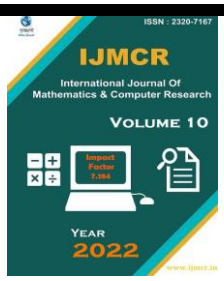
International Journal of Mathematics and Computer Research

ISSN: 2320-7167

Volume 10 Issue 06 June 2022, Page no. – 2716-2721

Index Copernicus ICV: 57.55, Impact Factor: 7.362

DOI: 10.47191/ijmcr/v10i6.03



Optimal Control in Modeling The Dyanmic Transmission of Infectious Disease

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ARTICLE INFO

Published Online:
07 June 2022

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ABSTRACT

This research paper considers the dynamics in epidemic model. Since understanding the mechanism of the spread and the transmission dynamics of a disease, is very crucial in preventing and controlling disease. We describe the mechanisms of disease transmission model of infectious agents. Optimal control theory was used to deduce the optimal strategy aimed at curtailing the spread of syphilis.

KEYWORDS: Optimal Control, Hamiltonian, Stability.

1 INTRODUCTION

Syphilis is a systemic disease from the outset and is caused by the *spirochaete, Treponema pallidum (T. pallidum)*. The infection can be classified as congenital (transmitted from mother to child in utero) or acquired (through sex or blood transfusion). More than 25 infectious organisms are transmitted primarily through sexual activity and studies reveal that sexually transmitted diseases (STDs) are among the many related factors that affect the board continuum of reproductive health [Okonko et al, 2012 & Shafer, M. & Moscicki, A. 2006]. In the 1930s and 1940s, syphilis was perhaps the most prominent public health issue in the U.S., with more federal dollars spent on syphilis than any other infectious disease [Brown, W, 1971]. Acquired syphilis is divided into early and late syphilis. Early syphilis comprises the primary, secondary and early latent stages. Late syphilis refers to late latent syphilis, gummatous, neurological and cardiovascular syphilis. Nowadays early stage of the disease can be easily treated by a single dose of antibiotics such as penicillin or azithromycin.

The first effective treatment (Salvarsan) was developed in 1910 by Paul Ehrlich, which followed by trials of penicillin and confirmation of its effectiveness in 1943. Despite the successful reduction in syphilis in the U.S. and other developed countries over the last half century, the trend appears to have reversed. Infection rates for syphilis are rising in North America, Western Europe and Australia [Fentol, K. et al, 2008]. The sharpest rise has occurred in men who have sex with men (MSM), accounting for over 60% of primary and secondary U.S. syphilis cases in 2004 as compared to only 4% of U.S. cases in 2000. This is an alarming demographic shift given the high-risk sexual behavior and elevated chance for HIV infection among MSM [Chen, S.et al, 2003 & Heffelfinger, J. et al, 2007]. Mathematical Model of (STDs) transmission was developed in 1970s [Yorke, J.A. & Hethcote, H. W., 1973] in response to concern over the dramatic increases in the number of reported gonorrhoea cases in the USA during the 1970s. After their model, researchers developed mathematical models to simulate the spread of a wide range of (STDs) such as syphilis, HIV/AIDS, gonorrhoea, Hepatitis B virus [World Health Organization (WHO), 2006].

Mathematical modelling continues to play a significant role in epidemiology by providing deeper insight into the underlying mechanisms for the spread of emerging and re-emerging infectious diseases and suggesting effective control strategies. Epidemiology modelling has contributed to the design and analysis of epidemiological surveys, suggested crucial data that should be collected, identified trends, made general forecasts, and estimate the uncertainty in forecasts [Hethcote 2000]. Optimal control theory has proven to be a successful tool in understanding ways to curtail the spread of infectious diseases by devising the optimal diseases intervention strategies.

In this paper, we develop a model for the transmission dynamics of syphilis, which is an extension of the existing models of syphilis which includes two susceptible class, two infected classes with complications and treated class inclusive and an optimal control model for syphilis dynamics.

