Available online at http://scik.org
Commun. Math. Biol. Neurosci. 2021, 2021:56
https://doi.org/10.28919/cmbn/5734
ISSN: 2052-2541

A DETERMINISTIC MODEL FOR THE TRANSMISSION DYNAMICS OF TUBERCULOSIS (TB) WITH OPTIMAL CONTROL

DOMINIC OTOO[1], SHAIBU OSMAN[2,*], STEPHEN ATTA POKU[1], ELVIS KOBINA DONKOH[1]

[1]Department of Mathematics and Statistics, University of Energy and Natural Resources, Sunyani, Ghana

[2]Department of Basic Sciences, University of Health and Allied Sciences, Ho, Ghana

Abstract. In this paper, we employed a deterministic model in the analysis of the dynamics of Tuberculosis with a keen interest in vaccination and drug resistance as the first line of treatment. It was assumed that some of the susceptible population were vaccinated but with temporal immunity. This is due to the fact that vaccines do not confer permanent immunity. Moreover, Part of the infected individual after treatment grow resistance to the drug. Infective immigrants were also considered to be part of the population. The basic reproductive number for the model is estimated using the Next Generation Matrix method. The equilibrium points of the TB model and their local and global stability were determined. It was established that if the basic reproductive number was less than unity $(R_0 < 1)$, then the disease free equilibrium is stable and unstable if $R_0 > 1$. Furthermore, we investigated the optimal prevention, treatment and vaccination as control measures for the disease. It was established that the best control measure in combating Tuberculosis infections is prevention and vaccination of susceptible population.

Keywords: TB model; vaccination; reproductive number; local and global stability; optimal control.

2010 AMS Subject Classification: 92D30, 37M05.

*Corresponding author

E-mail address: shaibuo@yahoo.com

Received March 19, 2021

1. INTRODUCTION

Respiratory disease can be described as infections in which can be treated with time. Commonest respiratory infections include pneumonia, Tuberculosis, and flu. Chronic conditions such as asthma and Chronic Bronchitis are persistent and sometimes long lasting. The study of the determinate and distribution in the study of the existing population of health-related events and descriptive research based on regularly collected data for this purpose according to [1] is known as Epidemiology.

In epidemiology, we try to find the factors associated with diseases and how we may protect humans and animals from such diseases. Proving that a certain risk factor directly causes a disease is difficult, if not impossible. This can only lead us to establish that this risk factor results in a higher incidence of disease among the population exposed to a certain risk factor. Tuberculosis is among the most ancient diseases worldwide. It is very contagious. The causative organism, Mycobacterium tuberculosis was discovered by the German Microbiologist, Robert Koch in 1882 [2].

TB which attacks the lungs is known as pulmonary TB. If any organ other than the lungs is affected by the illness, it is known as extra pulmonary TB. As with pulmonary TB, extra pulmonary TB is not as contagious. Through coughing, singing, and sneezing, pulmonary TB is spread from a sick TB patient as a droplet infection. Inhalation by an uninfected individual of these droplets may cause infection. With the frequency and duration of contact with people who have the disease, the risk of contracting TB rises.

In 1993, the WHO decreed TB a global epidemic [3]. It is estimated that the risk of contracting active TB after coming into contact with an infected person is between 5% and 10%, with a greater proportion of the disease playing a crucial role which happens in the very first few years after the initial infection with the arrival of HIV [4]. Drug-resistance TB is actually one of the world's key health issues today. Less than 50% of multi-drug resistance TB (MDR TB) patients are successfully treated, with HIV-coinfected patients showing poor results [5].

Biological models usually explain the transmission dynamics of infectious diseases and can determine the status of the disease in a population with time. The basic reproduction number is the threshold value that determines the persistence or die out of a disease in a population [6, 7, 8, 9].

Optimal control theory are usually employed in biological models to determine the best optimal control strategy in combating infections in a population [10, 11, 12, 13].

2. Model Description and Formulation

The model partitions the entire populace into six compartments accordant to their epidemiological status. We define $S(t)$, $V(t)$, $E(t)$, $I(t)$, $R_1(t)$ and $R(t)$ as the number of susceptible individuals, vaccinated individuals, exposed individuals, infectious individuals, individuals resistance to treatment and recovered individuals respectively at time $t \geq 0$.

Variables	Description
S	Susceptible persons
V	Vaccinated persons
E	Exposed persons
I	TB-Infected persons
R_1	Individuals resistant to treatment
R	Recovered persons

TABLE 1. Variable description

Parameters	**Description**
Λ	Recruitment of susceptible individuals
M	Immigrants into the susceptible and infectious compartments
α	Rate of inflow of immigrants into the susceptible compartment
σ	Rate at which the cured lose their immunity
μ	Rate of natural mortality
γ	Rate of vaccination of susceptible individuals
θ	Rate at which the vaccinated recover
β	Rate at which the susceptible individuals are exposed to Mtb
ρ	Rate at which unprotected individuals get infected
δ	Disease-induced death rate
κ	Rate of recovery after treatment
τ	Rate of resistance to the treatment
$(1-\alpha)$	Rate of inflows of immigrants into the infected compartment

TABLE 2. Parameter description

Table 1 and Table 2 show the variables and parameters used in the Tuberculosis model. Figure 1 shows the Tuberculosis (TB) model transmission dynamics.

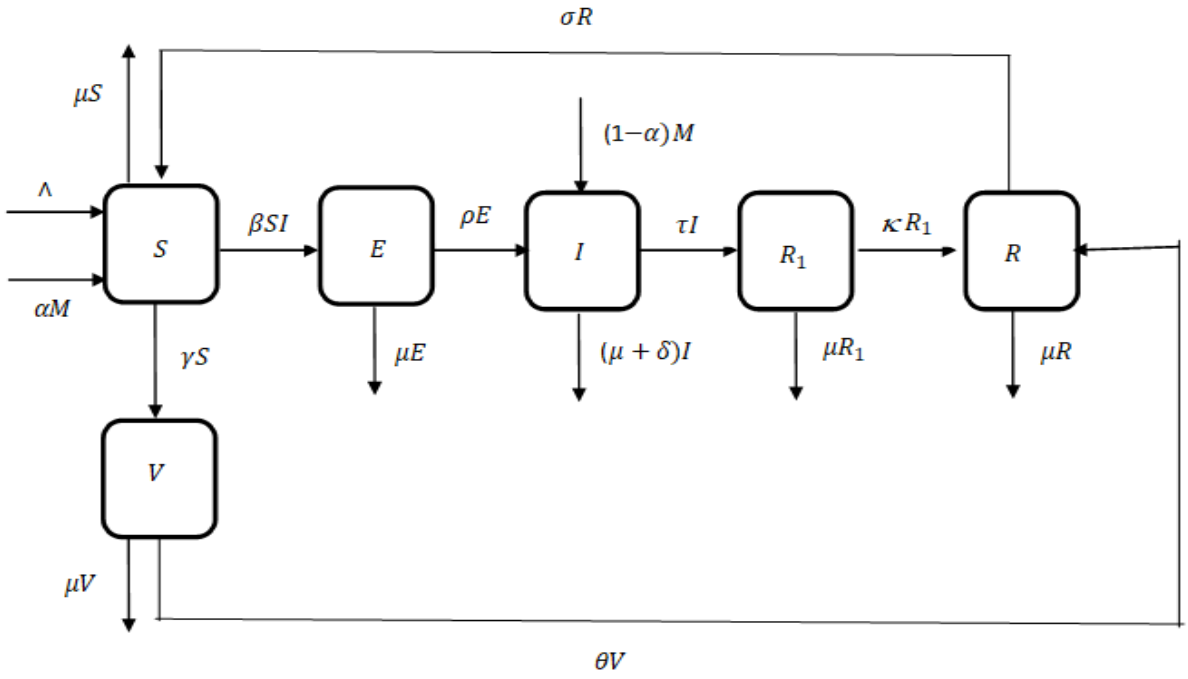

FIGURE 1. Flow diagram for the Tuberculosis disease transmission dynamics.

The following differential equations were obtained from the model flow diagram;

$$
\begin{aligned}
\frac{dS}{dt} &= \Lambda + \alpha M + \sigma R - \beta SI - (\gamma + \mu) S \\
\frac{dV}{dt} &= \gamma S - (\theta + \mu) V \\
\frac{dE}{dt} &= \beta SI - (\rho + \mu) E \\
\frac{dI}{dt} &= \rho E + (1 - \alpha) M - (\tau + \delta + \mu) I \\
\frac{dR_1}{dt} &= \tau I - (\kappa + \mu) R_1 \\
\frac{dR}{dt} &= \kappa R_1 + \theta V - (\sigma + \mu) R
\end{aligned} \tag{1}
$$

Thus the total population is given as;

$$N = S + V + E + I + R_1 + R \tag{2}$$

with initial conditions;

$$(S(0), V(0), E(0), I(0), R_1(0), R(0)) \in \mathrm{R}_+^6 \tag{3}$$

3. TUBERCULOSIS MODEL ANALYSIS

Tuberculosis (TB) model is about human population, hence model state variables ought to be non-negative and limited for all $t \geq 0$. In this section, we demonstrate that the TB model is numerically and epidemiologically sensible.

3.1. Positivity of the Solution. We prove the positivity of the variables in the model. Based on the concept of derivative of a function, the behavior of the function at a known point can be established [14, 15, 16].

