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RESEARCH ARTICLE

A Mathematical Model of Tuberculosis with Respect to Drug Resistance to the First and Second Line of the Treatment

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ABSTRACT

In this research paper work, we developed a mathematical model for tuberculosis (TB). Disease was formulated and rigorously analyzed. The model sub-divided into six compartments. The model has equilibria; the diseases-free equilibrium. The equilibrium states were obtained and analyzed for their stability relatively to the effective reproduction number. The result shows that the disease-free equilibrium state was stable state is established. We able to show that the TB disease free equilibrium is locally and globally asymptotically stable R_0<1. Using the number of treatment, individual increases as the rate at which recovery rate of which makes them recovery back from disease. The analytical solution was obtained using homotopy perturbation method and effective reproduction number was computed to measure the relative impact for individual or combined intervention for effective disease control. Numerical simulations of the model show that lose their immunity at the rate decreases at immunity wanes of which makes them susceptible back to disease is the most effective way to combat the epidemiology of TB.

Key words: Mathematical model, tuberculosis, resistance, second and fist line, treatment

INTRODUCTION

Tuberculosis (TB) is a worldwide pandemic disease. According to the World Health Organization (WHO) [1], one-third of the world's population is currently infected by the TB bacillus bacteria. Being a disease of poverty, the vast majority of TB deaths are in the developing world with more than half occurring in Asia (Bleed *et al.*, 2001) [2]. The estimated global incidence rate is falling very slowly from the peak of 141 cases per 100,000 population in 2002 to 128 cases per 100,000 population in 2010. The TB death rate has also fallen by 40% since 1990 and the number of deaths is also declining.

Globally, the percentage of people successfully treated reached its highest level at 87% in 2009. TB caused by infection with the bacillus *Mycobacterium tuberculosis* is a very common and an infectious airborne disease. It typically affects the lungs (pulmonary TB) but can affect other sites as well (extrapulmonary TB). It is estimated that one-third of the world's population has been infected with the *M. tuberculosis* (the WHO, 2010) [3]. Moreover, an estimated 8.6 million people developed TB and 1.3 million died from the disease (including 320 thousand deaths among HIV-positive people) in 2012 (Kochi, 2001)[3]. Although the rate of new TB cases and the TB incidence rates are falling worldwide and the TB mortality rate has been reduced, the absolute number of incident cases of TB is increasing due to population growth. Therefore, TB remains a major global health problem (the WHO, 2013) [4].

In 2011, the treatment success rate continued to be high at 87% among all new TB cases. However, there were about 3 million people who developed TB and were missed by national notification systems (the WHO, 2013)[4]. On the other hand, the treatment interruptions are frequent in active TB cases during the intensive phase and the continuation phase because of a wide range of reasons (Jakubowiak

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et al., 2009)[5]. It may be recognized that the treatment interruptions and the missed TB cases are the key factors to cause the more drug-resistant TB cases and the high TB mortality (Tsai *et al.*, 2010)[6]. The factor of treatment interruptions may result in more susceptible people infected as well. In 2012, there was estimation that 450 thousand individuals developed multidrug-resistant TB (MDR-TB) and an estimation of 170 thousand deaths from MDR-TB [2], which is currently a main threat to tuberculosis control programs and community health (van Helden *et al.*, 2006)[7].

According to the WHO, the number of people falling ill with TB each year is declining (the WHO, 2010)[1]. However, this downward trend is threaten by the increasing number of TB cases in immigrants especially in countries that have substantial levels of immigration from areas with a high prevalence of the disease (Jia *et al.,* 2008)[8]. The immigrants here are generally the people who are travelling from less to more economically developed geographical areas in search of jobs and better living conditions. As an air-borne infectious disease, it is impossible for any country to isolate itself. In long-term, the best defense against TB is to bring the disease under control worldwide.

The model subdivides the population into six mutually-exclusive classes, namely, susceptible $S(t)$, early latent $E_1(t)$, late latent $E_2(t)$, non-isolated infectious $I(t)$, isolated infectious $J(t)$, and treated or recovered $T(t)$.

