

# **OPTIMAL CONTROL STRATEGY ON MATHEMATICAL MODELING OF SYPHILIS INFECTION**



**Shewarega Cheru Ayanie**

**A Thesis Submitted to the Department of Mathematics  
College of Natural Science**

**Presented in Partial Fulfillment of the Requirement for the Degree of  
Master's in Applied Mathematics (Mathematical Modeling)**

**SALALE UNIVERSITY**

**May, 2024  
Fitcha, Ethiopia**

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**Co-advisor: Birke Siyum**

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## APPROVAL OF BOARD OF EXAMINERS

We, the undersigned, members of the board of examiners of the final open defense, Shewarega Cheru Ayanie have read and evaluated his thesis entitle **”Optimal Control Strategy on Mathematical Modeling of Syphilis Infection”** and examined the candidate. This is, therefore, to certify that the thesis has been accepted in partial fulfillment of the requirement of the degree of Master’s in Applied Mathematics (Mathematical Modeling).

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## DECLARATION

I hereby declare that this MSc Thesis is my original work and has not been presented for a degree in any other university, and all sources of material used for this thesis have been duly acknowledged.

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This MSc dissertation has been submitted for examination with my approval as-thesis advisor/ dissertation Supervisor.

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## **ABBREVIATION AND ACRONYMS**

DFEP	Disease Free Equilibrium Point
EEP	Endemic Equilibrium Point
EPHI	Ethiopia Public Health Institute
MSM	Male having Sex with Male
FSWs	Female Sex Workers
STI	Sexually Transmitted Infections
WHO	World Health Organization

## ABSTRACT

*In this thesis, our study focused on developing a mathematical model for the Syphilis disease, incorporating optimal control strategies. Initially, we rigorously established the positivity and boundedness of the model's solution within a specified domain. Moreover, utilizing the next generation matrix, we derived a basic reproduction number, which is crucial for assessing disease dynamics. Both local and global stability of the disease-free equilibrium and endemic equilibrium point of the model equation was established. The results show that, if the basic reproduction number is less than one, the solution converges to the disease-free steady-state, rendering the disease-free equilibrium asymptotically stable. To assess their impact on disease transmission dynamics, we conducted sensitivity analysis of the model equation on the key parameters. We extended the model to optimal control by incorporate control measures, such as preventive interventions for protecting susceptible individuals and treatment strategies for reducing infectious transmission, was obtained through the Pontryagin minimum principle. The efficacy of the proposed models was validated through numerical simulations, and sensitivity analysis provided valuable insights into their robustness. Our analysis suggests that integrating available treatment and prevention techniques to mitigate Syphilis outbreaks yields greater efficacy. Ultimately, numerical simulations emphasize that the most optimal approach involves a synergistic application of prevention and treatment strategies to minimize disease burden.*

**Keywords:** Modeling; Optimal; Stability; Simulation; Syphilis.

# CHAPTER 1

## INTRODUCTION

### 1.1 Background of the Study

Infectious diseases have the potential to cause significant mortality within a population and result in substantial healthcare expenses and disease control efforts. It is imperative to allocate adequate resources to prevent the spread of infectious diseases through the implementation of effective control mechanisms. Infectious diseases can stem from various sources including bacteria, parasites, fungi, and viruses ([Wagenlehner et al., 2016](#)). Prominent and impactful infectious diseases encompass Human Immunodeficiency Virus (HIV), Human Papillomavirus (HPV), Hepatitis B, Candidiasis, Syphilis, Gonorrhea, and Trichomoniasis. Among these, HIV, HPV, and Hepatitis B are viral diseases, while Gonorrhea and Syphilis are bacterial in nature. Candidiasis is attributed to fungal infection, and Trichomoniasis to parasitic

The infectious diseases mentioned above are commonly transmitted through sexual intercourse, including vaginal, anal, and oral sex ([Wagenlehner et al., 2016](#)), ([Low et al., 2006](#)). Other transmission routes include blood transfusion, injecting drug use (IDUs), childbirth, exchange of contaminated syringes and needles, travel by infected individuals, and sharing of sex toys ([Blower and Medley, 1992](#)), ([Ito et al., 2019](#)), ([Aral et al., 2005](#)). In addition, community transmission occurs among men who have sex with men (MSM) and female sex workers (FSW) in various countries, contributing to the spread of these infections ([Chen et al., 2011](#)), ([Aral et al., 2005](#)).

According to the World Health Organization fact sheet, more than one million cases of sexually transmitted infections are acquired globally every day, with an estimated 376 million new infections from diseases such as Syphilis, Chlamydia, Gonorrhea, and Trichomoniasis occurring annually ([Zimet et al., 2000](#)). Not all infectious diseases exhibit symptoms; some are symptomatic while others may be asymptomatic. HIV/AIDS, Human Papillomavirus, and Candidiasis

are symptomatic, while Syphilis, Hepatitis B, Gonorrhea, and Trichomoniasis are typically asymptomatic. Common symptoms of infectious diseases include headache, painless sores on the genitalia, weight loss, and burning during urination.

Syphilis is a bacterial sexually transmitted infection caused by the bacterium *Treponema pallidum*, a subspecies of pallidum ([Abbasi, 2017](#)). Many individuals with syphilis may be asymptomatic, and the manifestation of symptoms varies across the four stages of infection. Primary syphilis typically manifests within 10 days to 3 months, presenting as a painless sore commonly located on the penis, vagina, or within the oral cavity. Secondary syphilis develops several weeks after the disappearance of the initial sore, characterized by the appearance of body rashes, general malaise, weight loss, and the formation of skin growths around the vulva. During the latent stage, individuals may remain asymptomatic for several years. In the tertiary stage, syphilis can inflict severe damage on the heart, brain, and nervous system. Understanding the transmission mechanisms of this disease is crucial for effective prevention.

It is transmitted either directly through contact with an infected person's sore during vaginal, oral or anal sex or indirectly during pregnancy and childbirth and sometimes through breastfeeding. Less often, syphilis can transmit by kissing or touching an active sore on the lips, tongue, mouth, breasts or genitals. The bacteria enter the body through minor cuts or scrapes in the skin or in the moist inner lining of some body parts. But they can't be transmitted through casual contact with objects that an infected person has touched. So it cannot transmit by using the same toilet, bathtub, clothing, eating utensils, doorknobs, swimming pools or hot tubs. From this, it is clear that the transmission mechanisms of Syphilis disease, so we must take care ourselves from this transmission .

Syphilis is a disease that is both treatable and curable. Individuals who suspect they may have contracted syphilis are advised to seek consultation with a qualified healthcare professional. The initial phase of syphilis necessitates treatment with a benzathine penicillin injection, supplemented by doxycycline

as a secondary form of treatment. Subsequent stages of the disease also require penicillin-based treatment, albeit necessitating a greater number of doses. Typically, these doses are administered on a weekly basis over a three-week period, a regimen that remains consistent even in instances where the stage of infection cannot be conclusively determined (WHO).

In the field of mathematics, the widespread application of mathematical modeling serves to articulate the processes involved in disease transmission, pinpoint the key factors contributing to disease spread, and devise effective control or prevention intervention strategies. Furthermore, it facilitates an in-depth comprehension of the intricate dynamics of epidemic transmission. According to ([Oyeniya et al., 2017](#)), mathematical modeling presents innovative approaches to comprehend the increasingly complex behavior of technology, which forms the cornerstone of contemporary industrial output. In the domain of modeling, rigorous research analysis and informed decision-making are imperative, thereby signifying its paramount significance in technological advancement. Moreover, mathematical models foster expeditious innovation cycles, owing to their capability to promptly generate original responses and solutions ([Prabhakararao, 2014](#)).

The primary objective of optimal control theory is to minimize the spread of disease within specific regions by identifying the most effective intervention strategies through the application of mathematical models. This theory equips decision-makers with valuable tools for the strategic planning and assessment of disease control initiatives, facilitating the implementation of optimal control interventions and the allocation of resources to mitigate the disease burden. Key considerations encompassed in this framework include the cost of interventions, disease dynamics, and available resources. Moreover, optimal control models enable the evaluation of the cost-effectiveness of diverse interventions. Policy-makers are thereby empowered to prioritize interventions that maximize health benefits relative to costs, factoring in metrics such as quality-adjusted life years gained, the impact on disease reduction, and implementation costs.

The effective control of Syphilis disease is essential to diminish its prevalence within the community. Accurate information concerning the prevalence and severity of Syphilis in Ethiopia is a critical prerequisite for devising an effective control strategy. Despite the availability of control strategies, the disease continues to impose a substantial burden on human health, particularly in sub-Saharan Africa, including Ethiopia. Consequently, this study is designed with the primary objective of formulating a mathematical model with optimal control and analyzing the threshold dynamics of Syphilis to identify the most effective control strategies for the people of Ethiopia and the broader African population.

## 1.2 Statement of the Problem

Syphilis has emerged as a significant global public health concern, primarily stemming from unsafe sexual practices and contact. Its endemic status in numerous countries is troubling, with a substantial number of new cases reported worldwide. The World Health Organization (WHO) estimates that in 2020, approximately 7.1 million adults were afflicted with Syphilis (World Health Organization et al., 2020). Consequently, scientists have devoted considerable efforts to comprehensively study the dynamics of Syphilis, recognizing its substantial threat to public health. These endeavors have yielded valuable insights. For example, (Abdullahi et al., 2016) conducted a study on epidemiological modeling, emphasizing the methods and applicability of examining the transmission dynamics of Syphilis infection. Additionally, numerous other studies have been conducted on the prevention and control of Syphilis.

The dynamics of Syphilis present several practical questions that necessitate a reliable mathematical model to enrich the understanding and identification of crucial factors influencing disease dynamics. In response, we introduce an epidemiological model designed to offer long-term, quantitative, and qualitative insights. This model facilitates predictions of outbreaks and persistence, aids in response planning, enhances public health planning, and minimizes costs through optimal control strategies. Consequently, this study endeavors to address the following fundamental research questions:

1. In what ways can mathematical models be applied to accurately describe the dynamics of Syphilis infection?
2. What is the purpose of integrating optimal control strategies into the formulated mathematical model of Syphilis infection?
3. How can we determine the stability, sensitivity, and recommend the most effective strategy for reducing the prevalence of the disease within the community?



## **1.3 Objectives of the study**

### **1.3.1 General Objective**

The primary aim of this study is to develop a mathematical model for analyzing the dynamics of Syphilis disease, incorporating an optimal control strategy.

### **1.3.2 Specific Objectives**

The specific objectives of the study are to:

1. Formulate a mathematical model that accurately describes the dynamics of Syphilis infection.
2. Integrate optimal control strategies into the formulated mathematical model of Syphilis infection.
3. Conduct sensitivity analyses of evaluate the robustness of optimal control strategies derived from the mathematical model.
4. Identifying critical parameters and assessing their impact on disease dynamics.

## **1.4 Significance of the study**

This study endeavors to advance our comprehension of the intricate dynamics of Syphilis transmission by employing non-linear differential equations within a mathematical model. Through the incorporation of control strategies, we endeavor to unearth novel facets of the disease's behavior that may elude conventional models. The potential significance of this study includes:

1. enrich our comprehension of the complex dynamics governing Syphilis transmission. The incorporation of control strategy may unveil novel insights into the diseases behavior that conventional models might overlook.

2. identify and optimize control strategies within the mathematical model, presenting more effective and precisely targeted measures for the management and mitigation of Syphilis outbreaks.
3. establish a foundation for further research and exploration in the intersection of mathematical modeling, infectious disease dynamics, and the application of mathematics in epidemiological studies.

Further, the findings may inform public health policies, influencing decision-makers in crafting strategies to prevent, control, and respond to Syphilis outbreaks with a more informed and evidence-based approach.

## **1.5 The Scope of the Study**

This study investigated the dynamics of syphilis through the application of differential equations while integrating optimal control methods. The primary focus is on the key control strategies that govern the disease dynamics.

## CHAPTER 2

### LITERATURE REVIEW

Mathematical models have been developed to analyze the dynamics of syphilis infection transmission and its associated health complications, as well as to investigate the effectiveness of various intervention strategies against the bacterium. Numerous studies have been undertaken to examine the dynamics and control of syphilis.

[Valentim et al. \(2022\)](#) presented a mathematical model employing nonlinear differential equations to assess the impact of syphilis in Brazil. The country declared a syphilis epidemic in 2016 due to notably high morbidity and mortality rates, particularly in cases of maternal syphilis (MS) and congenital syphilis (CS) with adverse outcomes. The study aimed to quantitatively depict the correlation between reported MS and CS cases in Brazil from 2010 to 2020, accounting for the probability of diagnosis and effective maternal treatment during prenatal care. This approach sought to provide mathematical support for decision-making and coordination of syphilis response efforts. Notably, the analysis did not encompass control strategies.

In their study, ([Stuart et al., 2022](#)) examined the effects of sexual behavior, mass media reporting, and treatment of infected individuals on the dynamics of syphilis transmission. The authors conducted analyses on a full model and two sub-models, concluding that the disease-free equilibrium of the model exhibited both local and global asymptotic stability when the associated reproduction number was less than one. Their assessment of the reproduction number indicated that controlling syphilis transmission would be unattainable if the prevalence of risky sexual behavior remained high. Additionally, while late syphilis infection treatment proved beneficial to infected individuals, it did not impact the reproduction number. The study recommends that effective syphilis control strategies should prioritize reducing the proportion of the population engaging in risky sexual behavior and increasing treatment rates for early syphilis infections. Fur-

thermore, the study highlights the importance of media addressing safe sexual behavior, notwithstanding the absence of consideration of the exposed compartment in their model.

In their study, ([Iboi and Okuonghae, 2016](#)) proposed a deterministic mathematical model to analyze the transmission dynamics of syphilis. The study aimed to qualitatively evaluate the impact of loss of transitory immunity on the transmission process. It was demonstrated that loss of transitory immunity can lead to a phenomenon known as backward bifurcation when the associated reproduction number is less than one. The model indicated that in populations where early latent cases of syphilis do not progress to the primary and secondary stages of infection, the disease-free equilibrium of the model is globally asymptotically stable when the reproduction number is less than one. Conversely, the unique endemic equilibrium of the model is globally asymptotically stable when the reproduction number is greater than one. Furthermore, the study revealed an intricate relationship between the rates of progression from the primary and secondary stages of infection, the treatment rates for individuals in these stages, and the reproduction number and incidence of syphilis in the population. Numerical simulations suggested that high treatment rates for individuals in the primary and secondary stages of infection have a positive cascading effect on the number of infected individuals in the subsequent stages of infection.

The study by ([Korenromp et al., 2020](#)) emphasizes that achieving elimination of syphilis necessitates substantial enhancements in service coverage and investment, the feasibility of which warrants further assessment. Despite inherent uncertainties related to sexual network patterns, natural history parameters, baseline treatment coverage, and antibiotic exposure rates, the model presented serves as an analytical framework and a user-friendly tool to facilitate the formulation of tailored country programs.

The authors, as cited in ([Barro et al., 2018](#)), have devised a mathematical modeling framework to assess the cost-effectiveness of various approaches utilizing rapid tests for syphilis detection in prison populations. They assert that indi-

viduals deprived of liberty represent a vulnerable demographic, and emphasize that current control activities in prisons predominantly hinge on passive case detection. The authors advocate for the availability of affordable alternatives that would facilitate the adoption of active case-finding strategies. Their specific focus is on evaluating these strategies from a health system perspective, using a Chilean male prison population as a basis for exploration.

In a study conducted by (Tuite et al., 2013), it was observed that increasing the fraction of individuals tested, without a concurrent increase in test frequency, led to a smaller decline in incidence. This outcome was attributed to the fact that reductions in infectious syphilis through treatment were offset by an increase in incident syphilis among individuals with prior latent syphilis. Furthermore, the authors determined that, when computing an equivalent number of additional tests performed annually, increased test frequency consistently proved to be more effective than improved coverage.

The study by (Milner and Zhao, 2010) delves into the transmission of syphilis within MSM (men who have sex with men) populations, which have witnessed a resurgence of syphilis cases in recent times. The study formulates a system of ordinary differential equations to model the infection stages and treatment of syphilis. It also calculates a control reproduction number and demonstrates that if this threshold parameter is below one, syphilis will diminish; otherwise, if it exceeds one, a unique endemic equilibrium exists. In specific scenarios, it is shown that this equilibrium is globally asymptotically stable. The study utilizes data from the literature on MSM populations and employs numerical methods to assess the variation and robustness of the control reproduction number with respect to the model parameters, and to determine adequate treatment rates for syphilis eradication. By assuming a closed population with no return to susceptibility, an epidemic model is derived. The study numerically determines final outbreak sizes for various parameter values and investigates their variation and robustness to parameter changes. The findings underscore the significance of early treatment for syphilis control.

[Abdullahi et al. \(2016\)](#) presented a comprehensive analysis of the transmission dynamics of syphilis, with a focus on providing effective solutions to address the syphilis problem. The study employed mathematical modeling to explore various approaches to syphilis screening and their implications for epidemic dynamics and the health outcomes of men who have sex with men (MSM). Notably, the research encompassed the development and scrutiny of a non-linear mathematical model that captures the transmission dynamics of syphilis in a heterogeneous environment with associated complications. Furthermore, the investigation delved into the examination of the existence and uniqueness of the system of equations, along with the application of the Lipschitz criterion to analyze the model.

[Milner and Zhao \(2010\)](#) delineated the application of computational methods in data analysis to aid managerial decision-making in formulating new public policies for the prevention and control of sexually transmitted infections (STIs). These computational techniques integrate experiential knowledge and employ an inference mechanism to apply conditions to a database, elucidating data behavior. This systematic review scrutinized studies utilizing computational methods to establish or enhance aspects related to syphilis. The review underscores the efficacy of computational tools in advancing the comprehensive understanding of syphilis as a global health concern, guiding public policy and practice, and optimizing public health interventions including surveillance, prevention, health service delivery, and diagnostic tool utilization. Adhering to the PRISMA 2020 Statement, the review utilized stringent quality criteria to select relevant studies. Publications considered for this review were sourced from reputable databases including Science Direct, Web of Science, Springer, Scopus, ACM Digital Library, and PubMed, covering studies published between 2015 and 2022, yielding 1,991 studies. Following the application of inclusion, exclusion, and study quality assessment criteria, 26 primary studies were included in the final analysis. The author has proposed a compartmental model to examine the dynamics of syphilis spread within a sexually active population while considering disease

control measures. Through quantitative and qualitative analysis, the model was found to demonstrate backward bifurcation. Furthermore, the model exhibits a globally asymptotically stable disease-free equilibrium (DFE) when the cause of backward bifurcation is eliminated. Additionally, the model displays globally asymptotically stable endemic equilibrium points (EEP) under certain circumstances. Numerical simulations were conducted to propose effective treatment strategies for syphilis in primary and secondary infected individuals, aimed at reducing the incidence of the disease.

The study conducted by ([Omame et al., 2021](#)) presented a nonlinear ordinary differential equation aimed at examining the dynamics of syphilis transmission. The model integrates controls for the prevention and treatment of infected males and females. The author derived the syphilis-free equilibrium (SFE) and syphilis-present equilibrium (SPE) and calculated the basic reproduction number, which serves as a tool for disease transmission control and for establishing conditions governing the local and global stability of the syphilis-free equilibrium. The stability analysis indicates that the model achieves local asymptotic stability when the RouthHurwitz criteria are met and global asymptotic stability. The bifurcation analysis also reveals the manifestation of backward bifurcation in the model. Moreover, the author employed Pontryagin's maximum principle to formulate the optimality system for the syphilis model. This system was subsequently solved numerically to demonstrate that optimal control of syphilis transmission can be achieved through a combination of condom usage and treatment during the primary stage of infection in both infected male and female populations.

[Zhao et al. \(2022\)](#) introduced mathematical models to analyze the transmission dynamics of sexually transmitted infections. These models offer valuable insights for interpreting observed epidemiological patterns and devising effective control programs.

