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Modeling the Effect of Screening and Treatment on the Transmission of Tuberculosis Infections

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Abstract

Tuberculosis (TB) is a chronic airborne disease caused mainly by Mycobacterium tuberculosis and has caused many deaths globally and Tanzania in particular due to failure or delayed intervention. In this paper, a deterministic mathematical model for transmission dynamics of TB with vaccination and screening the population for the purpose of identifying those for immediate treatment is formulated. The effective reproduction number is computed in order to measure the relative impact for individual or combined intervention for effective disease control. Numerical simulations of the basic reproduction number shows that, the combination of vaccination, screening and treatment is the most effective intervention for minimizing the transmission of TB in a population.
Key words: Tuberculosis, Modeling, Screening, Treatment.

1. Introduction

Tuberculosis is a chronic infectious disease caused mainly by Mycobacterium tuberculosis (tubercle bacillus). Worldwide 8.6 million people fell ill due to TB, of which 1.3 million people die annually. In developing countries especially in Africa, the TB incidences, prevalence, and deaths per 100,000 population are 262, 293, and 26 respectively and Tanzania incidences, prevalence and deaths per 100,000 population are 177, 183, and 14 as per WHO (2013). Therefore it is becoming essential to find a viable alternative to minimize/reduce the prevalence of the disease. Basically there are two types of tuberculosis: pulmonary tuberculosis which affects the lungs and 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 (URT, 2006). This study concentrates only on the infectious pulmonary TB. 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. It is estimated that ten percent of infected individuals develop active tuberculosis and the rest have strong immunity which limits multiplication of tubercle bacilli (Castillo-Chavez and Feng, 1998; Feng et al., 2000; Castillo-Chavez and Song, 2004).

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 through the year 2020 (Murray and Lopez, 1997). The disease spreads 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 (Adetunde, 2008). 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 (Okyere, 2007). 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-complex and renewed concern over the disease.

The influence for the use of mathematical modelling 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. Okuonghae and Korobeinikov (2007) 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. Ssematimba *et al*. (2005), 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. Enagi and Ibrahim (2011) 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. Ziv *et al* (2001) 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 suggest 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 (Hove-Musekwa and Nyabadza, 2009).In this paper, we investigate the effect of vaccination, screening and treatment on transmission dynamics of TB infections in a homogenous population.

The outline of the rest of the paper is as follows; section 2: model formulation, section 3: model analysis, and section 4: numerical simulations.

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 mild stage $I_1(t)$, infectious at severe 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 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

- 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.
- Recruits are either vaccinated or susceptible.
- Individuals at mild stage may recover naturally or by treatment; otherwise they advance to severe stage.
- On recovery there is temporal immunity.
- People in each compartment have equal natural death rate μ

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

described in Table 1.

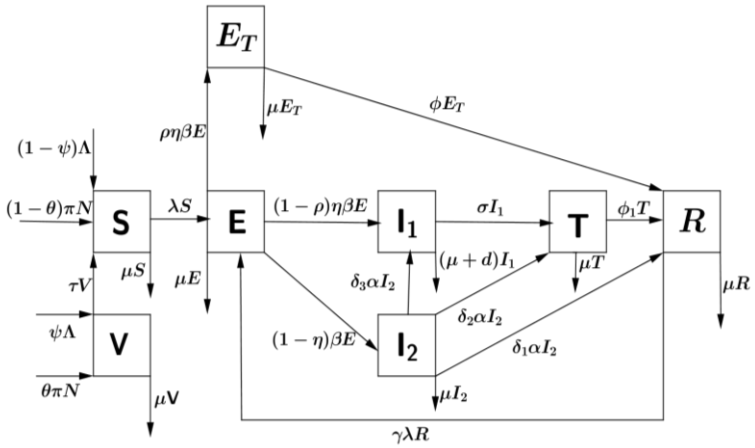

Figure 1: Compartmental diagram for a TB transmission model with vaccination, screening and treatment.

