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Optimal Control on a Discrete Time Model for Tuberculosis

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Abstract : An optimal control problem is studied in a discrete time model describing the dynamics of Tuberculosis transmission in which treatments in both latency and infectious periods are considered. Objectives include maximising the susceptible population at the final observational time and minimising the cost induced from the controls. The controls are characterised using Pontryagin's Optimality Principle, and are solved numerically, together with the state equations, using a forward-backward sweep method.

Keywords : optimal control; discrete time model; Pontryagin's optimality principle; forward-backward sweep method.
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1 Introduction

Background of the Study. Being among the top ten epidemic causes of death globally, Tubercolosis (TB) has been a great focus of study in the field of epidemic diseases. It is caused by a bacteria called *Mycobacterium Tu-*

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berculosis which is transmitted through air. In fact, almost thirty percent of the world's entire population is infected with the disease, albeit majority do not exhibit symptoms [1]. In line with this, TB has been proven to be curable and preventable, and even now, various efforts are being made to deal with the threat of the disease.

On the other hand, mathematical modelling have been of great help in studying disease transmission dynamics over the years, particularly that of communicable diseases. These models describe the dynamics as simple as possible while retaining a certain level of complexity just enough so as to account for the underlying processes governing it. Among the pioneers of mathematical modelling for epidemic diseases are Kermack and McKendrick [2], who divided the population into three compartments– the Susceptible, the Infected, and the Removed classes– commonly known as the SIR epidemic model. The susceptible class is composed of the members of the population who are vulnerable and may contract the disease under scrutiny via interaction with members of the infected class, while those in the removed class are the ones who have recovered from the disease, be it due to treatment or natural recovery. From then on, several models have been developed to further understand the dynamics of different diseases such as TB. One example, Tracy Atkins studied the transmission of Tuberculosis in her Master's thesis [3], dividing the population not only into the three such compartments, but also considered those infected individuals who have yet to exhibit symptoms and are non-infectious— that which was assigned as the Latent class.

Aparicio and Castillo-Chavez [4] studied the same epidemic but considered different levels of risks for contracting the disease in both infected classes. In this, Aparacio, et al. took into account the detail that there are individuals who could transmit the infection faster than the normal rate of transmission. They also took note of the portion of the population which develops pulmonary TB and those which do not. With that, the authors divided the population into seven classes instead.

Furthermore, in addition to using mathematical modelling for the study of epidemic diseases, several mathematicians also delved into the field of optimal controls applied to these models. Some of these focused on optimising the amount of treatment— or vaccination as a form of prevention— certain classes should get, given some certain, reasonable constraints. Lee, Chowell, and Castillo-Chavez [5] studied a variation of such problem, in which they considered a model of a pandemic influenza, with the treatment and interaction between classes as the control variables. Another similar model

was studied by Tchuenche, et al., [6], but they instead considered treatment and vaccination as the control variables.

Description of the Model. In this study, the researchers are interested in an epidemic model developed by Cao and Tan [7]. As such, the authors considered a discrete time tuberculosis model given as follows:

$$\begin{aligned} S_{t+1} &= \Lambda + p\left(1 - \frac{\beta I_t}{N_t}\right) S_t + pkmL_t + p\gamma I_t, \\ L_{t+1} &= q\frac{p\beta S_t I_t}{N_t} + p(1-\alpha)(1-m)L_t + p(1-k)mL_t, \\ I_{t+1} &= (1-q)\frac{p\beta S_t I_t}{N_t} + p\alpha(1-m)L_t + p(1-\gamma)I_t, \end{aligned}$$

where $S_0, L_0, I_0 \geq 0$, along with the following properties:

(i.) the entire population is compartmentalized into three classes: the Susceptible, the Latently infected, and the Infectiously infected, with their corresponding populations at time t denoted by S_t, L_t, and I_t, respectively;

(ii.) interaction between the members of the infectious and the susceptible classes may cause the susceptible individuals to contract the disease and get infected;

(iii.) the surviving members of the latent class may either get treatment from the disease or naturally progress into the infectious class, with m denoting the probability for getting treatment, and $(1-m)$ denoting the probability for natural progression;

(iv.) the parameter Λ denotes the recruitment rate into the population;

(v.) p is the survival probability;

(vi.) k is the probability that a latent individual recovers from the disease given that they received treatment;

(vii.) α denotes the probability that a member of the latent class becomes infectious;

(viii.) γ is the rate of recovery of an infectious individual;

(ix.) β is the probabilty of transmitting the disease; and

(x.) q is the probability that an infected individual enters the latently infected class, while $(1-q)$ is the probability that an infected individual enters the infectiously infected class.