2. MODEL FORMULATION

The model sub-divides the total human population at time t denoted by N(t) into six compartments of susceptible male $S_m(t)$, susceptible female $S_f(t)$, infected male $I_m(t)$, infected female $I_f(t)$, complications C(t) and Treated T(t), where N(t) is given as

$$N(t) = S_m(t) + S_f(t) + I_m(t) + I_f(t) + C(t) + T(t) \quad (1)$$

The susceptible are individuals that have not contracted the infection but may be infected through sexual contacts. The population recruits into the susceptible classes at the rate π_m for susceptible male and π_f for the susceptible female. Infected individuals are those with the infection and can transmit the disease to the susceptible classes during sexual intercourse. α_1, α_2 Represent the rate of movement of susceptible to infected classes. The complications are individuals in the population with the infection at the latent stage that can leads to other diseases or death, the progression rate into the complication class is through β_1, β_2 and r_1, r_2 denote the recovery rate of the infected classes. We assumed that the death rate is not negligible therefore, the natural death rate is represented by μ while the induce disease caused untreated syphilis is represented by v. Treated are people in the population that have recovered due to treatment. The model equation is given as:

$$\begin{aligned}
\frac{dS_m}{dt} &= \pi_m - \alpha_1 I_f S_m - \mu S_m \\
\frac{dS_f}{dt} &= \pi_f - \alpha_2 I_m S_f - \mu S_f \\
\frac{dI_m}{dt} &= \alpha_1 I_f S_m - (r_1 + \beta_1 + \mu) I_m \\
\frac{dI_f}{dt} &= \alpha_2 I_m S_f - (r_2 + \beta_2 + \mu) I_f \\
\frac{dC}{dt} &= \beta_1 I_m + \beta_2 I_f - (v + \mu + \delta) C \\
\frac{dT}{dt} &= r_1 I_m + r_2 I_f + vC - \mu T
\end{aligned} \quad (2)$$

2.1 Basic Properties of the Model

Lemma 1: If $S_m(0) > 0, S_f(0) > 0, I_m(0) > 0, I_f(0) > 0, C(0) > 0,$ and $T(0) > 0$, then the solutions $S_m(t), S_f(t), I_m(t), I_f(t), C(t),$ and $T(t)$ of the system of equations (2) are positive for all $t \geq 0$.

Proof: Under the given initial conditions, it is easy to prove that the solutions of the system of equations (2) are positive; if not, we assume a contradiction that there exists a first time t_1 such that

$$\begin{gathered}
S_m(0) > 0, \quad S_m(t_1) = 0, \quad S'_m(t_1) \leq 0, \\
S_f(t) > 0, \quad I_m(t) > 0, \quad I_f(t) > 0, \\
C(t) > 0, \; T(t) > 0, \quad 0 \leq t \leq t_1
\end{gathered}$$

In that case, from equation (2), we have

$$S'_m(t_1) = \pi_m > 0$$

Which is a contradiction meaning that $S_m(t) > 0, \; t > 0$.

Or there exists a t_2 such that

$$\begin{gathered}
S_f(0) > 0, \quad S_f(t_2) = 0, \quad S'_f(t_2) \leq 0, \\
S_m(t) > 0, \quad I_m(t) > 0, \quad I_f(t) > 0, \\
C(t) > 0, \; T(t) > 0, \quad 0 \leq t \leq t_2
\end{gathered}$$

From equation (2), we have

$$S'_f(t_1) = \pi_f > 0$$

Which is a contradiction meaning that $S_f(t) > 0, \; t > 0$.

Or there exists a t_3 such that

$$\begin{gathered}
I_m(0) > 0, \quad I_m(t_3) = 0, \quad I'_m(t_3) \leq 0, \\
S_m(t) > 0, \quad S_f(t) > 0, \quad I_f(t) > 0, \\
C(t) > 0, \; T(t) > 0, \quad 0 \leq t \leq t_3
\end{gathered}$$

From equation (3), we have

$$I'_m(t_3) = \alpha_1 I_f S_m > 0$$

Which is a contradiction meaning that $I_m(t) > 0, \; t > 0$.

Or there exists a t_4 such that

$$I_f(0) > 0, \quad I_f(t_3) = 0, \quad I'_f(t_3) \leq 0,$$
$$S_m(t) > 0, \quad S_f(t) > 0, \quad I_m(t) > 0,$$
$$C(t) > 0, \ T(t) > 0, \quad 0 \leq t \leq t_4$$

From equation (4), we have

$$I'_f(t_4) = \alpha_2 I_m S_f > 0$$

Which is a contradiction meaning that $I_f(t) > 0, \ t > 0$.

Similarly, it can be shown that $C(t) > 0, \ T(t) > 0$, for all $t \geq 0$. Thus the solutions $S_m(t)$, $S_f(t)$, $I_m(t)$, $I_f(t)$, $C(t)$, $and \ T(t)$ of the system of equations (2) are positive for all ≥ 0.

