Optimal Control Applied to Resistance Strategies for the Transmission Dynamics of Syphilis

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Abstract: Although syphilis is a highly treatable disease, its continuing occurrence illustrates that the control efforts still need to be further improved. We incorporate in an epidemiological model for the transmission dynamics of syphilis a control variable to assess the effects of resistance strategies against the disease. The existence of an optimal control for an objective functional that takes into account the number of susceptible and infectious individuals, and the cost of preventive strategies, the characterization of the optimal control, and the uniqueness of the optimality system are proved. The optimality system is solved numerically using the Forward-Backward Sweep method. Numerical simulations show the need to reevaluate the current control programs; the development of an effective vaccine associated with health education could be the best ways to control syphilis in high-risk populations.

Key–Words: Deterministic Model, Forward-Backward Sweep Method, Partial immunity, Pontryagin's Maximum Principle, Resistance, Syphilis.

1 Introduction

Syphilis is a sexually transmitted infection (STI) that can be successfully controlled by public health measures due to the availability of a highly sensitive diagnostic test and a highly effective and affordable treatment and effective prevention measures, such as condoms nevertheless it remains a global problem with an estimated 12 million new cases of syphilis in the world each year. Control of syphilis is vital because of its interactions with HIV. Its continuing occurrence illustrates that the control efforts need to be reevaluated and improved.

Syphilis is caused by the spirochete bacterium Treponema pallidum which enters via abraded skin or intact mucous membrane and distributes via the bloodstream and lymphatics after an incubation period of around 3 weeks (range 2-6 weeks). The primary route of transmission is through sexual contact; however, it may also be transmitted from mother to fetus during pregnancy or at birth, resulting in congenital syphilis which represents a major cause of stillbirth, childhood morbidity, and mortality worldwide.

We consider the modified SIR model of syphilis with suboptimal immunity introduced by Milner and Zhao [3] where we incorporate a control term representing the resistance against the disease, to assess the effects of biological protection consisting of vaccination and behavioral protection consisting of health education in high-risk populations.

2 Optimal Control applied to a Modified SIR Model of Syphilis

We consider the modified SIR model of syphilis with suboptimal immunity introduced by Milner and Zhao [3], which is a special case of a model in [4], where the population under consideration is divided into susceptible (S), infected (I), and recovered and resistant (R) individuals within a "core group" that is very sexually active and which is believed to cause the epidemic. Let $S(t)$, $I(t)$, and $R(t)$ be the fractions of susceptible, infected, and recovered and resistant individuals in the population at time t, respectively. The dynamics of transmission is described by the following system of ODEs :

$$\begin{cases} \frac{dS}{dt} = \mu - \beta IS + p\gamma I - u(t)S - \mu S \\ \frac{dI}{dt} = \beta IS + \sigma\beta IR - \gamma I - \mu I \\ \frac{dR}{dt} = (1-p)\gamma I - \sigma\beta IR + u(t)S - \mu R \end{cases} \quad (1)$$

where β is the transmission parameter, μ is per capita rate of death/birth, and γ is the natural recovery rate (i.e. $1/\gamma$ is the mean infectious period for untreated syphilis). The immunity acquired after treatment is

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temporary. The parameter σ is the factor of reduction of susceptibility for individuals in the class R. It is assumed that the infection with syphilis leads to partial immunity if it progresses to secondary or later stage of infection. Let p be the fraction of primary infections going back to the susceptible pool among all infected individuals. The incorporated control term u into the model represents resistance by vaccination and safe sex activity. The control, u, is bounded, Lebesgue integrable function. Our control problem involves the numbers of susceptible and infectious individuals, and the cost of implementing vaccination and health education strategies. This led us to define the objective functional to be minimized as

$$J(u) = \int_0^{T_f} \left(A\, S(t) + B\, I(t) + \frac{C}{2}\, u^2(t) \right) dt \quad (2)$$

subject to the state system (1) and non negative initial values $S(0)$, $I(0)$, $R(0)$. The coefficients A, B and C are balancing cost factors. The objective is to find an optimal control u^* and the corresponding path such that

$$J(u^*) = \min_{\Omega} J(u) \quad (3)$$

where

$$\Omega = \left\{ u(t) \in L^1(0, T_f),\ a \leq u(t) \leq b,\ 0 \leq t \leq T_f \right\}$$

and a, b are fixed positive constants.

Pontryagin proved that the necessary condition to solve an optimal control problem is to choose a control so as to minimize pointwise the Hamiltonian, $\mathcal{H}$,

$$\mathcal{H} = AS(t) + BI(t) + \frac{C}{2} u^2(t) + \sum_{i=1}^{3} \lambda_i f_i \quad (4)$$

with respect to u (see [1]), where f_i is the right hand side of the differential equation of the $i-th$ state variable and where λ_i $(1 \leq i \leq 3)$ are so-called adjoint variables. The characterization of the optimal control is given in the following theorem.