All of the aforementioned studies have developed mathematical models of syphilis dynamics from various perspectives. Some have focused on deterministic models, while others have explored stochastic models, and have subdivided the pop-

ulation into susceptible, infective, treated, and recovered groups. However, none of these studies have examined optimal control strategies in the mathematical modeling of syphilis infection within a community. This knowledge gap has motivated us to undertake this study in order to address this particular aspect.



## **CHAPTER 3**

### **RESEARCH METHODOLOGY**

This chapter describes an overview of the study area, study period, data sources, data collection and analysis methodologies, mathematical procedures, and a detailed description of the modified model employed to fulfill the objectives of the study.

#### **3.1 Description of the Study Area**

This study was conducted in Fitcha, North Shewa, Oromia region, Ethiopia. Fitcha, a town situated 110 kilometers from the capital city of Addis Ababa, is located within the North Shewa zone of the Oromia region. The chosen hospitals for this study are in close proximity to Salale University in the North Shewa region of Ethiopia.

#### **3.2 Study Period**

The study carried out in Fitcha, Ethiopia, from January 2024 to June 2024.

#### **3.3 Source of Data**

The study used secondary sources to procure the necessary data for analysis. These sources encompass Fitcha Hospital, the Ethiopian Public Health Institute (EPHI), and WHO situation reports. In the event that the data obtained from these sources is insufficient, supplementary data was taken from published

#### **3.4 Data Analysis**

In the proposed model analysis, we focused on the mathematical and statistical analysis of the datasets employing computational techniques and a numerical algorithm. We used Runge Kutta method within the MATLAB software to scrutinize the data. The ensuing results visually depicted in graphs to probe the influence of the model parameters on the prevalence of Syphilis within the

population.

### **3.5 Mathematical Procedure**

In the present study, we constructed a mathematical models using a system of non-linear differential equations that describe the dynamics of syphilis transmission. Firstly, we obtained the model's behavior in order to develop a better understanding of the dynamics of the suggested models. Next, we shown that both models are well-posed within a region that is biologically feasible. The equilibrium points of the model equations was analyzed for both local and global stability using the relevant Lyapunov functions and the Jacobian matrix, respectively. By carefully selecting (and estimating) the system parameter values with MATLAB software. Finally, we extend the formulated model to an optimal control problem. For the extended optimal control model, we plot numerical simulations using an iterative fourth-order Runge-Kutta integration scheme to support the analytical results.

## CHAPTER 4

### MODEL FORMULATION AND ANALYSIS

#### 4.1 Syphilis Model Description and Formulation

The total population denoted by  $N(t)$  and categorized into six classes based on their disease status at time  $t$ . Those are susceptible individuals,  $S(t)$ , consisting of individuals who are at risk for developing an infection from syphilis. Exposed individuals,  $E(t)$ , are individuals who are exposed to the syphilis infection. Early stage infected individuals,  $I_e(t)$ , are individuals who are infected at the early stage of syphilis infection. Late stage infected individuals,  $I_l(t)$ , are individuals who are infected at the late stage of syphilis infection. Treated individuals,  $T(t)$ , are individuals who fail treatment. Recovered individuals,  $R(t)$ , are individuals who recovered from syphilis infection.

The population recruited into susceptible class at a rate  $\Pi$ . Susceptible individuals acquire the infection when come in contact with individuals in the disease classes  $I_e(t)$ ,  $I_l(t)$  and  $T$  at a force of infection,  $\lambda = \frac{\beta(I_e(t) + \delta I_l(t) + \gamma T)}{N}$ , where  $\beta$  is the probability that a contact between a susceptible individuals and an infectious individuals will result to an infection. The modification parameter  $\delta$  and  $\gamma$ , explains the assumed variability implies increase and decrease in the relative infectiousness of individuals in  $I_l(t)$  and  $T$  classes respectively, in comparison to infected in the  $I_e(t)$  class. Early stage infected individuals move forward to the similar late stage of the infection at the rate  $\alpha$ . Infected individuals implies both early stage infected and late stage infected individuals are treated at the rate  $\tau$ . A fraction  $q$ , of treated individuals from the early stage of infection will recover and move to the recovery class, while the remaining fraction  $(1 - q)$ , will fail treatment and move to the treated class. A fraction  $p$ , of the treated individuals in the late stage of infection, will recover and move to the recovery class, while the remaining fraction  $(1 - \chi p)$  will fail treatment and move to the treated class, where  $\chi$  rate of individuals in the late stage of infection in comparison to those in the early stage of infection. Individuals who recovered in treated class move

to recovery class at a rate  $\phi$ . Recovered individuals may revert to the susceptible class after losing their immunity at rate  $\omega$ . All class are subjected to a natural death rate  $\mu$ . However, individuals in early stage infected, late stage infected and treated individuals who failed treatment of syphilis infection are induced to mortality at a rate  $\xi_1, \xi_2$  and  $\xi_3$  respectively. All parameters in the model are non-negative.

The schematic diagram of the formulated model is given in Figure 1.

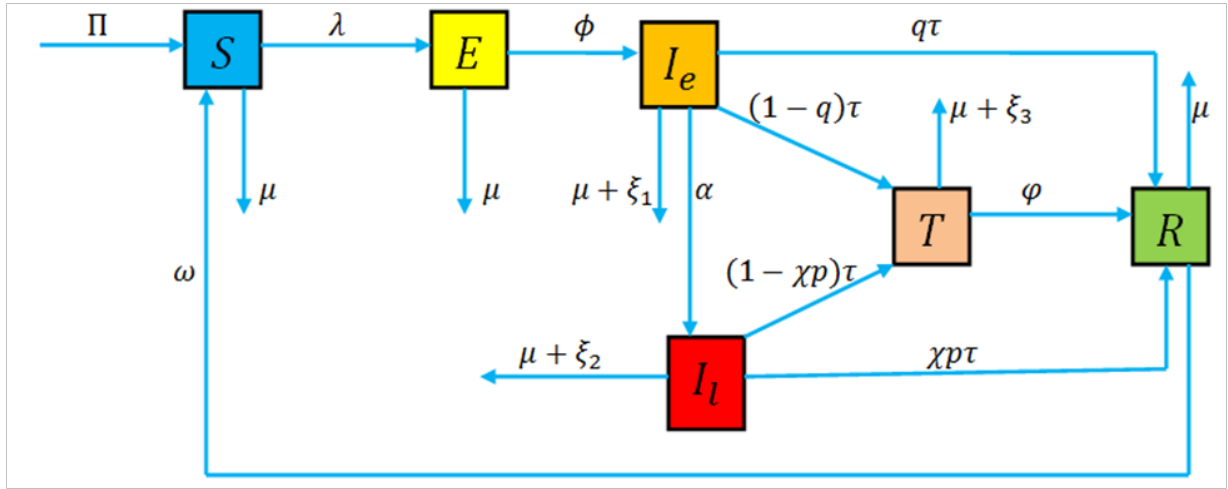


Figure 4.1: Schematic Diagram of Syphilis Model.

Based on the model assumption and schematic diagram, the model equations are given as follows;

$$\begin{cases} \frac{dS}{dt} = \Pi - \left( \frac{\beta(I_e(t) + \delta I_l(t) + \gamma T)}{N} \right) S - \mu S + \omega R, \\ \frac{dE}{dt} = \left( \frac{\beta(I_e(t) + \delta I_l(t) + \gamma T)}{N} \right) S - (\phi + \mu) E, \\ \frac{dI_e}{dt} = \phi E - (\tau + \alpha + \mu + \xi_1) I_e, \\ \frac{dI_l}{dt} = \alpha I_e - (\tau + \mu + \xi_2) I_l, \\ \frac{dT}{dt} = (1 - q)\tau I_e + (1 - \chi p)\tau I_l - (\phi + \mu + \xi_3) T, \\ \frac{dR}{dt} = q\tau I_e + \chi p\tau I_l + \phi T - (\omega + \mu) R. \end{cases} \quad (4.1)$$

With initial condition  $S(t) \geq 0, E(t) \geq 0, I_e(t) \geq 0, I_l(t) \geq 0, T \geq 0$  and  $R(t) \geq 0$ .

Table 4.1: Model parameters and its description

Parameters	Description
$\Pi$	Recruitment rate of susceptible
$\beta$	Probability of contact between a susceptible and an infectious
$\delta$	Rate of increase infectiousness in $I_l(t)$
$\gamma$	Rate of decrease infectiousness $T$
$\alpha$	Rate of Early stage infected become Late stage infected
$\tau$	Rate of both early stage infected and late stage infected are become treated
$q$	A fraction of treated from the early stage of infection become recover and move to the recovery
$p$	A fraction of the treated in the late stage of infection become recover and move to the recovery
$\chi$	rate late stage of infection in comparison to the early stage of infection
$\phi$	Rate of Exposed human become Early stage infected
$\omega$	Rate of recovered human become susceptible
$\mu$	Human population natural death rate
$\varphi$	Rate of Treated human become recovered
$\xi_1$	Rate of early stage infected who failed treatment is to mortality
$\xi_2$	Rate of late stage infected who failed treatment is to mortality
$\xi_3$	Rate of treated who failed treatment is to mortality

## 4.2 Basic Properties of Syphilis Model

### 4.2.1 Invariant Region

In this section, we obtain a region in which the solutions of model equation (4.1) are uniformly bounded in the proper subsets of  $\Omega \in \mathfrak{R}^{6+}$ . To obtain this, first we considered the total population  $N$  where  $N = S + E + I_e + I_l + T + R$ . Then, after differentiating  $N$  both sides with respect to  $t$  and substituting the expression for  $\frac{dS}{dt}, \frac{dE}{dt}, \frac{dI_e}{dt}, \frac{dI_l}{dt}, \frac{dT}{dt}, \frac{dR}{dt}$ , and from equation (4.1) we obtained;

$$\frac{dN}{dt} = \Pi - \mu - (\xi_1 I_e + \xi_2 I_l + \xi_3 T), \quad (4.2)$$

In the absence of mortality due to disease ( $\xi_1 = \xi_2 = \xi_3 = 0$ ), then equation (4.2) become

$$\frac{dN}{dt} \leq \Pi - \mu, \quad (4.3)$$

After solving equation (4.3) and equating it as time tends to infinity, we obtain  $0 \leq N(t) \leq \frac{\Pi}{\mu}$ .

Hence, the feasible solution set of model equation (4.1) remains in the region:

$$\Omega = \{(S, E, I_e, I_l, T, R) \in \mathfrak{R}^{6+} : N \leq \frac{\Pi}{\mu}\}. \quad (4.4)$$

#### 4.2.2 Positivity of the Solution

In this section, we show all the solution of the model equation (4.1) remain positive for future time if their respective initial values are positive.

**Lemma 1:** Let  $\Omega = \{(S, E, I_e, I_l, T, R) \in \mathfrak{R}^{6+}; S(0) \geq 0, E(0) \geq 0, I_e(0) \geq 0, I_l(0) \geq 0, T(0) \geq 0 \text{ and } R(0) \geq 0\}$ ; then the solutions of  $\{S, E, I_e, I_l, T, R\}$  are positive for all  $t \geq 0$ .

**Proof:** Positivity is verified separately for each of the model  $(S(t), E(t), I_e(t), I_l(t), R(t), T(t))$

**Positivity of  $S(t)$ :** From model equation (4.1) we have:

$$\begin{aligned} \frac{dS}{dt} &= \Pi - \left(\frac{\beta(I_e(t) + \delta I_l(t) + \gamma T)}{N}\right)S - \mu S + \omega R, \\ \frac{dS}{dt} &\geq -\left(\frac{\beta(I_e(t) + \delta I_l(t) + \gamma T)}{N}\right)S - \mu S \text{ by elimination positive term,} \\ \int \frac{dS}{S} &\geq \int -\left(\frac{\beta(I_e(t) + \delta I_l(t) + \gamma T) + \mu}{N}\right)dt \text{ by separable variable,} \\ \ln S &\geq -\left(\frac{\beta(I_e(t) + \delta I_l(t) + \gamma T) + \mu}{N}\right)t + c, \\ e^{\ln S} &\geq e^{(-\frac{\beta(I_e(t) + \delta I_l(t) + \gamma T) + \mu}{N})t + c}, \\ S &\geq e^{(-\frac{\beta(I_e(t) + \delta I_l(t) + \gamma T) + \mu}{N})t} \cdot e^c \text{ where } e^c = S_0, \\ S &\geq S_0 e^{(-\frac{\beta(I_e(t) + \delta I_l(t) + \gamma T) + \mu}{N})t} \text{ as } t \rightarrow \infty, \\ S &\geq 0. \end{aligned}$$

**Positivity of  $E(t)$ :** From model equation (4.1) we have:

$$\begin{aligned} \frac{dE}{dt} &= \left(\frac{\beta(I_e(t) + \delta I_l(t) + \gamma T)}{N}\right)S - (\phi + \mu)E, \\ \frac{dE}{dt} &\geq -(\phi + \mu)E \text{ by elimination positive term,} \\ \int \frac{dE}{E} &\geq \int -(\phi + \mu)dt \text{ by separable variable,} \\ \ln E &\geq -(\phi + \mu)t + c, \\ e^{\ln E} &\geq e^{-(\phi + \mu)t + c}, \\ E &\geq e^{-(\phi + \mu)t} \cdot e^c \text{ where } e^c = E_0, \\ E &\geq E_0 e^{-(\phi + \mu)t}, \text{ as } t \rightarrow \infty \end{aligned}$$

$$E \geq 0.$$

**Positivity of  $I_e(t)$ :** From model equation (4.1) we have:

$$\begin{aligned}\frac{dI_e}{dt} &= \phi E - (\tau + \alpha + \mu + \xi_1)I_e, \\ \frac{dI_e}{dt} &\geq -(\tau + \alpha + \mu + \xi_1)I_e \text{ by elimination positive term,} \\ \int \frac{dI_e}{I_e} &\geq \int -(\tau + \alpha + \mu + \xi_1)dt \text{ by separable variable,} \\ \ln I_e &\geq -(\tau + \alpha + \mu + \xi_1)t + c, \\ e^{\ln I_e} &\geq e^{-(\tau + \alpha + \mu + \xi_1)t + c}, \\ I_e &\geq e^{-(\tau + \alpha + \mu + \xi_1)t} \cdot e^c \text{ where } e^c = I_{e0}, \\ I_e &\geq I_{e0}e^{-(\tau + \alpha + \mu + \xi_1)t} \text{ as } t \rightarrow \infty, \\ I_e &\geq 0.\end{aligned}$$

**Positivity of  $I_l(t)$ :** From model equation (4.1) we have:

$$\begin{aligned}\frac{dI_l}{dt} &= \alpha I_e - (\tau + \mu + \xi_2)I_l, \\ \frac{dI_l}{dt} &\geq -(\tau + \mu + \xi_2)I_l \text{ by elimination positive term,} \\ \int \frac{dI_l}{I_l} &\geq \int -(\tau + \mu + \xi_2)dt \text{ by separable variable,} \\ \ln I_l &\geq -(\tau + \mu + \xi_2)t + c, \\ e^{\ln I_l} &\geq e^{-(\tau + \mu + \xi_2)t + c}, \\ I_l &\geq e^{-(\tau + \mu + \xi_2)t} \cdot e^c \text{ where } e^c = I_{l0}, \\ I_l &\geq I_{l0}e^{-(\tau + \mu + \xi_2)t} \text{ as } t \rightarrow \infty, \\ I_l &\geq 0.\end{aligned}$$

**Positivity of  $T(t)$ :** From model equation (4.1) we have:

$$\begin{aligned}\frac{dT}{dt} &= (1 - q)\tau I_e + (1 - \chi p)\tau I_l - (\phi + \mu + \xi_3)T, \\ \frac{dT}{dt} &\geq -(\phi + \mu + \xi_3)T \text{ by elimination positive term,} \\ \int \frac{dT}{T} &\geq \int -(\phi + \mu + \xi_3)dt \text{ by separable variable,} \\ \ln T &\geq -(\phi + \mu + \xi_3)t + c, \\ e^{\ln T} &\geq e^{-(\phi + \mu + \xi_3)t + c}, \\ T &\geq e^{-(\phi + \mu + \xi_3)t} \cdot e^c, \text{ where } e^c = T_0 \\ T &\geq T_0e^{-(\phi + \mu + \xi_3)t}, \text{ as } t \rightarrow \infty \\ T &\geq 0.\end{aligned}$$

**Positivity of  $R(t)$ :** From model equation (4.1) we have:

$$\begin{aligned}
\frac{dR}{dt} &= q\tau I_e + \chi p\tau I_l + \phi T - (\omega + \mu)R, \\
\frac{dR}{dt} &\geq -(\omega + \mu)R \text{ by elimination positive term,} \\
\int \frac{dR}{R} &\geq \int -(\omega + \mu)dt \text{ by separable variable,} \\
\ln R &\geq -(\omega + \mu)t + c, \\
e^{\ln R} &\geq e^{-(\omega + \mu)t + c}, \\
R &\geq e^{-(\omega + \mu)t} \cdot e^c \text{ where } e^c = R_0, \\
R &\geq R_0 e^{-(\omega + \mu)t} \text{ as } t \rightarrow \infty, \\
R &\geq 0.
\end{aligned}$$

The six dimensional solution space shows that all the solutions are positive. Hence, the feasible region containing all the solutions of the system of equations (4.1) is given by the set

$$\Omega = \{(S, E, I_e, I_l, T, R) \in \Re^6_+ : N \leq \frac{\Pi}{\mu}\}. \quad (4.5)$$

Here the variables  $E(t), I_e(t), I_l(t), T(t)$  and  $R(t)$  are all non-negatives.

