Optimal Isolation Control Strategy of a Tuberculosis Model

Schehrazad SELMANE
LAID3. Faculty of Mathematics, University of Science and Technology of Algiers. Algeria.

1. Introduction

Tuberculosis (TB), in spite of the fact that is a preventable and curable disease, is still and will remain a problem of public health world for several decades during the 3rd millennium. According to the World Health Organization a third of the world population is currently infected; 5 to 10% of the infected individuals (not infected by HIV) develop the disease. Only less than half of new annual cases are officially declared, causing 1.7 million deaths yearly. The majority of the new cases are in the populated area of Asia. The growth remains very strong in Africa with a significant proportion of seropositivity HIV. The economic decline and the increase in precariousness are recognized causes of the increase in the number of cases [4].

In order to minimize the transmission of the disease, we consider optimal control strategy associated with isolation of infectious individuals.

2. Tuberculosis Model

The model we consider monitors the dynamics of four sub-populations, namely susceptible $S(t)$, latently infected $L(t)$, infectious $I(t)$, and treated $R(t)$ individuals. We assume that the population is homogeneous mixed, and all people are equally likely to be infected by the infectious individuals in a case of adequate contact. We assume that the total population size $N(t) = S(t) + L(t) + I(t) + T(t)$ is constant and individuals are recruited into the population either by birth or immigration at rate $\Lambda = \mu N$ where the natural death rate, μ, in each class is assumed to be positive. Susceptible individuals can be infected only through contact with individuals having smear positive pulmonary TB disease; a proportion p degenerates into infectious class whereas the remaining proportion degenerates into latent infection class. The latently infected individuals progress to infectious class at rate α. All detected infectious individuals receive treatment at rate τ. The patients whose cases are not detected either die or self cure at rate e. An intervention to keep TB under control and to reduce the incidence, in addition to the prompt detection and treatment of active TB cases, may consist on identification and isolation of smear positive pulmonary TB individuals till they become smear negative, and isolation of treatment failure cases and drugs resistant cases. A control function, $u(t)$, is incorporated into the model, it represents the effort on isolation of of infectious, treatment failure, and drugs resistant TB patients to break the transmission of the disease.The interactions of the four compartments under the assumed assumptions is specified by the following system (I) :

$$\begin{cases} \overset{\bullet}{S} = \Lambda - \beta \frac{I}{N} S - \mu S \\ \overset{\bullet}{L} = (1-p)\beta \frac{I}{N} S - (\alpha + \mu) L \\ \overset{\bullet}{I} = p\beta \frac{I}{N} S + \alpha L - (e + u(t)\tau + \mu) I \\ \overset{\bullet}{R} = (e + u(t)\tau) I - \mu R \end{cases}$$

where $S(0)$, $L(0)$, $I(0)$, $R(0)$ are given and the control function, u, is bounded, Lebesgue integrable function. Our control problem involves the numbers of infectious individuals, and the cost for applying isolation strategy. This lead us to define the objective functional to be minimized as

$$J(u) = \int_0^{T_f} \left(A\ I(t) + \frac{B}{2}\ u^2(t) \right) dt \qquad (1)$$

subject to the state system (**??**). The coefficients, A, B are balancing cost factors due to size and importance of the two parts of (1). We require $B > 0$ so that this is a minimization problem. The objective is to find an optimal control u^* and the corresponding path such that

$$J(u^*) = \min_{\Omega} J(u) \qquad (2)$$

where $\Omega = \left\{ u(t) \in L^1(0, T_f) : a \le u(t) \le b,\ 0 \le t \le T_f \right\}$ and a, b are fixed positive constants.

3. Analysis of the Optimal Control

Pontryagin proved that a necessary condition for solving an optimal control problem is to chose a control so that to minimize pointwise a Hamiltonian, $\mathcal{H}$,

$$\mathcal{H} = A\ I(t) + \frac{B}{2}\ u^2(t) + \sum_{i=1}^{4} \lambda_i f_i \qquad (3)$$

with respect to u [2], where f_i is the right hand side of the differential equation (I) of the $i-th$ state variable, and where λ_i $(1 \leq i \leq 4)$ are so-called adjoint variables.

