Science Development
2026, Vol. 7, No. 1, pp. 1–22
https://doi.org/10.11648/j.scidev.20260701.11

Research Article

Mathematical Modelling and Optimal Control of Tuberculosis Transmission Dynamics in Werder District, Somali Regional State, Ethiopia

Tasew Ayele Taddese[1, *], Tsega Mhretab Gebre Silase[1], Tsegaw Muche Tessema[1], Sadam Dawud Adem[2]

[1]Department of Mathematics, Kebri Dehar University, Kebri Dehar, Ethiopia

[2]Department of Mathematics, Jigjiga University, Jigjiga, Ethiopia

Abstract

Tuberculosis (TB) is an infectious disease caused by mycobacterium tuberculosis bacteria (tubercle bacilli) and spreads through the air from an infectious person to a susceptible person. This research aims to investigate the transmission dynamics of tuberculosis (TB) using a mathematical model with optimal control and to estimate the reproduction number in the Werder district of the Somali regional state. To achieve the objective of the study, we employed different mathematical tools and available cumulative case data from the Werder district of the Somali regional state health officials. The model is developed using a system of nonlinear ordinary differential equations and basic reproduction number is determine to perform analysis for both local and global stability of the equilibrium points of the model. In addition to this, sensitivity analysis is studied based on the reproduction number to reveal influential parameters of transmission dynamics of tuberculosis. Then the optimal control strategy was found by minimizing the number of exposed and infected individual populations with tuberculosis taking into account the cost of implementation. The existence of optimal control and characterization was established with the help of Pontryagin's Maximum Principle and we conducted different numerical simulation cases to see agreements with analytical results. Moreover, the model was calibrated with real data collected from the Werder district of the Somali regional state health office from 2016 – 2022. The simulation results also clearly shown that the tuberculosis can be minimized by applying TB prevention programs to susceptible individuals and preventing the failure of treatment in active tuberculosis individuals through continuous supervision and helping patients during treatment period with optimal implementation cost. Furthermore, the optimal control model also predicted that tuberculosis is under control in Werder district.

Keywords

Tuberculosis (TB), Differential Equations, Basic Reproduction Number, Stability, Optimal Control

1. Introduction

Tuberculosis (TB) is an infectious disease caused by mycobacterium tuberculosis bacteria (tubercle bacilli) [2, 5, 42]. The bacteria live in the lungs of the infected host. Mycobacterium tuberculosis spreads through the air from an infectious

*Corresponding author: tasewayele99@gmail.com (Tasew Ayele Taddese)

Received: 18 January 2025; **Accepted:** 13 June 2025; **Published:** 16 January 2026

person to a susceptible person. Persons with active pulmonary or laryngeal tuberculosis generate droplet nuclei that contain Mycobacterium tuberculosis through communication, coughing, singing, shouting, sneezing, or any other forceful expiratory maneuver that shears respiratory secretions from the airways, with coughing being the most efficient at generating infectious aerosols [7, 45, 55].

Mycobacterium tuberculosis is the bacteria that caused tuberculosis and was identified by Nobel Laureate Robert Koch in March 1882 and the 1900s, Albert Chalmette and Camille Guerin achieved the first genuine success in immunizing against tuberculosis using attenuated bovine strain tuberculosis called BCG (Bacillus of Chalmette and Guerin) [11, 12, 26]. The genus of Mycobacterium is divided into two main groups: Mycobacterium tuberculosis complex and environmental mycobacterium. The Mycobacterium tuberculosis complex comprises the closely related species Mycobacterium tuberculosis, Mycobacterium Bovis, Mycobacterium africanum, Mycobacterium microti, and Mycobacterium canettii [8, 9, 51].

The highest risk groups to acquire TB when exposed to children under five years old, people who are immune-compromised especially those who are HIV-Positive, persons who have diabetes or kidney failure, people that take excessive alcohol and drugs, those with poor nutrition and lack of food, whom suffering from stress and living in poorly ventilated rooms [10, 16, 47]. Someone when infected with tuberculosis isn't contagious until symptoms appear. Symptoms of TB disease rely upon where within the body the TB bacteria grow. Active TB cases are also pulmonary where it affects the lungs.

The first symptoms usually include fatigue or weakness, unexplained weight loss, fever, chills, loss of appetite, and night sweats [13, 55]. Since the symptoms are abundantly the same as a standard cold people tend to treat it united. When the two infections within the lung worsen, it should cause pain, a bad cough that lasts 3 weeks or longer, and coughing up blood [13].

Tuberculosis occurs in every part of the world and affects all countries as well as all age groups. According to World Health Organization (WHO) Global TB 2020 Report, there was an estimated 10.0 million persons who fell ill with TB in 2019 such that 12% of cases were children (aged $\leq$ 15 years), 56% were male (aged $\geq$ 15 years) and 32% of cases were women. Among all those affected, 8.2% were people living with HIV (74% of them in Africa) and about 56% were from five countries: India, Indonesia, China, the Philippines and Pakistan [8, 50]. In the 2019 year, the largest number of new TB cases occurred in the South-East Asia and Western Pacific regions, with 64% of new cases, followed by the African region, with 25% of new cases [9, 52]. Additionally, in 2020, 86% of new TB cases occurred within the 30 high TB burden countries. Eight countries accounted for 2 thirds of the new TB cases: India, China, Indonesia, Philippines, Pakistan, Nigeria, Bangladesh and South Africa. These countries accounted more than 62% of the whole TB burden in the worldwide [14, 51]. Corresponding to the World Health Organization (WHO) 2021 report, TB is one of the top ten causes of death and the leading cause from a single infectious agent (ranking above HIV/AIDS) worldwide. Millions of people continue to fall sick with TB each year and an estimated 9.9 million people developed TB and 1.5 million died from the disease (including 214,000 deaths among HIV positive people) [10, 15, 51].

Drug-resistant TB has continued to be a major problem in the effective management and control of TB in a population [17, 21, 24]. In 2020 alone, there were an estimated 500,000 new TB cases with resistance to rifampicin (RR-TB), of which 78% a had cases of multidrug-resistant TB (MDR-TB) [28, 49]. The World Health Organization (WHO) estimates that 10.0 million cases of tuberculosis (TB) occurred worldwide in 2020, of which 500,000 were rifampicins (RR) or multidrug-resistant (MDR) TB which defined as Mycobacterium tuberculosis with resistance to at least rifampicin and isoniazid [30, 31]. Multidrug-resistant (MDR) is a common in Sub-Saharan Africans including Ethiopia [33, 36, 55].

Africa is that the world's second-largest and second-most having an oversized population continent. With 1.4 billion people as of 2021, it accounts for about 18% of the world's human population. Global TB incidence continues to be growing at one percent a year because of the rapid increase in Africa; intense control efforts are helping incidence fall or stabilize in other regions [36, 38]. The unprecedented growth of the tuberculosis epidemic in Africa due to several factors, the furthermost important is the HIV epidemic. Geographically, most TB cases in 2021 were within the WHO regions of Africa is 25% [39, 50]. The challenge in controlling TB in Africa is attributed to poverty, drug-resistant tuberculosis, endemic of the causative agents, and inefficient diagnostic methods, among others [6, 37].

In Ethiopia, tuberculosis (TB) is one of the first public health problems; HIV/AIDS, poverty, under nutrition, over-crowded living conditions and lack of knowledge about the disease have been known to increase the risk of spreading the bacteria and the risk of developing the disease [25, 44]. Ethiopia is one of the highest TB burden countries in Sub-Saharan African countries [3, 48]. Tuberculosis (TB) is the leading cause of death from an infectious disease in Ethiopia, killing more than 30 thousand people every year (more than 75 people per day), it also has a long-term corrosive impact on the health of Ethiopians population [55, 59]. According to the WHO report, Ethiopia is one of the 30 high-burden countries, and there were an estimated 172,000 (192 per 100,000 populations) incident cases of TB in 2020. Corresponding to the same report, there were an estimated 25,000 deaths (23 per 100,000) due to TB, excluding HIV related deaths [27, 60]. As in [55, 61], the economic consequences of TB include those due to lost income and productivity during diagnosis and treatment, direct household expenditures for TB care, and the unmeasured disabilities due to

permanent lung damage in up to 50% of survivors.

The situation, regarding TB, in Somali Regional State (SRS) largely contrasts with the progress seen at the national level. The national TB prevalence was adjusted to 224/100,000 from 421/100,000 in 2011 based on the national TB survey [4]. This prevalence is further found to be disproportionately distributed across population sectors. Pastoral and rural communities have a nearly 30% higher prevalence, compared to the national one. SRS has a TB prevalence of 240 per 100,000 populations [12, 43]. Based on this prevalence, it is estimated to have over 14,400 and 860 TB cases in SRS and Doolo zone respectively. Based on the national TB survey, the national case detection rate has increased from below 50% to over 70% [22]. Nonetheless, this detection rate varies widely between regions, with SRS having the lowest case detection rate (CDR) [18, 53]. A low CDR means that TB patients with open PTB, stay in the community and are contagious for longer periods before starting treatment. This increases incidence in the community (negative externality), leads to more morbidity, and might negatively affect the treatment outcome when commenced so late and the patient's condition is bad which a public health problem is. Between 2010 and 2016, there were 5357 patients tested for acid-fast bacilli (AFB), and 1113 commenced treatment in Werder Hospital of Doolo zone. This number of patients who commenced TB treatment is less than 19% of the expected number of patients over the past 7 years [18, 40, 41].

Tuberculosis (TB) becomes a serious public health problem and the major cause of death worldwide including in Ethiopia. For this reason, many epidemiologists and other scientists invest their effort in understanding the transmission dynamics of tuberculosis and controlling its transmission. From interactions with those scientists, mathematicians have developed a significant and effective tool, namely mathematical models of tuberculosis, giving an insight into the dynamics of communicable diseases effectively with the help of these mathematical models and providing useful information on the spread and how to control the communicable diseases. Mathematical modelling of the transmission dynamics of tuberculosis flourished in 1962 [47].

From Waaler [47] models, several models have been developed considering such as the compartmental model for the TB disease *[35]*, the non-linear mathematical model of TB with case detection and treatment (Athithan and Minighosh, 2013), the effect of vaccination and treatment on the spread of TB [29, 59], the effect of diabetes on the spread of TB [23,32], assess the impact of vaccination and effective contact rate in the spreads of TB [11, 34] and global stability analysis TB infection with incomplete treatment [54, 46] also offered a recent mathematical model on the transmission dynamics of tuberculosis in 2019. They confirmed their model with real data from Pakistan. But the authors do not consider optimal control intervention strategies. Hence, in this research, we modified the mathematical model proposed by Ullah *[47]*, by introducing optimal control function and studying both analytically and numerically with the help of Pontryagin's maximum principle.

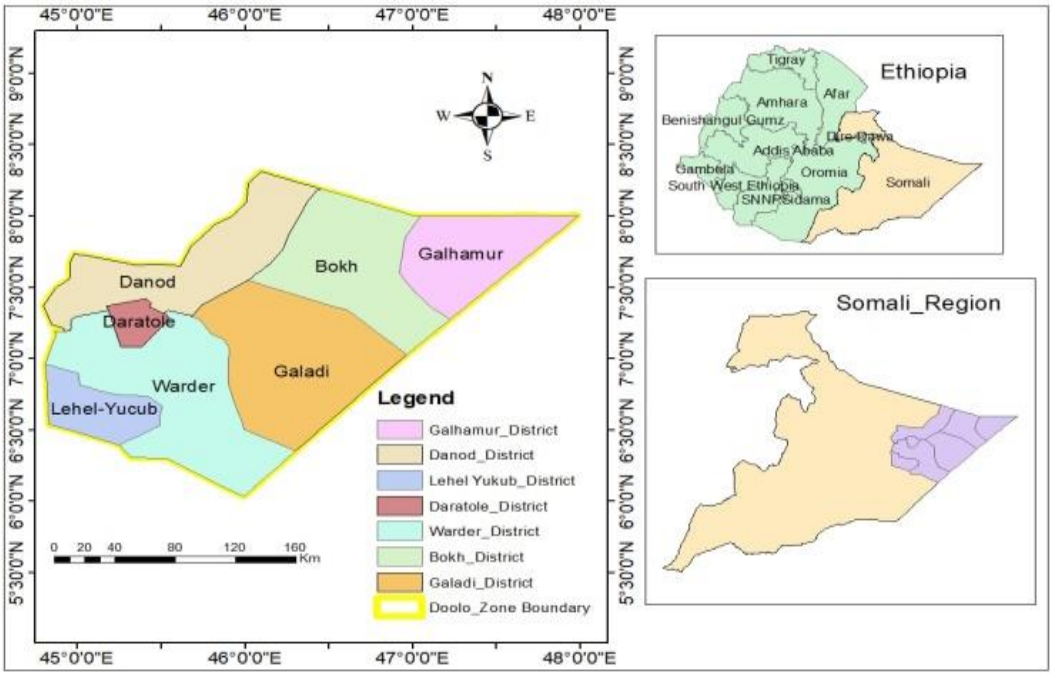

Figure 1. *Map of the study area.*

2. Study Area

The study is conducted in Werder district of Doolo zone, Somali region. Geographically, this district is found between $5^0 58' N$ latitude to $45^0 21' E$ longitude with an elevation of 541 meters above sea level. It is located at 1146 km away from Addis Ababa, the capital of Ethiopia and 528 km away from Jigjiga, the capital of Somali region. The climate of the study area is warm and temperate. A vast area of this zone experiences high temperature and low precipitation with mean annual temperature ranges between $20^0 C - 32^0 C$. The annual rainfall of the zone varies between 293 mm and 595 mm.