Theorem 1. *Let the initial set be* $S(0)$,$V(0)$,$E(0)$,$I(0)$,$R_1(0)$,*and* $R(0)$, *be non-negative, then the solution set of* $\{S(t), V(t), E(t), I(t), R_1(t), R(t)\}$ *of the equation* (1) *is positive and bounded for all* $t > 0$ *, wherever they exist.*

Proof. From Equation (1), we can state that

$$\frac{dS}{dt} \geqslant -(\gamma+\mu+\beta I)S$$

$$\frac{dS}{S} \geqslant -(\gamma+\mu+\beta I)dt$$

$$In|S| \geqslant -(\gamma+\mu+\beta I)t+c$$

$$S(t) \geqslant ce^{-(\gamma+\mu+\beta I)t}$$

At $t=0$, $S(0) \geqslant c$

$$S(t) \geqslant S(0)e^{-(\gamma+\mu+\beta I)t}$$

since

$$(\gamma+\mu+\beta I) > 0, S(t) \geqslant 0$$

Also

$$\frac{dV}{dt} \geqslant -(\theta+\mu)V$$

$$V(t) \geqslant ce^{-(\theta+\mu)t}$$

At $t=0$, $V(0) \geqslant c$

$$V(t) \geqslant V(0)e^{-(\theta+\mu)t}$$

since

$$(\theta+\mu)>0, V(t)\geqslant 0$$

Also

$$\frac{dE}{dt}\geqslant -(\rho+\mu)E$$

$$E(t)\geqslant ce^{-(\rho+\mu)t}$$

At $t=0,\ \ E(0)\geqslant c$

$$E(t)\geqslant E(0)e^{-(\rho+\mu)t}$$

since

$$(\rho+\mu)>0, E(t)\geqslant 0$$

Also,

$$\frac{dI}{dt}\geqslant -(\tau+\mu+\delta)I$$

$$I(t)\geqslant ce^{-(\tau+\mu+\delta)t}$$

At $t=0,\ \ I(0)\geqslant c$

$$I(t)\geqslant I(0)e^{-(\tau+\mu+\delta)t}$$

since

$$(\tau+\mu+\delta)>0, I(t)\geqslant 0$$

Also,

$$\frac{dR_1}{dt}\geqslant -(\kappa+\mu)R_1$$

$$R_1(t)\geqslant ce^{-(\kappa+\mu)t}$$

At $t=0,\ \ R_1(0)\geqslant c$

$$R_1(t)\geqslant R_1(0)e^{-(\kappa+\mu)t}$$

since

$$(\kappa+\mu)>0, R_1(t)\geqslant 0$$

Also

$$\frac{dR}{dt} \geqslant -(\sigma+\mu)R$$

$$R(t) \geqslant ce^{-(\sigma+\mu)t}$$

At $t=0,\ \ R(0) \geqslant c$

$$R(t) \geqslant R(0)\,e^{-(\sigma+\mu)t}$$

since

$$(\sigma+\mu) > 0, R(t) \geqslant 0$$

□

3.2. Region of Feasibility.

Theorem 2. *The positive solution set is a positively invariant set of the model and is given by*

$$\Gamma = \left\{ (S,V,E,I,R_1,R) \in R_+^6 : N \leqslant \frac{\Lambda+M-\delta I}{\mu}, \mu \neq 0 \right\} \tag{4}$$

Proof.

$$N = S+V+E+I+R_1+R$$

$$\frac{dN}{dt} = \Lambda-\mu N+M-\delta I$$

$$\frac{dN}{\Lambda-\mu N+M-\delta I} = dt$$

$$-\frac{1}{\mu}\int\left(\frac{-\mu}{\Lambda-\mu N+M-\delta I}\right)dN = \int dt$$

$$-\frac{1}{\mu}In\,|\Lambda-\mu N+M-\delta I| = t+c$$

$$In\,|\Lambda-\mu N+M-dI| = -\mu t+c_1$$

$$\Lambda-\mu N+M-\delta I = c_2e^{-\mu t}$$

$$N(t) = \frac{\Lambda+M-\delta I-c_2e^{-\mu t}}{\mu}$$

$$At\ \ t=0,\ N(0)=N_0,\ I(0)=I_0$$

$$N_0 = \frac{\Lambda+M-\delta I_0-c_2}{\mu}$$

$$c_2 = \Lambda+M-\delta I_0-\mu N_0$$

$$N(t) = \frac{\Lambda + M - \delta I - (\Lambda + M - \delta I_0 - \mu N_0)\, e^{-\mu t}}{\mu}$$

So as $t \to \infty$, $N \to \frac{\Lambda + M - \delta I}{\mu} \in R_+$

Therefore, Γ is positive invariant. □

3.3. Existence of Disease-Free Equilibrium Point. The disease-free equilibrium of the dynamical system (1) is obtained by setting $\frac{dS}{dt} = \frac{dV}{dt} = \frac{dE}{dt} = \frac{dI}{dt} = \frac{dR_1}{dt} = \frac{dR}{dt} = 0$ and since there is no disease $E = I = R_1 = R = 0$

$$\Lambda + \alpha M - (\gamma + \mu) S = 0 \quad \Rightarrow S = \frac{\Lambda + \alpha M}{\gamma + \mu}$$

Therefore, the disease-free equilibrium of the dynamical system (1) is

$$C^0 = \left(S^0, V^0, E^0, I^0, R_1^0, R^0\right) = \left(\frac{\Lambda + \alpha M}{\gamma + \mu}, \frac{\gamma(\Lambda + \alpha M)}{(\theta + \mu)(\gamma + \mu)}, 0, 0, 0, 0\right) \tag{5}$$

3.4. The Basic Reproductive Number, R_o. The basic reproductive number can be computed utilizing the cutting edge matrix approach. It is utilized to predict the stability of the disease equilibrium. The basic reproductive number is characterized as the quantity of secondary infections that one tainted person can create in a completely susceptible populace [17]. According to [17, 18], the next generation matrix is defined as $K = FG^{-1}$ and $R_0 = \rho\left(FG^{-1}\right)$, where $\rho\left(FG^{-1}\right)$ denotes the spectral radius of FG^{-1}.

Using the Next Generation Matrix, we consider only the infectious compartments in the system of differential equation in 4.2.1

$$\begin{aligned} \frac{dE}{dt} &= \beta SI - (\rho + \mu) E \\ \frac{dI}{dt} &= \rho E + (1 - \alpha) M - (\tau + \delta + \mu) I \\ \frac{dR_1}{dt} &= \tau I - (\kappa + \mu) R_1 \end{aligned} \tag{6}$$

Let f be the count of emerging infection moving into the system and g be the count of infections existing the system.

$f = (\beta SI,\ 0,\ 0)$ and $g = ((\rho + \mu) E,\ -\rho E - (1 - \alpha) M + (\tau + \mu + \delta) I,\ -\gamma I + (k + \mu) R_1)$

The Jacobian matrix of f and g are obtained by

$$F = \begin{pmatrix} 0 & \beta S & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix} \text{ and } G = \begin{pmatrix} \rho+\mu & 0 & 0 \\ -\rho & \tau+\mu+\delta & 0 \\ 0 & -\gamma & k+\mu \end{pmatrix} \tag{7}$$

But $R_0 = \rho\left(FG^{-1}\right)$

From the relation FG^{-1} , the inverse of G can be calculated:

$$G^{-1} = \begin{pmatrix} \frac{(\gamma+\mu+\delta)}{(\rho+\mu)(\tau+\mu+\delta)} & 0 & 0 \\ \frac{\rho}{(\rho+\mu)(\tau+\mu+\delta)} & \frac{1}{(\tau+\mu+\delta)} & 0 \\ \frac{\gamma\rho}{(\rho+\mu)(\tau+\mu+\delta)(k+\mu)} & \frac{\gamma}{(\tau+\mu+\delta)(k+\mu)} & \frac{(\gamma+\mu+\delta)}{(\tau+\mu+\delta)(k+\mu)} \end{pmatrix} \tag{8}$$

Computing the product of FG^{-1}

$$FG^{-1} = \begin{pmatrix} 0 & \beta S & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix} \begin{pmatrix} \frac{(\gamma+\mu+\delta)}{(\rho+\mu)(\tau+\mu+\delta)} & 0 & 0 \\ \frac{\rho}{(\rho+\mu)(\tau+\mu+\delta)} & \frac{1}{(\tau+\mu+\delta)} & 0 \\ \frac{\gamma\rho}{(\rho+\mu)(\tau+\mu+\delta)(k+\mu)} & \frac{\gamma}{(\tau+\mu+\delta)(k+\mu)} & \frac{(\gamma+\mu+\delta)}{(\tau+\mu+\delta)(k+\mu)} \end{pmatrix}$$

$$FG^{-1} = \begin{pmatrix} \frac{\beta\rho S}{(\rho+\mu)(\tau+\mu+\delta)} & \frac{\beta S}{(\tau+\mu+\delta)} & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix} \tag{9}$$

By selecting the dominant eigenvalue of FG^{-1}, the basic reproductive number is

$$R_0 = \frac{\beta\rho S}{(\rho+\mu)(\tau+\mu+\delta)} \tag{10}$$

At the disease-free equilibrium, we substitute $S = \frac{\Lambda+\alpha M}{\gamma+\mu}$ into the basic reproductive number, R_0.