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 ordinary differential equations.

$$\frac{dV}{dt} = \psi\Lambda + \theta\pi N - (\tau + \mu)V,$$

$$\frac{dS}{dt} = (1-\psi)\Lambda + (1-\theta)\pi N + \tau V - (\lambda + \mu)S,$$

$$\frac{dE}{dt} = \lambda S + \gamma\lambda R - (\beta + \mu)E \quad ,$$

$$\frac{dE_T}{dt} = \rho\eta\beta E - (\phi + \mu)E_T \qquad (1)$$

$$\frac{dI_1}{dt} = (1-\rho)\eta\beta E + \delta_3\alpha I_2 - (\sigma + \mu + d)I_1,$$

$$\frac{dI_2}{dt} = (1-\eta)\beta E - (\alpha + \mu)I_2 \quad ,$$

$$\frac{dT}{dt} = \sigma I_1 + \delta_2\alpha I_2 - (\phi_1 + \mu)T \quad ,$$

$$\frac{dR}{dt} = \phi E_T + \phi_1 T + \delta_1\alpha I_2 - (\gamma\lambda + \mu)R$$

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

$$v = \frac{V}{N}, s = \frac{S}{N}, e_T = \frac{E_T}{N}, e = \frac{E}{N}, i_1 = \frac{I_1}{N}, i_2 = \frac{I_2}{N}, h = \frac{T}{N} \text{ and } r = \frac{R}{N}$$

in classes

$$V,\ S,\ E,\ E_T,\ I_1,\ I_2, \text{T and } R.$$

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

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

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 $\Omega = \{(v, s, e, e_T, i_1, \mathrm{i}_2, h, r) \in R_+^{\,8} : v + s + e + e_T + i_1 + i_2 + h + r \le 1\}$ where the model makes biological sense that can be shown to be positively invariant and globally attracting in $R_+^{\,8}$ with respect to our system.

3. Model analysis

The Model (3) is analyzed qualitatively to get insights into its dynamical features which gives 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

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

and in case of no disease, $e_T = e = i_1 = i_2 = 0$ and the sum of susceptible and vaccinated populations equals to total population, that is to say $s^* + v^* = 1$.

The statement above reduces system (3) to:

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

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

Therefore, the disease free equilibrium (DFE) denoted by E_0 of the model (3.3) is given by:

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

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 (Diekman et al., 1990). 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.

From system (3), we derive $\mathcal{F}_i$ and $\mathcal{V}_i$ as

$$\mathcal{F}_i=\begin{bmatrix}\mathcal{F}_1\\ \mathcal{F}_2\\ \mathcal{F}_3\\ \mathcal{F}_4\end{bmatrix}=\begin{bmatrix}c\omega(\varphi i_1+i_2)(s+\gamma r)\\ 0\\ 0\\ 0\end{bmatrix}$$

and

$$\mathcal{V}_i=\begin{bmatrix}\mathcal{V}_1\\ \mathcal{V}_2\\ \mathcal{V}_3\\ \mathcal{V}_4\end{bmatrix}=\begin{bmatrix}-\gamma\lambda r+(\beta+k+\pi-di_1)e\\ -\rho\eta\beta e+(\phi+k+\pi-di_1)e_T\\ -(1-\rho)\eta\beta e-\delta_3\alpha i_2+(\sigma+d+k+\pi-di_1)i_1\\ -(1-\eta)\beta e+(\alpha+k+\pi-di_1)i_2\end{bmatrix}$$

Using the linearization method, the associated matrix at DFE for **F** is given by:

$$\mathbf{F}=\begin{bmatrix} \frac{\partial \mathcal{F}_1(E_0)}{\partial e_T} & \frac{\partial \mathcal{F}_1(E_0)}{\partial e} & \frac{\partial \mathcal{F}_1(E_0)}{\partial i_1} & \frac{\partial \mathcal{F}_1(E_0)}{\partial i_2} \\ \frac{\partial \mathcal{F}_2(E_0)}{\partial e_T} & \frac{\partial \mathcal{F}_2(E_0)}{\partial e} & \frac{\partial \mathcal{F}_2(E_0)}{\partial i_1} & \frac{\partial \mathcal{F}_2(E_0)}{\partial i_2} \\ \frac{\partial \mathcal{F}_3(E_0)}{\partial e_T} & \frac{\partial \mathcal{F}_3(E_0)}{\partial e} & \frac{\partial \mathcal{F}_3(E_0)}{\partial i_1} & \frac{\partial \mathcal{F}_3(E_0)}{\partial i_2} \\ \frac{\partial \mathcal{F}_4(E_0)}{\partial e_T} & \frac{\partial \mathcal{F}_4(E_0)}{\partial e} & \frac{\partial \mathcal{F}_4(E_0)}{\partial i_1} & \frac{\partial \mathcal{F}_4(E_0)}{\partial i_2} \end{bmatrix}=\begin{bmatrix} 0 & 0 & c\omega\varphi s & c\omega s \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix}$$