Based on the 2007 Census conducted by the Central Statistical Agency of Ethiopia (CSA 2007), this district has a total population of 58,005, of whom 32,743 are men and 25,292 women. While 9,211 or 15.87% are urban inhabitants, a further 13,493 or 23.25% are pastoralists. Based on the result of housing and population census of May, 2007, in 2017 the projected population of Werder district is 85,078 people, out of this 48001 are males and 37077 are females.

2.1. Model Formulation

To develop the mathematical model which describes the transmission dynamics of TB, the human population is divided into five epidemiological sub compartments which are mutually exclusive. The sub compartments are susceptible individuals $S(t)$, TB-exposed individuals $E(t)$, TB-infected individuals who have active TB diseases and infectious $I(t)$, TB-treated individuals $T(t)$, Recovered individuals $R(t)$. The flow between five compartments is shown in the schematic diagram presented in Figure 1.

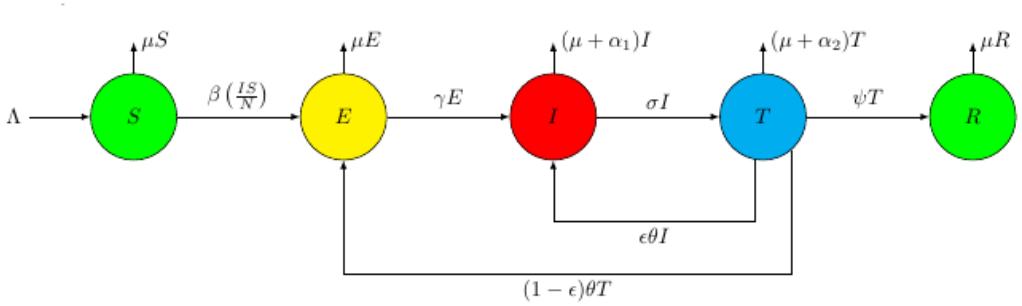

Figure 2. *Schematic diagram of Tuberculosis (TB).*

2.2. Model Assumption

Here, a mathematical model of TB transmission dynamics of TB is constructed based on the following assumptions. The total population at time $N(t)$is subdivide into susceptible $S(t)$, TB exposed $E(t)$, TB infectious $I(t)$, TB treated $T(t)$, Recovered individuals $R(t)$, such that

$$N(t) = S(t) + E(t) + I(t) + I(t) + R(t)$$

Thus, the following assumptions were made in the mathematical model: A number of susceptible populations are increased by the recruitment of individuals into population at a constant rate Λ. All individuals suffer from natural death, at a constant rate μ. Any susceptible class is infected when they come into effective contact with infectious class and the disease transmitted at rate β. Susceptible (S) class gets infected is proportional to infectious class (I). A number of infected class people increases at a rate proportional to both the number of infectious class and the number of susceptible class. The infectious class and treated class have additional death rate due to the disease with rate constants α_1 and α_2 respectively. The infectious class- individuals are treated with a constant rate σ, entering into the treatment class. The treated individuals enters to either latent (exposed) class due to the remainder of TB or infective class due to the failure of treatment at a constant rate θ. The term $(1-\epsilon)\theta T$, where the parameter ϵ reflects the treatment failure, further by considering $0 \leq \epsilon \leq 1$; that means, when $\epsilon = 0$, will mean that all the individuals under treatment become latent (exposed) and when $\epsilon = 1$, mean that the failure of treatment and all the treated individuals will still be infectious. Treated individuals are recovered at a constant rate ψ. All parameters and state variables are in the model are assumed to be non-negative.

Table 1. *State variables of the model.*

State variable	Description
$S(t)$	Susceptible individuals at a time t

State variable	Description
$E(t)$	Number of individuals which is not yet infectious at a time t
$I(t)$	Number of TB active individuals at a time t
$T(t)$	Number of treated individuals at a time t
$R(t)$	Number of recovered individuals at a time t

Table 2. *Parameters of the model.*

Parameters	Description
Λ	Recruitment rate
β	Disease contact rate
ψ	Progression rate from compartment T to R
σ	Treatment rate from compartment I to T
μ	Natural death rate
α_1	Disease related mortality rate of infected individuals
α_2	Disease related mortality rate in T
θ	Rate at which treated individuals leave the T
ϵ	Treatment failure rate
γ	Rate of moving from E to I

To represent this mathematically, we have the following system of nonlinear differential equations based on the assumption and the schematic diagram:

$$\begin{cases} \frac{dS}{dt} = \Lambda - \frac{\beta SI}{N} - \mu S \\ \frac{dE}{dt} = \frac{\beta SI}{N} - (\ \mu + \gamma)E + (1-\epsilon)\theta T \\ \frac{dI}{dt} = \gamma E + \epsilon\theta T - (\mu + \sigma + \alpha_1)I \\ \frac{dT}{dt} = \sigma I - (\mu + \theta + \alpha_2 + \psi)T \\ \frac{dR}{dt} = \psi T - \mu R \end{cases} \quad (1)$$

With initial conditions: $S(0) = S_0 > 0, E(0) = E_0 \geq 0, I(0) = I_0 \geq 0, T(0) = T_0 \geq 0, and$ $R(0) = R_0 \geq 0.$

2.3. Model Analysis

In this section, we investigate the invariant region, positivity, disease free-equilibrium, reproduction number, stability and sensitivity of the basic reproduction number.

2.4. Invariant Region

In this subsection, we study a region in which the feasible solution of the governing equation for the tuberculosis model is bounded. Summing the system of non-linear ordinary differential equation (1) we obtain.

$$\frac{d}{dt}(S + E + I + T + R)(t) = \Lambda - \mu(S + E + I + T + R)(t) - \alpha_1 I(t) - \alpha_2 T(t)$$

Since α_1 and α_2 are non-negative, we have

$$\frac{dN(t)}{dt} = \Lambda - \mu N(t) - \alpha_1 I(t) - \alpha_2 T(t) \leq \Lambda - \mu N(t)$$

$$\frac{dN(t)}{dt} + \mu N(t) = \Lambda$$

By integrating factor,

$$\frac{d}{dt}(N(t)e^{\mu t}) \leq \Lambda e^{\mu t} \tag{2}$$

Integrating both sides of the equation (2) and simplifying it, then we have

$$N(t) \leq \frac{\Lambda}{\mu} + N(0)e^{-\mu t} \tag{3}$$

Where $N(0)$ is obtain from initial condition and as $t \to \infty$ in equation (3), the population size $N(t) \leq \frac{\Lambda}{\mu}$ which implies that $0 \leq N(t) \leq \frac{\Lambda}{\mu}$. Thus, the feasible region of the system (1) is given by the set.

$$\Omega = \left\{\left(S(t), E(t), I(t), I(t), R(t)\right) \in R^5{}_+, N(t) \leq \frac{\Lambda}{\mu}, S(0) \geq 0, E(0) \geq 0, I(0) \geq 0, T(0) \geq 0, R(0) \geq 0\right\}$$

Hence, the system (1) is biologically meaningful and mathematically well-posed within the domain given by the region Ω.

$$\begin{cases} \Lambda - \frac{\beta SI}{N} - \mu S = 0 \\ \frac{\beta SI}{N} - (\ \mu + \gamma)E + (1-\epsilon)\theta T = 0 \\ \gamma E + \epsilon\theta T - (\mu + \sigma + \alpha_1)I = 0 \\ \sigma I - (\mu + \theta + \alpha_2 + \psi)T = 0 \\ \psi T - \mu R = 0 \end{cases} \tag{4}$$

Solving this equation, the disease free equilibrium is $\mathcal{E}_T = \left(\frac{\Lambda}{\mu}, 0,0,0,0\right)$

2.5. Basic Reproduction Number

The basic reproduction number has the key role in the disease modelling and intuitively from epidemiological point of view, the basic reproduction number, which is denoted by R_0, is the average number of new cases (infections), that one infected case will generate during its entire infectious lifetime. It is very important in determining whether the global dynamics of the disease can be spread or not. When the value of the basic reproduction number falls less than unity, then the disease will not be spread in the community, whereas, when its values cross the unity, then the disease can be spread in the community i.e., the disease becomes endemic and will produce deaths and sometimes outbreak which is called epidemics. In epidemiology, the epidemic is expected to be eliminated if $R_0 < 1$, and persists if $R_0 > 1$. Therefore, the basic reproduction number is a threshold parameter for a disease and its biological significance is obvious. We use the next generation method given in [58] to compute R_0. Let us assume that there are n compartments of which the m compartments correspond to infected individuals. In order to compute R_0, it is important to distinguish new infections from all other changes in population.

In order to compute R_0, it is important to distinguish new infections from all other changes in the population. Let $\mathcal{F}_i(x)$ be the rate of appearance of new infections in compartments, ${\mathcal{V}_i}^{in}$ be the rate of transfer of individuals into compartment. ${\mathcal{V}_i}^{out}$ be the rate of transfer of individuals out of compartment. It is assumed that each function ($\mathcal{F}_i(x)$, ${\mathcal{V}_i}^{in}(x)$ and ${\mathcal{V}_i}^{out}(x)$) is continuously differentiable with respect to each variable. We define $n \times n$ matrices, F and V,

$F_{ij}(x) = \frac{\partial f_i}{\partial j}$ for $1 \leq i, j \leq n$, $V_{ij}(x) = \frac{\partial \mathcal{V}_i}{\partial j}$ for $1 \leq i, j \leq n$, where $\mathcal{V}_i(x) = {\mathcal{V}_i}^{out} - {\mathcal{V}_i}^{in}$ Diekmann *et al* (1990) we call FV^{-1} the next generation matrix for the model and we shall set R_0, as equal to largest eigenvalue in magnitude of the matrix of $R_0 = FV^{-1}$.

The next step is the computation of the square matrices F and V of order $n \times n$, where n is the number of infected class, defined by:

$$F = \begin{bmatrix} \frac{\beta SI}{N} \\ 0 \\ 0 \end{bmatrix} \text{ and } V = \begin{bmatrix} (\ \mu + \gamma)E - (1-\epsilon)\theta T \\ \gamma E - \epsilon\theta T - (\mu + \sigma + \alpha_1)I \\ -\sigma I + (\mu + \theta + \alpha_2 + \psi)T \end{bmatrix} \text{ with } 1 \leq i, j \leq n.$$

Such that F is non-negative, V is non-singular matrix and $\mathcal{E}_T$ is the disease free equilibrium point. Now, the Jacobian matrices of $f(x)$ and $v(x)$ at the disease-free equilibrium $\mathcal{E}_T$ are:

$$Df(\ \mathcal{E}_T) = \begin{bmatrix} 0 & \frac{\beta S}{N} & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{bmatrix} \ \ and \ \ Dv(\ \mathcal{E}_T) = \begin{bmatrix} k_1 & 0 & -(1-\epsilon)\theta \\ -\gamma & k_2 & -\epsilon\theta \\ 0 & -\sigma & k_3 \end{bmatrix}$$

The linearization approach of the system (1) associated with matrix F and V at DFE point $\mathcal{E}_T$ is given by

$$F = \begin{bmatrix} 0 & \beta & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{bmatrix} \ \ and \ \ V = \begin{bmatrix} k_1 & 0 & -(1-\epsilon)\theta \\ -\gamma & k_2 & -\epsilon\theta \\ 0 & -\sigma & k_3 \end{bmatrix} \text{ respectively.}$$

Where $k_1 = (\ \mu + \gamma), k_2 = (\mu + \sigma + \alpha_1), k_3 = (\mu + \theta + \alpha_2 + \psi)$;
Then we denote the determinant of V by $det(V) = \ k_1(k_2k_3 - \epsilon\theta\sigma) - (1-\epsilon)\theta\sigma\gamma$.

$$V^{-1} = \begin{bmatrix} \frac{k_2k_3-\epsilon\theta\sigma}{det(V)} & \frac{(1-\epsilon)\theta\sigma}{det(V)} & \frac{(1-\epsilon)\theta\sigma k_2}{det(V)} \\ \frac{\gamma k_3}{det(V)} & \frac{k_1k_2}{det(V)} & \frac{(1-\epsilon)\theta+\epsilon\theta k_1}{det(V)} \\ \frac{\gamma\sigma}{det(V)} & \frac{\sigma k_1}{det(V)} & \frac{k_1k_2}{det(V)} \end{bmatrix} \text{ and } \ M = FV^{-1} = \begin{bmatrix} \frac{\beta k_3\gamma}{det(V)} & \frac{\beta k_1k_3}{det(V)} & \frac{\beta(1-\epsilon)\theta+\epsilon k_1}{det(V)} \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{bmatrix}$$

Since F is non-negative and V is non-singular, then V^{-1} is non-negative and FV^{-1} is non-negative. Hence, the matrix M is called next generation matrix for the model. From this matrix, we determine the value of an eigenvalues of the coefficient matrix$M$ or V^{-1}. Hence $\det(FV^{-1} - \lambda\mathrm{I}) = |FV^{-1} - \lambda I|$. This implies that

$$\begin{vmatrix} \frac{\beta k_3\gamma}{k_1(k_2k_3-\epsilon\theta\sigma)-(1-\epsilon)\theta\sigma\gamma} - \lambda & \frac{\beta k_1k_2}{k_1(k_2k_3-\epsilon\theta\sigma)-(1-\epsilon)\theta\sigma\gamma} & \frac{\beta(1-\epsilon)\theta+\epsilon k_1}{k_1(k_2k_3-\epsilon\theta\sigma)-(1-\epsilon)\theta\sigma\gamma} \\ 0 & 0-\lambda & 0 \\ 0 & 0 & 0-\lambda \end{vmatrix} = 0$$

From this we obtain

$|FV^{-1} - \lambda I| = \left(\frac{\beta k_3\gamma}{k_1(k_2k_3-\epsilon\theta\sigma)-(1-\epsilon)\theta\sigma\gamma} - \lambda\right)\lambda^2$. This show that $\frac{\beta k_3\gamma}{k_1(k_2k_3-\epsilon\theta\sigma)-(1-\epsilon)\theta\sigma\gamma}\lambda^2 = \lambda^3$

Hence, by cancelling λ^2 on both sides and solving we obtain $\lambda = \frac{\beta k_3\gamma}{k_1(k_2k_3-\epsilon\theta\sigma)-(1-\epsilon)\theta\sigma\gamma}$. Thus, the reproduction number is given by the spectral radius of FV^{-1} that is $R_0 = \lambda = \frac{\beta k_3\gamma}{k_1(k_2k_3-\epsilon\theta\sigma)-(1-\epsilon)\theta\sigma\gamma}$. Then $\rho(\mathrm{M})$ denotes the spectral radius of a matrix M which is the biggest non-negative eigenvalue of the next generation matrix.

