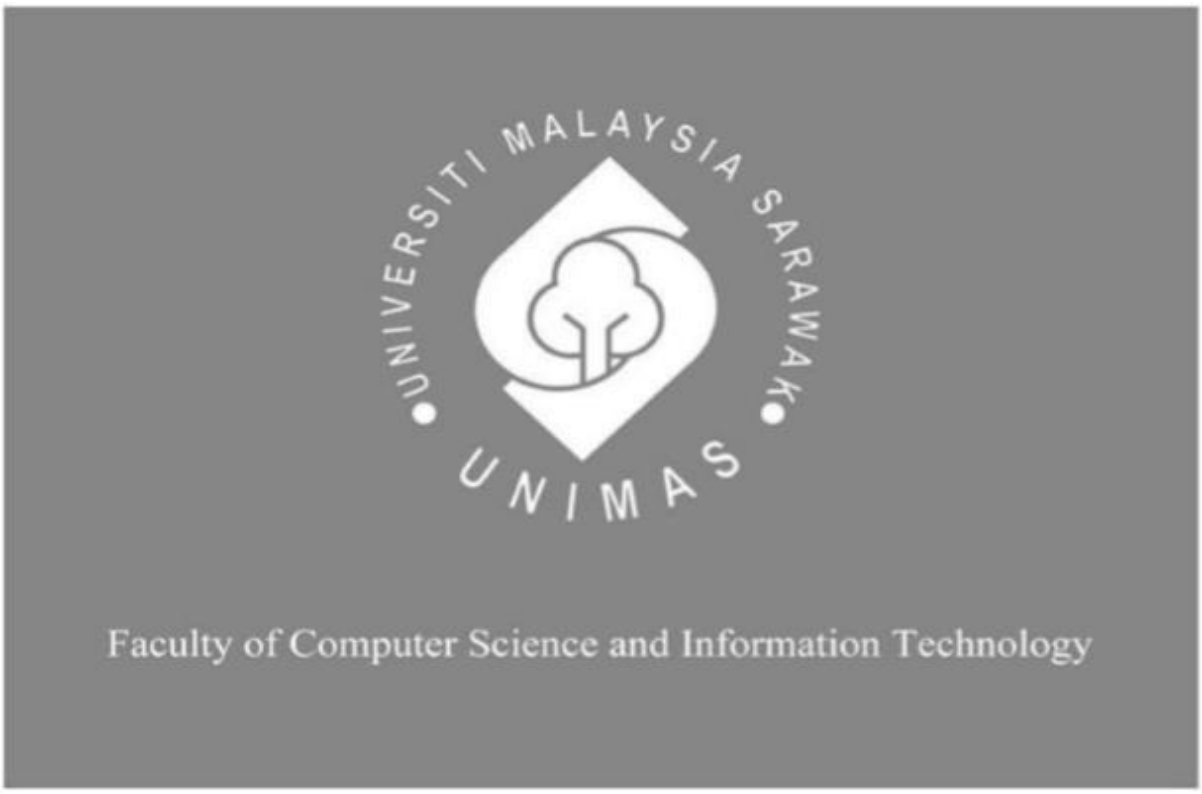


# *Evaluating the Effectiveness of Intervention Strategies in Controlling Dengue Fever Outbreaks with ASEI-SVIR Model*

Ibnu Ameerul Bin Abdul Halim

Bachelor of Computer Science with Honours

(Computational Science)

2025

# Evaluating the Effectiveness of Intervention Strategies in Controlling Dengue Fever Outbreaks with *ASEI-SVIR* Model

Ibnu Ameerul Bin Abdul Halim

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(Ibnu Ameerul Bin Abdul Halim)

78038@siswa.unimas.my

Computational Science Programme

Faculty of Computer Science and Information Technology

Universiti Malaysia Sarawak

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## ABSTRACT

Dengue fever remains a significant public health concern in Malaysia, where outbreaks are recurrent and challenging to control. Despite the availability of intervention strategies such as larvicide, fogging, and vaccination, there remains a lack of comprehensive studies that quantitatively evaluate their individual and combined effectiveness over time. This study addresses this gap by developing an ASEI-SVIR compartmental model integrated with optimal control theory to assess the impact of different dengue intervention strategies on disease transmission dynamics. The aim of this research is to identify the most effective intervention strategy for controlling dengue outbreaks using mathematical modelling. The model divides the human and mosquito populations into epidemiologically relevant compartments and introduces three control variables representing larvicide ($u_1$), fogging ($u_2$), and vaccination ($u_3$). These strategies, both individually and in combination, were simulated using the forward-backward sweep method with a fourth-order Runge-Kutta scheme in Python. The key findings reveal that fogging is the most effective strategy in the short term due to its immediate impact on adult mosquitoes, while vaccination provides more substantial benefits over the long term by reducing human susceptibility. Among all strategies tested, the combined application of larvicide, fogging, and vaccination resulted in the greatest reduction of both infected mosquito and human populations. This research contributes to epidemiological field by offering a quantitative framework for evaluating dengue control strategies, aiding policymakers in planning more effective intervention programs. However, the model's assumptions such as homogeneous mixing, constant parameters, and exclusion of environmental factors may not accurately reflect real-world dynamics. Future work should consider additional strategies such as *Wolbachia* deployment or alternative optimization techniques to improve accuracy and applicability in real-world scenarios.

## ABSTRAK

Demam denggi merupakan isu kesihatan awam yang kritikal di Malaysia. Walaupun terdapat pelbagai strategi intervensi seperti penggunaan larvisid, semburan, dan vaksinasi, kajian menyeluruh untuk menilai keberkesanan setiap strategi ini secara kuantitatif dalam jangka masa tertentu masih terhad. Kajian ini bertujuan untuk membangunkan model epidemiologi ASEI-SVIR yang digabungkan dengan teori kawalan optimum bagi menilai kesan pelbagai strategi intervensi denggi terhadap dinamik penularan penyakit denggi. Objektif kajian ini bertujuan untuk mengenal pasti strategi yang paling berkesan dalam mengawal penularan wabak denggi. Model epidemiologi ini membahagikan populasi manusia dan nyamuk kepada beberapa kompatmen serta memunyai tiga pemboleh ubah iaitu larvisid ($u_1$), semburan ($u_2$), dan vaksinasi ($u_2$). Strategi ini telah disimulasikan secara individu dan gabungan beberapa strategi menggunakan kaedah *forward-backward sweep* melalui Runge-Kutta tahap empat dalam Python. Dapatan utama menunjukkan bahawa semburan merupakan strategi paling berkesan untuk jangka masa pendek kerana kesannya yang segera terhadap nyamuk dewasa, manakala vaksinasi memberikan faedah jangka panjang dengan meningkatkan imunisasi manusia. Gabungan ketiga-tiga strategi ini memberikan pengurangan tertinggi dalam jumlah jangkitan bagi kedua-dua populasi manusia dan nyamuk. Kajian ini menyumbang kepada bidang epidemiologi dengan menyediakan kerangka kuantitatif bagi menilai strategi kawalan denggi, sekali gus membantu merancang program intervensi yang lebih berkesan. Namun, model ini bergantung kepada andaian seperti pencampuran homogen, parameter yang tetap, dan pengabaian faktor persekitaran yang mungkin tidak mencerminkan sepenuhnya situasi sebenar. Pengkaji seterusnya disarankan untuk mempertimbangkan strategi tambahan seperti penggunaan Wolbachia atau kaedah pengoptimuman lain bagi meningkatkan ketepatan dan kebolehgunaan dalam konteks dunia sebenar.

## TABLE OF CONTENTS

# LIST OF TABLES

# LIST OF FIGURES

# LIST OF EQUATIONS

# CHAPTER 1: INTRODUCTION

## 1.0 Chapter Overview

This chapter provides a comprehensive introduction to the study, which focuses on addressing the public health challenge posed by dengue fever in Malaysia. It begins with an introduction to the disease's background, emphasising its growing prevalence and the need for effective intervention strategies. The chapter identifies the research problem, emphasising gaps in understanding the effectiveness of various control measures. The objectives of the study are defined, including the development and application of the ASEI-SVIR model to evaluate interventions such as larvicide, fogging, and vaccination. The methodology is briefly outlined, detailing the model formulation, data collection, and simulation approaches. Additionally, the chapter describes the scope, significance, and expected outcomes of the research, stressing its potential to inform evidence-based dengue control policies in Malaysia. Lastly, the chapter provides an outline of the thesis structure, offering readers a roadmap for the subsequent sections of the study.

## 1.1 Background

Dengue fever is a mosquito-borne viral infection that poses a significant public health challenge in tropical and subtropical regions, including Malaysia. The disease is transmitted primarily by Aedes mosquitoes, and its incidence has been increasing globally due to factors such as urbanization, climate change, and increased human mobility (World Health Organization, 2023). Effective public health interventions are crucial to controlling the spread of dengue fever and reducing its impact on affected populations.

Recent studies have highlighted the escalating burden of dengue fever. Malavige et al. (2023) discuss the challenges and perspectives in managing dengue, emphasizing the role of climate change and urbanization in increasing the global burden of the disease. Xu et al. (2024)

analysed the long-term effects of climate factors on dengue fever, demonstrating the significant impact of temperature, humidity, and precipitation on dengue transmission dynamics. Additionally, a study by Buhler et al. (2019) provides a systematic review of environmental methods for dengue vector control, emphasizing the effectiveness of source reduction and community engagement in reducing mosquito breeding sites.

The increasing incidence of dengue fever in regions in Malaysia necessitates a comprehensive approach to intervention strategies. The integration of larvicide, fogging, and vaccination has shown promise in controlling dengue outbreaks. These strategies not only reduce the mosquito population but also enhance community immunity against dengue virus.

## 1.2 Problem Statement

Dengue fever remains a significant public health challenge in tropical regions, including Malaysia. Despite various public health interventions, there is limited understanding of how different strategies perform in controlling dengue outbreaks, particularly when considering the disease incubation period. Effective control of dengue fever is crucial to reducing its impact on affected populations. However, the lack of comprehensive evaluation of intervention strategies, such as larvicide, fogging, and vaccination, leaves a gap in guiding policy decisions during outbreaks. This project aims to fill this gap by using the ASEI-SVIR model to evaluate the effectiveness of these interventions. By understanding which strategies are most effective, public health authorities can implement more targeted and efficient measures to control the spread of dengue fever.

## 1.3 Objective

The objectives of this study include:

1. To formulate an extended ASEI-SVIR model by integrating elements from multiple existing epidemiological models, enabling the simulation of combined intervention strategies.
2. To simulate the impact of intervention strategies (larvicide, fogging, and vaccination) on the spread of dengue fever.
3. To compare the effectiveness of these interventions in reducing the peak number of infections, total infected population, and overall outbreak duration with historical data.
4. To provide recommendations for optimizing intervention strategies based on the model's results.

## 1.4 Brief Methodology

The methodology outlines the process of modelling dengue fever dynamics using the ASEI-SVIR model, incorporating human and mosquito populations. It integrates interventions such as vaccination, larvicide, and fogging as control variables ($u_1, u_2, \ and \ u_3$ ) to minimize infections and costs, based on parameter values gathered from reliable sources. The model is implemented in Python and simulated under various scenarios (no intervention, individual interventions, and combined strategies) to analyse outcomes like peak infections, total infections, and outbreak duration. Sensitivity, uncertainty, and cost-effectiveness analyses ensure robustness, and final recommendations are made for effective resource allocation in dengue control.

### 1.4.1 Data Collection for Model Parameters

Data on dengue fever cases, population demographics, and parameter values have been gathered from sources such as the Ministry of Health Malaysia, WHO, and relevant research papers.

### 1.4.2 Model Implementation

The ASEI-SVIR model is implemented using Python. It is divided into two populations which are human population denoted by $N_h$and mosquito (vector) population denoted by $N_v$. The human population consists of four compartments: Susceptible ($S_h$), Vaccinated ($V_h$), Infectious ($I_h$), and Recovered ($R_h$) while the mosquito population consists of four compartments: aquatic stage ($A_m$), susceptible ($S_m$ ), exposed ($E_m$), and infectious mosquitoes ($I_m$).

### 1.4.3 Incorporating Interventions

Intervention strategies that will be incorporated in the ASEI-SVIR model are larvicide (source reduction), fogging (adulticide) and vaccination. These interventions are represented by control variables $u_1, u_2,\ and\ u_3$ respectively.

#### 1.4.3.1 Source Reduction (Larvicide) and Fogging (Adulticide) Interventions

Abidemi and Aziz (2020) developed the ASEI-SEIR model for dengue transmission, incorporating control strategies like personal protection, larvicide, and adulticide across human, aquatic mosquito, and female mosquito populations. The study found combining adulticide and personal protection to be the most cost-effective intervention. Similarly, Bhuju et al. (2022) proposed a deterministic model employing fumigation and bed nets, assuming mosquitoes do not develop resistance to fumigation. This model treats key parameters, including transmission rate, recovery rate, and mosquito biting rate, as fuzzy numbers to account for uncertainty, using membership functions to reflect variability in virus load and the effectiveness of bed nets.

#### 1.4.3.2 Vaccination intervention

The SVIR model extends the SEIR framework by introducing a vaccinated (V) compartment as shown in a study by Rodrigues et al. (2014), replacing the exposed (E)

compartment, to simulate dengue transmission dynamics more accurately. It differentiates immunity acquired through vaccination from natural recovery while assuming perfect, lifelong immunity from vaccination. Continuous vaccination is modelled by vaccinating a proportion of newborns, reflecting real-world intervention strategies. While this approach highlights the potential of vaccination to reduce disease burden, it also imposes the risks in low-transmission settings, such as increased hospitalization among dengue-naïve individuals. The model simplifies mosquito dynamics, assuming the absence of a resistant phase due to their brief lifespan. This shows the importance of precise parameterisation and context-specific strategies to optimise vaccination outcomes.

### 1.4.4 Solving Optimal control Problem

The Optimal Control Problem (OCP) is a mathematical approach used to identify the best intervention strategies $(u_1, u_2, u_3)$ to minimize or achieve specific objectives while satisfying the constraints of a dynamic system. In the context of dengue fever transmission, the goal is to determine how to apply these control variables effectively to reduce the impact of the disease at the least cost. This method ensures that the optimal strategies effectively minimize the objective function while satisfying the system dynamics and constraints.

### 1.4.5 Model Simulation

Simulations of the ASEI-SVIR model have been run under different scenarios: no intervention, larvicide, fogging and vaccination. The results have been compared in terms of peak infections, total infected population, and the overall dynamics of disease spread.

### 1.4.6 Setting Up Parameters for Simulation and Analysis

The parameters in the model are set up to balance the objectives of minimizing the number of infected individuals and the cost of implementing control strategies. This is achieved by assigning weight constants ($W_1, W_2, W_3, W_4, W_5$) to various components of the objective function. These weights quantify the relative importance of reducing the infected populations and the costs of interventions.

#### 1.4.6.1 Baseline Scenario Analysis (No Interventions)

After the model is set up, the next step is to simulate a dengue outbreak without applying any interventions. This simulation serves as baseline scenario, representing the natural progression of the disease in the population. Key metrics to observe include the peak number of infections, time to peak, total number of infections, and the overall duration of the outbreak. This baseline analysis provides a benchmark against which the effects of different intervention strategies can be measured.

#### 1.4.6.2 Intervention Scenario Analysis (One-by-One Interventions)

With the baseline established, interventions have been introduced one at a time, such as larvicide, fogging and vaccination. Each intervention has been simulated individually, and its results have been compared against the baseline scenario. Key metrics to observe include changes in peak infections, time to peak, total infections, and the overall length of the outbreak. This step helps determine the effectiveness of each individual intervention in controlling the disease. By isolating the effects of each strategy, the intervention that provides the most significant benefits in terms of reducing disease spread is identified.

#### 1.4.6.3 Combined Intervention Analysis

After evaluating individual interventions, the next step is to examine the effects of combining multiple interventions. Simulations have been run where interventions like larvicide, fogging and vaccination are applied together to determine whether their effects are additive or if diminishing returns occur. The results of combined interventions have been compared against both the baseline and the single-intervention scenarios. This analysis assesses whether combining strategies provides significantly better outcomes than using them individually.

#### 1.4.6.5 Sensitivity and Uncertainty Analysis

To ensure the robustness of the findings, sensitivity and uncertainty analyses have been performed. In this step, control variables for intervention ($u_1, u_2, u_3$) have been varied to test how sensitive the model's outcomes are to small changes in these values. This analysis has revealed whether certain parameters significantly impact the effectiveness of interventions.

#### 1.4.6.6 Cost-Effectiveness and Practical Considerations

Beyond the technical aspects of the model, the cost-effectiveness and practicality of each intervention have been evaluated. In this step, the financial and logistical costs of interventions like larvicide, fogging and vaccination have been compared against the health outcomes they produce, such as reducing the number of infections. The real-world feasibility of implementing these interventions on a large scale has been considered, considering factors like public compliance and resource availability.

#### 1.4.6.7 Final Recommendations and Conclusion

Recommendation for the most suitable intervention have been provided for controlling dengue outbreaks based on the analysis of individual interventions, their combinations, timing, and cost-effectiveness. The most effective interventions for early, peak, and post-peak stages have been highlighted, along with guidelines for public health officials on best allocating resources.

## 1.5 Scope of Project

The scope of this project has focused on evaluating the effectiveness of intervention strategies for controlling dengue fever outbreaks in Malaysia, using the ASEI-SVIR epidemiological model. The study specifically targets dengue fever, excluding other vector-borne diseases, and emphasises the dynamics of disease spread and control within a defined regional context. The project has assessed the impact of larvicide (to eliminate breeding sites), fogging (to reduce mosquito populations), and vaccination (to increase immunity against dengue virus), analysing how these measures affect transmission rates and the overall progression of outbreaks.

Simulations have been conducted for different intervention strategies as well as in incorporating optimal control strategies (OCP) in managing disease spread by using Pontryagin's Maximum Principle (PMP) in solving OCPs in the dynamic systems. The project has used Python to implement the ASEI-SVIR model, focusing on a specific time frame rather than long-term impacts or year-over-year trends. Data has been sourced from publicly available epidemiological data from the Ministry of Health Malaysia, the World Health Organization (WHO), and relevant research studies on dengue transmission.

The project is constrained by several assumptions, such as homogeneous mixing of the population and fixed intervention effectiveness rates. It does not account for spatial factors or variables like climate change or human mobility. Additionally, the limitations of the ASEI-SVIR model, including the assumption of a closed population without external infections, have been acknowledged. This scope ensures that the project remains focused, feasible, and relevant to current public health concerns.

## 1.6 Significance of Project

This project has been significant because it provides a comprehensive analysis of the effectiveness of different intervention strategies in controlling dengue fever outbreaks. By using the ASEI-SVIR model, the research has offered valuable insights into how various interventions impact the transmission dynamics of dengue fever. The findings will help public health authorities in Malaysia, and other regions with similar epidemiological profiles to make informed decisions about which interventions to implement during dengue outbreaks. This can ultimately lead to more effective control measures, reduced disease burden, and improved public health outcomes.