The control space Ω is convex and closed by definition and the state system with respect to the state variables is uniformly Lipschitz continuous, and the integrand in the functional (1); $A\ I(t) + \frac{B}{2}\ u^2(t)$ is convex on the control $u(t)$, and there exists a constant $\nu > 1$, and positive numbers ξ_1 and ξ_2 such that $J(u) \geq \xi_2 + \xi_1 \|u\|^2$. So there exists an optimal control function u^* satisfying (2).

Theorem 1 *Given an optimal control variable u^* and solutions of the corresponding state system for the optimal control problem (I) and (1), there exist adjoint variables λ_i for $i = 1, ..., 4$ that satisfy*

$$\begin{aligned}
\frac{d\lambda_1}{dt} &= \lambda_1 \left(\beta \frac{I}{N} + \mu\right) - \lambda_2(1-p)\beta\frac{I}{N} - \lambda_3 p\beta\frac{I}{N} \\
\frac{d\lambda_2}{dt} &= \lambda_2\left(\alpha + \mu\right) - \lambda_3\alpha \\
\frac{d\lambda_3}{dt} &= -A\ + \lambda_1\beta\frac{S}{N} - \lambda_2(1-p)\beta\frac{S}{N} \\
&\quad -\lambda_3\left[p\beta\frac{S}{N} - (e + u(t)\tau + \mu)\right] \\
&\quad -\lambda_4\left(e + u(t)\tau\right) \\
\frac{d\lambda_4}{dt} &= \lambda_4\mu \qquad (4)
\end{aligned}$$

with transversality conditions

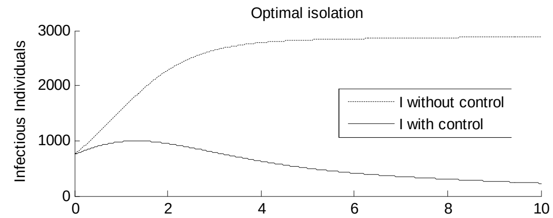
$$\lambda_i(T_f) = 0, \qquad i = 1, ..., 4$$

Furthermore the following characterization (called the characterization of the optimal control) holds

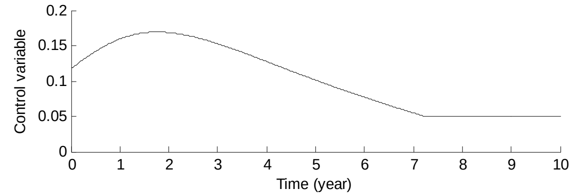
$$u^*(t) = \min\left(\max\left(a, \frac{1}{B}\left(\lambda_3 - \lambda_4\right)\tau I\right), b\right).$$

4. Numerical Illustrations and Conclusions

The state system coupled with the adjoint system, called the optimality system, is solved numerically using the Forward-Backward Sweep method [2]. In order to illustrate the theoretical results, we chose the following set of biologically-feasible parameters



The plot represents the population of infectious individuals I both with control and without control.



The control u is plotted as a function of time

[3] : $\mu = 1/70$, $p = 0.11$, $\alpha = 0.000113$, $e = 0.2$, $\tau = 0.63$, $\beta = 13$, $(a, b) = (0.05, 0.95)$, $A = 1$, $B = 1$, $N = 30000$, $S(0) = (76/120)\,N$, $L(0) = (40/120)\,N$, $I(0) = (3/120)\,N$, $R(0) = (1/120)\,N$, where year is used as the unit of time.

We observe in the above figure, that the total number of infectious individuals at time $T_f = 10$ years, is $I_{T_f} = 229.6$ with optimal isolation (u), while $I_{T_f} = 2889$ without control. In conclusion, control program that follow this strategy can effectively reduce the population of actively infected TB cases.

References

[1] Castillo-Chavez, C., Dynamical models of Tuberculosis and their applications, Mathematical biosciences and engineering. Vol. 1 (2004) 361-404.

[2] Lenhart, S.,Workman, J.T., Optimal control applied to biological models. Chapman&Hall/CRC, London, UK. 2007.

[3] E. Vynnycky, P.E.M. Fine, The natural history of tuberculosis : the implications of age-dependent risks of disease and the role of reinfection. Epidemiol. Infect. 119 (1997) 183–201.

[4] World Health Organization report 2008. WHO/HTM/TB/2008.393.