Optimal Control Strategy on Mathematical Modeling of Syphilis Infection

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Abstract

In this study, developed 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 Control, Stability, Simulation, Syphilis

1 Introduction

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 [18]. 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

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 [19]. 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 [1]. 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.

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 [13], 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 [14].

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. Optimal control models enable the evaluation

of the cost-effectiveness of diverse interventions. Policymakers 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.

Mathematical models have been developed to analyze the dynamics of syphilis infection transmission and its associated health complications. These models also serve 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.,[17] presented a mathematical model using nonlinear differential equations to assess the impact of syphilis in Brazil. The study aimed to quantitatively depict the correlation between reported cases of mother-to-child transmission and congenital syphilis in Brazil from 2010 to 2020, accounting for the probability of diagnosis and effective maternal treatment during prenatal care. Notably, the analysis did not encompass control strategies. Furthermore, a study [15] examined the effects of sexual behavior, mass media reporting, and treatment of infected individuals on the dynamics of syphilis transmission, emphasizing the importance of media addressing safe sexual behavior, despite the absence of consideration of the exposed compartment in their model. Additionally, a deterministic mathematical model was proposed by another study [7] to analyze the transmission dynamics of syphilis, revealing a complex 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. They have also developed a mathematical modeling framework to assess the cost-effectiveness of various approaches using rapid tests for syphilis detection in prison populations [4]. Furthermore, a study led by another researcher [16] observed that increasing the fraction of individuals tested, without a concurrent increase in test frequency, led to a smaller decline in incidence. Similarly, a study [11] proposed a system of ordinary differential equations to model the infection stages and treatment of syphilis. The findings emphasized the significance of early treatment for syphilis control. Additionally, a study led by another researcher [12] introduced a nonlinear ordinary differential equation aimed at examining the dynamics of syphilis transmission. They demonstrated 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. It is important to note that none of these studies considered optimal control strategies in the mathematical modeling of syphilis infection within a community. This knowledge gap has motivated further research to address this particular aspect.

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.

2 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 Π. 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 β is the probability that a contact between a susceptible individuals and an infectious individuals will result to an infection. The modification parameter δ and γ , 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 α. Infected individuals implies both early stage infected and late stage infected individuals are treated at the rate τ. 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 χ 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 ϕ. Recovered individuals may revert to the susceptible class after losing their immunity at rate ω. All class are subjected to a natural death rate μ. 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 ξ_1,ξ_2 and ξ_3 respectively. All parameters in the model are non-negative.
The schematic diagram of the formulated model is given in Figure 1.

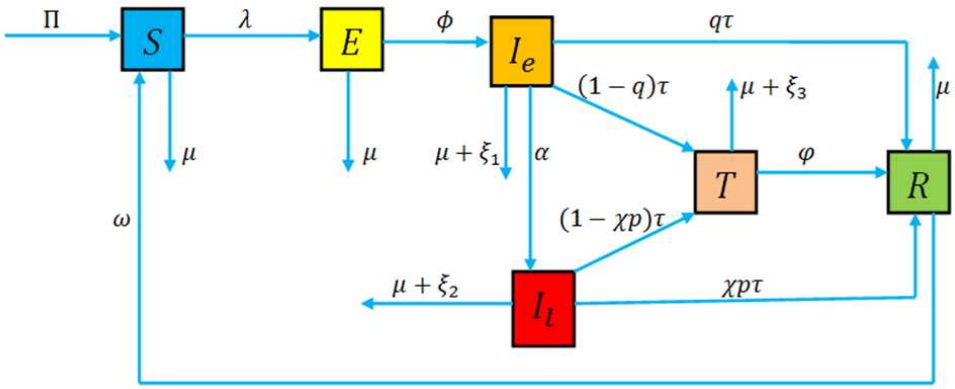

Fig. 1 Schematic Diagram of Syphilis Model.

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

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

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 $R(t) \geq 0$.

3 Basic Properties of Syphilis Model

3.1 Invariant Region

In this section, we obtain a region in which the solutions of model equation (1) are uniformly bounded in the proper subsets of $\Omega \in R^{6+}$. 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 (1) we obtained;

$$\frac{dN}{dt} = \Pi - \mu - (\xi_1 I_e + \xi_2 I_l + \xi_3 T), \tag{2}$$

In the absence of mortality due to disease ($\xi_1 = \xi_2 = \xi_3 = 0$), then equation (2)become

$$\frac{dN}{dt} \leq \Pi - \mu, \tag{3}$$

After solving equation (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 (1) remains in the region:

$$\Omega = \{(S, E, I_e, I_l, T, R) \in \Re^{6+} : N \leq \frac{\Pi}{\mu}\}. \tag{4}$$

3.2 Positivity of Solutions

In this section, we show all the solution of the model equation (1) remain positive for future time if their respective initial values are positive.
Lemma 1: Let $\Omega = \{(S, E, I_e, I_l, T, R) \in \Re^{6+}; S(0) \geq 0, E(0) \geq 0, I_e(0) \geq 0, I_l(0) \geq 0, T(0) \geq 0$ 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 (1) we have:

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

By the same procedure, the other state variables $E(t), I_e(t), I_l(t), T(t)$ and $R(t)$ are all non-negatives.

3.3 Equilibrium Analysis

3.4 Syphilis Free Equilibrium

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 (1) as

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

Thus, the Syphilis-free equilibrium point of the model equation in (1) above is given by

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

3.5 The Basic Reproduction Number

The basic reproduction number is denoted $\Re_0$ by and is defined as the expected number of people getting secondary infection among the whole susceptible population.The dominant eigenvalue of the next generation matrix is $\Re_0$, which is computed using the next-gen matrix method for the model system (1) the associated matrices and for the new infectious terms and the remaining transition terms are respectively given by:

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

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

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

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 $\Re_0$ 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 λ 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;

$$\Re_0 = [\frac{\beta\phi}{(\phi+\mu)(\tau+\alpha+\mu+\xi_1)} + \frac{\beta\delta\phi\alpha}{(\phi+\mu)(\tau+\alpha+\mu+\xi_1)(\tau+\mu+\xi_2)} - (\frac{\beta\gamma\phi\alpha(1-\chi\rho)\tau + \beta\gamma\phi(1-q)\tau}{(\phi+\mu)(\tau+\alpha+\mu+\xi_1)(\tau+\mu+\xi_2)(\varphi+\mu+\xi_3)})].$$

3.6 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 (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 (1) is locally asymptotically stable if $\Re_0 < 1$.
Proof: The Jacobian matrix J of model at the Syphilis free equilibrium E_0 reduces to;

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

where $J_{11} = -\mu(\frac{\beta(I_e(t)+\delta I_l(t)+\gamma T)}{\Pi} - \mu^2, J_{21} = (\frac{\beta(I_e(t)+\delta I_l(t)+\gamma T)}{\Pi}\mu), J_{33} = \tau+\alpha+\mu+\xi_1, J_{44} = -(\tau+\mu+\xi_2), J_{55} = -(\varphi+\mu+\xi_3).$
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:
$(J(E_0) - \Phi I)=$