## 1.7 Project Schedule

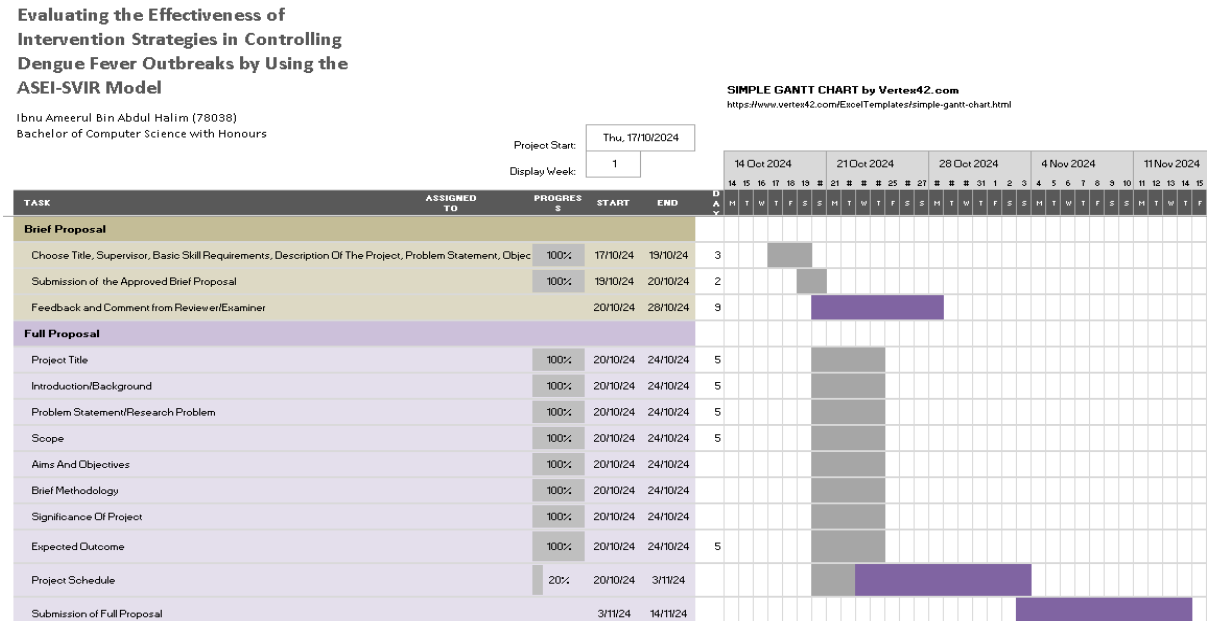


Figure 1. 1. Gantt chart for FYP 1

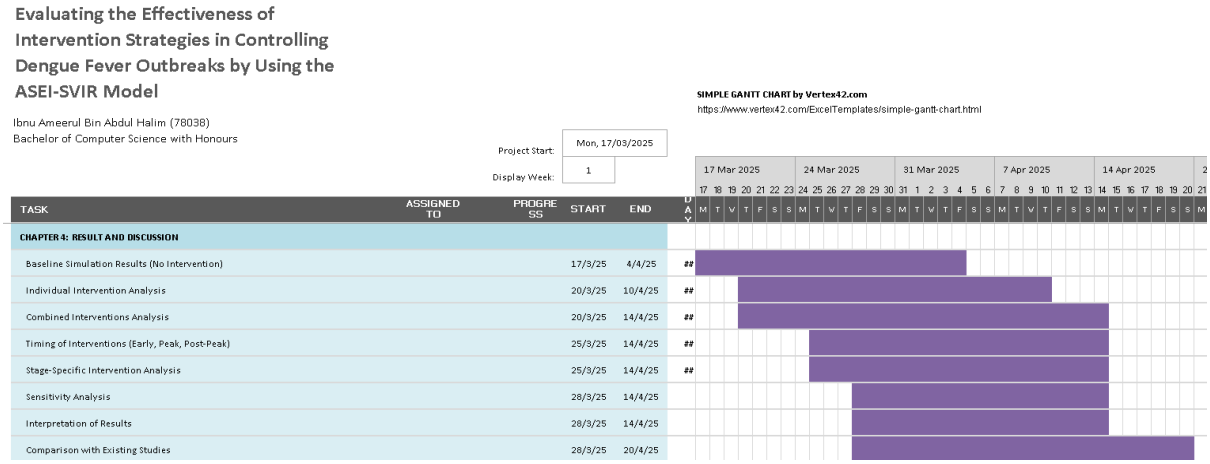


Figure 1. 2. Gantt chart for FYP 2

The Gantt chart has been meticulously prepared, as shown in Figure 1.1 and Figure 1.2, to outline the project timelines and tasks for analysing the effectiveness of intervention strategies against dengue outbreaks using the SEIR model. These schedules have incorporated specific start dates, with Final Year Project (FYP) 1 commencing on October 17, 2024, and FYP 2 beginning on March 17, 2025. Each task has been assigned, and progress stages have been tracked systematically to ensure efficient management of resources and time. The plans

have emphasized weekly tracking of milestones and deliverables, providing a comprehensive framework to monitor the projects until their respective end dates in mid and late 2025. This structured approach has ensured that all activities are well-organized, facilitating the achievement of the research objectives within the projected timeline.

## 1.8 Expected Outcome

This project will provide valuable insights into the effectiveness of various public health interventions for controlling dengue fever outbreaks in Malaysia. By simulating different epidemic scenarios using the ASEI-SVIR model, the project will offer evidence-based recommendations for optimizing intervention strategies like fogging, source reduction, and community engagement. These findings will be crucial for public health authorities in developing more effective outbreak control plans. Moreover, the project's modelling approach can be adapted to other regions or diseases, contributing to the broader field of infectious disease control.

## 1.9 Project Outlines

The project outline provides a structured summary of the study, detailing its focus on using the ASEI-SVIR model to analyse and optimize dengue intervention strategies. It begins with an introduction to the problem, followed by a review of relevant literature on dengue modelling and control measures. The methodology explains the model formulation, data setup, and simulations, while subsequent chapters present and discuss simulation results. Practical recommendations are provided based on findings, and the study concludes with key insights, limitations, and future research directions.

### 1.9.1 Chapter 1: Introduction

This chapter introduces the context of the project, focusing on dengue fever outbreaks and their impact in Malaysia. It explains the problem of controlling dengue and the importance

of using mathematical models like the ASEI-SVIR model to analyse intervention strategies. The objectives, methodology, project scope, significance, timeline, and expected outcomes are defined, providing readers with a clear understanding of the project's purpose and structure.

### 1.9.2 Chapter 2: Literature Review

This chapter reviews existing research related to dengue modelling, particularly using the SIR, SEIR, SVIR and human-vector SEIR model. It explores mathematical approaches used in epidemiology, discusses different dengue control interventions, and compares the model formulation for different models.

### 1.9.3 Chapter 3: Methodology

The methodology chapter details how the ASEI-SVIR model is formulated for this study, including the definitions of compartments and parameters. It describes optimal control problem, solving and setting up the parameters and how various intervention scenarios are simulated. Tools like Python will be used for simulations. The chapter also discusses the assumptions, limitations, and validation of the model, along with the optimal control problem for assessing intervention effectiveness.

### 1.9.4 Chapter 4: Results and Simulation

This chapter presents the results of the simulations. It starts with baseline scenarios without interventions, then by analysing individual strategies' effectiveness (fogging, larvicide, vaccination) and combinations thereof.

### 1.9.5 Chapter 5: Discussion and Recommendations

Results are interpreted and compared with findings from other studies. Based on the simulation results, this chapter offers practical policy recommendations for managing dengue outbreaks in Sarawak. It suggests targeted interventions for different outbreak stages, discusses the cost-effectiveness and feasibility of various strategies, and proposes a comprehensive

strategy for dengue control. The recommendations are grounded in simulation outcomes to provide evidence-based guidelines.

### 1.9.6 Chapter 6: Conclusion and Future Work

The final chapter summarizes the project's key findings, highlighting contributions to dengue modelling and intervention strategies. It also addresses the objective achievements gained from the simulation and analysis. It acknowledges limitations of the study and proposes directions for future works to enhance the effectiveness of dengue control efforts.

# CHAPTER 2: LITERATURE REVIEW

## 2.0 Overview

In this chapter, a comprehensive review of the existing literature is presented to provide a foundation for understanding the dynamics of dengue fever transmission and its control measures. The chapter begins by discussing the role of Aedes mosquitoes, particularly Aedes aegypti, as primary vectors of dengue fever, emphasizing the increasing incidence in Malaysia. It explores the application of mathematical modelling, particularly deterministic and stochastic approaches, in epidemiology, with a focus on SIR and SEIR frameworks. The SEIR model's relevance to dengue is highlighted, including its extensions to account for vector dynamics and vaccination strategies. Various dengue control interventions, such as larvicide, adulticide, and vaccination, are examined, alongside advancements in modelling these strategies through adaptations like the SEI-SEIR and SVIR models. Methods for parameter estimation and their integration into dynamic models are reviewed, emphasizing their importance in disease prediction and management. Additionally, the chapter discusses the role of optimal control theory in devising effective strategies to mitigate dengue transmission. The review identifies research gaps and sets the stage for further investigations into optimising dengue control interventions.

## 2.1 Aedes Mosquitoes and Dengue Fever

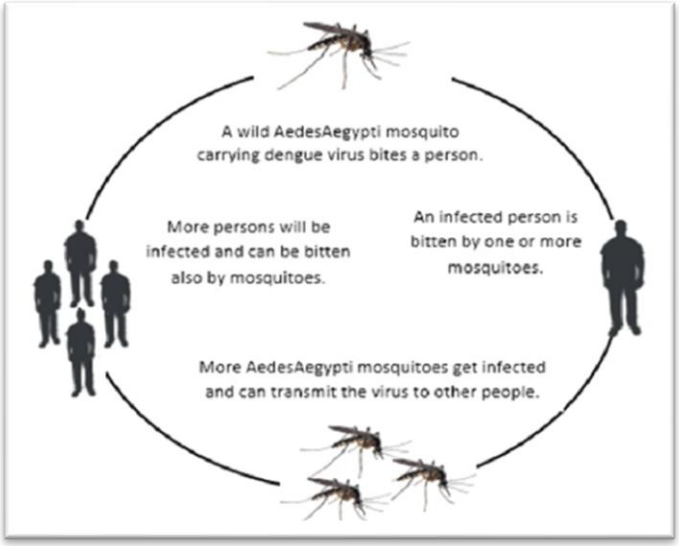


Figure 2. 1. Pictorial representation of dengue virus transmission process

Source: Emmanuel et al. (2023)

Dengue fever, caused by the dengue virus and primarily transmitted by Aedes mosquitoes, remains a critical public health issue in Malaysia. The Aedes Aegypti species is particularly notorious for its role as a vector for dengue transmission. In recent years, a significant surge in dengue cases in Malaysia has been witnessed, necessitating a comprehensive understanding of the factors contributing to these outbreaks and the development of effective intervention strategies. Aedes mosquitoes, especially Aedes Aegypti, are established as the primary vectors responsible for dengue fever transmission. Their life cycle, reproductive habits, and adaptability to urban environments make them particularly effective at spreading the virus. As shown in Figure 2.1, the transmission process occurs when an Aedes mosquito bites an infected individual, subsequently transmitting the virus to subsequent hosts (Utarini et al., 2021). This depicts the critical role of vector management in controlling dengue outbreaks, as the presence and population dynamics of these mosquitoes are directly linked to the incidence of the disease.

## 2.2 Mathematical Modelling in Epidemiology

Mathematical modelling has emerged as a vital tool in epidemiology, particularly in understanding the dynamics of infectious diseases such as dengue and formulating control strategies. The application of mathematical modelling in epidemiology is exemplified by its use during the COVID-19 pandemic. Wang et al. (2020) emphasize the importance of mathematical models, which estimate the potential spread of the virus. Such models have been instrumental in predicting outbreak trajectories, assessing the impact of asymptomatic carriers, and evaluating public health strategies, including social distancing and contact tracing.

Epidemiological modelling serves as a crucial tool in understanding the dynamics of infectious diseases. Two primary approaches dominate this field: deterministic and stochastic models. Deterministic models are characterised by fixed relationships among variables, allowing researchers to predict disease outcomes under specific conditions. Conversely, stochastic models account for randomness and variability in disease transmission, making them essential for capturing the complexities of real-world scenarios.

### 2.2.1 Deterministic Models in Epidemiology

Deterministic models have been widely adopted in epidemiological studies due to their straightforward structure and reduced data requirements. For instance, a study examining the spread of COVID-19 utilized a deterministic compartmental model to categorize the population based on disease status and awareness. This model effectively analysed the impact of social distancing measures on epidemic dynamics, demonstrating how fixed relationships between variables could predict the timing and magnitude of the epidemic's peak (Teslya et al., 2020). The advantages of deterministic models lie in their ability to simplify complex systems and facilitate the understanding of disease dynamics through clearly defined parameters. However, researchers have acknowledged limitations in these models, particularly regarding their

inability to account for variability inherent in disease transmission (Teslya et al., 2020). Therefore, motivated by the above study, the interest is to develop a compartmental deterministic model to evaluate the effectiveness of intervention strategies in controlling dengue fever outbreaks in Malaysia.

## 2.3 Overview of SIR

The SIR model, a cornerstone of epidemiological modelling, delineates the dynamics of disease spread among individuals in a population by classifying individuals into three groups: Susceptible (S), Infected (I), and Recovered (R), as shown in Equation 1. Initially presented by Kermack and McKendrick in 1927, the SIR simplicity allows for a foundational understanding of infectious disease transmission while serving as a basis for more complex models that incorporate additional factors (Brauer, 2005). In the SIR model, a population of size N is partitioned into three separate groups: susceptible (S), infectious (I), and removed (R) such as individuals who have recovered or been immunised (Grimm et al., 2021). Movement between these compartments is represented through a flow diagram shown in Figure 2.2. Epidemiological compartment models assume that all individuals within the same group share identical characteristics, making each group homogeneous (Grimm et al., 2021).

$$\frac{dS}{dt} = -\frac{\beta SI}{N} \tag{1.1}$$

$$\frac{dI}{dt} = \frac{\beta SI}{N} - \gamma I \tag{1.2}$$

$$\frac{dR}{dt} = \gamma I \tag{1.3}$$

Equation 1. Basic SIR model.

The SIR model is described mathematically as an initial value problem, where the starting values $S(t_0 \geq 0, I(t_0 \geq 0)$, and $R(t_0 \geq 0)$ are provided at an initial time $t_0$. The

parameter $\gamma$, commonly known as the mean infectious period, denotes the proportion of infected individuals who recover within a given time interval. It can be calculated as $\gamma = \frac{1}{D}$, Where D represents the average time duration during which an infected individual remains capable of transmitting the disease. The contact rate, denoted as $\beta$, indicates the average number of infectious contacts made by an infected person per unit time. As a result, $N.\beta$ indicates the average number of individuals an infected person is expected to infect per unit of time. The model maintains the total population size as constant, ensuring that the functions $S(t)$ , $I(t)$ , and $R(t)$ satisfy the equation $S(t) + I(t) + R(t) = N$ for all $t \geq t_0$ .

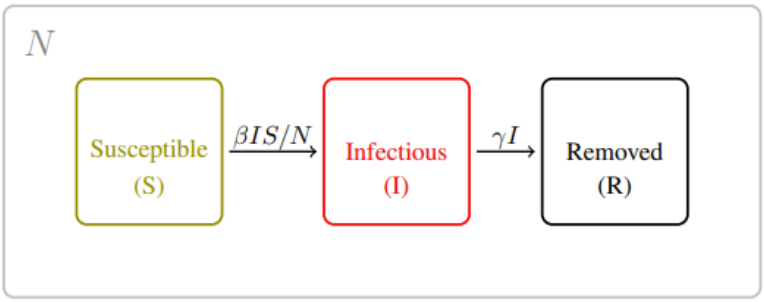


Figure 2. 2. SIR compartmental diagram

Source: (Grimm et al., 2021).

## 2.4 Overview of SEIR

In the standard SIR model, individuals are assumed to become infectious immediately upon infection. However, many infectious diseases include a notable incubation period during which an infected individual is not yet capable of transmitting the disease. To account for this latency phase, the SIR model is expanded to include a fourth compartment, labelled as Exposed (E), as shown in Equation 2. To be more specific, the SIR model is modified by allowing individuals to transition from the susceptible (S) compartment to the exposed (E) compartment, representing those who are infected but not yet infectious. After going through the exposed phase, they then move from the exposed (E) compartment to the infectious (I) compartment.

$$\frac{dS}{dt} = -\frac{\beta SI}{N} \tag{2.1}$$

$$\frac{dE}{dt} = \frac{\beta SI}{N} - kE \tag{2.2}$$

$$\frac{dI}{dt} = kE - \gamma I \tag{2.3}$$

$$\frac{dR}{dt} = \gamma I \tag{2.4}$$

Equation 2. Basic SEIR model

The resulting SEIR model is expressed as an initial value problem, with specified initial conditions $S(t_0 \geq 0), E(t_0 \geq 0), I(t_0 \geq 0)$, and $R(t_0 \geq 0)$. The parameters β and γ are defined as in the SIR model. The extra parameter, $1/k$, represents the mean of an assumed exponential distribution for the exposed period, which is the duration an individual remains in the exposed compartment (E). Movement between these compartments is represented through a flow diagram shown in Figure 2.3. In analogy to the SIR model, the SEIR model is also based on the assumption of a constant population size N with $S(t) + E(t) + I(t) + R(t) = N$ at any time $t \geq t_0$.

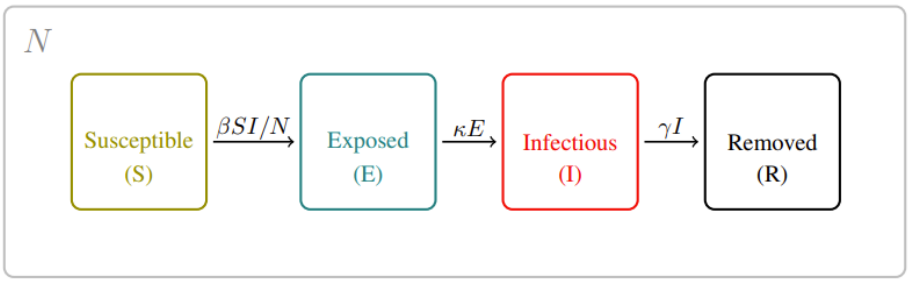


Figure 2. 3. SEIR compartmental diagram

Source: (Grimm et al., 2021).

### 2.4.1 Application to Dengue Fever

Dengue fever, transmitted primarily by Aedes mosquitoes, presents unique challenges and opportunities for modelling using the SEIR framework. The SEIR model is particularly appropriate for dengue due to its consideration of critical disease characteristics, including the incubation period (E) and the infectious period (I). Research indicates that the SEIR model effectively captures the dynamics of dengue transmission, as it mirrors the disease's progression from exposure to recovery (Fouque & Reeder, 2019; Phakhounthong et al., 2018).

For instance, Mwalili et al. (2020) and Morin et al. (2015) demonstrate that the SEIR model can be used to simulate dengue outbreaks in regions with high incidence rates, such as Selangor, Malaysia. These studies highlight the rapid spread of the disease and the importance of understanding how the virus propagates through the population. The findings suggest that the SEIR model provides valuable insights into infection rates and potential control measures, which are critical for public health strategies aimed at mitigating dengue outbreaks.

### 2.4.2 Adaptations in SEIR for Vector-Borne Diseases (SEI-SEIR)

One significant adaptation involves incorporating vector population dynamics into the SEIR framework. The role of Aedes mosquitoes as vectors necessitates modifications to transmission rates and the introduction of additional compartments or parameters to account for the interaction between the mosquito population and the human population (Bouzid et al., 2014; Eder et al., 2018).

According to Syafruddin and Noorani (2012), the SEIR model is adapted to account for transmission between human hosts and mosquito vectors, as shown in Equation 3. The human population ($N_h$) is divided into four compartments: individuals susceptible to dengue infection ($S_h$), those exposed to the virus ($E_h$), infected individuals ($I_h$), and individuals who have recovered ($R_h$). Meanwhile, the mosquito vector population ($N_v$) is classified into three groups:

mosquitoes susceptible to dengue infection ($S_v$), those exposed to the virus ($E_v$), and infected mosquitoes ($I_v$). This compartmentalisation as shown in Figure 2.4, allows for the modelling of disease dynamics and interactions between hosts and vectors, providing insights into the spread and control of dengue fever.

Human Population:

$$\frac{dS_h}{dt} = \mu_h N_h - (\frac{\beta_h b I_v}{N_h} + p + \mu_h) S_h \tag{3.1}$$

$$\frac{dE_h}{dt} = \left(\frac{\beta_h b I_v}{N_h} + p\right) S_h - (\mu_h + \varphi_h) E_h \tag{3.2}$$

$$\frac{dI_h}{dt} = \varphi_h E_h - (\mu_h + \gamma_h + \alpha_h) I_h \tag{3.3}$$

$$\frac{dR_h}{dt} = \gamma_h I_h - \mu_h R_h \tag{3.4}$$

Vector Population:

$$\frac{dS_v}{dt} = A - (\frac{\beta_v b I_h}{N_h} + \mu_v) S_v \tag{3.5}$$

$$\frac{dE_v}{dt} = \frac{\beta_v b I_h}{N_h} S_v - (\mu_v + \delta_v) E_v \tag{3.6}$$

$$\frac{dI_v}{dt} = \delta_v E_v - \mu_v I_v \tag{3.7}$$

Equation 3. Vector-human SEI-SEIR dengue model

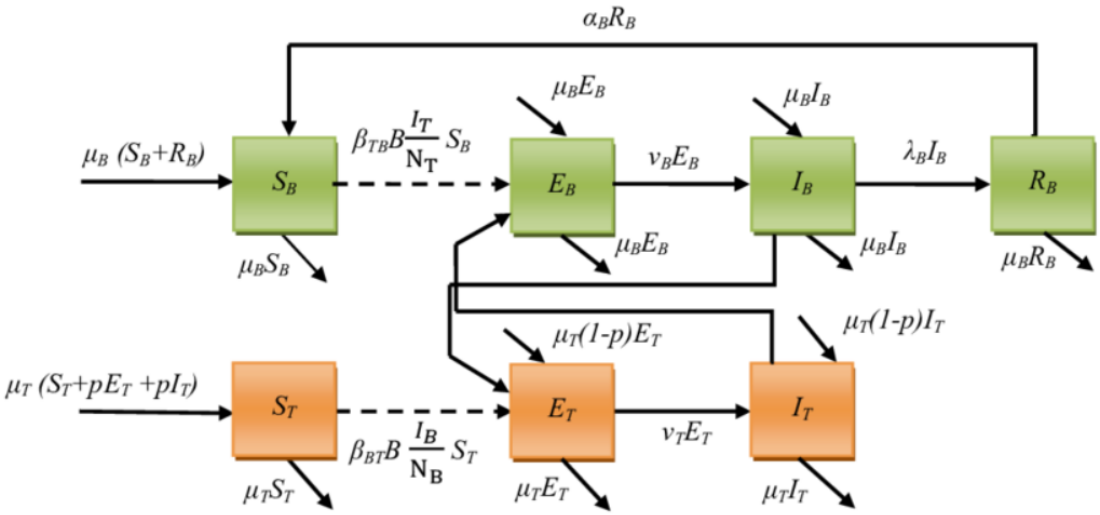


Figure 2. 4. SEI-SEIR dengue model compartmental diagram

Source: (Abdelheq et al., 2019)

Similarly, a study to analyse the transmission dynamics of dengue fever over time in subtropical Malaysia done by Emmanuel et al. (2023) has utilised this SEI-SEIR model which incorporated vector compartments in the formulation of the model.

