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BIFURCATION AND STABILITY ANALYSIS OF THE DYNAMICS OF TUBERCULOSIS MODEL INCORPORATING, VACCINATION, SCREENING AND TREATMENT

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Abstract: In this paper, a deterministic Tuberculosis (TB) model is formulated with the aim of assessing the effects of vaccination, screening and treatment on the transmission of TB infections. The analysis of the model shows that its dynamics are completely determined by the effective reproduction number, R_{eff}. If $R_{eff} < 1$ the disease-free equilibrium exists and is locally and globally asymptotically stable whereas an endemic equilibrium exists if $R_{eff} > 1$ and is globally asymptotically stable, the disease persistence occurs. Furthermore, when the effective reproduction number is equal to one, that is $R_{eff} = 1$, a backward bifurcation occurs. Numerical results are presented for the justifications of theoretical results.

Keywords: Analysis; Bifurcation, Stability; Dynamics; Tuberculosis.

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1. Introduction

Tuberculosis is a chronic infectious disease caused mainly by *Mycobacterium tuberculosis* (*M tuberculosis, Mtb*). Worldwide 8.6 million people fall ill due to TB, of which 1.3 million

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people die annually. In developing countries especially in Africa, the TB incidences, prevalence, and deaths per 100,000 populations is 262, 293, and 26 respectively and Tanzania incidences, prevalence and deaths per 100,000 populations is 177, 183, and 14 as per [25]. Therefore it is becoming essential to find a viable alternative to minimize the prevalence of the disease.

Basically there are two types of tuberculosis: pulmonary tuberculosis which affects the lungs and it is the commonest and infectious form of the disease and extra-pulmonary tuberculosis that affects organs other than the lungs, such as pleura, lymph nodes, pericardium, spine, joints, abdomen or genito-urinary tract [17]. In general, it can affect any part of the body. This study concentrates only on the pulmonary TB where person to person transmission of *Mtb* is via the respiratory route, which can occur both through close contacts between individuals and through infectious bacilli being carried throughout buildings by air currents that makes ventilation an important preventative measure [12]

Tuberculosis occurs in two forms namely: latent tuberculosis and active tuberculosis (progressive TB). The most common form of the disease is latent tuberculosis. Many people remain latent and are at risk of developing active TB as a consequence of either exogenous or endogenous re-infection of latent bacilli. In the absence of HIV, it is estimated that 10% of infected individuals develop active tuberculosis and the rest have strong immunity which limits multiplication of tubercle bacilli [3, 5, 13].

Tuberculosis is the seventh most important cause of global premature mortality and disability and is projected to remain among the 10 leading causes of disease burden even in the year 2020 [18]. The disease spread from one individual to another through air as an individual with active TB coughs, sneezes, speaks, spits, kisses and sings. Upon infection, the body slowly develops immunity within 1-2 months to kill the organisms and the infection heals, or it develops into active infection [1]. The symptoms include coughing up blood or sputum, excessive weight loss, fever, loss of appetite, shortness of breath to people at an advanced stage of TB, fatigue, night sweats, chest pain and a bad cough lasting longer than two weeks [21]. The realization that TB had not been defeated by effective antimicrobial treatment in developing countries where crowded accommodation, poor nutrition, emergence of AIDS and resistance to the limited number of antituberculosis drugs available lead to the need for more

comprehensive and renewed concern over the disease.

Modeling is used to quantify uncertainty due to different gaps in our knowledge to help identify research priorities. The influence for the use of mathematical modeling in theory and practice of disease management and control have increased due to the fact that, the approach helps in figuring out decisions that are of significant importance on the outcomes and provide comprehensive examinations that enter into decisions in a way that gives quick approach and control of the disease with main interest of developing more effective public health interventions. [20] developed a *SEIJT* (Susceptible-Exposed-Undetected Infected-Detected Infected-Treated) model on the effect of Direct Observation Therapy Strategy (DOTS) in Nigeria. Their results showed that, provided that the fraction of detected infectious individuals exceeded a critical value, there exists a globally stable disease free equilibrium. However, if this critical detection level is not reached, the disease-free equilibrium will be unstable even with the very high probability successful treatment under DOTS. [23], focused on the density of individuals with an aim of calculating the size of the area an individual is supposed to occupy in order to eliminate the TB epidemic. This study recommended that, in order to minimize the TB incidence in a population, the characteristic area per individual should be at least 0.25 square kilometres. [11] presented a mathematical model on of effect of bacillus calmette-guérin vaccine in preventing mother to child transmission of tuberculosis. Their findings show that, tuberculosis can be eradicated completely if the total removal rate from the infectious class is greater than the total number of latent infections produced throughout the infectious period. This can be achieved by effective immunization of new born infants against infection using BCG vaccines. [26] conducted a study on Early Therapy for Latent Tuberculosis Infection. Their results shows that tuberculosis control programmes develop the ability to find and treat active cases of disease; they further suggested that, the next step in tuberculosis control should be to develop methods of preventing new cases. Screening is a strategy used in a population to identify an unrecognized disease in individuals without signs or symptoms [14].

In this paper, we present a TB model with vaccination, screening and treatment interventions in a homogenous population. The bifurcation and stability of the equilibrium points for the model are investigated.

2. Model Formulation

The total population $N(t)$ is divided into eight compartments depending on the epidemiological status of individuals: Vaccinated $V(t)$, Susceptible $S(t)$, Exposed $E(t)$, Screened $E_T(t)$, infectious at severe stage $I_1(t)$, infectious at mild stage $I_2(t)$, Treated $T(t)$ and Recovered $R(t)$. In this model, individuals are recruited into the population by either immigration at the rate Λ or per capita birth rate π. We assume that proportions θ of newborns in the population and ψ of the immigrants were vaccinated at birth to protect them against infection. Furthermore, the immunized class increases due to the coming in of the immunized children and reduces due to expiration of duration of vaccine efficacy at the rate τ and death for reasons that are not related to the disease (natural death) at the rate μ. Susceptible population increases due to the coming in of new births not vaccinated against the infection and those who were vaccinated but lose their immunity. When some susceptible individuals come into contact with infectious individuals at a rate, c, they get infected and progress to latently infected class at a force of infection rate λ. More importantly, screening is done to individuals with no symptoms (the susceptible and exposed individuals) and a proportion ρ of those who found to be latently infected opt to go for treatment when their TB is still at latent stage and recovers at the rate, ϕ, while the remaining proportion $(1-\rho)$ of the latently infected individuals may not have opportunity for treatment or they stubbornly refuse to go for early treatment until their TB progresses to active stages at the rate β. A proportion η of the latent/exposed individuals that do not go for early treatment, their TB progress to severe infectious stage I_1 due to their weak immunity and later go for treatment after realizing the severity of the disease or been forced by their relatives or friends. This group goes for treatment at the rate σ and recover at the rate ϕ_1, where $\phi_1 < \phi$.Those with strong immunity $(1-\eta)$ will deviate to infectious class I_2 in which their TB status is at mild stage. Individuals leaves I_2 at the rate α in which, the proportion δ_1 recovers

naturally, δ_2 goes for treatment and the remaining proportion δ_3 their TB advances to severe stage. Due to the nature of the disease, the infection will only kill individuals whose TB progresses to the severe infectious class. In other words, there is no TB induced deaths at mild stage. Moreover, individuals in the recovery class, R are temporarily recovered. Soon they revert back to the latently infected class, E after been reinfected by either I_1 or I_2 at the rate $\gamma\lambda$ where γ is the reduction in susceptibility due to prior endogenous infection. We assume that each class conforms to natural death at the rate μ while infectious individuals in I_1 die due to TB at the rate d .

Furthermore, the following assumptions are made in formulation of the model

i. The mixing in this model is homogeneous, that is, all susceptible individuals are equally likely to be infected by infectious individuals in case of contact.

ii. Recruits are either vaccinated or susceptible.

iii. Individuals at mild stage may recover naturally or by treatment; otherwise advances to severe stage.

iv. On recovery there is temporal immunity.

v. People in each compartment have equal natural death rate μ

The above description leads to the compartmental diagram in Figure 1.The parameters indicated in Figure 1 are described in Table 1.