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

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;

$$(-(\omega+\mu) - \Phi)(-(\phi+\mu) - \Phi)(J_{11} - \Phi)(J_{55} - \Phi)(J_{33} - \Phi)(J_{44} - \Phi) = 0. \quad (5)$$

From equation (5)

$(-(\omega+\mu) - \Phi) = 0$, $\Phi_1 = -(\omega+\mu)$, $(-(\phi+\mu) - \Phi) = 0$, $\Phi_2 = -(\phi+\mu)$,
$(J_{11} - \Phi) = 0$, $\Phi_3 = J_{11}$, since $J_{11} = -\mu(\frac{\beta(I_e(t)+\delta I_l(t)+\gamma T)}{\Pi} - \mu^2$,
$\Phi_3 = -\mu(\frac{\beta(I_e(t)+\delta I_l(t)+\gamma T)}{\Pi} - \mu^2$,
$(J_{55} - \Phi) = 0$, $\Phi_4 = (J_{55})$, since $J_{55} = -(\varphi + \mu + \xi_3)$, $\Phi_4 = -(\varphi + \mu + \xi_3)$,
and from the last characteristic equation $(J_{33} - \Phi)(J_{44} - \Phi)$, we have;

$$\Phi^2 - a\Phi - b = 0, \quad (6)$$

where $a = (\alpha + \xi_1 - \xi_2), b = (\tau + \mu + \xi_1)(\tau + \mu + \xi_2)$.
By using Routh-Hurwitz criteria, equation (6) has real root that strictly negative if $a < 0$ and $b < 0$ so that;

$$b = (\tau + \mu + \xi_1)(\tau + \mu + \xi_2)[\frac{\beta\phi cf + \beta\delta\phi\alpha f - (\beta\gamma\phi\alpha e + \beta\gamma\phi d)}{(abcf)(\tau+\mu+\xi_1)(\tau+\mu+\xi_2)} - \frac{1}{(\tau+\mu+\xi_1)(\tau+\mu+\xi_2)}]$$
$$=((\tau + \mu + \xi_1)(\tau + \mu + \xi_2))^2(\frac{\beta\phi + \beta\delta\phi\alpha - (\beta\gamma\phi\alpha e + \beta\gamma\phi d)}{(abcf))} - 1)$$
$$=(\tau + \mu + \xi_1)(\tau + \mu + \xi_2))^2(\Re_0 - 1) < 0.$$

However, b to be negative, $(\tau+\mu+\xi_1)(\tau+\mu+\xi_2))^2(\Re_0-1)$ should be negative, which leads to $\Re_0 < 1$. Hence the Syphilis free equilibrium is locally asymptotically stable in Ω if $\Re_0 < 1$.

3.7 Global Stability of Syphilis Free Equilibrium

Theorem 2: The Syphilis free equilibrium of the system (1) is global asymptotically stable if $\Re_0 < 1$.

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

$$L = A_1 I_e + A_2 I_l \tag{7}$$

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

$$\frac{dL}{dt} = A_1 \frac{I_e}{dt} + A_2 \frac{I_l}{dt}$$
$$= A_1(\phi E - (\tau + \alpha + \mu + \xi_1)I_e) + A_2(\alpha I_e - (\tau + \mu + \xi_2)I_l)$$
$$= A_1(\phi E) - (\tau + \alpha + \mu + \xi_1)I_e A_1 + A_2(\alpha I_e) - (\tau + \mu + \xi_2)I_l A_2$$
$$= -(\tau + \alpha + \mu + \xi_1)I_e \frac{(\beta\gamma\phi\alpha e + \beta\gamma\phi d)}{(abcf))} + (\frac{(\beta\gamma\phi)}{(abc))}(\alpha I_e) \text{ By taking}$$
$$A_1 = \frac{(\beta\gamma\phi\alpha e + \beta\gamma\phi d)}{(abcf)}, A_2 = (\frac{(\beta\gamma\phi)}{(abc)}$$
$$\frac{dL}{dt} \leq [-(\tau + \alpha + \mu + \xi_1)\frac{(\beta\gamma\phi\alpha e + \beta\gamma\phi d)}{(abcf))} + (\frac{(\beta\gamma\phi\alpha)}{(abc)}]I_e$$
$$= [(\frac{-abcf}{(\tau+\alpha+\mu+\xi_1)(\beta\gamma\phi\alpha e + \beta\gamma\phi df + \beta\gamma\phi\alpha)} - \frac{(\tau+\alpha+\mu+\xi_1)(\beta\gamma\phi\alpha e + \beta\gamma\phi df + \beta\gamma\phi\alpha)}{\beta\phi cf + \beta\delta\phi\alpha f - (\beta\gamma\phi\alpha e + \beta\gamma\phi d)})$$
$$(-(\tau + \alpha + \mu + \xi_1)\frac{(\beta\gamma\phi\alpha e + \beta\gamma\phi d)}{(abcf))} + (\frac{(\beta\gamma\phi\alpha)}{(abc)})]I_e$$
$$= [(\frac{(\beta\gamma\phi\alpha)}{(abc)}(1 - \frac{\beta\phi + \beta\delta\phi\alpha - (\beta\gamma\phi\alpha e + \beta\gamma\phi d)}{(abcf))})]I_e$$
$$= [(\frac{(\beta\gamma\phi\alpha)}{(abc)}(1 - \Re_0)]I_e$$

Hence, we obtain $\frac{dL}{dt} < 0$ if $\Re_0 < 0$ and $\frac{dL}{dt} = 0$ if and only if $I_e = 0$. Thus, the singleton set SFE in Ω 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 $\Re_0 < 1$, the SFE is globally asymptotically stable in Ω.

3.8 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 (1) to zero and express each dependent variable in terms of I_e^* at equilibrium point and we obtain;

$$\begin{cases} S^* = \frac{\Pi^2 + R^*\omega\mu}{\mu(\beta(I_e(t)+\delta I_l(t)+\gamma T))}, \\ E^* = \frac{S^*\mu(\beta(I_e(t)+\delta I_l(t)+\gamma T))}{\Pi(\phi+\mu)}, \\ I_l^* = \frac{\alpha E^*}{\tau+\mu+\xi_2}, \\ T^* = \frac{(1-q)\tau I_e^* + (1-\chi p)\tau I_l^*}{\varphi+\mu+\xi_3}, \\ R^* = \frac{q\tau I_e^* + \chi p\tau I_l^* + \varphi T^*}{\omega\mu}. \end{cases} \tag{8}$$

From equation (8) the endemic equilibrium easily satisfies the following polynomial and I_e^* is obtained by solving the equation;

$$A(I_e^*)^2 + B(I_e^*) = 0 \tag{9}$$

where $A = \Pi^2 + R^*\omega\mu + (1-\chi p)$, $B = q\tau + \alpha(1-\Re_0)$. Hence $A > 0$ and $B > 0$ whenever $\Re_0 < 1$. 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 $\Re_0 < 1$.

3.9 Global Stability of Endemic Equilibrium

Theorem 1: The endemic equilibrium point of the model equation (1) is globally asymptotically stable whenever $\Re_0 > 1$.

