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Optimal Control Model for the Dynamics of Tuberculosis with Control Strategies

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Abstract
The optimal control model with five different control strategies; the control effort on vaccination (u_1), the control effort on public health campaigns (u_2), the control effort on tuberculosis case detection (u_3), the control effort on quarantine (u_4) and the control effort on sanitarium (u_5) is formulated and analyzed using Pontrayagin's maximum principle. The numerical simulations of the optimal control model have shown that tuberculosis infection can be effectively controlled in a given population provided that 35.69% control effort on vaccination (u_1), 35.69% control effort on public health campaign (u_2), 0.0642% control effort on tuberculosis case detection (u_3), 28.55% control effort on quarantine (u4), and 0.0021% control effort on sanitarium (u_5) are continuously implemented. In this paper, an optimal control model that incorporate five different control effort variables: vaccination (U_1), public health campaign (U_2), case detection (U_3), Quarantine (U_4) and sanitarium (U_5) as control strategies was proposed. And perform numerical simulation of the model

Keywords: Tuberculosis, Optimal Control, Public Health Campaign, Quarantine, Sanitarium.

Introduction

Tuberculosis (TB) is a chronic infectious disease caused by mycobacterium (tubercle bacillus). The disease spreads from one individual to another through air. Infected persons release droplets of Mycobacterium tuberculosis bacteria into the air by coughing, sneezing or spitting mucus containing the bacteria onto surfaces. This droplets or mucus contain large number of small respiratory droplets nuclei that evaporates and dispersed into the air almost instantly. These nuclei implant themselves in the lung when inhaled. In most cases, a competent immune system limits the multiplication of the tuberculosis bacilli, although some bacilli remain dormant but viable, rendering a condition known as Latent TB Infection (LTBI), (Center for Disease and control (CDC), 2000).

Basically, there are two types of TB, namely: Pulmonary TB which affects the lung (the commonest and infectious form of the disease) and Extra-pulmonary TB that affects organs such as pleura, lymph nodes, spine, joints, abdomen or genitourinary track.

Worldwide 8.6 million people fell ill due to TB, of which 1.3 million people die annually. In Africa, the TB incidences per 100,000 population is 262 while the prevalence is 293 as per World Health Organization (WHO), (2013). At global level, TB is the seventh most important cause of global premature mortality and disability and it is projected to remain among the ten leading causes of disease burden even in the year 2020 (Nyerere *et al*., 2014).

The use of mathematical modeling in the theory and practice of disease management and control have increase due to the fact that, the approach helps in figuring out control strategies and making decisions that are of significant importance to the control of the disease (Nyerere, *et al.*, 2014).

Optimal control theory is a powerful mathematical tool that can be used to proffer best control regiment to help in making decisions involving complex biological situations. For instance, what percentage of the population should be vaccinated as time evolves in a given epidemic model to minimize the number of infected and the cost of implementing vaccination strategy? The behavior of the underline dynamical system is described by a state variable(s). It is assumed that there is a way to steer the state variable by acting upon with suitable control function(s). The control enters the system ordinary differential equations and affects the dynamic of the system. The goal is to adjust the control in order to maximize (or minimize) a given objective functional (Suzanne & Workman, 2007). In general, the objective functional depends on one or more of the state and the control variables. Frequently the objective functional is given by an integral of the state and or control variables.

There exist several research works in which the simple compartment models for different infectious diseases have been proposed and analyze in some of them optimal control technique have been incorporated. For instance, Zaman *et al*. (2009) developed optimal control model of susceptible, infected, recovered, with time delay using treatment as control parameter to minimize the probability of infections transmission and to maximize the total number of susceptible and recovered individuals. Bowng & Alaoui (2013) developed tuberculosis model and analyzed using optimal control theory by introducing control terms on the chemoprophylaxis and case detection to reduce the number of individuals infected with active TB. Ahmadin & Fatmawati (2014) constructed a mathematical model of drug resistant in the tuberculosis disease transmission that include treatment measure as optimal control. Agusto & Adekunle (2014) developed a TB and HIV/AIDS co-infection model by incorporating nine control parameters. Optimal control of tuberculosis with case detection and treatment was proposed by (Athithan & Ghosh; 2015), they compared the result with result of fixed control and it was observed that optimal control gives better result than fixed control. Fatmawati & Hengki (2016) developed an optimal treatment control of TB-HIV co-infection that includes use of anti-TB and ARV treatment as optimal control strategies. They conclude that the combination of anti-TB and ARV treatments is the most effective to reduce the TB-HIV con-infection.

Quarantine
Refers to the separation and restriction of persons who, while not ill, have been exposed to an infectious agent and thereafter may become infectious. Quarantine may be used when a person has been exposed to a highly dangerous and infectious diseases and include a range of disease control strategies that may be used individually or in combination. Quarantine includes short-term voluntary home confinement; restrictions on travel by those who may have been exposed; and out of a geographic area. Quarantine also includes other measures to control the spread of disease, such as restriction on the assembly of groups of people (e.g. school events); suspension of public gathering and closure of mass transit system or broad restrictions on travel by air, rail or water may be used (CDC; 2014).

Sanitarium
This is a medical facility for long term illness management. It is a hospital where people who have had a serious illness like TB go so that health care workers can take care of them to recuperate. The efficiency of sanitarium treatment depends on early detection and reference of patients. Sanitarium can also be used as an educational center where TB patients receive both didactic and practical instructions.

Public campaign
This can be achieved or operate by addressing prisoners, refugees and other high risk groups on danger of a certain disease, strengthening of health systems, engaging all care providers through public-public and public-private mix approaches. Also through advocacy, communication and social mobilization on the risk of disease like TB.