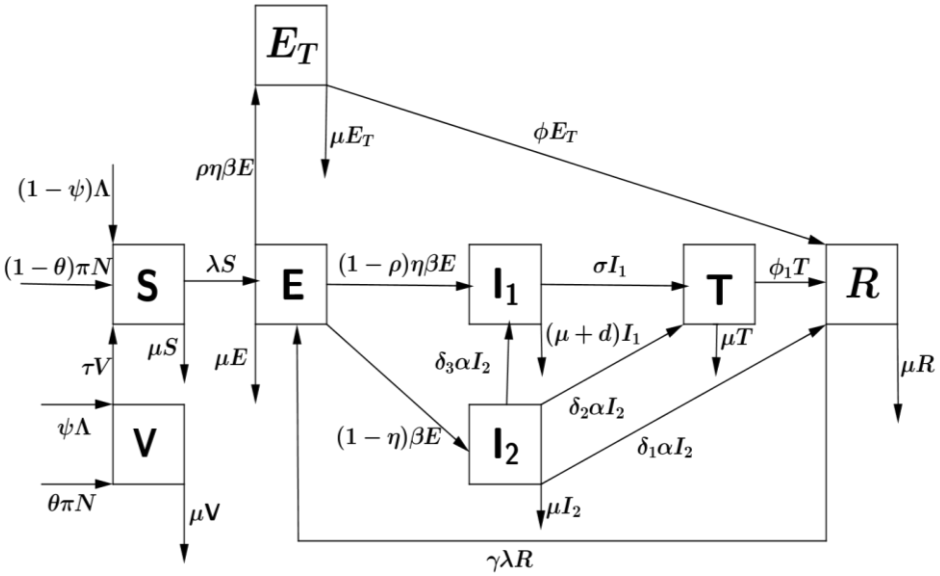

Figure 1: Flow diagram for a TB transmission model with vaccination, screening and treatment.

Table 1: Parameters used in the model formulation and their description

Parameter	Description
Λ	Recruitment rate of the immigrants into the population.
π	Per capita birth rate.
θ	Proportion of babies vaccinated at birth.
ψ	Proportion of vaccinated immigrant babies.
c	Per capita contact rate.
ω	Probability of acquiring TB infections per contact with one infectious individual.
φ	Level of infectiousness of severely infected.
ρ	Proportion of latently infected individuals who go for treatment after screening.
β	Progression rate from latency to active TB.
η	Proportion of latently infected individuals that progress to severe TB.
α	The departure rate from mild stage
δ_1	Proportion of infectious individuals at mild stage who recover naturally.
δ_2	Proportion of infectious individuals who are treated at mild stage.
δ_3	Proportion of infectious individuals at mild stage who progress to severe stage.
σ	Rate at which the infectious individuals at severe stage are isolated for treatment.
ϕ_1	Recovery rate of treated infectious individuals who are at severe conditions
d	The tuberculosis induced mortality rate.
μ	Per capita natural mortality death rate.
ϕ	The recovery rate after treatment of the aware infected individuals.
τ	Progression from immune to susceptible.
γ	Probability of individual to be passive infected from recovery.

2.1 The Model Equations

Based on the assumptions and the inter-relations between the variables and the parameters as shown in the model compartments in Figure 1, the effect of screening and treatment on tuberculosis transmission dynamics can be described by the following system of ordinary differential equations:

$$\begin{aligned}
\frac{dV}{dt} &= \psi\Lambda + \theta\pi N - (\tau + \mu)V, \\
\frac{dS}{dt} &= (1-\psi)\Lambda + (1-\theta)\pi N + \tau V - (\lambda + \mu)S, \\
\frac{dE}{dt} &= \lambda S + \gamma\lambda R - (\beta + \mu)E \quad , \\
\frac{dE_T}{dt} &= \rho\eta\beta E - (\phi + \mu)E_T \\
\frac{dI_1}{dt} &= (1-\rho)\eta\beta E + \delta_3\alpha I_2 - (\sigma + \mu + d)I_1, \qquad (1) \\
\frac{dI_2}{dt} &= (1-\eta)\beta E - (\alpha + \mu)I_2, \\
\frac{dT}{dt} &= \sigma I_1 + \delta_2\alpha I_2 - (\phi_1 + \mu)T, \\
\frac{dR}{dt} &= \phi E_T + \phi_1 T + \delta_1\alpha I_2 - (\gamma\lambda + \mu)R
\end{aligned}$$

where the total population size, $N = V + S + E_T + E + I_1 + I_2 + T + R$

satisfies the equation:

$$\frac{dN}{dt} = \Lambda + \pi N - \mu N - dI_1 \qquad (2)$$

derived by adding the state equations of (1)

and $\lambda = c\omega(\varphi I_1 + I_2)/N$.

2.2 Dimensionless transformation: We consider the equations for the normalized quantities because it is easier to analyze our model in terms of proportions of quantities than of actual populations. This can be done by scaling the population of each class by the total population.

We make the transformation: $v = \frac{V}{N}$, $s = \frac{S}{N}$, $e_T = \frac{E_T}{N}$, $e = \frac{E}{N}$, $i_1 = \frac{I_1}{N}$, $i_2 = \frac{I_2}{N}$, $h = \frac{T}{N}$

and $r = \frac{R}{N}$.

Differentiating the fractions with respect to time t and simplifying leads to the system:

$$\begin{aligned}
\frac{dv}{dt} &= \psi k + \theta\pi - (\tau + k + \pi - di_1)v \\
\frac{ds}{dt} &= (1-\psi)k + (1-\theta)\pi + \tau v - (\lambda + k + \pi - di_1)s \\
\frac{de}{dt} &= \lambda s + \gamma\,\lambda r - (\beta + k + \pi - di_1)e \\
\frac{de_T}{dt} &= \rho\eta\beta e - (\phi + k + \pi - di_1)e_T \\
\frac{di_1}{dt} &= (1-\rho)\eta\beta e + \delta_3\alpha i_2 - (\sigma + d + k + \pi - di_1)i_1 \\
\frac{di_2}{dt} &= (1-\eta)\beta e - (\alpha + k + \pi - di_1)i_2 \\
\frac{dh}{dt} &= \sigma i_1 + \delta_2\alpha i_2 - (\phi_1 + k + \pi - di_1)h\,, \\
\frac{dr}{dt} &= \phi e_T + \phi_1 h + \delta_1\alpha i_2 - (\gamma\lambda + k + \pi - di_1)r
\end{aligned} \tag{3}$$

subject to the restriction $v + s + e + e_T + i_1 + i_2 + h + r = 1$ that leads to studying system (3) in the region $\Omega = \{(v, s, e, e_T, i_1, i_2, h, r) \in \mathbb{R}_+^8 : v + s + e + e_T + i_1 + i_2 + h + r = 1\}$ where the model makes biological sense that can be shown to be positively invariant and globally attracting in $\mathbb{R}_+^8$ with respect to our system.

3. Model Analysis

The model (3) is analyzed qualitatively to get insights into its dynamical features that give better understanding of the effect of screening and treatment on the transmission of TB infection in a population.

3.1 Disease Free Equilibrium (DFE), E_0

The disease free equilibrium of the model (3) is obtained by setting

$$\frac{dv}{dt} = \frac{ds}{dt} = \frac{de}{dt} = \frac{de_T}{dt} = \frac{di_1}{dt} = \frac{di_2}{dt} = \frac{dh}{dt} = \frac{dr}{dt} = 0\,.$$

In case of no disease, $e_T = e = i_1 = i_2 = 0$ the sum of susceptible and vaccinated populations is equal to total population.

The statement above reduces system (3) to:

$$\psi k + \theta\pi - (\tau + k + \pi)v^* = 0 \Rightarrow v^* = \frac{\psi k + \theta\pi}{\tau + k + \pi} \quad \text{and}$$

$$(1-\psi)k + (1-\theta)\pi + \tau v - (k + \pi_1)s^* = 0 \Rightarrow s^* = \frac{\tau + (1-\psi)k + (1-\theta)\pi}{\tau + k + \pi} \tag{4}$$

Therefore, the disease free equilibrium (DFE) denoted by E_0 of the model (3.) is given by:

$$(v^*,\ s^*,\ 0,\ 0,\ 0,\ 0,\ 0,\ 0) = \left(\frac{\psi k + \theta\pi}{\tau + k + \pi},\ \ \frac{\tau + k + \pi - (\psi k + \theta\pi)}{\tau + k + \pi},\ \ 0,\ 0,\ 0,\ 0,\ 0,\ 0\right).$$

3.2 The Basic Reproduction Number, R_0

The basic reproduction number, R_0, is defined as the effective number of secondary infections caused by typical infected individual during his entire period of infectiousness [10]. This definition is given for the models that represent spread of infection in a population. We calculate the basic reproduction number by using the next generation operator method on the system (3).