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 **L** along the solution (1) we have

$\frac{dL}{dt} = [\frac{S-S^*}{S}]\frac{dS}{dt} + [\frac{E-E^*}{E}]\frac{dE}{dt} + [\frac{I_e-I_e^*}{I_e}]\frac{dI_e}{dt} + [\frac{I_l-I_l^*}{I_l}]\frac{dI_l}{dt} + [\frac{T-T^*}{T}]\frac{dT}{dt} + [\frac{R-R^*}{R}]\frac{dR}{dt}$

$= [\frac{S-S^*}{S}](\Pi - (\frac{\beta(I_e(t)+\delta I_l(t)+\gamma T)}{N})S - \mu S + R\omega)$

$+ [\frac{E-E^*}{E}]((\frac{\beta(I_e(t)+\delta I_l(t)+\gamma T)}{N})S - (\phi+\mu)E)$

$+ [\frac{I_e-I_e^*}{I_e}](\phi E - (\tau+\alpha+\mu+\xi_1)I_e)$

$+ [\frac{I_l-I_l^*}{I_l}](\alpha I_e - (\tau+\mu+\xi_2)I_l)$

$+ [\frac{T-T^*}{T}]((1-q)\tau I_e + (1-\chi p)\tau I_l - (\varphi+\mu+\xi_3)T)$

$+ [\frac{R-R^*}{R}](q\tau I_e + \chi p\tau I_l + \varphi T - (\omega+\mu)R),$

$= [1 - \frac{S^*}{S}](\Pi - (\frac{\beta(I_e(t)+\delta I_l(t)+\gamma T)}{N})S - \mu S + R\omega)$

$+ [1 - \frac{E^*}{E}]((\frac{\beta(I_e(t)+\delta I_l(t)+\gamma T)}{N})S - (\phi+\mu)E)$

$+ [1 - \frac{I_e^*}{I_e}](\phi E - (\tau+\alpha+\mu+\xi_1)I_e)$

$+ [1 - \frac{I_l^*}{I_l}](\alpha I_e - (\tau+\mu+\xi_2)I_l)$

$+ [1 - \frac{T^*}{T}]((1-q)\tau I_e + (1-\chi p)\tau I_l - (\varphi+\mu+\xi_3)T)$

$+ [1 - \frac{R^*}{R}](q\tau I_e + \chi p\tau I_l + \varphi T - (\omega+\mu)R).$

Then collecting positive and negative terms together we obtain

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

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

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

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 (1). By LaSalle?s invariant principle (LaSalle?s, 1976), it implies that E_1 is globally asymptotically stable in Ω if $M < N$.

4 Sensitivity Analysis of Model Parameters

In this section, we will see the sensitivity analysis of the parameters that found in the model (1) those can determine the value of the basic reproduction number. Because those parameters can increasing or decreasing a basic reproduction number $\Re_0$ 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 $\Re_0$ 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 $\Re_0$ that depends differentiable on a parameter **M** is defined as;

$$\tau_M^{\Re_0} = \frac{\partial \Re_0}{\partial M} \times \frac{\Re_0}{M}. \tag{10}$$

The sensitivity index of $\Re_0$ in relation to the parameter β is calculated as

$$\tau_\beta^{\Re_0} = \frac{\partial \Re_0}{\partial \beta} \times \frac{\beta}{\Re_0}$$

$$= [\frac{\phi}{(\phi+\mu)(\tau+\alpha+\mu+\xi_1)} + \frac{\delta\phi\alpha}{(\phi+\mu)(\tau+\alpha+\mu+\xi_1)(\tau+\mu+\xi_2)} -$$

$$(\frac{\gamma\phi\alpha(1-\chi\rho)\tau+\beta\gamma\phi(1-q)\tau}{(\phi+\mu)(\tau+\alpha+\mu+\xi_1)(\tau+\mu+\xi_2)((\phi+\mu)(\tau+\alpha+\mu+\xi_1)(\tau+\mu+\xi_2)(\varphi+\mu+\xi_3)})] \times$$

$$\frac{\beta}{[\frac{\beta\phi}{(\phi+\mu)(\tau+\alpha+\mu+\xi_1)} + \frac{\beta\delta\phi\alpha}{(\phi+\mu)(\tau+\alpha+\mu+\xi_1)(\tau+\mu+\xi_2)} - (\frac{\beta\gamma\phi\alpha(1-\chi\rho)\tau+\beta\gamma\phi(1-q)\tau}{(\phi+\mu)(\tau+\alpha+\mu+\xi_1)(\tau+\mu+\xi_2)((\phi+\mu)(\tau+\alpha+\mu+\xi_1)(\tau+\mu+\xi_2)(\varphi+\mu+\xi_3)})]} =$$

$$1 > 0$$

Taking the same approach as with rest parameters, $\tau_\phi^{\Re_0}$,$\tau_\delta^{\Re_0}$, $\tau_\tau^{\Re_0}$, $\tau_{\xi_1}^{\Re_0}$, $\tau_{\xi_2}^{\Re_0}$, $\tau_{\xi_3}^{\Re_0}$, $\tau_\alpha^{\Re_0}$, $\tau_\mu^{\Re_0}$, $\tau_\gamma^{\Re_0}$

Their sensitivity indices were written in Table 1 as follows.

Based on the described sensitivity indices of the basic reproduction number $\Re_0$ with respect to ten basic parameters is described in Table 1. The results showed that the parameters with a positive sensitivity index increased the value of $\Re_0$ 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 $\Re_0$.

Table 1 Sensitivity indices of parameters

Parameters symbol	Sensitivity index
β	1
ϕ	1
δ	0.23
τ	0.818
ξ_3	0.00003749
ξ_2	0.00001227
ξ_1	-0.00027
α	-0.0183
μ	-0.01204
γ	-0.296

5 Optimal Control Model Formulation

In this section, we apply optimal control strategies on model equations (1). This helps us to reduce the disease in the specified time. The optimal control model is an extension of Syphilis model (1) by including the following two controls defined as;

- u_1 represents prevention effort that helps to reduce contact rate of Syphilis infection,
- u_2 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 (1), we obtain the following state system;

$$\begin{cases} \frac{dS}{dt} = \Pi + R\omega - (1-u_1)(\frac{\beta(I_e(t)+\delta I_l(t)+\gamma T)}{N})S - \mu S, \\ \frac{dE}{dt} = (1-u_1)(\frac{\beta(I_e(t)+\delta I_l(t)+\gamma T)}{N})S - (\phi+\mu)E, \\ \frac{dI_e}{dt} = \phi E - (u_2+\tau)I_e - (\alpha+\mu+\xi_1)I_e, \\ \frac{dI_l}{dt} = \alpha I_e - (u_2+\tau)I_l - (\mu+\xi_2)I_l, \\ \frac{dT}{dt} = (1-u_2)(1-q)\tau I_e + (1-u_2)(1-\chi p\tau)I_l - (\varphi+\mu+\xi_3)T, \\ \frac{dR}{dt} = (u_2+q\tau)I_e + (u_2+\chi p\tau)I_l + \varphi T - (\omega+\mu)R. \end{cases} \tag{11}$$

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 model's objective functional (11) is given as

$$J(u_1, u_2) = \underbrace{\min}_{u_1,u_2} \int_0^{t_f} [M_1E + M_2I_e + M_3I_L + M_4T + \frac{1}{2}(W_1u_1^2 + W_2u_2^2)]dt \tag{12}$$

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 human,

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 . The objective functional (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 a double optimal controls u_1^*, and u_2^*, such that

$$J(u_1^*, u_2^*) = \min J(u_1, u_2) : u_1, u_2 \in \nu \tag{13}$$

where $\nu = (u_1, u_2) : u_i(t)$ 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.