Case detection
Case detection is the investigation of infectious disease through either laboratory means or Direct Observation Therapy Strategy **(DOTS).** Christopher & Martien (2008) conducted case detection over 11 years between 1994 and 2005, a total of 26.5 million TB patients were diagnosed and reported under DOTS. That in 2005, DOTS programs worldwide reported 4.8 million new and relapsed cases, among which 2.3 million were smear-positive. The smear-positive case detection was 60% (90% uncertainty limits, 52-69%) of the 3.9 million new cases estimate. The estimate of case detection was below the 70% target. The

estimated case detection rate increased almost linearly from 11% globally in 1995 to 28% in 2000. They concluded that case detection has since accelerated from 2003 to 2004.

Materials and Method

The following are the main assumptions made in in formulating the model:

(i) All exposed individuals suspected of TB case are quarantined.
(ii) Treatment of infected individuals occur in the sanitarium.
(iii) Quarantined individuals who are tested positive will be taken to sanitarium for immediate treatment.
(iv) Screening is done to the exposed individual to detect infected individuals.
(v) Natural death occurs across the compartments.
(vi) All exposed individuals that are tested negative are going to the quarantine.
(vii) Recruitment rate into the susceptible population remain constant.
(viii) Those on vaccine become exposed on expiration of the vaccine efficacy.

Table 1: Definitions of variables of the modified model

Variable	Definition
S(t)	The population of susceptible individuals at time, t
V(t)	The population of vaccinated individuals at time t
E(t)	The population of exposed individuals at time, t
Q(t)	The population of individuals suspected with the symptoms of the disease at time, t
I(t)	The population of infected individuals at time, t
J(t)	The population of individuals in a sanitarium at time, t
R(t)	The population of recovered/treated individuals at time, t
N(t)	Total population at time, t

Table 2: Definitions of parameters of the model

Parameters	**Definition**
Λ	Birth Rate
μ	Natural mortality rate
ρ	Proportion of vaccination at birth
$1-p$	Proportion of those not vaccinated at birth
d_2	TB-induced death rate for individuals in the sanitarium
d_1	TB=induced death rate for infected individuals
ω	Proportion of quarantined individual that are infected and go for treatment
$1-\omega$	Proportion of quarantine individuals that are not infected
q	The rate at which susceptible individuals are vaccinated
α	The rate at which infected individuals move to sanitarium
β	Per capita TB transmission rate
θ	The rate at which new born are vaccinated
r_1	The recovery rate of individuals in the sanitarium
π	The efficacy of vaccine
λ	The force of infection
τ	Rate at which the quarantine individuals are diagnose
p	The rate of progression from expose to infected class
γ	Proportion of exposed individuals that are quarantined

$1-\gamma$	Proportion of exposed individuals that are not quarantined
η	Probability of acquiring TB infections per contact with an infectious individual

Description of the Model

The total population at time t denoted by $N(t)$ is divided into seven mutual exclusive compartments (depending on the epidemiological status of individuals in the population). The compartments are; the population of susceptible individuals, $S(t)$, the population of vaccinated individuals, $V(t)$, the population of exposed individuals, $E(t)$, the population of quarantined individuals, $Q(t)$, the population of infected individuals, $I(t)$, the population of individuals under sanitarium $J(t)$, and the population of recovered individuals, $R(t)$. it is refer to a compartmental-based model as SVEQIJR model. Let the force of infection be given as $\lambda = \frac{\beta(I+\eta J)}{N}$, where the total population is given by:

$$N(t)=S(t)+E(t)+I(t)+Q(t)+J(t)+V(t)+R(t).$$

The population of susceptible individuals is generated by the proportion (1−ρ) Λ i.e. new births that were not vaccinated, vaccinated individuals who lose immunity at the rate θ and the proportion of quarantine individuals that are confirmed negative with TB given by $(1-\omega)\tau$. The susceptible population is reduced by natural death at the rate μ those that are vaccinated at the rate q and by those that become infected and move to the exposed compartment at the rate λ. Thus, the equation governing the dynamics of susceptible individuals is given by

$$\frac{dS}{dt}=(1-\rho)\Lambda+\theta V+(1-\omega)\tau Q-(\lambda+q+\mu)S \cdot$$

The population of vaccinated individuals is generated by the proportion of those that are successfully vaccinated at birth given by ρΛ and the susceptible individuals that are vaccinated at the rate q. This population is reduced by those who lose immunity against TB at the rate θV. The vaccinated population further reduces due to the natural death at the rate μ. Hence, the equation governing the dynamics of the vaccinated population is as follows:

$$\frac{dV}{dt}=\rho\Lambda+qS-(\theta+(1-\pi)\lambda+\mu)V \cdot$$

The population of exposed individuals is generated by those susceptible and vaccinated individuals that are suspected with TB at the rates λ and $\lambda(1-\pi)$, respectively. This population decreases due to the progression into the infected class at the rate $p(1-\gamma)$, those that are quarantine at the rate $p\gamma$ and by the natural death at the rate μ. Hence,

$$\frac{dE}{dt}=(S+(1-\pi)V)\lambda-(p+\mu)E \cdot$$

The population of quarantine individuals is generated by the proportion of those that are suspected with TB at the rate of γ. It reduces by those who move to the susceptible class after they are confirmed negative with TB at the rate $(1-\omega)\tau$, those that go for treatment at the rate $\omega\tau$ and the natural death at the rate μ. Thus, the equation:

$$\frac{dQ}{dt}=p\gamma E+\phi_1-(\tau+\mu)Q \cdot$$

The population of the infected individuals is generated by the proportion of those confirmed infected at the rate $p(1-\gamma)$ and reduced by TB-induced and natural deaths at the rates d_1 and μ, respectively. The population also reduces by αI, i.e. the proportion of those that go for treatment. Hence,

$$\frac{dI}{dt}=p(1-\gamma)E+\phi_2-(\alpha+d_1+\mu)I .$$

The population of individuals in the sanitarium compartment increases by proportion of those that go for treatment from the infected class at the rate α and from quarantine compartment at the rate $\omega\tau$. This population reduces by those who recover due to the effective treatment at the rate r_1, TB-induce death at the rate d_2 and natural death at the rate μ. Thus,

$$\frac{dJ}{dt} = \alpha I + \tau\omega Q - \left(r_1 + d_2 + \mu\right) J \cdot$$