Therefore,

$$R_0 = \frac{\beta k_3\gamma}{k_1(k_2k_3-\epsilon\theta\sigma)-(1-\epsilon)\theta\sigma\gamma}$$

2.6. Stability Analysis of Disease Free Equilibrium

The model (1) has a unique disease free equilibrium (DFE), $\mathcal{E}_T$, given by $\mathcal{E}_T = \left(\frac{\Lambda}{\mu}, 0,0,0,0\right)$.

Local stability of disease free equilibrium

Theorem 2.2: The disease-free equilibrium $\mathcal{E}_T = \left(\frac{\Lambda}{\mu}, 0,0,0,0\right)$ of the system (1) is locally asymptotically stable if $R_0 < 1$.

Proof. By considering the linearized system of the governing equation (1), we have

$$J(S+E+I+T+R) = \begin{Bmatrix} -\frac{\beta I}{N} - \mu & 0 & -\frac{\beta S}{N} & 0 & 0 \\ 0 & -(\ \mu+\gamma) & \frac{\beta S}{N} & (1-\epsilon)\theta & 0 \\ 0 & \gamma & -(\mu+\sigma+\alpha_1) & \epsilon\theta & 0 \\ 0 & 0 & \sigma & -(\mu+\theta+\alpha_2+\psi) & 0 \\ 0 & 0 & 0 & \psi & -\mu \end{Bmatrix}$$

Therefore, the Jacobian matrix J of model at the disease free equilibrium $\mathcal{E}_T$ reduces to

$$J(\ \mathcal{E}_T) = \begin{Bmatrix} -\mu & 0 & -\beta & 0 & 0 \\ 0 & -k_1 & \beta & (1-\epsilon)\theta & 0 \\ 0 & \gamma & -k_2 & \epsilon\theta & 0 \\ 0 & 0 & \sigma & -k_3 & 0 \\ 0 & 0 & 0 & \psi & -\mu \end{Bmatrix} \tag{5}$$

where $k_1 = (\ \mu + \gamma), k_2 = (\mu + \sigma + \alpha_1), k_3 = (\mu + \theta + \alpha_2 + \psi)$.

The eigenvalues of equation (5) are the solutions of the characteristics equation $|J(\ \mathcal{E}_T) - \lambda\ I_5| = 0$, where I_5 is the identity matrix of order 5. Then we have

$$|J(\ \mathcal{E}_T) - \lambda\ I_5| = \begin{vmatrix} -\mu-\lambda & 0 & -\beta & 0 & 0 \\ 0 & -k_1-\lambda & \beta & (1-\epsilon)\theta & 0 \\ 0 & \gamma & -k_2-\lambda & \epsilon\theta & 0 \\ 0 & 0 & \sigma & -k_3-\lambda & 0 \\ 0 & 0 & 0 & \psi & -\mu-\lambda \end{vmatrix} = 0$$

This implies that

$$|J(\ \mathcal{E}_T) - \lambda\ I_5| = -(\mu+\lambda)\left(\begin{vmatrix} -k_1-\lambda & \beta & (1-\epsilon)\theta & 0 \\ \gamma & -k_2-\lambda & \epsilon\theta & 0 \\ 0 & \sigma & -k_3-\lambda & 0 \\ 0 & 0 & \psi & -\mu-\lambda \end{vmatrix}\right)$$

$$= -(\mu+\lambda)^2\left(\begin{vmatrix} -k_1-\lambda & \beta & (1-\epsilon)\theta \\ \gamma & -k_2-\lambda & \epsilon\theta \\ 0 & \sigma & -k_3-\lambda \end{vmatrix}\right) \tag{6}$$

It follows that the characteristic equation computed from equation (6) is given by

$(\mu+\lambda)^2[\lambda^3 + (k_1+k_2+k_3)\lambda^2 + (k_1k_2 + k_1k_3 + k_2k_3 - \sigma\epsilon\theta - \gamma\beta)\lambda + (k_1k_2)k_3 - k_1\sigma\epsilon\theta - (1-\epsilon)\theta\sigma\gamma - \gamma\beta k_3] = 0$

Which equivalent to

$(\mu+\lambda)^2 = 0$ or $[\lambda^3 + (k_1+k_2+k_3)\lambda^2 + (k_1k_2 + k_1k_3 + k_2k_3 - \sigma\epsilon\theta - \gamma\beta)\lambda + (k_1k_2)k_3 - k_1\sigma\epsilon\theta - (1-\epsilon)\theta\sigma\gamma - \gamma\beta k_3] = 0$

We can write the characteristic equation as $\lambda_1 = \lambda_2 = -\mu$ or $\lambda^3 + a_1\lambda^2 + a_2\lambda + a_3 = 0$, where $a_1 = (k_1 + k_2 + k_3), a_2 = (k_1k_2 + k_1k_3 + k_2k_3 - \sigma\epsilon\theta - \gamma\beta), a_3 = k_1k_2k_3 - k_1\sigma\epsilon\theta - (1-\epsilon)\theta\sigma\gamma - \gamma\beta k_3$.

It can be observed that the first two eigenvalues λ_1 and λ_2 are absolutely negative quantities since the parameter is always positive. Hence, λ_1 and λ_2 are stable. Consider the following characteristic equation:

$$\lambda^3 + a_1\lambda^2 + a_2\lambda + a_3 = 0 \tag{7}$$

Using the Routh-Hurwitz criteria [56], it can be observed that all the eigenvalues of the characteristic equation (7) have negative real part if $a_1 > 0, a_2 > 0, a_3 > 0$ and $a_1a_2 - a_3 > 0$. We can see that a_1 is positive because of all parameters are positive and their sum is also positive. But in order to say a_2 to be positive $k_1k_2 + k_1k_3 + k_2k_3 - \sigma\epsilon\theta - \gamma\beta$ must be positive. Hence, $a_2 > 0$ if it fulfil that $k_1k_2 + k_1k_3 + k_2k_3 > \sigma\epsilon\theta + \gamma\beta$. Additionally, $a_1a_2 - a_3 > 0$. This is the same as $a_1a_2 > a_3$. From Routh-Hurwitz criterion, it follows that $a_3 > 0$

$$a_3 = k_1k_2k_3 - k_1\sigma\epsilon\theta - (1-\epsilon)\theta\sigma\gamma - \gamma\beta k_3$$

From this we get $k_1k_2k_3 - k_1\sigma\epsilon\theta - (1-\epsilon)\theta\sigma\gamma > \gamma\beta k_3$ and then dividing both sides by $k_1k_2k_3 - k_1\sigma\epsilon\theta - (1-\epsilon)\theta\sigma\gamma$ to get $1 > \frac{\gamma\beta k_3}{k_1k_2k_3 - k_1\sigma\epsilon\theta - (1-\epsilon)\theta\sigma\gamma}$ which demonstrate that $1 > R_0$. This implies that $a_3 > 0$ for $R_0 < 1$. Therefore, we can concluded that the disease free equilibrium point of the system (1) is locally asymptotically stable if $R_0 < 1$.

2.7. Global Stability of Disease Free Equilibrium

Theorem 2.3: The disease free equilibrium of system (1) is globally asymptotically stable if $R_0 < 1$.

Proof: To proof the global stability of the disease-free equilibrium, first we construct a Lyapunov function: $V(S+E+I+T+R): {R_+}^5 \longrightarrow R^+$ defined as $V(S+E+I+T+R) = A_1E + A_2I + A_3$, where A_i, for $i = 1, 2, 3$, are some positive constants. The Lyapunov function V is continuously differentiable.

$$V(\ \mathcal{E}_T) = 0$$

$$V(S+E+I+T+R) > 0,\ V(S+E+I+T+R) \in {R_+}^5 - \{\ \mathcal{E}_T\}$$

Now differentiating $V(S+E+I+T+R)$ with respect to time we obtain

$$\frac{dV}{dt} = A_1\frac{dE}{dt} + A_2\frac{dI}{dt} + A_3\frac{dT}{dt}$$

$$= A_1\left[\frac{\beta SI}{N} - (\ \mu+\gamma)E + (1-\epsilon)\theta T\right] + A_2[\gamma E + \epsilon\theta T - (\mu+\sigma+\alpha_1)I] + A_3[\sigma I - (\mu+\theta+\alpha_2+\psi)T]$$

$$\leq A_1[\beta I - (\ \mu+\gamma)E + (1-\epsilon)\theta T] + A_2[\gamma E + \epsilon\theta T - (\mu+\sigma+\alpha_1)I] + A_3[\sigma I - \ \ (\mu+\theta+\alpha_2+\psi)T]$$

$$= [A_1\beta + A_3\sigma - A_2k_2]I + [\gamma A_2 - A_1k_1]E + [A_1(1-\epsilon)\theta + A_2\epsilon\theta - A_3k_3]T$$

$$\leq A_2k_2\left(\frac{A_1\beta + A_3\gamma}{A_2k_2} - 1\right)I + (\gamma A_2 - A_1k_1)E + (A_1(1-\epsilon)\theta + A_2\epsilon\theta - A_3k_3)T$$

Now choosing $A_1 = \frac{\gamma k_2}{k_1}, A_2 = k_3, A_3 = \frac{(1-\epsilon)\theta\gamma + k_1\epsilon\theta}{k_1}$; then we have

$$\frac{dV}{dt} = \frac{1}{k_1}(\gamma\beta k_3 + (1-\epsilon)\theta\sigma\gamma + \epsilon\theta\sigma k_1 - k_1k_2k_3)$$

$\frac{dV}{dt} = \frac{1}{k_1}\left(\frac{\gamma\beta k_3}{k_1k_2k_3 - \epsilon\theta\sigma k_1 - (1-\epsilon)\theta\sigma\gamma} - 1\right)I$; This implies that $\frac{dV}{dt} = \frac{1}{k_1}(R_0 - 1)\ I$.

Hence, if $R_0 < 1$, then $\frac{dV}{dt}$ is negative. Therefore, the largest compact invariant set in Ω is the singleton set $\left(\frac{\Lambda}{\mu}, 0,0,0,0\right)$. Hence, by LaSalle's invariant principle [57], every solution to equations of model (1) with initial conditions in Ω which approaches the disease-free equilibrium point as time t tends to infinity $(t \longrightarrow \infty)$ whenever $R_0 < 1$. This implies that the disease-free equilibrium is globally asymptotically stable in Ω.

2.8. Stability Analysis of Endemic Equilibrium

The endemic equilibrium point which denoted by $\mathcal{E}_T{}^*$ is a steady state solution where the disease persists in the population. For the existence of endemic equilibrium $\mathcal{E}_T{}^* = (S^*, E^*, I^*, T^*, R^*\ )$, is equivalent to the endemic of tuberculosis in the population and it is obtained by setting rates of changes of variables with respect to time in the model equation (1) to zero. Then solving the system of differential equation simultaneously, we obtain

$$\begin{cases} S^* = \frac{N}{R_0} \\ E^* = \frac{(\mu+\alpha_1)+\sigma(\mu+\sigma_2\psi)+(1-\epsilon)\theta\sigma(R_0-1)}{R_0\{(\mu+\alpha_1)+\sigma(\mu+\alpha_2+\ \psi)(1-\epsilon)\theta\sigma+\gamma(\sigma+k_3)\}} \\ I^* = \frac{\gamma k_3N(R_0-1)}{R_0\{(\mu+\alpha_1)+\sigma(\mu+\alpha_2+\ \psi)(1-\epsilon)\theta\sigma+\gamma(\sigma+k_3)\}} \\ T^* = \frac{k_3\sigma N(R_0-1)}{R_0\{(\mu+\alpha_1)+\sigma(\mu+\alpha_2+\ \psi)(1-\epsilon)\theta\sigma+\gamma(\sigma+k_3)\}} \\ R^* = \frac{\psi T^*}{R_0\{(\mu+\alpha_1)+\sigma(\mu+\alpha_2+\ \psi)(1-\epsilon)\theta\sigma+\gamma(\sigma+k_3)\}} \end{cases}$$

Therefore, system (1) has a unique endemic equilibrium whenever $R_0 > 1$.