6 Optimal Control Problem Analysis

6.1 Existence of an Optimal Controls

Theorem : Given $J(u)$ subject to system (11) 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 $U = [0,1]^2$, $\upsilon = (u_1, u_2) \in \nu$, $x = (S^*, E^*, I_e^*, I_l^*, T^*, R^*)$ and $f(t, x, \upsilon)$ the right hand side of state system (11), is given by

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

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 (11) has bounded coefficients and hence any solutions are bounded on [0, T].

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, $0 \leq \lambda u_1 + (1 - \lambda)u_2 \leq$, 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 $g(\phi, u) \geq c_1 + c_2|u_1|^\tau + c_3|u_2|$. Thus, the state variables are being bounded. Let $c_1 = \inf_{t\in[0,T]}[M_1E + M_2I_e + M_3I_l + M_4T], c_2 = \frac{w_1}{2}, c_3 = \frac{w_2}{2}$ 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.

6.2 Characterization of an Optimal Control

The optimal control must satisfy the necessary conditions that are formulated by Pontryagin?s minimize Principle. This principle converts the system of equations (11) and (12) into a problem of minimizing point-wise a Hamiltonian (H), with respect to $u_1(t)$, $u_2(t)$ as

$$\begin{cases} H = [M_1E + M_2I_e + M_3I_L + M_4T + \frac{1}{2}(W_1u_1^2 + W_2u_2^2)] \\ +\lambda_1\frac{dS}{dt} + \lambda_2\frac{dI_e}{dt} + \lambda_3\frac{dI_e}{dt} + \lambda_4\frac{dI_l}{dt} + \lambda_5\frac{dT}{dt} + \lambda_6\frac{dR}{dt} \end{cases} \tag{14}$$

It follows that the system of equation (11) and equation (12) are substituted into a minimized Hamiltonian function with respect to u_1, u_2, as given by:

$$\begin{cases} H = [M_1E + M_2I_e + M_3I_L + M_4T + \frac{1}{2}(W_1u_1^2 + W_2u_2^2)] \\ +\lambda_1[\Pi + R\omega - (1 - u_1)(\frac{\beta(I_e(t)+\delta I_l(t)+\gamma T)}{N})S - \mu S] \\ +\lambda_2[(1 - u_1)(\frac{\beta(I_e(t)+\delta I_l(t)+\gamma T)}{N})S - (\phi + \mu)E] \\ +\lambda_3[\phi E - (u_2 + \tau)I_e - (\alpha + \mu + \xi_1)I_e] \\ +\lambda_4[\alpha I_e - (u_2 + \tau)I_l - (\mu + \xi_2)I_l] \\ +\lambda_5[(1 - u_2)(1 - q)\tau I_e + (1 - u_2)(1 - \chi p\tau)I_l - (\varphi + \mu + \xi_3)T] \\ +\lambda_6[(u_2 + q\tau)I_e + (u_2 + \chi p\tau)I_l + \varphi T - (\omega + \mu)R] \end{cases} \tag{15}$$

where λ_1, λ_2, λ_3, λ_4, λ_5 and λ_6 are adjoint variables. Next to obtaining the co-state variables by using Pontryagin?s minimize principle (11) with the existence result, 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 ν subject to equation (1), adjoint variables λ_1, λ_2, λ_3, λ_4,λ_5 and λ_6 are found, holding the adjoint system.

$$\begin{cases} \frac{d\lambda_1}{dt} = -(\lambda_2 - \lambda_1)(1-u_1)(\frac{\beta(I_e(t)+\delta I_l(t)+\gamma T)}{N}) + \mu\lambda_1, \\ \frac{d\lambda_2}{dt} = -M_1 + \phi(\lambda_3 - \lambda_2) + \phi\lambda_2, \\ \frac{d\lambda_3}{dt} = -M_2 - \alpha(\lambda_3 + \lambda_6) + \tau(\lambda_3 - \lambda_4) + \alpha(\lambda_3 - \lambda_4) + (\mu + \xi_1)\lambda_3 + q\tau(\lambda_5 - \lambda_6) \\ -u_2 q\tau\lambda_5 - q\tau\lambda_6 - u_2\tau\lambda_5, \\ \frac{d\lambda_4}{dt} = -M_3 + (u_2 + \tau + \mu + \xi_2)\lambda_4 - (\chi p\tau - u_2 + \chi p\tau u_2)\lambda_5 - u_2\lambda_6 - \chi p\tau\lambda_6, \\ \frac{d\lambda_5}{dt} = -M_4 - \varphi(\lambda_6 - \lambda_5) + (\mu + \xi_3)\lambda_5, \\ \frac{d\lambda_6}{dt} = (\omega + \mu)\lambda_6. \end{cases} \tag{16}$$

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:

$$\begin{cases} u_1^* = \min\{1, \max\{0, \frac{\beta(I_e(t)+\delta I_l(t)+\gamma T)S^*(\lambda_2-\lambda_1)}{w_1 N}\}\}, \\ u_2^* = \min\{1, \max\{0, \frac{\lambda_3 I_e^* + \lambda_4 I_l^* + (1-q)\tau I_e^*\lambda_5 + (1-xp\tau)I_l^*\lambda_5 - 2\lambda_6}{w_2}. \end{cases} \tag{17}$$

Proof: To obtain the form of the co-state equations we compute the derivative of the Hamiltonian function (H), equation (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;

$$\begin{cases} \frac{d\lambda_1}{dt} = -\frac{\partial H}{\partial S} = -(\lambda_2 - \lambda_1)(1-u_1)(\frac{\beta(I_e(t)+\delta I_l(t)+\gamma T)}{N}) + \mu\lambda_1, \\ \frac{d\lambda_2}{dt} = -\frac{\partial H}{\partial E} = -M_1 + \phi(\lambda_3 - \lambda_2) + \phi\lambda_2, \\ \frac{d\lambda_3}{dt} = -\frac{\partial H}{\partial I_e} = -M_2 - \alpha(\lambda_3 + \lambda_6) + \tau(\lambda_3 - \lambda_4) + \alpha(\lambda_3 - \lambda_4) + (\mu + \xi_1)\lambda_3 + q\tau(\lambda_5 - \lambda_6) \\ -u_2 q\tau\lambda_5 - q\tau\lambda_6 - u_2\tau\lambda_5, \\ \frac{d\lambda_4}{dt} = -\frac{\partial H}{\partial I_l} = -M_3 + (u_2 + \tau + \mu + \xi_2)\lambda_4 - (\chi p\tau - u_2 + \chi p\tau u_2)\lambda_5 - u_2\lambda_6 - \chi p\tau\lambda_6, \\ \frac{d\lambda_5}{dt} = -\frac{\partial H}{\partial T} = -M_4 - \varphi(\lambda_6 - \lambda_5) + (\mu + \xi_3)\lambda_5, \\ \frac{d\lambda_6}{dt} = -\frac{\partial H}{\partial R} = (\omega + \mu)\lambda_6, \end{cases} \tag{18}$$