### 4.2.3 The Syphilis Free Equilibrium (DFE)

Syphilis free equilibrium points are steady state solutions where there is no Syphilis in the population. Absence of Syphilis implies that  $E(t) = I_e(t) = I_l(t) = R(t) = T(t) = 0$  and the equilibrium points require that the right hand sides of the model equations set equal to zero. These requirements reflect in reducing the model equations (4.1) as

$$\begin{aligned}
\frac{dS}{dt} &= \Pi - \left( \frac{\beta(I_e(t) + \delta I_l(t) + \gamma T)}{N} \right) S - \mu S, \\
\Pi - \left( \frac{\beta(I_e(t) + \delta I_l(t) + \gamma T)}{N} \right) S - \mu S &= 0, \\
\text{then, } S^0 &= \frac{\Pi}{\mu}.
\end{aligned}$$

Thus, the Syphilis-free equilibrium point of the model equation in (4.1) above is given by

$$E_0 = \{S^0, E^0, I_e^0, I_l^0, T^0, R^0\} = \left\{ \frac{\Pi}{\mu}, 0, 0, 0, 0, 0 \right\}.$$



#### 4.2.4 The Basic Reproduction Number ( $\mathfrak{R}_0$ )

The basic reproduction number is denoted  $\mathfrak{R}_0$  by and is defined as the expected number of people getting secondary infection among the whole susceptible population (Oname et al., 2021). The dominant eigenvalue of the next generation matrix is  $\mathfrak{R}_0$ , which is computed using the next-gen matrix method for the model system (4.1) the associated matrices and for the new infectious terms and the remaining transition terms are respectively given by:

$$F_i = \begin{bmatrix} \frac{\beta(I_e(t) + \delta I_l(t) + \gamma T)}{N} S \\ 0 \\ 0 \\ 0 \end{bmatrix}, V_i = \begin{bmatrix} (\phi + \mu)E \\ (\tau + \alpha + \mu + \xi_1)I_e - \phi E \\ (\tau + \mu + \xi_2)I_l - \alpha I_e \\ (\phi + \mu + \xi_3)T - (1 - q)\tau I_e - (1 - \chi p)\tau I_l \end{bmatrix}.$$

The Jacobian matrices of  $F_i$  and  $V_i$  at the Syphilis free equilibrium point take the form respectively as;

$$F = \begin{bmatrix} 0 & \frac{\beta\Pi}{\mu N} & \frac{\beta\delta\Pi}{\mu N} & \frac{\beta\gamma\Pi}{\mu N} \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix}, V = \begin{bmatrix} \phi + \mu & 0 & 0 & 0 \\ -\phi & \tau + \alpha + \mu + \xi_1 & 0 & 0 \\ 0 & -\alpha & \tau + \mu + \xi_2 & 0 \\ 0 & -(1 - q)\tau & -(1 - \chi p)\tau & \phi + \mu + \xi_3 \end{bmatrix}.$$

It can be verified that the matrix  $V$  is non-singular as its determinant  $\det[V] = abcf$  is non-zero and after some algebraic computations its inverse matrix is constructed as;

$$V^{-1} = \begin{bmatrix} \frac{1}{a} & 0 & 0 & 0 \\ \frac{\phi}{ab} & \frac{1}{b} & 0 & 0 \\ \frac{\phi\alpha}{abc} & \frac{-\alpha}{bc} & \frac{1}{c} & 0 \\ \frac{-\phi\alpha e - \phi cd}{abcf} & \frac{a\alpha e + aed}{abcf} & \frac{e}{cf} & \frac{1}{f} \end{bmatrix}.$$

The product of the matrices  $F$  and  $V^{-1}$  can be computed as:

$$FV^{-1} = \begin{bmatrix} \frac{\beta\phi}{ab} + \frac{\beta\delta\phi\alpha}{abc} - (\frac{\beta\gamma\phi\alpha e + \beta\gamma\phi d}{abcf}) & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix}.$$

Now it is possible to calculate the eigenvalue to determine the basic reproduction number  $\mathfrak{R}_0$  by taking the spectral radius of the matrix  $FV^{-1}$ . Thus, the eigenvalues are computed by evaluating  $\det[FV^{-1} - \lambda I] = 0$  or equivalently solving;

$$FV^{-1} - \lambda = \begin{bmatrix} [\frac{\beta\phi}{ab} + \frac{\beta\delta\phi\alpha}{abc} - (\frac{\beta\gamma\phi\alpha e + \beta\gamma\phi d}{abcf})] - \lambda & 0 & 0 & 0 \\ 0 & 0 - \lambda & 0 & 0 \\ 0 & 0 & 0 - \lambda & 0 \\ 0 & 0 & 0 & 0 - \lambda \end{bmatrix} = 0.$$

It reduces to the equation for  $\lambda$  as  $\lambda^3 [[\frac{\beta\phi}{ab} + \frac{\beta\delta\phi\alpha}{abc} - (\frac{\beta\gamma\phi\alpha e + \beta\gamma\phi d}{abcf})] - \lambda]$  giving the four eigenvalues as  $\lambda_1 = [\frac{\beta\phi}{ab} + \frac{\beta\delta\phi\alpha}{abc} - (\frac{\beta\gamma\phi\alpha e + \beta\gamma\phi d}{abcf})]$ ,  $\lambda_2 = 0$ ,  $\lambda_3 = 0$ ,  $\lambda_4 = 0$ .

Hence, the largest eigenvalue here is  $\lambda_1 = [\frac{\beta\phi}{ab} + \frac{\beta\delta\phi\alpha}{abc} - (\frac{\beta\gamma\phi\alpha e + \beta\gamma\phi d}{abcf})]$  and is the basic reproductive number. Thus, it can be concluded that the reproduction number of the model is;

$$\mathfrak{R}_0 = \left[ \frac{\beta\phi}{(\phi+\mu)(\tau+\alpha+\mu+\xi_1)} + \frac{\beta\delta\phi\alpha}{(\phi+\mu)(\tau+\alpha+\mu+\xi_1)(\tau+\mu+\xi_2)} - \left( \frac{\beta\gamma\phi\alpha(1-\chi\rho)\tau + \beta\gamma\phi(1-q)\tau}{(\phi+\mu)(\tau+\alpha+\mu+\xi_1)(\tau+\mu+\xi_2)(\phi+\mu+\xi_3)} \right) \right].$$

#### 4.2.5 Local Stability of Syphilis Free Equilibrium

In absence of the infectious Syphilis, the model populations have a unique Syphilis free steady state  $E_0$ . To find the local stability of  $E_0$ , the Jacobian of the model equations evaluated at Syphilis free equilibrium,  $E_0$  is used. It is already shown that the Syphilis free equilibrium of model (4.1) is given by  $E_0 = \{\frac{\Pi}{\mu}, 0, 0, 0, 0, 0\}$ . Now, the stability analysis of Syphilis free equilibrium is conducted and the results are presented in the form of theorems and proofs as follows:

**Theorem 1:** The Syphilis free equilibrium of the system (4.1) is locally asymp-

totically stable if  $\mathfrak{R}_0 < 1$ .

**Proof:** The Jacobian matrix  $J$  of model at the Syphilis free equilibrium  $E_0$  reduces to;

$$J(E_0) = \begin{bmatrix} J_{11} & 0 & \beta & \beta\delta & \beta\gamma & 0 \\ J_{21} & -(\phi + \mu) & \beta & \beta\delta & \beta\gamma & 0 \\ 0 & \phi & J_{33} & 0 & 0 & 0 \\ 0 & 0 & I_e & J_{44} & 0 & 0 \\ 0 & 0 & (1-q)\tau & (1-\chi p)\tau & J_{55} & 0 \\ 0 & 0 & q\tau & xp\tau & \phi & -(\omega + \mu) \end{bmatrix},$$

$$\text{where } J_{11} = -\mu\left(\frac{\beta(I_e(t) + \delta I_l(t) + \gamma T)}{\Pi} - \mu^2\right), J_{21} = \left(\frac{\beta(I_e(t) + \delta I_l(t) + \gamma T)}{\Pi}\mu\right), J_{33} = \tau + \alpha + \mu + \xi_1, J_{44} = -(\tau + \mu + \xi_2), J_{55} = -(\phi + \mu + \xi_3).$$

Now, the eigenvalues of are required to be found. The characteristic equation  $\det[J(E_0) - \Phi I] = 0$  is expanded and simplified as follows:

$$(J(E_0) - \Phi I) =$$

$$\begin{bmatrix} J_{11} - \Phi & 0 & \beta & \beta\delta & \beta\gamma & 0 \\ J_{21} & [-(\phi + \mu)] - \Phi & \beta & \beta\delta & \beta\gamma & 0 \\ 0 & \phi & J_{33} - \Phi & 0 & 0 & 0 \\ 0 & 0 & I_e & J_{44} - \Phi & 0 & 0 \\ 0 & 0 & (1-q)\tau & (1-\chi p)\tau & J_{55} - \Phi & 0 \\ 0 & 0 & q\tau & xp\tau & \phi & -(\omega + \mu) - \Phi \end{bmatrix}.$$

The six column of Jacobian matrix is all zero except the six entry, which is  $-(\omega + \mu) - \Phi$ . Then, we have the six eigenvalue ;  $\Phi = (\omega + \mu)$ . The rest of the

eigenvalues are computed from the following Jacobian matrix.

$$J(E_0) - \Phi I = \begin{bmatrix} J_{11} - \Phi & 0 & \beta & \beta\delta & \beta\gamma \\ J_{21} & [-(\phi + \mu)] - \Phi & \beta & \beta\delta & \beta\gamma \\ 0 & \phi & J_{33} - \Phi & 0 & 0 \\ 0 & 0 & I_e & J_{44} - \Phi & 0 \\ 0 & 0 & (1 - q)\tau & (1 - \chi p)\tau & J_{55} - \Phi \end{bmatrix}.$$

The two column of Jacobian matrix is all zero except the two entry, which is  $-(\phi + \mu) - \Phi$ . Then, we have the two eigenvalue ;  $\Phi = (\phi + \mu)$ . The rest of the eigenvalues are computed from the following Jacobian matrix.

$$J(E_0) - \Phi I = \begin{bmatrix} J_{11} - \Phi & \beta & \beta\delta & \beta\gamma \\ 0 & J_{33} - \Phi & 0 & 0 \\ 0 & I_e & J_{44} - \Phi & 0 \\ 0 & (1 - q)\tau & (1 - \chi p)\tau & J_{55} - \Phi \end{bmatrix}.$$

The first column of Jacobian matrix is all zero except the first entry, which is  $J_{11} - \Phi$ . Then, we have the two eigenvalue ;  $\Phi = J_{11}$ . The rest of the eigenvalues are computed from the following Jacobian matrix.

$$J(E_0) - \Phi I = \begin{bmatrix} J_{33} - \Phi & 0 & 0 \\ I_e & J_{44} - \Phi & 0 \\ (1 - q)\tau & (1 - \chi p)\tau & J_{55} - \Phi \end{bmatrix}.$$

The third column of Jacobian matrix is all zero except the third entry, which is  $J_{55} - \Phi$ . Then, we have the two eigenvalue ;  $\Phi = J_{55}$ . The rest of the eigenvalues are computed from the following Jacobian matrix.

$$J(E_0) - \Phi I = \begin{bmatrix} J_{33} - \Phi & 0 \\ I_e & J_{44} - \Phi \end{bmatrix}.$$

Then, Jacobian matrix obtained as the polynomial function given by;

$$(-(\omega + \mu) - \Phi)(-(\phi + \mu) - \Phi)(J_{11} - \Phi)(J_{55} - \Phi)(J_{33} - \Phi)(J_{44} - \Phi) = 0. \quad (4.6)$$

From the equation (4.6)

$$\begin{aligned} &(-(\omega + \mu) - \Phi) = 0, \\ &\Phi_1 = -(\omega + \mu), \\ &(-(\phi + \mu) - \Phi) = 0, \\ &\Phi_2 = -(\phi + \mu), \\ &(J_{11} - \Phi) = 0, \\ &\Phi_3 = J_{11}, \\ &\text{since } J_{11} = -\mu \left( \frac{\beta(I_e(t) + \delta I_l(t) + \gamma T)}{\Pi} - \mu^2 \right), \\ &\Phi_3 = -\mu \left( \frac{\beta(I_e(t) + \delta I_l(t) + \gamma T)}{\Pi} - \mu^2 \right), \\ &(J_{55} - \Phi) = 0, \\ &\Phi_4 = J_{55}, \\ &\text{since } J_{55} = -(\varphi + \mu + \xi_3), \\ &\Phi_4 = -(\varphi + \mu + \xi_3), \end{aligned}$$

and from the last characteristic equation  $(J_{33} - \Phi)(J_{44} - \Phi)$ , we have;

$$\Phi^2 - a\Phi - b = 0, \quad (4.7)$$

where  $a = (\alpha + \xi_1 - \xi_2)$ ,  $b = (\tau + \mu + \xi_1)(\tau + \mu + \xi_2)$ .

By using Routh-Hurwitz criteria, the equation (4.8) has real root that strictly negative if  $a < 0$  and  $b < 0$  So that;

$$\begin{aligned} b &= (\tau + \mu + \xi_1)(\tau + \mu + \xi_2) \left[ \frac{\beta\phi cf + \beta\delta\phi\alpha f - (\beta\gamma\phi\alpha e + \beta\gamma\phi d)}{(abcf)(\tau + \mu + \xi_1)(\tau + \mu + \xi_2)} - \frac{1}{(\tau + \mu + \xi_1)(\tau + \mu + \xi_2)} \right] \\ &= ((\tau + \mu + \xi_1)(\tau + \mu + \xi_2))^2 \left( \frac{\beta\phi + \beta\delta\phi\alpha - (\beta\gamma\phi\alpha e + \beta\gamma\phi d)}{(abcf)} - 1 \right) \\ &= (\tau + \mu + \xi_1)(\tau + \mu + \xi_2)^2 (\mathfrak{R}_0 - 1) < 0. \end{aligned}$$

However,  $b$  to be negative,  $(\tau + \mu + \xi_1)(\tau + \mu + \xi_2)^2 (\mathfrak{R}_0 - 1)$  should be negative, which leads to  $\mathfrak{R}_0 < 1$ . Hence the Syphilis free equilibrium is locally asymptotically stable in  $\Omega$  if  $\mathfrak{R}_0 < 1$ .

#### 4.2.6 Global Stability of Syphilis Free Equilibrium

**Theorem 2:** The Syphilis free equilibrium of the system (4.1) is global asymptotically stable if  $\mathfrak{R}_0 < 1$ .

**Proof.** To establish the stability of the Syphilis free equilibrium point globally, we first developed the following Lyapunov function defined as;

$$L = A_1 I_e + A_2 I_l \quad (4.8)$$

By differentiating the above Lyapunov function with respect to time t, we obtain,

$$\begin{aligned} \frac{dL}{dt} &= A_1 \frac{I_e}{dt} + A_2 \frac{I_l}{dt} \\ &= A_1 (\phi E - (\tau + \alpha + \mu + \xi_1) I_e) + A_2 (\alpha I_e - (\tau + \mu + \xi_2) I_l) \\ &= A_1 (\phi E) - (\tau + \alpha + \mu + \xi_1) I_e A_1 + A_2 (\alpha I_e) - (\tau + \mu + \xi_2) I_l A_2 \\ &= -(\tau + \alpha + \mu + \xi_1) I_e \frac{(\beta \gamma \phi \alpha e + \beta \gamma \phi d)}{(abc f)} + \left( \frac{(\beta \gamma \phi)}{(abc)} \right) (\alpha I_e) \text{ By taking} \\ &\quad A_1 = \frac{(\beta \gamma \phi \alpha e + \beta \gamma \phi d)}{(abc f)}, A_2 = \left( \frac{(\beta \gamma \phi)}{(abc)} \right) \\ \frac{dL}{dt} &\leq [ -(\tau + \alpha + \mu + \xi_1) \frac{(\beta \gamma \phi \alpha e + \beta \gamma \phi d)}{(abc f)} + \left( \frac{(\beta \gamma \phi \alpha)}{(abc)} \right) ] I_e \\ &= \left[ \left( \frac{-abc f}{(\tau + \alpha + \mu + \xi_1)(\beta \gamma \phi \alpha e + \beta \gamma \phi d f + \beta \gamma \phi \alpha)} - \frac{(\tau + \alpha + \mu + \xi_1)(\beta \gamma \phi \alpha e + \beta \gamma \phi d f + \beta \gamma \phi \alpha)}{\beta \phi c f + \beta \delta \phi \alpha f - (\beta \gamma \phi \alpha e + \beta \gamma \phi d)} \right) \right. \\ &\quad \left. - (\tau + \alpha + \mu + \xi_1) \frac{(\beta \gamma \phi \alpha e + \beta \gamma \phi d)}{(abc f)} + \left( \frac{(\beta \gamma \phi \alpha)}{(abc)} \right) \right] I_e \\ &= \left[ \left( \frac{(\beta \gamma \phi \alpha)}{(abc)} \right) \left( 1 - \frac{\beta \phi + \beta \delta \phi \alpha - (\beta \gamma \phi \alpha e + \beta \gamma \phi d)}{(abc f)} \right) \right] I_e \\ &= \left[ \left( \frac{(\beta \gamma \phi \alpha)}{(abc)} \right) (1 - \mathfrak{R}_0) \right] I_e \end{aligned}$$

Hence, we obtain  $\frac{dL}{dt} < 0$  if  $\mathfrak{R}_0 < 0$  and  $\frac{dL}{dt} = 0$  if and only if  $I_e = 0$ . Thus, the singleton set SFE in  $\Omega$  is the dominant compact invariant set in  $(S, E, I_e, I_l, T, R)$  :  $\frac{dL}{dt} = 0$ . As a result of LaSalle's invariant principle (La Salle, 1976), as t tends to infinity, every solution that begins in the domain approaches SFE. Thus, if  $\mathfrak{R}_0 < 1$ , the SFE is globally asymptotically stable in  $\Omega$ .

#### 4.2.7 The Endemic Equilibrium

Endemic equilibrium point  $E_1$  is a steady state solution where the disease persists in the population. For the existence and uniqueness of endemic equilibrium  $E_1 = \{S^*, E^*, I_e^*, I_l^*, T^*, R^*\}$ , its coordinates should satisfy the conditions

$E_1 = \{S^*, E^*, I_e^*, I_l^*, T^*, R^*\} \neq 0$  where  $S^* > 0, E^* \geq 0, I_e^* \geq 0, I_l^* \geq 0, T^* \geq 0$  and  $R^* \geq 0$ . The endemic equilibrium point is obtained by setting left hand sides of equations of the system (4.1) to zero and express each dependent variable in terms of  $I_e^*$  at equilibrium point and we obtain;

$$\begin{cases} S^* = \frac{\Pi^2 + R^* \omega \mu}{\mu(\beta(I_e(t) + \delta I_l(t) + \gamma T))} \\ E^* = \frac{S^* \mu(\beta(I_e(t) + \delta I_l(t) + \gamma T))}{\Pi(\phi + \mu)} \\ I_l^* = \frac{\alpha E^*}{\tau + \mu + \xi_2} \\ T^* = \frac{(1-q)\tau I_e^* + (1-\chi p)\tau I_l^*}{\phi + \mu + \xi_3} \\ R^* = \frac{q\tau I_e^* + \chi p\tau I_l^* + \phi T^*}{\omega \mu} \end{cases} \quad (4.9)$$

From equation (4.10) the endemic equilibrium easily satisfies the following polynomial and  $I_e^*$  is obtained by solving the equation;

$$A(I_e^*)^2 + B(I_e^*) = 0 \quad (4.10)$$

where  $A = \Pi^2 + R^* \omega \mu + (1 - \chi p)$ ,  $B = q\tau + \alpha(1 - \mathfrak{R}_0)$ . Hence  $A > 0$  and  $B > 0$  whenever  $\mathfrak{R}_0 < 1$ . Solve for  $I_e^*$ , we have that  $I_e^* = -\frac{B}{A} < 0$ . From this, we see that, there is no endemic equilibrium for this model. Therefore, this condition shows that it is not possible for backward bifurcation in the model if  $\mathfrak{R}_0 < 1$ .

#### 4.2.8 Global Stability of Endemic Equilibrium

**Theorem 1:** The endemic equilibrium point of the model equation (4.1) is globally asymptotically stable whenever  $\mathfrak{R}_0 > 1$ .