This therefore implies that,

$$R_0 = \frac{\beta\rho(\Lambda+\alpha M)}{(\gamma+\mu)(\rho+\mu)(\tau+\mu+\delta)} \tag{11}$$

3.5. Local Stability of The Disease-Free Equilibrium Point.

Theorem 3. *The disease-free equilibrium point C^o of the dynamical system* (1) *is locally asymptotically stable if $R_0 < 1$ and unstable $R_0 > 1$.*

Proof. The Jacobian matrix of the dynamical system (1) at the DFE point $C^0 = \left(\frac{\Lambda+\alpha M}{\gamma+\mu}, \frac{\gamma(\Lambda+\alpha M)}{(\theta+\mu)(\gamma+\mu)}, 0, 0, 0, 0\right)$ is given by;

(12)
$$J\left(C^0\right) = \begin{pmatrix} -(\gamma+\mu) & 0 & 0 & -\frac{\beta(\Lambda+\alpha M)}{\gamma+\mu} & 0 & \sigma \\ \gamma & -(\theta+\mu) & 0 & 0 & 0 & 0 \\ 0 & 0 & -(\rho+\mu) & \frac{\beta(\Lambda+\alpha M)}{\gamma+\mu} & 0 & 0 \\ 0 & 0 & \rho & -(\tau+\mu+\delta) & 0 & 0 \\ 0 & 0 & 0 & \tau & -(\kappa+\mu) & 0 \\ 0 & \theta & 0 & 0 & \kappa & -(\sigma+\mu) \end{pmatrix}$$

The corresponding characteristics equation for the eigenvalues, λ is $\left|\lambda I - J\left(C^0\right)\right| = 0$ □

(13)
$$\begin{vmatrix} \lambda+(\gamma+\mu) & 0 & 0 & \frac{\beta(\Lambda+\alpha M)}{\gamma+\mu} & 0 & -\sigma \\ -\gamma & \lambda+(\theta+\mu) & 0 & 0 & 0 & 0 \\ 0 & 0 & \lambda+(\rho+\mu) & -\frac{\beta(\Lambda+\alpha M)}{\gamma+\mu} & 0 & 0 \\ 0 & 0 & -\rho & \lambda+(\tau+\mu+\delta) & 0 & 0 \\ 0 & 0 & 0 & -\tau & \lambda+(\kappa+\mu) & 0 \\ 0 & -\theta & 0 & 0 & -\kappa & \lambda+(\sigma+\mu) \end{vmatrix} = 0$$

$$(\lambda+\kappa+\mu)\left[(\lambda+\gamma+\mu)(\lambda+\theta+\mu)(\lambda+\sigma+\mu) - \gamma\theta\sigma\right]$$

(14)
$$\left[(\lambda+\tau+\mu+\delta)(\lambda+\rho+\mu) - \frac{\rho\beta(\Lambda+\alpha M)}{\gamma+\mu}\right] = 0$$

$$\lambda+\kappa+\mu = 0 \qquad \Rightarrow \lambda_1 = -\kappa-\mu$$

$$(\lambda+\gamma+\mu)(\lambda+\theta+\mu)(\lambda+\sigma+\mu)-\sigma\gamma\theta=0$$

$$\lambda^3+(\gamma+\theta+\sigma+3\mu)\lambda^2+[(\theta+\mu)(\sigma+\mu)(\gamma+\mu)(\theta+\sigma+2\mu)]\lambda+\left[\mu^3+(\gamma+\theta+\sigma)\mu^2+(\gamma\theta+\sigma\gamma+\sigma\theta)\mu\right]=0$$

This is,

$$\lambda^3+Q\lambda^2+R\lambda+T=0 \tag{15}$$

According to Routh-Hurwith criterion, since $Q>0$, $R>0$ and $T>0$ λ_2, λ_3 and λ_4 will have negative real part as roots.

Also;

$$(\lambda+\rho+\mu)(\lambda+\tau+\mu+\delta)-\frac{\rho\beta(\Lambda+\alpha M)}{\gamma+\mu}=0$$

$$\lambda^2+(\rho+\tau+\delta+2\mu)\lambda+(\rho+\mu)(\tau+\mu+\delta)-\frac{\rho\beta(\Lambda+\alpha M)}{\gamma+\mu}=0$$

The roots, λ_5 and λ_6 , of this characteristic polynomial will have negative real part if and only if

$$(\rho+\mu)(\tau+\mu+\delta)-\frac{\rho\beta(\Lambda+\alpha M)}{\gamma+\mu}>0 \tag{16}$$

$$1-\frac{\rho\beta(\Lambda+\alpha M)}{(\gamma+\mu)(\rho+\mu)(\tau+\mu+\delta)}>0$$

$$1-R_0>0$$

$$R_0<1$$

Therefore, C^0 is asymptotically stable since $R_0<1$ and unstable if $R_0>1$

3.6. Global Stability of The Disease-Free Equilibrium Point.

Theorem 4. *The disease-free equilibrium point C^0 of the dynamical system* (1) *is globally asymptotically stable in* Λ *if* $R_0<1$ *and unstable* $R_0>1$.

Proof. Using the Perron eigenvector to prove the global stability of the disease free equilibrium as in [19, 20] we apply the matrix-theoretic method. In the dynamical system, the disease compartment is $x=\begin{pmatrix}E & I & R_1\end{pmatrix}^T\in R^3$ and the non-disease compartment is $y\in R^6$

Taking the same path as[19, 20],

let us set

$$f(x,y) := (F-G)x - F(x,y) + G(x,y) \tag{17}$$

Then, the equation of the disease compartment can be written as

$$x^1 = (F-G)x - f(x,y) \tag{18}$$

□

Theorem 5. *Let R_o be defined as in 4.8. Then the threshold property holds for system* (1)

Proof. Using the instrument provided in subsection 3.4.3 and the conditions outlined in the theorem 3.4.3 in chapter 3, we set the Lyapunov function for the disease-free equilibrium (DFE). We first find w^T (the left eigenvector of the non-negative matrix $G^{-1}F$)

$$G^{-1}F = \begin{pmatrix} \frac{1}{(\rho+\mu)} & 0 & 0 \\ \frac{\rho}{(\rho+\mu)(\gamma+\mu+\delta)} & \frac{1}{(\gamma+\mu+\delta)} & 0 \\ \frac{\gamma\rho}{(\rho+\mu)(\gamma+\mu+\delta)(\kappa+\mu)} & \frac{\gamma}{(\gamma+\mu+\delta)(\kappa+\mu)} & \frac{1}{(\kappa+\mu)} \end{pmatrix} \begin{pmatrix} 0 & \beta S & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix}$$

$$= \begin{pmatrix} 0 & \frac{\beta S}{(\rho+\mu)} & 0 \\ 0 & \frac{\rho\beta S}{(\rho+\mu)(\gamma+\mu+\delta)} & 0 \\ 0 & \frac{\rho\beta\gamma S}{(\rho+\mu)(\gamma+\mu+\delta)(\kappa+\mu)} & 0 \end{pmatrix}$$

$$= \begin{pmatrix} 0 & R_0\frac{(\gamma+\mu+\delta)}{\rho} & 0 \\ 0 & R_0 & 0 \\ 0 & R_0\frac{\gamma}{\kappa+\mu} & 0 \end{pmatrix}$$

$$\Rightarrow \; w^T = \begin{pmatrix} 0 & R_0\frac{(\gamma+\mu+\delta)}{\rho} & 0 \\ 0 & R_0 & 0 \\ 0 & R_0\frac{\gamma}{\kappa+\mu} & 0 \end{pmatrix} \begin{pmatrix} n_1 \\ n_2 \\ n_3 \end{pmatrix} = \begin{pmatrix} n_1 \\ n_2 \\ n_3 \end{pmatrix} R_0$$

$$\Rightarrow \; R_0\frac{(\gamma+\mu+\delta)}{\rho}n_2 = R_0 n_1, \;\; R_0 n_2 = R_0 n_2 \text{ and } R_0\frac{\gamma}{\kappa+\mu}n_2 = R_0 n_3$$

$\therefore\ w^T = \begin{pmatrix} \frac{\gamma+\mu+\delta}{\rho} & 1 & \frac{\gamma}{\kappa+\mu} \end{pmatrix}$ and any multiple of this becomes our eigenvector.

From equation (15),

$$x^1 = (F-G)x - f(x,y)$$

That is $f(x,y) = (F-G)x - x^1$

(19)

$$f(x,y) = \left[\begin{pmatrix} 0 & \beta S & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix} - \begin{pmatrix} \rho+\mu & 0 & 0 \\ -\rho & \tau+\mu+\delta & 0 \\ 0 & -\gamma & \kappa+\mu \end{pmatrix} \right] x - \begin{pmatrix} \beta SI \\ 0 \\ 0 \end{pmatrix} + \begin{pmatrix} (\rho+\mu)E \\ -\rho E + (1-\alpha)M + (\tau+\mu+\delta)I \\ -\gamma I + (\kappa+\mu)R_1 \end{pmatrix}$$

$$= \begin{pmatrix} -(\rho+\mu) & \beta S & 0 \\ \rho & -(\tau+\mu+\delta) & 0 \\ 0 & \gamma & -(\kappa+\mu) \end{pmatrix} \begin{pmatrix} E \\ I \\ R_1 \end{pmatrix} + \begin{pmatrix} -\beta SI + (\rho+\mu)E \\ -\rho E + (1-\alpha)M + (\tau+\mu+\delta)I \\ -\gamma I + (\kappa+\mu)R_1 \end{pmatrix}$$

$$= \begin{pmatrix} \beta SI - (\rho+\mu)E \\ \rho E - (\tau+\mu+\delta)I \\ \gamma I - (\kappa+\mu)R_1 \end{pmatrix} + \begin{pmatrix} -\beta SI + (\rho+\mu)E \\ -\rho E + (1-\alpha)M + (\tau+\mu+\delta)I \\ -\gamma I + (\kappa+\mu)R_1 \end{pmatrix} = 0$$

where $\alpha = 1$ at the disease-free equilibrium

Therefore, $f(x,y) = 0$ and this satisfies the demand of Theorem 5. The Lyapunov function D as $D = w^T G^{-1} x$