### 2.4.3 Numerical Solutions for SEIR Models

The practical application of SEIR models in real-world scenarios necessitates robust numerical solutions. Common methods such as Euler's Method and the Runge-Kutta method have been employed to solve SEIR equations, as highlighted by Kumar et al. (2020b). These numerical techniques are essential for accurately simulating disease dynamics and evaluating intervention strategies. For instance, the integration of advanced numerical methods with SEIR modelling allows for improved forecasting accuracy, as demonstrated in studies assessing COVID-19 dynamics and intervention impacts (Sun et al., 2020).

Moreover, the incorporation of real-time data with mathematical modelling techniques, as seen in the COVID Symptom Study, exemplifies how mobile technology can enhance model

predictions by forecasting hotspots of incidence (Drew et al., 2020). This underscores the importance of numerical solutions in adapting models to evolving epidemiological landscapes.

## 2.5 Dengue Control Intervention Strategies

Dengue fever, transmitted primarily by Aedes mosquitoes, poses a significant public health challenge in tropical and subtropical regions. Effective control measures are critical for reducing disease incidence and mitigating outbreaks. This literature review synthesizes current research findings on various dengue control interventions, including fogging (adulticide), source reduction (larvicide), vaccination, and combined intervention approaches.

### 2.5.1 Larvicide and Adulticide Interventions (ASEI-SEIR)

Abidemi and Aziz (2020) proposed a mathematical model called ASEI-SEIR, which describes the transmission dynamics of dengue fever by incorporating control strategies such as personal protection, larvicide, and adulticide. The model considers three populations: humans, aquatic mosquitoes, and female mosquitoes. The human population is categorized into four groups: susceptible individuals ($S_h$), exposed individuals (infected but not yet infectious, $E_h$), infectious individuals ($I_h$), and recovered individuals ($R_h$). The aquatic mosquito population is modelled based on a proportion of the total human population. Meanwhile, the female mosquito population is divided into four compartments: aquatic stage ($A_m$), susceptible ($S_m$), exposed ($E_m$), and infectious mosquitoes ($I_m$). The compartmental model for ASEI-SEIR model is illustrated in Figure 2.5.

Three control variables, $0 \leq u_i(t) \leq 1$ $(for\ i = 1, 2, 3)$, are incorporated to represent efforts directed towards human personal protection (e.g., use of mosquito repellents, insecticide-treated bed nets, and wearing long-sleeved clothing), larvicide application, and adulticide application, respectively. The control $u_1(t)$ is implemented to reduce effective contact rates between infectious humans and mosquitoes, as well as between infectious

mosquitoes and humans. The control $u_2(t)$ targets the aquatic mosquito stage, focusing on reducing the population of mosquito eggs and larvae. Lastly, the control $u_3(t)$ is aimed at preventing the proliferation of the adult mosquito population. The study concludes that the most cost-effective strategy in their model combines adulticide controls with personal protection measures.

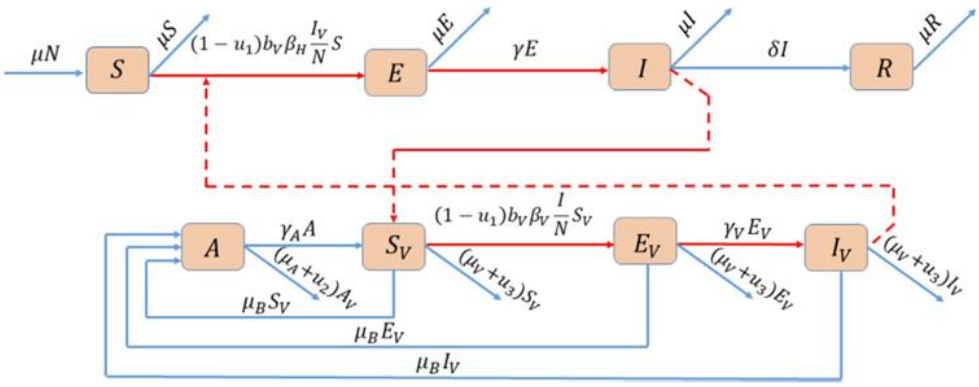


Figure 2. 5. ASEI-SEIR compartmental diagram

Source: (Abidemi and Aziz, 2020)

Another similar study conducted by Bhuju et al. (2022), where in this deterministic model, fumigation and bed nets are employed as intervention strategies to eliminate dengue, with the assumption that mosquitoes do not develop resistance to fumigation. However, the transmission and recovery processes of the disease are uncertain. The disease transmission coefficient ($\beta_h$) between susceptible and infected individuals, the recovery rate ($c_h$), and the mosquito biting rate ($b$) are treated as fuzzy numbers. To represent the variability of virus load on the parameters $\beta_h$ and $c_h$), membership functions $\beta_h(v)$ and $c_h(v)$ are utilized for the transmission rate and recovery rate, respectively. Similarly, the membership function $b(k,r)$ is applied to describe the biting rate, incorporating the impact of bed net usage ($k$) and the effectiveness of bed nets ($r$).

### 2.5.2 Integrating Vaccination into SEIR Model

The introduction of vaccines, such as Dengvaxia and Qdenga, into the SEIR model as an additional compartment (SVIR) is vital for accurately simulating dengue transmission dynamics. Flasche et al. (2016) underscore the importance of assessing the long-term safety and efficacy of the Dengvaxia vaccine across different transmission settings, advocating for its inclusion in modelling efforts to evaluate the impact on disease burden and hospitalization rates. The presence of a vaccination compartment allows researchers to explore how vaccination strategies can effectively reduce dengue incidence, especially in areas with moderate to high endemicity, thereby aligning with predictions made by the SEIR framework. However, the findings also reveal potential risks associated with vaccination in low transmission settings, emphasizing the need for careful modelling to avoid adverse outcomes, such as increased hospitalization among dengue-naïve individuals. This highlights a significant knowledge gap in understanding the nuanced effects of vaccination across varying epidemiological contexts is crucial for informing public health policies and intervention strategies. Moreover, Rodrigues et al. (2014) present a mathematical perspective on vaccination models, emphasizing the need for optimal control strategies in combating dengue. This research indicates that mathematical modelling can aid in identifying effective vaccination approaches and underscores the necessity of integrating vaccination dynamics into the SEIR model.

### 2.5.3 Overview of ASI-SVIR Model

A new compartment is introduced in this model, Vaccinated (V), replacing the Exposed (E) compartment in SEIR model as shown in Figure 2.6. The compartment $V_h$ represents the segment of the human population that has been vaccinated, distinguishing between immunity acquired through vaccination and that obtained from recovering after infection (Rodrigues et

al., 2014). For mosquitoes, there is no resistant phase due to their short lifespan and the assumption that the disease transmission coefficient remains constant. Additionally, it is assumed that both humans and mosquitoes are born susceptible to the disease (Rodrigues et al., 2014). Equation 4 below shows the comprehensive model equations for the ASI SVIR model according to Rodrigues et al. (2014).

$$\frac{dS_h}{dt} = (1-p)\mu_h N_h - (B\frac{\beta_{mh} I_m}{N_h} + \mu_h)S_h \quad (4.1)$$

$$\frac{dV_h}{dt} = p\mu_h N_h - \mu_h V_h \quad (4.2)$$

$$\frac{dI_h}{dt} = B\frac{\beta_{mh} I_m}{N_h} S_h - (\eta_h + \mu_h)I_h \quad (4.3)$$

$$\frac{dR_h}{dt} = \eta_h I_h - \mu_h R_h \quad (4.3)$$

$$\frac{dA_m}{dt} = \varphi\left(1 - \frac{A_m}{kN_h}\right)(S_m + I_v)) - (\eta_A + \mu_A)A_m \quad (4.4)$$

$$\frac{dS_m}{dt} = \eta_A A_m - (B\frac{\beta_{hm} I_h}{N_h} + \mu_m)S_m \quad (4.5)$$

$$\frac{dI_m}{dt} = B\frac{\beta_{hm} I_h}{N_h} S_m - \mu_m I_m \quad (4.6)$$

Equation 4. ASI-SVIR dengue model incorporating vaccinated compartment in human population

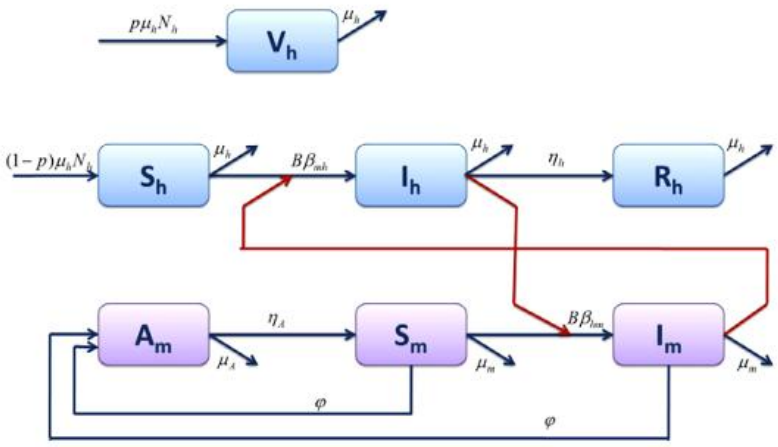


Figure 2. 6. ASI-SVIR compartmental diagram

Source: (Rodrigues et al., 2014)

In SVIR model, a continuous vaccination strategy is applied, where a proportion $p$ (where $0 \leq p \leq 1$) of newborns are vaccinated by default. The model assumes that immunity acquired through vaccination is identical to the natural immunity gained by individuals who recover from the disease without any intervention. It is assumed that the vaccine is perfect, providing lifelong immunity.

Similarly, in a study to investigate the influence of spatial heterogeneous environment on long-term dynamics of a reaction-diffusion SVIR epidemic model with relapse by Zhu et al. (2019), vaccines have become crucial in preventing and controlling disease transmission with advancements in science, technology, and medical standards and thus, the model incorporates a group of individuals who have received preventive vaccination. Another study related to the incorporation of the Vaccinated (E) compartment also has been done by Attaullah et al. (2022). In this study, an autonomous nonlinear epidemic model (SVIR model) was developed to analyse the transmission dynamics among susceptible, vaccinated, infected, and recovered individuals, incorporating nonlinear saturation incidence and vaccination rates. The inclusion of a nonlinear saturation incidence rate effectively enhances human immunity, thereby reducing the mortality rate of infected individuals (Attaullah et al., 2022). The study

provides a comprehensive examination of the model's equilibrium points, the basic reproduction number (R0), and both local and global stability. The findings reveal that the disease-free equilibrium is stable when R0 < 1, while an endemic equilibrium emerges, indicating the disease persists within the population, when R0 > 1 (Attaullah et al., 2022).

Table 1. Summary of reviewed models from research papers.

| Model | Description | Key Features | Limitations | Source |
|---|---|---|---|---|
| SIR | The SIR (Susceptible-Infected-Recovered) model is a foundational compartmental model in epidemiology that models the flow of individuals through the stages of being susceptible to a disease, becoming infected, and eventually recovering with immunity. | Simple structure that captures basic infection-recovery dynamics; mathematically tractable; widely used as the starting point for more complex models. | Assumes individuals become infectious immediately after exposure; does not account for latency or incubation period. | Grimm et al. (2021) |
| SEIR | The SEIR (Susceptible-Exposed-Infected-Recovered) model extends the SIR framework by adding an Exposed (E) compartment, allowing the model to account for the incubation period. | Accounts for incubation phase; better suited for diseases with latency; retains the mathematical simplicity of SIR with an added compartment. | Assumes constant population size and homogeneous mixing; does not model external factors like vector-borne transmission. | Grimm et al. (2021) |
| SEI-SEIR | This model modifies the SEIR framework to include mosquito vector | Effectively models vector-borne | Does not directly incorporate intervention | Syafruddin & Noorani (2012); |

| | | | | |
|---|---|---|---|---|
| (Human-Vector) | dynamics in addition to human compartments. | transmission; captures both host and vector states; suitable for studying dengue fever. | strategies; may require extensive parameter calibration. | Emmanuel et al. (2023) |
| ASEI-SEIR | The ASEI-SEIR model incorporates Aquatic (A), Susceptible (S), Exposed (E), and Infected (I) mosquito stages, along with standard SEIR compartments for humans. It introduces three optimal control interventions which are personal protection, larvicide. | Includes both larval and adult mosquito stages; integrates optimal control theory; can evaluate cost-effectiveness of intervention strategies. | Assumes control strategies act independently; fixed mosquito biting rate may not reflect environmental variability. | Abidemi & Aziz (2020); Bhuju et al. (2022) |
| ASI-SVIR | The ASI-SVIR model replaces the Exposed (E) compartment in humans with a Vaccinated (V) compartment to evaluate the impact of continuous vaccination strategies. | Focuses on vaccination as the primary control strategy; allows exploration of vaccination policies. | Oversimplifies the mosquito infection process by excluding the exposed stage. | Rodrigues et al. (2014) |

## 2.6 Parameter Estimation Methods for Epidemiological Models

Accurate parameter estimation is crucial in epidemiological modelling to understand the physical characteristics of diseases and develop effective control strategies. Adequate data availability further enhances parameter estimation and increases the reliability of the model for disease prediction and management. Various methods have been employed for parameter estimation in dynamic models, including ordinary least squares, maximum likelihood estimation, moments estimation, Markov Chain Monte Carlo (MCMC) methods, derivative-free optimization algorithms, and algorithms such as Levenberg-Marquardt and Trust-Region-Reflective (Berhe et al., 2019). Other researchers, including Agusto and Khan (2018), and Abidemi and Aziz (2020), have used various estimation techniques based on available data to explore the effects of epidemiological factors on disease transmission and control strategies.

One commonly used approach for parameter estimation in dynamic models is the nonlinear least squares method. This method involves solving a system of ordinary differential equations (ODEs) and fitting the model to observed data by minimizing the sum-of-squares error. The parameter estimation process involves formulating the system of ODEs as:

$$\frac{dy}{dt} = f(y, \theta, t), B \qquad y(t_0) = y_0 \tag{5}$$

Equation 5. Formulation of the system of ODEs for parameter estimation

where $y$ represents the dependent variables and $\theta$ denotes the parameters to be estimated (Berhe et al., 2019). The error, calculated as the sum-of-squares between observed data $\widehat{y_i}$ and model predictions $y_i(\theta)$, is represented as:

$$E(\theta) = \sum_{i=1}^{n} (\widehat{y_i} - y_i(\theta))^2 \tag{6}$$

Equation 6. Calculating parameter estimation error as sum-of-the squares

The objective function is then minimized as:

minimize E(θ), subject to the ODE constraints.

The algorithm typically begins with initial parameter guesses and uses numerical solvers, such as MATLAB's ode45, to solve the ODE system iteratively. Optimization routines like *lsqnonlin* with Trust-Region-Reflective algorithms are employed to minimize the error and update parameter estimates. This process continues until convergence criteria are met, yielding the optimal parameter values. Studies by Abidemi and Aziz (2020) and Agusto and Khan (2018) have successfully applied similar approaches to model dengue fever dynamics in Malaysia and Pakistan, respectively. These studies utilized least squares estimation methods to fit model parameters to real outbreak data, demonstrating the utility and reliability of this approach in epidemiological modelling. In summary, parameter estimation using nonlinear least squares provides a robust framework for fitting dynamic models to observed data, facilitating the accurate prediction and control of disease outbreaks. The integration of this method with advanced optimization algorithms enhances its efficiency, making it an essential tool in epidemiological research.

## 2.7 Optimal Control Problem to Control a Dynamic System

A foundational study by Aldila et al. (2013) introduces an OCP arising from a dengue disease transmission model, emphasizing the importance of optimal control strategies in managing disease spread. The authors highlight the significance of utilizing a quadratic cost functional to evaluate control measures aimed at reducing transmission rates. This study sets the stage for subsequent research that builds upon the theoretical framework established in the context of dengue fever and other diseases. Using Pontryagin's Maximum Principle (PMP) provides a robust analytical tool for solving OCPs in dynamic systems, including dengue

transmission models. The principle helps establish necessary conditions for optimal control, enabling researchers to derive strategies that minimize the spread of the disease while balancing societal and economic implications. The work of Chen et al. (2017) showcases the utility of PMP in developing control measures that incorporate both symptomatic and asymptomatic infectious classes, thereby enhancing the understanding of dengue dynamics.

The emphasis on quadratic cost functionals in the literature is significant, as it aligns with findings from studies in other fields. For instance, Wang et al. (2014) propose a mixed-integer quadratic programming (MIQP) approach for dynamic economic dispatch, which parallels the need for efficient control strategies in epidemiological contexts. Although these studies focus on different applications, the underlying mathematical principles of quadratic programming and cost optimization remain relevant. The sensitivity analysis of threshold dynamics is critical for understanding the factors that influence dengue transmission. The work by Chen et al. (2017) identifies key parameters such as the biting rate and the rate of asymptomatic cases as significant influencers of the basic reproduction number. This insight is valuable for public health initiatives aimed at reducing transmission, advocating for strategies that focus on mosquito population control and preventive measures.

## 2.8 Summary of Key Findings and Research Direction

The literature review highlights the significant role of Aedes mosquitoes, particularly *Aedes Aegypti*, in the transmission of dengue fever and underscores the necessity for robust intervention strategies to mitigate outbreaks in Malaysia. Mathematical models, such as the ASEI-SEIR and SVIR frameworks, are pivotal in understanding dengue dynamics and evaluating control measures. Deterministic compartmental models, including adaptations like SEIR for vector-host dynamics and SVIR for vaccination, offer valuable insights into disease progression and intervention impacts. Larvicide, adulticide (fogging), and vaccination have

emerged as key strategies, with studies advocating for integrated approaches to optimize effectiveness. These models facilitate quantitative evaluations of interventions, emphasizing the need for tailored strategies like combining adulticide with personal protection or integrating vaccination into control efforts. This research aims to build on these findings by employing the ASEI-SVIR model to systematically assess the effectiveness of vaccination, fogging, and larvicide interventions in controlling dengue outbreaks in Malaysia.

# CHAPTER 3: METHODOLOGY

## 3.0 Methodology Overview

This chapter explores the ASEI-SVIR epidemiological model, incorporating fogging, larvicide, and vaccination as control strategies to study dengue fever transmission dynamics. The model is calibrated using Malaysia's 2024 dengue case data to estimate parameters such as mosquito biting rates, transmission probabilities, and larval mortality rate. Optimal control theory is applied to analyse the impact of various intervention strategies, including combinations of larvicide, fogging, and vaccination. Simulations are performed using the fourth-order Runge-Kutta method in python. The findings aim to assist Malaysian authorities in assessing the effectiveness of mosquito control measures to reduce dengue incidence.

## 3.1 ASEI-SVIR Model Formulation

In this research, the model is based on the ASEI-SEIR model for the optimal control strategies for dengue fever, a study by Abidemi and Aziz (2020). This model also incorporated the SVIR models by Attaullah et al. (2022) and Rodrigues et al. (2014) where the Vaccinated (V) compartment is introduced in both of their studies, replacing the Exposed (E) compartment in the typical SEIR model.

### 3.1.1 Defining Compartments

The vector-host transmission model comprises four mosquito compartments which are Aquatic ($A_v$), Susceptible ($S_v$), Exposed ($E_v$), and Infected ($I_v$), and four human compartments which are Susceptible ($S_h$), Vaccinated ($V_h$), Infected ($I_h$), and Recovered ($R_h$). The total mosquito population ($N_v$) is the sum of $S_v$, $E_v$, and $I_v$, while the total human population ($N_h$) is the sum of $S_h$, $V_h$, $I_h$, and $R_h$, with $N_h$ set to 34,058,800, based on Malaysia's 2024 population (Department of Statistics Malaysia, 2024). This study introduces a new vaccinated class ($V_h$),

representing the segment of the human population that is vaccinated is considered to differentiate the immunity gained through vaccination from that acquired through recovery from the disease (Rodrigues et al., 2014).

### 3.1.2 Assumptions Made During Formulation

The study focuses on *Aedes aegypti* mosquitoes and a single dengue virus variant, assuming recovered individuals gain lifelong immunity while infected mosquitoes never recover (Khan et al., 2014). The dengue vaccine is not fully effective; vaccinated individuals may still be infected, and immunity wanes over 6–10 years (Thisyakorn et al., 2022). The vaccination is considered thorough, assuming 100% vaccination coverage across all age groups. Takeda's TAK-003 vaccine is used with an assumed efficacy of 80.2% (Upcoming Vaccines Dengue, 2023). The aquatic mosquito population $A(t)$ is modeled as proportional to the total human population, $A(t) = kN(t)$ (Abidemi and Aziz, 2020). The model incorporates three control variables $u_1(t), u_2(t),\ and\ u_3(t)$, targeting larvicide, fogging, and vaccination, respectively. Control $u_1(t)$ reduces mosquito eggs and larvae, $u_2(t)$ limits adult mosquito proliferation, and $u_3(t)$ boosts human immunity against dengue.