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:

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

Obviously, after derivation of function (H), equation (14), with respect to the controls, the result

becomes:

$$\begin{cases} \frac{\partial H}{u_1} = 0 = w_1 u_1 + \frac{\beta(I_e(t)+\delta I_l(t)+\gamma T)\lambda_1 S}{N} - \frac{\beta(I_e(t)+\delta I_l(t)+\gamma T)\lambda_2 S}{N}, \\ \frac{\partial H}{u_2} = 0 = w_2 u_2 - \lambda_3 I_e - \lambda_4 I_l - (1-q)\tau I_e \lambda_5 - (1-xp\tau) I_l \lambda_5 + 2\lambda_6. \end{cases} \tag{19}$$

Moreover, solving for the control variables from equation (19) we obtain

$$\begin{cases} u_1^* = \min\{1, \max\{0, \frac{\beta(I_e(t)+\delta I_l(t)+\gamma T)S^*(\lambda_2-\lambda_1)}{w_1 N}\}\}, \\ u_2^* = \min\{1, \max\{0, \frac{\lambda_3 I_e^* + \lambda_4 I_l^* + (1-q)\tau I_e^* \lambda_5 + (1-xp\tau) I_l^* \lambda_5 - 2\lambda_6}{w_2}. \end{cases} \tag{20}$$

Rearranging the solution of equation (20) with the boundary condition of each control, we get:

$$\begin{cases} u_1^* = \max\{0, \min\{1, \frac{\beta(I_e(t)+\delta I_l(t)+\gamma T)S^*(\lambda_2-\lambda_1)}{w_1 N}\}\}, \\ u_2^* = \max\{0, \min\{1, \frac{\lambda_3 I_e^* + \lambda_4 I_l^* + (1-q)\tau I_e^* \lambda_5 + (1-xp\tau) I_l^* \lambda_5 - 2\lambda_6}{w_2}. \end{cases} \tag{21}$$

6.3 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 λ_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.

7 Numerical Simulations

In this subsection, numerical simulation study of the autonomous system 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 2 parameters in model and their descriptions in model

Symbols	parameters	Initial values	Reference
Π	Recruitment rate of susceptible	1020	Estimated
β	Contact rate	0.3	Assumed
δ	Rate of increase infectiousness in $I_l(t)$	0.25	Estimated
γ	Rate of decrease infectiousness T	0.25	Assumed
α	Rate of Early stage infected become Late stage infected	0.3	Assumed
τ	Rate of treatment	0.6849	Assumed
q	A fraction of treated from the early stage	0.9	[7]
p	A fraction of the treated in the late stage	0.9	[7]
χ	Modification parameter	0.6849	[7]
ϕ	Rate of Exposed human become Early stage infected	0.9	Assumed
ω	Rate of recovered human become susceptible	0.3	Estimated
μ	Human population natural death rate	0.00548	Estimated
φ	Recovery rate	0.4762	Assumed
ξ_1	Induced death rate of early stage	0.0001	Estimated
ξ_2	Induced death rate of late stage	0.0001	Estimated
ξ_3	Induced death rate of treated	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 2, 3, 4 and 5 shows that an infectious individual goes to zero at the end of the implementation period. Therefore, applying this strategy is effective in eradicating Syphilis form the community in a specified period of time.