**Proof:** To prove the global asymptotic stability of the endemic equilibrium we use the method of Lyapunov functions.

Define

$$L(S^*, E^*, I_e^*, I_l^*, T^*, R^*) = [S - S^* - S^* \ln(\frac{S}{S^*})] + [E - E^* - E^* \ln(\frac{E}{E^*})] + [I_e - I_e^* - I_e^* \ln(\frac{I_e}{I_e^*})] + [I_l - I_l^* - I_l^* \ln(\frac{I_l}{I_l^*})] + [T - T^* - T^* \ln(\frac{T}{T^*})] + [R - R^* - R^* \ln(\frac{R}{R^*})].$$

By direct calculating the derivative of  $\mathbf{L}$  along the solution (4.1) we have

$$\begin{aligned} \frac{dL}{dt} &= [\frac{S-S^*}{S}] \frac{dS}{dt} + [\frac{E-E^*}{E}] \frac{dE}{dt} + [\frac{I_e-I_e^*}{I_e}] \frac{dI_e}{dt} + [\frac{I_l-I_l^*}{I_l}] \frac{dI_l}{dt} + [\frac{T-T^*}{T}] \frac{dT}{dt} + [\frac{R-R^*}{R}] \frac{dR}{dt} \\ &= [\frac{S-S^*}{S}] (\Pi - (\frac{\beta(I_e(t) + \delta I_l(t) + \gamma T)}{N})S - \mu S + R\omega) \end{aligned}$$

$$\begin{aligned}
& + \left[ \frac{E-E^*}{E} \right] \left( \left( \frac{\beta(I_e(t)+\delta I_l(t)+\gamma T)}{N} \right) S - (\phi + \mu) E \right) \\
& + \left[ \frac{I_e-I_e^*}{I_e} \right] (\phi E - (\tau + \alpha + \mu + \xi_1) I_e) \\
& + \left[ \frac{I_l-I_l^*}{I_l} \right] (\alpha I_e - (\tau + \mu + \xi_2) I_l) \\
& + \left[ \frac{T-T^*}{T} \right] ((1-q)\tau I_e + (1-\chi p)\tau I_l - (\phi + \mu + \xi_3) T) \\
& + \left[ \frac{R-R^*}{R} \right] (q\tau I_e + \chi p\tau I_l + \phi T - (\omega + \mu) R), \\
& = \left[ 1 - \frac{S^*}{S} \right] \left( \Pi - \left( \frac{\beta(I_e(t)+\delta I_l(t)+\gamma T)}{N} \right) S - \mu S + R\omega \right) \\
& + \left[ 1 - \frac{E^*}{E} \right] \left( \left( \frac{\beta(I_e(t)+\delta I_l(t)+\gamma T)}{N} \right) S - (\phi + \mu) E \right) \\
& + \left[ 1 - \frac{I_e^*}{I_e} \right] (\phi E - (\tau + \alpha + \mu + \xi_1) I_e) \\
& + \left[ 1 - \frac{I_l^*}{I_l} \right] (\alpha I_e - (\tau + \mu + \xi_2) I_l) \\
& + \left[ 1 - \frac{T^*}{T} \right] ((1-q)\tau I_e + (1-\chi p)\tau I_l - (\phi + \mu + \xi_3) T) \\
& + \left[ 1 - \frac{R^*}{R} \right] (q\tau I_e + \chi p\tau I_l + \phi T - (\omega + \mu) R).
\end{aligned}$$

Then collecting positive and negative terms together we obtain

$$\frac{dL}{dt} = M - N,$$

where  $M = [\Pi + \frac{S^*}{N}(\beta(I_e(t) + \delta I_l(t) + \gamma T)) + \mu N^* + \omega E^* \phi E + (\tau + \alpha + \xi_1) I_e^* + \alpha I_e + (\tau + \xi_2) I_l^* + (1-q)\tau I_e + (1-\chi p)\tau I_l + (\phi + \xi_3) T^* + q\tau I_e + \chi p\tau I_l + \phi T + \omega R^*]$

$N = [\mu N + \frac{S^*}{S}(\Pi) + \phi E + \frac{E^*(\beta(I_e(t)+\delta I_l(t)+\gamma T))}{EN} + (\tau + \alpha + \xi_1) I_e + \frac{I_e^*}{I_e}(\phi E) + (\tau + \xi_1) + \alpha I_e \frac{I_l^*}{I_l} + (\phi + \xi_3) T + \frac{T^*}{T}((1-q)\tau I_e + (1-\chi p)\tau I_l) + \omega R + \frac{R^*}{R}(q\tau I_e + \chi p\tau I_l + T)]$ .

Thus if  $M < N$ , then  $\frac{dL}{dt} \leq 0$ . Noting that  $\frac{dL}{dt} = 0$  if and only if

$S = S^*, E = E^*, I_e = I_e^*, I_l = I_l^*, T = T^*, R = R^*$ . Therefore, the largest compact invariant set in  $\{(S^*, E^*, I_e^*, I_l^*, T^*, R^*) \in \Omega : \frac{dL}{dt} = 0\}$  is the singleton  $E_1$  is the endemic equilibrium of the system (4.1). By LaSalle's invariant principle (LaSalle, 1976), it implies that  $E_1$  is globally asymptotically stable in  $\Omega$  if  $M < N$ .

### 4.3 Sensitivity Analysis of Model Parameters

In this section, we will see the sensitivity analysis of the parameters that found in the model (4.1) those can determine the value of the basic reproduction number. Because those parameters can increasing or decreasing a basic reproduction



number ( $\mathfrak{R}_0$ ) if their values increases or decreases and vice-versa. So that to identify the parameters that have a high impact on the basic reproduction number ( $\mathfrak{R}_0$ ) we should have applied the sensitivity analysis. Thus, to find the sensitivity analysis, we followed the technique outlined in and with the developed techniques defined as follows, we will obtain the sensitivity index of all the basic parameters.

**Definition** The normalized forward sensitivity index of  $\mathfrak{R}_0$  that depends differentiable on a parameter  $\mathbf{M}$  is defined as;

$$\tau_M^{\mathfrak{R}_0} = \frac{\partial \mathfrak{R}_0}{\partial M} \times \frac{\mathfrak{R}_0}{M} \quad (4.11)$$

The sensitivity index of  $\mathfrak{R}_0$  in relation to the parameter  $\beta$  is calculated as

$$\begin{aligned} \tau_\beta^{\mathfrak{R}_0} &= \frac{\partial \mathfrak{R}_0}{\partial \beta} \times \frac{\beta}{\mathfrak{R}_0} \\ &= \left[ \frac{\phi}{(\phi+\mu)(\tau+\alpha+\mu+\xi_1)} + \frac{\delta\phi\alpha}{(\phi+\mu)(\tau+\alpha+\mu+\xi_1)(\tau+\mu+\xi_2)} - \right. \\ &\quad \left. \left( \frac{\gamma\phi\alpha(1-\chi\rho)\tau+\beta\gamma\phi(1-q)\tau}{(\phi+\mu)(\tau+\alpha+\mu+\xi_1)(\tau+\mu+\xi_2)((\phi+\mu)(\tau+\alpha+\mu+\xi_1)(\tau+\mu+\xi_2)(\phi+\mu+\xi_3))} \right) \right] \times \\ &\quad \frac{\beta\phi}{\left[ \frac{\beta\phi}{(\phi+\mu)(\tau+\alpha+\mu+\xi_1)} + \frac{\beta\delta\phi\alpha}{(\phi+\mu)(\tau+\alpha+\mu+\xi_1)(\tau+\mu+\xi_2)} - \left( \frac{\beta\gamma\alpha(1-\chi\rho)\tau+\beta\gamma(1-q)\tau}{(\phi+\mu)(\tau+\alpha+\mu+\xi_1)(\tau+\mu+\xi_2)((\phi+\mu)(\tau+\alpha+\mu+\xi_1)(\tau+\mu+\xi_2)(\phi+\mu+\xi_3))} \right) \right]} = \\ &\quad 1 > 0 \end{aligned}$$

The sensitivity index of  $\mathfrak{R}_0$  in relation to the parameter  $\beta$  is calculated as

$$\begin{aligned} \tau_\phi^{\mathfrak{R}_0} &= \frac{\partial \mathfrak{R}_0}{\partial \phi} \times \frac{\phi}{\mathfrak{R}_0} \\ &= \left[ \frac{\beta}{(\phi+\mu)(\tau+\alpha+\mu+\xi_1)} + \frac{\delta\beta\alpha}{(\phi+\mu)(\tau+\alpha+\mu+\xi_1)(\tau+\mu+\xi_2)} - \right. \\ &\quad \left. \left( \frac{\gamma\phi\alpha(1-\chi\rho)\tau+\beta\gamma\phi(1-q)\tau}{(\phi+\mu)(\tau+\alpha+\mu+\xi_1)(\tau+\mu+\xi_2)((\phi+\mu)(\tau+\alpha+\mu+\xi_1)(\tau+\mu+\xi_2)(\phi+\mu+\xi_3))} \right) \right] \times \\ &\quad \frac{\phi}{\left[ \frac{\beta\phi}{(\phi+\mu)(\tau+\alpha+\mu+\xi_1)} + \frac{\beta\delta\phi\alpha}{(\phi+\mu)(\tau+\alpha+\mu+\xi_1)(\tau+\mu+\xi_2)} - \left( \frac{\beta\gamma\alpha(1-\chi\rho)\tau+\beta\gamma(1-q)\tau}{(\phi+\mu)(\tau+\alpha+\mu+\xi_1)(\tau+\mu+\xi_2)((\phi+\mu)(\tau+\alpha+\mu+\xi_1)(\tau+\mu+\xi_2)(\phi+\mu+\xi_3))} \right) \right]} = \\ &\quad 1 > 0 \end{aligned}$$

The sensitivity index of  $\mathfrak{R}_0$  in relation to the parameter  $\delta$  is calculated as

$$\tau_\delta^{\mathfrak{R}_0} = \frac{\partial \mathfrak{R}_0}{\partial \delta} \times \frac{\delta}{\mathfrak{R}_0}$$

$$= \left[ \frac{\beta\phi\alpha}{(\phi+\mu)(\tau+\alpha+\mu+\xi_1)\delta} \times \right. \\ \left. \frac{\left[ \frac{\beta\phi}{(\phi+\mu)(\tau+\alpha+\mu+\xi_1)} + \frac{\beta\delta\phi\alpha}{(\phi+\mu)(\tau+\alpha+\mu+\xi_1)(\tau+\mu+\xi_2)} - \left( \frac{\beta\gamma\alpha(1-\chi\rho)\tau+\beta\gamma(1-q)\tau}{(\phi+\mu)(\tau+\alpha+\mu+\xi_1)(\tau+\mu+\xi_2)(\phi+\mu)(\tau+\alpha+\mu+\xi_1)(\tau+\mu+\xi_2)(\phi+\mu+\xi_3)} \right) \right]}{0.23} \right] > 0$$

The sensitivity index of  $\mathfrak{R}_0$  in relation to the parameter  $\delta$  is calculated as

$$\tau_\alpha^{\mathfrak{R}_0} = \frac{\partial \mathfrak{R}_0}{\partial \alpha} \times \frac{\alpha}{\mathfrak{R}_0} \\ = \left[ \frac{\beta\phi\delta}{(\phi+\mu)(\tau+\alpha+\mu+\xi_1)(\tau+\mu+\xi_2)} - \frac{\beta\delta\alpha\phi(1-\chi\rho)\tau}{(\phi+\mu)(\tau+\alpha+\mu+\xi_1)(\tau+\mu+\xi_2)(\phi+\mu+\xi_3)} \right] \times \\ \frac{\left[ \frac{\beta\phi}{(\phi+\mu)(\tau+\alpha+\mu+\xi_1)} + \frac{\beta\delta\phi\alpha}{(\phi+\mu)(\tau+\alpha+\mu+\xi_1)(\tau+\mu+\xi_2)} - \left( \frac{\beta\gamma\alpha(1-\chi\rho)\tau+\beta\gamma(1-q)\tau}{(\phi+\mu)(\tau+\alpha+\mu+\xi_1)(\tau+\mu+\xi_2)(\phi+\mu)(\tau+\alpha+\mu+\xi_1)(\tau+\mu+\xi_2)(\phi+\mu+\xi_3)} \right) \right]}{-0.0183} < 0$$

The sensitivity index of  $\mathfrak{R}_0$  in relation to the parameter  $\delta$  is calculated as

$$\tau_\gamma^{\mathfrak{R}_0} = \frac{\partial \mathfrak{R}_0}{\partial \gamma} \times \frac{\gamma}{\mathfrak{R}_0} \\ = - \left[ \frac{\beta\phi\alpha(1-\chi\rho)\tau+\beta\phi(1-q)\tau}{(\phi+\mu)(\tau+\alpha+\mu+\xi_1)(\tau+\mu+\xi_2)(\phi+\mu+\xi_3)} \right] \times \\ \frac{\left[ \frac{\beta\phi}{(\phi+\mu)(\tau+\alpha+\mu+\xi_1)} + \frac{\beta\delta\phi\alpha}{(\phi+\mu)(\tau+\alpha+\mu+\xi_1)(\tau+\mu+\xi_2)} - \left( \frac{\beta\gamma\alpha(1-\chi\rho)\tau+\beta\gamma(1-q)\tau}{(\phi+\mu)(\tau+\alpha+\mu+\xi_1)(\tau+\mu+\xi_2)(\phi+\mu)(\tau+\alpha+\mu+\xi_1)(\tau+\mu+\xi_2)(\phi+\mu+\xi_3)} \right) \right]}{-0.296} < 0$$

The sensitivity index of  $\mathfrak{R}_0$  in relation to the parameter  $\mu$  is calculated as

$$\tau_\mu^{\mathfrak{R}_0} = \frac{\partial \mathfrak{R}_0}{\partial \mu} \times \frac{\mu}{\mathfrak{R}_0} \\ = \left[ -\frac{\beta\phi}{\phi(\tau+\alpha+\xi_1)\mu^3} - 3\frac{\beta\delta\phi\alpha}{\phi(\tau+\alpha+\xi_1)\mu^4} + 4\left( \frac{\beta\gamma\phi\alpha(1-\chi\rho)\tau+\beta\gamma\phi(1-q)\tau}{\phi(\tau+\alpha+\xi_1)(\tau+\xi_2)(\phi+\xi_2)\mu^5} \right) \right] \times \\ \frac{\left[ \frac{\beta\phi}{(\phi+\mu)(\tau+\alpha+\mu+\xi_1)} + \frac{\beta\delta\phi\alpha}{(\phi+\mu)(\tau+\alpha+\mu+\xi_1)(\tau+\mu+\xi_2)} - \left( \frac{\beta\gamma\alpha(1-\chi\rho)\tau+\beta\gamma(1-q)\tau}{(\phi+\mu)(\tau+\alpha+\mu+\xi_1)(\tau+\mu+\xi_2)(\phi+\mu)(\tau+\alpha+\mu+\xi_1)(\tau+\mu+\xi_2)(\phi+\mu+\xi_3)} \right) \right]}{-0.01204} < 0$$

The sensitivity index of  $\mathfrak{R}_0$  in relation to the parameter  $\tau$  is calculated as

$$\tau_\tau^{\mathfrak{R}_0} = \frac{\partial \mathfrak{R}_0}{\partial \tau} \times \frac{\tau}{\mathfrak{R}_0} \\ = \left[ \frac{\beta\phi}{(\phi+\mu)(\epsilon+\mu+\xi_1)\ln \tau} - 2\frac{\beta\delta\phi\alpha}{(\phi+\mu)(\epsilon+\mu+\xi_1)(\mu+\xi_2)\tau^3} + 2\left( \frac{\beta\gamma\phi\alpha(1-\chi\rho)\tau+\beta\gamma\phi(1-q)\tau}{(\phi+\mu)(\epsilon+\mu+\xi_1)(\mu+\xi_2)(\phi+\mu+\xi_3)\tau^3} \right) \right] \times \\ \frac{\left[ \frac{\beta\phi}{(\phi+\mu)(\tau+\alpha+\mu+\xi_1)} + \frac{\beta\delta\phi\alpha}{(\phi+\mu)(\tau+\alpha+\mu+\xi_1)(\tau+\mu+\xi_2)} - \left( \frac{\beta\gamma\alpha(1-\chi\rho)\tau+\beta\gamma(1-q)\tau}{(\phi+\mu)(\tau+\alpha+\mu+\xi_1)(\tau+\mu+\xi_2)(\phi+\mu)(\tau+\alpha+\mu+\xi_1)(\tau+\mu+\xi_2)(\phi+\mu+\xi_3)} \right) \right]}{88.189} > 0$$

The sensitivity index of  $\mathfrak{R}_0$  in relation to the parameter  $\xi_1$  is calculated as

$$\begin{aligned} \tau_{\xi_1}^{\mathfrak{R}_0} &= \frac{\partial \mathfrak{R}_0}{\partial \xi_1} \times \frac{\xi_1}{\mathfrak{R}_0} \\ &= \left[ \frac{\beta\phi}{(\phi+\mu)(\tau+\alpha+\mu)\ln \xi_1} + \frac{\beta\delta\phi\alpha}{(\phi+\mu)(\tau+\alpha+\mu)(\tau+\mu+\xi_2)\ln \xi_1} - \right. \\ &\quad \left. \left( \frac{\beta\gamma\phi\alpha(1-\chi\rho)\tau+\beta\gamma\phi(1-q)\tau}{(\phi+\mu)(\tau+\alpha+\mu)(\tau+\mu+\xi_2)(\phi+\mu+\xi_3)\ln \xi_1} \right) \right] \times \\ &\quad \frac{\xi_1}{\mathfrak{R}_0} \\ &= \left[ \frac{\beta\phi}{(\phi+\mu)(\tau+\alpha+\mu+\xi_1)} + \frac{\beta\delta\phi\alpha}{(\phi+\mu)(\tau+\alpha+\mu+\xi_1)(\tau+\mu+\xi_2)} - \left( \frac{\beta\gamma\alpha(1-\chi\rho)\tau+\beta\gamma(1-q)\tau}{(\phi+\mu)(\tau+\alpha+\mu+\xi_1)(\tau+\mu+\xi_2)(\phi+\mu+\xi_3)} \right) \right] \times \\ &\quad -0.00027 < 0 \end{aligned}$$

The sensitivity index of  $\mathfrak{R}_0$  in relation to the parameter  $\xi_2$  is calculated as

$$\begin{aligned} \tau_{\xi_2}^{\mathfrak{R}_0} &= \frac{\partial \mathfrak{R}_0}{\partial \xi_2} \times \frac{\xi_2}{\mathfrak{R}_0} \\ &= \left[ \frac{\beta\alpha\delta\phi}{(\phi+\mu)(\tau+\alpha+\mu+\xi_1)(\tau+\mu)\ln \xi_2} - \frac{\beta\gamma\alpha(1-\chi\rho)\tau+\beta\gamma(1-q)\tau}{(\phi+\mu)(\tau+\alpha+\mu+\xi_1)(\tau+\mu)(\phi+\mu+\xi_3)\ln \xi_2} \right] \times \\ &\quad \frac{\xi_2}{\mathfrak{R}_0} \\ &= \left[ \frac{\beta\phi}{(\phi+\mu)(\tau+\alpha+\mu+\xi_1)} + \frac{\beta\delta\phi\alpha}{(\phi+\mu)(\tau+\alpha+\mu+\xi_1)(\tau+\mu+\xi_2)} - \left( \frac{\beta\gamma\alpha(1-\chi\rho)\tau+\beta\gamma(1-q)\tau}{(\phi+\mu)(\tau+\alpha+\mu+\xi_1)(\tau+\mu+\xi_2)(\phi+\mu+\xi_3)} \right) \right] \times \\ &\quad 0.0000122 > 0 \end{aligned}$$

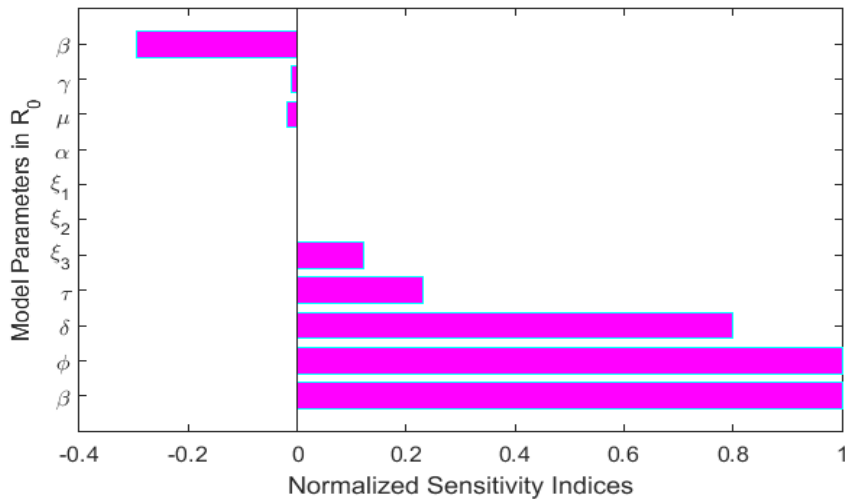
The sensitivity index of  $\mathfrak{R}_0$  in relation to the parameter  $\xi_3$  is calculated as

$$\begin{aligned} \tau_{\xi_3}^{\mathfrak{R}_0} &= \frac{\partial \mathfrak{R}_0}{\partial \xi_3} \times \frac{\xi_3}{\mathfrak{R}_0} \\ &= \left[ -\frac{\beta\gamma\alpha(1-\chi\rho)\tau+\beta\gamma(1-q)\tau}{(\phi+\mu)(\tau+\alpha+\mu+\xi_1)(\tau+\mu+\xi_2)(\phi+\mu)\ln \xi_3} \right] \times \\ &\quad \frac{\xi_3}{\mathfrak{R}_0} \\ &= \left[ \frac{\beta\phi}{(\phi+\mu)(\tau+\alpha+\mu+\xi_1)} + \frac{\beta\delta\phi\alpha}{(\phi+\mu)(\tau+\alpha+\mu+\xi_1)(\tau+\mu+\xi_2)} - \left( \frac{\beta\gamma\alpha(1-\chi\rho)\tau+\beta\gamma(1-q)\tau}{(\phi+\mu)(\tau+\alpha+\mu+\xi_1)(\tau+\mu+\xi_2)(\phi+\mu+\xi_3)} \right) \right] \times \\ &\quad 0.00003749 > 0 \end{aligned}$$

Their sensitivity indices were written in Table 4.2 as follows.