2.8.1. Local Stability of Endemic Equilibrium (EE)

Theorem 4.4: The Endemic equilibrium (EE) of system (1) at $\mathcal{E}_T{}^*$ is locally asymptotically stable if $R_0 > 1$.

Proof: The Jacobian matrix $J(\ \mathcal{E}_T{}^*\ )$ of the system (1)around the EE, $\mathcal{E}_T{}^*$ is obtained by

$$J(\ \mathcal{E}_T{}^*\ ) = \begin{pmatrix} \frac{I^*(N-S^*)\beta}{N^2} - \mu & \frac{I^*S^*\beta}{N^2} & -\frac{(N-I^*)S^*\beta}{N^2} & \frac{I^*S^*\beta}{N^2} \\ \frac{I^*(N-S^*)\beta}{N^2} & -\frac{I^*S^*\beta}{N^2} - k_1 & \frac{(N-I^*)S^*\beta}{N^2} & (1-\epsilon)\theta - \frac{I^*S^*\beta}{N^2} \\ 0 & \gamma & -k_2 & \theta\epsilon \\ 0 & 0 & \sigma & -k_3 \end{pmatrix} \quad (8)$$

where $\mathcal{E}_T{}^* = (S^*, E^*, I^*, T^*, R^*\ )$ is the endemic equilibrium of the system (1). The eigenvalues of equation (8) are the solutions of the characteristic equation $|J(\ \mathcal{E}_T{}^*\ ) - \lambda\ \ I| = 0$, where I is the identity matrix.

Then we have $|J(E^*\ ) - \lambda\ \ I| = \begin{pmatrix} -\left(\frac{I^*(N-S^*)\beta}{N^2} + \mu\right) - \lambda & \frac{I^*S^*\beta}{N^2} & -\frac{(N-I^*)S^*\beta}{N^2} & \frac{I^*S^*\beta}{N^2} \\ \frac{I^*(N-S^*)\beta}{N^2} & -\left(\frac{I^*S^*\beta}{N^2} + k_1\right) - \lambda & \frac{(N-I^*)S^*\beta}{N^2} & (1-\epsilon)\theta - \frac{I^*S^*\beta}{N^2} \\ 0 & \gamma & -k_2 - \lambda & \theta\epsilon \\ 0 & 0 & \sigma & -k_3 - \lambda \end{pmatrix}$

The characteristic equation associated to $J(\ \mathcal{E}_T{}^*\ )$ is

$$\lambda^4 + b_1\lambda^3 + b_2\lambda^2 + b_3\lambda + b_4 = 0 \tag{9}$$

where, the coefficients are: $b_1 = k_1 + k_2 + k_3 + \mu + \frac{I^*S^*\beta}{N^2}$

$$b_1 = \frac{1}{N}\{k_3(\mu N^2 + I^*S^*\beta) + QN^2 + k_2(\mu N^2 + I^*S^*\beta) + k_1\big((k_1 + k_2 + k_3 + \mu)N^2 + I^*\beta(N - S^*)\big)\ + S^*\beta\big(I^*\mu + (N - I^*)\big)\}$$

$$b_3 = \frac{1}{N^2}\Big\{k_1\Big(k_3\big(\mu N^2 + I^*\beta(N - S^*)\big)\Big) + QN^2 + k_2\big(\mu N^2 + I^*\beta(N - S^*)\big) + k_2(k_3(\mu N^2 + S^*I^*\beta) + I^*S^*\mu\beta) + \beta k_3 I^*S^* + \beta I^*S^*\big(\sigma + \mu\gamma(1 + I^*N)\big) - \Big(\beta\epsilon k_3 I^*S^*N + \beta\sigma\epsilon\theta + \sigma\theta N^2\big((1-\epsilon)\gamma + \epsilon\mu\big)\Big)\Big\}$$

$$b_4 = \frac{1}{N^2}\{k_1Q\big(\mu N^2 + I^*\beta(N - S^*)\big) + \beta I^*S^*(k_1k_3 + \sigma\mu\gamma)\ - \big(\beta\gamma\mu k_3 S^*(N - I^*) + \mu\sigma(\theta\gamma(1-\epsilon)N^2 + \beta\epsilon\theta S^*I^*) + \beta\sigma\theta\gamma I^*(1-\epsilon)(N - S^*)\big)\}$$

where $Q = \{k_3(\mu + \alpha_1) + \sigma(\mu + \alpha_2 + \psi) + \sigma\theta(1-\epsilon)\}$.

Then the eigenvalues of the characteristic polynomial (9) will be negative if it fulfil the Routh-Hurwitz conditions that are $b_i > 0$, for $i = 1, 2, 3, 4$ and $b_1b_2b_3 > {b_3}^2 + {b_1}^2b_4$. Hence, the EE of the model (1) will be locally asymptotically stable if $R_0 > 1$.

2.8.2. Global Stability of Endemic Equilibrium (EE)

In this subsection, we prove the global asymptotic stability property of the endemic equilibrium (EE) of the model (1) at the endemic equilibrium (EE), we have from system (1) by using the approach given in (Wang and Jinde, 2014., Wang and Jinde, 2015).

$$\begin{cases} \Lambda = \frac{I^*S^*\beta}{N^2} + \mu S^* \\ k_1E^* = \frac{I^*S^*\beta}{N^2} + (1-\epsilon)\theta\, T^* \\ k_2I^* = \gamma E^* + \theta\epsilon T^* \\ \sigma I^* = k_3T^* \end{cases}$$

Theorem 2.5: The unique endemic equilibrium (EE) at $\mathcal{E}_T{}^*$ of model equation (1) is globally asymptotically stable if $R_0 > 1$.

Proof. To proof the result, we define the following Lyapunov function

$$V(t) = \epsilon\left(S(t) - S^* - S^*\ln\left(\frac{S(t)}{S^*}\right)\right) + \epsilon\left(E(t) - E^* - E^*\ln\left(\frac{E(t)}{E^*}\right)\right) + k_1\left(I(t) - I^* - I^*\ln\left(\frac{I(t)}{I^*}\right)\right) + \frac{\theta T^*(k_1\epsilon + \gamma(1-\epsilon))}{\epsilon I^*}\left(T(t) - T^* - T^*\ln\left(\frac{T(t)}{T^*}\right)\right)$$

After differentiating $V(t)$with respect to time gives

$$\frac{dV(t)}{dt} = \gamma\left[\left(1 - \frac{S^*}{S}\right)\frac{dS}{dt} + \left(1 - \frac{E^*}{E}\right)\frac{dE}{dt}\right] + k_1\left[\left(1 - \frac{I^*}{I}\right)\frac{dI}{dt}\right] + \frac{\theta T^*(k_1\epsilon + \gamma(1-\epsilon))}{\sigma I^*}\left[\left(1 - \frac{T^*}{T}\right)\frac{dT}{dt}\right] \tag{10}$$

From direct calculation we have:

$$\begin{cases} \gamma\left(1 - \frac{S^*}{S}\right)\frac{dS}{dt} = \gamma\left(1 - \frac{S^*}{S}\right)\left(\Lambda - \frac{\beta SI}{N} - \mu S\right) \\ \gamma\left(1 - \frac{S^*}{S}\right)\frac{dS}{dt} = \gamma\left(1 - \frac{S^*}{S}\right)\left[\frac{I^*S^*\beta}{N} + \mu S^* - \frac{\beta SI}{N} - \mu S\right] \\ \gamma\left(1 - \frac{S^*}{S}\right)\frac{dS}{dt} = \gamma\mu S^*\left(2 - \frac{S^*}{S} - \frac{S}{S^*}\right) + \frac{\gamma I^*S^*\beta}{N}\left(2 - \frac{S^*}{S} - \frac{IN}{I^*N}\right) - \frac{\gamma\beta SI}{N} \end{cases} \tag{11}$$

$$\begin{cases} \gamma\left(1-\frac{E^*}{E}\right)\frac{dE}{dt} = \gamma\left(1-\frac{E^*}{E}\right)\left[\frac{\beta SI}{N} - k_1E + (1-\epsilon)\theta T\right] \\ \gamma\left(1-\frac{E^*}{E}\right)\frac{dE}{dt} = \frac{\gamma\beta SI}{N} - \frac{\gamma\beta SIE^*}{NE} - \gamma k_1E + \gamma k_1E^* + \gamma(1-\epsilon)\theta T - \frac{\gamma(1-\epsilon)\theta TE^*}{E} \\ \gamma\left(1-\frac{E^*}{E}\right)\frac{dE}{dt} = \frac{\gamma\beta SI}{N} - \frac{\gamma\beta SIE^*}{NE} - \gamma k_1E + \frac{\gamma\beta S^*I^*E^*}{NE} + \gamma(1-\epsilon)\theta T^* + \gamma(1-\epsilon)\delta T \\ -\gamma(1-\epsilon)\theta T \end{cases} \tag{12}$$

$$\begin{cases} \gamma k_1\left(1-\frac{I^*}{I}\right)\frac{dI}{dt} = k_1\left(1-\frac{I^*}{I}\right)[\gamma E + \epsilon\theta T - k_2I] = \gamma k_1E - \frac{\gamma k_1EI^*}{I} + k_1\epsilon\theta T - \frac{k_1\epsilon\theta I^*}{I} \\ -k_1k_2I + k_1k_2I^* \\ \gamma k_1\left(1-\frac{I^*}{I}\right)\frac{dI}{dt} = k_1\gamma E - \frac{\gamma k_1E^*EI^*}{IE^*} + k_1\epsilon\theta T - \frac{k_1\epsilon T\theta I^*}{I} + \frac{\gamma\beta I^*S^*}{N} + k_1\epsilon\theta T^* + \\ \quad \gamma(1-\epsilon)\theta T^* - \frac{\gamma\beta I^*S^*I}{NI^*} - \frac{\gamma(1-\epsilon)\theta T^*I}{I^*} - \frac{k_1\epsilon\theta T^*I}{I^*} \\ \gamma k_1\left(1-\frac{I^*}{I}\right)\frac{dI}{dt} = \frac{k_1\gamma E - \gamma\beta I^*S^*EI^*}{NIE^*} - \gamma(1-\epsilon)\theta T^*\frac{EI^*}{IE^*} + k_1\epsilon\theta T - k_1\epsilon\theta T\frac{I^*}{I} + \frac{\gamma\beta S^*I^*}{N} + \\ \quad k_1\epsilon\theta T^* + \gamma(1-\epsilon)\theta T^* + \frac{\gamma\beta S^*I^*}{N}\frac{I^*}{I} - \gamma(1-\epsilon)\theta T^*\frac{I}{I^*} - k_1\epsilon\theta T^*\frac{I}{I^*} \end{cases} \tag{13}$$

$$\begin{cases} \frac{\delta T^*(k_1\epsilon+\gamma(1-\epsilon))}{\sigma I^*}\left(1-\frac{T^*}{T}\right)\frac{dT}{dt} = \frac{\theta T^*(k_1\epsilon+\gamma(1-\epsilon))}{\sigma I^*}\left[\left(1-\frac{T^*}{T}\right)\ (\sigma I - k_3T)\right] \\ \qquad = \frac{\theta T^*(k_1\epsilon+\gamma(1-\epsilon))}{I^*}\left(1-\frac{T^*}{T}\right)\left(I-\frac{I^*T}{T^*}\right) \\ \frac{\theta T^*(k_1\epsilon+\gamma(1-\epsilon))}{\sigma I^*}\left(1-\frac{T^*}{T}\right)\frac{dT}{dt} = \theta T^*k_1\epsilon\frac{I}{I^*} + \gamma(1-\epsilon)\theta T^*\frac{I}{I^*} - \epsilon\theta T^*\frac{IT^*}{I^*T} - \gamma(1-\epsilon)\theta T^*\frac{IT^*}{I^*T} \\ \qquad -k_1\epsilon\theta T - \gamma(1-\epsilon)\theta T + k_1\epsilon\theta T^* + \gamma(1-\epsilon)\theta T^* \end{cases} \tag{14}$$

.

Using equation (11) up to equation (14) into equation (10), then we obtained the following equation:

$$\frac{dV(t)}{dt} = \gamma\mu S^*\left(2-\frac{S^*}{S}-\frac{S}{S^*}\right) + \frac{\gamma\beta I^*S^*}{N}\left(3-\frac{S^*}{S}-\frac{I}{I^*}-\frac{EI^*}{IE^*}-\frac{SIE^*N}{I^*S^*NE}\left(1-\frac{ES^*}{SE^*}\right)\right) + \gamma(1-\epsilon)\theta T^*\left(3-\frac{EI^*}{IE^*}-\frac{TE^*}{ET^*}-\frac{IT^*}{TI^*}\right) + k_1\epsilon\theta T^*\left(2-\frac{TI^*}{IT^*}-\frac{IT^*}{TI^*}\right) \tag{15}$$

Using properties of the arithmetic mean and geometric mean in Equation (15)we have

$$\begin{cases} \left(2-\frac{S^*}{S}-\frac{S}{S^*}\right) \le 0 \\ \left(3-\frac{S^*}{S}-\frac{I}{I^*}-\frac{EI^*}{IE^*}-\frac{SIE^*N}{I^*S^*NE}\left(1-\frac{ES^*}{SE^*}\right)\right) \le 0 \\ \left(3-\frac{EI^*}{IE^*}-\frac{TE^*}{ET^*}-\frac{IT^*}{TI^*}\right) \le 0 \\ \left(2-\frac{TI^*}{IT^*}-\frac{IT^*}{TI^*}\right) \le 0 \end{cases} \tag{16}$$

As all the parameters are non-negative, therefore it follows that $\frac{dV(t)}{dt} \le 0$ when $R_0 > 1$. Hence, by the LaSalle's Invariance Principle (Lasalle, 1976), $(S, E, I, T) \longrightarrow (S^*, E^*, I^*, T^*)$ as $t \longrightarrow \infty$.

