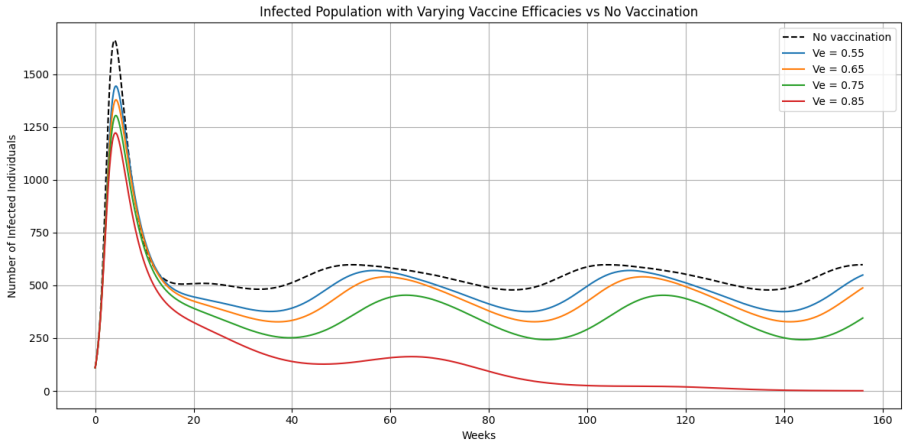

Figure 3: Effect of different vaccine efficacies ($V_e = 0.55, 0.65, 0.75, 0.85$) on the long-term dynamics of dengue infection.

Figure 3 illustrates the impact of varying vaccine efficacies (Ve = 0.55, 0.65, 0.75, and 0.85) on the dynamics of dengue infection among children aged 10-14 in Rio de Janeiro over three years, maintaining a constant vaccination rate ($\psi = 0.12$). In the absence of vaccination, an early peak in infection rates is observed, followed by periodic oscillations in subsequent years. The introduction of vaccination—even at the lowest efficacy of 0.55—markedly suppresses these infection peaks relative to the no-vaccination baseline. As vaccine efficacy increases, this suppressive effect on peak infection rates becomes more pronounced, with the scenario involving a vaccine efficacy of 0.85 demonstrating the most substantial reduction in infections. Additionally, an increase in vaccine efficacy correlates with a delayed onset of the infection peak. This observation underscores the critical role of vaccine efficacy in managing dengue outbreaks and highlights the potential benefits of high-efficacy vaccines in delaying and reducing peak infection periods.

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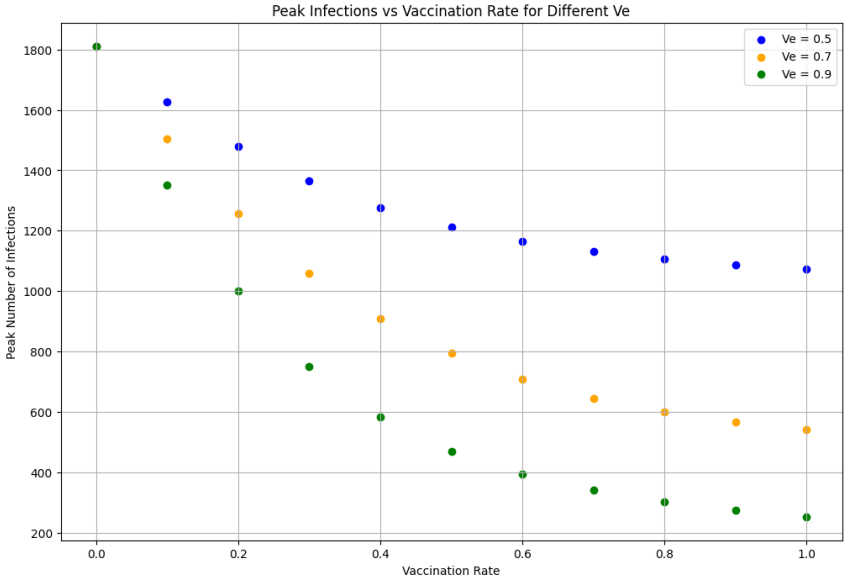

Figure 4: Effect of vaccination rates, ψ on the peak of infections for different values of V_e.

Figure 4 shows the relationship between peak infection numbers and vaccination rates for three different values of vaccine efficacy (Ve). Each point on the graph corresponds to the maximum number of infections observed for a given vaccination rate (on the x-axis) and vaccine efficacy (indicated by color). The blue points represent a vaccine efficacy of 0.5, the orange points represent a vaccine efficacy of 0.7, and the green points represent a vaccine efficacy of 0.9. As we move from left to right along the x-axis, the vaccination rate increases from 0 to 1.0. The y-axis shows the peak number of infections, ranging from 200 to over 1800 infections. The graph indicates a clear trend: as the vaccination rate increases, the peak number of infections decreases. This trend is consistent across all three vaccine efficacy levels. However, the decline in infections is steepest for the green points, which represent the highest vaccine efficacy (0.9). Even at lower vaccination rates, high vaccine efficacy leads to a significantly lower number of peak infections. Conversely, for a vaccine efficacy of 0.5, even high vaccination rates cannot reduce the peak infections to the levels achieved by the higher efficacy vaccines at the same rates.

Figure 5 depicts the impact of vaccination timing on dengue infection rates among children aged 10-14 in Rio de Janeiro, highlighting the importance of early vaccination, even with lower-efficacy vaccines, in reducing infections. The simulation indicates a critical start time for vaccination at 4 weeks, after which the peak number of infections stabilizes, illustrating a diminishing return on delaying vaccination. This plateau is attributed to herd immunity and the dynamics of disease transmission, where increasing vaccination coverage reduces disease spread. Once a significant portion of the population is vaccinated, further delays in vaccination do not substantially alter peak infection rates due to the slowed disease transmission and the small number of susceptible individuals remaining.