On the other hand, the matrix **V** for the transfer of individuals out of the compartment i is given by;

$$\mathbf{V}=\begin{bmatrix} \frac{\partial \mathcal{V}_1(E_0)}{\partial e_T} & \frac{\partial \mathcal{V}_1(E_0)}{\partial e} & \frac{\partial \mathcal{V}_1(E_0)}{\partial i_1} & \frac{\partial \mathcal{V}_1(E_0)}{\partial i_2} \\ \frac{\partial \mathcal{V}_2(E_0)}{\partial e_T} & \frac{\partial \mathcal{V}_2(E_0)}{\partial e} & \frac{\partial \mathcal{V}_2(E_0)}{\partial i_1} & \frac{\partial \mathcal{V}_2(E_0)}{\partial i_2} \\ \frac{\partial \mathcal{V}_3(E_0)}{\partial e_T} & \frac{\partial \mathcal{V}_3(E_0)}{\partial e} & \frac{\partial \mathcal{V}_3(E_0)}{\partial i_1} & \frac{\partial \mathcal{V}_3(E_0)}{\partial i_2} \\ \frac{\partial \mathcal{V}_4(E_0)}{\partial e_T} & \frac{\partial \mathcal{V}_4(E_0)}{\partial e} & \frac{\partial \mathcal{V}_4(E_0)}{\partial i_1} & \frac{\partial \mathcal{V}_4(E_0)}{\partial i_2} \end{bmatrix}$$

This gives,

$$\mathbf{V}=\begin{bmatrix} \beta+k+\pi & 0 & 0 & 0 \\ -\rho\eta\beta & \phi+k+\pi & 0 & 0 \\ -(1-\rho)\eta\beta & 0 & \sigma+d+k+\pi & -\delta_3\alpha \\ -(1-\eta)\beta & 0 & 0 & \alpha+k+\pi \end{bmatrix}$$

Finding the inverse of $\mathbf{V}$ above, we get:

$$\mathbf{V}^{-1}=\begin{bmatrix} \frac{1}{\beta+k+\pi} & 0 & 0 & 0 \\ \frac{\rho\eta\beta}{(\beta+k+\pi)(\phi+k+\pi)} & \frac{1}{\phi+\mu} & 0 & 0 \\ \frac{(1-\eta)\delta_3\alpha\beta+(\alpha+k+\pi)\eta\beta}{(\beta+k+\pi)(\sigma+d+k+\pi)(\alpha+k+\pi)} & 0 & \frac{1}{\sigma+d+k+\pi} & \frac{\delta_3\alpha}{(\alpha+k+\pi)(\sigma+d+k+\pi)} \\ \frac{(1-\eta)\beta}{(\alpha+k+\pi)(\beta+k+\pi)} & 0 & 0 & \frac{1}{\alpha+k+\pi} \end{bmatrix}$$

For simplicity, $\mathbf{FV}^{-1}$ can be written as

$$\mathbf{FV}^{-1} = \begin{bmatrix} a & 0 & b & p \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix} \tag{5}$$

where,

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

$$b = \frac{c\omega\varphi}{(\sigma+d+k+\pi)},$$

and

$$p = \frac{\delta_3\alpha c\omega\varphi s^*}{(\sigma+d+k+\pi)(\alpha+k+\pi)} + \frac{c\omega s^*}{(\alpha+k+\pi)}$$

from (3.4)

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

The eigenvalues, $\boldsymbol{\lambda}$ of matrix (5) can be computed from the characteristic equation: $\left|\mathbf{FV}^{-1} - \lambda\mathbf{I}\right| = \mathbf{0}$. And we see that from our matrix that $\lambda_2 = \lambda_3 = \lambda_4 = 0$ and

$$\lambda_1 = \frac{((1-\eta)\delta_3\alpha + (\alpha+k+\pi)(1-\rho)\eta)c\omega\varphi\beta s^*}{(\beta+k+\pi)(\sigma+d+k+\pi)(\alpha+k+\pi)} + \frac{(1-\eta)c\omega\beta s^*}{(\beta+k+\pi)(\alpha+k+\pi)}$$