### 3.1.3 ASEI-SVIR Model

The dynamics of host-vector dengue fever are described using a nonlinear system of differential equations, presented as a set of ordinary differential equations (ODEs) as shown in Equation 7. These equations outline the changes in the number of individuals within each compartment over time. Additionally, a detailed list of parameter definitions is displayed in Table 1, along with compartmental diagrams, is provided as shown in Figure 3.1 and Figure 3.2, to enhance understanding of the model structure.

Mosquito Compartment:

Pre-adult / Larva: $$\frac{dA_v}{dt} = \varphi\left(1 - \frac{A_v}{kN_h}\right)(S_v + E_v + I_v) - (\omega + \mu_A + u_1)A_v \quad (7.1)$$

Susceptible Adult: $$\frac{dS_v}{dt} = \omega A_v - (B\frac{\beta_v I_h}{N_h} + \mu_v + u_2)S_v \quad (7.2)$$

Exposed Adult: $$\frac{dE_v}{dt} = B\frac{\beta_v I_h}{N_h}S_v - (\delta + \mu_v + u_2)E_v \quad (7.3)$$

Infected Adult: $$\frac{dI_v}{dt} = \delta E_v - (\mu_v + u_2)I_v \quad (7.4)$$

Human Compartments:

Susceptible: $$\frac{dS_h}{dt} = \mu_h N_h + \theta V_h - (B\frac{\beta_h I_v}{N_h} + \mu_h + u_3)S_h \quad (7.5)$$

Vaccinated: $$\frac{dV_h}{dt} = u_3 S_h - (\theta + \sigma B\frac{\beta_h I_v}{N_h} + \mu_h)V_h \quad (7.6)$$

Infected: $$\frac{dI_h}{dt} = B\frac{\beta_h I_v}{N_h}S_h + \sigma B\frac{\beta_h I_v}{N_h}V_h - (\gamma + \mu_h)I_h \quad (7.7)$$

Recovered: $$\frac{dR_h}{dt} = \gamma I_h - \mu_h R_h \quad (7.8)$$

Equation 7. ASEI-SVIR dengue vector model with control variables

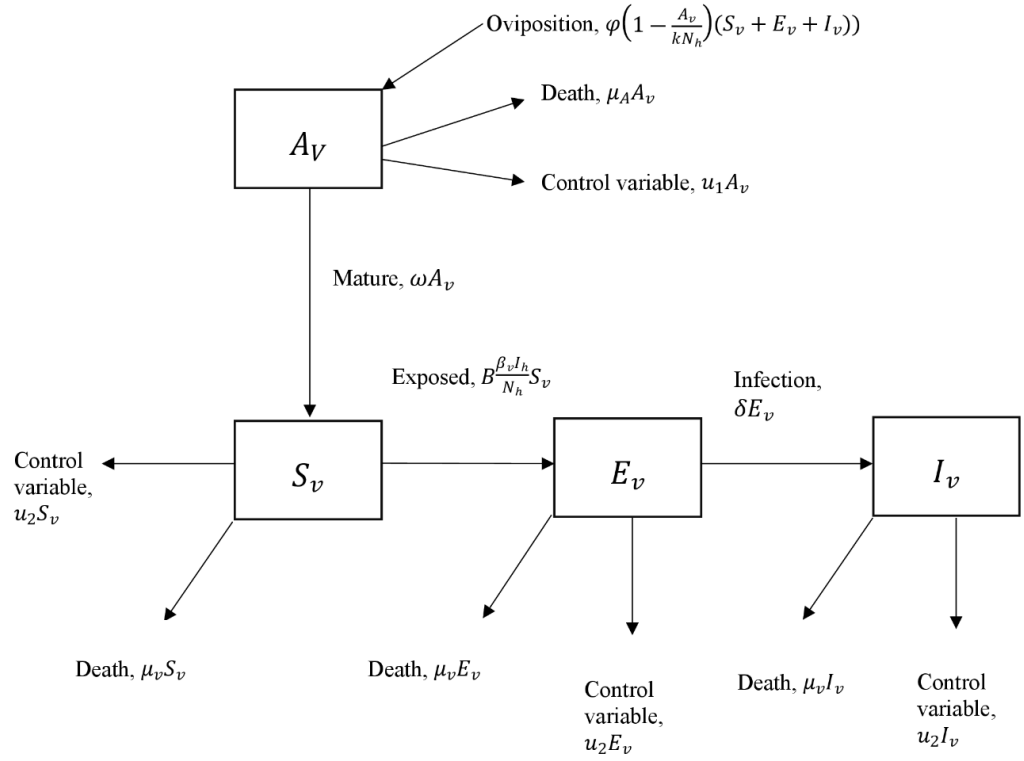


Figure 3. 1. Vector population compartmental diagram in ASEI-SVIR model

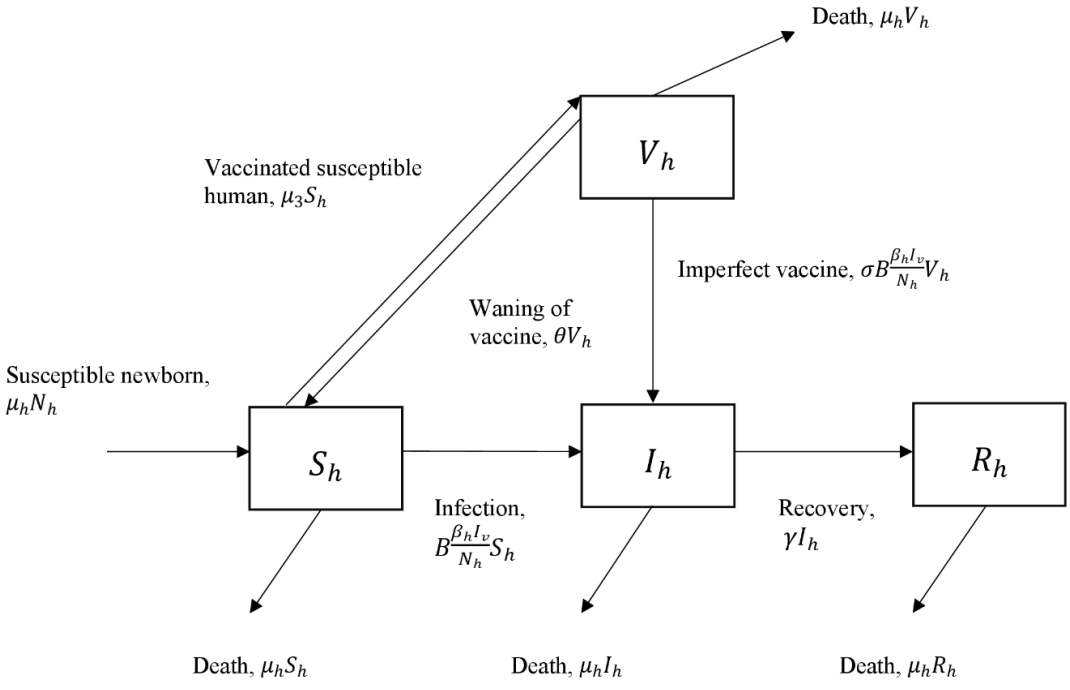


Figure 3. 2. Human population compartmental diagram in ASEI-SVIR model

Table 2. Parameters description for the ASEI-SVIR model

| Parameter | Description |
|---|---|
| $A_v$ | Pre-adult mosquito |
| $S_v$ | Susceptible adult female mosquito |
| $E_v$ | Exposed adult female mosquito |
| $I_v$ | Infected adult female mosquito |
| $N_v$ | Total adult female population mosquito |
| $S_h$ | Susceptible human group |
| $V_h$ | Vaccinated human group |
| $I_h$ | Infected human group |
| $R_h$ | Recovered human group |
| $N_h$ | Overall human group |
| $t$ | Duration of time |
| $\varphi$ | Oviposition rate (egg deposition rate per individual) |
| $k$ | Mosquito larvae density per person |
| $\omega$ | Larvae development rate to adult |
| $\mu_A$ | Larvae natural death rate |
| $B$ | Mosquito bite rate |
| $\beta_v$ | Infection transmission rate from infected humans to susceptible mosquitoes |
| $\mu_v$ | Mosquito death rate |
| $\delta$ | Rate of disease advancement in exposed mosquitoes |
| $\mu_h$ | Human death rate / birth rate |
| $\theta$ | Vaccine waning rate |

| | |
|---|---|
| $\boldsymbol{\beta_h}$ | Infection transmission rate from infected mosquitoes to susceptible humans |
| $\boldsymbol{\sigma}$ | Proportion of vaccinated human being infected (vaccine efficacy = 1 - $\sigma$) |
| $\boldsymbol{\gamma}$ | Human recovery rate |
| $\boldsymbol{u_1}$ | Control variables for larvicide |
| $\boldsymbol{u_2}$ | Control variables for fogging |
| $\boldsymbol{u_3}$ | Control variables for vaccination |

### 3.1.4 Pre-intervention Model

According to Abidemi and Aziz (2020), the parametrization of the dengue fever (DF) model involves examining a scenario where no efforts are allocated to any of the three control measures, represented $u_1(t) = u_2(t) = u_3(t) = 0$. Under these conditions, the non-autonomous DF model simplifies into an autonomous system of ordinary differential equations (ODEs), expressed as shown in Equation 8 below:

Mosquito Compartment:

Pre-adult / Larva: $$\frac{dA_v}{dt} = \varphi\left(1 - \frac{A_v}{kN_h}\right)(S_v + E_v + I_v) - (\omega + \mu_A)A_v \quad (8.1)$$

Susceptible Adult: $$\frac{dS_v}{dt} = \omega A_v - (B\frac{\beta_v I_h}{N_h} + \mu_v)S_v \quad (8.2)$$

Exposed Adult: $$\frac{dE_v}{dt} = B\frac{\beta_v I_h}{N_h}S_v - (\delta + \mu_v)E_v \quad (8.3)$$

Infected Adult: $$\frac{dI_v}{dt} = \delta E_v - \mu_v I_v \quad (8.4)$$

Human Compartments:

Susceptible: $$\frac{dS_h}{dt} = \mu_h N_h + \theta V_h - (B\frac{\beta_h I_v}{N_h} + \mu_h)S_h \quad (8.5)$$

Vaccinated: $$\frac{dV_h}{dt} = -(\theta + \sigma B\frac{\beta_h I_v}{N_h} + \mu_h)V_h \quad (8.6)$$

Infected: $$\frac{dI_h}{dt} = B\frac{\beta_h I_v}{N_h}S_h + \sigma B\frac{\beta_h I_v}{N_h}V_h - (\gamma + \mu_h)I_h \quad (8.7)$$

Recovered: $$\frac{dR_h}{dt} = \gamma I_h - \mu_h R_h \quad (8.8)$$

Equation 8. Pre-intervention ASEI-SVIR dengue vector model

### 3.2 Data Fitting

To establish the parameters for the dengue fever (DF) model, the initial conditions (ICs) for the state variables are specified to represent the 2024 dengue outbreak in Malaysia. According to the Department of Statistics Malaysia (2024), the total human population in 2024 is approximated at $N_h(0)$ = 34,058,800. Initially, the vaccinated population is set to $V_h(0)$ = 0, while the infectious population begins with $I_h(0)$ = 3,181. Assuming no recovered individuals at the outbreak's onset, $R_h(0)$ = 0. Therefore, the initial susceptible human population is calculated as $S_h(0) = N_h(0) - V_h(0) - I_h(0) - R_h(0)$ = 34,055,619. For the mosquito population, the aquatic stage population at the start is given by $A_v(0) = k.N_h(0) = 3.N_h(0)$ = 102,176,400. The exposed and infectious mosquito populations are both initially assumed to be $E_v(0)$ = 100,000 and $I_v(0)$ = 100,000 respectively. Consequently, the initial susceptible mosquito population is determined as $S_v(0) = 4.N_h(0) - E_v(0) - I_v(0)$ = 136,035,200.

Table 3. Parameter estimation values for the dengue model

| Parameter | Value | Source |
|---|---|---|
| $\varphi$ | 5.1 | Fitted |
| $k$ | 39.9 | Fitted |
| $\omega$ | 0.897548 | Fitted |
| $\mu_A$ | 0.42 | (Abidemi and Aziz, 2020) |
| $B$ | 0.71 | Fitted |
| $\beta_v$ | 0.51 | Fitted |
| $\mu_v$ | 0.7 | (Rodrigues et al., 2014) |
| $\delta$ | 0.51 | Fitted |
| $\mu_h$ | 0.0069 | (MOH, 2023) |
| $\theta$ | 0.00189 | (Shafie et al., 2017) |
| $\beta_h$ | 0.11 | Fitted |
| $\sigma$ | 0.198 | (Upcoming Vaccines Dengue, 2023) |
| $\gamma$ | 0.7 | (Abidemi and Aziz, 2020) |

Additionally, certain parameter values are sourced from existing literature, while others are estimated or calibrated using dengue outbreak data from Malaysia in 2024, retrieved from the Ministry of Health (MOH) website. The remaining parameters are fitted to the data using nonlinear least squares, implemented via the curve fit function from the SciPy library as shown in Table 3.2.

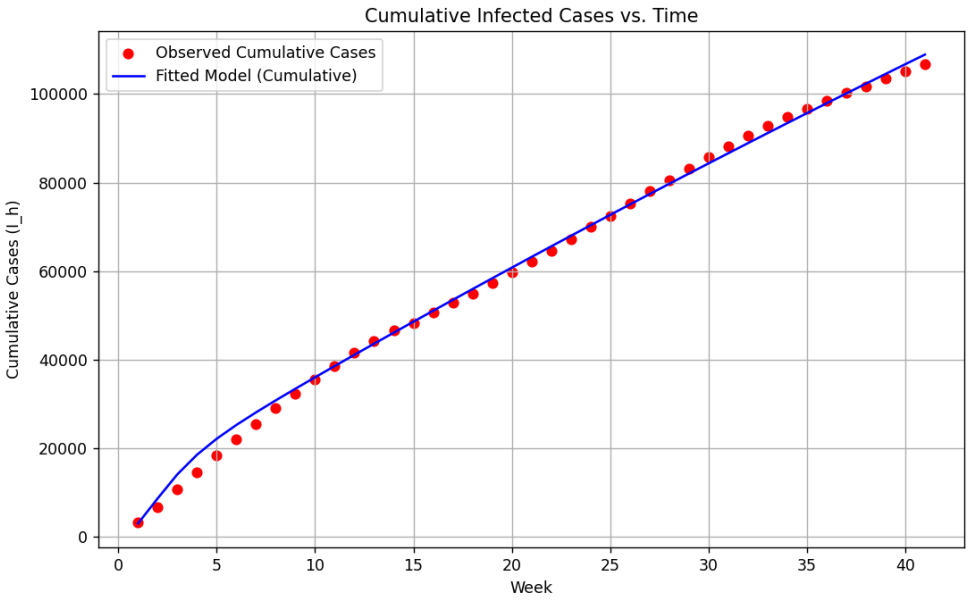


Figure 3. 3. Result of the data fitted of the number of infected individuals in 2024 Malaysia outbreak to the ASEI-SVIR model

After calibrating the DF model to the 2024 Malaysia dengue outbreak data as, the estimated parameter values are as follows: $\varphi = 5.1$, $k = 39.9$, $\omega = 0.897548$, $B = 0.71$, $\beta_h = 0.11$, $\beta_v = 0.51$, and $\delta = 0.51$. Figure 3.3 illustrates the cumulative reported DF cases alongside the model's output.

## 3.3 Optimal Control Problem Formulation

This section focuses on formulating the optimal control problem (OCP) for the non-autonomous system that models Dengue Fever transmission dynamics. Pontryagin's Maximum Principle (PMP) is applied to facilitate a detailed analysis, as it is a commonly employed method in studies addressing optimal control (OC) within dynamic systems (Abidemi and Aziz, 2020). The cost functional (CF) in this formulation is quadratic with respect to the control terms, aligning with similar research approaches (Abidemi and Aziz, 2020). Hence, the problem is given as follows:

$$minimize\ J(u_1, u_2, u_3) = \int_0^{t_f} (W_1 I_v + W_2 I_h + \frac{W_3}{2} u_1^2 + \frac{W_4}{2} u_2^2 + \frac{W_5}{2} u_3^2)\, dt \qquad (9)$$

Equation 9. Objective function for optimal control problem

where $t_f$ is the final time for control administration. The specification of CF involves minimization of the sizes of infectious mosquitoes and infectious individual subpopulations, and the costs associated with implementing the controls $u_1, u_2$ and $u_3$. In the integrand (Lagrangian) of CF expressed, the coefficients $W_i$, i = 1, 2, 3…5 are positive weight constants where $W_i > 0$. Besides, $W_1$ and $W_2$ measure the importance of reducing the size of infected mosquito and infected human populations in dengue transmission. Then, $W_3$, $W_4$ and $W_5$ are the relative measures of the costs or efforts required to implement the respective controls.

### 3.4 Characterization of Optimal Controls

Let $H$ denote the Hamiltonian associated with the optimal control problem (OCP), which has been determined as follows:

$$H = W_1 I_v + W_2 I_h + \frac{W_3}{2} u_1^2 + \frac{W_4}{2} u_2^2 + \frac{W_5}{2} u_3^2 + \lambda_1 \frac{dA_v}{dt} + \lambda_2 \frac{dS_v}{dt} + \lambda_3 \frac{dE_v}{dt} \qquad (10)$$
$$+ \lambda_4 \frac{dI_v}{dt} + \lambda_5 \frac{dS_h}{dt} + \lambda_6 \frac{dV_h}{dt} + \lambda_7 \frac{dI_h}{dt} + \lambda_8 \frac{dR_h}{dt}$$

Equation 10. Hamiltonian associated with OCP

To achieve the optimal solution for the OCP associated with the non-autonomous dengue model, a non-trivial vector function (costate system) has been derived as follows:

$$\frac{d\lambda_1}{dt} = -\frac{\partial H}{\partial A_v} = -\left[\lambda_1\left(-\frac{(S_v + E_v + I_v)}{kN_h} - \omega - \mu_A - u_1\right) + \lambda_2\omega\right] \tag{11.1}$$

$$\frac{d\lambda_2}{dt} = -\frac{\partial H}{\partial S_v} = -\left[\lambda_2\left(-\frac{B\beta_v I_h}{N_h} - \mu_v - u_2\right) + \lambda_1\varphi\left(1 - \frac{A_v}{kN_h}\right) + \lambda_3\left(\frac{B\beta_v I_h}{N_h}\right)\right] \tag{11.2}$$

$$\frac{d\lambda_3}{dt} = -\frac{\partial H}{\partial E_v} = -\left[\lambda_3(-\delta - \mu_v - u_2) + \lambda_1\varphi\left(1 - \frac{A_v}{kN_h}\right) + \lambda_4\delta\right] \tag{11.3}$$

$$\frac{d\lambda_4}{dt} = -\frac{\partial H}{\partial I_v} = -\left[\lambda_4(-\mu_v - u_2) + \lambda_1\varphi\left(1 - \frac{A_v}{kN_h}\right) + \lambda_5\left(\frac{B\beta_h S_h}{N_h}\right)\right. \tag{11.4}$$

$$\left. - \lambda_6\left(\frac{\sigma B\beta_h V_h}{N_h}\right) + \lambda_7\left(\frac{B\beta_h S_h}{N_h} + \frac{\sigma B\beta_h V_h}{N_h}\right) + W_1\right]$$

$$\frac{d\lambda_5}{dt} = -\frac{\partial H}{\partial S_h} = -\left[\lambda_5\left(-\frac{B\beta_h I_v}{N_h} - \mu_h - u_3\right) + \lambda_6 u_3 + \lambda_7\left(\frac{B\beta_h I_v}{N_h}\right)\right] \tag{11.5}$$

$$\frac{d\lambda_6}{dt} = -\frac{\partial H}{\partial V_h} = -\left[\lambda_6\left(-\theta - \frac{\sigma B\beta_h I_v}{N_h} - \mu_h\right) + \lambda_5\theta + \lambda_7\left(\frac{\sigma B\beta_h I_v}{N_h}\right)\right] \tag{11.6}$$

$$\frac{d\lambda_7}{dt} = -\frac{\partial H}{\partial I_h} = -\left[\lambda_7(-\gamma + \mu_h) + \lambda_8\gamma - \lambda_2\left(\frac{B\beta_v S_v}{N_h}\right) + \lambda_3\left(\frac{B\beta_v S_v}{N_h}\right) + W_2\right] \tag{11.7}$$

$$\frac{d\lambda_8}{dt} = -\frac{\partial H}{\partial R_h} = \lambda_8\mu_h \tag{11.8}$$

Equation 11. Costate system (adjoint equations)

The following transversality or boundary conditions are used in the simulation:

$$\lambda_i(t_f) = 0, i = 1, 2, 3, \ldots, 8 \tag{12}$$

Equation 12. Boundary conditions in simulation

Where $t_f$ is the final time.