Figure 6 illustrates the effects of variable vaccination rates on the spread of dengue among 10-14-year-olds over three years. It compares the number of infections under three scenarios: no vaccination, a fixed vaccination rate, and a variable (stochastic) vaccination rate modeled with a Gaussian distribution. The line representing no vaccination shows the highest infection peaks, emphasizing the importance of vaccination. The fixed-rate vaccination scenario shows consistently

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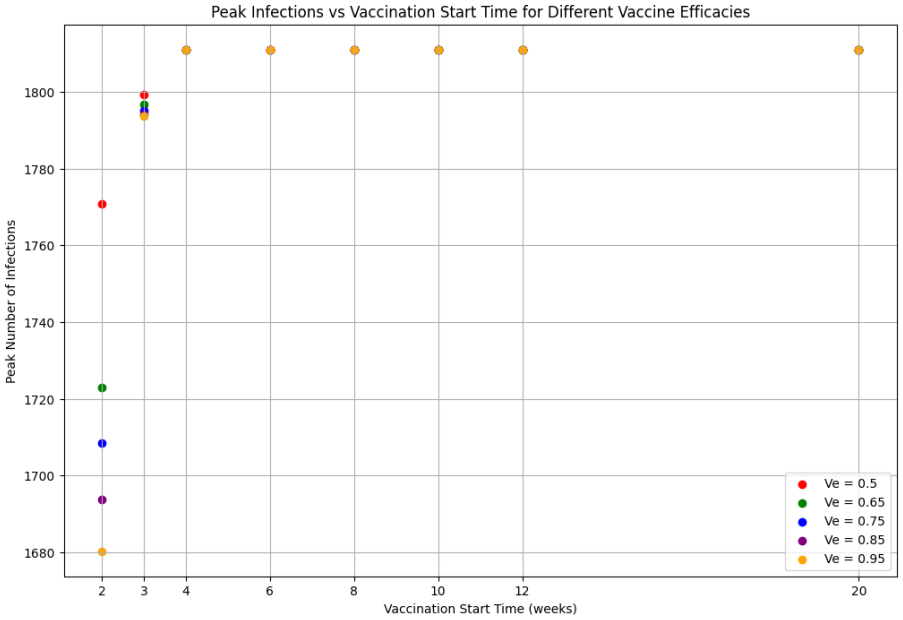

Figure 5: Effect of the vaccination start time on the infection dynamics for different vaccine efficacies.

lower infection levels, demonstrating the effectiveness of a steady vaccination strategy. In contrast, the stochastic model, which incorporates randomness in vaccination rates, displays a fluctuation in infection levels, with peaks sometimes approaching the levels seen without vaccination. This variability suggests that while vaccination reduces infections, inconsistent vaccination rates can compromise disease control, underlining the value of maintaining a consistent vaccination program.

4 Conclusion

We have developed a dengue vaccine model that underscores the importance of vaccination timing and efficacy in controlling dengue outbreaks. Our findings highlight the critical roles of vaccine timing and efficacy in reducing infection rates. However, the model requires fine-tuning to better reflect observed data. We suggest employing Bayesian inference to enhance the predictive accuracy of our model in future iterations. Anticipating challenges such as limited vaccine availability, we aim to adapt our model to address these issues effectively. Additionally, our future research will include the effects of antibody-dependent enhancement (ADE) to better understand its impact on vaccination outcomes and inform robust vaccination strategies against the complex dynamics of dengue virus infections.

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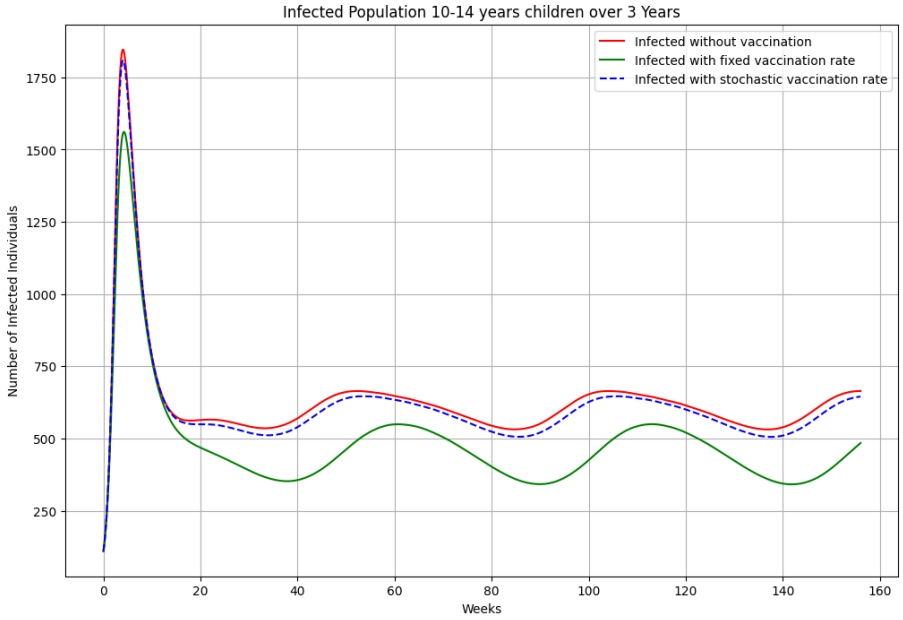

Figure 6: Effect of stochastic vaccination rate on the long-term dynamics of dengue.

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