Clearly λ_1 is the dominant eigenvalue and thus is the effective reproduction number, R_{eVT1} of our normalised model system (3) with vaccination, screening and treatment.
Therefore:

$$R_{eVT1} = \frac{((1-\eta)\delta_3\alpha + (\alpha+k+\pi)(1-\rho)\eta)c\omega\varphi\beta s^*}{(\beta+k+\pi)(\sigma+d+k+\pi)(\alpha+k+\pi)} + \frac{(1-\eta)c\omega\beta s^*}{(\beta+k+\pi)(\alpha+k+\pi)} \tag{6}$$

where,

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

When there is no screening, (i.e. $\rho = 0$) the effective reproduction number with vaccination and treatment only is given by:

$$R_{eVT2}=\frac{((1-\eta)\delta_3\alpha+(\alpha+k+\pi)\eta)c\omega\varphi\beta s^*}{(\beta+k+\pi)(\sigma+d+k+\pi)(\alpha+k+\pi)}+\frac{(1-\eta)c\omega\beta s^*}{(\beta+k+\pi)(\alpha+k+\pi)} \quad (7)$$

Considering equation (6), when some of individuals progress to infectious stage and no treatment is provided, the parameters $\rho=\sigma=0$, consequently the effective reproduction number with vaccination only (R_{eV}) is given by:

$$R_{eV}=\frac{((1-\eta)\delta_3\alpha+(\alpha+k+\pi)\eta)c\omega\varphi\beta s^*}{(\beta+k+\pi)(d+k+\pi)(\alpha+k+\pi)}+\frac{(1-\eta)c\omega\beta s^*}{(\beta+k+\pi)(\alpha+k+\pi)} \quad (8)$$

It can be noted that the term $(\alpha+k+\pi)\eta\beta$ is multiplied by a proportion $(1-\rho)$ in R_{eVT1} which implies that $R_{eVT1}<R_{eV}$ and we conclude that the endemicity of the infection is reduced more when the combination of vaccination, screening and treatment are introduced. Furthermore, if there is no vaccination then, the proportion of children vaccinated at birth θ and that of immigrants ψ becomes zero. Subsequently, the expiry rate of the vaccination efficacy τ is zero and $s=1$. Thus, the reproduction number for screening and treatment only becomes:

$$R_{eT1}=\frac{((1-\eta)\delta_3\alpha+(\alpha+k+\pi)(1-\rho)\eta)c\omega\varphi\beta}{(\beta+k+\pi)(\sigma+d+k+\pi)(\alpha+k+\pi)}+\frac{(1-\eta)c\omega\beta}{(\beta+k+\pi)(\alpha+k+\pi)} \quad (9)$$

Also we note that $R_{eVT}=sR_{eT1}$ where $0<s^*<1$, which implies that $R_{eVT1}<R_{eT1}$.Thus, the endemicity of the infection is reduced when vaccination, screening and treatment are introduced rather than screening and treatment only. In addition to that, if there is no vaccination and screening the parameters ψ,θ and ρ are zero and the reproduction number for our model with treatment only becomes:

$$R_{eT2}=\frac{((1-\eta)\delta_3\alpha+(\alpha+k+\pi)\eta)c\omega\varphi\beta}{(\beta+k+\pi)(\sigma+d+k+\pi)(\alpha+k+\pi)}+\frac{(1-\eta)c\omega\beta}{(\beta+k+\pi)(\alpha+k+\pi)} \quad (10)$$

Finally, we compute the basic reproduction number R_0 from the equation for R_{eVT}, that is if there is no vaccination and treatment. That is, $\theta=\tau=\psi=\rho=\sigma=0$.

Thus,

$$R_0=\frac{((1-\eta)\delta_3\alpha+(\alpha+k+\pi)\eta)c\omega\varphi\beta}{(\beta+k+\pi)(d+k+\pi)(\alpha+k+\pi)}+\frac{(1-\eta)c\omega\beta}{(\beta+k+\pi)(\alpha+k+\pi)} \quad (11)$$

Moreover, equation (11) shows that the basic reproduction number for system (3) is the sum of the basic reproduction numbers for severe infection, R_{0i_1} and mild infection, R_{0i_2}.