(20)
$$D = \begin{pmatrix} \frac{\gamma+\mu+\delta}{\rho} & 1 & \frac{\gamma}{\kappa+\mu} \end{pmatrix} \begin{pmatrix} \frac{1}{(\rho+\mu)} & 0 & 0 \\ \frac{\rho}{(\rho+\mu)(\gamma+\mu+\delta)} & \frac{1}{(\gamma+\mu+\delta)} & 0 \\ \frac{\rho\gamma}{(\rho+\mu)(\gamma+\mu+\delta)(\kappa+\mu)} & \frac{\gamma}{(\gamma+\mu+\delta)(\kappa+\mu)} & \frac{1}{(\kappa+\mu)} \end{pmatrix} \begin{pmatrix} E \\ I \\ R_1 \end{pmatrix}$$

$$= \begin{pmatrix} \frac{\gamma+\mu+\delta}{\rho} & 1 & \frac{\gamma}{\kappa+\mu} \end{pmatrix} \begin{pmatrix} \frac{1}{(\rho+\mu)}E \\ \frac{\rho}{(\rho+\mu)(\gamma+\mu+\delta)}E + \frac{1}{(\gamma+\mu+\delta)}I \\ \frac{\rho\gamma}{(\rho+\mu)(\gamma+\mu+\delta)(\kappa+\mu)}E + \frac{\gamma}{(\gamma+\mu+\delta)(\kappa+\mu)}I + \frac{1}{(\kappa+\mu)}R_1 \end{pmatrix}$$

$$= \left(\left(\frac{\gamma+\mu+\delta}{\rho(\rho+\mu)} + \frac{\rho}{(\rho+\mu)(\gamma+\mu+\delta)} + \frac{\rho\gamma^2}{(\rho+\mu)(\gamma+\mu+\delta)(\kappa+\mu)^2} \right) E + \left(\frac{1}{(\gamma+\mu+\delta)} + \frac{\gamma^2}{(\gamma+\mu+\delta)(\kappa+\mu)^2} \right) I + \frac{\gamma}{(\kappa+\mu)^2} R_1 \right)$$

$$= \left(\frac{(\gamma+\mu+\delta)^2(\kappa+\mu)^2 + \rho^2(\rho+\mu)(\kappa+\mu) + \rho^2\gamma^2}{\rho(\rho+\mu)(\gamma+\mu+\delta)(\kappa+\mu)^2} \right) E + \left(\frac{(\kappa+\mu)^2+\gamma^2}{(\gamma+\mu+\delta)(\kappa+\mu)^2} \right) I + \left(\frac{\gamma}{(\kappa+\mu)^2} \right) R_1$$

But

$$D^1 = w^T V^{-1} x^1 = w^T V^{-1} (F-V)x - w^T V^{-1} f(x,y)$$

$$D^1 = (R_0 - 1)\, w^T x - w^T V^{-1} f(x,y)$$

Since $w^T > 0$, V^{-1} and $f(x,y) = 0$

$$\Rightarrow D^1 < 0 \text{ if } R_0 < 1$$

From the derivative of the Lyapunov function, $D^1 < 0$ when $R_0 < 1$, which satisfy the condition that the disease-free equilibrium is asymptotically stable, and unstable when $R_0 > 1$. □

3.7. Existence of The Endemic Equilibrium Point. The endemic equilibrium point is acquired by mounting the right-hand side of the dynamical system (4) equal to zero and solve them simultaneously. The endemic equilibrium point is $C^* = (S^*, V^*, E^*, I^*, R_1^*, R^*)$ where

$$\begin{aligned}
S^* &= \frac{(\theta+\mu)[(\Lambda+\alpha M)(\sigma+\mu)(\kappa+\mu)+\kappa\sigma\tau I^*]}{(\kappa+\mu)[(\sigma+\mu)(\theta+\mu)(\gamma+\mu+\beta I^*)-\sigma\theta\gamma]} \\
V^* &= \frac{\gamma[(\Lambda+\alpha M)(\sigma+\mu)(\kappa+\mu)+\kappa\sigma\tau I^*]}{(\kappa+\mu)[(\sigma+\mu)(\theta+\mu)(\gamma+\mu+\beta I^*)-\sigma\theta\gamma]} \\
E^* &= \frac{\beta(\theta+\mu)[(\Lambda+\alpha M)(\sigma+\mu)(\kappa+\mu)+\kappa\sigma\tau I^*]I^*}{(\rho+\mu)(\kappa+\mu)[(\sigma+\mu)(\theta+\mu)(\gamma+\mu+\beta I^*)-\sigma\theta\gamma]} \qquad (21) \\
R_1^* &= \frac{\tau I^*}{(\kappa+\mu)} \text{ and} \\
R^* &= \frac{1}{(\sigma+\mu)(\kappa+\mu)}\left[\kappa\tau I^* + \frac{\theta\gamma[(\Lambda+\alpha M)(\sigma+\mu)(\kappa+\mu)+\kappa\sigma\tau I^*]}{[(\sigma+\mu)(\theta+\mu)(\gamma+\mu+\beta I^*)-\sigma\theta\gamma]}\right]
\end{aligned}$$

I^* is the positive root of $AI^{*2} + BI^* + C = 0$ that is $I^* = \frac{-B+\sqrt{B^2-4AC}}{2A} > 0$

We have three possibilities of getting the value of I^*

(1) If $B^2 - 4AC < 0$, then there is no endemic equilibrium state;

(2) If $B^2 - 4AC = 0$, then again, the endemic equilibrium point does not exist.

(3) If $B^2 - 4AC > 0$, then the endemic equilibrium point exists when $AC < 0$

where $A = \kappa\sigma\tau\rho\beta\,(\theta+\mu)$

$$B = \beta\,(\sigma+\mu)\,(\kappa+\mu)\,[\rho\,(\theta+\mu)\,(\Lambda+\alpha M) + (\rho+\mu)\,(\tau+\mu+\delta)\,(\theta+\mu) + (\rho+\mu)\,(1-\alpha)\,M]$$

$$C = (\rho+\mu)\,(\kappa+\mu)\,[\theta\gamma\sigma - (\sigma+\mu)\,(\theta+\mu)\,(\gamma+\mu)]\,[(\tau+\mu+\delta) - (1-\alpha)\,M]$$

3.8. Local Stabilty of The Endemic Equilibrium Point.

Theorem 6. *The positive endemic equilibrium point C^* of the system (4.1) is locally asymptotically stable if $R_o > 1$*

Proof. The Jacobian matrix of the system of the equations (1) at the endemic point is

$$J(C^*) = \begin{pmatrix} M_{11} & 0 & 0 & M_{14} & 0 & \sigma \\ \gamma & M_{22} & 0 & 0 & 0 & 0 \\ M_{31} & 0 & M_{33} & M_{34} & 0 & 0 \\ 0 & 0 & \rho & M_{44} & 0 & 0 \\ 0 & 0 & 0 & \tau & M_{55} & 0 \\ 0 & \theta & 0 & 0 & \kappa & M_{66} \end{pmatrix} \tag{22}$$

where $M_{11} = -(\gamma+\mu+\beta I^*)$, $M_{14} = -\beta S^*$, $M_{22} = -(\theta+\mu)$, $M_{31} = -\beta I^*$, $M_{33} = -(\rho+\mu)$, $M_{34} = -\beta S^*$, $M_{44} = -(\tau+\mu+\delta)$, $M_{55} = -(\kappa+\mu)$, and $M_{66} = -(\sigma+\mu)$

The corresponding characteristic equation is $J(C^*)$ is denoted by $|\lambda I - J(C^*)| = 0$ and is given as

$$\begin{vmatrix} \lambda - M_{11} & 0 & 0 & M_{14} & 0 & \sigma \\ \gamma & \lambda - M_{22} & 0 & 0 & 0 & 0 \\ M_{31} & 0 & \lambda - M_{33} & M_{34} & 0 & 0 \\ 0 & 0 & \rho & \lambda - M_{44} & 0 & 0 \\ 0 & 0 & 0 & \tau & \lambda - M_{55} & 0 \\ 0 & \theta & 0 & 0 & \kappa & \lambda - M_{66} \end{vmatrix} = 0 \tag{23}$$

The matrix $J(C^*)$ is a strictly column diagonally dominant matrix. Again, all the diagonal entries are negative. Hence, all eigenvalues of $J(C^*)$ have negative real part. Now applying the Gershgorin circle theorem [21], C^* is locally asymptotically stable if $|M_{11}| > |M_{14}+\sigma|$, $|M_{22}| > |\gamma|$, $|M_{33}| > |M_{31}+M_{34}|$, $|M_{44}| > |\rho|$, $|M_{55}| > |\tau|$ and $|M_{66}| > |\theta+\kappa|$ □

3.9. Global Stabilty of The Endemic Equilibrium Point.

Theorem 7. *The dynamical system* (1) *is said to have an endemic equilibrium if $R_o > 1$, and it is globally asymptotically stable.*

Proof. Consider the Lyapunov function defined by

$$\begin{aligned} Q(C^*) &= \left(S-S^*-S^*In\tfrac{S^*}{S}\right)+\left(V-V^*-V^*In\tfrac{V^*}{V}\right)+\left(E-E^*-E^*In\tfrac{E^*}{E}\right) \\ &+ \left(I-I^*-I^*In\tfrac{I^*}{I}\right)+\left(R_1-R_1^*-R_1^*In\tfrac{R_1^*}{R_1}\right)+\left(R-R^*-R^*In\tfrac{R^*}{R}\right) \end{aligned} \tag{24}$$