The population of recovered individuals increases by those that recovered from the disease at the rate r_1 and reduces by natural death at the rate μ. Hence the equation:

$$\frac{dR}{dt} = r_1 J - \mu R$$

The General transfer diagram for the model

From the assumptions (2.1) and the model description (2.2) the model flow diagram is:

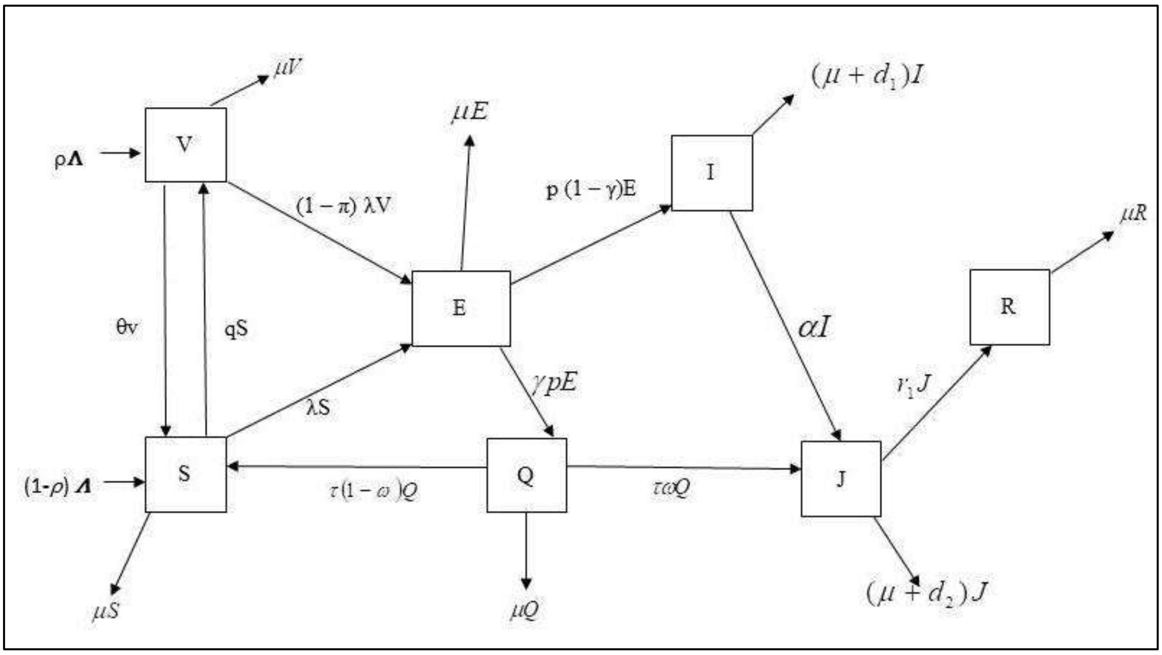

Figure 1: A general transfer diagram for the model (SEIQJVR)

Model equations (model with constant controls)

Based on the assumptions, the description and the schematic flow diagram of the model in Figure 2.1, we present the following set of first order nonlinear ordinary differential equation for the model (SVEQIJR).

$$\left.\begin{aligned}
\frac{dS}{dt} &= (1-\rho)\Lambda + \theta V + (1-\omega)\tau Q - (\lambda + q + \mu)S, \\
\frac{dV}{dt} &= \rho\Lambda + qS - (\theta + (1-\pi)\lambda + \mu)V, \\
\frac{dE}{dt} &= (S + (1-\pi)V)\lambda - (p + \mu)E, \\
\frac{dQ}{dt} &= p\gamma E - (\tau + \mu)Q, \\
\frac{dI}{dt} &= p(1-\gamma)E - (\alpha + d_1 + \mu)I, \\
\frac{dJ}{dt} &= \alpha I + \tau\omega Q - (r_1 + d_2 + \mu)J, \\
\frac{dR}{dt} &= r_1 J - \mu R,
\end{aligned}\right\} \quad (3.2)$$

where

$$\lambda = \frac{\beta(I + \eta J)}{N},$$

$$N(t) = S(t) + V(t) + E(t) + Q(t) + I(t) + J(t) + R(t).$$

Subject to the following initial condition:

$$S(0) > 0, V(0) \geq 0, E(0) \geq 0, Q(0) \geq 0, I(0) \geq 0, J(0) \geq 0, R(0) \geq 0.$$

The formulation of the optimal control model

An optimal control problem is developed by incorporating the time dependent control strategies into the model with constant controls given by system (2.1). The time dependent control strategies to be implemented are as follows:

(i) $u_1(t)$, with $0 \leq u_1 \leq 1$, denotes the control efforts on vaccination of children at birth and the susceptible individuals.

(ii) $u_2(t)$, with $0 \leq u_2 \leq 1$, represents the control effort on public health campaign of susceptible individuals.

(iii) $u_3(t)$, with $0 \leq u_3 \leq 1$, represents the control effort on case detection of infected individuals.

(iv) $u_4(t)$, with $0 \leq u_4 \leq 1$, denotes the control effort on quarantine of individual suspected with TB.

(v) $u_5(t)$, with $0 \leq u_5 \leq 1$, denotes the control effort on the sanitarium of infected.