Theorem 1 *There exists an optimal control variable u^* and corresponding solution, S^*, I^* and R^*, that minimizes $J(u^*)$ over Ω. Furthermore, there exists adjoint functions $\lambda_i(t)$ for $i = 1, ..., 3$ that satisfy*

$$\begin{cases} \frac{d\lambda_1}{dt} = & -A + \lambda_1 \left(\beta I + u(t) + \mu\right) \\ & -\lambda_2 \beta I - \lambda_3 u(t) \\ \frac{d\lambda_2}{dt} = & -B - \lambda_1 \left(-\beta S + p\gamma\right) \\ & -\lambda_2 \left(\beta S + \sigma\beta R - \gamma - \mu\right) \\ & -\lambda_3 \left[(1-p)\gamma - \sigma\beta R\right] \\ \frac{d\lambda_3}{dt} = & -\lambda_2 \sigma\beta I + \lambda_3 \left(\sigma\beta I + \mu\right) \end{cases} \quad (5)$$

with transversality conditions $\lambda_i(T_f) = 0$, for $i = 1, 2, 3$. Furthermore the characterization of the optimal control holds

$$u^*(t) = \min\left(\max\left(a, \frac{1}{C} \left(\lambda_1 - \lambda_3\right) S \right), b \right) \quad (6)$$

Incorporating the representation of the optimal control, we obtain the state system coupled with the adjoint system which characterizes the optimal control, and is called the optimality system. The uniqueness of the optimal control follows from the uniqueness of the optimality system for small T_f.

3 Conclusion

The simulations were carried out using the following biological feasible parameter values taken from Breban et al. [2] : $\beta = 9.045$, $\gamma = 6$, $\mu = 0.03$ for which the basic reproduction is greater than one and therefore the disease is not expected to die out without intervention strategies. As the factor of reduction of susceptibility for individuals in the recovered class, σ, and the infection acquired immunity uptake, $1 - p$, affect the model without control, it is therefore crucial to investigate how the optimal control depends on these parameters. Thus we used several values for σ and p. We set the initial values $S(0) = 0.66667$; $I(0) = 0.00707$; $R(0) = 0.32626$ for a total population size $N = 10^5$ [2]. The cost associated with u will include the cost of vaccination and treatment and education; we took the weight factor $A = 10$, $B = 1$, and $C = \frac{1}{2}$. We chose the upper bound b equal to 0.95 and the lower bound a equal to 0.05.

Figure 1 and Figure 2 show the outcome of the model for susceptible, infectious, and recovered individuals with and without control, the control is plotted as a function of time and this is done for different values of p and σ.

Figure 1 shows the outcome of the model for susceptible, infectious, and recovered individuals when the optimal resistance strategy is applied (solid curve) and when only treatment is applied (dashed curve) for $\sigma = 0.6333$ and $p = 0.232$. We observe that the total number of infectious individuals at final time $T_f = 10$ is $I_{10} = 481$ with optimal control and $I_{10} = 6250$ without optimal control, thus the total number of infectious prevented after 10 years of application of the resistance strategy is 5769. The number of individuals in the resistance class increases to $R_{10} = 93670$ and the number of susceptible individuals decreases to $S_{10} = 5849$ with optimal control while without control $R_{10} = 74260$ and $S_{10} = 19490$. In the same figure the control is plotted as a function of time.

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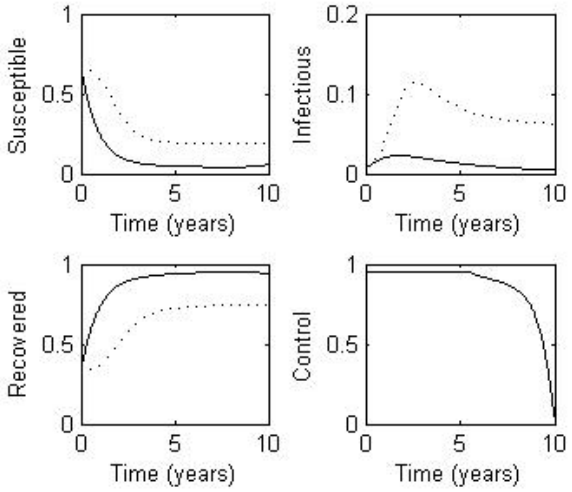

Figure 1: The outcome of the model for suceptible, infectious, and recovered individuals when the optimal resistance strategy is applied (solid curve) and when only treatment is applied (dashed curve) for $\sigma = 0.6333$ and $p = 0.232$.

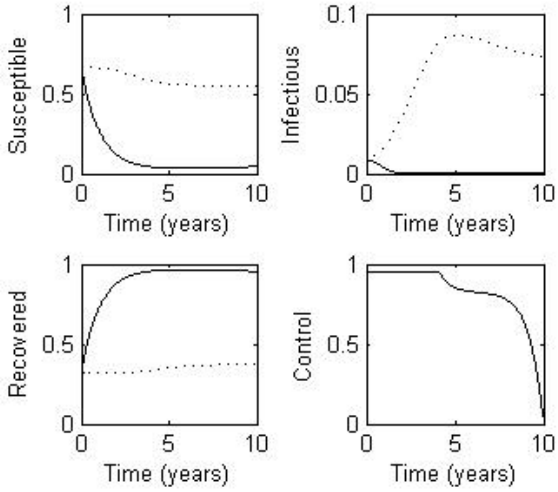

Figure 2: The outcome of the model for suceptible, infectious, and recovered individuals when the optimal resistance strategy is applied (solid curve) and when only treatment is applied (dashed curve) for $\sigma = 0.3$ and $p = 0.8$

Numerical simulations show that vaccination associated with health education could be the best ways to control syphilis epidemic.

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