Computing the derivative of Q along the solution of the dynamical system in (1) directly,

$$\begin{aligned} \frac{dQ}{dt} &= \left(\tfrac{S-S^*}{S}\right)\tfrac{dS}{dt}+\left(\tfrac{V-V^*}{V}\right)\tfrac{dV}{dt}+\left(\tfrac{E-E^*}{E}\right)\tfrac{dE}{dt} \\ &+ \left(\tfrac{I-I^*}{I}\right)\tfrac{dI}{dt}+\left(\tfrac{R_1-R_1^*}{R_1}\right)\tfrac{dR_1}{dt}+\left(\tfrac{R-R^*}{R}\right)\tfrac{dR}{dt} \end{aligned} \tag{25}$$

$$\begin{aligned} \tfrac{dQ(C^*)}{dt} &= \left(\tfrac{S-S^*}{S}\right)(\Lambda+\alpha M+\sigma R-(\gamma+\mu)S-\beta SI)+\left(\tfrac{V-V^*}{V}\right)(\gamma S-(\theta+\mu)S) \\ &+ \left(\tfrac{E-E^*}{E}\right)(\beta SI-(\rho+\mu)E)+\left(\tfrac{I-I^*}{I}\right)(\rho E+(1-\alpha)M-(\tau+\delta+\mu)I) \\ &+ \left(\tfrac{R_1-R_1^*}{R_1}\right)(\tau I-(\kappa+\mu)R_1)+\left(\tfrac{R-R^*}{R}\right)(\kappa R_1+\theta V-(\sigma+\mu)R) \end{aligned} \tag{26}$$

$$\begin{aligned} \tfrac{dQ}{dt} &= (\Lambda+M+\mu N^*+\gamma S^*+\sigma V^*+\rho E^*+(\tau+\delta)I^*+\kappa R_1^*+\sigma R^*+\beta S^*I) \\ &- \begin{pmatrix} \mu N+(\Lambda+\alpha M+\sigma R)\tfrac{S^*}{S}+\gamma\tfrac{SV^*}{V}+\beta\tfrac{SIE^*}{E}+\delta I \\ +(\rho E+(1-\alpha)M)\tfrac{I^*}{I}+\tau\tfrac{IR_1^*}{R_1}+(\kappa R_1+\theta V)\tfrac{R^*}{R} \end{pmatrix} \end{aligned} \tag{27}$$

$$\Rightarrow \frac{dQ}{dt} = Z-Y$$

where $Z = \Lambda+M+\mu N^*+\gamma S^*+\sigma V^*+\rho E^*+(\tau+\delta)I^*+\kappa R_1^*+\sigma R^*+\beta S^*I$

and $Y = \mu N+(\Lambda+\alpha M+\sigma R)\tfrac{S^*}{S}+\gamma\tfrac{SV^*}{V}+\beta\tfrac{SIE^*}{E}+\delta I+(\rho E+(1-\alpha)M)\tfrac{I^*}{I}+\tau\tfrac{IR_1^*}{R_1}+(\kappa R_1+\theta V)\tfrac{R^*}{R}$

Imposing the condition that $Z<Y$, the derivative of the Lyapunov function with respect to time is less than or equal to zero.

If $Z<Y$, then $\frac{dQ}{dt}\leqslant 0$

But $\dfrac{dQ}{dt}=0$ if and only if $S=S^*, V=V^*, E=E^*, I=I^*, R_1=R_1^*$ and $R=R^*$

Therefore, the endemic equilibrium point C^* is globally asymptotically stable in Γ if $Z<Y$

The largest invariant set in: $\left\{C^* = (S^*, V^*, E^*, I^*, R_1^*, R^*) \in \Gamma : \frac{dQ}{dt} = 0\right\}$ is a singleton, where C^* is the endemic equilibrium point. □

4. Extension of TB Model to Optimal Control

In this section, we will carry out an analysis of the optimal controls to ascertain its effects on the model. The optimal control problem is obtained by integrating the undermentioned control functions into the Tuberculosis model (1) and introducing an objective functional that desires to minimize the controls (u_1, u_2, u_3),

where u_1 is the vaccination of the susceptible population (S) as a control measure;

u_2 is the treatment of the infected individuals (I) as a control measure; and

u_3 is the education/sensitization of the exposed population (E) as a control measure.

By inserting the various controls, the system with the optimal controls becomes

$$\begin{aligned}
\frac{dS}{dt} &= \Lambda + \alpha M + \sigma R - u_1\gamma S - \mu S - \beta SI \\
\frac{dV}{dt} &= u_1\gamma S - (\theta + \mu)V \\
\frac{dE}{dt} &= \beta SI - (1-u_3)\rho E - \mu E \\
\frac{dI}{dt} &= (1-u_3)\rho E + (1-\alpha)M - u_2\tau I - (\delta + \mu)I \\
\frac{dR_1}{dt} &= u_2\tau I - (1-u_2)\kappa R_1 - \mu R_1 \\
\frac{dR}{dt} &= (1-u_2)\kappa R_1 - (1-u_1)\theta V - (\sigma + \mu)R
\end{aligned} \tag{28}$$

Let the optimal levels of the control set be u, which is Lesbesgue measurable and defined as:

$U = \left\{(u_1(t), u_2(t), u_3(t)) : 0 \leqslant u_1 < 1, 0 \leqslant u_2 < 1, 0 \leqslant u_3 < 1, 0 \leqslant t \leqslant t_f\right\}$

The problem is to find a control $u(t)$ and its associated state variables $S(t)$, $V(t)$, $E(t)$, $I(t)$, $R_1(t)$ and $R(t)$ to minimize the objective functional J given by

$$J = \min_{(u_1,u_2,u_3)} \int_0^{t_f} \left(a_1 I + a_2 R_1 + \sum_{i=1}^{3} w_i {u_i}^2\right) dt \tag{29}$$

That is $J = \min_{(u_1,u_2,u_3)} \int_0^{t_f} \left(a_1 I + a_2 R_1 + w_1 u_1^2 + w_2 u_2^2 + w_3 u_3^2\right) dt$ subject to the differential equations system (28).

Where a_1,a_2, w_1 , w_2 and w_3 are the weight constants to balance the terms in the integrals to abstain the ascendance of one over the other(s).

Also a_1, I and $a_2 R_1$ are the cost associated with the infected individuals and the individuals resistance to treatment, respectively; while $w_1 u_1^2$, $w_2 u_2^2$ and $w_3 u_3^2$ are the cost associated with vaccination, treatment and sensitization as preventive measures. t_f is the period of the intervention.

The purpose of inserting the controls is to minimize the number of infections and at the same time reduce the cost of treatment.

Our task at this point is to find the optimal functions; $u_1^*(t)$, $u_2^*(t)$, $u_3^*(t)$ such that $J(u_1^*(t), u_1^*(t), u_1^*(t)) = \min_{(u_1,u_2,u_3)} \in \cup J(u_1, u_2, u_3)$,

where $U = \{u_i : 0 \leqslant u_i(t) \leqslant 1, t \in [0, t_f], i = 1,2,3\}$ is referred to as the control set [22, 23, 24].

4.1. Pontryagin's Maximum Principle. Consider the Lagrangian function:

$$L(I, R_1, u_1, u_2, u_3, t) = a_1 I + a_2 R_1 + w_1 u_1^2 + w_2 u_2^2 + w_3 u_3^2 \tag{30}$$

The Pontryagin's maximum principle provides the essential condition that the optimal must satisfy. This change the system of the differential equation into minimization problem pointwise Hamiltonian (H) with respect to (u_1, u_2, u_3).

Hence, the Hamiltonian (H) becomes

$$H(S, V, E, I, R_1, R, t) = L(I, R_1, u_1, u_2, u_3, t) + \lambda_1 \frac{dS}{dt} + \lambda_2 \frac{dV}{dt} + \lambda_3 \frac{dE}{dt} + \lambda_4 \frac{dI}{dt} + \lambda_5 \frac{dR_1}{dt} + \lambda_6 \frac{dR}{dt}$$

where $\lambda_1, \lambda_2, \lambda_3, \lambda_4, \lambda_5,$ and , λ_6 are disjoint variables.

(31)

$$\begin{aligned} H &= a_1 I + a_2 R_1 + w_1 u_1^2 + w_2 u_2^2 + w_3 u_3^2 + \lambda_1 \{\Lambda + \alpha M + \sigma R - u_1 \gamma S - \mu S - \beta SI\} \\ &+ \lambda_2 \{u_1 \gamma S - (\theta + \mu) V\} + \lambda_3 \{\beta SI - (1 - u_3) \rho E - \mu E\} \\ &+ \lambda_4 \{(1 - u_3) \rho E + (1 - \alpha) M - u_2 \tau I - (\delta + \mu) I\} \\ &+ \lambda_5 \{u_2 \tau I - (1 - u_2) \kappa R_1 - \mu R_1\} \\ &+ \lambda_6 \{(1 - u_2) \kappa R_1 + (1 - u_1) \theta V - (\sigma + \mu) R\} \end{aligned}$$

considering the relation

$$\frac{d\lambda_i}{dt} = -\frac{\partial H}{\partial \overset{\bullet}{x}(t)} \tag{32}$$

By taking partial derivatives of the Hamiltonian function with respect to (S,V,E,I,R_1,R) and negating each of them, the following co-state variables are the solutions of the adjoint systems.

$$\begin{aligned}
\tfrac{d\lambda_1}{dt} &= -\tfrac{\partial H}{\partial S} = (\lambda_1-\lambda_2)\,u_1\gamma + (\lambda_1-\lambda_3)\,\beta I + \mu\lambda_1 \\
\tfrac{d\lambda_2}{dt} &= -\tfrac{\partial H}{\partial V} = (\lambda_2-\lambda_6)\,\theta + u_2\lambda_2 + u_1\theta\lambda_6 \\
\tfrac{d\lambda_3}{dt} &= -\tfrac{\partial H}{\partial E} = (1-u_3)\,(\lambda_3-\lambda_4)\,\rho + \mu\lambda_3 \\
\tfrac{d\lambda_4}{dt} &= -\tfrac{\partial H}{\partial I} = (\lambda_1-\lambda_3)\,\beta S + (\lambda_4-\lambda_5)\,u_2\tau + (\mu+\delta)\,\lambda_4 \\
\tfrac{d\lambda_5}{dt} &= -\tfrac{\partial H}{\partial R_1} = (1-u_2)\,(\lambda_5-\lambda_6)\,\kappa + \mu\lambda_5 \\
\tfrac{d\lambda_6}{dt} &= -\tfrac{\partial H}{\partial R} = (\lambda_6-\lambda_1)\,\sigma + \mu\lambda_6
\end{aligned} \tag{33}$$