The objective function to be minimize is;

$$J(u_1, u_2, u_3, u_4, u_5) = \int_0^T \left(Z_1 I + \frac{1}{2}\sum_{i=1}^{5} C_i u_i \right) dt$$

Subject to

$$
\begin{aligned}
\frac{dS}{dt} &= (1-\rho)u_1\Lambda + \theta V + (1-\omega)u_4\tau Q - ((1-u_2)\lambda + u_1 q + \mu)S, \\
\frac{dV}{dt} &= u_1\rho\Lambda + u_1 qS - (\theta + (1-\pi)\lambda + \mu)V, \\
\frac{dE}{dt} &= ((1-u_2)S + (1-\pi)V)\lambda - (u_3 p + \mu)E, \\
\frac{dQ}{dt} &= u_3 p\gamma E - (u_4\tau + \mu)Q, \\
\frac{dI}{dt} &= u_3 p(1-\gamma)E - (u_4\alpha + d_1 + \mu)I, \\
\frac{dJ}{dt} &= u_4\alpha I + u_4\tau\omega Q - (u_5 r_1 + d_2 + \mu)J, \\
\frac{dR}{dt} &= u_5 r_1 J - \mu R,
\end{aligned} \tag{3.3}
$$

with the following initial condition:

$S(0) > 0, V(0) \geq 0, E(0) \geq 0, Q(0) \geq 0, I(0) \geq 0, J(0) \geq 0, R(0) \geq 0\cdot$

The parameters, C_1, C_2, C_3, C_4 and C_5 in the objective function are the weight constants for the control efforts on vaccination, public health campaign, case detection, quarantine and sanitarium respectively and Z_1 is the cost coefficient corresponding to the population of individuals infected with TB. The quadratic terms $\frac{C_1u_1^2}{2}, \frac{C_2u_2^2}{2}, \frac{C_3u_3^2}{2}, \frac{C_4u_4^2}{2}$ and $\frac{C_5u_5^2}{2}$, describe the cost associated with the control efforts on vaccination, public health campaign, case detection, quarantine and sanitarium respectively. A quadratic cost function is chosen because the cost of control effort are generally assumed nonlinear. The aim is to minimize the population of individuals with TB infection while keeping the cost of applying control efforts on vaccination, public health campaign, case detection, quarantine and sanitarium at minimum levels. The aim is to search for the controls functions $(u_1^*, u_2^*, u_3^*, u_4^*, u_5^*)$ such that

$J(u_1^*, u_2^*, u_3^*, u_4^*, u_5^*) = \underset{U}{\text{Min}}\, J(u_1, u_2, u_3, u_4, u_3)$, where $U = \{u_1, u_2, u_3, u_4, u_5 \mid 0 \leq u_i \leq 1, i = 1, 2, ..., 5\}$, is the control set and is Lebesgue measurable.

The following methods will be employed for the analysis of the modified model:

(i) Pontrayagin's Maximum Principle will be used to analyze the optimal control model;
(ii) MATLAB software for the numerical simulations of the optimality system derived.

Optimal Control Analysis

The optimal control problem is***:***

$$
\begin{aligned}
&J(x(t), u(t)) = \text{optimize}\int_{t_0}^{t_1} f(t, x(t), u(t))dt \\
&\text{subject to } x'(t) = g(t, x(t), u(t)) \\
&x(t_0) = x_0 \text{ and } x(t_1) \text{ unrestructed}
\end{aligned} \tag{2.3}
$$

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

If $u^*(t)$) and $x^*(t)$ are optimal solutions for the optimal control problem (3.3), then there exists a piecewise differentiable adjoint variable $\lambda(t)$ such that

$$H(t, x^*(t), u(t), \lambda(t)) \leq H(t, x^*(t), u^*(t), \lambda(t)) \tag{2.4}$$

For control variables $u(t)$ at each time *t*, where the Hamiltonian *H* is given by

$$H\left(t,x^{*}(t),u(t),\lambda(t)\right)=f\left(t,x(t),u(t)\right)+\lambda(t)g\left(t,x(t),u(t)\right) \text{ and}$$

$$\frac{d\lambda}{dt}=\frac{\partial H\left(t,x^{*}(t),u^{*}(t),\lambda(t)\right)}{\partial x}, \tag{2.5}$$

$$\lambda(t_1)=0$$

Numerical Simulations

In this section, numerical experiments to determine the impact of vaccine, public campaign, case detection, quarantine and sanitarium in the control of TB in a population were consided. The optimality system will be solve numerical using ODE45 solver in MATLAB and the values of parameters in table 3.

Table 3: Description of parameters with their values

Parameters	Descriptions	Values	Reference
Λ	The Proportion of New born	0.1891	Estimated
μ	Natural mortality rate	0.2041	Andreir, 2007
ρ	Proportion of vaccination at birth	0.8	Estimated
$1-p$	Proportion of those not vaccinated at birth	0.97	Estimated
d_2	TB induced death rate for individuals in the sanitarium	0.3	Athithan, 2015
d_1	TB induced death rate for infected individuals	0.365	Adetunde, 2007
ω	Proportion of quarantined individual that are infected go for treatment	0.22	Estimated
$1-\omega$	Proportion of quarantine individuals that are not infected	0.78	Estimated
q	The rate at which susceptible individuals are vaccinated	0.2	Estimated
α	The rate at which infected individuals move to sanitarium	0.8	Estimated
θ	The rate at which new born are vaccinated	0.7	Estimated
β	per capita transmission rate from susceptible to exposed class	0.35	Agusto, 2009
r_1	The recovery rate of individuals in the sanitarium	0.9	Estimated
Π	The efficacy of vaccine	0.8	Nyerere, et al.,2014
Λ	The force of infection	0.042	Estimated
τ	rate at which quarantine individuals are diagnose	0.2	Estimated
P	The rate of movement from expose to infected class	0.03	Nyerere, et al.,2014
Γ	Proportion of exposed individuals quarantined	0.6	Estimated
$1-\gamma$	Proportion of exposed individuals that are not quarantined	0.4	Estimated
η	probability of acquiring TB infections	0.3	Estimated

Results

The Analysis of the Optimal control Model

The Lagrangian of the optimal control problem given by system (2.2) is presented as;

$$L = Z_1 I + \frac{C_1 u_1}{2} + \frac{C_2 u_2}{2} + \frac{C_3 u_3}{2} + \frac{C_4 u_4}{2} + \frac{C_5 u_5}{2} \quad (3.1)$$