3. ANALYSIS OF THE MODEL

Disease Free Equilibrium

The Disease free of the syphilis model exists and is given by

$$E_0 = \left(\frac{\pi_m}{\mu}, \ \frac{\pi_f}{\mu}, \ 0, \ 0, \ 0, \ 0\right) \quad (3)$$

In the absence of syphilis, the susceptible male and susceptible female changes in proportion to the ratio of their recruitment rates to the death rate.

Existence of Endemic Equilibrium

Calculating the endemic point, where$I_m \neq 0, \ I_f \neq 0, \ C \neq 0$ we obtain,

$$I^*_f = \frac{\pi_m - \mu S^*_m}{\alpha_1 S^*_m}$$
$$I^*_m = \frac{\pi_f - \mu S^*_f}{\alpha_1 S^*_f}$$
$$C^* = \frac{\alpha_1\beta_1 S^*_m(\pi_f - \mu S^*_f) + \alpha_2\beta_2 S^*_f(\pi_m - \mu S^*_m)}{\alpha_1\alpha_2 S^*_m S^*_f(v + \mu + \delta)}$$
$$T^* = \frac{(v+\mu+\delta)+(K_1+K_2)+K_3+K_4}{\alpha_1\alpha_2 S^*_m S^*_f(v+\mu+\delta)\mu} \quad (4)$$

Where

$$K_1 = \alpha_1 r_1 S_m(\pi_f - \mu S_f)$$
$$K_2 = \alpha_2 r_2 S_f(\pi_m - \mu S_m)$$
$$K_3 = \alpha_1\beta_1 S_m(\pi_f - \mu S_f)$$
$$K_4 = \alpha_2\beta_2 S_f(\pi_m - \mu S_m)$$

4. BASIC REPRODUCTION NUMBER (R_0)

The Basic Reproduction Number which is defined as the average number of secondary infections that occur when one infection is introduced into a complete susceptible host population [Derick, N. & Grossman, S. (1976)]. For this research work the method of next generation matrix was used. It is given by

$$F = \begin{pmatrix} 0 & \alpha_1 S_m & 0 \\ \alpha_2 S_f & 0 & 0 \\ \beta_1 & \beta_2 & 0 \end{pmatrix}$$

$$V = \begin{pmatrix} (r_1+\beta_1+\mu) & 0 & 0 \\ 0 & (r_2+\beta_2+\mu) & 0 \\ 0 & 0 & (v+\mu+\delta) \end{pmatrix}$$

$$R_0 = \rho(FV^{-1}) = \frac{\sqrt{(r_2+\beta_2+\mu)(r_1+\beta_1+\mu)\alpha_1\alpha_2\pi_m\pi_f}}{(r_2+\beta_2+\mu)(r_1+\beta_1+\mu)\mu} \quad (5)$$

5. ANALYSIS OF OPTIMAL CONTROL

We now incorporate time-dependent controls into the model (2) to obtain the following:

$$\frac{dS_m}{dt} = \pi_m - (1-u_1)\,\alpha_1 I_f S_m - \mu S_m + u_2 \emptyset\, I_m$$
$$\frac{dS_f}{dt} = \pi_f - (1-u_1)\alpha_2 I_m S_f - \mu S_f + u_2 \emptyset\, I_f$$
$$\frac{dI_m}{dt} = (1-u_1)\alpha_1 I_f S_m - (r_1 + \beta_1 + \mu + u_2 \emptyset)I_m$$
$$\frac{dI_f}{dt} = (1-u_2)\alpha_2 I_m S_f - (r_2 + \beta_2 + \mu + u_2 \emptyset)I_f$$
$$\frac{dC}{dt} = \beta_1 I_m + \beta_2 I_f - (v + \mu + \delta)\,C$$
$$\frac{dT}{dt} = r_1 I_m + r_2 I_f + vC + \mu T. \qquad (6)$$

where u_1 and u_2 are time dependent controls, $0 \le u_1 \le 1$ is a preventive control measure on the susceptible from becoming infected with the disease (e.g proper education campaign and use of condoms) and the control $0 \le u_2 \le 1$ deals with the effort necessary to curtail the Infection i.e the control on treatment.