Objective. The goal of this paper is to study an optimal control problem at a finite time period $t = 0, 1, \ldots, T$, applied to the model investigated by Cao et.al. [7]. The controls that will be considered in this model are the treatments for both of the infected classes. The aim is to maximise the population of the susceptible class at the final time T. Due to the possible scarcity of resources on implementing both treatments, the problem will also be formulated as to minimise the cost induced from applying these controls. This study, unlike the optimal control problems that makes use of models of differential equations cited before, deals with a discrete time model. The reason behind this is the fact that the data used for estimating the parameters in the model are usually collected periodically, which makes a discrete time model a natural candidate for describing such phenomena.

This paper is organized as follows. In the next section, the formulation of the optimal control problem will be shown, and the optimal controls will be characterised using Pontryagin's Optimality Principle. In the third section, using the characterisation of the controls, numerical examples using a forward-backward sweep method will be illustrated, and the results will be discussed. Lastly, conclusions and possible future works will be discussed.

2 Formulation of the Optimal Control Problem

Going back to the Discrete Tuberculosis Model (cf. [7]), we have

$$\begin{aligned} S_{t+1} &= \Lambda + p\left(1 - \frac{\beta I_t}{N_t}\right) S_t + pkmL_t + p\gamma I_t, \\ L_{t+1} &= q\frac{p\beta S_t I_t}{N_t} + p(1-\alpha)(1-m)L_t + p(1-k)mL_t, \\ I_{t+1} &= (1-q)\frac{p\beta S_t I_t}{N_t} + p\alpha(1-m)L_t + p(1-\gamma)I_t, \end{aligned}$$

for $t = 0, 1 \ldots, T-1$, where the parameters are defined as in [7]. The solutions for the model are established to be bounded, making it possible for us to apply controls.

For each $t = 0, 1, \ldots, T-1$, we consider controls $u_{1,t}, u_{2,t}$ such that $u_{i,t} \in [0, b_i]$, where $b_i \leq 1$, for each $i = 1, 2$. These control variables are considered to be treatments for the disease. Meaning to say, instead of the

parameters k and γ we shall respectively use the control variables $u_{1,t}$ and $u_{2,t}$ for each $t = 0, 1, \ldots, T-1$. This, in turn, results in to making the treatment rates dependent on time $t = 0, 1, \ldots, T-1$.

Hence, the controlled model (*state equations*), satisfied for each $t = 0, 1, \ldots, T-1$, is given as follows.

$$\begin{cases} S_{t+1} &= \Lambda + p\left(1 - \frac{\beta I_t}{N_t}\right) S_t + p u_{1,t} m L_t + p u_{2,t} I_t, \\ L_{t+1} &= q\frac{p\beta S_t I_t}{N_t} + p(1-\alpha)(1-m)L_t + p(1-u_{1,t})mL_t, \\ I_{t+1} &= (1-q)\frac{p\beta S_t I_t}{N_t} + p\alpha(1-m)L_t + p(1-u_{2,t})I_t, \end{cases} \tag{2.1}$$

$$\text{with initial states } S_0, L_0, I_0 \geq 0, \text{ and } 0 \leq u_{i,t} \leq b_i \text{ for all } i = 1, 2. \tag{2.2}$$

Note that the parameters b_1 and b_2 depend on the highest effectivity rate of treatment among various TB medicines.