The optimality condition is given as follows:

$$\frac{\partial H}{\partial u_1} = 0 \tag{13.1}$$

$$\frac{\partial H}{\partial u_2} = 0 \tag{13.2}$$

$$\frac{\partial H}{\partial u_3} = 0 \tag{13.3}$$

Equation 13. Optimality condition

Thus, the control variables $u_1, u_2,\ and\ u_3$ will be solved as the following:

$$u_1 = \frac{\lambda_1 A_v}{W_3} \tag{14.1}$$

$$u_2 = \frac{\lambda_2 S_v + \lambda_3 E_v + \lambda_4 I_v}{W_4} \tag{14.2}$$

$$u_3 = \frac{\lambda_5 S_h - \lambda_6 S_h}{W_5} \tag{14.3}$$

Equation 14. Solution for control variables

### 3.5 Numerical Simulation

Optimal control and optimal state are found by solving numerically the optimality system which consists of the non-autonomous differential equation model, together with initial conditions, and the costate system, with its boundary conditions coupled with the control variables solution. The forward-backward sweep method is implemented in Python to obtain the solution. This approach aims to analyse the numerical outcomes of the model both with and without control and to simulate the optimal solution using the forward-backward sweep method. The optimal control problem is solved numerically using the fourth-order Runge-Kutta (RK4) method. Widely recognized for its simplicity, accuracy, and efficiency, RK4 is a fourth-order numerical technique frequently employed to solve ordinary differential equations. This method calculates the estimated solution of an ODE at each time step through four stages: evaluating slopes at the initial point, midpoint, and endpoint. The solution for the subsequent

time step is then estimated by averaging these slopes with appropriate weights (Mukhsar et al., 2023).

To demonstrate the impact of various strategies combining optimal controls $u_1$ (larvicide), $u_2$ (fogging), and $u_3$ (vaccination) in minimizing the fractions of infectious mosquitoes ($I_v$) and the infectious human population ($I_h$), thus the total mosquito population ($N_v$), as well as the costs associated with these controls as shown in Table 3.3, the state variables and the parameter values provided in Table 3.2 have been utilized. The values of $W_1$ and $W_2$ have been set to 100, signifying the priority given to reducing the populations of infected mosquitoes ($I_v$) and infected humans ($I_h$) in the context of dengue transmission (Pongsumpun et al., 2019). On the other hand, $W_3$, $W_4$, and $W_5$ denote the expenditure or effort required to implement the corresponding control measures. Based on prior research and presuming the application of advanced technology, the weights are established as follows: $W_3$ = 1,000,000,000, $W_4$ = 2,500,000,000, and $W_5$ = 100,000,000,000, expressed in MYR (Suwantika et al., 2021; España et al., 2021).

Table 4. Definition and value of control balancing weight constant

| **Respective To** | **Weight Constant, $W_i$** | **Value** |
|---|---|---|
| Infected mosquito population, $\boldsymbol{I_v}$ | $W_1$ | 100 |
| Infected human population, $\boldsymbol{I_h}$ | $W_2$ | 100 |
| Larvicide, $\boldsymbol{u_1}$ | $W_3$ | 1,000,000,000 |
| Fogging, $\boldsymbol{u_2}$ | $W_4$ | 2,500,000,000 |
| Vaccination, $\boldsymbol{u_3}$ | $W_5$ | 100,000,000,000 |

## 3.6 Strategies Implementation

The study investigates seven intervention strategies for controlling dengue transmission dynamics. Firstly, optimal larvicide ($u_1$) is implemented, followed by optimal fogging ($u_2$), and optimal vaccination ($u_3$). Fourthly, larvicide and fogging ($u_1$ and $u_2$) are applied together, while the fifth strategy combines larvicide and vaccination ($u_1$ and $u_3$). Sixthly, fogging and vaccination ($u_2$ and $u_3$) are implemented simultaneously. Lastly, all three controls ($u_1$, $u_2$, and $u_3$) are deployed in combination to effectively minimize both infected mosquito and human populations.

## 3.7 Methodology Summary

This chapter details the methodology used to study dengue transmission dynamics and evaluate the effectiveness of interventions using the ASEI-SVIR model. The model incorporates mosquito (aquatic, susceptible, exposed, infected) and human (susceptible, vaccinated, infected, recovered) compartments, with control variables for larvicide, fogging, and vaccination. Parameters are calibrated using Malaysia's 2024 dengue data, and the optimal control problem is formulated using Pontryagin's Maximum Principle to minimize infections and intervention costs. The forward-backward sweep method and the fourth-order Runge-Kutta method are implemented in Python for numerical simulations, analysing seven intervention strategies, including individual and combined controls. The study aims to identify cost-effective strategies for reducing infected human and mosquito populations while considering the resource implications of each intervention.

# CHAPTER 4: RESULTS AND SIMULATION

## 4.0 Result Overview

The numerical simulation incorporates several control strategies, each associated with specific control variables such as larvicide ($u_1$), insecticide ($u_2$), and vaccination ($u_3$). The ASEI-SVIR model is employed to simulate seven distinct intervention scenarios, ranging from single measures, such as the application of larvicide or insecticide alone, to combined strategies involving all three interventions. These simulations facilitate a comparative analysis of each strategy's effectiveness, enabling the identification of the most efficient approach for controlling dengue outbreaks under varying conditions. This section presents the findings on the effectiveness of dengue intervention strategies based on the ASI-SVIR model. Seven strategies were assessed, consisting of individual implementations of larvicide ($u_1$), fogging ($u_2$), and vaccination ($u_3$), as well as various combinations of these control measures. The analysis is based on the dynamics of infected mosquito and human populations as depicted in Figures 4.1.1 to 4.7.8.

## 4.1 Strategies for dengue intervention

This section discusses various strategies implemented in the model which involve the solo effect of intervention strategy such as larvicide ($u_1$), fogging ($u_2$) and vaccination ($u_3$) and the combination of two to three of these interventions to evaluate which intervention is the most optimal for dengue control strategy.

### 4.1.1 Strategy 1: Implementation of optimal larvicide ($u_1$)

This intervention approach illustrates the effect of larvicide ($u_1$) on the transmission dynamics of dengue fever within the population. The outcomes of implementing this strategy are presented in figure 4.1.1, figure 4.1.2 and figure 4.1.3 below.

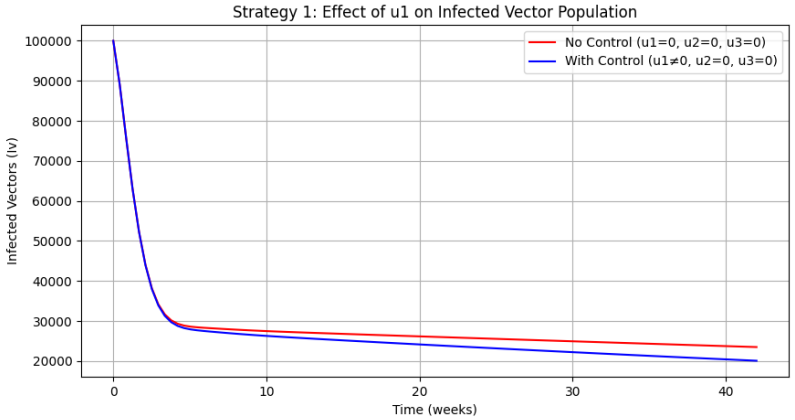


Figure 4.1. 1. Subpopulation of infected mosquito, $I_v$

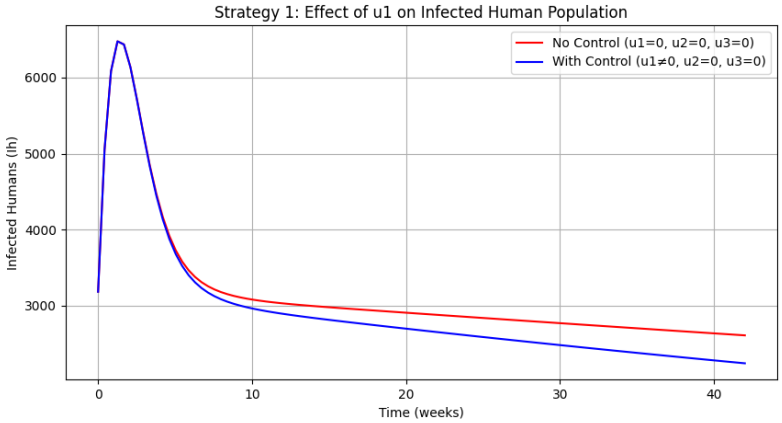


Figure 4.1. 2. Subpopulation of infected human, $I_h$


Figure 4.1. 3. Control measures of larvicide, $u_1$

Implementation of optimal larvicide ($u_1$) demonstrates a moderate reduction in both the infected mosquito population (Figure 4.1.1) and the infected human population (Figure 4.1.2). Although fluctuations in infection levels persist throughout the time horizon, the larvicide

intervention appears to delay and slightly suppress the transmission cycle. Figure 4.1.3 shows a rapid increase in larvicide application, quickly reaching its maximum level early in the simulation. This early and sustained rise indicates an aggressive initial deployment of larvicide to quickly suppress the mosquito larvae population, which is critical during the early outbreak phase. The stabilization of the control level after reaching its peak suggests that a consistent, ongoing application is necessary to maintain low vector levels throughout the simulation period.

### 4.1.2 Strategy 2: Implementation of optimal fogging ($u_2$)

This intervention strategy highlights the influence of fogging ($u_2$) on the transmission dynamics of dengue fever within the population. The results obtained from implementing this approach are illustrated in figure 4.2.1, figure 4.2.2 and figure 4.2.3 below.

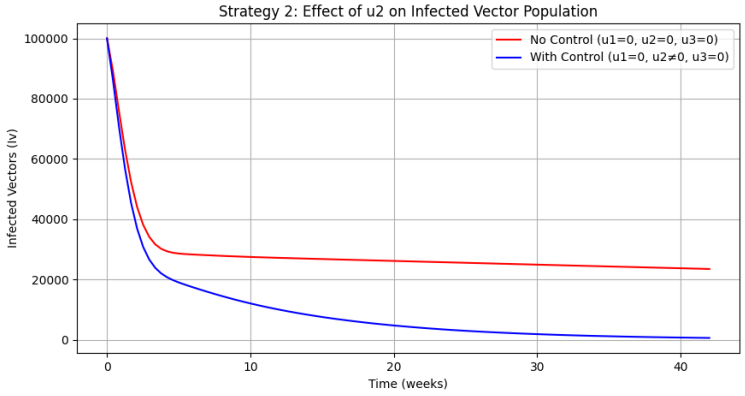


Figure 4.2. 1. Subpopulation of infected mosquito, $I_v$

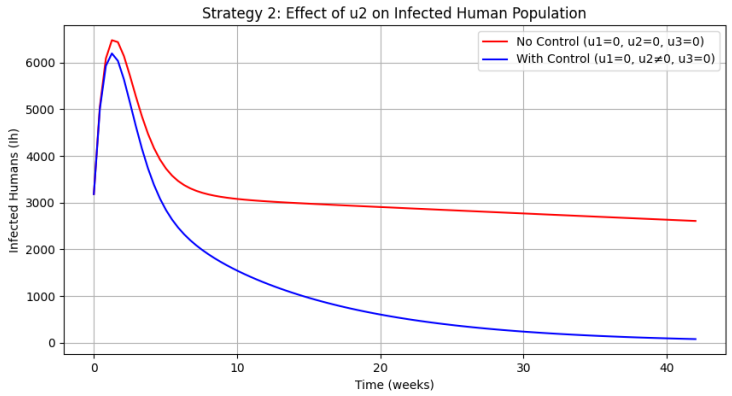


Figure 4.2. 2. Subpopulation of infected human, $I_h$


Figure 4.2. 3. Control measures of fogging, $u_2$

Implementation of optimal fogging ($u_2$) yields a more substantial and immediate reduction in the infected mosquito population (Figure 4.2.1). This consequently contributes to a more noticeable decline in human infections (Figure 4.2.2) when compared to larvicide ($u_1$). Figure 4.2.3 indicates that fogging is deployed intensively at the beginning and then reaches a plateau around the 10th week. After this point, the level of fogging remains consistently high for the remainder of the simulation period. This behaviour suggests an aggressive and sustained deployment of fogging early in the outbreak to reduce adult mosquito populations, followed by a continued but steady application to maintain low vector levels and prevent resurgence of infections.

### 4.1.3 Strategy 3: Implementation of optimal vaccination ($u_3$)

This intervention strategy illustrates the effect of vaccination ($u_3$) on the transmission dynamics of dengue fever within the population. The outcomes resulting from the implementation of this strategy are depicted in figure 4.3.1, figure 4.3.2 and figure 4.3.3 below.

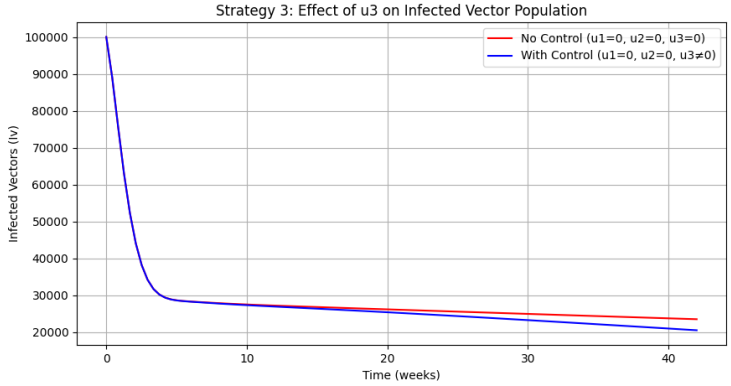


Figure 4.3. 1. Subpopulation of infected mosquito, $I_v$

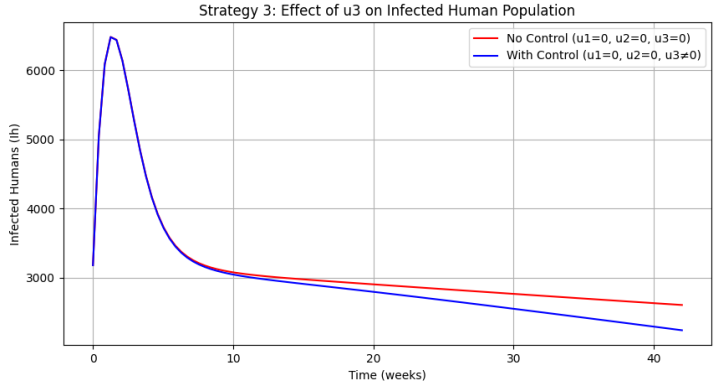


Figure 4.3. 2. Subpopulation of infected human, $I_h$

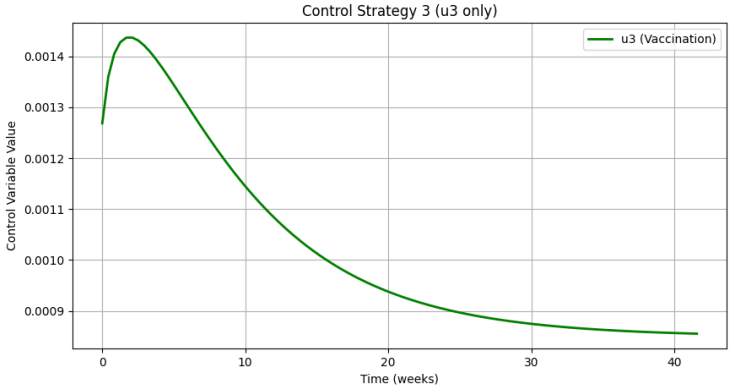


Figure 4.3. 3. Control measures of vaccination, $u_3$

Strategy 3 employed optimal vaccination ($u_3$) as a control measure. The resulting trend in the infected mosquito population (Figure 4.3.1) remains relatively unaffected in the early phase, as this strategy does not act on vectors directly. However, the infected human population (Figure 4.3.2) exhibits a gradual and sustained decline, particularly in the latter half of the

simulation period. This trend aligns with the anticipated delay in vaccine-induced immunity, which typically requires several weeks to become effective. The application of vaccination control as shown in Figure 4.3.3 begins with a rapid increase, reaching its peak at around the second week, and then gradually declines over the remaining simulation period. This indicates that the optimal strategy involves an initial surge in vaccination efforts to quickly boost immunity within the population during the early stages of the outbreak. Following this, the intensity of vaccination efforts decreases as a sufficient level of herd immunity is achieved, reducing the need for aggressive continued immunization. The smooth, tapering decline also reflects a sustained but diminishing effort to maintain immunity as the infection risk lowers.

### 4.1.4 Strategy 4: Implementation of optimal larvicide ($u_1$) and fogging ($u_2$)

This intervention strategy demonstrates the combined effects of larvicide ($u_1$) and fogging ($u_2$) on the transmission dynamics of dengue fever within the population. The results from implementing this approach are presented in figure 4.4.1, figure 4.4.2 and figure 4.4.3 below.

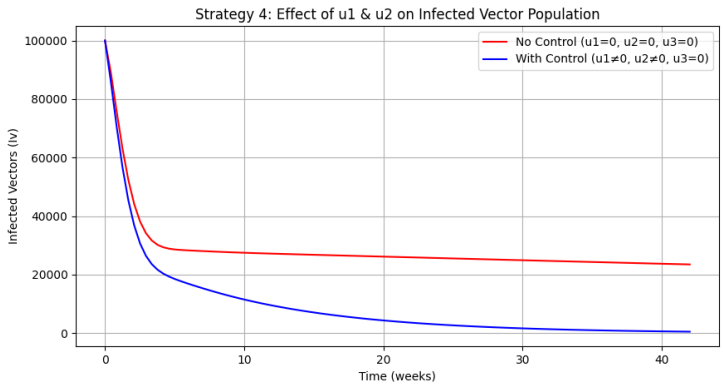


Figure 4.4. 1. Subpopulation of infected mosquito, $I_v$

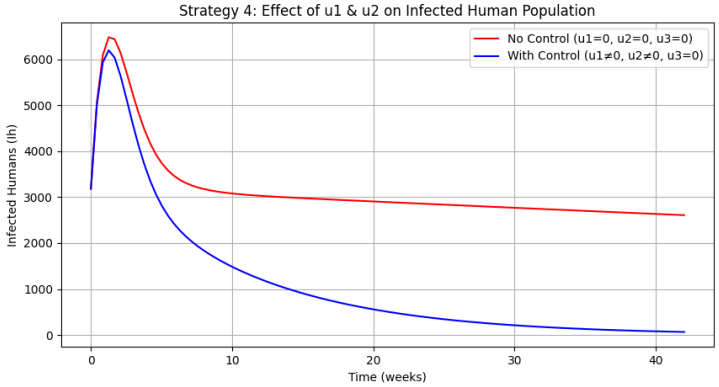


Figure 4.4. 2. Subpopulation of infected human, $I_h$

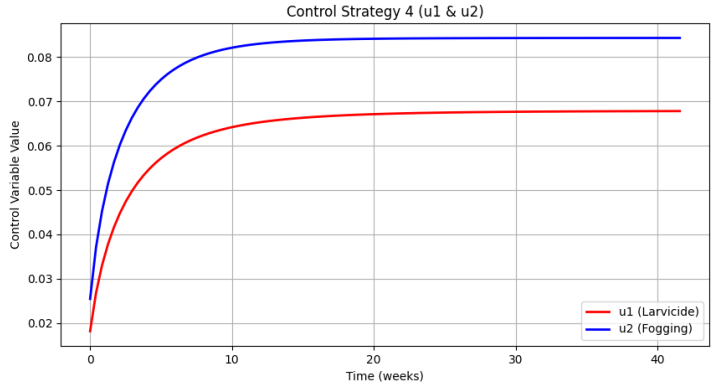


Figure 4.4. 3. Control measures of larvicide, $u_1$ and fogging, $u_2$

Implementation of optimal larvicide ($u_1$) and fogging ( $u_2$) demonstrates improved effectiveness over individual applications. As shown in Figure 4.4.1, the infected mosquito population declines at a faster rate, while Figure 4.4.2 illustrates a corresponding reduction in the infected human population. In this dual-control strategy, both larvicide and fogging are applied with increasing intensity during the early weeks, peaking at around week 10. The fogging control ($u_2$) reaches a slightly higher plateau than the larvicide ($u_1$), indicating a heavier reliance on fogging in this strategy. Both control measures stabilize after the initial rise, implying a balanced and sustained effort in which fogging targets the adult mosquito population while larvicide focuses on eliminating larvae, working in tandem to comprehensively suppress vector proliferation throughout the outbreak.

### 4.1.5 Strategy 5: Implementation of optimal larvicide ($u_1$) and vaccination ($u_3$)

This intervention strategy shows the combined effects of larvicide ($u_1$) and vaccination ($u_3$) on the transmission dynamics of dengue fever within the population. The results of applying this strategy are presented in figure 4.5.1, figure 4.5.2 and figure 4.5.3 below.