The above satisfy the transversality condition;

$$\lambda_1(t_f) = \lambda_2(t_f) = \lambda_3(t_f) = \lambda_4(t_f) = \lambda_5(t_f) = \lambda_6(t_f) = 0 \tag{34}$$

Moreover, the characterization of the optimal control is obtained by solving

$$\frac{\partial H}{\partial u_i} = 0 \tag{35}$$

Where $u_i = u_i^*,\ i = 1,2,3$

$$\frac{\partial H}{\partial u_1} = 2w_1u_1 + (\lambda_2-\lambda_1)\,\gamma S - \lambda_6\theta V$$

$$\Rightarrow\ 2w_1u_1 + (\lambda_2-\lambda_1)\,\gamma S - \lambda_6\theta V = 0$$

$$\therefore u_1^* = \frac{(\lambda_1-\lambda_2)\,\gamma S^* + \lambda_6\theta V^*}{2w_1}$$

$$\frac{\partial H}{\partial u_2} = 2w_2u_2 - (\lambda_4-\lambda_5)\,\tau I^* - (\lambda_6-\lambda_5)\,\kappa R_1^*$$

$$\Rightarrow\ 2w_2u_2 - (\lambda_4-\lambda_5)\,\tau I^* - (\lambda_6-\lambda_5)\,\kappa R_1^* = 0$$

$$\therefore u_2^* = \frac{(\lambda_4-\lambda_5)\,\tau I^* + (\lambda_6-\lambda_5)\,\kappa R_1^*}{2w_2}$$

$$\frac{\partial H}{\partial u_3} = 2w_3u_3 - (\lambda_4-\lambda_3)\,\rho E^*$$

$$\Rightarrow\ 2w_3u_3 - (\lambda_4-\lambda_3)\,\rho E^* = 0$$

$$\therefore u_3^* = \frac{(\lambda_4 - \lambda_3)\rho E^*}{2w_3}$$

$$\begin{aligned} u_1^* &= \tfrac{(\lambda_2-\lambda_1)\gamma S^*+\lambda_6\theta V^*}{2w_1} \\ u_2^* &= \tfrac{(\lambda_4-\lambda_5)\tau I^*+(\lambda_6-\lambda_5)\kappa R_1^*}{2w_2} \\ u_1^* &= \tfrac{(\lambda_4-\lambda_3)\rho E^*}{2w_3} \end{aligned} \tag{36}$$

Theorem 8. *The optimal control vector* $\left(u_1^*(t), u_2^*(t), u_3^*(t)\right)$ *that maximizes the objective function* (J) *over* $\cup$ *is given by*

$$\begin{aligned} u_1^*(t) &= \max\left\{0, \min\left(1, \tfrac{(\lambda_2-\lambda_1)\gamma S^*+\lambda_6\theta V^*}{2w_1}\right)\right\} \\ u_2^*(t) &= \max\left\{0, \min\left(1, \tfrac{(\lambda_4-\lambda_5)\tau I^*+(\lambda_6-\lambda_5)\kappa R_1^*}{2w_2}\right)\right\} \\ u_3^*(t) &= \max\left\{0, \min\left(1, \tfrac{(\lambda_4-\lambda_3)\rho E^*}{2w_3}\right)\right\} \end{aligned} \tag{37}$$

where $\lambda_1, \lambda_2, \lambda_3, \lambda_4, \lambda_5,$ and , λ_6 are the solutions of equation (4.28) and (4.30)

Proof. The presence of optimal control is as an aftereffect of the convexity of the integral of J regarding u_1 , u_2 and u_3 , the Lipschitz property of the state system concerning the state factors from the earlier boundedness of the state arrangements [25]

The differential conditions administering the adjoint factors are acquired by separation of the Hamiltonian work, assessed at the ideal control. By standard control contentions including the limits on the control, we conclude

$$
\begin{aligned}
u_1^* &= \begin{cases} 0, \text{ if } \eta_1^* \leqslant 0 \\ \eta_1^*, \text{ if} 0 < \eta_1^* < 1 \\ 1, \text{if } \eta_1^* \geqslant 1 \end{cases} \\
u_2^* &= \begin{cases} 0, \text{ if } \eta_2^* \leqslant 0 \\ \eta_2^*, \text{ if} 0 < \eta_2^* < 1 \\ 1, \text{if } \eta_2^* \geqslant 1 \end{cases} \\
u_3^* &= \begin{cases} 0, \text{ if } \eta_3^* \leqslant 0 \\ \eta_3^*, \text{ if} 0 < \eta_3^* < 1 \\ 1, \text{if } \eta_3^* \geqslant 1 \end{cases}
\end{aligned} \tag{38}
$$

where $\eta_1^* = \frac{(\lambda_1-\lambda_2)\gamma S^* + \lambda_6 \theta V^*}{2w_1}$, $\eta_2^* = \frac{(\lambda_4-\lambda_5)\tau I^* + (\lambda_6-\lambda_5)\kappa R_1^*}{2w_2}$ and $\eta_3^* = \frac{(\lambda_4-\lambda_3)\rho E^*}{2w_3}$ □

5. NUMERICAL RESULTS

The state systems, adjoint equations, and the transversality terms are solved simultaneously to get the optimal strategies. The optimal problem is a two-point boundary-value problem with two abstracted boundary conditions at initial times $t = 0$ and $t = t_f$, where $t_f = 3$ months. This represents the period at which preventive strategies and treatment are expected to be stopped. The numerical simulation was conducted by solving the state equations, the adjoint equations, and the transversality conditions using Runge-Kutta fourth-order scheme by guessing the controls over a simulated time. We then use the current iteration of the state equation, the adjoint equations, and the transversality conditions by a backward method. Further iterations are done until values of the unknown variables at the previous iteration are very closed to those in at the present iteration [20, 26, 27, 28].

Parameter	Value	Reference
Λ	10	Assumed
α	0.9	[29]
β	0.05	Assumed
γ	0.2	Assumed
σ	0.4	Assumed
μ	0.01874	[30]
θ	0.1	Assumed
ρ	0.00114	[30]
δ	0.1577	[30]
κ	1.00	Assumed
τ	0.4	[31]

TABLE 3. Numerical Values

Table 3 shows the various parameter values used the TB model simulations.

5.1. Strategy 1: Treatment, Prevention and Vaccination of Susceptible. Objective functional was optimised by using treatment, prevention and vaccination as control measures. As a result of these control measures, there have been significant reduction of infections and an increase in the number of recoverpopulations as shown in Figure 2 and Figure 3.

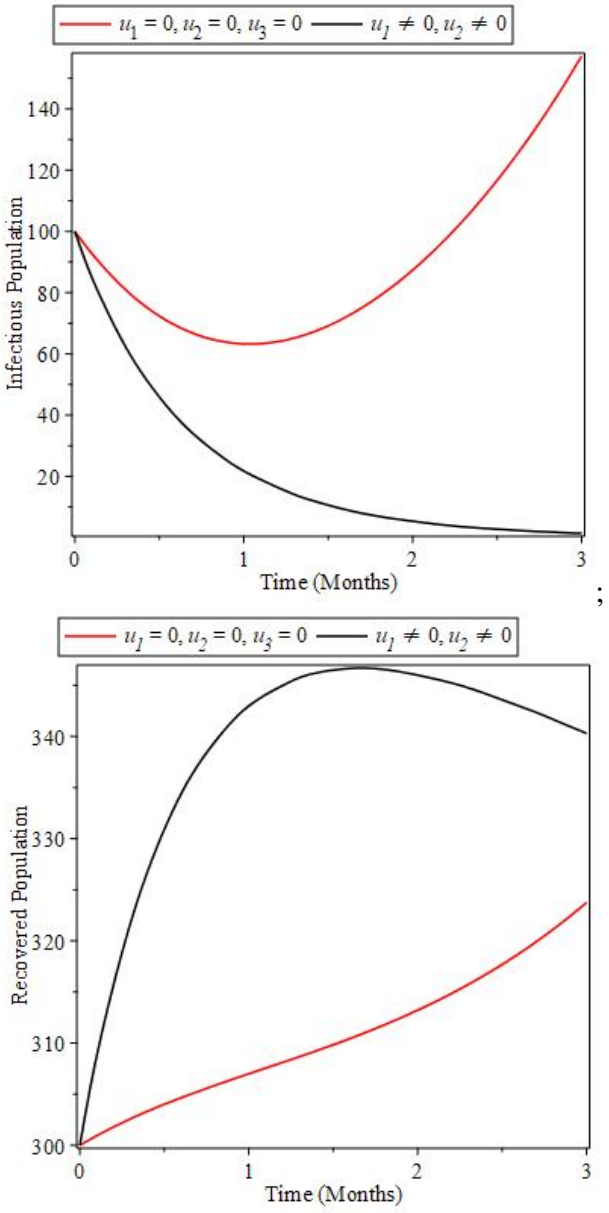

FIGURE 2. Optimal treatment of population infected.