Some of the limitations are;

i. Unavailability of records of TB disease case
ii. Poor data documentation habit of public servants
iii. Scanty scholarly article on TB disease
iv. Is not age structured?

MODEL FORMATION

Following Andrawus *et al.*, 2020[9], the model considers human population N. The population at time t is divided into six (6) subpopulations. Susceptible $S(t)$ this class includes those individuals who are at risk for developing an infection from TB. Latent Class $E(t)$ this class refers to susceptible individuals who become infected. Infected $I(t)$: This class includes all individuals who are showing the symptom of the disease. First Line Treatment $T_N(t)$: This class includes all individual that failed to take drugs (treatment). Second Line Treatment $T_D(t)$: This class includes all individual that failed to take drugs (treatment) for the second treatment term. Recovered $R(t)$: This class includes all individuals that have recovered from the disease and got temporary immunity. The susceptible class is increased by birth or emigration at the rate of π: The susceptible class will get TB when they mingled with infectious individuals at the, β is the effective contact rate. The latent class is generated at a rate βSI, it decreases at rate α which is the progression rate. The infectious class is generated at a rate α, it also reduces at rate of the treatment r_1 and it further reduces at a rate γ_1 which is default of the treatment. The first line treatment is generated at rate γ_1, it reduces at a rate of the treatment r_1 and it further reduces at a rate γ_2 which is second default of the treatment. The second line treatment class is generated at rate γ_2, it reduces at a rate of the treatment r_1 and recovered class is generated at rate r_1, r_2 and r_3 The infectious, first line treatment, and second line treatment class are reduced at the rates δ_1, δ_2 and δ_3 while the whole classes reduce at the rate $\propto$ those who lose their partial immunity at the rate σ which recovered humans become susceptible. Which is the natural mortality rate, Hence, Figure 1, shows the schematic diagram:

Mathematical Model

Our assumptions are as follow;

- That the population size in a compartment is differentiable with respect to time and that the epidemic process is deterministic
- That the population is heterogeneous. That is, the individuals that make up the population can be grouped into different compartments or groups according to their epidemiological state
- That a proportion of the population of newborn in immunized against TB infection through treatment

- That the immunity conferred on individuals by the treatment expires after some time at given rate
- That people in each compartment have equal natural death rate of $\propto$
- That there are no immigrants and emigrants. The only way of entry into the population is through new-born babies and the only way of exit is through death from natural causes of death from TB-related causes
- That the infection does not confer immunity to the curved and recovered individuals and so they go back to the susceptible class at a given rates
- That all newborns are previously uninfected by TB and therefore joint either the immunized compartment or the susceptible compartment depending on whether they are treated or not.

The model equations are;

$$\frac{dS}{dt} = \pi + \sigma R - \beta SI - \mu S \tag{1}$$

$$\frac{dE}{dt} = \beta SI - (\mu + \alpha) E \tag{2}$$

$$\frac{dI}{dt} = \alpha E - (\gamma_1 + r_1 + \mu + \delta_1) I \tag{3}$$

$$\frac{dT_N}{dt} = \gamma_1 I - (\gamma_2 + r_2 + \mu + \delta_2) T_N \tag{4}$$

$$\frac{dT_D}{dt} = \gamma_2 T_N - (r_3 + \mu + \delta_3) T_D \tag{5}$$

$$\frac{dR}{dt} = r_1 I + r_2 T_N + r_3 T_D - (\mu + \sigma) R \tag{6}$$

Positive Invariant Region

The entire population size N can be determined from equations (1) to (6).

The total population size is $N=S+E+I+T_N+T_D+R$ 7)

Adding equation (1) to equation (6)

$$\frac{dN}{dt} = \frac{dS}{dt} + \frac{dE}{dt} + \frac{dI}{dt} + \frac{dT_N}{dt} + \frac{dT_D}{dt} + \frac{dR}{dt} \tag{8}$$

$$\frac{dN}{dt} = \pi - \mu S - \mu E - \mu I - \delta_1 I - \mu T_N - \delta_2 T_N - \mu T_D - \delta_3 T_D - \mu R \tag{9}$$

In the absence of the disease ($\delta_1=\delta_2=\delta_3=0$) then (9) given
The positive invariant region can be obtained using the following theorem.