The goals, which are to maximise the population of the susceptible class at the final time T and to minimise the cost induced from applying both controls, will be realised by maximising the objective functional

$$J(u_{i,t}) := S_T - \frac{1}{2}\sum_{t=0}^{T-1} [A u_{1,t}^2 + B u_{2,t}^2].$$

In summary, the formulated optimal control problem can be written as

$$\max_{u,v \in U} J(u_{i,t}) \quad \text{subject to (2.1) and (2.2).} \tag{P}$$

3 Characterisation of the Controls

To characterise the optimal controls of the problem (P), we will be employing Pontryagin's Optimality Principle (POP). This characterisation is done by devising the necessary conditions for the optimal controls $u_{1,t}^*, u_{2,t}^*$ presented in [8]. The POP presents a way of translating problem (P) into maximising the Hamiltonian with respect to $u_{1,t}^*, u_{2,t}^*$, where the hamiltonian is defined as

$$H_t(u_{1,t}, u_{2,t}, S_t, L_t, I_t) = -\frac{1}{2}(A u_{1,t} + B u_{2,t}) + \Gamma_{t+1} \cdot G_t, \quad t = 0, 1, \ldots, T-1.$$

where $\Gamma_t = (\lambda_{1,t}, \lambda_{2,t}, \lambda_{3,t})^T$ is the adjoint vector, with $\lambda_{i,t}$ known to be the adjoint variables, and $G_t = (f_{1,t}, f_{2,t}, f_{3,t})^T$ is a vector with variables

$f_{i,t}$ denoting the right hand side of the state equations, for each $i = 1, 2, 3$. The existence of the optimal controls is established, and are characterised through the theorem below.

Theorem 3.1. *There exists $u^*_{1,t}, u^*_{2,t}$, with the corresponding state variables S^*_t, L^*_t and I^*_t, such that $J(u_{i,t})$ is maximised for all $t = 0, 1, \ldots, T-1$. Furthermore, there exists an adjoint vector, Γ_t, with adjoint variables satisfying the following:*

$$\begin{cases} \lambda_{1,t} &= \lambda_{1,t+1} p \left(1 - \frac{\beta I_t}{N_t}\right) + \lambda_{2,t+1} q \frac{p\beta I_t}{N_t} + \lambda_{3,t+1}(1-q)\frac{p\beta I_t}{N_t}, \\ \lambda_{2,t} &= \lambda_{1,t+1} p u_{1,t} m + \lambda_{2,t+1}[p\{(1-\alpha)(1-m) + (1-u_{1,t})\}] \\ &\quad + \lambda_{3,t+1} p\alpha(1-m), \\ \lambda_{3,t} &= \lambda_{3,t+1}\left[p\left(\frac{(1-q)\beta S_t}{N_t} + (1-u_{2,t})\right)\right] + \lambda_{2,t+1} p \frac{q\beta S_t}{N_t} \\ &\quad + \lambda_{1,t+1}\left[p\left(u_{2,t} - \frac{\beta S_t}{N_t}\right)\right], \end{cases} \tag{3.1}$$

with transversality conditions $\lambda_{1,T} = 1$, and $\lambda_{2,T} = \lambda_{3,T} = 0$. And, the optimal controls are characterised for each $t = 0, 1, \ldots, T-1$ as

$$u_{1,t} = \max\left(0, \min\left(b_1, \frac{pmL_t(\lambda_{1,t+1} - \lambda_{2,t+1})}{A}\right)\right), \tag{3.2}$$

and

$$u_{2,t} = \max\left(0, \min\left(b_1, \frac{pI_t(\lambda_{1,t+1} - \lambda_{3,t+1})}{B}\right)\right). \tag{3.3}$$

Proof. Notice that $-\frac{1}{2}\left(Ax^2 + By^2\right)$ is convex, that the *Lipschitz property* is satisfied by the state system, and that it has been established in [7] that the solutions of the state equations are bounded. These facts assure us of the existence of the optimal controls $u^*_{1,t}$ and $u^*_{2,t}$ for problem (P), through Corollary 4.1 of [9]. Moreover, the objective functional can also be easily shown to be strictly convex which establishes the unique existence of both controls.

The derivation of the adjoint equations, and the characterisation of the controls are standard and are based on the computations in [8]. The adjoint equations satisfy the following conditions:

$$\begin{cases} \lambda_{1,t} = \partial_{S_t} H \\ \lambda_{2,t} = \partial_{L_t} H \\ \lambda_{3,t} = \partial_{I_t} H \end{cases}$$