. In order to accomplish this, the Hamiltonian, H for the control problem is defined as:

$$\begin{aligned} H &= L(I, u_1, u_2, u_3, u_4, u_4) + \lambda_1 \frac{dS}{dt} + \lambda_2 \frac{dV}{dt} + \lambda_3 \frac{dE}{dt} + \lambda_4 \frac{dQ}{dt} + \lambda_5 \frac{dI}{dt} + \lambda_6 \frac{dJ}{dt} + \lambda_7 \frac{dR}{dt} \\ &= Z_1 I + \frac{C_1 u_1}{2} + \frac{C_2 u_2}{2} + \frac{C_3 u_3}{2} + \frac{C_4 u_4}{2} + \lambda_1 \left[(1-\rho) u_1 \Lambda + \theta V + (1-\omega) u_4 \tau Q - ((1-u_2)\lambda + u_1 q + \mu) S \right] \\ &+ \lambda_2 \left[u_1 \rho \Lambda + u_1 q S - (\theta + (1-\pi)\lambda + \mu) V \right] + \lambda_3 \left[((1-u_2) S + (1-\pi) V) \lambda - (u_3 p + \mu) E \right] \\ &+ \lambda_4 \left[u_3 p \gamma E - (u_4 \tau + \mu) Q \right] + \lambda_5 \left[u_3 p (1-\gamma) E - (u_4 \alpha + d_1 + \mu) I \right] \\ &+ \lambda_6 \left[u_4 \alpha I + u_4 \tau \omega Q - (u_5 r_1 + d_2 + \mu) J \right] + \lambda_7 \left[u_5 r_1 J - \mu R \right] \end{aligned}$$

(3.2)

The Optimality System

In order to find the optimal solution, the Pontryagin's Maximum Principle is employed to the Hamiltonian given by equation (3.2), such that if (x, u) is an optimal solution of an optimal control problem, then there exists a non-trivial vector $\lambda_1, \lambda_2, ..., \lambda_7$ satisfying the following conditions:

$$\frac{dx}{dt} = \frac{\partial H(t, x, u, \lambda)}{\partial \lambda}, \frac{\partial H(t, x, u, \lambda)}{\partial u} = 0, \frac{d\lambda}{dt} = -\frac{\partial H(t, x, u, \lambda)}{\partial x} \quad (3.3)$$

The necessary conditions to the Hamiltonian in equation (4.1) that optimal control functions and corresponding states must satisfy are driven through the following theorem:

Theorem 3.1

Let $S^*, V^*, E^*, Q^*, I^*, J^*$ and R^* be the optimal solutions corresponding to the optimal control problem given by system (3.3) associated with the optimal control variables $(u_1^*, u_2^*, u_3^*, u_4^*, u_5^*)$. Then there exist adjoint variables $\lambda_i, (i = 1, 2, 3, ..., 7)$ satisfying

$$\begin{aligned} \frac{d\lambda_1}{dt} &= (1-u_2)(\lambda_1 - \lambda_3)(J^* \eta + I^*) \frac{\beta}{N^*} + ((q u_1 + \mu)\lambda_1 - q u_1 \lambda_2), \\ \frac{d\lambda_2}{dt} &= (1-\pi)(\lambda_2 - \lambda_3)(J^* \eta + I^*) \frac{\beta}{N^*} + ((\mu + \theta)\lambda_2 - \theta \lambda_1), \\ \frac{d\lambda_3}{dt} &= p(\lambda_3 + (1-\gamma)\lambda_5 + \gamma \lambda_4) u_3 + \mu \lambda_3, \\ \frac{d\lambda_4}{dt} &= ((1-\omega)\lambda_1 - \omega \lambda_6 + \lambda_4) \tau u_4 + \mu \lambda_4, \\ \frac{d\lambda_5}{dt} &= (((1-u_2) S^* (\lambda_1 - \lambda_3)) + (1-\pi) V^* (\lambda_2 - \lambda_3)) \frac{\beta}{N^*} + ((\alpha u_4 + \mu + d_1)\lambda_5 - u_4 \alpha \lambda_6 - Z_1), \\ \frac{d\lambda_6}{dt} &= ((1-u_2) S^* (\lambda_1 - \lambda_3) + (1-\pi) V^* (\lambda_1 - \lambda_3)) \frac{\eta\beta}{N^*} + ((r_1 u_5 + \mu + d_2)\lambda_6 - u_5 r_1 \lambda_7), \\ \frac{d\lambda_7}{dt} &= \mu \lambda_7, \end{aligned} \quad (3.4)$$

with transversality conditions (i.e. terminal conditions)

$$\lambda_i(T) = 0, (i = 1, 2, 3, ..., 7). \quad (3.5)$$

Expressed as

$u_i^* = 0, \text{if } u_i \leq 0, \quad u_i^* = u_i \text{ if } 0<u_i<1 \quad u_i^* = 1 \text{if } u_i \geq 1$. In addition, the optimal controls $(u_1^*, u_2^*, u_3^*, u_4^*, u_5^*)$ satisfy the following optimality conditions:

$$
\begin{aligned}
u_1^* &= \max\left(\min\left[\frac{\Lambda\rho(\lambda_1-\lambda_2)+(\lambda_1-\lambda_2)qS^*-\Lambda\lambda_1}{C_1},1\right],0\right).\\
u_2^* &= \max\left(\min\left[\frac{(\lambda_3-\lambda_1)(\eta J^*+I^*)\beta S^*}{C_2N^*},1\right],0\right),\\
u_3^* &= \max\left(\min\left[\frac{((\lambda_5-\lambda_4)\gamma+\lambda_3-\lambda_5)pE^*}{C_3},1\right],0\right),\\
u_4^* &= \max\left(\min\left[\frac{(\lambda_1-\lambda_6)\omega\tau Q^*+(\lambda_4-\lambda_1)\tau Q^*+(\lambda_5-\lambda_6)\alpha I^*}{C_4},1\right],0\right),\\
u_5^* &= \max\left(\min\left[\frac{(\lambda_6-\lambda_7)r_1J^*}{C_5},1\right],0\right).
\end{aligned}
\tag{3.6}
$$

Proof:

To determine the adjoint equations and the transversality conditions, the Hamiltonian H is minimized with respect to the controls $(u_1^*, u_2^*, u_3^*, u_4^*, u_5^*)$ at the optimal control functions.