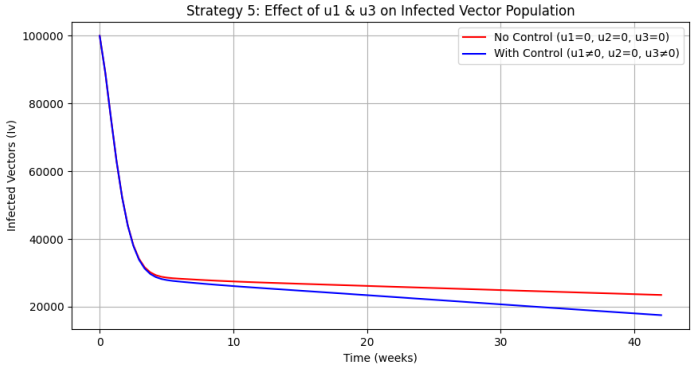


Figure 4.5. 1. Subpopulation of infected mosquito, $I_v$

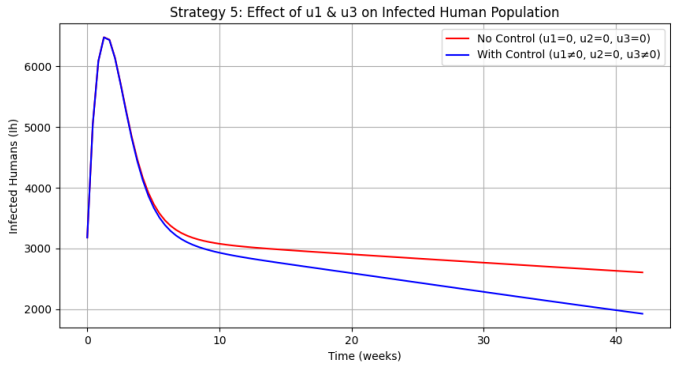


Figure 4.5. 2. Subpopulation of infected human, $I_h$

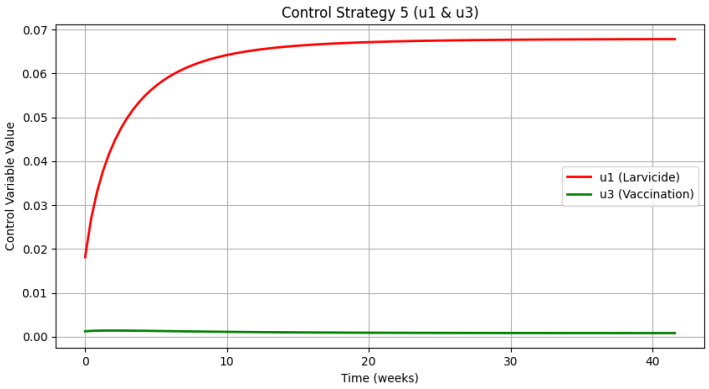


Figure 4.5. 3. Control measures of larvicide, $u_1$ and vaccination, $u_3$

Combination of larvicide and vaccination ($u_1$ and $u_3$), yields a more gradual decline in infection levels. While the infected mosquito population in Figure 4.5.1 decreases at a modest rate, the impact on the human population (Figure 4.5.2) becomes more pronounced over time. This reflects the delayed yet durable benefits of vaccination, complemented by the long-term vector control provided by larvicide. In figure 4.5.3, the larvicide control ($u_1$) follows a similar pattern of rapid increase during the first 10 weeks before leveling off at a stable value, reflecting a strong early push to disrupt mosquito breeding. In contrast, the vaccination control ($u_3$), remains minimal and nearly flat across the entire simulation period. This suggests that in this combined strategy, the larvicide plays the dominant role in vector control, while vaccination is minimally used, possibly due to cost constraints, logistical limitations, or a model optimization outcome favouring vector suppression over direct human immunization.

### 4.1.6 Strategy 6: Implementation of optimal fogging ($u_2$) and vaccination ($u_3$)

This intervention strategy examines the combined effects of fogging ($u_2$) and vaccination ($u_3$) on the transmission dynamics of dengue fever within the population. The results from implementing this strategy are shown in figure 4.6.1, figure 4.6.2 and figure 4.6.3 below.

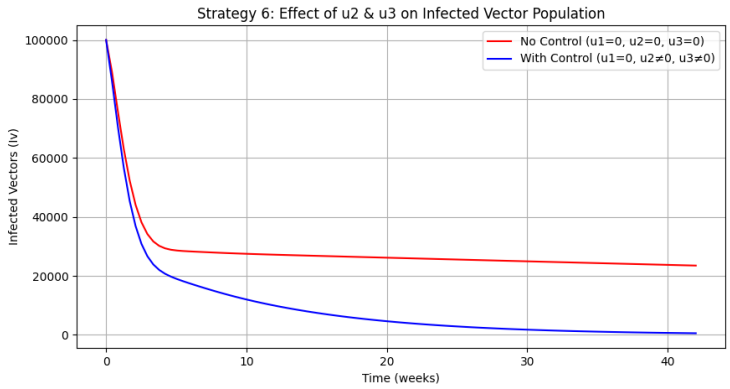


Figure 4.6. 1. Subpopulation of infected mosquito, $I_v$

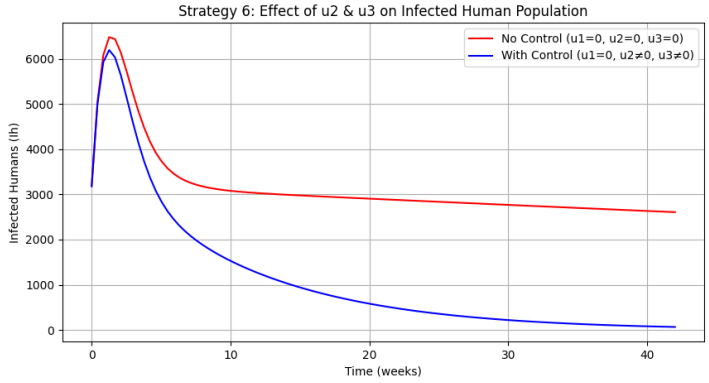


Figure 4.6. 2. Subpopulation of infected human, $I_h$

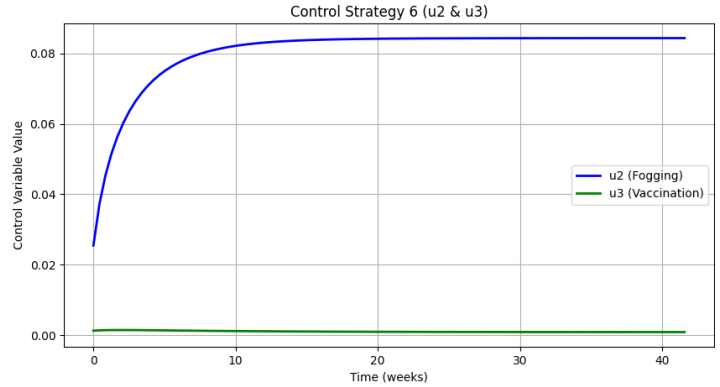


Figure 4.6. 3. Control measures of fogging, $u_2$ and vaccination, $u_3$

Strategy 6, involving the implementation of fogging and vaccination ($u_2$ and $u_3$), shows one of the most favourable outcomes among the paired strategies. Figures 4.6.1 and 4.6.2 display a rapid and consistent reduction in both vector and human infections. Figure 4.6.3 shows that fogging control ($u_2$) is applied aggressively from the beginning, with a steep increase during the first few weeks, peaking around week 10 and then stabilizing at a high level for the remainder of the simulation. This reflects the need for early and persistent fogging to eliminate adult mosquitoes and rapidly reduce transmission. In contrast, vaccination control ($u_3$) remains extremely low and nearly constant, indicating a minimal role in this strategy.

### 4.1.7 Strategy 7: Implementation of optimal larvicide ($u_1$), fogging ($u_2$) and vaccination ($u_3$)

This intervention strategy evaluates the combined effects of larvicide ($u_1$), fogging ($u_2$), and vaccination ($u_3$) on the transmission dynamics of dengue fever within the population. The outcomes of applying this strategy are presented as follows:

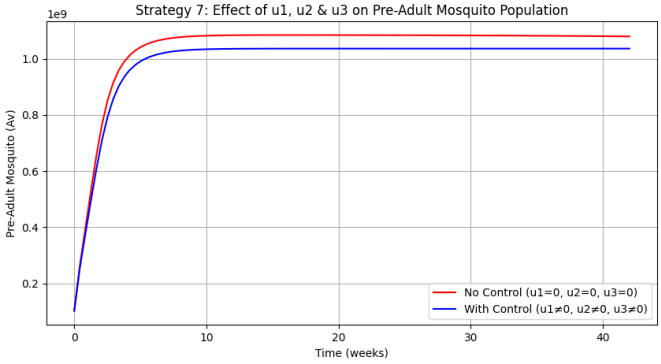


Figure 4.7. 1. Population of pre-adult mosquito, $A_v$

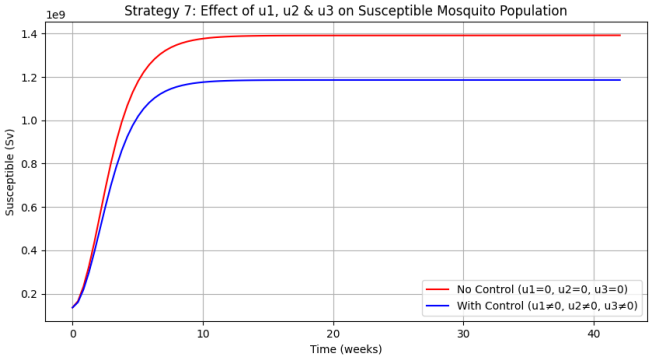


Figure 4.7. 2. Subpopulation of susceptible mosquito, $S_v$

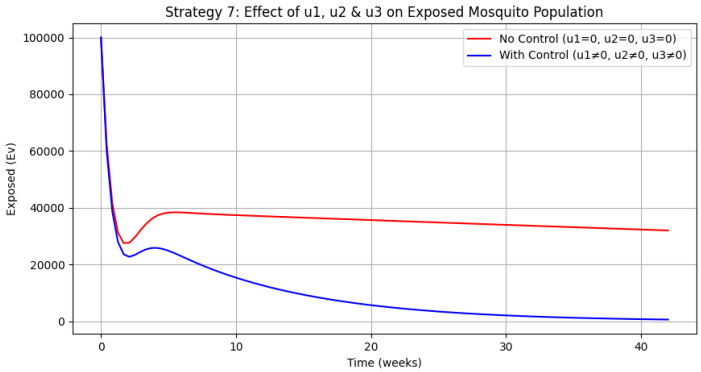


Figure 4.7. 3. Subpopulation of exposed mosquito, $E_v$

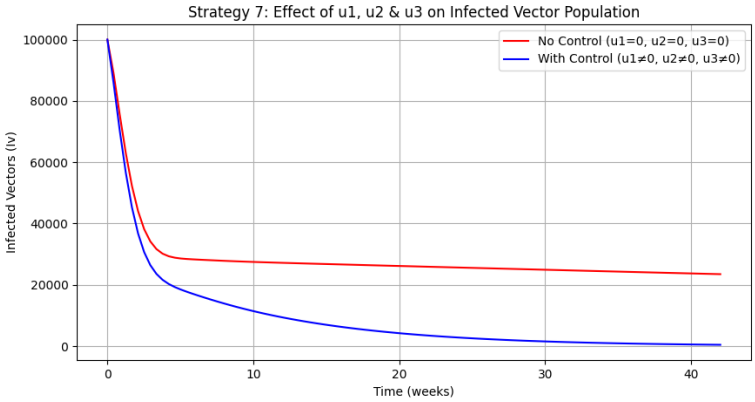


Figure 4.7. 4. Subpopulation of infected mosquito, $I_v$

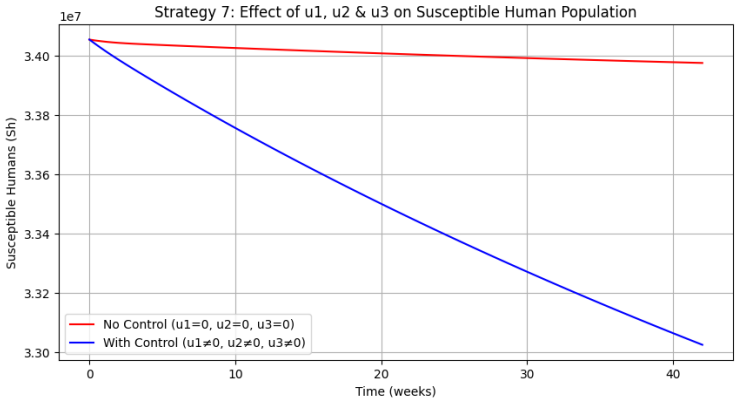


Figure 4.7. 5. Subpopulation of susceptible human, $S_h$

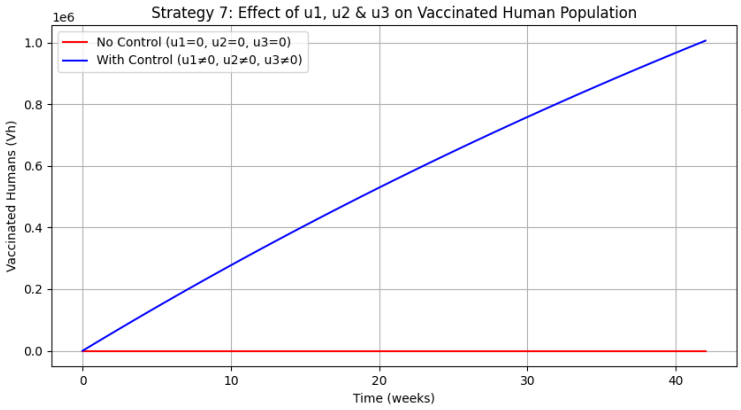


Figure 4.7. 6. Subpopulation of vaccinated human, $V_h$

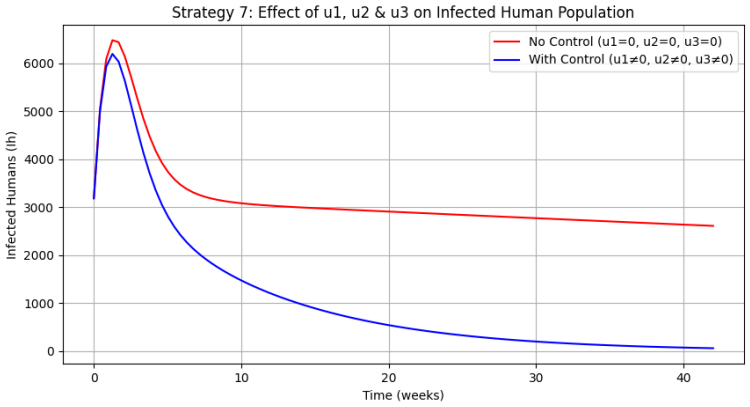


Figure 4.7. 7. Subpopulation of infected human, $I_h$


Figure 4.7. 8. Subpopulation of recovered human, $R_h$

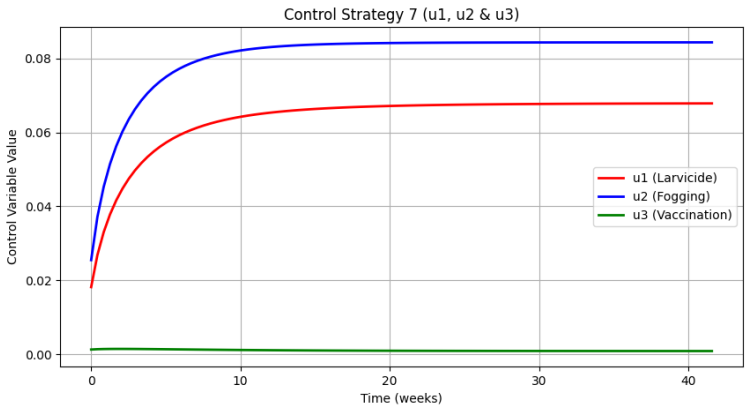


Figure 4.7. 9. Control measures of larvicide, $u_1$, fogging, $u_2$ and vaccination, $u_3$

Implementation of optimal larvicide ($u_1$), fogging ($u_2$) and vaccination ($u_3$) produces the most significant reductions in both infected mosquito and human populations. As indicated in Figure 4.7.4, the infected mosquito population experiences a steep and sustained decline.

Simultaneously, Figure 4.7.7 reveals a marked decrease in the human infection rate, with values approaching zero by approximately the 50th week of the simulation. In this combined strategy, fogging ($u_2$) shows the highest and most rapid increase, peaking early and maintaining a high, stable level throughout the period, highlighting its dominant role in controlling adult vectors. Larvicide ($u_1$) also rises quickly and stabilizes slightly below fogging, suggesting it is used as a strong complementary measure to suppress larvae. Vaccination ($u_3$) remains the lowest among all three controls and shows a flat trend, indicating minimal utilization or effect.

## 4.2 Summary of Simulation and Result

In summary, while fogging provides the most immediate benefits and vaccination offers the strongest long-term impact, the integration of all three interventions under 7$^{th}$ strategy proves to be the most effective overall. This strategy achieves the greatest reduction in both vector and human infections across the simulation period. In comparative terms, the implementation of all three interventions demonstrates superior performance, followed by the implementation of fogging and vaccination in strategy 6, the 4$^{th}$ strategy which is the implementation of larvicide and fogging, and the 5$^{th}$ strategy which is the implementation of larvicide and vaccination. Therefore, based on the observation of the results, the multi-faceted intervention strategies yield the most successful outcomes in controlling dengue transmission.

# CHAPTER 5: DISCUSSION AND RECOMMENDATION

## 5.0 Overview

This chapter provides a detailed interpretation of the simulation results and their implications for real-world dengue control. Each intervention strategy was evaluated for its effectiveness in reducing dengue transmission, with comparisons made between the observed outcomes and existing literature. The strategies were assessed not only based on their short-term and long-term impacts but also in terms of their practicality, sustainability, and relevance to public health implementation. By examining both the strengths and limitations of each intervention whether used alone or in combination, this chapter offers critical insights into how dengue control measures can be optimized. The following sections highlight key findings from the simulations and provide evidence-based recommendations for improving future dengue prevention efforts.

## 5.1 Discussion of Simulation Results

This section discusses the outcomes of the simulation in the context of real-world dengue control, focusing on how each intervention strategy performed, both individually and in combination. The simulation outcomes were compared against initial expectations and existing findings in the literature to assess the practicality and relevance of each approach in real-world dengue control efforts. Overall, while the results were generally consistent with biological and epidemiological expectations, although some deviations offered additional insights into the relative strengths and limitations of each strategy.

The implementation of optimal larvicide ($u_1$) as a standalone intervention, demonstrated a moderate and delayed reduction in both infected mosquito and human populations. This finding aligns with the biological mechanism of larvicides, which primarily target the immature stages of mosquitoes and thus require time to impact the adult vector population and subsequently disease transmission. The observed limited effectiveness is

further supported by existing literature. For instance, Kumar et al. (2020) and Perera et al. (2022) highlight the growing concern over resistance development in mosquito populations due to continuous larvicide use, which can compromise the long-term efficacy of such interventions. Additionally, Liu et al. (2020) emphasize that certain larvicides, such as *Bacillus thuringiensis israelensis* (Bti), have a relatively short duration of action and require frequent reapplication to maintain their effectiveness. These findings support the conclusion that while larvicide can play a valuable role in vector control, it is most effective when incorporated into a comprehensive, multi-pronged intervention strategy, particularly in regions with persistent mosquito breeding sites.

Implementation of optimal fogging ($u_2$) as the sole intervention, produced immediate and notable reductions in the infected mosquito and human populations, a result that is consistent with its mechanism of action, targeting and rapidly eliminating adult mosquitoes. This short-term effectiveness makes fogging a valuable tool during periods of outbreak when rapid suppression of the vector population is critical. However, the sustainability of its impact is questionable when used in isolation. Espinoza (2021) points out that while fogging may yield quick results, relying on it as a long-term strategy without complementary interventions can lead to a resurgence in dengue incidence over time. This is because fogging is a reactive strategy and does not address the mosquito breeding cycle or the larval stages, allowing vector populations to rebound (Espinoza, 2021). Therefore, fogging is best utilized as an emergency response measure during epidemic peaks rather than a standalone, ongoing solution for dengue control.

Implementation of optimal vaccination ($u_3$) resulted in a delayed but sustained reduction in human dengue cases, aligning with the time-dependent nature of immune response development following immunization. This pattern is well-supported by clinical findings on the TAK-003 tetravalent dengue vaccine, which has demonstrated long-lasting efficacy across

multiple studies. Sirivichayakul et al. (2020) and Rivera et al. (2021) reported high seropositivity rates maintained for up to 36 months, with vaccine efficacy reaching 62% against virologically confirmed dengue and 83.6% against hospitalizations. Furthermore, Tricou et al. (2024) confirmed the vaccine's broad effectiveness, showing protection against all four dengue serotypes in seropositive individuals and specifically against DENV-1 and DENV-2 in seronegative individuals. Given its durable protective effect, vaccination emerges as a crucial long-term intervention and should be integrated into public health strategies, particularly in endemic regions. However, due to past concerns associated with other vaccines like Dengvaxia, careful implementation, especially with pre-vaccination screening for seropositivity, is strongly recommended to ensure safety and public trust.

Implementation of optimal larvicide ($u_1$) and fogging ($u_2$) demonstrated stronger vector control compared to implementing either method alone. This outcome is supported by the logical synergy of targeting both life stages of the mosquito: larvicides like pyriproxyfen (PPF) disrupt the development of larvae, while fogging eliminates adult mosquitoes, resulting in a more comprehensive suppression of the vector population. Studies by Hustedt et al. (2020) and Chen et al. (2020) highlight the effectiveness of this dual approach in significantly reducing mosquito density, especially when cryptic larval habitats are difficult to eliminate through source reduction alone. Additionally, the success of such integrated vector management (IVM) strategies often depends on community engagement, with Durrance-Bagale et al. (2024) and Demers et al. (2020) emphasizing the importance of local participation in sustaining source control efforts and improving compliance. Therefore, this strategy is recommended as a pre-emptive measure before peak dengue transmission periods to enhance readiness and reduce outbreak risks.

