Optimal Control of Exogenous Reinfection Prevention and Treatment on a Tuberculosis Model

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Abstract: We apply optimal control for a system of ordinary differential equations in modelling tuberculosis disease with exogenous reinfection. Reducing the contact between exposed and infectious tuberculosis people and increasing the population of the medication compartment can be done to overcome the spreading of tuberculosis disease. We use control strategy of the tuberculosis disease to represent the prevention of exogenous reinfection and optimal treatment. Using Pontryagin's maximum principle, we have discussed optimal control of the tuberculosis disease. We use Forward-Backward Sweep Method to gain optimal system numerically. Numerical results show that the performance of 2-control model is highly effective for reducing the number of infected individuals in the Tuberculosis model by considering the simulation results from Susceptible, Exposed, Infectious and Treated population satisfying from each expected condition.

1 INTRODUCTION

Tuberculosis (TBC) is a disease caused by bacteria and one-third of the human population becomes infected with TBC. Of all patients (TB), there are only 10% of the active patients (Bloom, 1993) (Miller, 1993). Most individuals are considered capable for increasing the immune response to bacteria in their body because the individual has been an active TB patient. In other words, the body will adjust immune to the previous condition so that it will not be infected again (Feng, Capurro and Castillo, 2000). On the other hand, individuals who are infected with latent clinical infection will be able to transmit TB. Infected individuals may remain in this latent stage for long and uncertain periods, but the reality in the field shows that many individuals die without having to suffer active TB (Miller, 1993).

Most people who previously have been infected have a declining immune capability when they are old, and they may also be at risk of developing active TB in two ways: exogenous reinfection (acquiring new infections from other infections) or endogenous latent bacilli reactivity (reactivation of inactive and pre-existing infection) (Styblo, 1991 (Smith, 1994). In the disease spreading, exogenous reinfection plays a key role in the transmission of tuberculosis in areas with the highest incidence, especially in Africa (where HIV cases are very high) and in developed countries.

Prevention on individuals infected with inactive tuberculosis disease may be performed with chemoprophylaxis by administering Isoniazid Anti-tuberculosis Drugs. In order to cope with individuals who are already infected with active tuberculosis, WHO has recommended to administer anti-tuberculosis drugs that are isoniazid, rifampicin, pyrazinamide, ethambutol, and streptomycin throughout health care units in the world (Crofton, Horne and Miller, 2002).

Zhilan Feng, Carlos Castillo-Chavez and Angel F. Capurro have incorporated exogenous reinfection into the epidemiological model for the dynamics of tuberculosis transmission and have addressed the

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control of this disease by looking at the transmission parameter role of the disease at the reduction of R 0 and the prevalence of disease (Feng, Capurro and Castillo, 2000).

In this paper, we add into the model two optimal controls related to the prevention of reinfection to see the effect of the exogenous reinfection to become as minimal as possible and the optimal treatment control within efforts to reduce the number of infected compartment individuals and increase the number of individual treatment compartments.

2 MODEL OF TUBERCULOSIS DEVELOPMENT

In this section, we describe the model of *Tuberculosis* with reinfection exogenous, consisting of four population groups namely *susceptible S(t)*, *exposed E(t)*, *infectious I(t)*, and *treated T(t)*. *Susceptible S(t)* is a healthy human population but likely to be infected TB bacteria, *exposed E(t)* is a population of infected humans but the symptoms of the disease are still not seen, *infectious I(t)* is an infected human population in which the symptoms of the disease is already visible and can transmit to other susceptible individuals and *treated T(t)* is the population of the human being who is being treated or in the healing period. We assume that individuals infected with TB bacteria are only individuals who are in contact with other infected individuals.

The model of the spread of TB disease can be expressed as a system of nonlinear differential equations as follows:

$$\frac{dS}{dt} = \Lambda - \mu S - \beta c S \frac{I}{N} \quad (1)$$

$$\frac{dE}{dt} = \beta c S \frac{I}{N} - \rho \beta c E \frac{I}{N} - (\mu + k)E + \sigma \beta c T \frac{I}{N} \quad (2)$$

$$\frac{dI}{dt} = \rho \beta c E \frac{I}{N} + kE - (\mu + d + r)I \quad (3)$$

$$\frac{dT}{dt} = rI - \mu T - \sigma \beta c T \frac{I}{N} \quad (4)$$

with the addition of control variables $u\,(t)$ and $u_1\,(t)$, $(1 - u\,(t))$ represents a preventive attempt against exogenous reinfection and $(1 + u1\,(t))$ is the treatment effort against the individual infections (Hattaf, Rachik, Saadi, Tabit and Yousfi, 2009) (Nainggolan, 2017), the new model is as follows:

$$\frac{dS}{dt} = \Lambda - \mu S - \beta c S \frac{I}{N} \quad (5)$$

$$\frac{dE}{dt} = \beta c S \frac{I}{N} - \rho \beta c (1-u) E \frac{I}{N} - (\mu + k)E + \sigma \beta c T \frac{I}{N} \quad (6)$$

$$\frac{dI}{dt} = \rho \beta c (1-u) E \frac{I}{N} + kE - (\mu + d + r)I \quad (7)$$

$$\frac{dT}{dt} = r(r + u_1)I - \mu T - \sigma \beta c T \frac{I}{N} \quad (8)$$

The initial conditions of the above equation system are given by:

$$S(0) = S_0, E(0) = E_0, I(0) = I_0, T(0) = T_0$$

The parameters used in the TB model in this paper can be seen in the table below (Hattaf, Rachik, Saadi, Tabit and Yousfi, 2009):

Table 1: This caption has one line so it is centered.