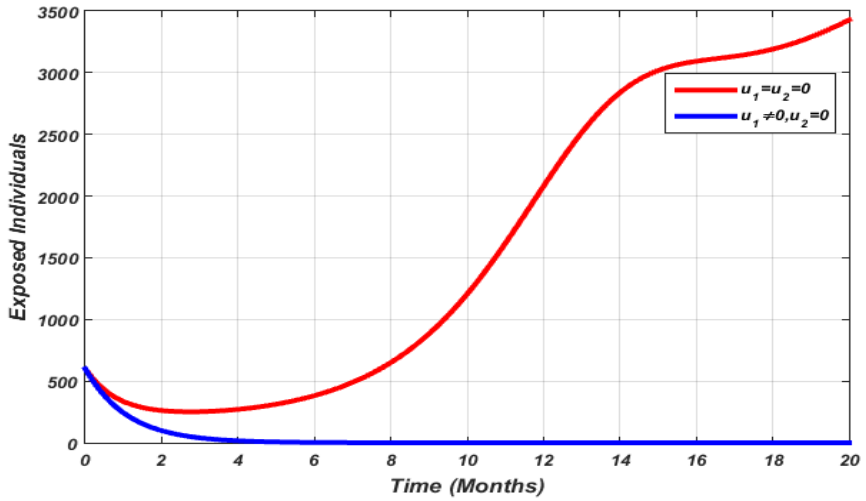

Fig. 2 Dynamics of Syphilis Exposed Individuals

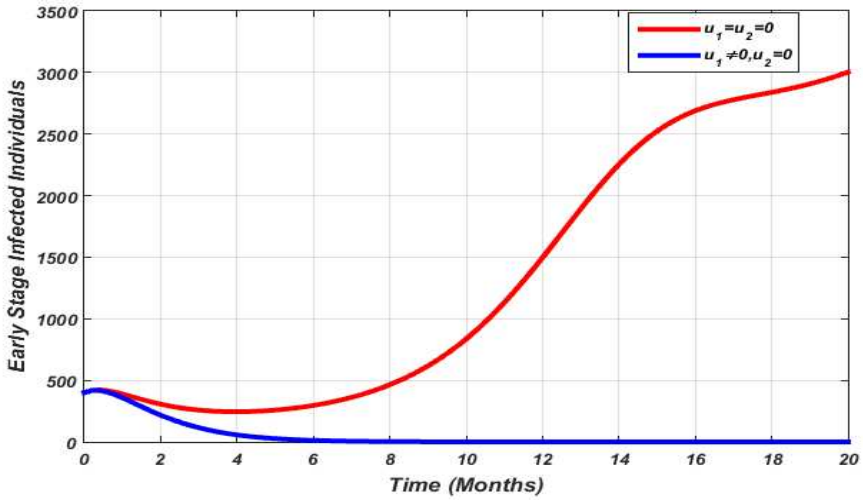

Fig. 3 Dynamics of Early Stage Infected Individuals

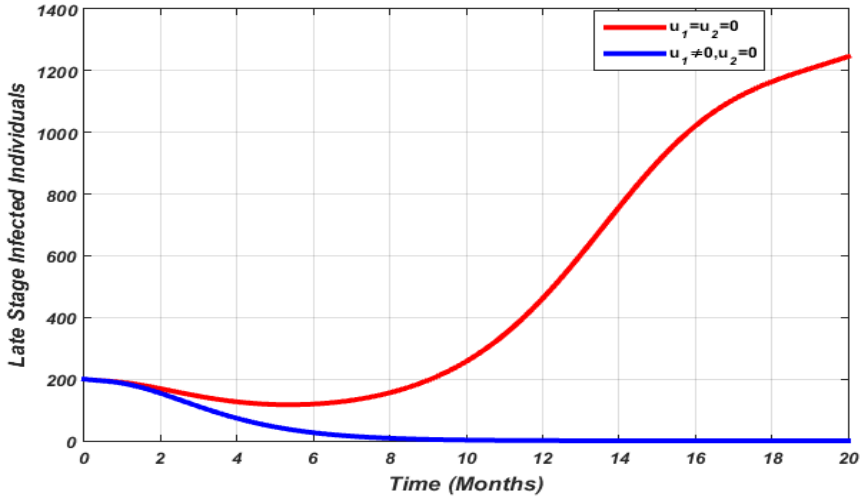

Fig. 4 Dynamics of late Stage Infected Individuals

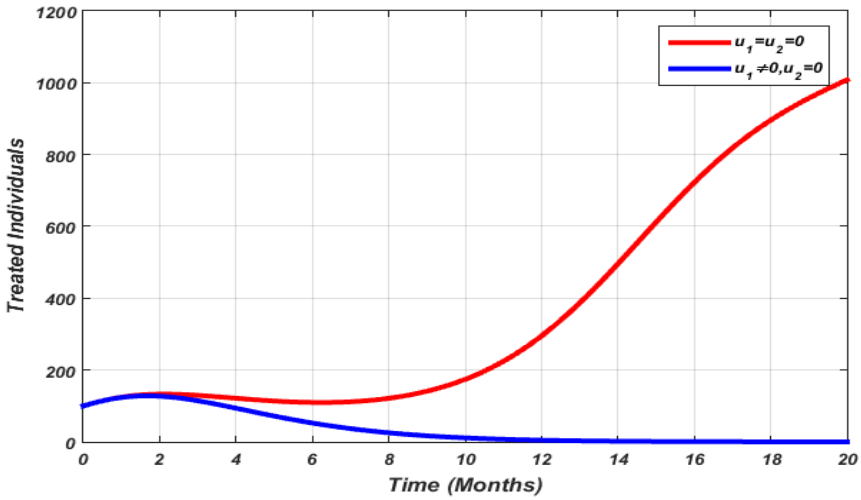

Fig. 5 Dynamics of Treated Individuals

Scenario II: Optimal use of Treatment

We applied treatment only as intervention that is treating individuals who have Syphilis disease infection. Figures 6, 7, 8 and 9 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.