Table 4.2: Sensitivity indices of parameters

Parameters symbol	Sensitivity index
$\beta$	1
$\phi$	1
$\delta$	0.23
$\tau$	0.123
$\xi_3$	0.00003749
$\xi_2$	0.00001227
$\xi_1$	-0.00027
$\alpha$	-0.0183
$\mu$	-0.01204
$\gamma$	-0.296

Figure 4.2: Sensitivity indices of basic reproduction number  $\mathfrak{R}_0$ 

Based on the described sensitivity indices of the basic reproduction number  $\mathfrak{R}_0$  with respect to five basic parameters is described in Table 4.2 and Figure 4.2. The results showed that the parameters with a positive sensitivity index increased the value of  $\mathfrak{R}_0$  as their values increased, whereas the other parameters remained constant. Furthermore, increasing the values of the parameters with negative indices while keeping the values of the other parameters constant reduces the value of  $\mathfrak{R}_0$ .

#### 4.4 Optimal Control Model Formulation

In this section, we apply optimal control strategies on model equations (4.1). This helps us to reduce the disease in the specified time. The optimal control model is an extension of Syphilis model (4.1) by including the following two controls defined as;

- represents prevention effort that helps to reduce contact rate of Syphilis infection,
- represents treatment effort that increases recovery of infectious individuals, implies early stage infected individuals, late infected individuals and treated individuals.

Time is specified and relatively short and is given by  $t \in [0, T]$ ,  $T$  is the terminal time. After incorporating control functions  $u_1(t)$  and  $u_2(t)$  in Syphilis model equation (4.1), we obtain the following state system;

$$\begin{cases} \frac{dS}{dt} = \Pi + R\omega - (1 - u_1)\left(\frac{\beta(I_e(t) + \delta I_l(t) + \gamma T)}{N}\right)S - \mu S, \\ \frac{dE}{dt} = (1 - u_1)\left(\frac{\beta(I_e(t) + \delta I_l(t) + \gamma T)}{N}\right)S - (\phi + \mu)E, \\ \frac{dI_e}{dt} = \phi E - (u_2 + \tau)I_e - (\alpha + \mu + \xi_1)I_e, \\ \frac{dI_l}{dt} = \alpha I_e - (u_2 + \tau)I_l - (\mu + \xi_2)I_l, \\ \frac{dT}{dt} = (1 - u_2)(1 - q)\tau I_e + (1 - u_2)(1 - \chi p\tau)I_l - (\phi + \mu + \xi_3)T, \\ \frac{dR}{dt} = (u_2 + q\tau)I_e + (u_2 + \chi p\tau)I_l + \phi T - (\omega + \mu)R. \end{cases} \quad (4.12)$$

Our main objective is to minimize the objective function  $J$  considering the total amount of treatment human  $T(t)$ , the total amount of Exposed individuals  $E(t)$ , the total amount of early stage infected individuals  $I_e(t)$ , the total amount of late stage infected individuals  $I_l(t)$  and costs of controls  $u_i(t)$ . The optimal control models objective functional (4.11) is given as

$$J(u_1, u_2) = \min_{u_1, u_2} \int_0^{t_f} [M_1 E + M_2 I_e T + M_3 I_l + M_4 T + \frac{1}{2}(W_1 u_1^2 + W_2 u_2^2)] dt \quad (4.13)$$

where  $t_f$  is the terminal time,  $M_1, M_2, M_3$  and  $M_4$  were the weight constants for the Exposed human, early stage infected, late stage infected and treatment hu-

man, respectively, while  $W_1, W_2$  are weight constants for use controls efforts, respectively. The expression  $\frac{1}{2}(W_i u_i^2)$  represents the cost function that corresponds to the controls  $u_i(t)$  and is quadratic as in the other literature (Zhao et al., 2022). The objective functional (4.12) is to minimize the Exposed human  $E(t)$ , early stage infected  $I_e(t)$ , late stage infected  $I_l(t)$ , treatment human  $T(t)$ , and control costs  $u_i(t)$ . The main point is to compute an a double optimal controls  $u_1^*$ , and  $u_2^*$ , Such that

$$J(u_1^*, u_2^*) = \min J(u_1, u_2) : u_1, u_2 \in \mathbf{v} \quad (4.14)$$

Where  $\mathbf{v} = (u_1, u_2) : u_i(t)$  are Lebesgue measurable on  $t \in [0, t_f]$

Hence, the basic setup of the optimal control problem is to check the existence and uniqueness of the optimal controls and to characterize them.

## 4.5 Optimal Control Problem Analysis

### 4.5.1 Existence of an optimal controls

**Theorem :** Given  $J(u)$  subject to system (4.22) with  $S(0) \geq 0, E(0) \geq 0, I_e(0) \geq 0, I_l(0) \geq 0, T(0) \geq 0, R(0) \geq 0$ , then there exists an optimal control  $u^*$  and corresponding  $(S^*, E^*, I_e^*, I_l^*, T^*, R^*)$ , that minimizes  $J(u)$  over  $U$ .

Let the control set  $U = [0, 1]^2$ ,  $\mathbf{v} = (u_1, u_2) \in U$ ,  $x = (S^*, E^*, I_e^*, I_l^*, T^*, R^*)$  and  $f(t, x, \mathbf{v})$  the right hand side of state system (4.22), is given by

$$f(t, x, \mathbf{v}) = \begin{bmatrix} \theta \Pi - (\phi - \mu)P \\ \Pi + R\omega - (1 - u_1) \left( \frac{\beta(I_e(t) + \delta I_l(t) + \gamma T)}{N} \right) S - \mu S, \\ (1 - u_1) \left( \frac{\beta(I_e(t) + \delta I_l(t) + \gamma T)}{N} \right) S - (\phi + \mu)E, \\ \phi E - (u_2 + \tau)I_e - (\alpha + \mu + \xi_1)I_e, \\ \alpha I_e - (u_2 + \tau)I_l - (\mu + \xi_2)I_l, \\ (1 - u_2)(1 - q)\tau I_e + (1 - u_2)(1 - \chi p \tau)I_l - (\phi + \mu + \xi_3)T, \\ (u_2 + q\tau)I_e + (u_2 + \chi p \tau)I_l + \phi T - (\omega + \mu)R. \end{bmatrix}.$$

The proof is based on the following assumption and by Fleming and Rishel's

theorem.

1. The set of controls and corresponding state variable is nonempty.
2. The measurable control set is convex and closed.
3. All the right hand sides of equations of the state system is continuous, bounded above by a sum of bounded control and state, and can be written as a linear function of  $u$  with coefficients depending on time and state.
4. The integrand  $g(\phi, u)$  of the objective functional is convex.
5. There exist constants  $c_1, c_2, c_3 \geq 0$  and  $\tau^* \geq 1$  such that the integrand of the objective functional satisfies  $g(\phi, u) \geq c_1 + c_2|u_1|^\tau + c_3|u_2|^\tau$ .

**Proof:**

1.  $U$  is a nonempty set of measurable functions on  $0 \leq T$  with values in real numbers  $\mathbb{R}$ . The system (4.22) has bounded coefficients and hence any solutions are bounded on  $[0, T]$ . The corresponding solutions for the system (??) exists.
2. Assume that  $u_1, u_2, u_3 \in U$  such that  $\|u_i\| \leq 1, i = 1, 2$ . Now, let us take any controls  $u_1, u_2 \in U$  and  $\lambda \in [0, 1]$ , then  $0 \leq \lambda u_1 + (1 - \lambda)u_2$ . Additionally, we observe that

$$\|\lambda u_1\| \leq \lambda \|u_1\| \leq \lambda \text{ and } \|(1 - \lambda)u_2\| \leq (1 - \lambda)\|u_2\| \leq (1 - \lambda).$$

Then for any  $\lambda \in [0, 1]$ ,

$$\begin{aligned} & \|\lambda u_1 + (1 - \lambda)u_2\|, \\ & \leq \|\lambda u_1\| + \|(1 - \lambda)u_2\|, \\ & \leq \lambda \|u_1\| + (1 - \lambda)\|u_2\|, \\ & \leq \lambda + (1 - \lambda) = 1. \end{aligned}$$

Hence,  $0 \leq \lambda u_1 + (1 - \lambda)u_2 \leq 1$ , for all  $u_1, u_2 \in U$  and  $\lambda \in [0, 1]$ .

Therefore, the control space  $U = \{u = (u_1, u_2), 0 \leq u_i \leq u_{i_{max}}, i = 1, 2\}$  and  $t \in [0, T]$  is convex and closed by definition.

3. The integrand in the objective functional, which is a cost function is an affine function. Recall that any affine function is a convex and the sum of a convex function is a convex. Therefore, cost function is convex on  $U$ .
4. Assume that there exists constants  $c_1, c_2, c_3 \geq 0$  and  $\tau^* \geq 1$  such that  $g(\phi, u)$  satisfies  $g(\phi, u) \geq c_1 + c_2|u_1|^\tau + c_3|u_2|^\tau$ . Thus, the state variables are being bounded.

Let  $c_1 = \inf_{t \in [0, T]} [M_1 E + M_2 I_e + M_3 I_l + M_4 T]$ ,  $c_2 = \frac{w_1}{2}$ ,  $c_3 = \frac{w_2}{2}$  and  $\tau = 2$  then it follows that

$$g(\phi, u) \geq c_1 + c_2|u_1|^\tau + c_3|u_2|^\tau.$$

Thus, this assumption is justified.

#### 4.5.2 Characterization of an optimal control

The optimal control must satisfy the necessary conditions that are formulated by Pontryagin's Maximum Principle. This principle converts the system of equations (4.11) and (4.12) into a problem of minimizing point-wise a Hamiltonian (H), with respect to  $u_1(t)$ ,  $u_2(t)$  as

$$\begin{cases} H = [M_1 E + M_2 I_e T + M_3 I_L + M_4 T + \frac{1}{2}(W_1 u_1^2 + W_2 u_2^2)] \\ + \lambda_1 \frac{dS}{dt} + \lambda_2 \frac{dI_e}{dt} + \lambda_3 \frac{dI_e}{dt} + \lambda_4 \frac{dI_l}{dt} + \lambda_5 \frac{dT}{dt} + \lambda_6 \frac{dR}{dt} \end{cases} \quad (4.15)$$

It follows that the system of equation (4.11) and equation (4.12) are substituted



into a minimized Hamiltonian function with respect to  $u_1, u_2$ , as given by:

$$\left\{ \begin{array}{l} H = [M_1 E + M_2 I_e + M_3 I_L + M_4 T + \frac{1}{2}(W_1 u_1^2 + W_2 u_2^2)] \\ + \lambda_1 [\Pi + R\omega - (1 - u_1) \left( \frac{\beta(I_e(t) + \delta I_L(t) + \gamma T)}{N} \right) S - \mu S] \\ + \lambda_2 [(1 - u_1) \left( \frac{\beta(I_e(t) + \delta I_L(t) + \gamma T)}{N} \right) S - (\phi + \mu) E] \\ + \lambda_3 [\phi E - (u_2 + \tau) I_e - (\alpha + \mu + \xi_1) I_e] \\ + \lambda_4 [\alpha I_e - (u_2 + \tau) I_L - (\mu + \xi_2) I_L] \\ + \lambda_5 [(1 - u_2)(1 - q)\tau I_e + (1 - u_2)(1 - \chi p \tau) I_L - (\phi + \mu + \xi_3) T] \\ + \lambda_6 [(u_2 + q\tau) I_e + (u_2 + \chi p \tau) I_L + \phi T - (\omega + \mu) R] \end{array} \right. \quad (4.16)$$

Where  $\lambda_1, \lambda_2, \lambda_3, \lambda_4, \lambda_5$  and  $\lambda_6$  are adjoint variables. Next to obtaining the co-state variables by using Pontryagin's maximum principle (4.11) with the existence result (4.15), the following theorem is stated:

**Theorem** For given optimal control triples  $u_1^*, u_2^*$  and  $S^*, E^*, I_e^*, I_L^*, T^*, R^*$  of the corresponding state system that minimizes  $J(u_1^*, u_2^*)$  over  $v$  subject to equation (4.1), adjoint variables  $\lambda_1, \lambda_2, \lambda_3, \lambda_4, \lambda_5$  and  $\lambda_6$  are found, holding the adjoint system.

$$\left\{ \begin{array}{l} \frac{d\lambda_1}{dt} = -(\lambda_2 - \lambda_1)(1 - u_1) \left( \frac{\beta(I_e(t) + \delta I_L(t) + \gamma T)}{N} \right) + \mu \lambda_1, \\ \frac{d\lambda_2}{dt} = -M_1 + \phi(\lambda_3 - \lambda_2) + \phi \lambda_2, \\ \frac{d\lambda_3}{dt} = -M_2 - \alpha(\lambda_3 + \lambda_6) + \tau(\lambda_3 - \lambda_4) + \alpha(\lambda_3 - \lambda_4) + (\mu + \xi_1)\lambda_3 + q\tau(\lambda_5 - \lambda_6) \\ - u_2 q \tau \lambda_5 - q \tau \lambda_6 - u_2 \tau \lambda_5, \\ \frac{d\lambda_4}{dt} = -M_3 + (u_2 + \tau + \mu + \xi_2)\lambda_4 - (\chi p \tau - u_2 + \chi p \tau u_2)\lambda_5 - u_2 \lambda_6 - \chi p \tau \lambda_6, \\ \frac{d\lambda_5}{dt} = -M_4 - \phi(\lambda_6 - \lambda_5) + (\mu + \xi_3)\lambda_5, \\ \frac{d\lambda_6}{dt} = (\omega + \mu)\lambda_6. \end{array} \right. \quad (4.17)$$

With transversely conditions

$$\lambda_1(t_f) = \lambda_2(t_f) = \lambda_3(t_f) = \lambda_4(t_f) = \lambda_5(t_f) = \lambda_6(t_f) = 0$$

Thus, the optimal control  $u_1^*, u_2^*$  and  $u_3^*$  are represented by:

$$\begin{cases} u_1^* = \min\{1, \max\{0, \frac{\beta(I_e(t) + \delta I_l(t) + \gamma T)S^*(\lambda_2 - \lambda_1)}{w_1 N}\}\}, \\ u_2^* = \min\{1, \max\{0, \frac{\lambda_3 I_e^* + \lambda_4 I_l^* + (1-q)\tau I_e^* \lambda_5 + (1-xp\tau)I_l^* \lambda_5 - 2\lambda_6}{w_2}\}. \end{cases} \quad (4.18)$$

**Proof:** To obtain the form of the co-state equations we compute the derivative of the Hamiltonian function (H), equation (4.14), with respect to S, E,  $I_e$ ,  $I_l$ , T and R respectively. Then the adjoint or co-state equations obtained are given by;

$$\begin{cases} \frac{d\lambda_1}{dt} = -\frac{\partial H}{\partial S} = -(\lambda_2 - \lambda_1)(1 - u_1)\left(\frac{\beta(I_e(t) + \delta I_l(t) + \gamma T)}{N}\right) + \mu\lambda_1, \\ \frac{d\lambda_2}{dt} = -\frac{\partial H}{\partial E} = -M_1 + \phi(\lambda_3 - \lambda_2) + \phi\lambda_2, \\ \frac{d\lambda_3}{dt} = -\frac{\partial H}{\partial I_e} = -M_2 - \alpha(\lambda_3 + \lambda_6) + \tau(\lambda_3 - \lambda_4) + \alpha(\lambda_3 - \lambda_4) + (\mu + \xi_1)\lambda_3 + q\tau(\lambda_5 - \lambda_6) \\ \quad - u_2 q \tau \lambda_5 - q \tau \lambda_6 - u_2 \tau \lambda_5, \\ \frac{d\lambda_4}{dt} = -\frac{\partial H}{\partial I_l} = -M_3 + (u_2 + \tau + \mu + \xi_2)\lambda_4 - (\chi p \tau - u_2 + \chi p \tau u_2)\lambda_5 - u_2 \lambda_6 - \chi p \tau \lambda_6, \\ \frac{d\lambda_5}{dt} = -\frac{\partial H}{\partial T} = -M_4 - \phi(\lambda_6 - \lambda_5) + (\mu + \xi_3)\lambda_5, \\ \frac{d\lambda_6}{dt} = -\frac{\partial H}{\partial R} = (\omega + \mu)\lambda_6. \end{cases} \quad (4.19)$$

With transversely conditions

$$\lambda_1(t_f) = \lambda_2(t_f) = \lambda_3(t_f) = \lambda_4(t_f) = \lambda_5(t_f) = \lambda_6(t_f) = 0$$

To obtain the control values, we compute the partial derivative of the Hamiltonian, given by:

$$\frac{\partial H}{\partial u_i} = 0$$

Obviously, after derivation of function (H), equation (4.14), with respect to the controls, the result

becomes:

$$\begin{cases} \frac{\partial H}{\partial u_1} = 0 = w_1 u_1 + \frac{\beta(I_e(t) + \delta I_l(t) + \gamma T) \lambda_1 S}{N} - \frac{\beta(I_e(t) + \delta I_l(t) + \gamma T) \lambda_2 S}{N}, \\ \frac{\partial H}{\partial u_2} = 0 = w_2 u_2 - \lambda_3 I_e - \lambda_4 I_l - (1-q)\tau I_e \lambda_5 - (1-xp\tau) I_l \lambda_5 + 2\lambda_6. \end{cases} \quad (4.20)$$

Moreover, solving for the control variables from equation (4.19) we obtain

$$\begin{cases} u_1^* = \min\{1, \max\{0, \frac{\beta(I_e(t) + \delta I_l(t) + \gamma T) S^* (\lambda_2 - \lambda_1)}{w_1 N}\}\}, \\ u_2^* = \min\{1, \max\{0, \frac{\lambda_3 I_e^* + \lambda_4 I_l^* + (1-q)\tau I_e^* \lambda_5 + (1-xp\tau) I_l^* \lambda_5 - 2\lambda_6}{w_2}\}. \end{cases} \quad (4.21)$$

Rearranging the solution of equation (4.20) with the boundary condition of each control, we get:

$$\begin{cases} u_1^* = \max\{0, \min\{1, \frac{\beta(I_e(t) + \delta I_l(t) + \gamma T) S^* (\lambda_2 - \lambda_1)}{w_1 N}\}\}, \\ u_2^* = \max\{0, \min\{1, \frac{\lambda_3 I_e^* + \lambda_4 I_l^* + (1-q)\tau I_e^* \lambda_5 + (1-xp\tau) I_l^* \lambda_5 - 2\lambda_6}{w_2}\}. \end{cases} \quad (4.22)$$

### 4.5.3 Uniqueness of the optimality system

In order to successively discuss uniqueness of the optimality system we notice that the adjoint system is also linear in  $\lambda_i$  for  $i = 1, 2, 3, 4, 5, 6$  with bounded coefficients. Thus, there exists a  $M > 0$  such that  $|\lambda_i(t)| < M$  for  $i = 1, 2, 3, 4, 5, 6$  on  $[0, T]$ .