To investigate the optimal level of efforts that would be needed to control the disease, we give the objective functional *J*, which is to minimize the number of human infective and the cost of applying the control u_1 , u_2 .

$$J = \max_{u_1,u_2} \int_0^{t_f} a_0 I_m + a_1 I_f + \frac{c{u_1}^2}{2} + \frac{d{u_2}^2}{2}\, dt \qquad (7)$$

With a_0 , a_1 , c , d are positive weights, where we want to minimize the infected groups while also keeping the cost of controls $u_1(t)$ and $u_2(t)$ low. It is generally assumed that the cost of control is usually nonlinear with the quadratic form which is a convex function. The $a_0 I_m$, $a_1 I_f$ represents the cost of infection, while the term $\frac{c{u_1}^2}{2}(t), \frac{d{u_2}^2}{2}(t)$, represents the cost of controls at the time t. The goal is to find an optimal control, ${u_1}^*$, ${u_2}^*$, such that

$$J({u_1}^*, {u_2}^*) = \min_{\Omega_1} J(u_1, u_2) \qquad (8)$$

Where $\Omega_1 = \{u \mid 0 \le u_1, u_2 \le 1, \quad Lebesque\ measurable\}$

The necessary conditions that an optimal must satisfy come from Pontryagin's Maximum Principle [Pontryagin L. S. et al, 1962].

Theorem 2.1 (Pontryagin's Maximum Principle Lenhart and Workman (2007)

If $u^*(t)$ and $x^*(t)$ are optimal for the problem

$$\max_u J[x(t), u(t)]$$

$$\text{Where } J[x(t), u(t)] = \max_u \int_{t_0}^{t_f} f(t,\ x(t),\ u(t))\, dt$$

$$\text{Subject to } \begin{cases} \frac{dx}{dt} = g(t, x(t), u(t)) \\ x(t_0) = x_0 \end{cases},$$

Then there exists a piecewise differentiable adjoint variable $\lambda(t)$ such that

$$H\big(t, x(t), u(t), \lambda(t)\big) \le H\,(t, x^*(t), u^*(t), \lambda(t))$$

For all controls u at each time t, where the Hamiltonian H is given by

$$H\big(t, x(t), u(t), \lambda(t)\big) = f\,\big(t, x(t), u(t)\big) + \lambda(t) g(t, x(t), u(t))$$

And

$$\begin{cases} \lambda'(t) = \dfrac{\partial H((t, x^*(t), u^*(t), \lambda(t))\,)}{\partial x} \\ \lambda(t_f) = 0 \end{cases}$$

While the Pontryagin's Maximum Principle gives the necessary conditions for the existence of an optimal solution. This principle converts (1) into a problem of minimizing pointwise a Hamiltonian H with respect to u_1 and u_2.

$$H = a_0 I_m + a_1 I_f + \frac{c{u_1}^2}{2} + \frac{d{u_2}^2}{2} + \lambda_{S_m}\{\pi_m - (1-u_1)\alpha_1 I_f S_m - \mu S_m + u_2 \emptyset\, I_m\}$$
$$+ \lambda_{S_f}\{\pi_f - (1-u_1)\alpha_2 I_m S_f - \mu S_f + u_2 \emptyset\, I_f\}$$
$$+ \lambda_{I_m}\{(1-u_1)\alpha_1 I_f S_m - (r_1 + \beta_1 + \mu + u_2 \emptyset)I_m\}$$
$$+ \lambda_{I_f}\{(1-u_2)\alpha_2 I_m S_f - (r_2 + \beta_2 + \mu + u_2 \emptyset)I_f\}$$
$$+ \lambda_C\{\beta_1 I_m + \beta_2 I_f - (v + \mu + \delta)C\}$$
$$+ \lambda_T\{r_1 I_m + r_2 I_f + vC - \mu T\}, \qquad (9)$$

Where λ_{S_m}, λ_{S_f}, λ_{I_m},λ_{I_f}, λ_C and λ_T are the adjoint variables or co-state variables. By applying Pontryagin's Maximum Principle and the existence result for the optimal control [Fleming, W. H. et al, 1975], we obtain

Preposition 1. For optimal control pair $u_1{}^*$ and $u_2{}^*$ that minimizes $J(u_1,\ u_2)$ overΩ_1, there exists adjoint varibales λ_{S_m}, λ_{S_f},λ_{I_m},λ_{I_f}, λ_C and λ_T satisfying

$$-\frac{d\lambda_{S_m}}{dt} = \left((1-u_1)\alpha_1 I_f\right)\left(\lambda_{S_m} - \lambda_{I_m}\right) - \mu\,\lambda_{S_m}\ ,$$

$$-\frac{d\lambda_{S_f}}{dt} = \left((1-u_1)\alpha_2 I_m\right)\left(\lambda_{S_f} - \lambda_{I_m}\right) - \mu\,\lambda_{S_f}\ ,$$

$$-\frac{d\lambda_{I_m}}{dt} = -a_0 + \left((1-u_1)\alpha_2 S_f\right)\left(\lambda_{S_f} - \lambda_{I_f}\right) + \left(\lambda_{I_m} - \lambda_{S_m}\right)u_2\,\emptyset + \mu\,\lambda_{I_m} - \beta_1\lambda_C - r_1\lambda_T$$