Thus,

$$R_0=R_{0i_1}+R_{0i_2}.$$

where,

$$R_{0i_1} = \frac{((1-\eta)\delta_3\alpha + (\alpha+k+\pi)\eta)c\omega\varphi\beta}{(\beta+k+\pi)(d+k+\pi)(\alpha+k+\pi)} \quad \text{and} \quad R_{0i_2} = \frac{(1-\eta)c\omega\beta}{(\beta+k+\pi)(\alpha+k+\pi)}$$

However, the comparison between most of the reproduction numbers in (6), (7), (8), (9), (10) and (11) analytically is not that direct. Hence we go for numerical simulations.

4. Simulation and Discussion

A Tuberculosis model with vaccination, screening and treatment is formulated and analyzed. The main objective of this study was to assess the effect of these control strategies, individually or in combination on the transmission dynamics of the disease. In order to support the analytical results, graphical representations showing the variations in reproduction numbers with respect to exposure rate, $c\omega$ are provided in Figure 2. However, most of the parameters are not readily available and we use values from the literature and others are estimated for the purpose of illustration. Table 2 shows the set of parameter values which were used.

Table 2: Parameters used in model simulations

Parameters	value	Source
k	0.0006yr^{-1}	Estimated
π	0.03725yr^{-1}	Estimated
θ	0.4	Estimated
ψ	0.2	Estimated
c	2	Feng *et al* (2000)
ω	0.5	Geomira (2008)
φ	0.2	Estimated
ρ	0.3	WHO(2013)
β	0.03yr^{-1}	Cohen *et al* (2007)
η	0.004	Egbetade (2012)
α	0.37	Egbetade (2012)
δ_3	0.02	Estimated
σ	2	Feng et al (2000)
d	0.3yr^{-1}	Adetunde(2008)
τ	0.04yr^{-1}	Estimated

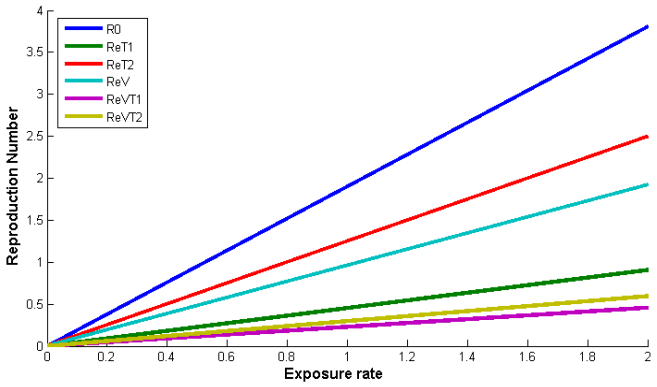

Figure 2: Variations in reproduction number with respect to exposure rate

Figure 2 shows that, $R_{eVT1} < R_{eVT2} < R_{eT1} < R_{eV} < R_{eT2} < R_0$. This implies combination of vaccination, screening and treatment is the most effective strategy in controlling the transmission of TB infection in a population followed by the combination of vaccination and treatment. The combination of screening and treatment is the third advisable while vaccination only and treatment only are not advisable in combating TB.

On the other hand, the contribution of severe and mild infectious individuals to the disease transmission were investigated, Figure 3 shows the graphical results.

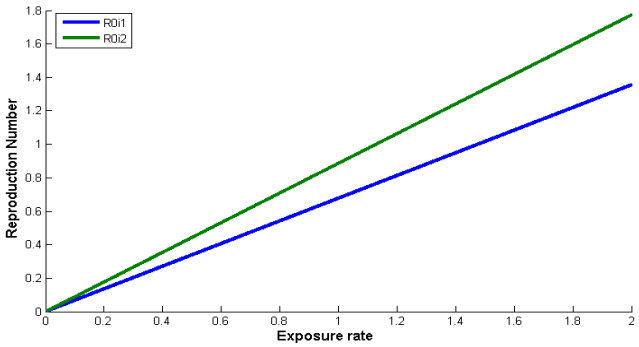

Figure 3: Variations in basic reproduction number for mild and severe infectives

Figure 3 shows that the basic reproduction number for individual at mild stage is greater than or equal to that of individuals at severe stage. This implies that infectious individuals who are at mild stage have a significant contribution on the transmission of the infection and keeping the disease endemic in the population compared to the one at severe conditions whose TB status are well known and most of them expected to be hospitalized. This conforms to the intuition that individuals at mild stage stay in a population for a long time and interact with many people compared to those at severe stage. Therefore, they are more dangerous than the sick ones (infectious at severe stage).

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