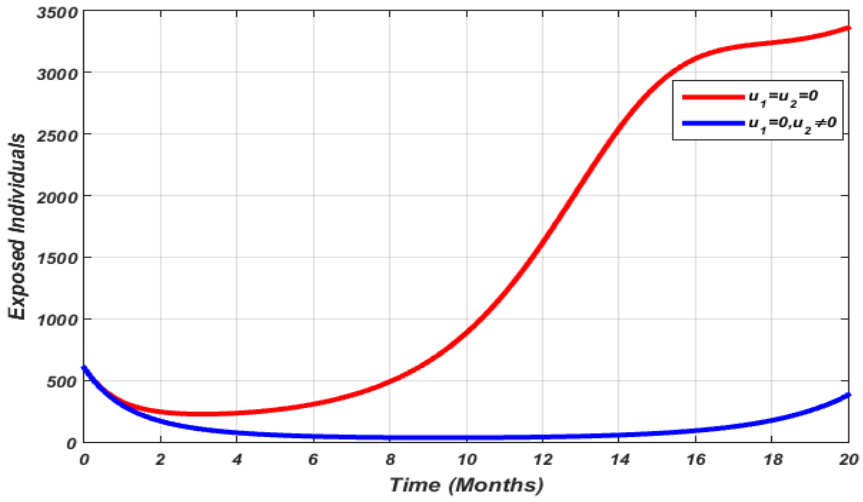

Fig. 6 Dynamics of Syphilis Exposed Individuals

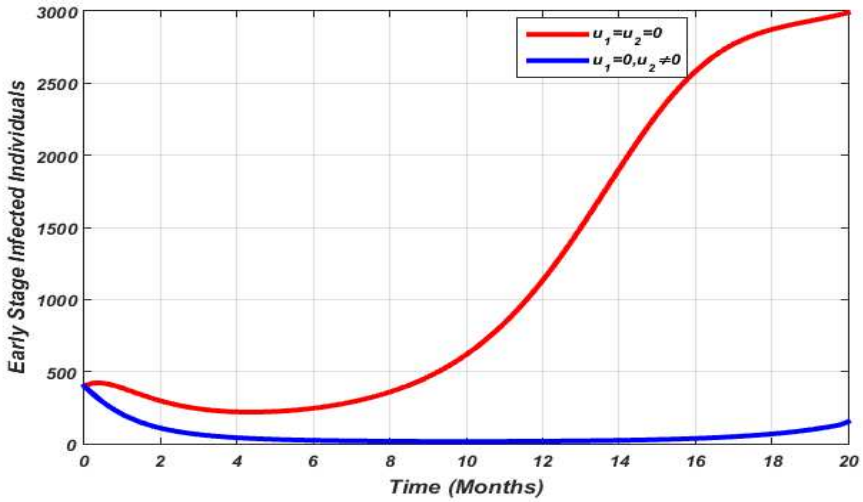

Fig. 7 Dynamics of Early Stage Infected Individuals

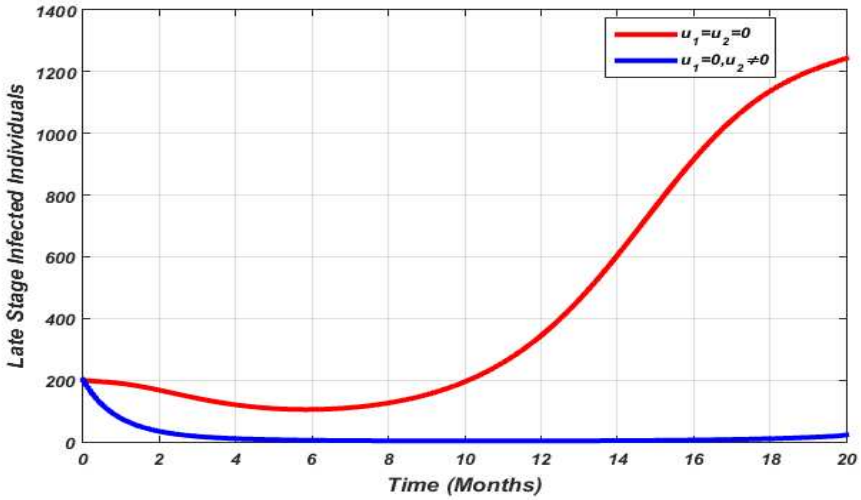

Fig. 8 Dynamics of Late Stage Infected Individuals

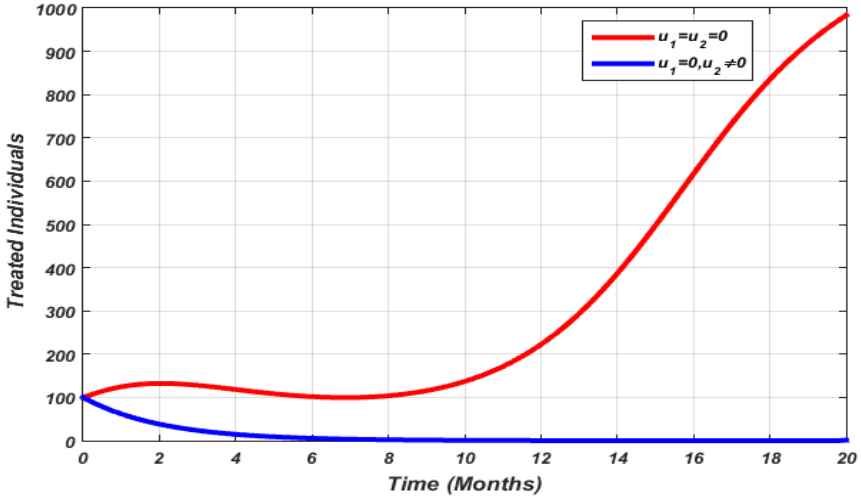

Fig. 9 Dynamics of Treated Individuals

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 10, 11, 12 and 13 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. The control profile for this strategy is described in Figure 14.