2.9. Sensitivity of the Basic Reproduction Number

We carried out sensitivity analysis in order to determine the relative significance of model parameters on disease transmission. The analysis will enable us to find out parameters that have high impact on the basic reproduction number and which should be targeted by intervention strategies. We perform sensitivity analysis by calculating the sensitivity indices of the basic reproduction number R_0 in order to determine whether tuberculosis (TB) can be spread in the population or not. To carry out this analysis, we use the normalized forward sensitivity index of a variable to a parameter.

Definition: The normalized forward sensitivity index of R_0 depending on the differentiability on a parameter Ψ.

$$S_\Psi^{R_0} = \frac{\Psi}{R_0} \times \frac{\partial R_0}{\partial \Psi}$$

We obtain the sensitivity analysis of R_0 separately in the following way:

$$S_\beta^{R_0} = \frac{\beta}{R_0} \times \frac{\partial R_0}{\partial \beta} = 1$$

$$S_{\gamma}^{R_0}=\frac{\gamma}{R_0}\times\frac{\partial R_0}{\partial\gamma}=1=\frac{\beta\mu(\theta+\mu+\psi+\alpha_2)(\theta(\mu+\sigma-\epsilon\sigma)+(\mu+\sigma)(\mu+\psi)+(\mu+\sigma)\alpha_2+\alpha_1(\theta+\mu+\psi+\alpha_2))}{(\mu(\gamma+\mu)(\theta+\mu)+\mu(\gamma+\theta-\epsilon\theta+\mu)\sigma+(\gamma+\mu)(\mu+\sigma)\psi+(\gamma+\mu)((\mu+\sigma)\alpha_2+\alpha_1(\theta+\mu+\psi+\alpha_2)))^2}\times\frac{\gamma}{R_0}>0$$

$$S_{\mu}^{R_0}=\frac{\mu}{R_0}\times\frac{\partial R_0}{\partial\mu}=\frac{\begin{matrix}\beta\gamma(\gamma(-1+\epsilon)\theta\sigma+(\gamma+\mu)(-\epsilon\theta\sigma+(\mu+\sigma+\alpha_1)(\theta+\mu+\psi+\alpha_2))-(\theta+\mu+\psi+\alpha_2)\\(-\epsilon\theta\sigma+(\mu+\sigma+\alpha_1)(\theta+\mu+\psi+\alpha_2)+(\gamma+\mu)(\theta+2\mu+\sigma+\psi+\alpha_1+\alpha_2)))\end{matrix}}{\left(\gamma(-1+\epsilon)\theta\sigma+(\gamma+\mu)\left(-\epsilon\theta\sigma+(\mu+\sigma+\alpha_1)(\theta+\mu+\psi+\alpha_2)\right)\right)^2}\times\frac{\mu}{R_0}<0$$

$$S_{\epsilon}^{R_0}=\frac{\epsilon}{R_0}\times\frac{\partial R_0}{\partial\epsilon}=\frac{\beta\gamma(\gamma\theta\sigma-\theta(\gamma+\mu)\sigma)(\theta+\mu+\psi+\alpha_2)}{\left((\gamma+\mu)\left((\mu+\sigma+\alpha_1)(\theta+\mu+\psi+\alpha_2)-\epsilon\theta\sigma\right)-\gamma(1-\epsilon)\theta\sigma\right)^2}\times\frac{\epsilon}{R_0}>0$$

$$S_{\alpha_1}^{R_0}=\frac{\alpha_1}{R_0}\times\frac{\partial R_0}{\partial\alpha_1}=-\frac{\beta\gamma(\gamma+\mu)(\theta+\mu+\psi+\alpha_2)^2}{\left(\gamma(-1+\epsilon)\theta\sigma+(\gamma+\mu)\left(-\epsilon\theta\sigma+(\mu+\sigma+\alpha_1)(\theta+\mu+\psi+\alpha_2)\right)\right)^2}\times\frac{\alpha_1}{R_0}<0$$

$$S_{\alpha_2}^{R_0}=\frac{\alpha_2}{R_0}\times\frac{\partial R_0}{\partial\alpha_2}=-\frac{\beta\gamma\theta(\gamma+\epsilon\mu)\sigma}{\begin{matrix}(\mu(\gamma+\mu)(\theta+\mu)+\mu(\gamma+\theta-\epsilon\theta+\mu)\sigma+(\gamma+\mu)\\(\mu+\sigma)\psi+(\gamma+\mu)((\mu+\sigma)\alpha_2+\alpha_1(\theta+\mu+\psi+\alpha_2)))\end{matrix}^2}\times\frac{\alpha_2}{R_0}<0$$

$$S_{\theta}^{R_0}=\frac{\theta}{R_0}\times\frac{\partial R_0}{\partial\theta}=\frac{\beta\gamma(\gamma+\epsilon\mu)\sigma(\mu+\psi+\alpha_2)}{\begin{matrix}(\mu(\gamma+\mu)(\theta+\mu)+\mu(\gamma+\theta-\epsilon\theta+\mu)\sigma+(\gamma+\mu)\\(\mu+\sigma)\psi+(\gamma+\mu)((\mu+\sigma)\alpha_2+\alpha_1(\theta+\mu+\psi+\alpha_2)))\end{matrix}^2}\times\frac{\theta}{R_0}>0$$

$$S_{\psi}^{R_0}=\frac{\psi}{R_0}\times\frac{\partial R_0}{\partial\psi}=-\frac{\beta\gamma\theta(\gamma+\epsilon\mu)\sigma}{\begin{matrix}(\mu(\gamma+\mu)(\theta+\mu)+\mu(\gamma+\theta-\epsilon\theta+\mu)\sigma+(\gamma+\mu)\\(\mu+\sigma)\psi+(\gamma+\mu)((\mu+\sigma)\alpha_2+\alpha_1(\theta+\mu+\psi+\alpha_2)))\end{matrix}^2}\times\frac{\psi}{R_0}<0$$

$$S_{\sigma}^{R_0}=\frac{\sigma}{R_0}\times\frac{\partial R_0}{\partial\sigma}=-\frac{\beta\gamma(\theta+\mu+\psi+\alpha_2)(\gamma(\mu+\psi)+\mu(\theta-\epsilon\theta+\mu+\psi)+(\gamma+\mu)\alpha_2)}{(\gamma(-1+\epsilon)\theta\sigma+(\gamma+\mu)(-\epsilon\theta\sigma+(\mu+\sigma+\alpha_1)(\theta+\mu+\psi+\alpha_2)))^2}\times\frac{\sigma}{R_0}<0$$

These sensitivity indices along with signs are provide information that how crucial each parameter is to disease transmission and prevalence. A positive (+) sign indicates that those parameters have great impact on expanding the disease in the community if their values are increasing. Due to the reason that the basic reproduction number increases as their values increase. On the other hand, an index with negative (-) indicates that those parameters have an influence of minimizing the burden of the disease in the community as their values increase and also as their values increase, the basic reproduction number decreases, which leads to minimizing the endemic nature of the disease in the community.

3. TB Model with Optimal Control

In chapter four, we presented a mathematical model for the transmission dynamics of tuberculosis and studied its well-possedness mathematically and epidemiologically without giving intervention mechanism. In this chapter, the intervention mechanism is addressed using the theory of optimal control. Optimal control theory has been applied to various mathematical models for studying the transmission dynamics of TB for example, see in ([19, 61]) and references cited therein. It deals with the problem of finding a control law for a given system such that a certain optimality criterion is achieved with minimum implementation cost. A control problem includes a cost functional that is a function of state and control variables. An optimal control is a set of differential equations describing the paths of the control variables that minimize the cost function. Our objective is to minimize the number of infectious by reducing treatment failure and the overall cost of the treatment during a fixed time period. For this, we introduce and analyze a control function in the TB model (1). After we present the existence of optimal control and characterization, we study the transmission dynamics of TB through numerical simulation.

3.1. Optimal Control Problem

In this section, we consider an SEITR compartmental model presented in chapter 4 to study the transmission dynamics of TB epidemic. In the model, we introduce tow control functions $u_1(\cdot)$ and $u_2(\cdot)$ representing prevention effort of TB disease, that protect TB susceptible from contacting the disease and the effort that prevents the failure of treatment in active TB individuals I respectively. It corresponds to supervising the patients, helping them to take the TB medications regularly on time and complete the TB treatment. The resulting dynamical control system is given by the following system of nonlinear ordinary differential equations:

$$\begin{cases}\frac{dS}{dt}=\Lambda-\frac{(1\ -\ u_1)\beta SI}{N}-\mu S\\ \frac{dE}{dt}=\frac{(1\ -\ u_1)\beta SI}{N}-(\ \mu+\gamma)E+(1-\epsilon)(1\ -\ u_2)\theta T\\ \frac{dI}{dt}=\gamma E+(1\ -\ u_2)\epsilon\theta T-(\mu+\sigma+\alpha_1)I\\ \frac{dT}{dt}=\sigma I-(\mu+\theta+\alpha_2+\psi)T\\ \frac{dR}{dt}=\psi T-\mu R\end{cases}\tag{17}$$

with initial conditions: $S(0)=S_0>0, E(0)=E_0\geq$

$0, I(0) = I_0 \geq 0, T(0) = T_0 \geq 0, and \ \ R(0) = R_0 \geq 0.$

The aim is to find the optimal values u^* of the controls u such that the associated state trajectories S^*, E^*, I^*, T^*, R^* are solution of the system (17) in the treatment time interval $[0, T]$ with given initial conditions and minimize the objective functional. For this, we consider the objective function.

$$J(u) = \int_0^T \left(AI(t) + \frac{1}{2} W_1 u_1^2 + \frac{1}{2} W_2 u_2^2 \right) dt \quad \longrightarrow min \quad (18)$$

Subject to (17) with its initial condition where A is relative constant that measures the relative importance of reducing the associated classes on the spread of the disease and the relative weight constants W_1 and W_2 is a measure of the relative cost of the interventions associated with the control u_1 and u_2. Clearly, u depends on the amount of resources available to effectively implement the control measure. The case $u = 0$, implies no control measure is taken and the model equation (17) is equivalent to (1). On the other hand, $u = 1$ implies a 100% success of intervention which is unrealistic. Thus we assume that $0 \leq u_1(t), u_2(t) \leq u_{max} < 1$ for numerical implementation. In the cost functional, the term $AI(t)$ describe the cost incurred related to TB infectious. Additionally, the function J represents the total cost incurred due to TB infectious and its control strategies. Further, the integrand function $F(t, S, E, I, T, R, u) = AI(t) + \frac{1}{2} W_1 u_1^2 + \frac{1}{2} W_2 u_2^2$ measures the current cost at time t. Lastly, the fixed constant T denotes the terminal treatment time.

The set of admissible control functions is defined by

$$\Omega = \{u(\cdot) \in (L^\infty(0,T)) : 0 \leq u_1(t), u_2(t) \leq 1, \forall t \in [0,T]\} \quad (19)$$

Then we consider the optimal control problem of determining $(S^*(\cdot), E^*(\cdot), I^*(\cdot), T^*(\cdot), R^*(\cdot))$, associated with an admissible control $u^* \in \Omega$ on the treatment time interval $[0, T]$, subjected to the state control system (17) in $\mathbb{R}^5$ with its initial condition and minimizing the cost functional (18). More precisely, the optimal control problem can be defined as

$$J[u^*] = \min_{\Omega} J[u(\cdot)] \quad (20)$$

satisfying (17) and its initial conditions.

Remark 1. The optimal control problem is to minimize the objective functional J considering active tuberculosis infections and the costs of treatment of infected individuals. The control functions u is also a bounded Lebesgue measurable function defined on the interval [0, 1].

3.2. Existence of the Optimal Control Problem

In this subsection, we will investigate the existence of an optimal control of our model (20). The Boundednes of solutions to system (1) for finite time interval is needed to establish the existence of an optimal control and the uniqueness of the optimality system. For model system (17) to be epidemiologically meaningful, it is important to prove that all its state variables are nonnegative for all time. To establish the upper bounds for the solutions, we consider an equation for the total population size N. The rate of change of the total population, obtained by adding all the equations in model (17) is given by

$$\frac{dN(t)}{dt} = \Lambda - \mu N(t) - \alpha_1 I(t) - \alpha_2 T(t) - \theta T u \leq \Lambda - \mu N(t)$$

Now, by applying integral factor we obtain $N(t) \leq \left(N(0) - \frac{\Lambda}{\mu}\right) e^{-\mu t} + \frac{\Lambda}{\mu} \leq \frac{\Lambda}{\mu}$. Thus, N is bounded above by $\frac{\Lambda}{\mu}$. The upper bound for N is also the upper bound for S, E, I, T and R since they are nonnegative from our assumption.

Theorem 3.2.1. There exist an optimal control u^* and a corresponding solution vector $(S^*, E^*, I^*, T^*, R^*)$ to the state initial value problem (17) that minimizes the cost functional $J(u)$ of (18) over the set of admissible control Ω.