The basic reproduction number is obtained by taking the largest (dominant) eigenvalue (spectral radius) of:

$$\mathbf{FV}^{-1} = \left[\frac{\partial \mathcal{F}_i(E_0)}{\partial x_j}\right]\left[\frac{\partial \mathcal{V}_i(E_0)}{\partial x_j}\right]^{-1}$$

where $\mathcal{F}_i$ is the rate of appearance of new infection in compartment i, $\mathcal{V}_i$ is the transfer of infections from one compartment i to another and E_0 is the disease-free equilibrium.

The effective reproduction number, R_{eff} of the normalised model system (3) with vaccination, screening and treatment is:

$$R_{eff} = \frac{((1-\eta)\delta_3\alpha + (\alpha + k + \pi)(1-\rho)\eta)c\omega\varphi\beta s^*}{(\beta + k + \pi)(\sigma + d + k + \pi)(\alpha + k + \pi)} + \frac{(1-\eta)c\omega\beta s^*}{(\beta + k + \pi)(\alpha + k + \pi)} \tag{5}$$

where,

$$s^* = \frac{(\tau + k + \pi) - (\psi k + \theta\pi)}{(\tau + k + \pi)}$$

Furthermore, the basic reproduction number for the model system (3) is given by:

$$R_0 = \frac{((1-\eta)\delta_3\alpha + (\alpha+k+\pi)\eta)c\omega\varphi\beta}{(\beta+k+\pi)(d+k+\pi)(\alpha+k+\pi)} + \frac{(1-\eta)c\omega\beta}{(\beta+k+\pi)(\alpha+k+\pi)} \tag{6}$$

The details for the computation of the basic reproduction number and the comparison between the effective reproduction numbers with individual or combination of different interventions are shown in [19].

3.3 Local Stability of the Disease Free Equilibrium (DFE), E_0

Theorem 3.1. *The disease free equilibrium of the vaccination, screening and treatment model system (3) is locally asymptotically stable if* $R_{eff} < 1$ *and unstable if* $R_{eff} > 1$.

Proof. We show that, the variational matrix, $\mathbf{J}(E_0)$ of the normalised model system (3) has negative trace and positive determinant. The partial differentiation of (3) with respect to $(v, s, e, e_T, i_1, i_2, h, r)$ at the disease free equilibrium gives:

$$\mathbf{J}(E_0) = \begin{bmatrix} -m_1 & 0 & 0 & 0 & dv & 0 & 0 & 0 \\ \tau & -(k+\pi) & 0 & 0 & -(c\omega\varphi - d)s & -c\omega s & 0 & 0 \\ 0 & 0 & -m_2 & 0 & c\omega\varphi s & c\omega s & 0 & 0 \\ 0 & 0 & \rho\eta\beta & -m_3 & 0 & 0 & 0 & 0 \\ 0 & 0 & (1-\rho)\eta\beta & 0 & -m_4 & \delta_3\alpha & 0 & 0 \\ 0 & 0 & (1-\eta)\beta & 0 & 0 & -m_5 & 0 & 0 \\ 0 & 0 & 0 & 0 & \sigma & \delta_2\alpha & -(\phi_1+k+\pi) & 0 \\ 0 & 0 & 0 & \phi & 0 & \delta_1\alpha & \phi_1 & -(k+\pi) \end{bmatrix}$$

where ,

$$m_1 = \tau + k + \pi, \quad m_2 = (\beta + k + \pi), \quad m_3 = \phi + k + \pi, \quad m_4 = \sigma + d + k + \pi \quad \text{and}$$

$$m_5 = \alpha + k + \pi.$$

The trace of our matrix $\mathbf{J}(E_0)$ is given by:

$$\mathrm{Tr}\mathbf{J}(E_0) = -(m_1 + m_2 + m_3 + m_4 + m_5 + (k+\pi)^2 + (\phi_1 + k + \pi)) < 0$$

$$\text{Now} \quad \det(\mathbf{J}(E_0)) = -A_1 \begin{vmatrix} -(\beta+k+\pi) & c\omega\varphi s & c\omega s \\ (1-\rho)\eta\beta & -(\sigma+d+k+\pi) & \delta_3\alpha \\ (1-\eta)\beta & 0 & -(\alpha+k+\pi) \end{vmatrix}$$

where,

$$A_1 = (\phi_1 + k + \pi)(\phi + k + \pi)(\tau + k + \pi)(k+\pi)^2$$

$$\Rightarrow \det(\mathbf{J}(E_0)) = A_2\left[1-\frac{((1-\eta)\delta_3\alpha\beta+(\alpha+k+\pi)(1-\rho)\eta)c\omega\varphi\, s\beta}{(\beta+k+\pi)(\sigma+d+k+\pi)(\alpha+k+\pi)}+\frac{(1-\eta)c\omega s\beta}{(\beta+k+\pi)(\alpha+k+\pi)}\right]$$

$$= A_2\ (1\ \text{-}_{e\ f}\mathrm{R}$$

where, $A_2 = A_1(\beta+k+\pi)(\sigma+d+k+\pi)(\alpha+k+\pi).$

This implies that the determinant of our variational matrix, is positive if and only if $R_{eff}<1.$ Since, the trace of our matrix $\mathbf{J}(\mathbf{E}_0)$ is less than zero and its determinant is positive when $R_{eff}<1$ then, model system (3) is locally asymptotically stable at disease free equilibrium, $\mathbf{E}_0$.

Theorem 3.1 implies that TB can be eliminated from the community when $R_{eff}<1$ if the initial size of the sub-populations of the model are in the basin of attraction of the disease free equilibrium $\mathbf{E}_0$. That means if $R_{eff}<1$, then on average, an infected individual produce less than one new infected individual over the course of infectious period and the infection cannot grow.

3.4 Global stability of the disease-free equilibrium, $\mathbf{E_0}$

In this section, we analyze the global stability of the disease-free equilibrium point by applying the [4] approach.

We write model system (1) in the form:

$$\begin{cases}\dfrac{\mathrm{d}\,\mathbf{X}_s}{\mathrm{dt}} = \mathbf{A}(\mathbf{X}_s - \mathbf{X}_{DFE,s}) + \mathbf{A}_1\mathbf{X}_i \\ \dfrac{\mathrm{d}\,\mathbf{X}_i}{\mathrm{dt}} = \mathbf{A}_2\mathbf{X}_i\end{cases}$$

where $\mathbf{X}_s$ is the vector representing the non-transmitting compartments and $\mathbf{X}_i$ is the vector representing the transmitting components. The DFE is globally asymptotically stable if $\mathbf{A}$ has real negative eigenvalues and $\mathbf{A}_2$ is a Metzler matrix (i.e. the off-diagonal elements of $\mathbf{A}_2$ are non-negative).

From system (1) we have: $\mathbf{X}_i = (e,\ i_1,\ i_2)^T$, $\mathbf{X}_s = (s,\ v,\ e_T,\ h,\ r)^T$,

$$\mathbf{X}_s - \mathbf{X}_{DFE,s} = \begin{bmatrix} \nu - \frac{\psi k + \theta\pi}{\tau + k + \pi} \\ s - 1 + \frac{\psi k + \theta\pi}{\tau + k + \pi} \\ e_T \\ h \\ r \end{bmatrix}$$

We need to check whether a matrix $\mathbf{A}$ for the non-transmitting compartments has real negative eigenvalues and that $\mathbf{A}_2$ is a Metzler matrix.