**Theorem :** For  $T$  sufficiently small the solution to the optimality system is unique.

## 4.6 Numerical Simulations

In this subsection, numerical simulation study of the autonomous system (4.22) are carried out using the software MATLAB R2015b with ODE45 solver. To conduct the study, a set of physically meaningful values are assigned to the model parameters. These values are either taken from literature or assumed on the basis of reality. Using the parameter values given in Table 5.3 and the initial conditions  $S(0) = 1000, E(0) = 600, I_e(0) = 400, I_l(0) = 200, T(0) = 100$

and  $R(0) = 20$  and also coefficients of the state and controls that we used are  $M_1 = 250, M_2 = 250, M_3 = 250, M_4 = 250, w_1 = 100, w_2 = 100$  a simulation study is conducted. Finally, an optimal control strategy is designed and discussed using different control strategies. To solve the optimal controls and states, we use the Runge-Kutta numerical method using MATLAB program. It needs to solve thirteen-state equations and thirteen adjoint equations. For that, first we solve system 2 with a guess for the controls forward in time and then using the transversality conditions as initial values and the adjoint system is solved backward in time using the current iteration solution of the state system.

Table 4.3: Parameter Description and Values

Parameters	Description	Value	Source
$\Pi$	Recruitment rate of susceptible	1020	Estimated
$\beta$	Probability of contact between a susceptible and an infectious	0.3	Assumed
$\delta$	Rate of increase infectiousness in $I_l(t)$	0.25	Estimated
$\gamma$	Rate of decrease infectiousness $T$	0.25	Assumed
$\alpha$	Rate of Early stage infected become Late stage infected	0.3	Assumed
$\tau$	Rate of both early stage infected and late stage infected are become treated	0.6849	Assumed
$q$	A fraction of treated from the early stage of infection become recover and move to the recovery	0.9	(Iboi and Okuonghae, 2016)
$p$	A fraction of the treated in the late stage of infection become recover and move to the recovery	0.9	(Iboi and Okuonghae, 2016)
$\chi$	rate late stage of infection in comparison to the early stage of infection	0.6849	(Iboi and Okuonghae, 2016)
$\phi$	Rate of Exposed human become Early stage infected	0.9	Assumed
$\omega$	Rate of recovered human become susceptible	0.3	Estimated
$\mu$	Human population natural death rate	0.00548	Estimated
$\varphi$	Rate of Treated human become recovered	0.4762	Assumed
$\xi_1$	Rate of early stage infected who failed treatment is to mortality	0.0001	Estimated
$\xi_2$	Rate of late stage infected who failed treatment is to mortality	0.0001	Estimated
$\xi_3$	Rate of treated who failed treatment is to mortality	0.0001	Estimated

### Scenario I: Optimal use of Prevention

We simulated the optimality control system by incorporating prevention intervention only to eradicate Syphilis infection from the community. Figures 4.3, 4.4, 4.5 and 4.6 shows that an infectious individual goes to zero at the end of the implementation period. Therefore, applying this strategy is effective in eradicating Syphilis from the community in a specified period of time.

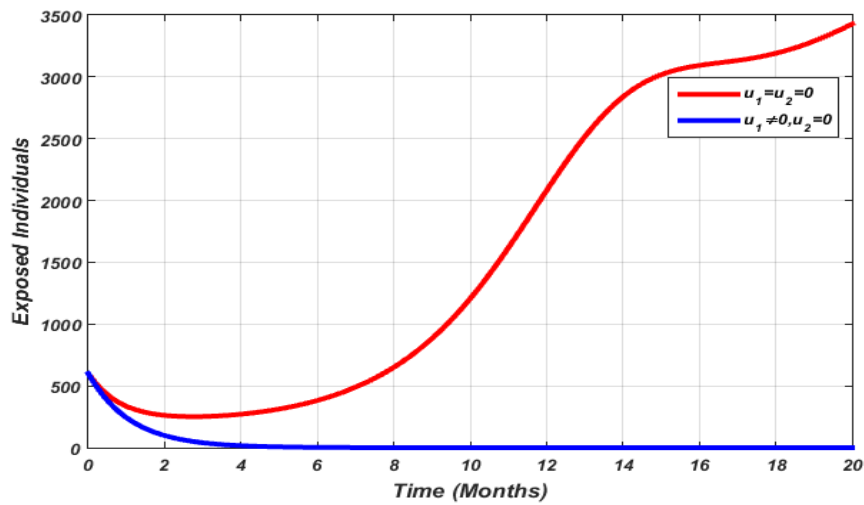


Figure 4.3: Dynamics of Syphilis Exposed individuals

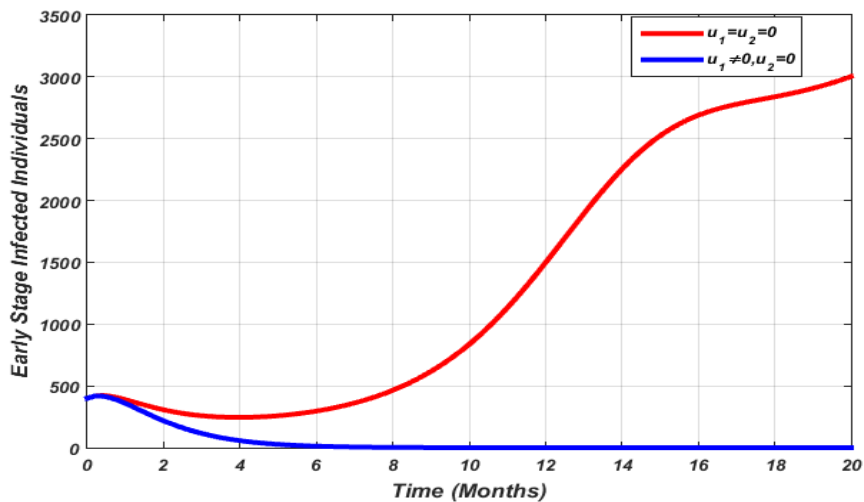


Figure 4.4: Dynamics of Early Stage Infected individuals

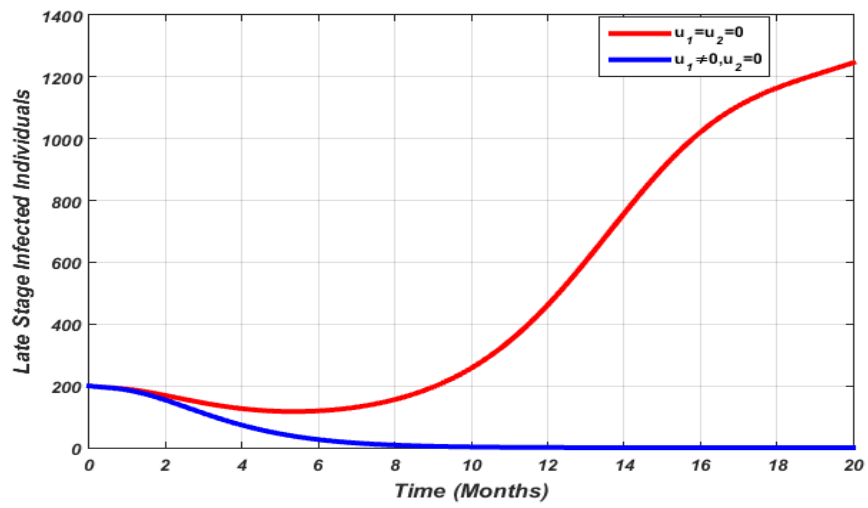


Figure 4.5: Dynamics of Syphilis Exposed individuals

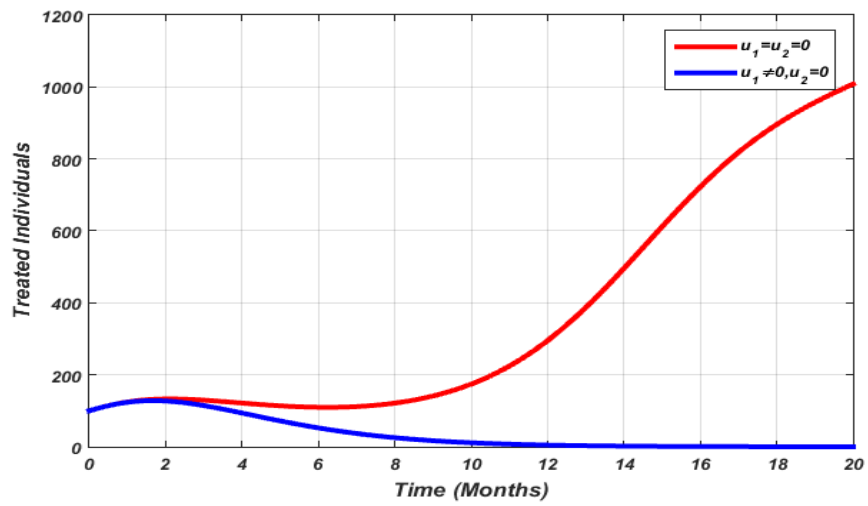


Figure 4.6: Dynamics of Early Stage Infected individuals

## Scenario II: Optimal use of Treatment

We applied treatment only as intervention that is treating individuals who have Syphilis disease infection. Figures 4.7, 4.8, 4.9 and 4.10 clearly show that all infectious individuals have gone to zero at the end of the implementation period. Therefore, we conclude that this strategy is effective in eradicating the Syphilis from the community in a specified period of time.

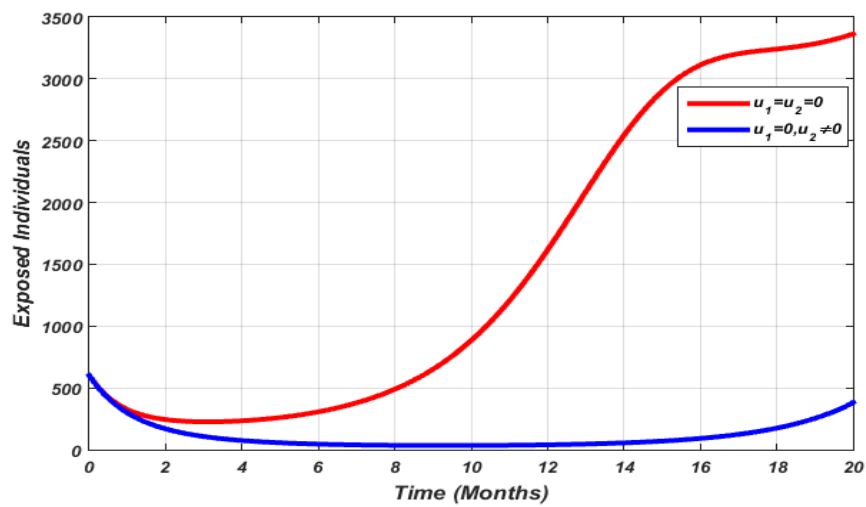


Figure 4.7: Dynamics of Syphilis Exposed individuals

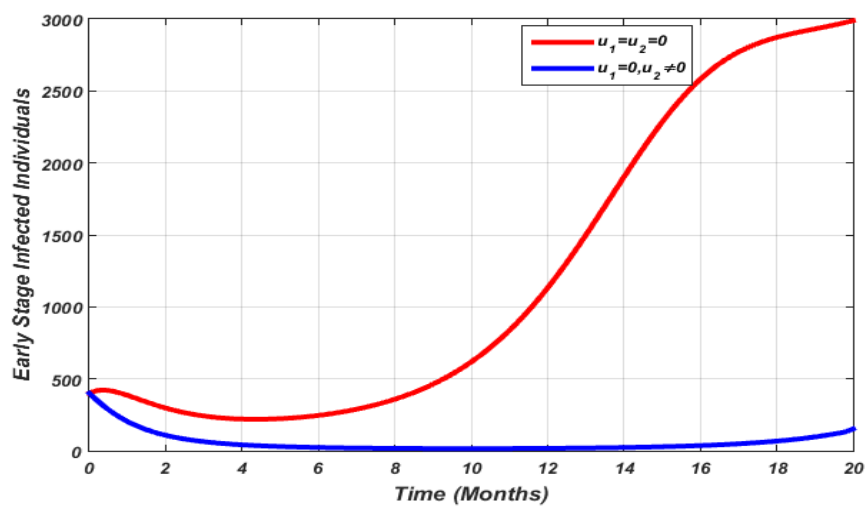


Figure 4.8: Dynamics of Early Stage Infected individuals



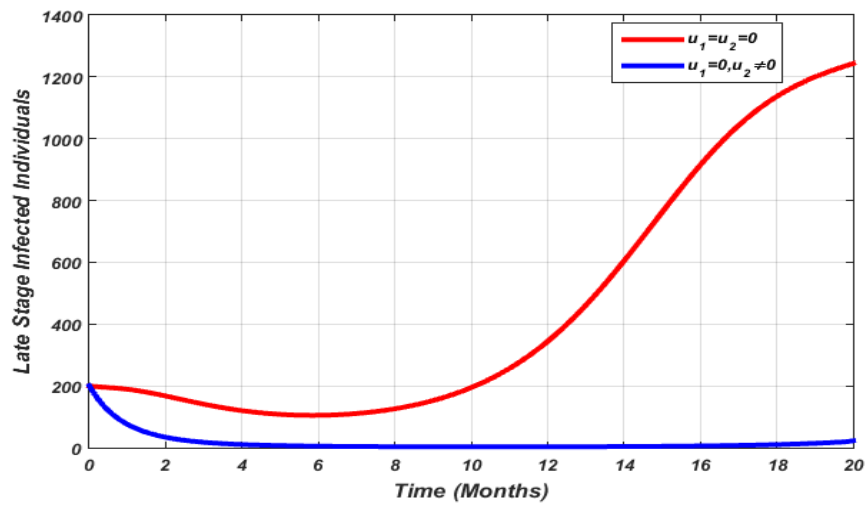


Figure 4.9: Dynamics of Syphilis Exposed individuals

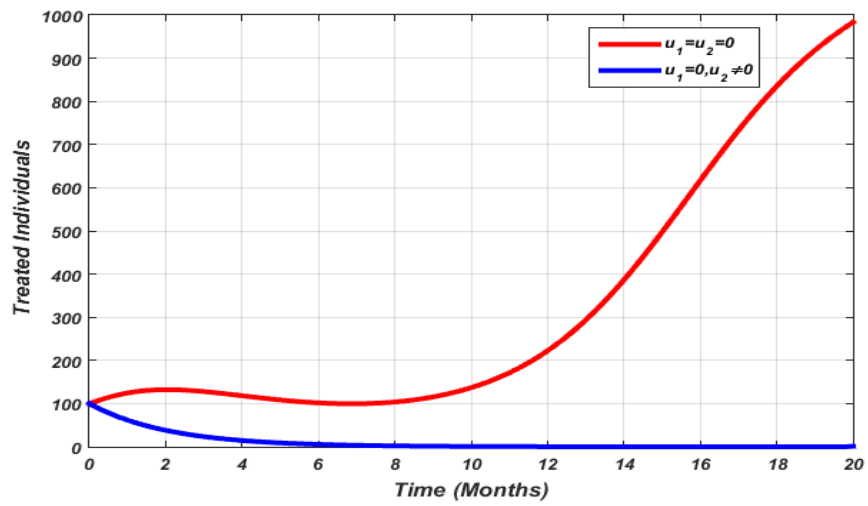


Figure 4.10: Dynamics of Early Stage Infected individuals

### Scenario III: Optimal use of Prevention and Treatment

We simulate the model using a combination of prevention and treatment as intervention strategy for control of Syphilis in the community. Figures 4.10, 4.12, 4.13 and 4.14 shows that infectious individuals goes to zero over the period of implementation of this intervention strategy. Therefore, this strategy is effective in eradicating the Syphilis in the specified period of time.