Strategy 5, which integrates larvicide application and vaccination ($u_1$ and $u_3$), yielded a slower yet cumulative reduction in dengue infections, consistent with expectations. This

outcome stems from the gradual buildup of herd immunity through vaccination and the steady suppression of mosquito populations via larval control. Although the impact may not be immediate, the combined strategy becomes increasingly effective over time. According to Knerer et al. (2020) and Hladish et al. (2020), this combination is not only more epidemiologically impactful than single interventions but also offers greater cost-effectiveness, making it a practical choice for sustained dengue control. Its success, however, relies on the presence of robust infrastructure for both vaccine distribution and consistent larval source reduction. Therefore, this strategy is best suited for communities with strong healthcare systems and active public health engagement.

The implementation of fogging ($u_2$) and vaccination ($u_3$), emerged as one of the most effective dual-intervention approaches, leveraging both immediate and long-term control mechanisms. Fogging offers rapid suppression of adult mosquito populations, crucial during outbreak scenarios, while vaccination builds lasting immunity in the population over time. This compounding effect aligns with findings by Hladish et al. (2020) and Zhang et al. (2022), who emphasize that integrated strategies encompassing vaccination and vector control are significantly more effective than single measures. Such combinations can lead to the short-term elimination of dengue cases and sustained reductions in transmission rates. Given its dual-phase impact, this strategy is particularly suitable for densely populated urban areas frequently facing dengue outbreaks, where swift action and durable prevention are both essential. Interestingly, the outcomes from the dual-intervention strategies were in some cases more effective than expected. This may be due to idealised assumptions in the model, such as perfect compliance and timely intervention deployment, which may not fully reflect field conditions. Nevertheless, these simulations provide useful insights into the potential effectiveness of coordinated control strategies under optimal conditions.

## 5.2 Recommendation of Intervention

Strategy 7, which combines all three interventions which are larvicide, fogging, and vaccination ($u_1, u_2, u_3$) has demonstrated the most effective outcome in the simulation, nearly eradicating dengue infection. This strong result can be attributed to the synergistic action across all stages of transmission: larvicide disrupts mosquito breeding at the larval stage, fogging rapidly reduces adult vector populations, and vaccination strengthens host immunity over time. By targeting the disease cycle from multiple angles, the combined strategy significantly reduces both mosquito populations and the number of susceptible individuals, thereby curbing overall transmission.

The observed synergy in this strategy is consistent with existing literature. Rawson et al. (2020) and Hladish et al. (2020) emphasize that integrated interventions are more effective than single strategies, as each method addresses a different aspect of dengue transmission. While fogging and larvicides provide immediate vector control, vaccination introduces a sustained immunity barrier, together leading to a compounded and more durable reduction in disease burden. Moreover, Hladish et al. (2020) caution that the combination of vector control and vaccination can sometimes result in interference depending on vaccine type, but when chosen and implemented appropriately, as with TAK-003, the combination is largely synergistic.

From a policy and economic perspective, integrated strategies are not only epidemiologically effective but also cost-efficient. Knerer et al. (2020) demonstrate that combining vaccination with larvicide and fogging yields greater health and economic benefits than deploying each method in isolation, especially in densely populated areas. These findings reinforce the model outcome, suggesting that comprehensive intervention packages can optimize dengue control outcomes and justify the higher initial investment through long-term benefits.

## 5.3 Summary of Discussion and Recommendation

The simulation results reveal that while single interventions such as larvicide, fogging, or vaccination each have their merits, their impact on dengue transmission is often limited when applied in isolation. Larvicide and fogging are effective in targeting mosquito populations at different life stages but may not offer lasting protection unless maintained consistently. Vaccination, though slower to show impact, provides long-term immunity and reduces overall disease susceptibility. Combination strategies demonstrated notably greater effectiveness, especially those that integrate both vector control and immunization. The dual-intervention strategies (e.g., fogging with vaccination or larvicide with vaccination) leveraged both immediate and sustained mechanisms of control, proving more efficient than single measures. Among all, the triple-intervention strategy, combining larvicide, fogging, and vaccination, achieved the most successful outcome, nearly eradicating dengue transmission in the model. These findings support the adoption of integrated intervention packages in real-world public health planning. While implementation may require greater coordination and investment, the long-term benefits, in terms of disease reduction, cost-effectiveness, and public health resilience, justify such efforts. Moving forward, public health authorities should prioritize multi-layered approaches that align with local epidemiological conditions, community engagement capacity, and healthcare infrastructure to effectively combat dengue outbreaks.

# CHAPTER 6: CONCLUSION AND FUTURE WORK

## 6.0 Summary

This project was undertaken with the primary aim of evaluating the effectiveness of various dengue control strategies with an ASEI-SVIR compartmental model. The study focused on simulating the transmission dynamics of dengue fever in a population and assessing how different intervention strategies could alter these dynamics. The model incorporated distinct human and mosquito compartments to reflect the natural disease transmission cycle and was enhanced with control variables representing larvicide ($u_1$), fogging ($u_2$), and vaccination ($u_3$) efforts.

A mathematical modelling approach was employed, supported by optimal control theory to determine the most efficient allocation of interventions over time. The model was implemented and simulated using Python, utilizing the forward-backward sweep method with the fourth-order Runge-Kutta numerical scheme. Simulations were conducted for each of the seven control strategies, including individual and combined interventions, to evaluate their respective impacts on dengue transmission.

Key findings indicate that fogging ($u_2$) is the most effective intervention in the short term, rapidly reducing the infected mosquito population. Vaccination ($u_3$), while slower in showing impact due to the time required for immunity development, provides the most long-lasting effect by significantly reducing human infections over the duration of the simulation. Larvicide ($u_1$), though beneficial, is less effective when applied independently. The strategy combining all three interventions which are larvicide, fogging, and vaccination ($u_1$, $u_2$, and $u_3$) was found to be the most comprehensive and impactful, effectively reducing both mosquito and human infections throughout the simulation period.

## 6.1 Objectives Achievements

This project was guided by three important objectives, all of which were successfully accomplished through the course of the study. The main objective was to develop an ASEI-SVIR model to simulate the transmission dynamics of dengue fever. This was achieved by constructing a mathematical compartmental model that accounted for both human and mosquito populations. The model included compartments for susceptible, exposed, infected, vaccinated, and recovered individuals in the human population, as well as for susceptible, exposed, and infected vectors in the mosquito population. Another objective was to simulate the impact of intervention strategies (larvicide, fogging, and vaccination) on the spread of dengue fever. To achieve this, the system of differential equations representing the model was formulated and implemented using Python, providing a computational framework to simulate and analyse disease progression over time under various intervention scenarios.

The second objective was to compare the effects of individual and combined intervention strategies on the spread of dengue. To fulfil this, seven different control strategies were simulated, each incorporating various combinations of larvicide ($u_1$), fogging ($u_2$), and vaccination ($u_3$). The impact of each strategy was evaluated by observing the resulting trends in both infected mosquito and human populations over the simulation period. The control measures were applied using optimal control theory through the Pontryagin's Maximum Principle, allowing for efficient simulation of each intervention's dynamics and their respective control profiles.

The third objective was to provide recommendation by identifying the most effective intervention strategy in reducing dengue transmission. This was achieved by analysing the outcomes of all simulated strategies in terms of the peak infection levels and total number of infections throughout the simulation period. Based on the results, it was concluded that the combination of all three control measures which are larvicide, fogging, and vaccination to be

the most effective approach. This strategy resulted in the lowest number of infections and a sustained decline in both mosquito and human populations, thereby highlighting the importance of integrated intervention planning in the control of dengue outbreaks.

## 6.2 Project Limitations

Despite achieving the intended objectives, this study is subject to several limitations. First, the findings are based on dengue incidence data from Malaysia, specifically from the year 2024. As such, the findings are specifically tailored to the context of Malaysia and may not be directly generalizable to other geographic regions or states within Malaysia due to variations in environmental, social, and infrastructural conditions. Additionally, the model relies on certain simplifying assumptions, including homogeneous mixing within the population and constant parameter values, which might not precisely represent actual real-world conditions, which are often influenced by heterogeneous contact patterns, behavioural differences, and fluctuating environmental conditions.

Moreover, the simulation does not incorporate environmental factors such as rainfall, temperature, or urban infrastructure, all of which can significantly influence mosquito breeding and disease transmission. The use of historical data means that some parameter values may be outdated, potentially leading to discrepancies between simulated and actual outbreak patterns. As a result, the simulation outcomes could differ if updated or region-specific data were employed.

## 6.3 Future Works

Future improvements can enhance the accuracy and applicability of the model. One possible extension involves incorporating biological control measures such as the introduction of *Wolbachia*-infected mosquitoes. *Wolbachia*-based strategies have shown promising results in reducing dengue transmission; however, studies such as Calle-Tobón et al. (2024) indicate

that in some regions like Medellín, Colombia, their prevalence may decline over time, suggesting the need for further research into sustainability and long-term effectiveness. Moreover, individual control strategies, such as those discussed by Abdemi and Aziz (2020), could be integrated into the model to explore more nuanced intervention approaches tailored to personal protection and community-level awareness.

In terms of computational enhancement, the model could be extended by exploring alternative optimization techniques beyond Pontryagin's Maximum Principle, such as genetic algorithms, particle swarm optimization, or differential evolution methods. Additionally, different numerical schemes such as implicit Runge-Kutta or adaptive step-size methods could be employed to improve the stability and accuracy of long-term simulations.

In future extensions of this project, the ASEI-SVIR model can be extended by integrating artificial intelligence (AI) and machine learning (ML) to improve adaptability and predictive accuracy. While the current ASEI-SVIR model uses fixed parameters, ML can be used to estimate key parameters like transmission or biting rates dynamically based on real-time data such as weather, population density, or recent case counts. Reinforcement learning may also be applied to optimize the timing and intensity of interventions like fogging or vaccination by learning from repeated simulations. Additionally, a hybrid approach that combines this mechanistic model with data-driven ML techniques could enhance outbreak forecasting and enable more responsive, localized intervention strategies. The model can also be used to generate synthetic outbreak data, which is useful for training AI models in low-data settings. Overall, integrating AI would support the development of a more intelligent, real-time public health response system for dengue control, improving the effectiveness and efficiency of future intervention planning.

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## APPENDIX

Figure 5. 1. Coding for generating data fitted graph

```
import numpy as np
import matplotlib.pyplot as plt
from scipy.integrate import solve_ivp
from scipy.optimize import curve_fit

# Define the differential equations for the model
def mosquito_human_model(t, y, ϕ, k, ω, B, β_h, β_v, δ):
    A_v, S_v, E_v, I_v, S_h, V_h, I_h, R_h = y
    N_h = 34058800  # Total human population
    μ_A = 0.42      # Natural mortality of larvae (per week)
    μ_h = 0.0069    # Natural mortality rate of humans (per week)
    θ = 0.0018      # Vaccine waning rate (per week)
    σ = 0.198       # Proportion of vaccinated humans infected
    γ = 0.7         # Human recovery rate (per week)
    μ_v = 0.7       # Natural mortality of mosquitoes (per week)

    # Mosquito equations
    dA_v = ϕ * (1 - A_v / (k * N_h)) * (S_v + E_v + I_v) - (ω + μ_A) * A_v
    dS_v = ω * A_v - (B * β_v * I_h / N_h + μ_v) * S_v
    dE_v = (B * β_v * I_h / N_h) * S_v - (δ + μ_v) * E_v
    dI_v = δ * E_v - μ_v * I_v

    # Human equations
    dS_h = μ_h * N_h + θ * V_h - (B * β_h * I_v / N_h + μ_h) * S_h
    dV_h = -(θ + σ * B * β_h * I_v / N_h + μ_h) * V_h
    dI_h = (B * β_h * I_v / N_h) * S_h + σ * (B * β_h * I_v / N_h) * V_h - (γ
+ μ_h) * I_h
    dR_h = γ * I_h - μ_h * R_h

    return [dA_v, dS_v, dE_v, dI_v, dS_h, dV_h, dI_h, dR_h]

# Function to solve the ODE system
def solve_model(week, ϕ, k, ω, B, β_h, β_v, δ):
    # Initial conditions
    N_h = 34058800
    S_h0 = N_h - 3181
    V_h0 = 0
    I_h0 = 3181
    R_h0 = 0
    A_v0 = 3 * N_h
    S_v0 = (4 * N_h) - 200000
    E_v0 = 100000
    I_v0 = 100000
    y0 = [A_v0, S_v0, E_v0, I_v0, S_h0, V_h0, I_h0, R_h0]
```

```
    # Time vector
    t = np.linspace(0, week[-1], len(week))

    # Solve the system using solve_ivp
    sol = solve_ivp(
        lambda t, y: mosquito_human_model(t, y, ϕ, k, ω, B, β_h, β_v, δ),
        [0, t[-1]], y0, t_eval=t, method="RK45"
    )

    return sol.t, sol.y[6]  # Return time and infected humans (I_h)

# Load data for weeks and number of cases
weeks = np.arange(1, 42)  # Week numbers
cases = np.array([3181, 3525, 3971, 3781, 3969, 3631, 3483, 3572, 3268, 3238,
                  2905, 3041, 2579, 2487, 1698, 2321, 2237, 1995, 2338, 2461,
                  2426, 2522, 2508, 2900, 2438, 2788, 2805, 2373, 2690, 2609,
                  2515, 2278, 2294, 1980, 1765, 1870, 1794, 1514, 1760, 1639,
1624])

# Compute cumulative real infected cases
cumulative_cases = np.cumsum(cases)

# Define a wrapper function for curve fitting
def fit_function(week, ϕ, k, ω, B, β_h, β_v, δ):
    t, I_h = solve_model(week, ϕ, k, ω, B, β_h, β_v, δ)
    cumulative_I_h = np.cumsum(I_h)  # Compute cumulative infected humans
    return cumulative_I_h

# Adjusted initial parameter guesses
initial_guess = [7.5, 35, 0.75, 0.78, 0.15, 0.65, 0.55]  # Modify as needed

# Adjusted parameter bounds
param_bounds = (
    [5.1, 25.5, 0.51, 0.71, 0.11, 0.51, 0.51],  # Lower bounds
    [9.9, 39.9, 0.99, 0.89, 0.99, 0.89, 0.89]   # Upper bounds
)

# Modify initial conditions for mosquitoes and humans
def solve_model(week, ϕ, k, ω, B, β_h, β_v, δ):
    N_h = 34058800  # Total human population
    # Adjust initial conditions for better early-week dynamics
    S_h0 = N_h - 3000  # Modify as needed
    I_h0 = 3000  # Modify as needed
    R_h0 = 0
    A_v0 = 2.5 * N_h  # Adjust mosquito larvae population
    S_v0 = (3.5 * N_h) - 150000  # Modify mosquito susceptible population
    E_v0 = 80000  # Modify mosquito exposed population
    I_v0 = 90000  # Modify mosquito infectious population
```

```
    V_h0 = 0  # Vaccinated humans remain 0 initially

    y0 = [A_v0, S_v0, E_v0, I_v0, S_h0, V_h0, I_h0, R_h0]

    t = np.linspace(0, week[-1], len(week))

    sol = solve_ivp(
        lambda t, y: mosquito_human_model(t, y, ϕ, k, ω, B, β_h, β_v, δ),
        [0, t[-1]], y0, t_eval=t, method="RK45"
    )

    return sol.t, sol.y[6]

# Define a wrapper function for curve fitting
def fit_function(week, ϕ, k, ω, B, β_h, β_v, δ):
    t, I_h = solve_model(week, ϕ, k, ω, B, β_h, β_v, δ)
    cumulative_I_h = np.cumsum(I_h)
    return cumulative_I_h

# Adjust fitting to prioritize earlier weeks (optional)
weights = np.concatenate([np.ones(15) * 2, np.ones(len(weeks) - 15)])  #
Double weight for weeks 1-15

# Curve fitting
popt, pcov = curve_fit(
    fit_function, weeks, cumulative_cases, p0=initial_guess,
bounds=param_bounds, sigma=1 / weights, maxfev=30000
)

# Extract fitted parameters
ϕ_fit, k_fit, ω_fit, B_fit, β_h_fit, β_v_fit, δ_fit = popt

# Solve model with fitted parameters
t_fitted, fitted_I_h = solve_model(weeks, ϕ_fit, k_fit, ω_fit, B_fit, β_h_fit,
β_v_fit, δ_fit)
fitted_cumulative_cases = np.cumsum(fitted_I_h)

# Plot cumulative cases
plt.figure(figsize=(10, 6))
plt.scatter(weeks, cumulative_cases, label="Observed Cumulative Cases",
color="red")
plt.plot(weeks, fitted_cumulative_cases, label="Fitted Model (Cumulative)",
color="blue")
plt.xlabel("Week")
plt.ylabel("Cumulative Cases (I_h)")
plt.title("Cumulative Infected Cases vs. Time")
plt.legend()
plt.grid()
```

```
plt.show()

# Print fitted parameters
print("Fitted Parameters:")
print(f"ϕ = {ϕ_fit:.6f}, k = {k_fit:.6f}, ω = {ω_fit:.6f}, B = {B_fit:.6f}")
print(f"β_h = {β_h_fit:.6f}, β_v = {β_v_fit:.6f}, δ = {δ_fit:.6f}")
```

Figure 5. 2. Coding for State functions

```
import numpy as np

def mosquito_human_model(t, y, u1, u2, u3, phi, muA, muh, muv, k, omega, B,
Beta_h, Beta_v, delta, theta, sigma, gamma, Nh):
    Av, Sv, Ev, Iv, Sh, Vh, Ih, Rh = y

    # Mosquito equations
    # Pre-adult / Larva
    dAv_dt = phi * (1 - (Av / (k * Nh))) * (Sv + Ev + Iv) - (omega + muA + u1)
* Av
    # Susceptible Mosquito
    dSv_dt = omega * Av - ((B * (Beta_v * Ih / Nh)) + muv + u2) * Sv
    # Exposed Mosquito
    dEv_dt = (B * (Beta_v * Ih / Nh) * Sv) - (delta + muv + u2) * Ev
    # Infected Mosquito
    dIv_dt = (delta * Ev) - (muv + u2) *
Iv

    # Human equations
    # Susceptible Human
    dSh_dt = (muh * Nh) + (theta * Vh) - ((B * (Beta_h * Iv / Nh)) + muh + u3)
* Sh
    # Vaccinated Human
    dVh_dt = (u3 * Sh) - (theta + ((sigma * B * Beta_h * Iv) / Nh) + muh) *
Vh
    # Infected Human
    dIh_dt = ((B * Sh * Beta_h * Iv) / Nh) + ((sigma * Vh * B * Beta_h * Iv) /
Nh) - (gamma + muh) * Ih
    # Recovered Human
    dRh_dt = (gamma * Ih) - (muh *
Rh)

    return np.array([dAv_dt, dSv_dt, dEv_dt, dIv_dt, dSh_dt, dVh_dt, dIh_dt,
dRh_dt])
```

Figure 5. 3. Coding for adjoint functions

```
import numpy as np

def adjoint(t, lam, y, u1, u2, u3, phi, muA, muh, muv, k, omega, B, Beta_h,
Beta_v, delta, theta, sigma, gamma, Nh):
    Av, Sv, Ev, Iv, Sh, Vh, Ih, Rh = y
    lambda_Av, lambda_Sv, lambda_Ev, lambda_Iv, lambda_Sh, lambda_Vh,
lambda_Ih, lambda_Rh = lam

    # Weight constants
    # Iv
    W1 = 100
    # Ih
    W2 = 100
    # larvicide
    W3 = 1000000000
    # insecticide
    W4 = 2500000000
    # vaccination
    W5 = 100000000000

    # Adjoint equations
    d_lambda_Av = -(lambda_Av * ((-(Sv + Ev + Iv)/(k * Nh)) - omega - muA -
u1) + lambda_Sv * omega)
    d_lambda_Sv = -(lambda_Sv * (-((B * Beta_v * Ih) / Nh) - muv - u2) +
lambda_Av * phi * (1 - (Av / (k * Nh))) + lambda_Ev * (B * Beta_v * Ih / Nh))
    d_lambda_Ev = -(lambda_Ev * (- delta - muv - u2) + lambda_Av * phi * (1 -
(Av / (k * Nh))) + lambda_Iv * delta)
    d_lambda_Iv = -(lambda_Iv * (- muv - u2) + lambda_Av * phi * (1 - (Av / (k
* Nh))) + lambda_Sh * (B * Beta_h * Sh / Nh) -  lambda_Vh * (sigma * B *
Beta_h * Vh / Nh) + lambda_Ih * ((B * Beta_h * Sh / Nh) + (sigma * B * Beta_h
* Vh / Nh)) + W1)
    d_lambda_Sh = -(lambda_Sh * (-(B * Beta_h * Iv / Nh) - muh - u3) +
lambda_Vh * u3 + lambda_Ih * (B * Beta_h * Iv / Nh))
    d_lambda_Vh = -(lambda_Vh * (- theta - (sigma * B * Beta_h * Iv / Nh) -
muh) + (lambda_Sh * theta) +  lambda_Ih * (sigma * B * Beta_h * Iv / Nh))
    d_lambda_Ih = -(lambda_Ih * (- gamma + muh) + (lambda_Rh * gamma) -
lambda_Sv * (B * Beta_v * Sv / Nh) + lambda_Ev * (B * Beta_v * Sv / Nh) + W2)
    d_lambda_Rh = lambda_Rh * muh

    return np.array([d_lambda_Av, d_lambda_Sv, d_lambda_Ev, d_lambda_Iv,
d_lambda_Sh, d_lambda_Vh, d_lambda_Ih, d_lambda_Rh])
```