From the equation for non-transmitting compartments in (3) we have:

$$\mathbf{A} = \begin{bmatrix} -(\tau + k + \pi) & 0 & 0 & 0 & 0 \\ \tau & -(k + \pi) & 0 & 0 & 0 \\ 0 & 0 & -(\phi + k + \pi) & 0 & 0 \\ 0 & 0 & 0 & -(\phi_1 + k + \pi) & 0 \\ 0 & 0 & \phi & \phi_1 & -(k + \pi) \end{bmatrix},$$

$$\mathbf{A}_1 = \begin{bmatrix} 0 & d\nu & 0 \\ 0 & -(c\omega\varphi - d)s & c\omega s \\ \rho\eta\beta & de_T & 0 \\ 0 & \sigma + dh & \delta_2\alpha \\ 0 & -(\gamma c\omega\varphi - d)r & -\gamma c\omega r + \delta_1\alpha \end{bmatrix}$$

and

$$\mathbf{A}_2 = \begin{bmatrix} -(\beta + k + \pi) & de + (s + \gamma r)c\omega\varphi & (s + \gamma r)c\omega \\ (1-\rho)\eta\beta & -(\sigma + k + \pi + d(1 - i_1)) & \delta_3\alpha \\ (1-\eta)\beta & di_2 & -(\alpha + k + \pi) \end{bmatrix}$$

A direct computation shows that, the eigenvalues of $\mathbf{A}$ are real and negative. This implies that the system $\frac{\mathrm{d}\mathbf{X}_s}{\mathrm{dt}} = \mathbf{A}(\mathbf{X}_s - \mathbf{X}_{DFE,s}) + \mathbf{A}_1\mathbf{X}_i$ is globally asymptotically stable at DFE. Furthermore, since $0 \le i_1 < 1$ we have, $(1 - i_1) > 0$ and this implies $\mathbf{A}_2$ a Metzler matrix. Thus, the DFE is globally asymptotically stable.

Theorem 3.2. *The disease-free equilibrium point is globally asymptotically stable in* Ω *if* $R_{eff} < 1$ *and unstable if* $R_{eff} > 1$.

3.5 Endemic Equilibrium Point (EEP), E_1

Let the endemic equilibrium of our normalised model system (3) be denoted by $E_1^*(v^*, s^*, e_T^*, e^*, i_1^*, i_2^*, h^*, r^*)$. It is obtained by setting the right hand side of each equation of the normalised model system (3) equal to zero.

However, due to the complexity of the problem, we derive the endemic equilibrium point $E_1^*(s^*, e^*, i_1^*, i_2^*, r^*)$ without any intervention.

If we let $a = k + \pi - di_1^*$, from system (3), we have:

i) $s^* = \dfrac{k+\pi}{\lambda + a}$, where $\lambda = c\omega(\varphi i_1^* + i_2^*)$

ii) $e^* = \dfrac{\lambda(\gamma\lambda + a)(\alpha + a)(k+\pi)}{(a_1\lambda + a_2)(\lambda + a)}$,

where $a_1 = \gamma((\beta + a)(\alpha + a) - \delta_1\alpha(1-\eta)\beta)$, $a_2 = a(\beta + a)(\alpha + a)$ and

iii) $i_2^* = \dfrac{\lambda(\gamma\lambda + a)(k+\pi)(1-\eta)\beta}{(a_1\lambda + a_2)(\lambda + a)}$

iv) $i_1^* = \lambda(\gamma\lambda + a)(k+\pi)\beta\dfrac{(1-\rho)\eta(\alpha + a) + (1-\eta)\delta_3\alpha}{(a_1\lambda + a_2)(\lambda + a)(\sigma + d + a)}$

v) $r^* = \dfrac{\lambda(\gamma\lambda + a)(k+\pi)(1-\eta)\delta_1\alpha\beta}{(a_1\lambda + a_2)(\lambda + a)(\gamma\lambda + a)}$

Substituting i_1^* and i_2^* in the equation for the force of infection

$\lambda = c\omega(\varphi i_1^* + i_2^*)$ we have:

$$\lambda = \lambda(\gamma\lambda + a)(k+\pi)c\omega\varphi\beta\frac{(1-\rho)\eta(\alpha + a) + (1-\eta)\delta_3\alpha}{(a_1\lambda + a_2)(\lambda + a)(\sigma + d + a)} + c\omega\left(\frac{\lambda(\gamma\lambda + a)(k+\pi)(1-\eta)\beta}{(a_1\lambda + a_2)(\lambda + a)}\right)$$

$$\lambda = \lambda(\gamma\lambda + a)(k+\pi)c\omega\beta\left(\frac{\varphi((1-\rho)\eta(\alpha + a) + (1-\eta)\delta_3\alpha) + (1-\eta)(\sigma + d + a)}{(a_1\lambda + a_2)(\lambda + a)(\sigma + d + a)}\right)$$

$$\lambda(a_1\lambda + a_2)(\lambda + a) = a_3\lambda(\gamma\lambda + a),$$

where,

$$a_3 = \frac{(k+\pi)c\omega\beta(\varphi((1-\rho)\eta(\alpha + a) + (1-\eta)\delta_3\alpha) + (1-\eta)(\sigma + d + a))}{(\sigma + d + a)}$$

This implies that:

$$a_1\lambda^3 + (a_1a + a_2 - \gamma a_3)\lambda^2 + (a_2a - a_3a)\lambda = 0$$

This can be written as a polynomial:

$$\lambda(A\lambda^2 + B\lambda + C) = 0 \tag{7}$$

where, $A = a_1$, $B = (a_1a + a_2) - \gamma a_3$ and $C = a_2a - a_3a$

The solutions for the cubic polynomial (7) are $\lambda = 0$ and $A\lambda^2 + B\lambda + C = 0$. In this case $\lambda = 0$ corresponds to the disease free equilibrium, already discussed and $A\lambda^2 + B\lambda + C = 0$ corresponds to the existence of two endemic equilibria points.

Furthermore, $A = \gamma((\beta + a)(\alpha + a) - \delta_1\alpha(1-\eta)\beta)$,

$$B = a(\beta + a)(\alpha + a)(1 + \gamma(1 - R_0)) - \gamma\delta_1\alpha(1-\eta)\beta, \text{ and}$$

$$C = a_2a - a_3a$$

$$C = a_2a - \frac{a(k+\pi)c\omega\beta(\varphi((1-\rho)\eta(\alpha+a) + (1-\eta)\delta_3\alpha) + (1-\eta)(\sigma+d+a)}{(\sigma+d+a)}$$

$$C = a^2(\beta+a)(\alpha+a) - a(k+\pi)c\omega\beta(\varphi((1-\rho)\eta(\alpha+a) + (1-\eta)\delta_3\alpha) + (1-\eta)(\sigma+d+a)$$

Dividing both sides by $a^2(\sigma+d+a)(\beta+a)(\alpha+a)$, we get:

$$\frac{C}{a^2(\sigma+d+a)(\beta+a)(\alpha+a)} = 1 - \frac{(k+\pi)c\omega\beta(\varphi((1-\rho)\eta(\alpha+a) + (1-\eta)\delta_3\alpha) + (1-\eta)(\sigma+d+a)}{a(\sigma+d+a)(\beta+a)(\alpha+a)}$$

This implies,

$$\frac{C}{a^2(\beta+a)(\alpha+a)} = 1 - R_0$$

Thus:

$$C = a^2(\beta+a)(\alpha+a)(1-R_0) \tag{8}$$

Significant assessment of the quadratic equation (7) shows that there is a unique endemic equilibrium point if $B < 0$ and $C = 0$ or $B^2 - 4AC = 0$. There are two endemic equilibria if $C > 0$, $B < 0$ and $B^2 - 4AC > 0$, otherwise there is none. It is also important to

note that the coefficient A is always positive and C is positive if $R_0 < 1$ and negative if $R_0 > 1$. This leads to the following theorem:

Theorem 3.3.

The tuberculosis model (3) has:

i. precisely one unique endemic equilibrium if $C < 0$, $R_0 > 1$,

ii. precisely one unique endemic equilibrium if $B < 0$ *and* $C = 0$ *or* $B^2 - 4AC = 0$,

iii. precisely two endemic equilibria if $C > 0$, $B < 0$ *and* $B^2 - 4AC > 0$, *and*

iv. *no endemic equilibrium otherwise.*

From iii. we see that backward bifurcation is possible if we set the discriminant $B^2 - 4AC = 0$ and solve for the critical value of R_0.

That is,

$$R_0{}^c = 1 - \frac{B^2}{4Aa^2(\beta + a)(\alpha + a)}$$

from which it can be shown that backward bifurcation occurs for values of R_0 that are in the range $R_0{}^c < R_0 < 1$.

In addition to that, Theorem 4 gives the condition for existence of endemic equilibrium, E_1

Theorem 3.4. *The endemic equilibrium point* $\mathbf{E}_1{}^*$ *exists if* $R_0 > 1$.