To solve for the equations above, let $\mathbf{J} = (\partial_{\mathbf{S_t}}\mathbf{G_t} \;\; \partial_{\mathbf{L_t}}\mathbf{G_t} \;\; \partial_{\mathbf{I_t}}\mathbf{G_t})$ denote the Jacobian of the state system (2.1). Where the resulting components are solved as

$$\partial_{S_t}G_t = \begin{pmatrix} p\left(1-\frac{\beta I_t}{N_t}\right) \\ q\frac{p\beta I_t}{N_t} \\ (1-q)\frac{p\beta I_t}{N_t} \end{pmatrix}, \quad \partial_{I_t}G_t = \begin{pmatrix} p\left(u_{2,t}-\frac{\beta S_t}{N_t}\right) \\ p\frac{q\beta S_t}{N_t} \\ p\left(\frac{(1-q)\beta S_t}{N_t}+(1-u_{2,t})\right) \end{pmatrix}$$

and

$$\partial_{L_t}G_t = \begin{pmatrix} pu_{1,t}m \\ p\{(1-\alpha)(1-m)+(1-u_{1,t})\} \\ p\alpha(1-m) \end{pmatrix}.$$

And thus,

$$\Gamma_t = \Gamma_{t+1}^T \cdot \mathbf{J},$$

which results into the system (3.1).

Now, for the characterisation of the controls, the optimality condition derived by Lenhart et al. [8] will again be used, i.e.,

$$\begin{cases} u_{i,t} = 0 & \text{if} \quad \partial_{u_{i,t}}H_t < 0, \\ u_{i,t} \in [0, b_i] & \text{if} \quad \partial_{u_{i,t}}H_t = 0, \\ u_{i,t} = b_i & \text{if} \quad \partial_{u_{i,t}}H_t > 0, \end{cases} \tag{3.4}$$

for all $i = 1, 2$, and $t = 0, 1, \ldots, T-1$. Computing for $\partial_{u_{i,t}}H_t$ for both $i = 1, 2$, yields

$$\partial_{u_{1,t}}H = -Au_{1,t} + pmL_t(\lambda_{1,t+1} - \lambda_{2,t+1}),$$

and

$$\partial_{u_{2,t}}H = -Bu_{2,t} + pI_t(\lambda_{1,t+1} - \lambda_{3,t+1}).$$

Thus, the characterisation (3.4) results into

$$u_{1,t} = \begin{cases} 0 & \text{if} \quad \partial_{u_{1,t}}H < 0, \\ \frac{pmL_t(\lambda_{1,t+1}-\lambda_{2,t+1})}{A} & \text{if} \quad \partial_{u_{1,t}}H = 0, \\ 1 & \text{if} \quad \partial_{u_{1,t}}H > 0, \end{cases}$$

and

$$u_{2,t} = \begin{cases} 0 & \text{if} \quad \partial_{u_{2,t}}H < 0, \\ \frac{pI_t(\lambda_{1,t+1}-\lambda_{3,t+1})}{B} & \text{if} \quad \partial_{u_{2,t}}H = 0, \\ 1 & \text{if} \quad \partial_{u_{2,t}}H > 0. \end{cases}$$

Therefore, we get the characterisations (3.2) and (3.3). □

4 Numerical Results and Discussion

Here, the first order necessary conditions derived from the previous section are used to illustrate several scenarios numerically, i.e., with varied values of certain chosen parameters. This is done using a forward-backward sweep method on the conditions.

Using the discrete timeline $t = 0, 1, 2, \ldots, 20$, we first show the effect of changing the values of the weight parameters A and B on the strategy of applying the controls. Here, the parameter values are taken from the endemic equilibrium analysed by Cao et.al. in [7], except of course for the parameters k and γ, which were altered as the controls u_1 and u_2, respectively.

For convergence's sake, the values $A = B = 10$ are initially simulated, as shown in Figure 1. Figure 2, shows a scenario where the weight parameter B is increased, i.e. $B = 15$. While in Figure 3, the weight parameter A is changed from $A = 10$ to $A = 15$.

Evidently, since increasing the weight parameter B is *equivalent* to increasing the price for the treatment u_2, Fig. 2 shows a decrease in application between the interval [10, 20] as compared to the application of u_2 in Fig. 1. Similarly, the application of treatment u_1 is affected when the weight paramater A is changed, i.e., from having $u_{1,t} = 0.5$ for $t = 1, 2, 3$ when $A = 10$ to $u_{1,t} = 0.5$ only for $t = 1, 2$, and $u_{1,3} \in [0.4, 0.45]$ when $A = 15$.