Theorem 2.1
The solutions of the system of equations (1) to (6) are feasible for $t>0$ if they enter that the invariant region D is given as equation (10).

Proof

Let $D = (S, E, I, T_N, T_D, R) \in R^6$ (10)

Be any solution of the system of equations (1) to (6) with non-zero initial conditions.
Assuming there is no disease-induced deaths equation (9)

$$\frac{dN}{dt} \leq \pi - \mu N \tag{11}$$

$$\frac{dN}{dt} + \mu N \leq \pi \tag{12}$$

The integrating fact for equation (13) is multiplying both sides of equation (12) by give

$$\frac{dN}{dt} + \mu N e^{-\mu t} \leq \pi e^{\mu t} \tag{13}$$

$$\frac{dN}{dt} \leq \mu \tag{14}$$

Integrating both sides we have

$$N(t) \tag{15}$$

$$N(t) = \frac{\pi}{\mu} + c \tag{16}$$

Applying the initial condition t=0, N (0)=N_0

$$N_0 \leq \frac{\pi}{\mu} + c \Rightarrow N_0 - \frac{\pi}{\mu} \leq c \tag{17}$$

$$\rightarrow N \leq \frac{\pi}{\mu} + \left(N_0 - \frac{\pi}{\mu} \right) e^{-\mu t} \tag{18}$$

Therefore, as t=∞ in (18) to humans N approaches $K = \frac{\pi}{\mu}$ (that is $N \rightarrow K = \frac{\pi}{\mu}$) the parameter $K = \frac{\pi}{\mu}$ is called the carrying capacity. Hence, all feasible solution set of the human of the model equation (1) to (6) enter the region.

$$D = \left\{ (S, E, I, T_N, T_D, R) \in R^6 : S > 0, E > 0, I > 0, T_N > 0, \mathrm{T}_D > 0, \mathrm{R} > 0, \mathrm{N} \leq \frac{\pi}{\mu}) \right\} \tag{19}$$

With is positively invariant (i.e., solution remain positive for all time t) and the model is epidemiologically meaningful and mathematically well pose.

POSITIVE OF SOLUTIONS

Since equation (1) to (6) represent the population in each compartment and all model parameters are all positive, then if lies in region D defined by

Theorem 2

Let the initial data for the model equation be given as this

$S(0)\geq 0, E(0)\geq 0, I(0)\geq 0, T_N(0)\geq 0, T_D(0)\geq 0, R(0)\geq 0$ (20)

Then, the solutions ($S(t)$, $E(t)$, $I(t)$, $T_N(t)$, $T_D(t)$, R) of the model equation with non-negative initial data with remain non-negative for at time $t>0$

Proof

For equation (1)

$$\frac{dS}{dt} = \pi + \sigma R - \beta IS - \mu S \geq -\mu S(t) \quad (21)$$

$$\frac{dS}{dt} \geq -\mu S \mu S(t) \quad (22)$$

Separating the variables and integrating both sides, we have

$$\frac{dS}{S} \geq -\mu dt \quad (23)$$

$$InS(t) \geq \propto t + c \quad (24)$$

$$S(t) = e^{-\propto t + c} \quad (25)$$

$$S(t) = e^{-\propto t} \quad (26)$$

Where $k = e^c$ (27)

Using the initial condition $t=0 \Rightarrow S(0) \geq k$

Therefore, $S(t) \geq S(0)e^{-\propto t} \geq 0$ (28)