Proof. From the quadratic equation in (7) we have $\lambda^* = \frac{-B + \sqrt{B^2 - 4AC}}{2A}$ which implies that, the disease will be endemic if $\lambda^* > 0$. In other words, the disease will be endemic if $AC < 0$ suggesting from (8) that $Aa^2(\beta + a)(\alpha + a)(1 - R_0) < 0$. This is true if and only if $R_0 > 1$.

Therefore, the endemic equilibrium point $\mathbf{E}_1{}^*$ exists if and only if $R_0 > 1$.

3.6 Stability Analysis Using Bifurcation Analysis

Endemic equilibrium points are steady state solutions where the disease persists in the

population (all state variables are positive). We use general bifurcation theory to prove the existence of at least one endemic equilibrium point for all $R_{eff} > 1$ [6].

When $R_{eff} > 1$, it is expected that the disease would be able to invade in the case of a backward bifurcation. The centre manifold theory can be used to analyse the stability of DFE (E_0) near $R_{eff} = 1$.

From equation (5):

$$R_{eff} = \frac{((1-\eta)\delta_3\alpha + (\alpha+k+\pi)(1-\rho)\eta)c\omega\varphi\beta s^*}{(\beta+k+\pi)(\sigma+d+k+\pi)(\alpha+k+\pi)} + \frac{(1-\eta)c\omega\beta s^*}{(\beta+k+\pi)(\alpha+k+\pi)}$$

we let the average number of effective contacts a susceptible has per unit of time $c\omega = \vartheta$ be the bifurcation parameter and $R_{eff} = 1$ be the bifurcation point.

If we equate $R_{eff} = 1$, and $c\omega = \vartheta^*$ we obtain:

$$\vartheta^* = \frac{(\beta+k+\pi)(\sigma+d+k+\pi)(\alpha+k+\pi)}{((1-\eta)\delta_3\alpha + (\alpha+k+\pi)(1-\rho)\eta)\varphi\beta s^* + (\sigma+d+k+\pi)(1-\eta)\beta s^*}$$

Again, let $x_1 = v, x_2 = s, x_3 = e_T, x_4 = e, x_5 = i_1, x_6 = i_2$, $x_7 = h$ and $x_8 = r$

The model system equation (3) becomes:

$$\begin{aligned}
\frac{dx_1}{dt} &= f_1(x_1, x_2, ..., x_8) = \psi k + \theta\pi - (\tau + k + \pi - dx_5)x_1 \\
\frac{dx_2}{dt} &= f_2(x_1, x_2, ..., x_8) = (1-\psi)k + (1-\theta)\pi + \tau x_1 - (\vartheta(\varphi x_5 + x_6) + k + \pi - dx_5)x_2 \\
\frac{dx_3}{dt} &= f_3(x_1, x_2, ..., x_8) = \vartheta(\varphi x_5 + x_6)(x_2 + \gamma x_8) - (\beta + k + \pi - dx_5)x_3 \\
\frac{dx_4}{dt} &= f_4(x_1, x_2, ..., x_8) = \eta\rho\beta x_3 - (\phi + k + \pi - dx_5)x_4 \qquad (9) \\
\frac{dx_5}{dt} &= f_5(x_1, x_2, ..., x_8) = (1-\rho)\eta\beta x_3 + \delta_3\alpha x_6 - (\sigma + d + k + \pi - dx_5)x_5 \\
\frac{dx_6}{dt} &= f_6(x_1, x_2, ..., x_8) = (1-\eta)\beta x_3 - (\alpha + k + \pi - dx_5)x_6 \\
\frac{dx_7}{dt} &= f_7(x_1, x_2, ..., x_8) = \sigma x_5 + \delta_2\alpha x - (\varphi_1 + k + \pi - dx_5)x_7
\end{aligned}$$

$$\frac{dx_8}{dt} = f_8(x_1, x_2, ..., x_8) = \phi x_4 + \phi_1 x_7 + \delta_1 \alpha\, x_6 - (\gamma \vartheta(\varphi\, x_5 + x_6) + k + \pi - dx_5)x_8$$

Therefore, the Jacobian matrix at DFE (E_0) is given by

$$\mathbf{J}(E_0) = \begin{bmatrix} -m_1 & 0 & 0 & 0 & dx_1 & 0 & 0 & 0 \\ \tau & -(k+\pi) & 0 & 0 & -(\vartheta\varphi - d)x_2 & -\vartheta x_2 & 0 & 0 \\ 0 & 0 & -m_2 & 0 & \vartheta\varphi x_2 & \vartheta x_2 & 0 & 0 \\ 0 & 0 & \rho\eta\beta & -m_3 & 0 & 0 & 0 & 0 \\ 0 & 0 & (1-\rho)\eta\beta & 0 & -m_4 & \delta_3\alpha & 0 & 0 \\ 0 & 0 & (1-\eta)\beta & 0 & 0 & -m_5 & 0 & 0 \\ 0 & 0 & 0 & 0 & \sigma & \delta_2\alpha & -(\varphi_1 + k + \pi) & 0 \\ 0 & 0 & 0 & \phi & 0 & \delta_1\alpha & \varphi_1 & -(k+\pi) \end{bmatrix}$$

where, $m_1 = \tau + k + \pi$, $m_2 = (\beta + k + \pi)$, $m_3 = \phi + k + \pi$, $m_4 = \sigma + d + k + \pi$ and $m_5 = \alpha + k + \pi$.

We calculate the left eigenvector $\mathbf{v}$ and the right eigenvector $\mathbf{y}$ which are associated with the zero eigenvalue of $\mathbf{J}(E_0)$.

Let the right eigenvector be given by $\mathbf{y} = (y_1, y_2, y_3, y_4, y_5, y_6, y_7, y_8)^T$.

Multiplying this vector with our Jacobian matrix $\mathbf{J}(E_0)$ and equating to zero we have:

$$y_1 = dx_1 \frac{(\alpha + k + \pi)(1-\rho)\eta\beta + (1-\eta)\delta_3\alpha\beta}{(\sigma + d + k + \pi)(\alpha + k + \pi)(\tau + k + \pi)} y_3,$$

$$y_2 = -\beta \frac{((\alpha + k + \pi)(1-\rho)\eta + (1-\eta)\delta_3\alpha)(\vartheta\varphi - d)x_2 - d\tau x_1) + g(1-\eta)\vartheta x_2}{g(k+\pi)(\alpha + k + \pi)} y_3$$

where, $g = (\sigma + d + k + \pi)(\tau + k + \pi)$

$$y_3 = y_3 > 0 \text{ free}$$

$$y_4 = \frac{\rho\eta\beta}{\phi + k + \pi} y_3$$

$$y_5 = \frac{(\alpha + k + \pi)(1-\rho)\eta\beta + (1-\eta)\delta_3\alpha\beta}{(\sigma + k + \pi)(\alpha + k + \pi)} y_3$$

$$y_6 = \frac{(1-\eta)\beta}{\alpha + k + \pi} y_3$$

$$y_7 = \frac{\sigma((\alpha + k + \pi)(1-\rho)\eta\beta + \delta_3\alpha(1-\eta)\beta) + \delta_2\alpha(1-\eta)\beta(\sigma + d + k + \pi)}{(\phi_1 + k + \pi)(\alpha + k + \pi)(\sigma + d + k + \pi)} y_3$$

$$y_8 = (\frac{(\alpha + k + \pi)\phi\rho\eta\beta + (\phi + k + \pi)(1-\eta)\delta_1\alpha\beta}{(k + \pi)(\phi + k + \pi)(\alpha + k + \pi)} + \phi_1 \frac{y_7}{k + \pi}) y_3$$

Similarly, we calculate the left eigenvectors $\mathbf{v} = (v_1, v_2, v_3, v_4, v_5, v_6, v_7, v_8)$ satisfying $\mathbf{v}.\mathbf{y} = 1$