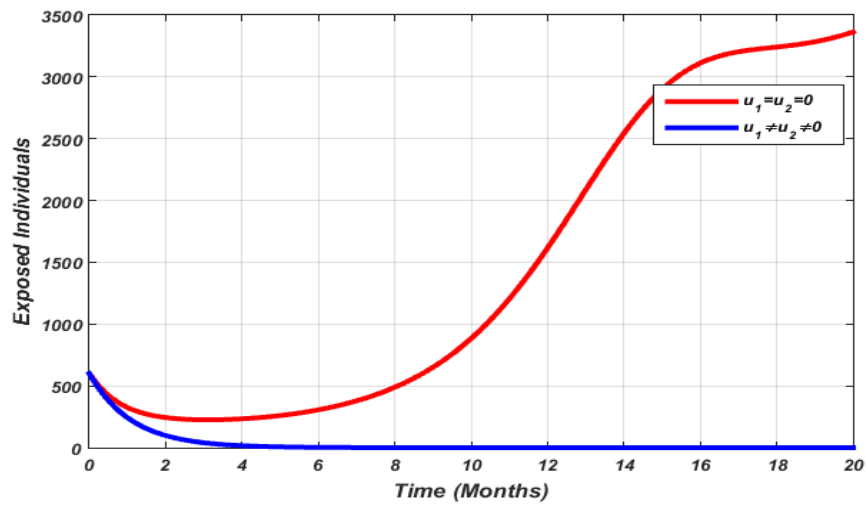


Figure 4.11: Dynamics of Syphilis Exposed individuals

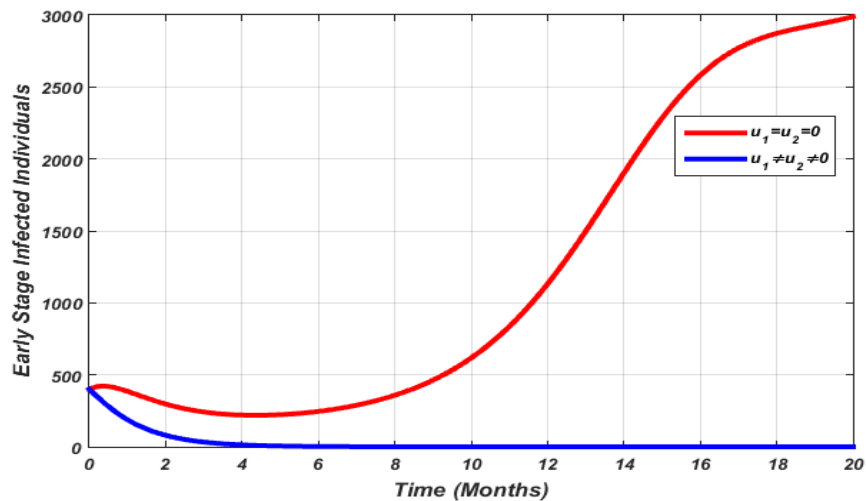


Figure 4.12: Dynamics of Early Stage Infected individuals

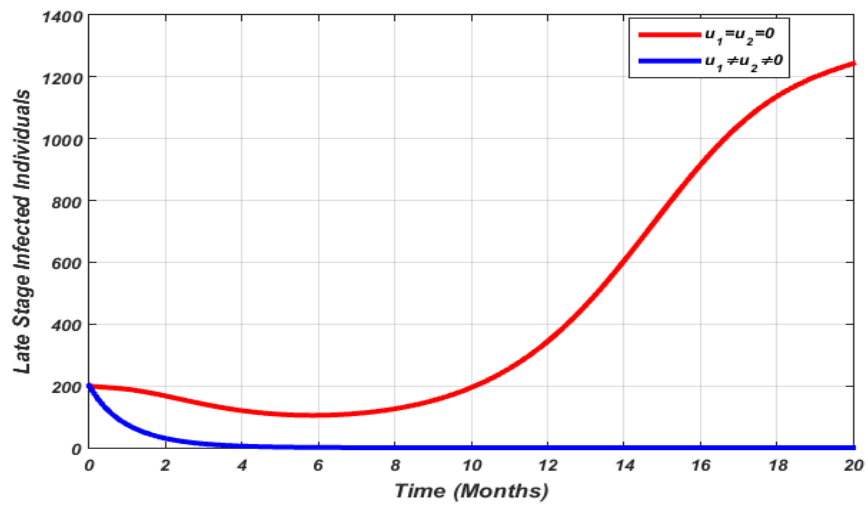


Figure 4.13: Dynamics of Syphilis Exposed individuals

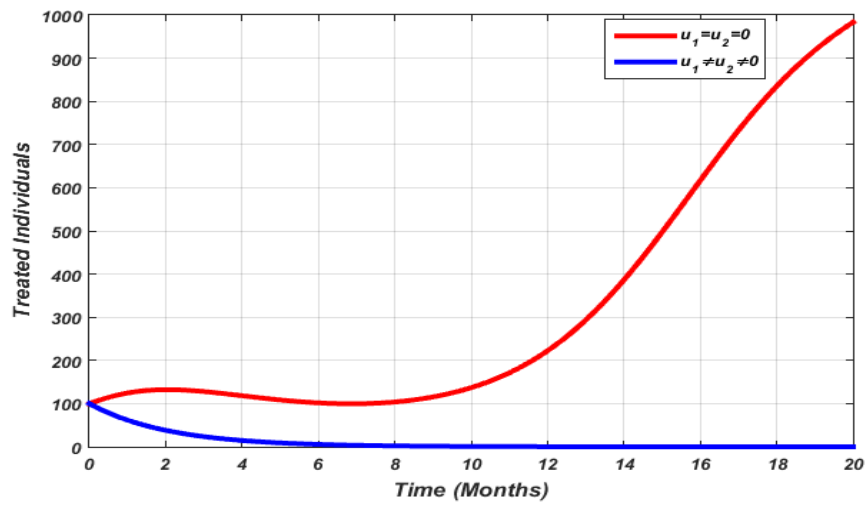


Figure 4.14: Dynamics of Early Stage Infected individuals

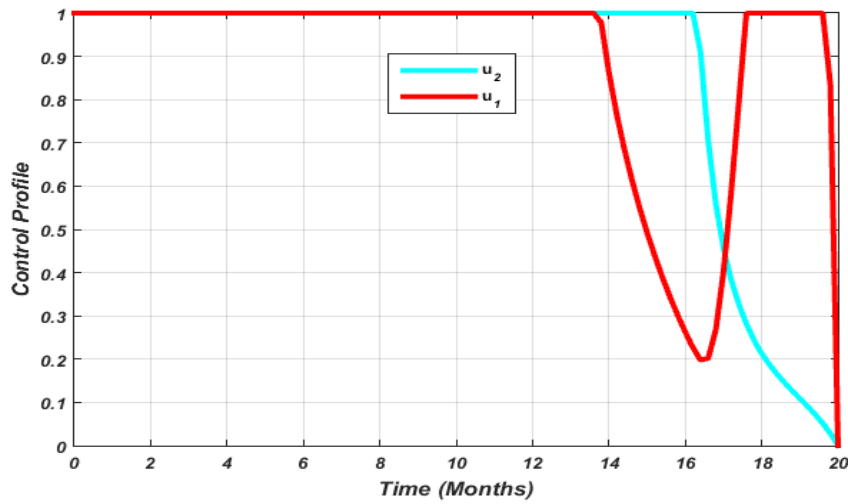


Figure 4.15: Control Profile

## 4.7 Cost Effective Analysis

To determine the most cost effective strategy we used controls only prevention, only treatment and the combination of prevention and treatment. To achieve this purpose we need to compare the differences between the costs and health outcomes of these interventions. This is done by calculating the incremental cost-effectiveness ratio (ICER) which is generally described as the additional cost per additional health outcome. When comparing two or more competing intervention strategies incrementally, one intervention should be compared with the next-less effective alternative. The ICER denominator is the differences in health outcomes. It is calculated using the following formula;

$$ICER = \frac{\text{Difference in costs between strategies}}{\text{Difference in health effects between strategies}}.$$

We rank the strategies in increasing order of effectiveness, namely strategy B, strategy D, strategy C and strategy A based on the model simulation results. The difference between the total infectious individuals without control and the total infectious individuals with control was used to determine the "total number of infections averted" described in the Table 4.3 and 4.4 of cost-effectiveness analysis.

Table 4.4: Control strategies in order of increasing averted

Strategies	Total infectious averted	Total cost (\$)
Strategy II	6243.458	999.9696
Strategy I	9796.0299	944.5708
Strategy III	9798.5031	1.7075

Table 4.5: Total number of infection averted and total cost with their ICER

Strategies	Total infectious averted	Total cost (\$)	ICER
Strategy II	6243.458	999.9696	0.16016
Strategy I	9796.0299	944.5708	-0.01559
Strategy III	9798.5031	1.7075	-381.232

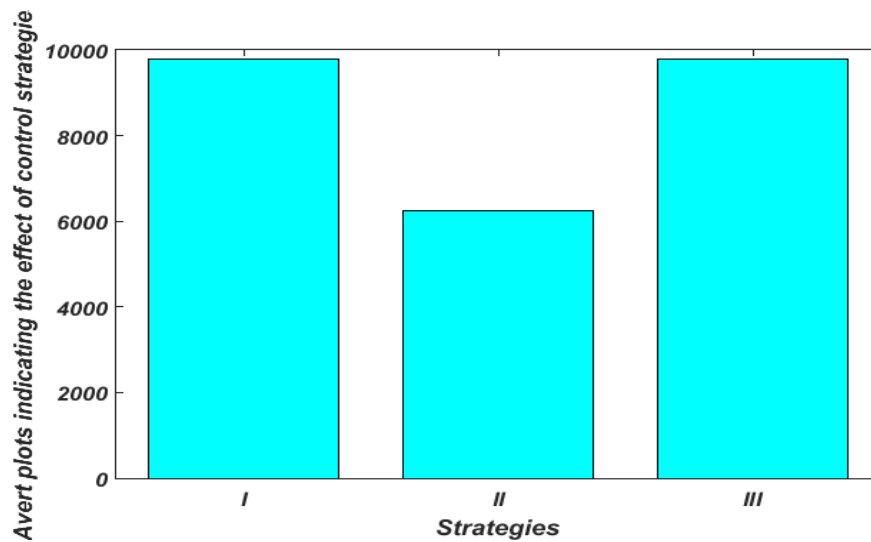


Figure 4.16: Total infectious averted plots indicating the effect of control strategies A, B, C, D and E

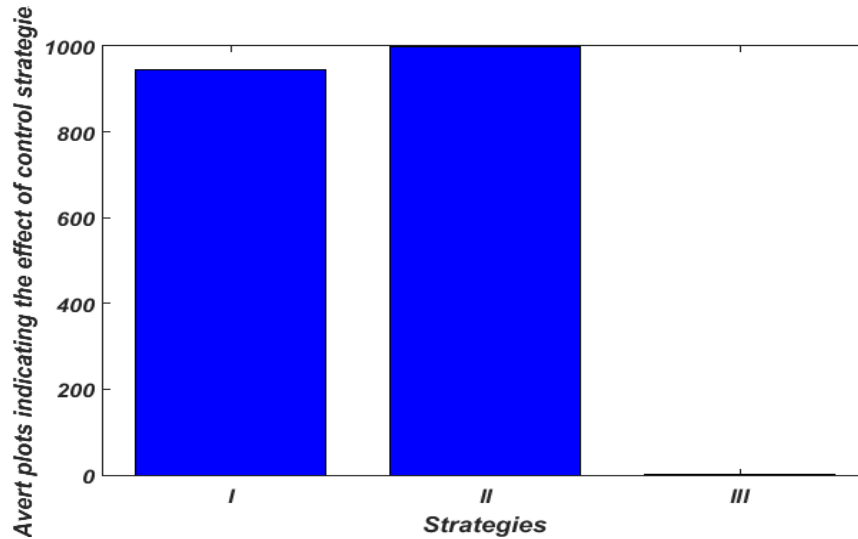


Figure 4.17: The total cost plots indicating the effect of control strategies A, B, C, D and E

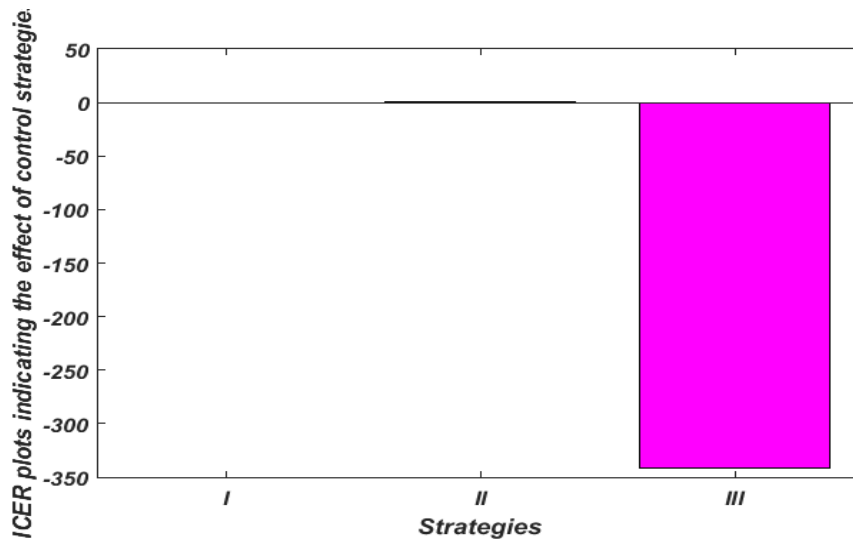


Figure 4.18: Incremental cost effective ration (ICER) plots indicating the effect of control strategies A, B, C, D and E

From the strategies B and D with their comparison in Table 4.4, we can observe that ICER (I) is less than ICER (II). This implies that strategy I is dominated by strategy II. It means that strategy II is more expensive than strategy I. Thus, we have deleted II from the comparison strategies. Then again re-calculate the ICER for the remaining comparison strategies I, and II as given in Table 4.5.

Table 4.6: Total number of infection averted and total cost with their ICER

<b>Strategies</b>	<b>Total infectious averted</b>	<b>Total cost (\$)</b>	<b>ICER</b>
Strategy I	9796.0299	944.5708	0.0964
Strategy III	9798.5031	1.7075	-381.232

In Table 4.5, there is a comparison between strategies I and III. From this the ICER (III) is less than ICER (I). This shows that strategy I is strongly dominated by strategy III. Based upon the result, we suggest that strategy III is a combination of prevention and treatment is the most effective and least cost to reduce Syphilis disease from the community. This result agrees with the results obtained in figure 4.18 for the objective functional for the various control strategies.

## CHAPTER 5

### CONCLUSION AND RECOMMENDATIONS

#### 5.1 Conclusion

In this thesis, a nonlinear differential equations were utilized to portray the dynamics of Syphilis. The analysis of the model demonstrated that all solutions of the systems are positive and bounded when initial conditions are within a specified set. The computation of the basic reproduction number in relation to the disease-free equilibrium was obtained using the next generation matrix technique. If the basic reproduction number is less than one, then the disease-free equilibrium is locally and globally asymptotically stable. Conversely, if the basic reproduction number exceeds unity, the positive endemic equilibrium is locally and globally asymptotically stable. A sensitivity analysis of the model equation was conducted on the key parameters to ascertain their influence on the disease transmission dynamics. Additionally, optimal control theory was employed to delineate the model, which integrates two controls: prevention of Syphilis and treatment of infectious individuals. Pontryagin's maximum principle is introduced to obtain the necessary condition for the optimal control problem. Ultimately, the simulation outcome of the optimal control problem and the analysis of cost-effectiveness indicated that a combined approach of prevention and treatment presents the most effective and economically viable strategy for mitigating the prevalence of Syphilis within the community.

#### 5.2 Future work

In this thesis, we have developed deterministic models that can be expanded in many ways in the future. It will be interesting to see how the model in this thesis can be expanded to include disease progression, specifically focusing on the susceptible stage of Syphilis and the onset of clinical symptoms. The expansion of the model will involve gradual progression of Syphilis. Additionally, we plan to include a drug resistance compartment in the model, and explore the



development of a fractional differential equation model.

### **5.3 Recommendations**

The eradication of syphilis poses a significant challenge for health organizations in many developing countries. Effective public health policy necessitates the utilization of optimal strategies and their appropriate implementation to mitigate the prevalence of syphilis. Consequently, this study stands to serve as a foundational framework for establishing a nexus between mathematics and public health organizations over the long term. Our study strongly advocates for the guidance of public health policymakers by optimal control strategies in managing the disease, particularly in light of the limited resources available in the sector.

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## APPENDIX

### MATHEMATICAL PRELIMINARIES

This chapter introduces some basic mathematical theories and methodologies that will be used in this dissertation.

Mathematical modeling can be defined as the use of mathematical signs, symbols and equations to represent a real-life situation in order to make it (real-life problem) easier to understand, solve, and infer a reasonable the conclusion from the solution of the problem. Mathematical models of infectious diseases have been used as a tool to study and understand the dynamics of diseases, make predictions about future outbreaks of the disease, and to suggest intervention measures that have to be implemented in order to control the disease. Mathematical models can be classified in various ways:

- Static versus dynamic models. Static models are time-independent while dynamic models are time-dependent.
- Continuous versus discrete time models. Continuous time models are models in which the independent variable is continuous, e.g,  $\frac{dx}{dt} = ax$ , while discrete time models are models used for life phenomena in which the independent variables are observed at discrete intervals, e.g,  $x_{t+1} = ax_t$ .
- Stochastic versus deterministic models. Stochastic models are models in which probabilistic concepts are used and distributions of possible behaviours are present, while deterministic models are models in which the behaviour of a population is determined completely by its history and by the rules which describe the model.
- Homogeneous versus detailed models. A detailed model involves the spatial or physiological distribution of each state variable specification while homogeneous models regard state variables as having the same spatial or

physiological distribution.

The tools used are ordinary differential equations (ODE), partial differential equations (PDE), delay differential Equation (DDE), Stochastic differential equations (SDE), integrated equations, Markov chains, game theory, etc.

## Differential Equations

Ordinary differential equations (ODEs) are equations that involve the derivatives of one or more dependent variables with respect to an independent variable. In compartmental disease models, the independent variable is time  $t$ , the rate of transfer between compartments are expressed mathematically by the derivatives of the compartments with respect to time, with an underlying assumption that the number of individuals in a compartment is a differentiable function with respect to time. The formulation of models as ordinary differential equations follows the assumption that the behaviour of a population can be determined completely by its history and the rules that govern the models.

A first order ordinary differential equation is defined as

$$\frac{dx(t)}{dt} = f(t, x(t)) \quad (5.1)$$

where  $t \in \mathbb{R}$  is an independent variable,  $x(t)$  is a dependent variable (unknown function) and  $f : \mathbb{R}^{\times} \rightarrow \mathbb{R}^{\times}$  is a vector field. Equation (5.1) is known as a nonautonomous ordinary differential equation.

When no ambiguity arises,  $\frac{dx(t)}{dt}$  is often written as  $\bar{x}$  so that (5.1) is written as

$$x' = f(t, x) \quad (5.2)$$

where the dependence of  $x(t)$  on  $t$  is also omitted unless this gives rise to ambiguities. If  $f$  does not depend explicitly on time, then (5.2) is called autonomous and takes the form

$$x' = f(x) \quad (5.3)$$

and the general solution is

$$x(t) = \int_{t_0}^t f(\tau) d\tau \quad (5.4)$$

For  $f_i : \mathbb{R}^\times \longrightarrow \mathbb{R}^\times$  and  $x_i \in \mathbb{R}^\times$ , a system of ordinary differential equations is defined when  $n > 1$ ; otherwise, for  $n = 1$  the equation is scalar.

In applications, a particular solution, which requires initial conditions is usually sought for rather than a general solution.

**Definition 1: (Initial Value Problem).** A first order ODE together with an initial condition

$$\begin{cases} x' = f(t, x) \\ x(t_0) = x_0 \end{cases} \quad (5.5)$$

is called an initial value problem. The initial condition  $x(t_0) = x_0$  represents the position of the objects at some initial time  $t_0$ . Solutions of a system of ordinary differential equations are sought for within a given interval (say, I) that contains  $t_0$ , so that the solution curves passes through the point  $(t_0, x(t_0))$ .

A solution of an initial value problem is a differentiable function  $x(t)$  such that

1.  $x' = f(t, x(t))$  for all  $t$  in an interval containing  $t_0$  where  $x(t)$  is defined, and
2.  $x(t_0) = x_0$ .

Thus, the solution can be expressed in integral form as

$$x(t) = x_0 + \int_{t_0}^t f(\tau, x(\tau)) d\tau \quad (5.6)$$

The system of ODEs to be analysed in this dissertation is autonomous and takes the form  $\bar{x} = f(x)$  with  $x \in \mathbb{R}_+^\times$  and  $f : \mathbb{R}_+^\times \longrightarrow \mathbb{R}_+^\times$ .

## Existence and Uniqueness of Solutions

In this subsection, we state some basic theorems describing general properties of solution of differential equations.

**Definition 2: (Well-posedness).** System (5.5) is well-posed if solutions exist,

are unique, and for systems describing populations, remain bounded and non-negative for all nonnegative initial conditions.

**Theorem (Cauchy- Lipschitz).** Consider the differential equation (5.5) with  $x \in \mathbb{R}^{\times}$ , and suppose that  $f \in C'$ . Then there exists a unique solution of (5.5) such that  $x(t_0) = x_0$ , where  $t_0 \in \mathbb{R}$  and  $x_0 \in \mathbb{R}^{\times}$  defined on the largest interval  $t_0 \in I$  on which  $f \in C'$ .

**Theorem** Let  $f$  and its partial derivatives  $(\partial f_i / \partial x_j)$  in (5.3) be continuous in  $\mathbb{R}^{\times}$  and let  $x_0 \in \mathbb{R}^{\times}$  and  $t_0 \in \mathbb{R}$ . Then there is an interval  $|t - t_0| < h$  in which there exists a unique solution  $x(t) = \phi(t)$  of the system that also satisfies the initial conditions.

**Definition 3: (Flow).** Consider System (5.5). The flow  $\phi(t, x_0)$  of (5.5) represents the solution of (5.5) over time given an initial condition, provided that the solutions to the differential equation exist and are unique.

**Definition 4:** An equilibrium solution of (5.3) is a solution  $\bar{x} \in \mathbb{R}^{\times}$  such that  $f(\bar{x}) = 0$ , i.e., a solution which does not change with time. The term "equilibrium point" can be used interchangeably with the following: "fixed point", "stationary point", "singularity point", "critical point" or "steady state".

**Definition 5: (Stable and unstable equilibrium point).** Let  $\phi(t)$  be the flow of (5.3), assumed to be defined for all  $t \in \mathbb{R}$ . An equilibrium solution  $\bar{x}$  of (5.3) is said to be locally stable if for all  $\epsilon > 0$ , there exists  $\delta = \delta(\epsilon) > 0$  such that for all  $x \in N_{\delta}(\bar{x})$  and  $t \geq 0$ , there holds

$$\phi_t(x) \in N_{\epsilon}(\bar{x}).$$

The equilibrium point is unstable if it is not stable.