Figure 5. 4. Coding for control functions

```
import numpy as np


def update_controls(y, lam, W3, W4, W5, u1_prev, u2_prev, u3_prev,
alpha=0.5):
    Av, Sv, Ev, Iv, Sh, Vh, Ih, Rh = y
    lambda_Av, lambda_Sv, lambda_Ev, lambda_Iv, lambda_Sh, lambda_Vh,
lambda_Ih, lambda_Rh = lam

    # Compute new control values
    computed_u1 = np.clip((lambda_Av * Av) / W3, 0, 1)
    computed_u2 = np.clip(((lambda_Sv * Sv) + (lambda_Ev * Ev) + (lambda_Iv *
Iv)) / W4, 0, 1)
    computed_u3 = np.clip(((lambda_Sh * Sh) + (lambda_Vh * Sh)) / W5, 0, 1)

    # Apply relaxation factor to smooth updates
    u1 = (1 - alpha) * u1_prev + alpha * computed_u1
    u2 = (1 - alpha) * u2_prev + alpha * computed_u2
    u3 = (1 - alpha) * u3_prev + alpha * computed_u3

    # Ensure values remain within [0,1]
    u1 = np.clip(u1, 0, 1)
    u2 = np.clip(u2, 0, 1)
    u3 = np.clip(u3, 0, 1)

    return u1, u2, u3
```

Figure 5. 5. Coding for plotting graphs of simulation results

```
import matplotlib.pyplot as plt

def plot_strategy(time, Ih_control, Ih_comparison, label_control,
label_comparison, title, ylabel):
    plt.figure(figsize=(10, 5))
    plt.plot(time, Ih_comparison, 'r-', label=label_comparison)
    plt.plot(time, Ih_control, 'b-', label=label_control)
    plt.xlabel('Time (weeks)')
    plt.ylabel(ylabel)
    plt.title(title)
    plt.legend()
    plt.grid()
    plt.show()

def plot_controls(time, u1=None, u2=None, u3=None, title="Control Strategy
Over Time"):
    plt.figure(figsize=(10, 5))
```

```
    if u1 is not None:
        plt.plot(time, u1, 'r-', linewidth=2, label='u1 (Larvicide)')
    if u2 is not None:
        plt.plot(time, u2, 'b-', linewidth=2, label='u2 (Fogging)')
    if u3 is not None:
        plt.plot(time, u3, 'g-', linewidth=2, label='u3 (Vaccination)')

    plt.xlabel('Time (weeks)')
    plt.ylabel('Control Variable Value')
    plt.title(title)
    plt.legend()
    plt.grid()
    plt.show()
```

Figure 5. 6. Coding for the main python program

```
import numpy as np
import matplotlib.pyplot as plt
from State_Function import mosquito_human_model
from Adjoint_Function import adjoint
from Control_Function import update_controls
from Plot_Graph import plot_strategy, plot_controls

# Time parameters
t0 = 0
T = 42              # Total time in weeks
N = 100             # Number of time steps
dt = (T - t0) / N

# Initialize state and adjoint variables
y = np.zeros((N + 1, 8))    # State variables
lam = np.zeros((N + 1, 8))  # Adjoint variables

#parameters value
Nh = 34058800     # Total human population
muA = 0.42        # Natural mortality of larvae (per week)
muh = 0.0069      # Natural mortality rate of humans (per week)
theta = 0.0018    # Vaccine waning rate (per week)
sigma = 0.198     # Proportion of vaccinated humans infected
gamma = 0.7       # Human recovery rate (per week)
muv = 0.7         # Natural mortality of mosquitoes (per week)
phi = 5.1         # Oviposition rate
k = 39.9          # Mosquito larvae density per person
omega = 0.897548  # Larvae development rate to adult
B = 0.71          # Mosquito bite rate
Beta_h = 0.11     # Infection transmission rate from infected mosquitoes to
susceptible humans
```

```
Beta_v = 0.51     # Infection transmission rate from infected humans to
susceptible mosquitoes
delta = 0.51      # Rate of disease advancement in exposed mosquitoes


# Initial conditions (same as defined in State_Function.py)
Sh0 = 34058800 - 3181
Vh0 = 0
Ih0 = 3181
Rh0 = 0
Av0 = 3 * 34058800
Sv0 = (4 * 34058800) - 200000
Ev0 = 100000
Iv0 = 100000
y[0] = [Av0, Sv0, Ev0, Iv0, Sh0, Vh0, Ih0, Rh0]

# Initial controls
u1, u2, u3 = 0.001, 0.001, 0.001

# Weights for control
W3, W4, W5 = 1e9, 2.5e9, 1e11

# RK4 Forward function
def RK4_forward(y, u1, u2, u3):
    for i in range(N):
        k1 = np.array(mosquito_human_model(i * dt, y[i], u1, u2, u3, phi, muA,
muh, muv, k, omega, B, Beta_h, Beta_v, delta, theta, sigma, gamma, Nh))
        k2 = np.array(mosquito_human_model((i + 0.5) * dt, y[i] + 0.5 * dt *
k1, u1, u2, u3, phi, muA, muh, muv, k, omega, B, Beta_h, Beta_v, delta, theta,
sigma, gamma, Nh))
        k3 = np.array(mosquito_human_model((i + 0.5) * dt, y[i] + 0.5 * dt *
k2, u1, u2, u3, phi, muA, muh, muv, k, omega, B, Beta_h, Beta_v, delta, theta,
sigma, gamma, Nh))
        k4 = np.array(mosquito_human_model((i + 1) * dt, y[i] + dt * k3, u1,
u2, u3, phi, muA, muh, muv, k, omega, B, Beta_h, Beta_v, delta, theta, sigma,
gamma, Nh))
        y[i + 1] = y[i] + (dt / 6) * (k1 + 2 * k2 + 2 * k3 + k4)
    return y

# RK4 Backward function
def RK4_backward(lam, y, u1, u2, u3):
    lam[-1] = np.zeros(8)  # Final boundary conditions
    for i in range(N - 1, -1, -1):
        k1 = np.array(adjoint(i * dt, lam[i], y[i], u1, u2, u3, phi, muA, muh,
muv, k, omega, B, Beta_h, Beta_v, delta, theta, sigma, gamma, Nh))
        k2 = np.array(adjoint((i - 0.5) * dt, lam[i] - 0.5 * dt * k1, y[i],
u1, u2, u3, phi, muA, muh, muv, k, omega, B, Beta_h, Beta_v, delta, theta,
sigma, gamma, Nh))
```

```
        k3 = np.array(adjoint((i - 0.5) * dt, lam[i] - 0.5 * dt * k2, y[i],
u1, u2, u3, phi, muA, muh, muv, k, omega, B, Beta_h, Beta_v, delta, theta,
sigma, gamma, Nh))
        k4 = np.array(adjoint((i - 1) * dt, lam[i] - dt * k3, y[i], u1, u2,
u3, phi, muA, muh, muv, k, omega, B, Beta_h, Beta_v, delta, theta, sigma,
gamma, Nh))
        lam[i - 1] = lam[i] - (dt / 6) * (k1 + 2 * k2 + 2 * k3 + k4)
    return lam

# Initialize previous control variables for relaxation
u1_prev, u2_prev, u3_prev = 0.001, 0.001, 0.001  # Small initial values

# Define relaxation factor (controls smoothness)
alpha = 0.1  # Adjust this value between 0 and 1 for more gradual updates

# Arrays to store control values over time
u1_values, u2_values, u3_values = [], [], []

# Forward-Backward Sweep Method
for _ in range(100):                                    # Iterate to find
optimal control
    y = RK4_forward(y, u1_prev, u2_prev, u3_prev)          # Forward
simulation
    lam = RK4_backward(lam, y, u1_prev, u2_prev, u3_prev)  # Backward adjoint

    # Compute new control values based on costates (lambda)
    u1_new, u2_new, u3_new = update_controls(y[-1], lam[-1], W3, W4, W5,
u1_prev, u2_prev, u3_prev)

    # Apply relaxation for smooth transitions
    u1_prev = (1 - alpha) * u1_prev + alpha * u1_new
    u2_prev = (1 - alpha) * u2_prev + alpha * u2_new
    u3_prev = (1 - alpha) * u3_prev + alpha * u3_new

    # Store control values for plotting
    u1_values.append(u1_prev)
    u2_values.append(u2_prev)
    u3_values.append(u3_prev)

# Convert lists to numpy arrays for plotting
u1_values = np.array(u1_values)
u2_values = np.array(u2_values)
u3_values = np.array(u3_values)


# Time array
time = np.linspace(t0, T, N + 1)

# Run simulation with u1 = 0, u2 = 0, u3 = 0
```

```
u1_zero, u2_zero, u3_zero = 0, 0, 0
y_zero_control = RK4_forward(np.copy(y), u1_zero, u2_zero, u3_zero)

# Extract Ih and Iv for no control scenario
Av_zero_control = y_zero_control[:, 0]
Sv_zero_control = y_zero_control[:, 1]
Ev_zero_control = y_zero_control[:, 2]
Iv_zero_control = y_zero_control[:, 3]
Sh_zero_control = y_zero_control[:, 4]
Vh_zero_control = y_zero_control[:, 5]
Ih_zero_control = y_zero_control[:, 6]
Rh_zero_control = y_zero_control[:, 7]

# Strategy 1: u1 ≠ 0, u2 = 0, u3 = 0
y_u1_control = RK4_forward(np.copy(y), u1_prev, 0, 0)
Ih_u1_control = y_u1_control[:, 6]
Iv_u1_control = y_u1_control[:, 3]

# Strategy 2: u1 = 0, u2 ≠ 0, u3 = 0
y_u2_control = RK4_forward(np.copy(y), 0, u2_prev, 0)
Ih_u2_control = y_u2_control[:, 6]
Iv_u2_control = y_u2_control[:, 3]

# Strategy 3: u1 = 0, u2 = 0, u3 ≠ 0
y_u3_control = RK4_forward(np.copy(y), 0, 0, u3_prev)
Ih_u3_control = y_u3_control[:, 6]
Iv_u3_control = y_u3_control[:, 3]

# Strategy 4: u1 ≠ 0, u2 ≠ 0, u3 = 0
y_u1_u2_control = RK4_forward(np.copy(y), u1_prev, u2_prev, 0)
Ih_u1_u2_control = y_u1_u2_control[:, 6]
Iv_u1_u2_control = y_u1_u2_control[:, 3]

# Strategy 5: u1 ≠ 0, u2 = 0, u3 ≠ 0
y_u1_u3_control = RK4_forward(np.copy(y), u1_prev, 0, u3_prev)
Ih_u1_u3_control = y_u1_u3_control[:, 6]
Iv_u1_u3_control = y_u1_u3_control[:, 3]

# Strategy 6: u1 = 0, u2 ≠ 0, u3 ≠ 0
y_u2_u3_control = RK4_forward(np.copy(y), 0, u2_prev, u3_prev)
Ih_u2_u3_control = y_u2_u3_control[:, 6]
Iv_u2_u3_control = y_u2_u3_control[:, 3]

# Strategy 7: u1 ≠ 0, u2 ≠ 0, u3 ≠ 0
y_u1_u2_u3_control = RK4_forward(np.copy(y), u1_prev, u2_prev, u3_prev)
Av_u1_u2_u3_control = y_u1_u2_u3_control[:, 0]
Sv_u1_u2_u3_control = y_u1_u2_u3_control[:, 1]
Ev_u1_u2_u3_control = y_u1_u2_u3_control[:, 2]
```

```
Iv_u1_u2_u3_control = y_u1_u2_u3_control[:, 3]
Sh_u1_u2_u3_control = y_u1_u2_u3_control[:, 4]
Vh_u1_u2_u3_control = y_u1_u2_u3_control[:, 5]
Ih_u1_u2_u3_control = y_u1_u2_u3_control[:, 6]
Rh_u1_u2_u3_control = y_u1_u2_u3_control[:, 7]

# Plot for Strategy 1 - Human Infections
plot_strategy(
    time,
    Ih_u1_control,
    Ih_zero_control,
    label_control='With Control (u1≠0, u2=0, u3=0)',
    label_comparison='No Control (u1=0, u2=0, u3=0)',
    title='Strategy 1: Effect of u1 on Infected Human Population',
    ylabel='Infected Humans (Ih)'
)

# Plot for Strategy 1 - Vector Infections
plot_strategy(
    time,
    Iv_u1_control,
    Iv_zero_control,
    label_control='With Control (u1≠0, u2=0, u3=0)',
    label_comparison='No Control (u1=0, u2=0, u3=0)',
    title='Strategy 1: Effect of u1 on Infected Vector Population',
    ylabel='Infected Vectors (Iv)'
)

# Strategy 1: Only u1
plot_controls(time[:-1], u1=u1_values, title='Control Strategy 1 (u1 only)')


# Plot for Strategy 2 - Human Infections
plot_strategy(
    time,
    Ih_u2_control,
    Ih_zero_control,
    label_control='With Control (u1=0, u2≠0, u3=0)',
    label_comparison='No Control (u1=0, u2=0, u3=0)',
    title='Strategy 2: Effect of u2 on Infected Human Population',
    ylabel='Infected Humans (Ih)'
)

# Plot for Strategy 2 - Vector Infections
plot_strategy(
    time,
    Iv_u2_control,
    Iv_zero_control,
    label_control='With Control (u1=0, u2≠0, u3=0)',
```

```
    label_comparison='No Control (u1=0, u2=0, u3=0)',
    title='Strategy 2: Effect of u2 on Infected Vector Population',
    ylabel='Infected Vectors (Iv)'
)

# Strategy 2: Only u2
plot_controls(time[:-1], u2=u2_values, title='Control Strategy 2 (u2 only)')

# Plot for Strategy 3 - Human Infections
plot_strategy(
    time,
    Ih_u3_control,
    Ih_zero_control,
    label_control='With Control (u1=0, u2=0, u3≠0)',
    label_comparison='No Control (u1=0, u2=0, u3=0)',
    title='Strategy 3: Effect of u3 on Infected Human Population',
    ylabel='Infected Humans (Ih)'
)

# Plot for Strategy 3 - Vector Infections
plot_strategy(
    time,
    Iv_u3_control,
    Iv_zero_control,
    label_control='With Control (u1=0, u2=0, u3≠0)',
    label_comparison='No Control (u1=0, u2=0, u3=0)',
    title='Strategy 3: Effect of u3 on Infected Vector Population',
    ylabel='Infected Vectors (Iv)'
)

# Strategy 3: Only u3
plot_controls(time[:-1], u3=u3_values, title='Control Strategy 3 (u3 only)')

# Plot for Strategy 4 - Human Infections
plot_strategy(
    time,
    Ih_u1_u2_control,
    Ih_zero_control,
    label_control='With Control (u1≠0, u2≠0, u3=0)',
    label_comparison='No Control (u1=0, u2=0, u3=0)',
    title='Strategy 4: Effect of u1 & u2 on Infected Human Population',
    ylabel='Infected Humans (Ih)'
)

# Plot for Strategy 4 - Vector Infections
plot_strategy(
    time,
    Iv_u1_u2_control,
```

```
    Iv_zero_control,
    label_control='With Control (u1≠0, u2≠0, u3=0)',
    label_comparison='No Control (u1=0, u2=0, u3=0)',
    title='Strategy 4: Effect of u1 & u2 on Infected Vector Population',
    ylabel='Infected Vectors (Iv)'
)

# Strategy 4: u1 and u2
plot_controls(time[:-1], u1=u1_values, u2=u2_values, title='Control Strategy 4
(u1 & u2)')

# Plot for Strategy 5 - Human Infections
plot_strategy(
    time,
    Ih_u1_u3_control,
    Ih_zero_control,
    label_control='With Control (u1≠0, u2=0, u3≠0)',
    label_comparison='No Control (u1=0, u2=0, u3=0)',
    title='Strategy 5: Effect of u1 & u3 on Infected Human Population',
    ylabel='Infected Humans (Ih)'
)

# Plot for Strategy 5 - Vector Infections
plot_strategy(
    time,
    Iv_u1_u3_control,
    Iv_zero_control,
    label_control='With Control (u1≠0, u2=0, u3≠0)',
    label_comparison='No Control (u1=0, u2=0, u3=0)',
    title='Strategy 5: Effect of u1 & u3 on Infected Vector Population',
    ylabel='Infected Vectors (Iv)'
)

# Strategy 5: u1 and u3
plot_controls(time[:-1], u1=u1_values, u3=u3_values, title='Control Strategy 5
(u1 & u3)')

# Plot for Strategy 6 - Human Infections
plot_strategy(
    time,
    Ih_u2_u3_control,
    Ih_zero_control,
    label_control='With Control (u1=0, u2≠0, u3≠0)',
    label_comparison='No Control (u1=0, u2=0, u3=0)',
    title='Strategy 6: Effect of u2 & u3 on Infected Human Population',
    ylabel='Infected Humans (Ih)'
)
```

```
# Plot for Strategy 6 - Vector Infections
plot_strategy(
    time,
    Iv_u2_u3_control,
    Iv_zero_control,
    label_control='With Control (u1=0, u2≠0, u3≠0)',
    label_comparison='No Control (u1=0, u2=0, u3=0)',
    title='Strategy 6: Effect of u2 & u3 on Infected Vector Population',
    ylabel='Infected Vectors (Iv)'
)

# Strategy 6: u2 and u3
plot_controls(time[:-1], u2=u2_values, u3=u3_values, title='Control Strategy 6
(u2 & u3)')

# Plot for Strategy 7 - Pre-Adult Mosquito
plot_strategy(
    time,
    Av_u1_u2_u3_control,
    Av_zero_control,
    label_control='With Control (u1≠0, u2≠0, u3≠0)',
    label_comparison='No Control (u1=0, u2=0, u3=0)',
    title='Strategy 7: Effect of u1, u2 & u3 on Pre-Adult Mosquito
Population',
    ylabel='Pre-Adult Mosquito (Av)'
)

# Plot for Strategy 7 - Susceptible Mosquito
plot_strategy(
    time,
    Sv_u1_u2_u3_control,
    Sv_zero_control,
    label_control='With Control (u1≠0, u2≠0, u3≠0)',
    label_comparison='No Control (u1=0, u2=0, u3=0)',
    title='Strategy 7: Effect of u1, u2 & u3 on Susceptible Mosquito
Population',
    ylabel='Susceptible (Sv)'
)

# Plot for Strategy 7 - Exposed Mosquito
plot_strategy(
    time,
    Ev_u1_u2_u3_control,
    Ev_zero_control,
    label_control='With Control (u1≠0, u2≠0, u3≠0)',
    label_comparison='No Control (u1=0, u2=0, u3=0)',
    title='Strategy 7: Effect of u1, u2 & u3 on Exposed Mosquito Population',
    ylabel='Exposed (Ev)'
```

```
)

# Plot for Strategy 7 - Vector Infections
plot_strategy(
    time,
    Iv_u1_u2_u3_control,
    Iv_zero_control,
    label_control='With Control (u1≠0, u2≠0, u3≠0)',
    label_comparison='No Control (u1=0, u2=0, u3=0)',
    title='Strategy 7: Effect of u1, u2 & u3 on Infected Vector Population',
    ylabel='Infected Vectors (Iv)'
)

# Plot for Strategy 7 - Susceptible Human
plot_strategy(
    time,
    Sh_u1_u2_u3_control,
    Sh_zero_control,
    label_control='With Control (u1≠0, u2≠0, u3≠0)',
    label_comparison='No Control (u1=0, u2=0, u3=0)',
    title='Strategy 7: Effect of u1, u2 & u3 on Susceptible Human Population',
    ylabel='Susceptible Humans (Sh)'
)

# Plot for Strategy 7 - Vaccinated Human
plot_strategy(
    time,
    Vh_u1_u2_u3_control,
    Vh_zero_control,
    label_control='With Control (u1≠0, u2≠0, u3≠0)',
    label_comparison='No Control (u1=0, u2=0, u3=0)',
    title='Strategy 7: Effect of u1, u2 & u3 on Vaccinated Human Population',
    ylabel='Vaccinated Humans (Vh)'
)

# Plot for Strategy 7 - Human Infections
plot_strategy(
    time,
    Ih_u1_u2_u3_control,
    Ih_zero_control,
    label_control='With Control (u1≠0, u2≠0, u3≠0)',
    label_comparison='No Control (u1=0, u2=0, u3=0)',
    title='Strategy 7: Effect of u1, u2 & u3 on Infected Human Population',
    ylabel='Infected Humans (Ih)'
)

# Plot for Strategy 7 - Recovered Human
plot_strategy(
```

```
    time,
    Rh_u1_u2_u3_control,
    Rh_zero_control,
    label_control='With Control (u1≠0, u2≠0, u3≠0)',
    label_comparison='No Control (u1=0, u2=0, u3=0)',
    title='Strategy 7: Effect of u1, u2 & u3 on Recovered Human Population',
    ylabel='Recovered Humans (Rh)'
)

# Strategy 7: u1, u2, and u3
plot_controls(time[:-1], u1=u1_values, u2=u2_values, u3=u3_values,
title='Control Strategy 7 (u1, u2 & u3)')
```