In this case, we get:

$$v_1 = v_2 = v_4 = v_7 = v_8 = 0,$$

$$v_3 = v_3 > 0 \text{ free},$$

$$v_5 = \frac{\vartheta\varphi\, x_2}{(\sigma + d + k + \pi)} v_3,$$

$$v_6 = \frac{\vartheta\, x_2(\varphi\delta_3\alpha + (\sigma + d + k + \pi))}{(\sigma + d + k + \pi)(\alpha + k + \pi)} v_3.$$

where

$$x_2 = \frac{(\tau + k + \pi) - (\psi k + \theta\pi)}{\tau + k + \pi}$$

After computing the right and left eigenvalues we use Theorem 2.5 in [5] to establish the conditions for the existence of backward bifurcation by determining the sign of **a** and **b** as indicated in the theorem which is restated as Theorem 3.5:

Theorem 3.5. *Consider the following general system of ordinary differential equations with a parameter* ϑ. $\frac{dx}{dt} = f(x, \vartheta) : \mathbf{R}^n \times \mathbf{R} \to \mathbf{R}^n$ *and* $f \in \mathbf{C}^2(\mathbf{R}^n \times \mathbf{R})$ *where 0 is an equilibrium point of the system, that is,* $f(0, \vartheta) \equiv 0 \; \forall \, \vartheta$ *and*

1. $A = D_x f(0,0) = \left[\frac{\partial f_i}{\partial x_i}(0,0) \right]$ *is the linearization matrix of the system around the equilibrium 0 with* ϑ *evaluated at 0.*

2. Zero is a simple eigenvalue of A and all other eigenvalues of A have negative real parts.

3. Matrix **A** *has a right eigenvector* **y** *and a left eigenvector* **v** *corresponding to the zero*

eigenvalue.

Let f_k *be the* k^{th} *component of* f *and* $a = \sum_{k,i,j=1}^{n} v_k y_i y_j \frac{\partial^2 f_k}{\partial x_i \partial x_j}(0,0)$,

$b = \sum_{k,i,j=1}^{n} v_k y_i \frac{\partial^2 f_k}{\partial x_i \partial \vartheta}(0,0)$, *the local dynamics of system (9) around 0 is totally governed by the signs of* a *and* b.

1. $a>0,\ b>0$. *when* $\vartheta<0$ *with* $|\vartheta|<<1$, *0 is locally asymptotically stable, and there exists a positive unstable equilibrium; when* $0<\vartheta<<1$, *0 is unstable and there exists a negative and locally asymptotically stable equilibrium.*
2. $a<0,\ b<0$. *when* $\vartheta<0$ *with* $|\vartheta|<<1$, *0 is unstable; when* $0<\vartheta<<1$, *0 is locally asymptotically stable, and there exists a positive unstable equilibrium.*
3. $a>0,\ b<0$. *when* $\vartheta<0$ *with* $|\vartheta|<<1$, *0 is unstable, and there exists a locally asymptotically stable negative equilibrium; when* $0<\vartheta<<1$, *0 is stable, and a positive unstable equilibrium appears.*
4. $a<0,\ b>0$. *when* $\vartheta<0$ *changes from negative to positive, 0 changes its stability from stable to unstable. Corresponding to a negative unstable equilibrium becomes positive and locally asymptotically stable.*

Particularly if $a>0$ *and* $b>0$ *then a backward bifurcation occurs at* $\vartheta=0$.

Computation of a **and** b

Since $v_1 = v_2 = v_4 = v_7 = v_8 = 0$ (for $k = 1, 2, 4, 7, 8$) we can only consider $k = 3, 5, 6$.

The only partial derivatives different from zero are:

$$\frac{\partial^2 f_3}{\partial x_5 \partial x_2} = \vartheta\varphi, \qquad \frac{\partial^2 f_3}{\partial x_6 \partial x_2} = \vartheta, \quad \frac{\partial^2 f_3}{\partial x_3 \partial x_5} = d \text{ and } \quad \frac{\partial^2 f_6}{\partial x_6 \partial x_5} = d$$

$$a = c\omega v_3 y_2(\varphi y_5 + y_6) + d v_3 y_2 y_6 + d v_6 y_5 y_6 \tag{10}$$

where

$$y_2 = -\beta \frac{((\alpha+k+\pi)(1-\rho)\eta + (1-\eta)\delta_3\alpha)(\vartheta\varphi - d)x_2 - d\tau x_1) + (\sigma+d+k+\pi)(\tau+k+\pi)(1-\eta)\vartheta x_2}{(k+\pi)(\sigma+d+k+\pi)(\alpha+k+\pi)(\tau+k+\pi)} y_3$$

$$y_5 = \frac{(\alpha + k + \pi)(1-\rho)\eta\beta + (1-\eta)\delta_3\alpha\beta}{(\sigma + k + \pi)(\alpha + k + \pi)} y_3, \quad y_6 = \frac{(1-\eta)\beta}{\alpha + k + \pi} y_3,$$

$$v_6 = \frac{\vartheta\, x_2(\delta_3\alpha + (\sigma + d + k + \pi))}{(\sigma + d + k + \pi)(\alpha + k + \pi)} v_3, \text{ and } \quad y_3, v_3 > 0$$

From (10) we see that $a > 0$ if $y > x$ and $a < 0$ if $y < x$,

where $y = \vartheta v_3 y_2(\phi\, y_5 + y_6) + d v_3 y_2 y_6$ and $x = d v_6 y_5 y_6$.

On the other hand, the value of b can be obtained from:

$$b = v_3\left[y_5 \frac{\partial^2 f_3}{\partial x_5 \partial \vartheta} \right] + v_3\left[y_6 \frac{\partial^2 f_3}{\partial x_6 \partial \vartheta} \right]$$

where $\frac{\partial^2 f_3}{\partial x_5 \partial \vartheta} = \varphi\, x_2$ and $\frac{\partial^2 f_3}{\partial x_6 \partial \vartheta} = x_2$ are the only partial derivatives different from zero.

Thus,

$$b = v_3 x_2(\varphi\, y_5 + y_6) > 0$$

Since $b > 0$ and $a < 0$ or $a > 0$ depending on whether x is greater or smaller than y, then the following theorem holds:

Theorem 3.6. *If $y > x$, $a > 0$, then model system (9) has backward bifurcation at $R_{eff} = 1$. If $\vartheta < 0$, this implies that there exists unstable negative endemic equilibrium point and when $\vartheta > 0$ it implies that there exists a stable positive endemic equilibrium point. Therefore the endemic equilibrium point EEP is locally asymptotically stable for $R_{eff} > 1$ but close to 1.*

Figure 2, illustrates a backward bifurcation diagram of the force of infection at equilibrium against the basic reproduction number, R_0 of the TB model (3) at $R_0 = 1$. Furthermore, EE and DFE represent endemic equilibrium and disease-free equilibrium respectively. It can be observed from the diagram that as R_0 approaches one, the number of TB cases rapidly increases giving rise to a situation whereby the disease-free equilibrium co-exist with the endemic equilibrium.

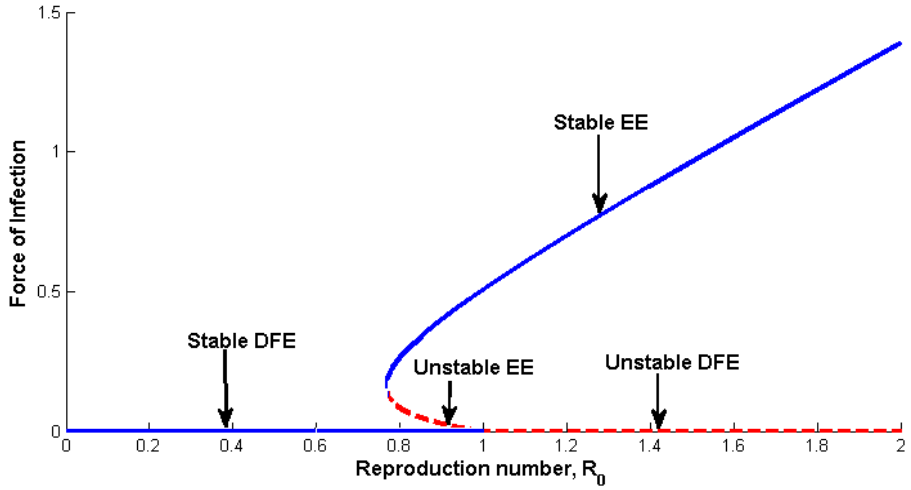

Figure 2: Backward bifurcation for a screening and treatment model

3.7 Global Stability of the Endemic Equilibrium Point (EEP), E_1

In this section, we study the global properties of the endemic equilibrium point. The following theorem provides the global property of the endemic equilibrium point.