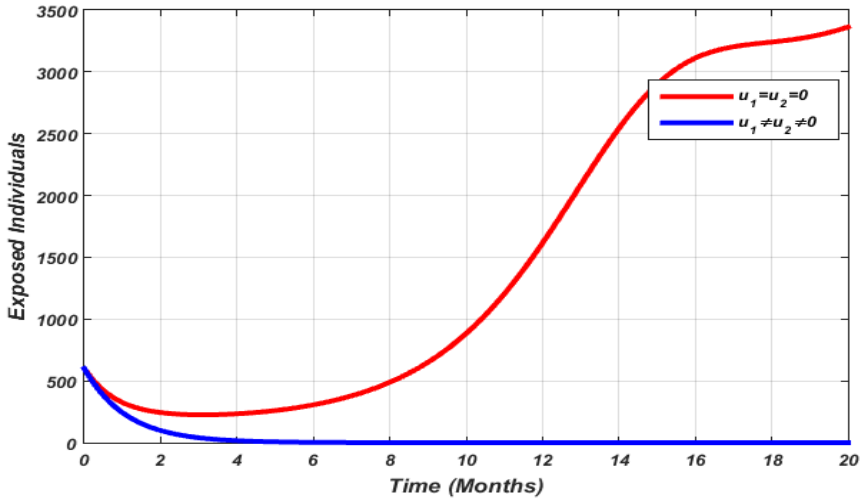

Fig. 10 Dynamics of Syphilis Exposed Individuals

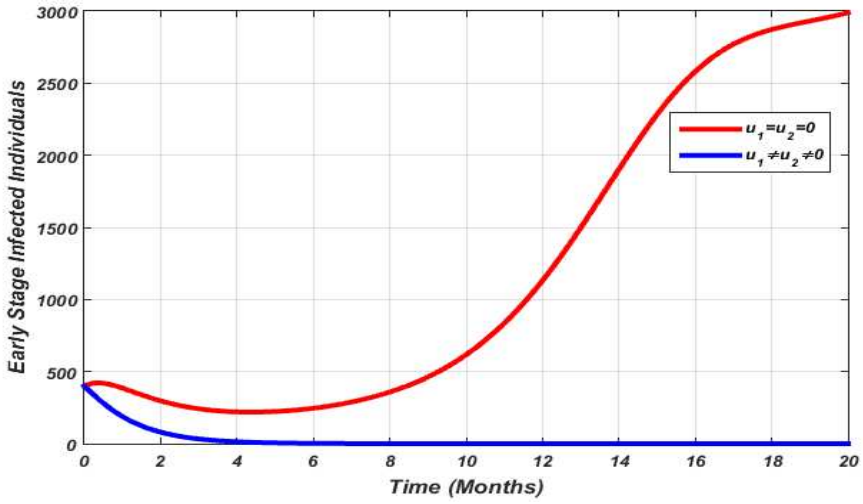

Fig. 11 Dynamics of Early Stage Infected Individuals

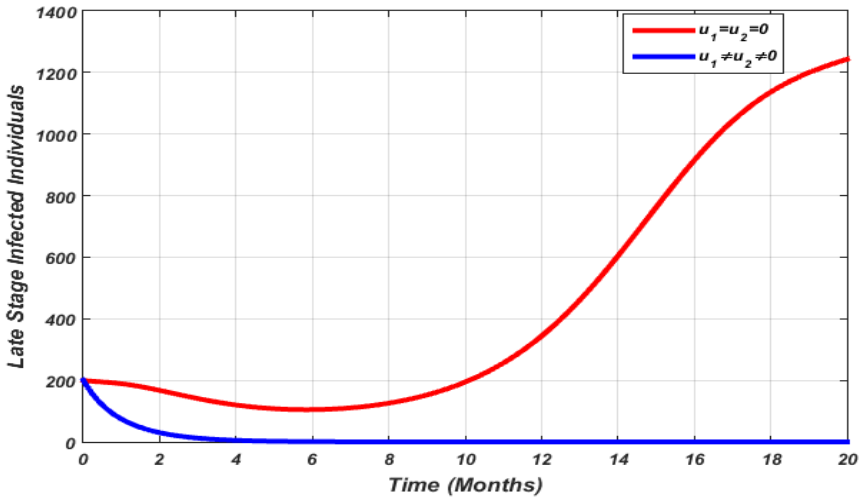

Fig. 12 Dynamics of Late Infected Individuals

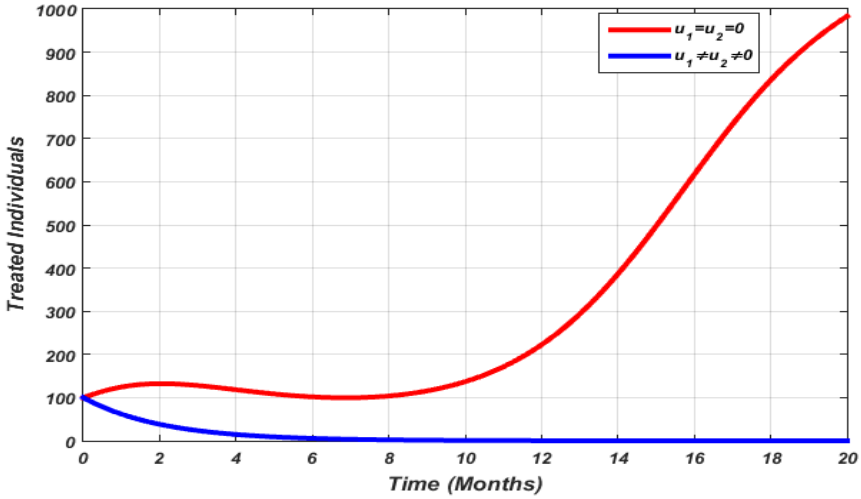

Fig. 13 Dynamics of Treated Individuals

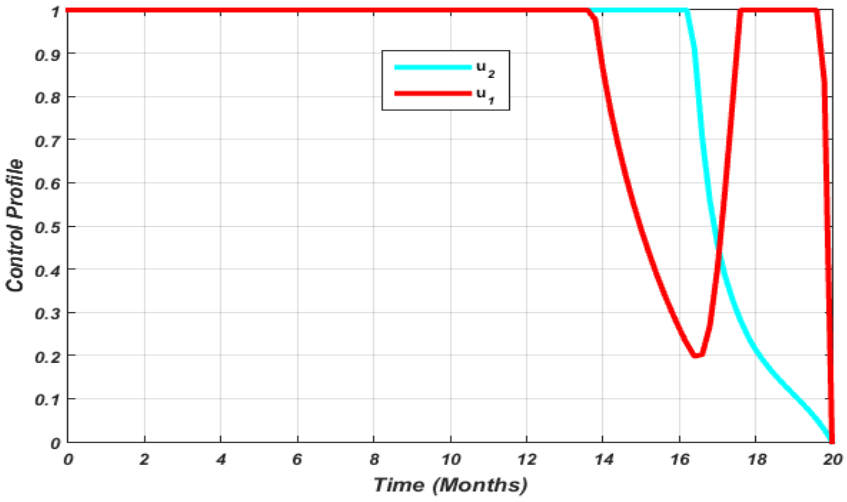

Fig. 14 Control Profile

8 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 II, strategy I, and strategy III 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 3 and 4 of cost-effectiveness analysis.

Table 3 Control strategies in order of increasing averted

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

Table 4 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

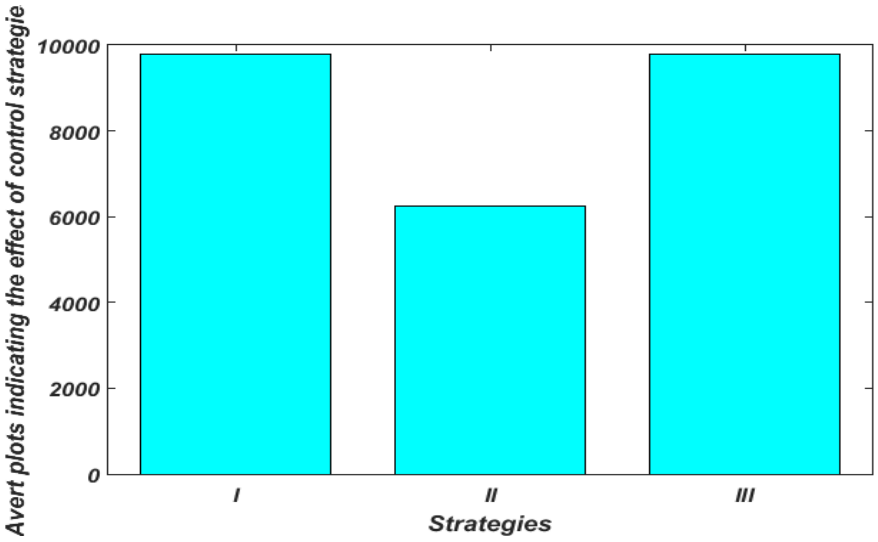

Fig. 15 Total infectious averted plots indicating the effect of control strategies I, II and III

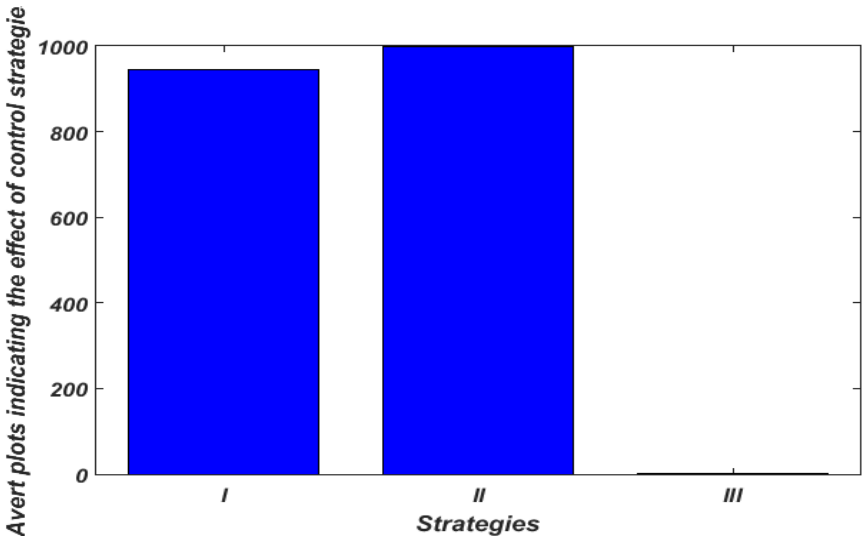

Fig. 16 The total cost plots indicating the effect of control strategies I, II and III

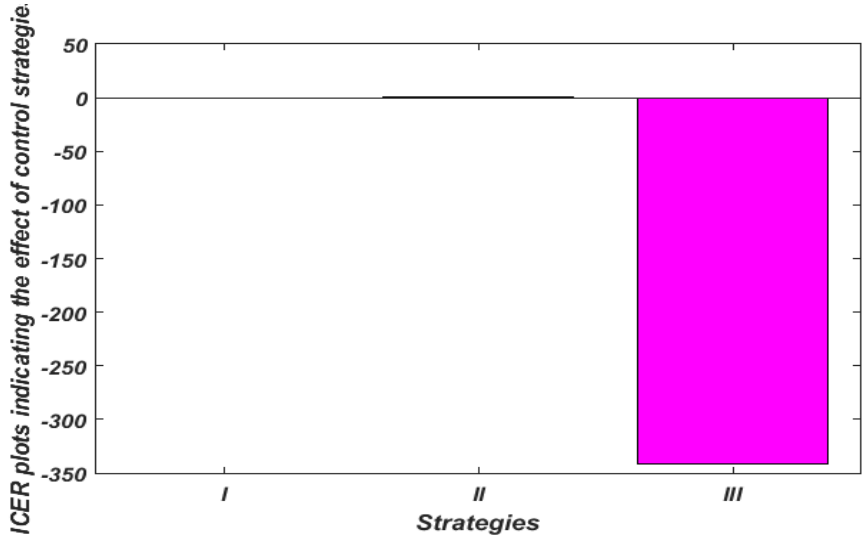

Fig. 17 Incremental cost effective ration (ICER) plots indicating the effect of control strategies I, II and III

From the strategies I and II with their comparison in Table 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 5.

Table 5 Total number of infection averted and total cost with their ICER

Strategies	Total infectious averted	Total cost ($)	ICER
Strategy I	9796.0299	944.5708	0.0964
Strategy III	9798.5031	1.7075	-381.232

In Table 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 figures 15, 16 and 17 for the objective functional for the various control strategies.

9 Conclusion

In this paper, 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.

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