$$-\frac{d\lambda_{I_f}}{dt} = -a_1 + \left((1-u_1)\alpha_1 S_m\right)\left(\lambda_{S_m} - \lambda_{I_m}\right) + \left(\lambda_{I_f} - \lambda_{S_f}\right)u_2\,\emptyset + \mu\,\lambda_{I_f} - \beta_2\lambda_C - r_2\lambda_T$$

$$-\frac{d\lambda_C}{dt} = \lambda_C(v + \mu + \delta) - v\,\lambda_T$$

$$-\frac{d\lambda_T}{dt} = \mu\,\lambda_T \qquad (10)$$

And with transversality conditions

$$\lambda_{S_m}(t_f) = \lambda_{S_f}(t_f) = \lambda_{I_m}(t_f) = \lambda_{I_f}(t_f) = \lambda_C(t_f) = \lambda_T(t_f),$$

$$u_1{}^* = max\left\{0, min\ \frac{\left(1,\ \alpha_1 I_f S_m{}^*(\lambda_1 - \lambda_3) + \alpha_2 I_m S_f{}^*(\lambda_2 - \lambda_4)\right) + \alpha_2 S_f I_m{}^*(\lambda_2 - \lambda_4) + \alpha_1 S_m I_f{}^*(\lambda_1 - \lambda_3)}{2c}\right\}$$

$$u_2{}^* = max\left\{0, min\ \frac{\left(1,\ \emptyset I_m{}^*(\lambda_3 - \lambda_1) + \emptyset I_f{}^*(\lambda_4 - \lambda_2)\right)}{2d}\right\}$$

Proof: Corollary 4.1 of [Fleming W. H.E, et al, 1975] gives the existence of an optimal control due to the convexity of the integrand of J with respect to u_1, u_2, a priori boundedness of the state solutions, and the Lipschitz property of the state system with respect to the state variables. The differential equations governing the adjoint are obtained by differentiation of Hamiltonian function evaluated at the optimal control.

By standard control arguments involving the bounds on the controls, we conclude

$$u_1{}^* = \begin{cases} 0 & If\ \varphi_1{}^* \le 0 \\ 0 & If\ 0 < \varphi_1{}^* < 1 \\ 1 & If\ \varphi_1{}^* \ge 1 \end{cases}$$

$$u_2{}^* = \begin{cases} 0 & If\ \varphi_2{}^* \le 0 \\ 0 & If\ 0 < \varphi_2{}^* < 1 \\ 1 & If\ \varphi_2{}^* \ge 1 \end{cases}$$

Where

$$\varphi_1{}^* = \left(\frac{\left(1,\ \alpha_1 I_f S_m{}^*(\lambda_1 - \lambda_3) + \alpha_2 I_m S_f{}^*(\lambda_2 - \lambda_4)\right) + \alpha_2 S_f I_m{}^*(\lambda_2 - \lambda_4) + \alpha_1 S_m I_f{}^*(\lambda_1 - \lambda_3)}{c}\right)$$

And

$$\varphi_2{}^* = \left(\frac{\left(1,\ \emptyset I_m{}^*(\lambda_3 - \lambda_1) + \emptyset I_f{}^*(\lambda_4 - \lambda_2)\right)}{d}\right) \qquad (11)$$

Due to the a priori boundedness of the state system, adjoint system, and the resulting Lipschitz structure of the ODEs, we obtain the uniqueness of the optimal control for small t_f. The uniqueness of the optimal control follows from the uniqueness of the optimality system, which consists of (9) and (10), with characterization (11). There is a restriction on the length of the time interval in order to guarantee the uniqueness of the optimality system. This smallness restriction of the length on the time is due to the opposite time orientations of (9) and (10); the state problem has initial values, and the adjoint problem has final values. This restriction is very common in control problems [Lenhart S. & Yong, J. 1995].

6.CONCLUSION

In this paper, a deterministic model for the transmission of syphilis in a heterogeneous setting with complications. We calculated the basic reproduction number and investigated the existence and stability of the disease free equilibrium (DFE) in which the (DFE) is said to be locally asymptotically stable due to $R_0 < 1$ which implies that syphilis will die out of the population, and performed

optimal control analysis of the model. Applying the control, we derived and anlayzed the conditions for optimal control of the disease with effective measures. Adequate control measures which adhered to these controls strategies would be a very effective way to curtail the disease.

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