Setting

$S(t)=S^*(t), V(t)=V^*(t), E(t)=E^*(t), Q(t)=Q^*(t), I(t)=I^*(t), J(t)=J^*(t), R(t)=R^*(t)$ and differentiating the Hamiltonian equation (4.58) with respect to $S, V, E, Q, I, J,$ and R, respectively, equation (). is gotten:

$$\frac{\partial H}{\partial u_i} = 0, (i = 1, 2, ..., 5), \tag{3.7}$$

On the interior of the control set using the optimality conditions and the property of the control set **U**, equation (3.6). is driven Because of the fact that the state and the adjoint functions are bounded and the Lipschitz structure of the ordinary differential equations, the uniqueness of the optimal control is obtained. Thus, the proof is complete.

The optimality system is made up of the state system presented in equation (3.2) with the initial conditions, the adjoint system (3.4) with the transversality conditions in equation (3.5) and the control characterization given by equation (3.6).

Numerical Simulation and Discussion

In this section, the analytic results of the work was numerically simulated using (MATLAB R 2018a).

Numerical Simulations of the Optimal Control Model

The numerical simulations conducted in order to investigate the effects of the control strategies on the transmission dynamics of Tuberculosis. The simulations are performed using MATLAB and time in years. The estimated initial values of the state variables of the model are $S_0 = 15000, V_0 = 8000, E_0 = 10000, Q_0 = 2000, I_0 = 5000, J_0 = 1500$ and $R_0 = 1300$ for the adjoint system and the terminal conditions are $\{\lambda_i(T) \forall \, i = 1,2,3,4,5,6,7\} = 0$, where $T = 10$ years. The cost coefficient corresponding to state variables are estimated to be $Z_1 = 0.001$. The quadratic cost coefficient corresponding to control measures is estimated to be $C_1 = 0.03, C_2 = 0.02, C_3 = 0.01, C_4 = 0.4$ and $C_5 = 0.05$ while the values of the remaining parameters are presented in Table 3.6.

The graphs were plotted to show the effects of the control strategies (vaccination, public campaign, case detection, quarantine, and sanitarium) in eradicating tuberculosis infection. Graphs were plotted when no control strategy is implemented and then compare with when the control strategies are implemented, as shown in Figures 2–5.4,

The Numerical simulation of the optimal control model with and without control strategies

The optimal control results are presented in Figure 2 to Figure 5.

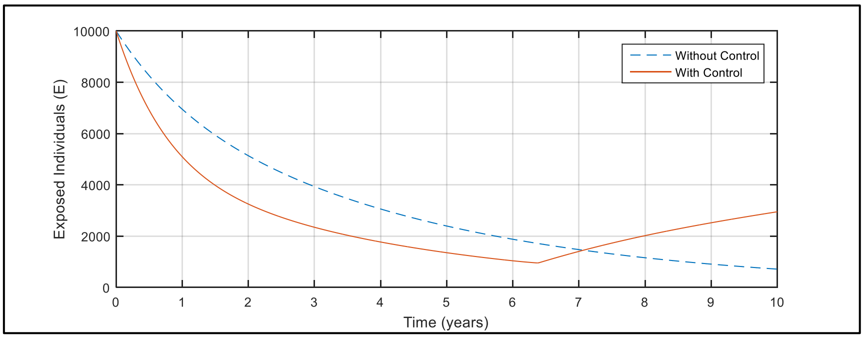

Figure 2: Graph showing the effects of applying control strategies on the population of exposed individuals.

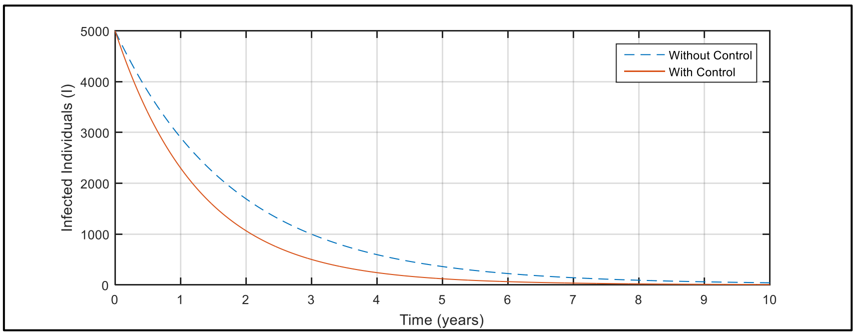

Figure 3: Graph showing the effects of applying all control strategies on the population of infected individuals.

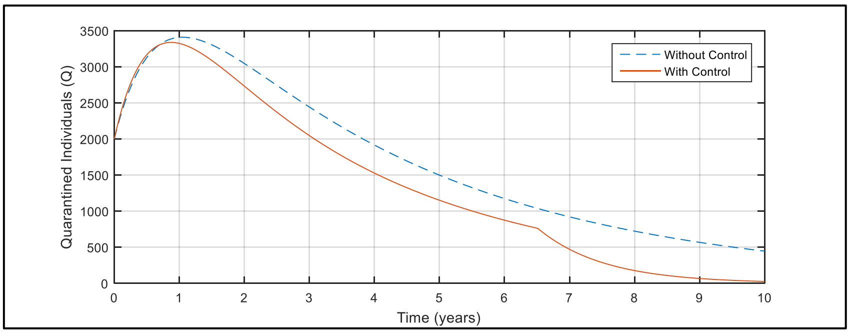

Figure 4: Graph showing the effects of applying all the control strategies on the population of quarantined individuals.