Parameter	Definition and value
Λ	Birth, 192
μ	Dead, 0.016
d	Death due to Tb, 0.1
β	Average number of unexpected individuals, 13
$\sigma\beta, 0 \leq \sigma \leq 1$	The average number of individuals treated for infection, 0.9
c	Human interaction, 1
k	Progress is Infected, 0.005
r	Treatment, 2
N	Total population, 12000
ρ	Exogenously Infected level, 0,4

2.1 Prevention Control of Reinfection and Optimal Treatment on Tuberculosis Transmission

The objective function J relating to the problem of this equation is to reduce the number of *I (t)* or actively infected individuals, so it is obtained:

$$\mathcal{J}(u_1, u_2) = \int_0^{tf} [I(t) + Au^2(t) + Bu_1^2(t)]dt \quad (9)$$

This problem is solved by minimizing (9). In this discussion, the numerical approach *Forward Backward Sweep Method* is used. The procedure of completion is further described as follows.

Step 1: Form the Hamiltonian function to get the optimal solution (Workman and Lenhart, 2007) (Subchan and Zbikowski, 2009)

$$H = I(t) + Au^2(t) + Bu_1^2(t) + \lambda_1 \left(\Lambda - \mu S - \beta c S \frac{I}{N}\right) + \lambda_2 \left(\beta c S \frac{I}{N} - \rho \beta c (1-u) E \frac{I}{N} - (\mu + k)E + \sigma \beta c T \frac{I}{N}\right) +$$

$$\lambda_3\left(\rho\beta c(1-u)E\frac{I}{N}+kE-(\mu+d+r(1+u_1))I\right)+$$
$$\lambda_4\left(r(1+u_1)I-\mu T-\sigma\beta cT\frac{I}{N}\right) \quad (10)$$

Step 2: Find that $u\,(t)$ and $u_1\,(t)$ that are optimal. Using $\left(\frac{\partial H}{\partial u}\right)=0$, we get

$$0=2Au+\rho\beta cE\frac{I}{N}\lambda_2-\rho\beta cE\frac{I}{N}\lambda_3$$
$$2Au=\left(\rho\beta cE\frac{I}{N}\right)(\lambda_3-\lambda_2)$$
$$u^*=\frac{I}{2AN}\left(\rho\beta cE\frac{I}{N}\right)(\lambda_2-\lambda_3) \quad (11)$$

Step 3: Determine the costate of H that is not yet optimal.

$$0=2Bu_1-rI\lambda_1+rI\lambda_4$$
$$Bu_1=rI(\lambda_1-\lambda_4)$$
$$u_1^*=\frac{1}{2B}rI(\lambda_1-\lambda_4) \quad (12)$$

with the *boundary conditions*

$$S(0)=S_0,E(0)=E_0,I(0)=I_0,T(0)=T_0$$
$$\dot{\lambda}_1=-\left(\frac{\partial H}{\partial S}\right)=0,\lambda_1(tf)=0$$
$$\dot{\lambda}_2=-\left(\frac{\partial H}{\partial E}\right)=0,\lambda_2(tf)=0$$
$$\dot{\lambda}_3=-\left(\frac{\partial H}{\partial I}\right)=0,\lambda_3(tf)=0$$
$$\dot{\lambda}_4=-\left(\frac{\partial H}{\partial T}\right)=0,\lambda_4(tf)=0$$

3 RESULTS AND ANALYSIS

In this chapter, we discussed the simulation of the Tuberculosis model using the Forward-Backward Sweep Method numerical approach to see how the effect of one-control administration on exogenous reprevention and 2-control administration on exogenous reprevention and treatment.

The simulation results in the untreated TB model. The TB model given 1 control and the TB model given 2 controls using matlab software can be seen as follows and after the simulation process was done using MATLAB software, the result of comparison of the TB model without controls and TB model with the controls (controlling individual contact against infectious and controlling the treatment) can be seen as follows:

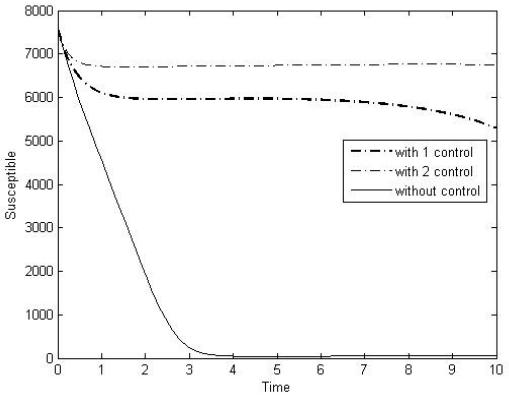

Figure 1: Suscebtible $S(t)$

From Figure 1, it is clear that with the use of 1 control on model, the population of susceptible increased. This is because the contact between the susceptible population and Exposed population was safer, since the exposed population decreased and minimized the chance of Susceptible to be infected or reinfected from the Exposed population. The use of 2 controls further increased the susceptible population. Because of the same reason, Exposed population was diminishing. The treatment subjects were controlled in infectious populations.