From equation (2)

$$\frac{dE}{dt} = \beta SI - (\mu + \alpha)E \geq -(\mu + \alpha)E \quad (29)$$

$$\frac{dE}{dt} \geq -(\mu + \alpha)E \quad (30)$$

Separating the variables and integrating both sides, we have

$$\frac{dE}{E} \geq -(\mu + \alpha)dt \quad (31)$$

$$InE(t) \geq -(\mu + \alpha) + c \quad (32)$$

$$E(t) = e^{-(\propto + \alpha)t + c} \quad (33)$$

$$E(t) = e^{-(\propto + \alpha)t} \quad (34)$$

Where $k = e^c$ (35)

Using the initial condition $t=0 \Rightarrow E(0) \geq k$

From equation (3)

$$\frac{dI}{dt} = \alpha E - (\gamma_1 + r_1 + \mu + \delta_1) I \geq -(\gamma_1 + r_1 + \mu + \delta_1) I \quad (36)$$

$$\frac{dI}{dt} \geq -(\gamma_1 + r_1 + \mu + \delta_1) I \quad (37)$$

Separating the variables and integrating both sides, we have

$$\frac{dI}{I} \geq -(\gamma_1 + r_1 + \mu + \delta_1) dt \quad (38)$$

$$InI(t) \geq -(\gamma_1 + r_1 + \infty + \delta_1) \quad (39)$$

$$I(t) = e^{-(\gamma 1 + r1 + \infty + \delta 1) + c} \quad (40)$$

$$I(t) = e^{-(\gamma 1 + r1 + \infty + \delta 1) t} \quad (41)$$

Where $k = e^c$ (42)

Using the initial condition $t=0 \Rightarrow I(0) \geq k$
Therefore, $I(t) \geq I(0) e^{-(\gamma 1 + r1 + \infty + \delta 1) t} \geq 0$ (43)
From equation (4)

$$\frac{dT_N}{dt} = \gamma_1 I - (\gamma_2 + r_2 + \mu + \delta_2) T_N \geq -(\gamma_2 + r_2 + \mu + \delta_2) T_N \quad (44)$$

$$\frac{dT_N}{dt} \geq -(\gamma_2 + r_2 + \mu + \delta_2) T_N \quad (45)$$

Separating the variables and integrating both sides, we have

$$\frac{dT_N}{T_N} \geq -(\gamma_2 + r_2 + \mu + \delta_2) dt \quad (46)$$

$$InT_N(t) \geq -(\gamma_2 + r_2 + \mu + \delta_2) + c \quad (47)$$

$$T_N(t) = e^{-(\gamma_2 + r_2 + \mu + \delta_2) t + c} \quad (48)$$

$$T_N(t) = e^{-(\gamma_2 + r_2 + \mu + \delta_2) t} \quad (49)$$

Where $k = e^c$ (50)

Using the initial condition $t=0 \Rightarrow T_D(0) \geq k$

Therefore, $T_N(t) \geq T_N(0) e^{-(\gamma_2 + r_2 + \mu + \delta_2) t} \geq 0$ (51)

From equation (5)

$$\frac{dT_D}{dt} = \gamma_2 T_N - (r_3 + \mu + \delta_3) T_D \geq -(r_3 + \mu + \delta_3) T_D \quad (52)$$

$$\frac{dT_D}{dt} \geq -\left(r_3 + \mu + \delta_3\right) T_D \tag{53}$$

Separating the variables and integrating both sides, we have

$$\frac{dT_D}{T_D} \geq -\left(r_3 + \mu + \delta_3\right) dt \tag{54}$$

$$InT_D(t) \geq -\left(r_3 + \mu + \delta_3\right) + c \tag{55}$$

$$T_D(t) = e^{-(r_3+\mu+\delta_3)t+c} \tag{56}$$

$$T_D(t) = e^{-(r_3+\mu+\delta_3)t} \tag{57}$$

Where $k=e^c$ (58)

Using the initial condition $t=0 \Rightarrow T_D(0) \geq k$

Therefore, $T_D(t) \geq T_D(0) e^{-(r_3+\mu+\delta_3)t} \geq 0$ (59)