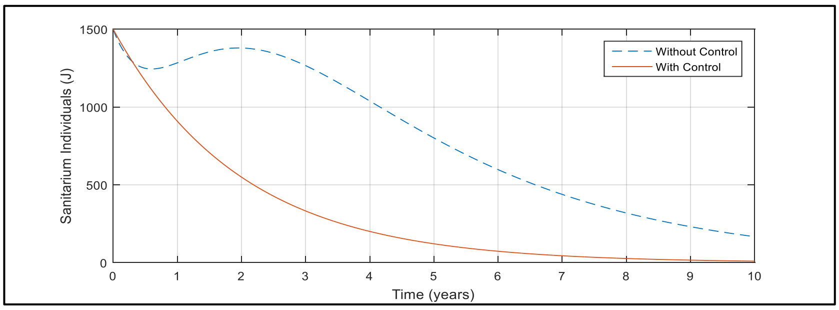

Figure 5: Graph showing the effects of applying all the control strategies on the population of sanitarium.

It can be observed from Figures 2 to 5 that with the application of optimal control strategies: vaccination, public campaign, case detection, quarantine, and sanitarium, there is a significant reduction in the number of exposed, infectious, quarantined, and sanitarium individuals at a given time. The simulation results presented in Figure 2 show that the implementation of all the control strategies is effective in reducing the number of exposed individuals for a period of six years, and four months after this period of time, it becomes ineffective. Furthermore, the simulation results in Figure 3 revealed that when all the control strategies are implemented, the number of infected individuals reduces significantly for the first seven years as compared to when the control strategies were not implemented. This result suggests that the implementation of all control strategies is less beneficial after approximately seven years' time. The simulation results in Figures 4 and 5 clearly show that implementing all the control strategies is highly beneficial in reducing the number of individuals in the quarantined and sanitarium classes throughout the period of implementation. Therefore, with respect to the simulation results presented, shows that the eradication of tuberculosis infection is possible.

The Control profile of the extended model

The control profiles are presented in Figure 6 to Figure 10.

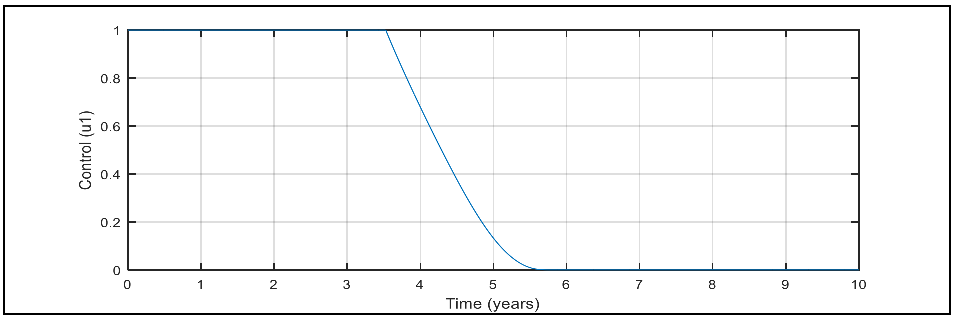

Figure 6: The profile of the control variable (u_1)

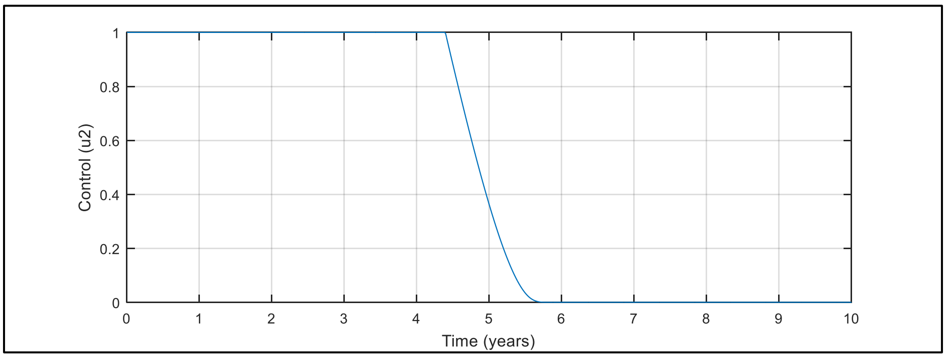

Figure 7: The profile of the control variable (u_2)

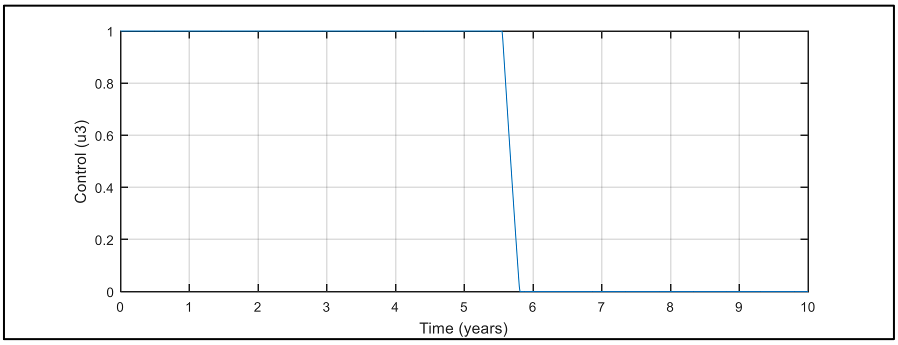

Figure 8: The profile of the control variable, (u_3)

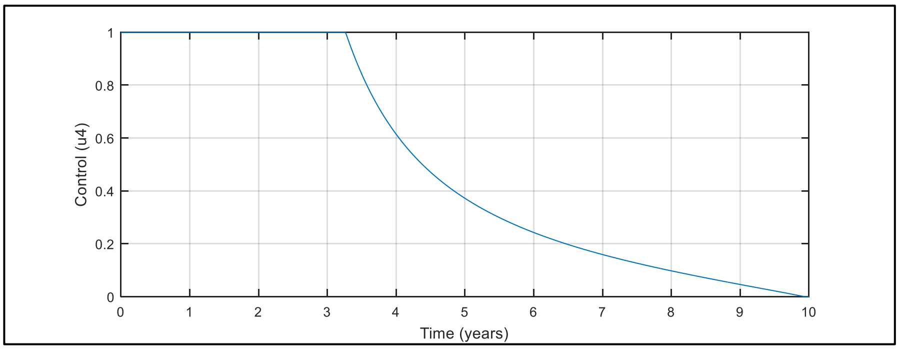

Figure 9: The profile of the control variable, (u_4)