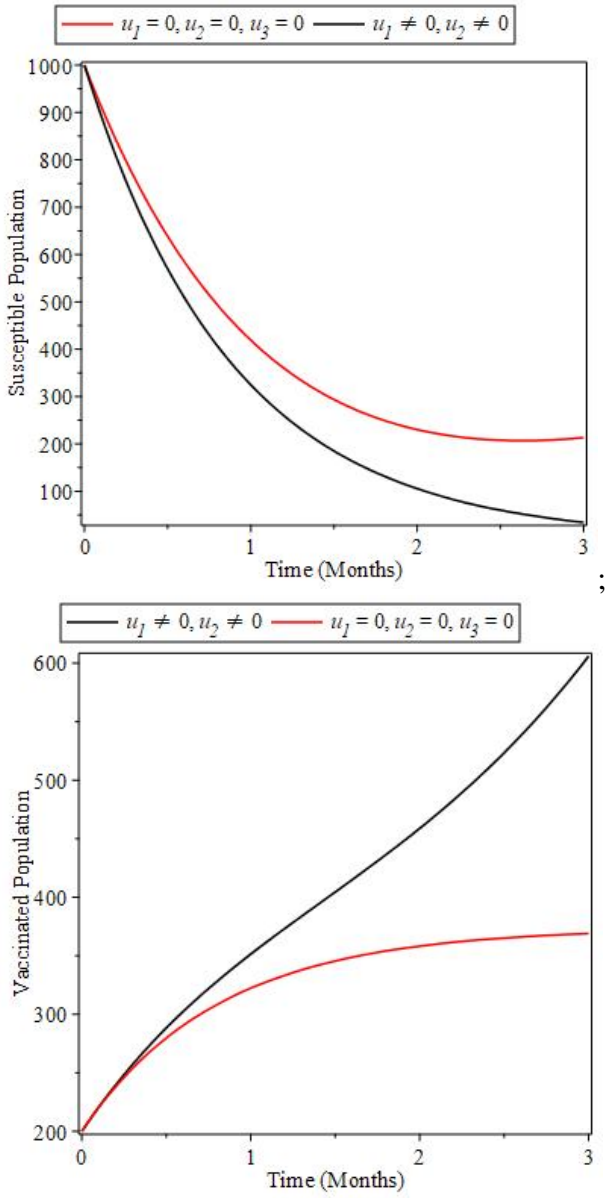

FIGURE 3. Optimal prevention and vaccination of population susceptible.

5.2. Strategy 2: Prevention and Treatment of Infected population. Objective functional was optimised by using prevention, vaccination and treatment as control measures. The outcome of these control measures indicates a reduction of population infected and increased recoveries. An indication that these variables have greatly impacted in the combat of the spread of infections as shown in Figure 4 and Figure 5.

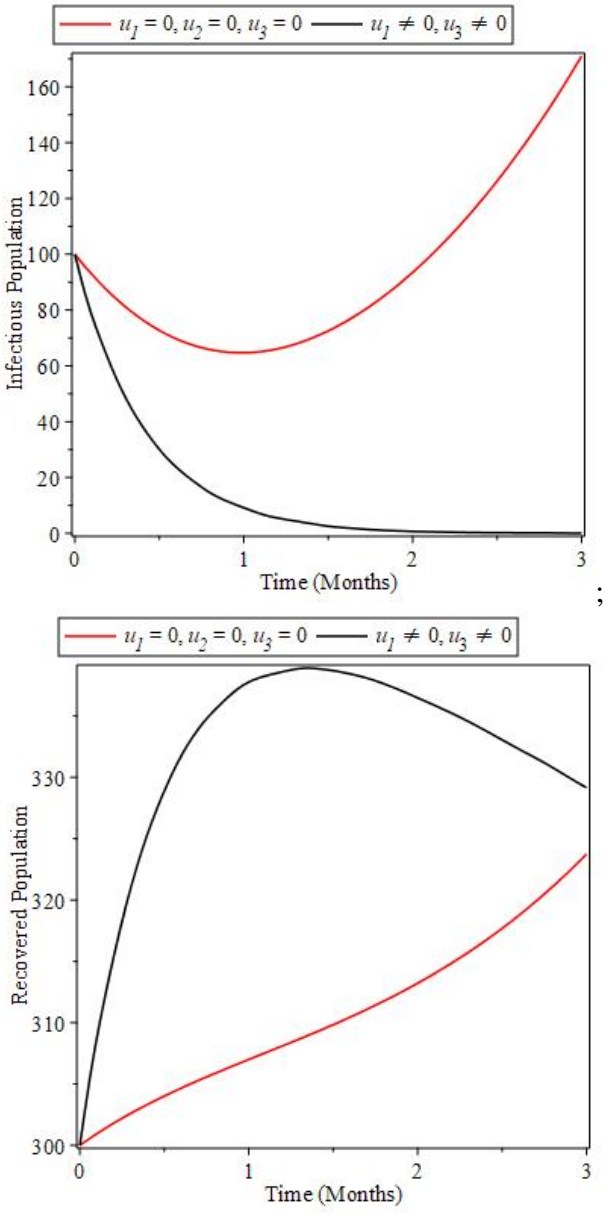

FIGURE 4. Optimal prevention and treatment of population infected.

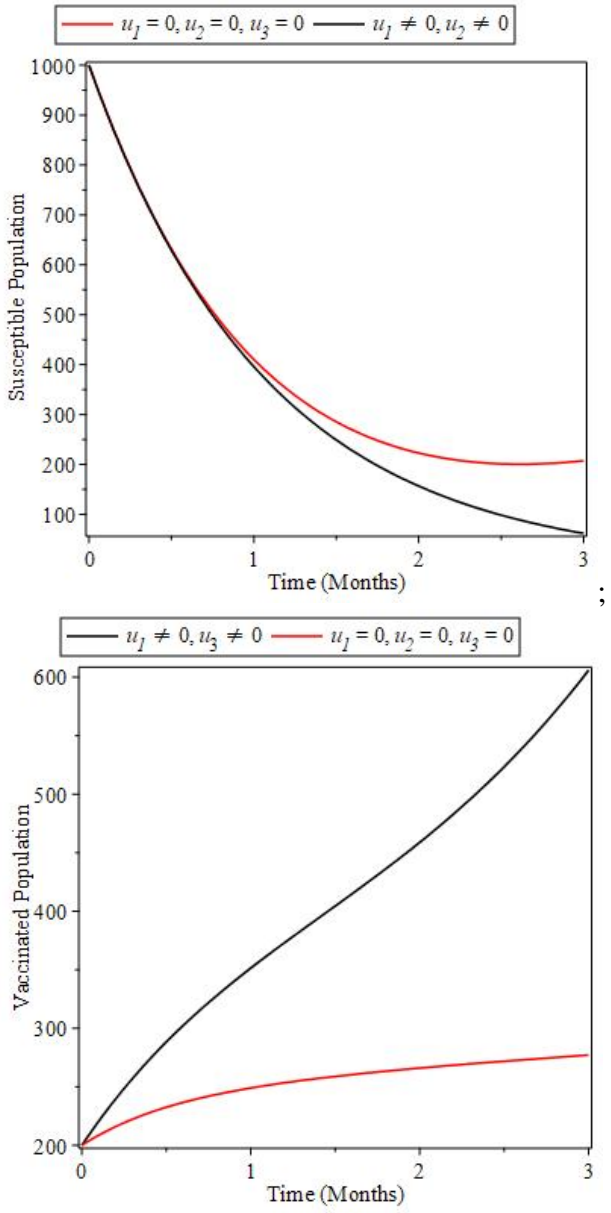

FIGURE 5. Optimal prevention and vaccination of susceptible population.

5.3. Strategy 3: Vaccination and Treatment of Infected population. Objective functional was optimised by using treatment, vaccination and prevention of suscepttible population as control measures. Figure 6 and Figure 7 show the effects of treatment and vaccination respectively. An increased in recovery population, a decreased in infectious population and a decreased in the number of population susceptible.

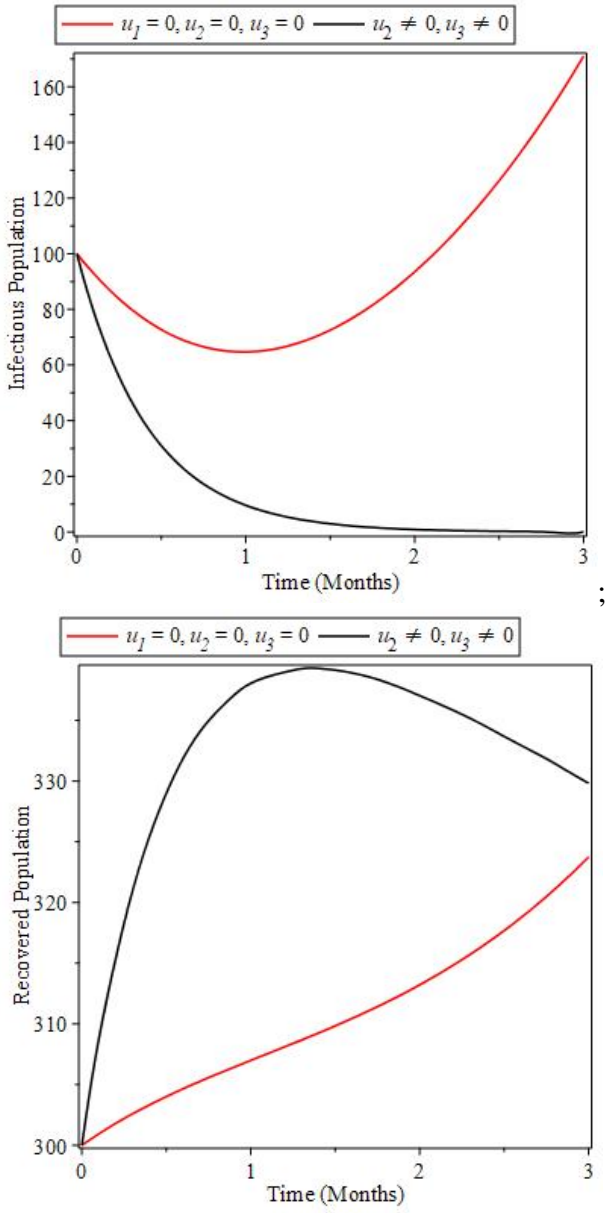

FIGURE 6. Optimal treatment of population infected.