Proof. We refer to the conditions in Theorem 2.1 and its corresponding corollary 2.1 in (Fleming et al., 2012). The requirements there on the set of admissible controls and on the set of end conditions are clearly met here. The following non-trivial requirement from Fleming and Rishel's theorem are listed and verified below:

1) The set of all solutions to system (17) with corresponding control functions inΩ is non-empty.
2) The control set is convex and closed.
3) The integral of the objective functional is convex.
4) The integrand $F(t, S, E, I, T, R, u)$ in equation (21) is convex with respect to control variables and additionally fulfills that $F(t, S, E, I, T, R, u) \geq f(u)$, where f is continuous and $|u|^{-1} f(u) \to +\infty$ as $|u| \to +\infty$.

In order to established condition (i), we refer to Picard-Lindelof existence theorem [62]. If the solutions of the state equations are a prior bounded and if the state equations are continuous and Lipschitz continuous in the state variables, then there is a unique solution corresponding to every admissible control in the given domain. With the result that, if $g(t, x, u)$ is bounded, continuous, and Lipschitz in the state variable, then there exists a unique solution corresponding to every admissible control Ω. Hence, for any $u \in \Omega$ and the state variables, we have

$$0 \leq N(t) \leq \frac{\Lambda}{\mu} \quad (21)$$

and nonempty by model assumption. Furthermore, with the bounded established (21), it implies that the state system is continuous and bounded. It is possible to show the Bound-

ednes of the partial derivative with respect to the state variable, i.e. $\frac{\partial g}{\partial x}$, exist and finite, which established the system is Lipschitz with respect to the state variables [62]. This established that the proof of condition *(i)* is complete.

To proof *(ii)*, consider

$\Omega = \{u \in \mathbb{R} : \|(u_1, u_2)\| \leq 1\}$

Assume that $u_1, u_2 \in \Omega$ such that $|u_1| \leq 1$ and $|u_2| \leq 1$. Then for any $\alpha \in [0,1]$,

$|\alpha u_1 + (1-\alpha)u_2| \leq \alpha|u_1| + (1-\alpha)|u_2| \leq 1.$

This implies that the control set Ω is convex and closed.

Next we verify condition *(iii)*, the integral of the cost function is given by

$$F(t,S,E,I,T,R,u) = AI(t) + \frac{1}{2}W_1u_1^2 + \frac{1}{2}W_2u_2^2$$

Recall that any affine function is convex and the sum of convex function is also convex (Chong et al., 2023). Therefore, F is convex on Ω. Finally, to verify condition *(iv)*, we note that the integrand $F(t,S,E,I,T,R,u)$ of the objective functional is clearly convex in control. To prove the bound on the $F(t,S,E,I,T,R,u)$ we note that the state system (17) is linear in control variable u with coefficients depending on state variables.

The integrand of the cost functional $F(t,S,E,I,T,R,u) = AI(t) + \frac{1}{2}W_1u_1^2 + \frac{1}{2}W_2u_2^2$ is the sum of convex function and hence convex with respect to control variables. Furthermore,

$$F(t,S,E,I,T,R,u) = AI(t) + \frac{1}{2}W_1u_1^2 + \frac{1}{2}W_2u_2^2 \geq \frac{1}{2}W_1u_1^2 + \frac{1}{2}W_2u_2^2 \tag{22}$$

Let $r = \frac{W}{2} > 0$ and and define a continuous function $f(u) = r|u|^2$. Then from equation (21) we have $F(t,S,E,I,T,R,u) \geq f(u)$. Clearly $|u|^{-1}f(u) \to +\infty$ as $|u| \to +\infty$. Thus, condition *(iv)* is achieved. With this we conclude that the existence of an optimal control $(S^*, E^*, I^*, T^*, R^*, u^*)$ that minimizes the cost functional of (18) over the set of admissible control Ω.

The Pontryagin's Maximum Principle (PMP) stated in ([17], theorem 2.1) gives the required necessary optimality condition as given in the following theorem. Note that since we look for minimization, we use Pontryagin's Minimum Principle.

3.3. Characterization of Optimal Control Solutions

Pontryagin's Maximum Principle [58] provides the necessary conditions that an optimal pair must satisfy. According to this principle, for u^* to be optimal with corresponding optimal states S^*, E^*, I^*, T^*, R^*, which minimizes the objective functional (18) for a fixed final time T, then there exists a non-trivial absolutely continuous mapping

$\lambda: [0,T] \to \mathbb{R}^5, \lambda = (\lambda_1(t), \lambda_2(t), \lambda_3(t), \lambda_4(t), \lambda_5(t))$ called the adjoint vector, such that

1) the Hamiltonian function is defined as

$$\mathcal{H} = AI(t) + \frac{1}{2}W_1u_1^2 + \frac{1}{2}W_2u_2^2 + \sum_{i=1}^{5}\lambda_i(t)g_i(t,S,E,I,T,R,u), \tag{23}$$

where g_i stands for the right hands of the constraints (20) for $i = 1,2,3,4,5$.

2) the control system

$$S' = \frac{\partial \mathcal{H}}{\partial \lambda_1}, E' = \frac{\partial \mathcal{H}}{\partial \lambda_2}, I' = \frac{\partial \mathcal{H}}{\partial \lambda_3}, T' = \frac{\partial \mathcal{H}}{\partial \lambda_4}, R' = \frac{\partial \mathcal{H}}{\partial \lambda_5} \tag{24}$$

3) The adjoint system

$$\lambda_1' = \frac{-\partial \mathcal{H}}{\partial S}, \lambda_2' = \frac{-\partial \mathcal{H}}{\partial E}, \lambda_3' = \frac{-\partial \mathcal{H}}{\partial I}, \lambda_4' = \frac{-\partial \mathcal{H}}{\partial T}, \lambda_5' = \frac{-\partial \mathcal{H}}{\partial R} \tag{25}$$

4) and the optimality condition

$$\mathcal{H}(S^*, E^*, I^*, T^*, R^*, u^*, \lambda^*) = \min_{u \in \Omega} \mathcal{H}(S, E, I, T, R, u, \lambda) \tag{26}$$

5) Moreover, the transversality condition

$$\lambda_i(T) = 0, i = 1, \ldots, 5 \tag{27}$$

also holds true.

In the following result, we give the characterization of optimal control.

Theorem 5.3.1. There exists an optimal solution, S^*, E^*, I^*, T^*, R^* and corresponding optimal controls u^* that minimizes $J(u)$ over the set of admissible control Ω. Moreover, there exist an adjoint function $\lambda_i^*(t)$, for $i = 1,2,3,4,5$ such that

$$\begin{cases} \lambda_1' = (1-u_1)\frac{\beta I}{N}(\lambda_1-\lambda_2)+\mu\lambda_1, \\ \lambda_2' = \lambda_2(\gamma+\mu)-\lambda_3\gamma, \\ \lambda_3' = -A+\frac{\lambda_1\beta S}{N}-\frac{\lambda_1\beta S}{N}+\lambda_3(\mu+\alpha_1+\varepsilon)-\lambda_4\varepsilon, \\ \lambda_4' = -\lambda_2(1-\varepsilon)(1-u)\theta-\lambda_3(1-u)\varepsilon\theta+\lambda_4(\mu+\theta+\alpha_2+\psi)-\lambda_5\psi, \\ \lambda_5' = \lambda_5\mu. \end{cases} \tag{28}$$

With transiversality conditions $\lambda_i^*(T)=0$, for $i=1,2,3,4,5$.
Moreover, the optimal control $u^*(t)$ is given by

$$u_1^*(t)=\min\left\{\max\left\{0,\frac{\beta SI(\lambda_2-\lambda_1)}{W_1}\right\},1\right\}, u_2^*(t)=\min\left\{\max\left\{0,\frac{T\theta(\varepsilon(\lambda_3-\lambda_2)+\lambda_2)}{W_2}\right\},1\right\} \tag{29}$$

Proof. By Corollary 2.1 in Fleming and Rishel [20], the convexity of the integrand (of the objective functional) in (28) with respect to u guarantees the existence of an optimal control as proved above. The adjoint equations and transversality conditions can be obtained via the Pontryagin's Maximum Principle such that:

$$\frac{d\lambda_1}{dt}=-\frac{\partial\mathcal{H}(t,S,u,\lambda)}{\partial S},\lambda_1(T)=0,$$

$$\frac{d\lambda_2}{dt}=-\frac{\partial\mathcal{H}(t,E,u,\lambda)}{\partial E},\lambda_2(T)=0,$$

$$\frac{d\lambda_3}{dt}=-\frac{\partial\mathcal{H}(t,I,u,\lambda)}{\partial I},\lambda_3(T)=0,$$

$$\frac{d\lambda_4}{dt}=-\frac{\partial\mathcal{H}(t,T,u,\lambda)}{\partial T},\lambda_4(T)=0,$$

$$\frac{d\lambda_5}{dt}=-\frac{\partial\mathcal{H}(t,R,u,\lambda)}{\partial R},\lambda_5(T)=0.$$

Considering the optimality conditions given by $\frac{\partial\mathcal{H}}{\partial u}=0$, the optimal control u^* can be explicitly obtained in terms of state and adjoint variables. That means for the optimality condition, we differentiate the Hamiltonian function with respect to u and equate it to zero by taking into account the boundedness on u. For this reason, we have the following optimality condition:

$$\frac{\partial\mathcal{H}}{\partial u_i}=0$$

which implies that

$$u_1^*(t)=\frac{\beta SI(\lambda_2-\lambda_1)}{W_1} \quad and \quad u_2^*(t)=\frac{T\theta(\varepsilon(\lambda_3-\lambda_2)+\lambda_2)}{W_2}$$

For Boundednes of $u_i^*(t)$ and minimality condition, we have:

$$u_1^*(t)=\begin{cases} 0, & if \ \frac{\partial\mathcal{H}}{\partial u}>0 \\ \frac{\beta SI(\lambda_2-\lambda_1)}{W_1}, & if \ \frac{\partial\mathcal{H}}{\partial u}=0 \\ 1, & if \ \frac{\partial\mathcal{H}}{\partial u}<0 \end{cases}$$

$$u_2^*(t)=\begin{cases} 0, & if \ \frac{\partial\mathcal{H}}{\partial u}>0 \\ \frac{T\theta(\varepsilon(\lambda_3-\lambda_2)+\lambda_2)}{W_2}, & if \ \frac{\partial\mathcal{H}}{\partial u}=0 \\ 1, & if \ \frac{\partial\mathcal{H}}{\partial u}<0 \end{cases}$$

Concluding that, the optimal control $u_i^*(t)$ can be summarized as

$$u_1^*(t)=\min\left\{\max\left\{0,\frac{\beta SI(\lambda_2-\lambda_1)}{W_1}\right\},1\right\},$$

$$u_2^*(t)=\min\left\{\max\left\{0,\frac{T\theta(\varepsilon(\lambda_3-\lambda_2)+\lambda_2)}{W_2}\right\},1\right\}.$$

This completes the proof of the theorem.

4. Numerical Simulation

This chapter present and discusses numerical results for the system (1) for different values of parameters given in the model. The simulation process is carried out using MATLAB software. We start by defining and estimating the values of parameter used in the model. Then we illustrate the simulation results graphically.

4.1. Parameter Estimations

In this section, we fit the proposed model to cumulative cases of TB infection data and estimate the unknown model parameters. Table 3 depicts the cumulative cases of TB infection from 2016 to 2022 extracted from Werder district of Doolo zone, Somali region, Ethiopia. The squared sum of errors (SSE) between model solution and the data can be computed as

$$SSE(\varphi)=argmin\sum_{i=1}^{n}\|I(t)-\bar{I}(t)\|^2 \tag{30}$$

where $\|\cdot\|$ denotes the Euclidean norm in $\mathbb{R}^n$ and n is the number of available real data points. The expression $\bar{I}_i(t)$ represents the actual cumulative TB infected cases and $I_i(t)$ are the corresponding model solutions at time t_i. In the process of least-squares fitting, we are looking for a value $\bar{\varphi}$ of model parameter φ such that the squared sum of errors is the

minimum. Clearly, such a problem is nonlinear least squares problem, since the dependence of a solution $I(t,\varphi)$ on the parameter φ is through a highly nonlinear system of differential equations.

Table 3. *Cumulative cases of TB infection from 2016 - 2022 (In Werder district, Somali region, Ethiopia).*

Year	2016	2017	2018	2019	2020	2021	2022
TB cases	123	186	112	155	132	180	162

In the next section, we study the dynamics of TB through numerical simulations by estimating the values of parameters in the proposed model with appropriate initial conditions with the help of least square technique.

4.2. Simulation Results and Discussion

Here, we illustrate numerically the solution of the optimal control problem proposed in Section (17) and explain the impact of control strategy on the spread of Tuberculosis. For this purpose, we use the forward-backward sweep method presented in the book of Lenhart and Workman [6, 62].

To briefly summarize the procedure; first we solve the control system with an initial guess for the control variables using forward fourth-order Runge-Kutta scheme and transversality conditions. The adjoint system is then solved applying the backward fourth-order Runge-Kutta scheme using the current solution of state variables. Then, the controls are updated by means of convex combination of the previous controls and the values computed in the characterizations process. The updated controls are then utilized to repeat the solution of state and adjoint systems. The iteration continued until a predefined convergence criterion is met.