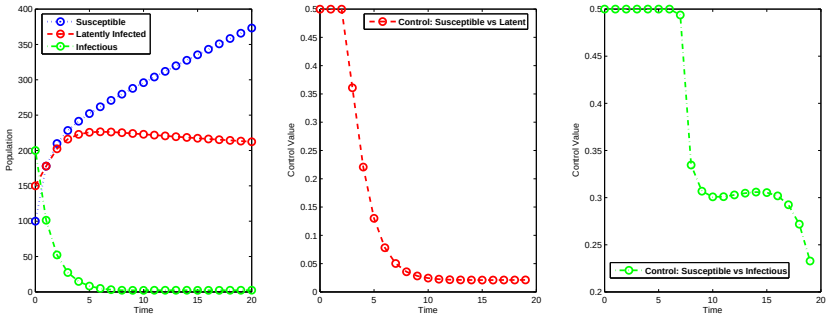

Figure 1: A=10, B =10

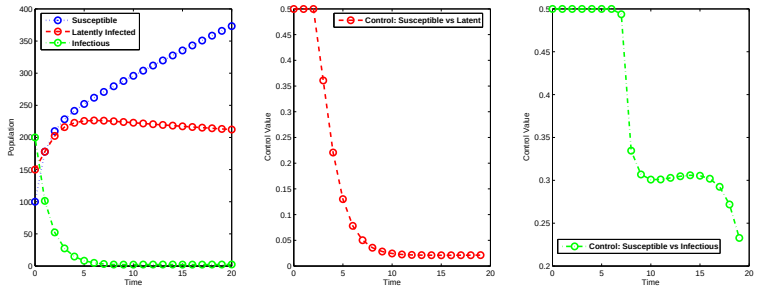

Figure 2: A = 10, B = 15

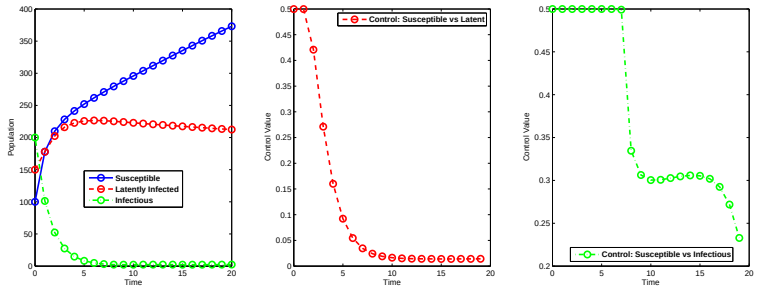

Figure 3: A = 15, B = 10

The next simulation shows the effect of using varied values for the parameter α on both controls. For convergence's sake, we take $A = B = 1$ and $T = 10$ (*Note:* The variation of α is of increasing order, i.e., $\alpha 1 < \alpha 2 < \alpha 3 < \alpha 4$). As can be observed (cf. Figure 4), the control u_1 is more sensitive to the variation relative to the control u_2. This could be attributed to the fact that an increase in α increases the rate of transmission from the latent class to the infectious class. Meaning to say, the control u_1 need not be focused on treating the members of the latent class.

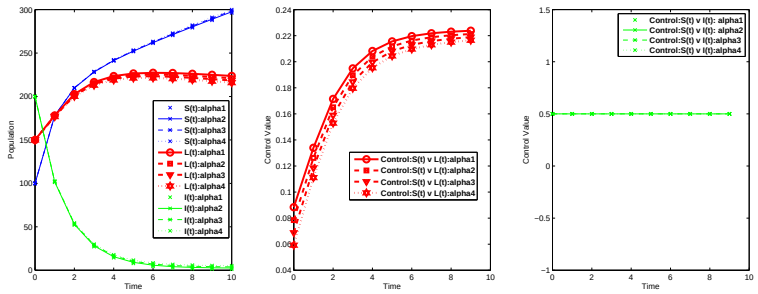

Figure 4: Simulations for varied values of α

Meanwhile, varying the values of β, as shown in Figure 5 (with $\beta 1 < \beta 2 < \beta 3 < \beta 4$), we see noticeable increases in both controls u_1 and u_2. This is expected as β represents the transmission rate of the disease. An increase in the value of the transmission rate would naturally cause a decrease in the susceptible population while increasing both of the infected populations. This would, in turn, result into a greater need for better quality of treatments in both classes.