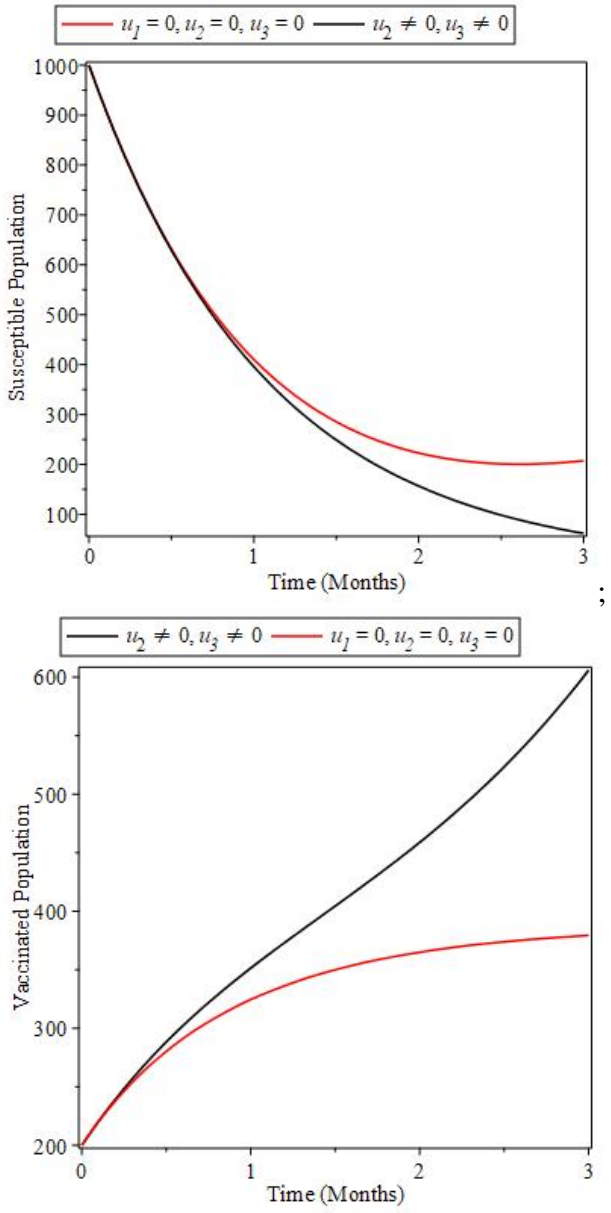

FIGURE 7. Optimal vaccination of susceptible population.

6. CONCLUSION

A deterministic model for tuberculosis was formulated and analysed. The basic reproductive number for the TB model is estimated using the Next Generation Matrix method.

The equilibrium points of the TB model and their local and global stability were determined. It was established that if the basic reproductive number was less than unity $(R_0 < 1)$, then the disease free equilibrium is stable and unstable if $R_0 > 1$. Furthermore, we investigated the optimal

prevention, treatment and vaccination as control measures for the disease.

Objective functional was optimised by using treatment, prevention and vaccination as control measures. As a result of these control measures, there have been significant reduction of infections and an increase in the number of recovered populations as shown in Figure 2 and Figure 3.

Objective functional was optimised by using prevention, vaccination and treatment as control measures. The outcome of these control measures indicates a reduction of population infected and increased recoveries as shown in Figure 4 and Figure 5. An indication that these variables have greatly impacted in the combat of the spread of infections.

Objective functional was optimised by using treatment, vaccination and prevention of susceptible population as control measures. An increased in recovery population, a decreased in infectious population and a decreased in the number of population susceptible as shown in Figure 6 and Figure 7.

It was established that the best control measure in combating Tuberculosis infections is prevention and vaccination of susceptible population.

ACKNOWLEDGMENT

Authors acknowledged the support of faculty members in their respective departments. Heartfelt appreciation to the numerous review comments and suggestions. We expressed our profound gratitude for such a wonderful support.

SOURCE OF FUNDING

There are no sources of funding for this research. Authors are solely responsible for the entire cost of this research.

DATA AVAILABILITY STATEMENT

Some of the parameter values are assumed and others are taken from published articles and are cited in this paper. These published articles are also cited at relevant places within the text as references.

CONFLICT OF INTERESTS

The author declares that there is no conflict of interests.

REFERENCES

[1] F.I. Bray, Cancer: Global Burden/Trends and Projections, in: International Encyclopedia of Public Health, Elsevier, 2008: pp. 424–451.

[2] I. Barberis, N. Bragazzi, L. Galluzzo, M. Martini, The history of tuberculosis: From the first historical records to the isolation of Koch's bacillus, J. Prevent. Med. Hyg. 58 (21017), 9–12.

[3] H. Kheiri, B. Song, F. Nazari, C. Castillo-Chavez, A. Jabbari, A two-strain TB model with multiple latent stages, Math. Biosci. Eng. 13 (2016), 741–785.

[4] C.p. Bhunu, W. Garira, A two strain tuberculosis transmission model with therapy and quarantine, Math. Model. Anal. 14 (2009), 291–312.

[5] D. Meressa, R.M. Hurtado, J.R. Andrews, et al. Achieving high treatment success for multidrug-resistant TB in Africa: initiation and scale-up of MDR TB care in Ethiopia—an observational cohort study, Thorax. 70 (2015), 1181–1188.

[6] S. Osman, D. Otoo, O. D. Makinde, et al., Modeling anthrax with optimal control and cost effectiveness analysis, Appl. Math. 11 (2020), 255-275.

[7] K. Okosun, O. Makinde, A co-infection model of malaria and cholera diseases with optimal control, Math. Biosci. 258 (2014), 19–32.

[8] O. D. Makinde, K. O. Okosun, Impact of chemo-therapy on optimal control of malaria disease with infected immigrants, BioSystems, 104 (2011), 32–41.

[9] D. W. Muia, S. Osman, M. Wainaina, Modelling and analysis of trypanosomiasis transmission mechanism, Glob. J. Pure Appl. Math. 14 (10) (2018), 1311–1331.

[10] S. Osman, Mathematical modelling of anthrax and listeriosisco-dynamics with optimal control, Ph.D. thesis, PhD thesis, PAUST, JKUAT (2019).

[11] O.D. Makinde, Adomian decomposition approach to a sir epidemic model with constant vaccination strategy, Appl. Math. Comput. 184 (2) (2007), 842–848.

[12] G. T. Tilahun, O. D. Makinde, D. Malonza, Modelling and optimal control of pneumonia disease with cost-effective strategies, J. Biol. Dyn. 11 (sup2) (2017), 400–426.

[13] S. Osman, D. Otoo, C. Sebil, O.D. Makinde, Bifurcation, sensitivity and optimal control analysis of modelling anthrax-listeriosis co-dynamics, Commun. Math. Biol. Neurosci. 2020 (2020), Article ID 98.

[14] S. Osman, H.A. Togbenon, D. Otoo, Modelling the dynamics of campylobacteriosis using nonstandard finite difference approach with optimal control, Comput. Math. Meth. Med. 2020 (2020), 8843299.

[15] D. Otoo, G.T. Tilahun, S. Osman, G.A. Wole, Modeling the dynamics of tuberculosis with drug resistance in north shoa zone, oromiya regional state, ethiopia, Commun. Math. Biol. Neurosci. 2021 (2021), Article ID 12.

[16] S. Osman, D. Otoo, C. Sebil, Analysis of listeriosis transmission dynamics with optimal control, Appl. Math. 11 (7) (2020), 712–737.

[17] O. Diekmann, J. Heesterbeek, J. Metz, On the definition and the computation of the basic reproduction ratio R_0 in models for infectious diseases in heterogeneous populations, J. Math. Biol. 28 (4) (1990), 365–382.

[18] K.O. Okosun, O.D. Makinde, Optimal control analysis of hepatitis c virus with acute and chronic stages in the presence of treatment and infected immigrants, Int. J. Biomath. 7 (02) (2014), 1450019.

[19] Z. Shuai, P. van den Driessche, Global stability of infectious disease models using Lyapunov functions, SIAM J. Appl. Math. 73 (2013), 1513–1532.

[20] P. Van den Driessche, J. Watmough, Reproduction numbers and sub-threshold endemic equilibria for compartmental models of disease transmission, Math. Biosci. 180 (2002), 29–48.

[21] R.A. Horn, C.R. Johnson, Matrix Analysis, Cambridge University Press, Cambridge, (2012).

[22] S. Osman, O.D. Makinde, D.M. Theuri, Stability analysis and modelling of listeriosis dynamics in human and animal populations, Glob. J. Pure Appl. Math. 14 (2018), 115–137.

[23] S. Osman, O.D. Makinde, D.M. Theuri, Mathematical modelling of transmission dynamics of anthrax in human and animal population, Math. Theory Model. 8 (2018), 47–67.

[24] K.A. Eustace, S. Osman, M. Wainaina, Mathematical modelling and analysis of the dynamics of cholera, Glob. J. Pure Appl. Math. 14 (9) (2018), 1259–1275.

[25] W.H. Fleming, H.M. Soner Controlled Markov processes and viscosity solutions, Applications of Mathematics, vol. 25, Springer-Verlag, New York (1993).

[26] S. Osman, O.D. Makinde, D.M. Theuri, Mathematical modelling of listeriosis epidemics in animal and human population with optimal control, Tamkang J. Math. 51 (4) (2020), 261–287.

[27] S. Osman, O.D. Makinde, A mathematical model for coinfection of listeriosis and anthrax diseases, Int. J. Math. Math. Sci. 2018 (2018), 1725671.

[28] G.T. Tilahun, Modeling co-dynamics of pneumonia and meningitis diseases, Adv. Differ. Equ. 2019 (2019), 149.

[29] N.A. Halim, Tuberculosis Model: A Mathematical Analysis/Nadhirah bt Abdul Halim. Masters thesis, University of Malaya, (2013)

[30] D.P. Moualeu, S. Bowong, J. Kurths, Parameter estimation of a tuberculosis model in a patchy environment: case of Cameroon, in: Biomat 2013, World Scientific, Toronto, Ontario, Canada, 2014: pp. 352–373.

[31] V.K. Gupta, S.K. Tiwari, S. Sharma, L. Nagar, Mathematical model of tuberculosis with drug resistance to the first and second line of treatment, J. New Theory, 21 (2018), (94–106).