We assume that initial population of exposed individuals $E(0) = 1000$. The initial infected population based on collected data $I(0) = 123$ as given Table 3. Initially, we assumed the treated and recovered populations as $T(0) = 50$ and $R(0) = 30$ respectively while the initial susceptible population is given by $S(0) = N(0) - L(0) - I(0) - T(0) - R(0) = 83{,}875$. The natural death rate is computed as $\mu = \frac{1}{66.71}$ per year, where 66.71 year is the average life expectancy in Ethiopia (Kereyu & Demie, 2021). The total population of Werder district in 2017 was estimated as $N(0) = 85{,}078$. The recruitment rate Λ, is then calculated as $\Lambda = \mu N(0) = 1{,}275.3410283316$ per year. The remaining model parameters are estimated using least-square fitting methods which provide a better fit for the model solution to the real data as shown in Figure 3 and the corresponding parameters value are depicted in Table 4. The red-circle shows the yearly TB cases reported in Weder district while the solid line denotes the model fit. Residuals plots for the model and the real data in Table 3 are given in Figure 4 and the residuals seem to be random and the standard errors are generally small for the model.

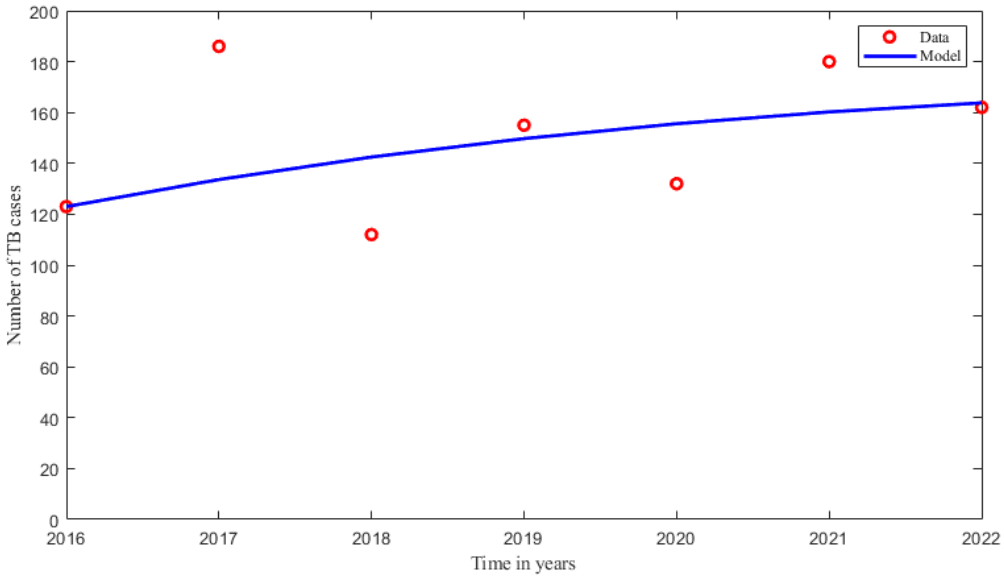

Figure 3. *TB model fit with real data on the number of TB cases in Werder district.*

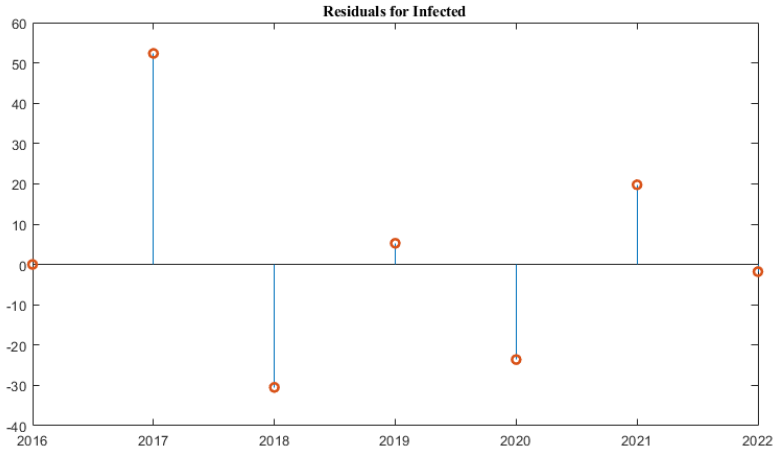

Figure 4. *Residual of estimated parameters.*

Table 4. *Fitted and estimated values for the parameters of the model.*

Parameters	Description	Value	References
$N(0)$	Initial population	85,078	(CSA 2007)
Λ	Recruitment rate	1,275.3410283316	Calculated
β	Disease contact rate	0.0341	Fitted
ψ	Progression rate from compartment T to R	0.1098	Fitted
σ	Treatment rate from compartment I to T	0.0734	Fitted
μ	Natural death rate	$\frac{1}{66.71}$	(Kereyu & Demie, 2021)
α_1	Disease related mortality rate of infected individuals	0.0159	Fitted
α_2	Disease related mortality rate in T	0.0046	Fitted
θ	Rate at which treated individuals leave the T	0.0251	Fitted
ϵ	Treatment failure rate	0.0178	Fitted
γ	Rate of moving from E to I	0.0244	Fitted

The associated parameters values of the model (1) are tabulated in Table 4 above. Consequently, using these parameter values we obtained in this study, the value of reproduction number R_0 for the 2016-2022 TB cases in Werder district is

$$R_0 = \frac{\beta(\mu+\theta+\alpha_2+\psi)\gamma}{(\mu+\gamma)((\mu+\sigma+\alpha_1)(\mu+\theta+\alpha_2+\psi)-\epsilon\theta\sigma)-(1-\epsilon)\theta\sigma\gamma} \approx 0.218232 < 1.$$

The result shows that disease will not break out under current situation by Theorem 2.2.

The numerical solutions are illustrated using MATLAB program. The optimality system, which consists of the state system and the adjoint system, is solved to obtain the optimal control solution. An iterative scheme, fourth order Runge-Kutta, is used to solve the optimality system. The adjoint equations are solved by the backward fourth order Runge-Kutta scheme using the current iterations solutions of the state equations because of the transversality conditions of (12). Then the controls are updated by using a convex combination of the previous controls and the value from the characterizations (13). This process is repeated and the iterations are stopped if the values of the unknowns at the previous iterations are very close to the ones at the present iteration (for more detail see [62].

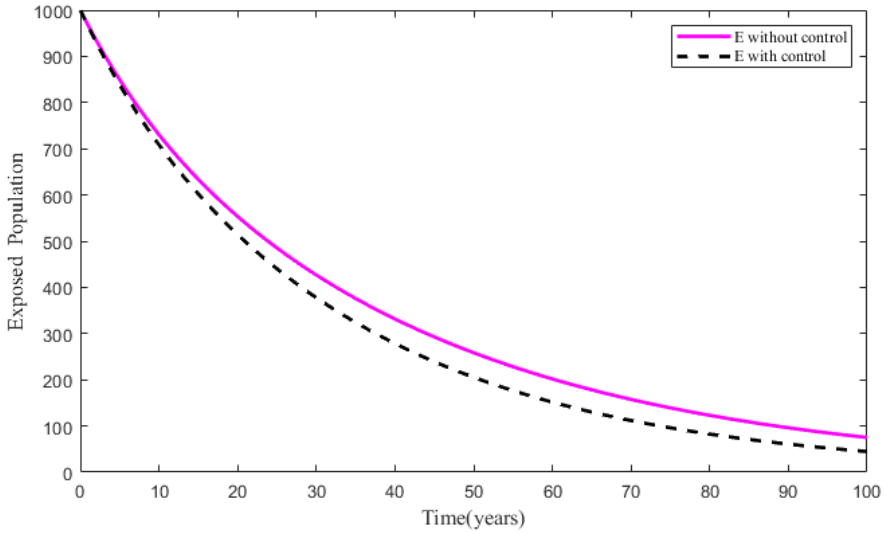

Figure 6. *The figure illustrates the impact of optimal control on the exposed populations.*

We conducted numerical simulation in order to investigate the effects of the control strategies on the transmission dynamics of TB. The initial values of model state variables are

$$\big(S(0), E(0), I(0), T(0), R(0)\big) = (83875, 1000, 123, 50, 30)$$

The corresponding parameter values used were illustrated in Table 4. For the adjoint system we set terminal conditions $\lambda_i(T) = 0;\ i = 1, \ldots, 5$, where $T = 100$ is simulation time. We considered the numerical value of the controls $u_i; i = 1, 2$ between zero and one as they are not 100% effective. The constants in the cost functional are taken as follows: coefficients for cost of infection (weight constants) are $A = 1.2$ and coefficients for cost of the control efforts (cost weight) are $W_1 = 5$ and $W_2 = 10$.

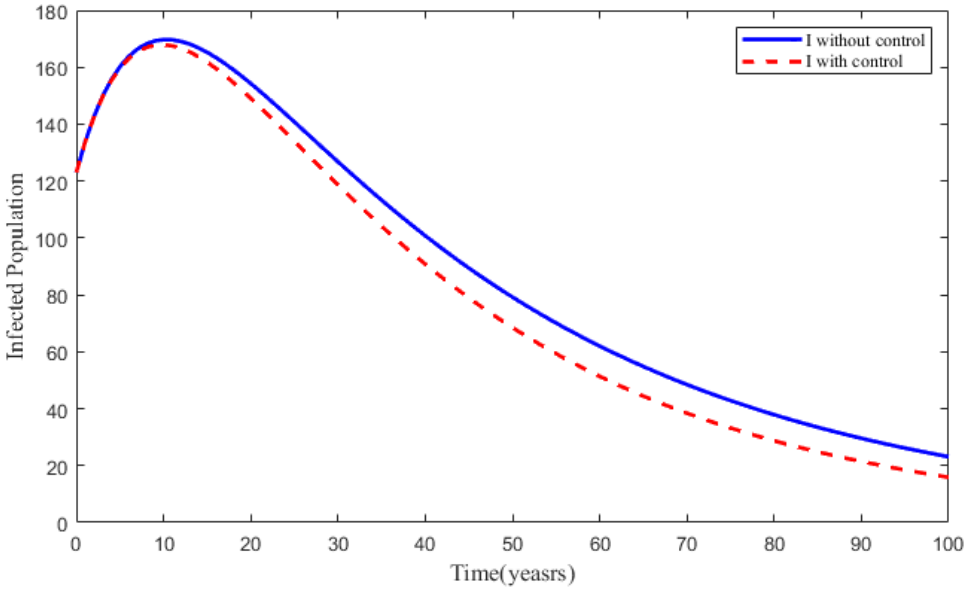

Figure 7. *The figure illustrates the impact of optimal control on the infected population.*

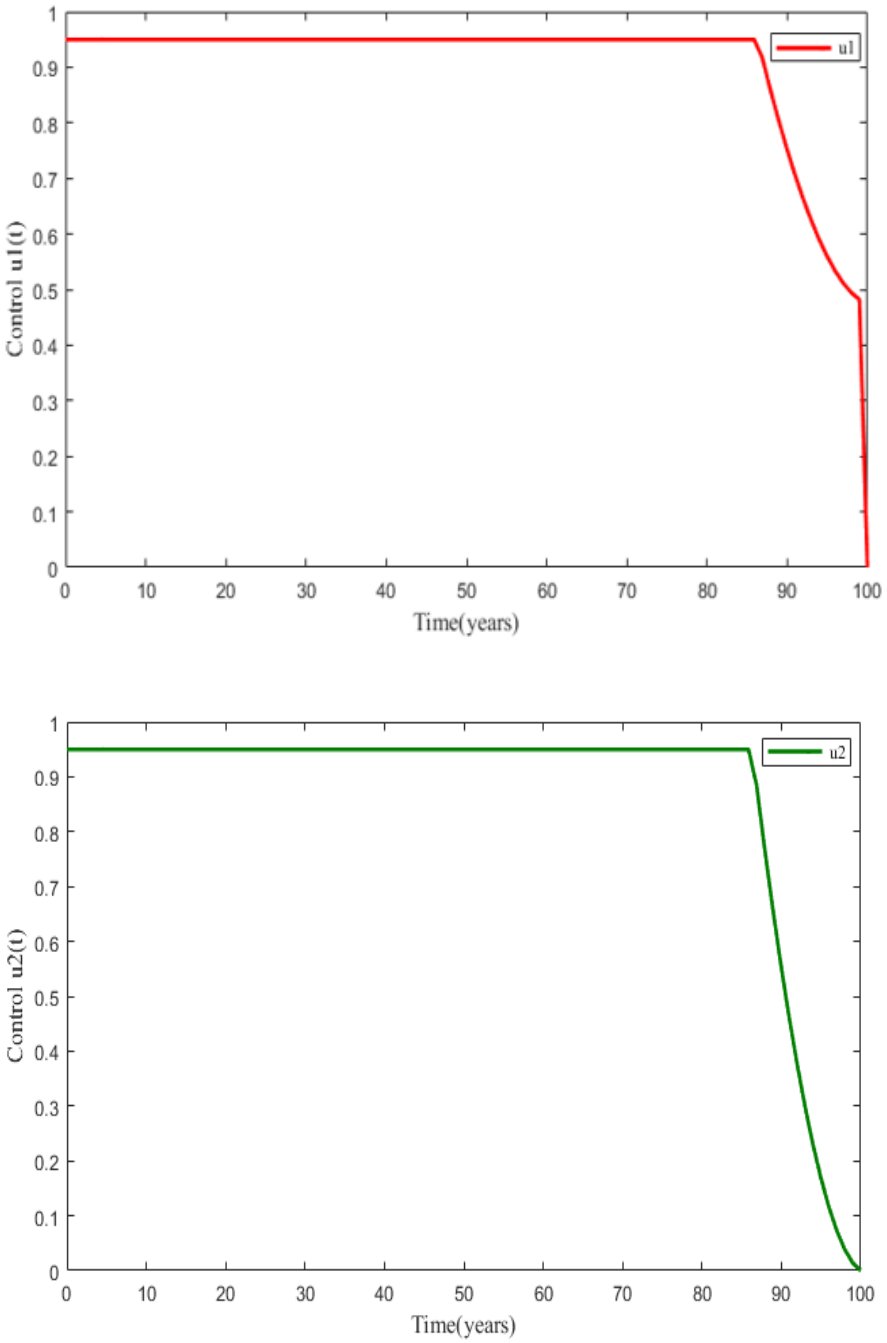

Figure 8. *Control profile when A = 1.2 and* $W_1 = 5$ *and* $W_2 = 10$.