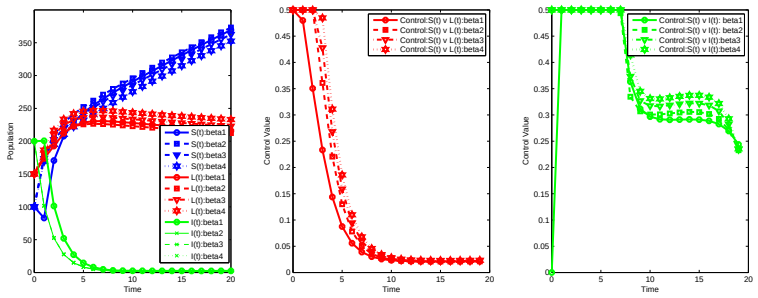

Figure 5: Simulations for varied values of β

In the next simulation (cf. Figure 6), we vary the values of q, or the probability that an infected individual from the susceptible class enters the latently infected class, in an increasing manner. This would then mean that the probability of an infected individual entering the infectious class, which is $(1-q)$, is changed in a decreasing manner. And so, as can be seen in Fig. 6, both controls are affected, although differently. The control u_1 shows an increasing trend, implying the need for better treatments in the latent class as q increases. On the other hand, the control in our infectious class, u_2, decreases as q increases, or $1-q$ decreases, which is reasonable, since there would be lower transmission rates from the susceptible population into the infectious population.

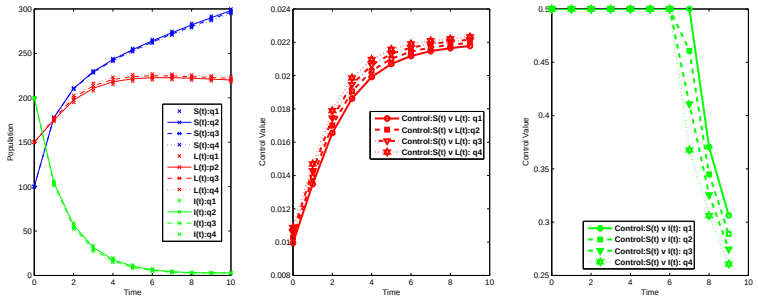

Figure 6: Simulations for varied values of q

Lastly, Figure 7 shows simulations when m is varied ($m1 < m2 < m3 < m4$). There is a very slight change in the control u_2 (less than 0.0001) as the parameter m denotes the probability of an individual from the latent class getting treatment. Hence, treatments in the infectious class are not prioritized. However, there is a significant increase in the control u_1 for all $t = 0, 1, \ldots, 20$. This is due to the fact that an increase in the number of treatments in the latent class requires better treatment success rates, which is the control u_1, in order for us to maximize the susceptible population and, at the same time, minimize the cost induced from implementing the controls.

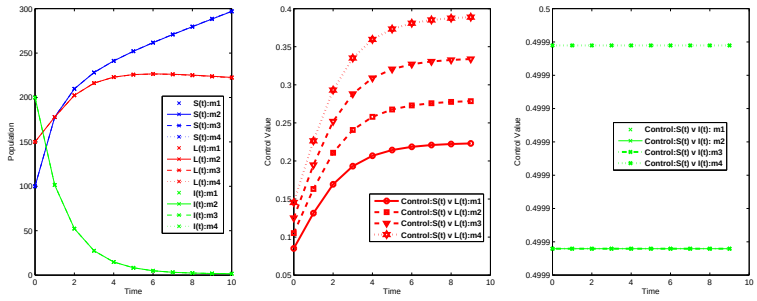

Figure 7: Simulations for varied values of m

5 Conclusion

Both of the optimal controls were characterised using the first order necessary conditions which were solved with the aid of Pontryagin's Optimality Principle. Furthermore, the sufficient conditions were shown, proving that the characterised controls are indeed optimal for the given control problem. With simulations done by varying the parameters— so as to consider different scenarios— maximisation of the susceptible population by using cost-effective control programs was done through a forward-backward sweep method on the equations derived from the necessary conditions. Maximisation of the susceptible population— while minimising the cost induced from applying both controls– in turn, effectively reduces both the latent TB and the infectious TB populations.

The authors recommend the reader to consider different control strategies. In particular, one may use a separating control for the problem, i.e., isolation or confinement of the members of the infectious class from the rest of the population.

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