**Definition 6: (Asymptotically stable equilibrium point)** Let  $\phi(t)$  be the flow of (5.3) is (locally) asymptotically stable if there exists  $\delta > 0$  such that for all  $x \in N_{\delta}(\bar{x})$  and  $t \geq 0$ , there holds

$$\lim_{t \rightarrow \infty} \phi(t) = \bar{x}$$

## Linearization

The behaviour of system (5.3) near a hyperbolic equilibrium point  $\bar{x}$  is linked to the behaviour of the linearized system

$$x' = Df(\bar{x})(x - \bar{x}) \quad (5.7)$$

about the same equilibrium, where

$$J(\bar{x}) = Df(\bar{x}) = \begin{bmatrix} \frac{\partial f_1}{\partial x_1}(\bar{x}) & \frac{\partial f_1}{\partial x_2}(\bar{x}) & \cdots & \frac{\partial f_1}{\partial x_{n-1}}(\bar{x}) & \frac{\partial f_1}{\partial x_n}(\bar{x}) \\ \frac{\partial f_2}{\partial x_1}(\bar{x}) & \frac{\partial f_2}{\partial x_2}(\bar{x}) & \cdots & \frac{\partial f_2}{\partial x_{n-1}}(\bar{x}) & \frac{\partial f_2}{\partial x_n}(\bar{x}) \\ \vdots & & \ddots & & \\ \frac{\partial f_{n-1}}{\partial x_1}(\bar{x}) & \frac{\partial f_{n-1}}{\partial x_2}(\bar{x}) & \cdots & \frac{\partial f_{n-1}}{\partial x_{n-1}}(\bar{x}) & \frac{\partial f_{n-1}}{\partial x_n}(\bar{x}) \\ \frac{\partial f_n}{\partial x_1}(\bar{x}) & \frac{\partial f_n}{\partial x_2}(\bar{x}) & \cdots & \frac{\partial f_n}{\partial x_{n-1}}(\bar{x}) & \frac{\partial f_n}{\partial x_n}(\bar{x}) \end{bmatrix} \quad (5.8)$$

matrix  $Df(\bar{x})$  is the Jacobian matrix of (5.3) evaluated at the equilibrium point  $\bar{x}$ .

**Definition 7: (Hyperbolic fixed point)** Let  $x = \bar{x}$  be a fixed point of  $x' = f(x)$ ,  $x \in \mathbb{R}^\kappa$ . Then  $\bar{x}$  is called a hyperbolic fixed point if none of the eigenvalues of  $Df(\bar{x})$  have zero real part. A hyperbolic fixed point is called a saddle if some, but not all, of the eigenvalues have positive real parts. If all eigenvalues have negative real part, then the hyperbolic fixed point is called a stable node or sink and if all of the eigenvalues have positive real part, then the hyperbolic fixed point is called an unstable node or source.

**Definition 8:** A non hyperbolic fixed point is a fixed point having the real part of some of the eigenvalues associated to the linearized system equal to zero, that is, these eigenvalues are purely imaginary. (Such fixed point is said to be a center if the system is linear.)

**Theorem (Hartman and Grobman)** Assume that  $\bar{x} \in \mathbb{R}^\kappa$  is a hyperbolic equilibrium (all eigenvalues of the Jacobian matrix evaluated at  $\bar{x}$  have nonzero real part). Then, in a small neighbourhood of  $\bar{x}$ , the nonlinear system behaves in a



similar manner as the linearized system.

## Stability

The Hartman-Grobman theorem tells us that, in a neighbourhood of a hyperbolic equilibrium point, we can get a qualitative idea of the behaviour of solutions of the nonlinear system by studying its corresponding linear system. Thus, we can determine whether solution trajectories approach or move away from the equilibrium point over time, that is, we can determine the stability of equilibria in System (5.3) without finding explicit solutions.

**Theorem** Let  $\bar{x}$  be an equilibrium point of the autonomous system (5.3), where  $f \in C^1$  in a neighborhood of  $\bar{x}$ .

1. If all the eigenvalues of  $J = Df(\bar{x})$  have negative real part, then  $\bar{x}$  is a locally asymptotically stable equilibrium point.
2. If  $J = Df(\bar{x})$  has at least one eigenvalue with positive real part, then  $\bar{x}$  is an unstable equilibrium point.

## Lyapunov functions and LaSalle's invariance Principle

Lyapunov functions and LaSalle's Invariance Principle are some of the methods often used to establish the global stability property of an equilibrium point.

**Definition 9:** A point  $x_0 \in \mathbb{R}^n$  is called an  $\omega$ -limit point of  $x_0 \in \mathbb{R}^n$  and denoted by  $\omega(x)$ , if there exists a sequence  $t_i$  such that

$$\phi(t_i, x) \rightarrow x_0 \text{ as } t_i \rightarrow \infty.$$

**Definition 10:** A point  $x_0 \in \mathbb{R}^n$  is called an  $\alpha$ -limit point of  $x_0 \in \mathbb{R}^n$  and denoted by  $\alpha(x)$ , if there exists a sequence  $t_i$  such that

$$\phi(t_i, x) \rightarrow x_0 \text{ as } t_i \rightarrow -\infty.$$

**Definition 11.** The set of all  $\omega$ -limit points of a flow is called the  $\omega$ -limit set. Similarly, the set of all  $\alpha$ -limit points of a flow is called the  $\alpha$ -limit set.

**Definition 12.** Let  $S \subseteq \mathbb{R}^n$  be a set. Then  $S$  is said to be invariant under the flow generated by (5.3) if for any  $x_0 \in S$ , we have  $x(t, x_0) \in S$  for all  $t \in \mathbb{R}$ .

If the region is restricted to positive times (*i.e.*,  $t \geq 0$ ), then  $S$  is said to be a positively-invariant set (this implies that solutions in the positive invariant set remain there for all time). The set is negatively-invariant if solutions remain there when we go backward in time.

**Definition 13:** A function  $V : \mathbb{R}^n \rightarrow \mathbb{R}$  is said to be a positive definite function if:

- $V(x) > 0$  for all  $x \neq 0$
- $V(x) = 0$  if and only if  $x = 0$

**Theorem (Lyapunov):** Consider the autonomous system defined by (5.3). Let  $\bar{x}$  be a fixed point of (5.3) and let  $V : U \rightarrow \mathbb{R}$  be a  $C^1$  function defined on some neighbourhood  $U$  of  $\bar{x}$  such that

1.  $V(\bar{x}) = 0$  and  $V(x) > 0$  if  $x \neq \bar{x}$ ,
2.  $\frac{dV(x)}{dx} \leq 0$  in  $U - \bar{x}$ .

Then  $\bar{x}$  is stable. Moreover, if

3.  $\frac{dV(x)}{dx} < 0$  in  $U - \bar{x}$ .

Then  $\bar{x}$  is asymptotically stable. Any function  $V$  that satisfies the conditions from Theorem (Lyapunov) is said to be a Lyapunov function.

**Theorem (LaSalle's Invariance Principle).** Consider system (5.3). Let

$$S = \{x \in U \mid \frac{dV(x)}{dt} = 0\} \quad (5.9)$$

and let  $M$  be the largest invariant set of (5.3) in  $S$ . If  $V$  is a Lyapunov function on  $U$  and  $\gamma^+(x_0)$  is a bounded orbit of (5.3) which lies in  $S$ , then the  $\omega$ -limit set of  $\gamma^+(x_0)$  belongs to  $M$  (that is,  $x(t, x_0) \rightarrow M$  as  $t \rightarrow \infty$ .)

- $\gamma^+(x_0)$ : part of solution trajectory where  $t \geq t_0$  (Positive orbit).

- $\gamma^-(x_0)$ : part of solution trajectory where  $t \leq t_0$  (negative orbit).

**Corollary:** If  $V(x) \rightarrow \infty$  as  $|x| \rightarrow \infty$  and  $\frac{dV}{dt} < 0$  on  $\mathbb{R}$ , then every solution of (5.3) is bounded and approaches the largest if  $M = 0$ , then the solution  $x = 0$  is globally asymptotically stable.

Subsequently  $V' = \frac{dV}{dt}$ .

## Routh-Hurwitz Criteria

**Theorem (Routh Hurwitz Stability Criteria)** Consider the  $n^{th}$  degree polynomial with real constant coefficients  $P(\lambda) = \lambda^n + a_1\lambda^{(n-1)} + \dots + a_{(n-1)}\lambda + a_n$ . Define  $n$  Hurwitz matrices using the coefficients  $a_i$  of the characteristic polynomial:

$$\begin{aligned}
 H_1 &= \begin{bmatrix} a_1 \end{bmatrix} \\
 H_2 &= \begin{bmatrix} a_1 & 1 \\ a_3 & a_2 \end{bmatrix} \\
 H_3 &= \begin{bmatrix} a_1 & 1 & 0 \\ a_3 & a_2 & a_1 \\ a_5 & a_4 & a_3 \end{bmatrix} \\
 H_4 &= \begin{bmatrix} a_1 & 1 & 0 & 0 & \dots & 0 \\ a_3 & a_2 & a_1 & 1 & \dots & 0 \\ a_5 & a_4 & a_3 & a_2 & \dots & 0 \\ \vdots & \vdots & \vdots & \vdots & \dots & \vdots \\ 0 & 0 & 0 & 0 & \dots & a_n \end{bmatrix}
 \end{aligned}$$

Here  $a_j = 0$  if  $j > n$ . All roots of the polynomial  $P(\lambda)$  are negative or have negative real part if and only if the determinants of all Hurwitz matrices are positive i.e.  $\text{Det}H_j > 0, \forall j = 1, 2, \dots$ , **Theorem (Derrick and Groosman, 1976)** Let  $D$  denote the region  $|t - t_0| \leq a, \|x - x_0\| \leq 1, x = (x_1, x_2, \dots, x_n), x_0 = (x_{10}, x_{20}, \dots, x_{n0})$  and suppose that  $f(t, x)$  satisfies the Lipschitz condition  $\|f(t, x_1) - f(t, x_2)\| \leq k\|x_1 - x_2\|$ . Whenever the pairs  $(t, x_1)$  and  $(t, x_2)$  belong to  $D$  where  $k$  is positive constant then, there is a constant  $\delta \geq 0$  such that there exist a unique

n	Coefficient signs	Additional Conditions
1	$a_1 > 0, a_2 > 0$	
2	$a_1 > 0, a_2 > 0, a_3 > 0$	$a_1 a_2 > a_3$
3	$a_1 > 0, a_2 > 0, a_3 > 0, a_4 > 0$	$a_1 a_2 a_3 > a_3^2 + a_1^2 a_4$
4	$a_1 > 0, a_2 > 0, a_3 > 0, a_4 > 0, a_5 > 0$	$a_1 a_2 a_3 > a_3^2 + a_1^2 a_4,$ $(a_1 a_4 - a_5)(a_1 a_2 a_3 - a_3^2 - a_1^2 a_4) > a_5(a_1 a_2 - a_3)^2 +$ $a_1 a_5^2.$

Table 5.1: Routh-Hurwitz Criteria

continuous vector solution of  $x(t)$  of the system in the interval  $|t - t_0| \leq \delta$ . It is important to note that the condition is satisfied by the requirement that  $\frac{(\partial f_i)}{(\partial x_i)}$ ,  $\forall i, j = 1, 2, \dots$  be continuous and bounded in D.

## Basic Reproduction Number $\mathfrak{R}_0$

The concept of the basic reproduction number is one of the central topics in mathematical Modelling of infectious diseases due to its meaning and extreme importance. Hardly can one find a publication on a mathematical model without mention of this number. It is also called the basic reproduction ratio among other variant forms. It is very important in disease Modelling because it gives an indication regarding the future state of the infection. It tells us whether or not the disease will persist or will be eradicated in due course.

**Definition 14** The basic reproduction number denoted by  $\mathfrak{R}_0$  and is defined as the expected number of people getting secondary infection among the whole susceptible population. This number determines the potential for the spread of disease within a population. When  $\mathfrak{R}_0$  each infected individual produces on average less than one new infected individual so that the disease is expected to die out. On the other hand if  $\mathfrak{R}_0$  then each individual produces more than one new infected individual so that the disease is expected to continue spreading in the population. This means that the threshold quantity for eradicating the disease is to reduce the value of  $\mathfrak{R}_0$  to less than one.

The basic reproductive number  $\mathfrak{R}_0$  can be determined using the next generation matrix. In this method,  $\mathfrak{R}_0$  is defined as the largest eigenvalue of the next

generation matrix. The formulation of this matrix involves classification of all compartments of the model into two classes: infected and non-infected. That is, the basic reproduction number cannot be determined from the structure of the mathematical model alone but depends on the definition of infected and uninfected compartments.

### **Description of the Method of Driessche and Watmough**

Consider a heterogeneous population whose individuals are distinguishable by age, behavior, spatial position, and/or stage of disease, but can be grouped into  $n$  homogeneous compartments. A general epidemic model for such a population is developed in this section. Let  $x = (x_1, x_2, \dots, x_n)^t$ , with each  $x_i \geq 0$ , the number of individuals in each bucket. For clarity, we order the compartments so that the first compartments of  $M$  correspond to the infected people. The distinction between infected and uninfected compartments must be determined by the epidemiological interpretation of the Model and can not be deduced from the structure alone equations, as we will discuss below. The basic reproduction number cannot be determined from the structure of the mathematical model alone, but depends on the definition of infected and uninfected compartments. We define  $X_s$  to be all states under discussion. That is  $X_s = \{x \geq 0 : x_i = 0, i = 1, \dots, m\}$ .

In order to compute  $\mathcal{R}_0$ , it is important to distinguish new infections from all other changes in population. Let  $f_i(x)$  be the rate of appearance of new infections in compartment  $i$ ,  $V_i^+(x)$  and the transfer rate of individuals into compartment  $i$  by all other means, and  $V_i^-(x)$  be the rate of transfer of individuals out of compartment  $i$ . It is assumed that each function is continuously differentiable at least twice in each variable. The disease transmission model consists of nonnegative initial conditions together with the following system of equations:

$$\dot{x} = f_i(x) - V_i(x), i = 1, \dots, n,$$

where  $V_i = V_i^- - V_i^+$  and the functions satisfy assumptions  $(A_1) - (A_5)$  described below. Since each function represents a direct transfer of individuals, they are not

negative. Thus,

A<sub>1</sub>. If  $x \geq 0$  then  $f_i, V_i^+, V_i^- \geq 0, \forall i = 1, \dots, n$ .

A<sub>2</sub>. If  $x_i = 0$  then  $V_i = 0$ . In particular if  $x \in X_s$  then  $V_i = 0 \forall i = 1, \dots, m$

A<sub>3</sub>.  $f_i = 0$  if  $i > m$ .

A<sub>4</sub>. If  $x \in X_s$  then  $f_i(x) = 0$  and  $V_i^+ = 0, \forall i = 1, \dots, m$

A<sub>5</sub>. If  $f(x)$  is set to zero, then all *dfeigenvalue*( $x_0$ ) have genuine actual parts.

Then the Jacobian matrix  $Df(x_0)$  can be partitioned as given in the following lemma.

**Lemma 1.** If  $x_0$  is a DFE of (5.3) and  $f_i(x)$  satisfies (A<sub>1</sub>) – (A<sub>5</sub>), then the derivatives  $Df(x_0)$  and  $DV(x_0)$  are partitioned as follows

$$DF(X_0) = \begin{bmatrix} F & 0 \\ 0 & 0 \end{bmatrix}, DV(X_0) = \begin{bmatrix} V & 0 \\ J_3 & J_4 \end{bmatrix}$$

where  $F$  and  $V$  are  $m \times m$  matrices defined by

$$F = [\frac{\partial f_i}{\partial x_i}(x_0)] \text{ and } V = [\frac{\partial V_i}{\partial x_i}(x_0)] \text{ with } i \leq m, j \leq m.$$

Further,  $F$  is non-negative,  $V$  is a non-singular M-matrix and all eigenvalues of  $J_4$  have positive real parts. The following theorem then is used to compute the threshold parameter  $\mathfrak{R}_0$ .

**Theorem .** Consider the disease transmission model given by (5.3) with  $f(x)$  satisfying conditions (A<sub>1</sub>) – (A<sub>5</sub>). If  $x_0$  is a DFE of the model, then  $x_0$  is locally asymptotically stable if  $\mathfrak{R}_0 < 1$ , where  $\mathfrak{R}_0$  is defined by

$$\mathfrak{R}_0 = \rho(FV^{-1})$$

where  $\rho(A)$  denotes the spectral radius of  $A$ .

Thus, the threshold quantity  $\mathfrak{R}_0$  plays a major role in determining the qualitative behavior of epidemic models. We note that at  $\mathfrak{R}_0 = 1$  the disease-free equilibrium and endemic equilibrium exchange stability. This phenomenon of change of stability is known as forwarding bifurcation. When forward bifurcation occurs, then  $\mathfrak{R}_0 \leq 1$  is a necessary and sufficient condition for disease elimination.

Another important concept related to the condition  $\mathfrak{R}_0 \leq 1$  is that of backward bifurcation. This occurs when a stable endemic equilibrium co-exists with a stable disease-free equilibrium. When this happens, then  $\mathfrak{R}_0 \leq 1$  only remains a necessary but not sufficient condition for disease elimination and hence disease eradication can not just be achieved by making  $\mathfrak{R}_0$

## Optimal Control Theory

The mathematical theory used to obtain optimal control strategies that vary over time are called the theory of optimal control. The simplest optimal control problem is an optimization problem that seeks to maximize/minimize an objective function subject to a dynamical system in the form of equation together with some initial or boundary conditions. Formally, the simplest optimal control problem is one of the form

$$\begin{aligned} & \text{Maximize } \int_{t_0}^{t_f} g(t, X, u) dt \\ & \text{Subject to } \frac{dx}{dt} = f(t, x, u), x(t_0) = x_0, x(t_f) \text{ free} \\ & \text{and } u(t) \in \mathcal{U}, \forall t \in [0, t_f] \end{aligned}$$

## Pontryagin Maximum Principle

Pontryagin's maximum principle, often referred to as the maximum principle, is the primary tool used to solve optimal control problems. It provide first-order necessary conditions for optimal solution of the problem. The principle provides direction as to how the control  $u$ , state variable  $x$  and a third variable known as co-state or adjoint variable  $\lambda$  should change overtime through equations of motions for  $x$  and  $\lambda$ . The Pontryagin's maximum principle is given in the following theorem.

**Theorem** Let  $u(t)$  be a time optimal control and  $X(t)$  be the corresponding response of the system. Then there exists a function  $\lambda(t) : [0, t_f] \rightarrow R^n$ , such that:

$$\begin{aligned} \dot{x} &= \frac{\partial H}{\partial \lambda}(x, \lambda, u), x(t_0 = x_0) \text{ (State Equation)} \\ \dot{\lambda} &= -\frac{\partial H}{\partial x}(x, \lambda, u) \text{ (Co-state Equation)} \end{aligned}$$

$$\lambda(t_f) = 0 \text{ (Transversality Condition)}$$

$$H(x, \lambda, u) = \max_{u \in A} H(x, \lambda, u) \left\{ \text{or } \frac{\partial H}{\partial u} = 0 \right\} \quad (5.10)$$

Where  $H = g(t, x, u) + \lambda(t)f(t, x, u)$  is called the Hamiltonian of the optimal control problem. Equation (5.10) is given in two forms because, when the Hamiltonian is differentiable with respect to  $u$ , the condition  $\frac{\partial H}{\partial u} = 0$  can often be used to replace  $H(x^*, \lambda^*, u^*) = \max_{u \in A} H(x, \lambda, u)$ .

## Sensitivity Analysis

Sensitivity analysis is commonly used to determine the robustness of model predictions parameter values a because there are usually errors in data collection and assumed parameter values. It is used to discover parameters that have a high impact on  $R_0$  and should be targeted by intervention strategies. More precisely, sensitivity indices allow measuring the relative change in a variable when the parameter changes. If the result is negative, then the relationship between the parameters and  $R_0$  is inversely proportional. In this case, we will take the sensitivity index module so that we can deduce the dimensions of the effect to change this parameter. A positive sensitivity index, on the other hand, signifies an increase in the value of a parameter.

For that, we use the normalized forward sensitivity index of a variable, with Compared to a specific parameter, which is defined as the ratio between the relative changes of the variable for the relative variation of the parameter. If this variable is differentiable with respect to the parameter, then the sensitivity index is defined by the partial derivatives, as follows:

**Definition 15** The normalized forward sensitivity index of  $R_0$ , which is differentiable with respect to a given parameter  $p$ , is defined by:

$$\Upsilon_p^{R_0} = \frac{\partial R_0}{\partial p} \cdot \frac{p}{R_0} \quad (5.11)$$