Figures 5, 6 and 7 presents the impact of control on the susceptible, exposed and infected populations respectively. It shows the density of susceptible populations is increasing rapidly in the presence of control while the population of exposed and infected are damped down when controls are applied. Thus, as expected the number of susceptible $S(t)$ is increases in the presence of control and at the same time the number of TB exposed $E(t)$ and TB infected $I(t)$are decreases in the presence of control. Figure 8 illustrates control profile of control interventions $u_1(t)$ and $u_2(t)$.

5. Conclusion

In this study, we studied a mathematical model of the transmission dynamics of TB with optimal control. The well-possedness of the model was established both in the mathematical and epidemiological sense by showing that all solutions of the model are positive and bounded with initial conditions in a certain meaningful set. The model has two non-negative equilibria, namely, the disease-free and the endemic equilibrium. The existence and stability of the dis-

ease-free and endemic equilibria of the model were performed. For the sack of completeness both local and global stability of the disease-free and the endemic equilibrium are determined by a threshold quantity (basic reproduction number R_0). Sensitivity indices of R_0 with respect to the model parameters reveal the transmission dynamics of tuberculosis. The optimal control strategy is found by minimizing the number of TB exposed and infected population taking into account the cost of implementation. The existence of optimal controls and characterization is established with the help of Pontryagin's Maximum Principle. The model is then fitted with cumulative cases of infected TB by collecting real data from Werder district Health Office from 2016 to 2022 years. Further, different simulation cases were comparatively performed to obtain the best control strategies. In general, the numerical simulation results demonstrate good agreement with our analytical results. The simulation results also clearly shown that the epidemic of TB can be minimized by creating awareness and preventing the failure of treatment in active TB infectious individuals through continuous supervision and helping patients during treatment period with optimal implementation cost.

Recommendation

Based on the findings of this study, we recommend to government and concerned stake holders to implement a combination of all prevention programs and continuous supervision and helping patients during treatment period to prevent failure of treatment in active TB infectious individuals.

Acknowledgments

First and foremost, we like to express our gratitude to the Almighty God. Then we would strive to convey our heartfelt gratitude to Kabridahar University for their help, such as by allocating funds to the project. Our gratitude also goes to Kabridahar University's Research and Technology Transfer Directorate for assisting us in getting the budget into our hands so that we could work on it. Finally, we want to convey our heartfelt gratitude to the werder district health office, werder general hospital, our respondents, and all those parties that assisted us in completing this research.

Conflicts of Interest

The authors declare no conflicts of interest.

References

[1] Adebisi, B., Yusuff. A and Adebayo. M., 2020. Burden of tuberculosis and challenges facing its Eradication in West Africa.

[2] Agyeman. D., Akosua. A and Richard. O., 2017. Tuberculosis-an overview. Journal of Pub Health and Emergency.

[3] Alene. A., Kefyalew. Aand Alachew. A., 2019. Mapping tuberculosis treatment outcomesin Ethiopia. BMC Infectious diseases.

[4] Alebachew, Z., 2011. Ethiopian National TB Prevalence survey 2010 - 2011 PreliminaryResult. Available from: http://www.who.int/tb/advisory_bodies/impact_Measurement taskforce/meetings/lille _oct11_ethiopia.pdf

[5] Annabel. B., Anna. D and Hannah. M., 2021. Global tuberculosis report 2021. Geneva: World Health Organization.

[6] Athithan, S., and Mini Ghosh. M., 2013. Mathematical modelling of TB with the effects ofCase Detection and treatment. International Journal of Dynamics and Control.

[7] Banerjee. K and Sandip. S., 2014. Mathematical modeling: models, analysis andApplications. *CRC Press.*

[8] Castillo. C and Baojun. S., 2004. Dynamical models of tuberculosis and their applications. *Mathematical Biosciences and Engineering.*

[9] CDC, 2022. Tuberculosis - Disease Surveillance Epidemiology Program https://www.maine.gov/dhhs/mecdc/infectiousdisease/epi/tuberculosis/index.shtml

[10] CSA, 2007. Population and Housing Census Report: Somali Region. Available from: *http://www.csa.gov.et/newcsaweb/images/documents/surveys/PopulationandHousingcensus/ETH-pop-2007/survey0/data/Doc/Reports/Somali_Statistical.pdf*

[11] Daniel. M., 2006. The history of tuberculosis. Respiratory medicine, 100(11): 1862-1870.

[12] Egonmwan. A and Okuonghae. D., 2019. Analysis of a mathematical model forTuberculosis with Diagnosis. *Journal of Applied Mathematics and Computing.*

[13] Elshafie. M., 2017. Review of the access to tuberculosis care in Doolo Zone in SomaliRegion State of Ethiopia. https://bibalex.org/baifa/Attachment/Documents/NwBhyyenvZ_20180404111238547.pdf

[14] Fatmawati. J and Ahmadin. A., 2018. Mathematical modelling of Tuberculosis in aLogistically growing human population with optimal control. *World Journal ofModelling and Simulation.*

[15] Fleming. W., Wendell. H., and Raymond. W., 2012. Deterministic and stochastic optimalcontrol. *Springer Science and Business Media.*

[16] FMOH., 2015. Annual TBL Bulletin 2015.

[17] FMOH., 2020. Health Sector Strategic Plan III, 2015 - 2020.

[18] Gaff. A., Holly. J and Elsa. S., 2009. Optimal control applied to vaccination and treatment.

[19] Strategies for various epidemiological models. *Mathematical Biosciences and Engineering.*

[20] Gugsa. N., Abebe. M and Desalew. T., 2018. Knowledge, Attitude And Practice OnPrevention And Control Of Tuberculosis Among Bilida Kebele Residents, Mana Woreda, Jimma Zone, Oromia Region, South West Ethiopia.

[21] Herzog., 1998. History of tuberculosis. Respiration.

[22] Kelemu. M., Ashenafi. B and Peter. J., 2019. Modeling the Effects of Vaccination andTreatment On Tuberculosis Transmission Dynamics. *Journal of Applied Mathematics.*

[23] Kereyu, D., & Demie, S., 2021. Transmission dynamics model of Tuberculosis with optimal control strategies in Haramaya district, Ethiopia. *Advances in Difference Equations*, *2021*(1).

[24] Kokomo, E. and Emvudu, Y. (2016). Mathematical modeling: Proposal of a generalmethodology and application of this methodology to epidemiology. *Academic Journal of Applied Mathematical Sciences, 2(11): 147–156.*

[25] Liu. J. and Zhang. T., 2011. Global stability for a tuberculosis model. *Mathematical and Computer Modelling.*

[26] Julie. H and Marias. J., 2019. Multidrug-resistant tuberculosis infection and disease in children: a review of new and repurposed drugs. *National center for biotechnology information.*

[27] Malik. M., Monica. L and Aldila. D., 2018 Mathematical modeling and numerical Simulation of Tuberculosis spread with diabetes effect. *IOP Conf. Series: Journal of Physics.*

[28] MOFED., 2022. Federal Government of Ethiopia Ministry of Finance and EconomicDevelopment Public Finance Management Assessment Somali RegionalGovernment.. *Available from:* *https://pefa.org/sites/default/files/ETSomaliRegion-Jun15-PFMPR SN-Public. pdf*

[29] Nkamba. A., Leontine. S and Nkague. M., 2019. Mathematical model to assess vaccinationand Effective contact rate impact in the spread of tuberculosis. *Journal of Biological Dynamics.*

[30] Raviglione. M., Mario. A and Giorgia. S., 2016. Tuberculosis 2015: burden, challengesand Strategy for control and elimination. *Infectious disease reports.*

[31] Revelle. L., Charles. S., Walter. R and Feldmann. F., 1967. Mathematical models for the economic Allocation of tuberculosis control activities in developing nations. *American review of Respiratory disease.*

[32] Reves. R and Sahil. A., 2016. Ethiopia moves toward tuberculosis elimination, success Requires Higher investment. *Washington DC: Center for Strategic and International Studies.*

[33] Ricks, M., Philip. M and Richard. O., 2009. Estimating the burden of tuberculosis among foreign-born persons Acquired prior to entering the US.

[34] Rosa. S and Torres. D., 2018. Optimal control and sensitivity analysis of a fractional order TB Model.

[35] Shirima. S., Theresia. J., Ismail. I and Kuznetsov. D., 2020. Modeling the Transmission Dynamics of Bovine Tuberculosis. *International Journal of Mathematics andMathematical Sciences.*

[36] Silva. H and Torres. M., 2017. Optimal control of a tuberculosis model with state and Control Delays. *Math. Biosci.*

[37] Silva. J and Torres. M., 2015. Optimal control of tuberculosis: a review. Dynamics, Games and Science. *Springer, Cham.*

[38] SRS Bureau of Health., 2016. Somali Adjusted Woreda overview July final 2016.

[39] Tahir. M., Ali. Sh and Gul. Z., 2019. Prevention strategy for super infection mathematical model Tuberculosis and HIV associated with AIDS. *Cogent Mathematics*] *and Statistics*.

[40] Turner. S., Richard. D and Graham. H., 2015. Cough and the transmission of tuberculosis. *The Journal of infectious diseases.*

[41] Ullah. S., Zhien. M., Liu. L., Yang. Y., Jianquan. L., 2019. Modeling and analysis of Tuberculosis (TB) in Khyber Pakhtunkhwa, Pakistan. *Mathematics and Computers in Simulation.*

[42] Waaler. H., Geser. A and Andersen. S., 1962. The Use of Mathematical Models in the Study of The Epidemiology of Tuberculosis. *American Journal of Public Healthand the Nation Health.*

[43] Wallis. K and Robert. S., 2016. Mathematical models of tuberculosis reactivation and relapse. Frontiers in Microbiology.

[44] WHO, 2020. Global Tuberculosis report 2020 Geneva. WHO Report.

[45] WHO, 2022. Global tuberculosis report 2021 Geneva. WHO Report.

[46] WHO, 2021. Media Centre-Visual Impairment and Blindness Fact Sheet.

[47] WHO*a*., 2020. Guidelines for treatment of drug-susceptible tuberculosis and patient care.

[48] Woldeyohannes. D., Sisay, S., Mengistu, B., Kassa, H., 2015. Directly observed treatment short course (DOTS) for treatment of new tuberculosis cases in Somali Regional State, Eastern Ethiopia: ten years retrospective study. BMC Res Notes.

[49] Yang. D., Yali. M and Liu, L., 2010. Global stability of two models with incomplete treatment for tuberculosis. Chaos, Solitons and Fractals, *Elsevier.*

[50] Yohanes. F and Temesgen. T. 2021. Post exposure vaccination for the dynamics of Tuberculosis with fast and slow latent period: *A Mathematical model analysis.*

[51] Merkin, David R. Introduction to the Theory of Stability. Vol. 24. Springer Science & Business Media, 2012.

[52] La Salle, Joseph P. The stability of dynamical systems. Society for Industrial and Applied Mathematics, 1976.

[53] Van den Driessche, Pauline, and James Watmough. "Reproduction numbers and sub-threshold endemic equilibria for compartmental models of disease transmission." Mathematical biosciences 180.1-2 (2002): 29-48.

[54] Wang, Yi, and Jinde Cao. "Global dynamics of multi-group SEI animal disease models with indirect transmission." Chaos, Solitons & Fractals 69 (2014): 81-89.

[55] Wang, Yi, and Jinde Cao. "Global stability of general cholera models with nonlinear incidence and removal rates." Journal of the Franklin Institute 352.6 (2015): 2464-2485.

[56] Gaff, H. and Schaefer, E., 2009. Optimal control applied to vaccination and treatment strategies for various epidemiological models. *Math. Biosci. Eng*, *6*(3), pp. 469-492.

[57] Coddington, E. A. and Levinson, N., Tata McGraw-Hill Education; 1955. *Theory of ordinary differential equations.*

[58] Pontryagin, L. S. and Boltyanskii, V. G., 1962. R. V. Gamkrelidze, and E. *F. Mishchenko,"The Mathematical Theory of Optimal Processes," translated by K. N. Trirogoff, Interscience. New York.*

[59] Chong, E. K., Lu, W. S. and Żak, S. H., 2023. *An introduction to optimization*. John Wiley & Sons.

[60] Lenhart, S. and Workman, J. T., 2007. *Optimal control applied to biological models*. CRC press.

[61] Rodrigues, H. S. F., 2012. *Optimal control and numerical optimization applied to epidemiological models* (Doctoral dissertation, Universidade de Aveiro. (Portugal).

[62] Parvaneh. E., Baba, A., Abdullahi. I., Rabiu. A 2020. Analysis of tuberculosis model withSaturated incidence rate and optimal control. *Statistical Mechanicsand its Applications*.