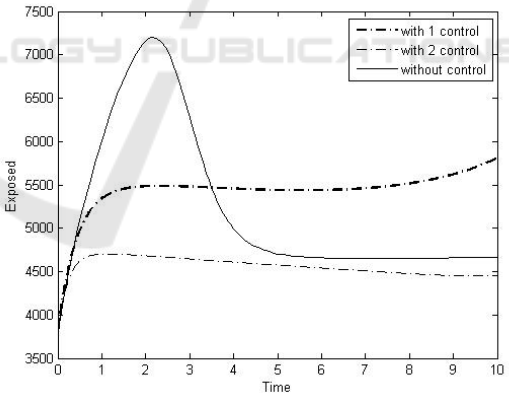

Figure 2: Exposed $E(t)$

From Figure 2, it is seen that with the use of 1 control on the model, the population of Exposed decreased, it caused the decrease of frequency contact between the Exposed population and the Infectious population, so the Exposed population could get healthy again and move on to the susceptible population. However, in Figure 2, it is clear that by using 1 control, initially, the Exposed population decreased over a period of time (approximately at 3 to 4) and increased again and

became more than the uncontrolled model. It is contrast to the inclusion of 2 controls on the model so that it looked better and stable with fewer populations than uncontrolled models and models with 1 control. In other words, the addition of medication control successfully suppressed the growing Infectious population and infecting Exposed population.

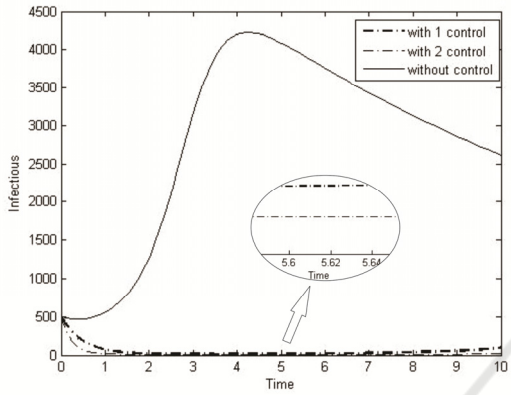

Figure 3: Infectious $I(t)$

From Figure 3, it can be seen that with 1 control in the reduction of the frequency of contacts in the model, the Infectious population tended to decrease, but at certain intervals, at t=9 from Figure 3, the Infectious population would increase again. It was different with the model subjected to 2 controls. The addition of optimal treatment control was faster to reduce Infectious populations. The results were better than models with 1 control and without control because Infectious stable populations did not increase again.

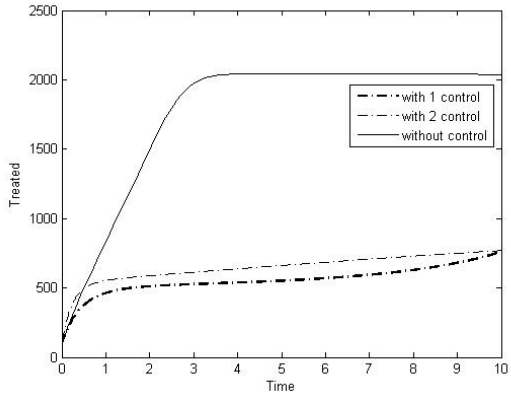

Figure 4: Treated $R(t)$

Figure 4 shows the same thing that with the implementation of 1 control on the model, the Treated population decreased, illustrating that many individuals have returned to good health after receiving treatment, but the decrease was temporary because the Treated population increased again sometimes. We see in the model subjected 2 controls, at first, it appears that Treated population number was more than Treated population number in the model with 1 control. It does not mean a model with 1 control was better because in the end, the model with 2 controls had fewer populations than the model with 1 control and without control. At the beginning of time, the model with 2 controls had more population than the model with 1 control due to the addition of medication controls to the Infectious population so that infectious populations were treated and the Treated population increased. Thus, the Treated population would decrease optimally because the Infectious population also decreased significantly.

4 CONCLUSIONS

From the exposure of the model of TB disease that has been given 1 control in the form of reduction of contact with the infectious individual population, then it can be drawn outline that the controls were applied well. However, there are some conditions that describe those controls but need to be refined, such as when the declining population of Susceptible, population of Exposed, Infectious and Treated wetr increasing. With the application of 2 controls, i.e., the addition of optimal treatment control, then the weakness of the model with 1 control can be resolved.

This 2-control model (5)(6)(7)(8) is highly effective for reducing the number of infected individuals in the Tuberculosis model by considering the simulation results from Susceptible, Exposed, Infectious and Treated population satisfying from each expected condition.

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