Theorem 3.7. *The endemic equilibrium point,* $\boldsymbol{E_1}$ *is globally asymptotically stable if* $R_{eff} > 1$.

Proof. In proving this theorem, we apply [15] approach to construct of a suitable Lyapunov function of the form:

$$L = \sum a_i (x_i - x_i^* \ln x_i)$$

where a_i is properly selected positive constant, x_i is the population of i^{th} compartment and x_i^* is the equilibrium point. This approach has been found to be useful for more complex compartmental epidemic models.

Now, we consider the Lyapunov function candidate, L for system (3.3) as:

$$L = B_1(v - v^* \ln v) + B_2(s - s^* \ln s) + B_3(e - e^* \ln e) + B_4(e_T - e_T^* \ln e_T)$$

$$+ B_5(i_1 - i_1^* \ln i_1) + B_6(i_2 - i_2^* \ln i_2 + B_7(h - h^* \ln h) + B_8(r - r^* \ln r)$$

where $B_1, B_2, B_3, ..., B_8$ are positive constants.

Differentiating our Lyapunov function with respect to time we get:

$$\frac{dL}{dt} = B_1(1-\frac{v^*}{v})\frac{dv}{dt} + B_2(1-\frac{s^*}{s})\frac{ds}{dt} + B_3(1-\frac{e^*}{e})\frac{de}{dt} + B_4(1-\frac{e_T{}^*}{e_T})\frac{de_T}{dt})$$

$$+ B_5(1-\frac{i_1{}^*}{i_1})\frac{di_1}{dt} + B_6(1-\frac{i_2{}^*}{i_2})\frac{di_2}{dt} + B_7(1-\frac{h^*}{h})\frac{dh}{dt} + B_8(1-\frac{r^*}{r})\frac{dr}{dt}$$

At the endemic equilibrium point, $\mathbf{E_1}$ we have:

$$\psi k + \pi\theta = (\tau + k + \pi - di_1{}^*)v^*,$$

$$(1-\psi)k + (1-\theta)\pi = (c\omega(\varphi i_1{}^* + i_2{}^*) + k + \pi - di_1{}^*)s^* - \tau v^*$$

$$\beta + k + \pi = \frac{(c\omega(\varphi i_1{}^* + i_2{}^*)(s^* + \gamma r^*)}{e^*} + di_1{}^*,$$

$$\phi + k + \pi = \frac{\rho\eta\beta e^*}{e_T{}^*} + di_1{}^*,$$

$$\sigma + d + k + \pi = \frac{(1-\rho)\eta\beta e^* + \delta_3\alpha i_2{}^*}{i_1{}^*} + di_1{}^*,$$

$$\alpha + k + \pi = \frac{(1\quad\eta)\beta e^*}{i_2{}^*} + di_1{}^*,$$

$$\phi_1 + k + \pi = \frac{\sigma i_1{}^* + \delta_2\alpha i_2{}^*}{h^*} + di_1{}^*,$$

$$k + \pi = \frac{\phi e_T{}^* + \phi_1 h^* + \delta_1\alpha i_2{}^* - \gamma c\omega(\varphi i_1{}^* + i_2{}^*)}{r^*} + di_1{}^*$$

Substituting in the derivative for the Lyapunov function and collecting like terms we have:

$$\frac{dL}{dt} = -(\tau + k + \pi)vB_1(1-\frac{v^*}{v})^2 + di_1vB_1(1-\frac{v^*}{v})(1-\frac{v^*i_1{}^*}{vi_1})$$

$$-(k+\pi)B_2(1-\frac{s^*}{s})^2 - B_2(1-\frac{s^*}{s})\left[c\omega\varphi si_1(1-\frac{i_1{}^*s^*}{i_1s}) + c\omega si_1(1-\frac{i_2{}^*s^*}{i_2s}) - di_1s(1-\frac{i_1{}^*s^*}{i_1s}) - \tau v(1-\frac{v^*}{v})\right]$$

$$-\frac{B_3}{e^*}(1-\frac{e^*}{e})\left[c\omega\varphi es^*i_1{}^*(1-\frac{e^*i_1s}{ei_1{}^*s^*}) + \gamma c\omega e\varphi i_1{}^*r^*(1-\frac{i_2{}^*s^*}{i_2s}) - di_1s(1-\frac{e^*i_1r}{ei_1{}^*r^*}) + c\omega es^*i_2{}^*(1-\frac{e^*i_2s}{ei_2{}^*s^*})\right]$$

$$-\frac{B_3}{e^*}(1-\frac{e^*}{e})\left[\gamma c\omega ei_2{}^*r^*(1-\frac{i_2{}^*s^*}{i_2s}) + di_1e^*e(1-\frac{i_1{}^*}{i_1})\right]$$

$$-\frac{B_4}{e_T^*}(1-\frac{e_T^*}{e_T})\left[\rho\eta\beta e^* e_T(1-\frac{e_T^* e}{e_T e^*})-di_1 e_T^* e_T(1-\frac{i_1^*}{i_1})\right]$$

$$-\frac{B_5}{i_1^*}(1-\frac{i_1^*}{i_1})\left[(1-\rho)\eta\beta e^* i_1(1-\frac{i_1^* e}{i_1 e^*})+\delta_3\alpha i_1 i_2^*(1-\frac{i_1^* i_2}{i_2^* i_1})-di_1^2 i_1^*(1-\frac{i_1^*}{i_1})\right]$$

$$-\frac{B_6}{i_2^*}(1-\frac{i_2^*}{i_2})\left[(1-\eta)\beta e^* i_2(1-\frac{i_2^* e}{i_2 e^*})-di_1 i_2 i_2^*(1-\frac{i_1^*}{i_1})\right]$$

$$-\frac{B_7}{h^*}(1-\frac{h^*}{h})\left[\sigma h i_1^*(1-\frac{h^* i_1}{h i_1^*})+\delta_2\alpha i_2^* h(1-\frac{h^* i_2}{h i_2^*})-di_1 h^* h(1-\frac{i_1^*}{i_1})\right]$$

$$-\frac{B_7}{h^*}(1-\frac{i_1^*}{i_1})\left[\sigma h i_1^*(1-\frac{h^* i_1}{h i_1^*})+\delta_2\alpha i_2^* h(1-\frac{h^* i_2}{h i_2^*})-di_1 h^* h(1-\frac{i_1^*}{i_1})\right]$$

$$-\frac{B_8}{r^*}(1-\frac{r^*}{r})\left[\phi e_T^* r(1-\frac{r^* e_T}{r e_T^*})+\phi_1 h^* r(1-\frac{r^* h}{r h^*})+\alpha\delta_1 i_2^* r(1-\frac{r^* i_2}{r i_2^*})+\gamma c\omega\varphi i_2^* r(1-\frac{r^* i_1}{r i_1^*})\right]$$

$$-\frac{B_8}{r^*}(1-\frac{r^*}{r})\left[\gamma c\omega i_1^* r(1-\frac{r^* i_2}{r i_2^*})-di_1 r r^*(1-\frac{i_1^*}{i_1})\right] \qquad (11)$$

This can be written as:

$$\frac{dL}{dt}=-(\tau+k+\pi)vB_1(1-\frac{v^*}{v})^2-(k+\pi)B_2(1-\frac{s^*}{s})^2+\mathrm{P}(v,s,e,e_T,i_1,i_2,h,r)$$

where,

$$P(v,s,e,e_T,i_1,i_2,h,r)$$

is the balance of the right hand terms of (11).

Following the approach of [2, 15, 16], P is non-positive for $v,s,e_T,e,i_1,i_2,h,r>0$. Therefore, $\frac{dL}{dt}=0$ if $v=v^*$, $s=s^*$, $e=e^*$, $e_T=e_T^*$, $i_1=i_1^*$, $i_2=i_2^*$, $h=h^*$, $r=r^*$ and $\frac{dL}{dt}<0$ for $v,s,e_T,e,i_1,i_2,h,r>0$.Thus if $R_{eff}>1$ then, model system (3) has a unique endemic equilibrium point **E_1** which is globally asymptotically stable.

4. Numerical Simulations

In this section we give numerical simulation for model system (3) for the purpose of verifying some of the analytical results. This is done by using a set of parameter values whose sources are mainly from literature as well as estimation in order to have more realistic

simulation results. Table 2 presents the parameter values and their respective sources.