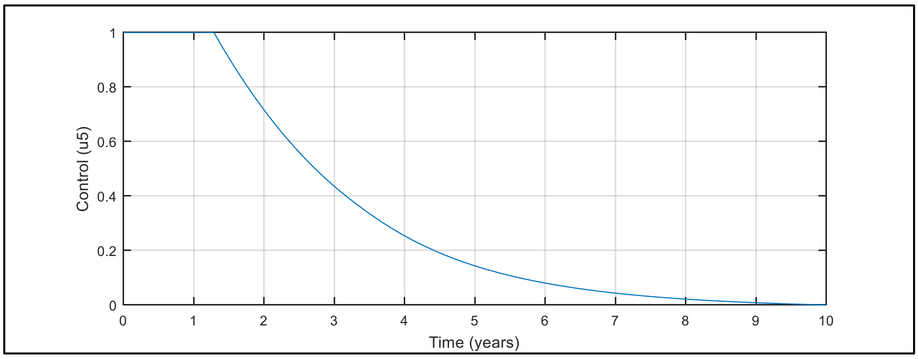

Figure 10: The profile of the control variable, (u_5)

Interpretation of the control profiles

The simulation results presented in Figure 6 to Figure 10 are the control profiles of the time-dependent optimal control variables $u_1, u_2, u_3, u_4,$ and u_5 respectively. It can be observed that the control variable u_1 is at maximum level (i.e. $u_{1\max} = 1.0000$) at $t = 0$ and remains constant for t = 3 years and 8 months before it gradually drops to its minimum level $\left(\text{i.e } u_{1\min} = 0\right)$ at the final time t = 5 years and 6 months. The control variable u_2 starts at maximum level $\left(\text{i.e. } u_{2\max} = 1.0000\right)$ at $t = 0$ and remains constant for t = 4 years and 5 months before it sharply drops to its minimum level $\left(\text{i.e. } u_{2\min} = 0\right)$ at the final t = 5years, 8months. The control variable u_3 remains at its maximum level $\left(\text{i.e. } u_{3\max} = 1.0000\right)$ at t = 5years, 7months and finally drops to its minimum level $\left(\text{i.e. } u_{3\min} = 0\right)$ at the final time t = 5years, 10months. The control variable u_4 is at the maximum level $\left(\text{i.e. } u_{4\max} = 1.0000\right)$ at $t = 0$

and remains constant for t = 3years, 4months before it gradually drops to its minimum level $(\text{i.e. } u_{4\,\min} = 0)$ at the final time t = 9years, 10months. The control variable u_5 is at the maximum level $(\text{i.e. } u_{5\,\max} = 1.0000)$ at $t = 0$ and remains constant for t = 1year, 4months before it gradually drops to its minimum level $(\text{i.e. } u_{5\,\min} = 0)$ at the final time t = 9years.

The analysis and interpretation of the graph of the control values

The controls u_1, u_2, u_3, u_4 and u_5 were used to optimize the objective function and the following observations were made:

The optimal control values observed are:

$u_1 = 0.9999$

$u_2 = 0.9999$

$u_3 = 0.0018$

$u_4 = 0.8000$

$u_5 = 0.0000575$

Now the proportion of each control needed to achieve effective control of TB in a population in terms of percentage is computed as follows:

Proportion of $u_1 = \dfrac{u_1}{u_1 + u_2 + u_3 + u_4 + u_5}$

$$u_1 = \frac{0.9999}{2.8017} \times 100 = 35.69\%$$

Proportion of $u_2 = \dfrac{u_2}{u_1 + u_2 + u_3 + u_4 + u_5}$

$$u_2 = \frac{0.9999}{2.8017} \times 100 = 35.69\%$$

Proportion of $u_3 = \dfrac{u_3}{u_1 + u_2 + u_3 + u_4 + u_5}$

$$u_3 = \frac{0.0018}{2.8017} \times 100 = 00642\%$$

Proportion of $u_4 = \dfrac{u_4}{u_1 + u_2 + u_3 + u_4 + u_5}$

$$u_4 = \frac{0.8}{2.8017} \times 100 = 28.55\%$$

Proportion of $u_5 = \dfrac{u_5}{u_1 + u_2 + u_3 + u_4 + u_5}$

$$u_5 = \frac{0.0000575}{2.8017} \times 100 = 0.0021\%$$

These results imply that for Tuberculosis to be controlled effectively in a community, 35.69% effort on vaccination of newborn babies and susceptible individuals. 35.69% effort on public health campaign of susceptible individuals, 0.0642% of effort on case detection, 28.55% effort on quarantined of suspected is needed and 0.0021% effort on sanitarium of individuals infected with TB are required to be continuously implemented.

Conclusion

The optimal analysis of the non-autonomous control model considering five different control strategies (i.e., control effort on vaccination, public health campaign, case detection, quarantine, and sanitarium) is performed. A comparison between an optimal control system and a system without control is presented. The numerical simulation results further showed that continuous implementation of vaccination, public health campaigns, case detection, quarantine, and sanitariums can bring the TB outbreak under effective control.

The numerical simulation results of the optimal control model have shown that to minimize the number of cases of TB transmission in the population, there is a need for continuous implementation of the five control strategies, i.e., vaccination, public health campaigns, case detection, quarantine, and sanitarium.

Recommendations

i. Proper education and sensitization on TB should be given to the general public by the government and non-governmental organizations (NGO).
ii. Government at national, state, local level should create an awareness program for early diagnoses of TB disease.

iii. Health care workers should ensure that patients have completed their treatments.
iv. Government should implement a 35.69% control effort on vaccination of new births and susceptible individuals, a 35.69% effort on a public health campaign for susceptible individuals, a 0.0642% effort on TB case detection, a 28.55% effort on the quarantine of suspected TB cases, and a 0.0021% control effort on the sanitarium to eradicate tuberculosis infection.

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