Table 2: Model Parameter values

Parameter	Value	Source
Λ	0.0006yr-1	Estimated
π	0.03767yr-1	Estimated
θ	0.4	Estimated
ψ	0.2	Estimated
c	2	[13]
ω	0.5	[22]
φ	0.3	Estimated
ρ	0.2	[25]
β	0.03yr-1	[9]
η	0.004	[8]
α	0.37yr-1	[8]
δ_1	0.2	[20]
δ_2	0.798	Estimated
δ_3	0.02	Estimated
σ	2	[13]
ϕ_1	1.5	[23]
d	0.3yr-1	[1]
ϕ	2	[23]
τ	0.07yr-1	Estimated
γ	0.06	[20]

In Figures 3 and 4: We show variation of subpopulations with respect to time.

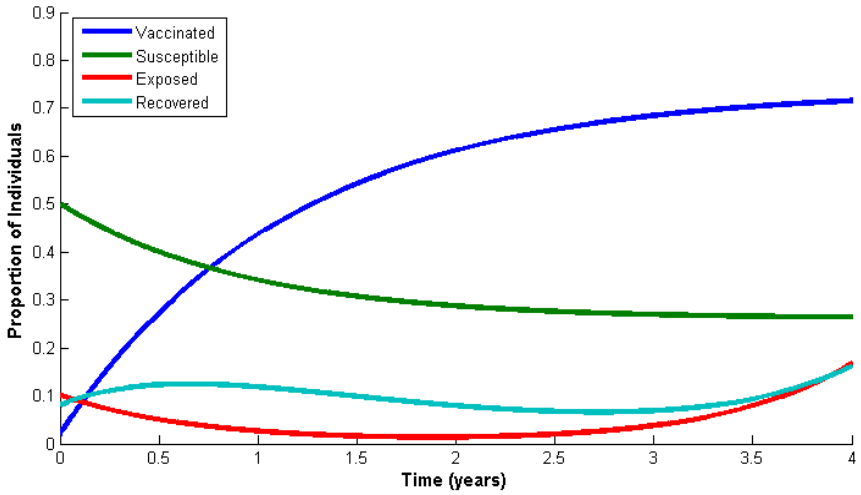

Figure 3: Variations of vaccinated, susceptible, exposed and recovered individuals.

In Figure 3: The susceptible class decreases because some of them progress to latent stage after getting infected by infectious individuals, whereas the number of vaccinated individuals increases due to increase in number of children vaccinated at birth and arrival of vaccinated immigrants. The increase in the proportion of individuals vaccinated is due country policies for instance in Tanzania, where the first vaccine (BCG) for newborns is given to every child as per the child immunization schedules. In the case of the exposed group, the decrease is as a result of screening and treatment intervention and after some years (3.5years) as per our graph, an increase is due to exogenous or endogenous reinfection.

Furthermore, the recovered class increases as a result of the incoming of effectively treated infectious individuals from both severe and infectious stages, as well as screened and treated latent individuals.

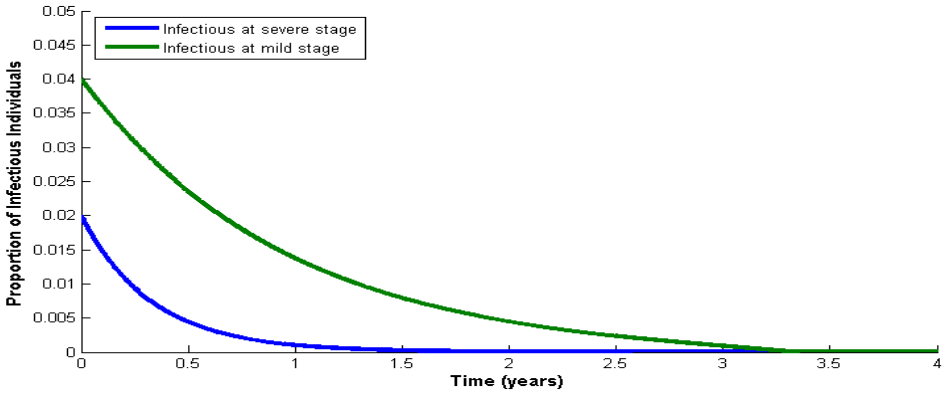

Figure 4: Variations in the infectious population

In Figure 4: Both infectious individuals at mild and severe stages decrease to zero; this

implies that, if all infectious individual are treated, a disease free equilibrium can be attained.

5. Sensitivity Analysis

To determine how best we can do in order to reduce human mortality and morbidity due to TB, it is necessary to know the relative importance of different factors responsible for its transmission and prevalence. We know that, initial disease transmission is directly related to R_0.We calculate the sensitivity indices of the reproductive number, R_0 to the parameters in the model. These indices tell us how vital each parameter is to disease transmission and prevalence. Sensitivity analysis is commonly used to determine the robustness of model predictions to parameter values (since there are usually errors in data collection and presumed parameter values). Thus we use it to discover parameters that have a high impact on R_0 and should be targeted by intervention strategies. The explicit expression of R_0 is given by the equation (6). Since R_0 depends only on ten parameters, we derive an analytical expression for its sensitivity to each parameter using the normalized forward sensitivity index [7] as follows:

$$\Upsilon_{c}^{R_0} = \frac{\partial R_0}{\partial c} \times \frac{c}{R_0} = +1$$

$$\Upsilon_{\omega}^{R_0} = \frac{\partial R_0}{\partial \omega} \times \frac{\omega}{R_0} = +1$$

$$\Upsilon_{\beta}^{R_0} = \frac{\partial R_0}{\partial \beta} \times \frac{\beta}{R_0} = +\ 0.560779$$

In a similar fashion, we compute the sensitivity indices for all parameters used in equation (10). Table 3 shows the sensitivity indices of R_0 with respect to the ten parameters.

Table 3: Sensitivity indices of R_0 with respect to each parameter

Parameter	Sensitivity Index
c	+1
ω	+1
β	+0.561
α	-0.901
π	-1.851
k	-0.0103
δ_3	+0.0043
η	-0.00305
φ	+0.0053
d	-0.0153

From Table 3, we see that, the most sensitive parameters are per capita birth rate, π, per capita contact rate, *c*, probability of transmission of the disease from an infectious individual to a susceptible individual per contact, ω, and the progression rate from latent to infectious stage. For almost all parameters, the sign of the sensitivity indices of R_0 (i.e., whether R_0 increases or decreases when a parameter increases) agrees with an intuitive expectation from the model parameters. For, $\Upsilon_c^{R_0} = \Upsilon_\omega^{R_0} = +1$, this means that, increasing (or decreasing) of c or ω by 10% increases (or decreases) R_0 by 10%. Similarly, $\Upsilon_\beta^{R_0} = +0.561$ means that, increasing (or decreasing) of β by 10% increases (or decreases) R_0 by 5.61%. The negative sign of the sensitivity index of R_0 with respect to d, η, k, α and π imply an inverse relationship between these parameters and R_0. For instance, 10% increase (or decrease) in α leads to approximately a 9.01% decrease (or increase) in R_0. Indeed, if a large number of infectious individuals are treated while their TB status is at mild stage then a decrease in the transmission rate of the disease is expected. Furthermore, the negative sign on the per capita birth rate is due the fact that most of the people are vaccinated at birth to reduce the probability of being infected hence an increase in π reduces R_0 and vice versa.

Therefore, to minimize TB transmission in a population, this study recommends that, the combination of vaccination, screening and treatment should be implemented. This is due the fact that, vaccination reduces the likelihood of an individual to get infected, screening and treatment of latently infected people reduces the progression rate to infectious stage and treatment of infectious people will stop them from transmitting the disease.

6. Conclusion

A deterministic TB model has been formulated with the aim of assessing the effect of vaccination, screening and treatment on the transmission of TB infections. It has been proved that the disease-free equilibrium is locally and globally asymptotically stable if $R_{eff} < 1$ and unstable otherwise while the endemic equilibrium is locally and globally stable if $R_{eff} > 1$. Furthermore, when the effective reproduction number is equal to one, $R_{eff} = 1$, a backward bifurcation occurs. Analytical solutions and numerical simulation shows that, TB incidence can be minimized in a population if the combination of vaccination, screening and treatment are implemented.

Conflict of Interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

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