From equation (6)

$$\frac{dR}{dt} = r_1 I + r_2 T_N + r_3 T_D - (\sigma + \mu) R \geq -(\sigma + \mu) R \tag{60}$$

$$\frac{dR}{dt} \geq -(\sigma + \mu) R \tag{61}$$

Separating the variables and integrating both sides, we have

$$\frac{dR}{R} \geq -(\sigma + \mu) dt \tag{62}$$

$$InR(t) \geq -(\sigma + \mu) t + c \tag{63}$$

$$R(t) = e^{-(\sigma+\mu)t+c} \tag{64}$$

$$R(t) = e^{-(\sigma+\mu)t} \tag{65}$$

Where $k=e^c$ (66)

Using the initial condition $t=0 \Rightarrow R(0) \geq k$

Therefore, $R(t) \geq R(0) e^{-(\sigma+\mu)t} \geq 0$ (67)

THE EXISTENCE AND UNIQUENESS OF SOLUTION

The validity and implementation of any mathematical model depend on whether the given system of equations has a solution, and if it has, there is need to check if the solution is unique (Ayoade *et al.,* 2019) [10].

Theorem 4.1

Let D denotes the region $\pi \in \Re^{+}$. Then, the model system (1) to (6) has a unique solution if it is established that $\frac{\partial m_i}{\partial m_i}, \mathrm{i} = 1,2,3,4,5,6$ are continuous and bounded in D.

Proof

Let equations (1) to (2) be represented by m_1, m_2, m_3, m_4, m_5 and m_6 respectively

From equation (1), the following partial derivatives are obtain

$$\left.\begin{aligned} &\left|\frac{\partial m_1}{\partial S}\right| = \left|-\beta I - \mu\right| < \infty; \left|\frac{\partial m_1}{\partial E}\right| = 0 < \infty; \left|\frac{\partial m_1}{\partial I}\right| = \left|-\beta S\right| < \infty; \\ &\left|\frac{\partial m_1}{\partial T_N}\right| = 0 < \infty; \left|\frac{\partial m_1}{\partial T_D}\right| = 0 < \infty; \left|\frac{\partial m_1}{\partial R}\right| = \left|\sigma\right| < \infty \end{aligned}\right\} \tag{68}$$

The above partial derivatives exist, continuous and are bounded. From equation (2), we obtained the following partial derivatives

$$\left.\begin{aligned} &\left|\frac{\partial m_1}{\partial S}\right| = \left|\beta I\right| < \infty; \left|\frac{\partial m_1}{\partial E}\right| = \left|-(\alpha + \mu)\right| < \infty; \left|\frac{\partial m_1}{\partial I}\right| = \left|\beta S\right| < \infty; \\ &\left|\frac{\partial m_1}{\partial T_N}\right| = 0 < \infty; \left|\frac{\partial m_1}{\partial T_D}\right| = 0 < \infty; \left|\frac{\partial m_1}{\partial R}\right| = 0 < \infty \end{aligned}\right\} \tag{69}$$

The above partial derivatives exist, continuous and are bounded. From equation (3), we obtained the following partial derivatives

$$\left.\begin{aligned} &\left|\frac{\partial m_1}{\partial S}\right| = 0 < \infty; \left|\frac{\partial m_1}{\partial E}\right| = \left|\alpha\right| < \infty; \left|\frac{\partial m_1}{\partial I}\right| = \left|-(\gamma_1 + r_1 + \mu + \delta_1)\right| < \infty; \\ &\left|\frac{\partial m_1}{\partial T_N}\right| = 0 < \infty; \left|\frac{\partial m_1}{\partial T_D}\right| = 0 < \infty; \left|\frac{\partial m_1}{\partial R}\right| = 0 < \infty \end{aligned}\right\} \tag{70}$$

The above partial derivatives exist, continuous, and are bounded. From equation (4), we obtained the following partial derivatives

$$\left.\begin{aligned} &\left|\frac{\partial m_1}{\partial S}\right| = 0 < \infty; \left|\frac{\partial m_1}{\partial E}\right| = \left|\alpha\right| < \infty; \left|\frac{\partial m_1}{\partial I}\right| = \left|\gamma_1\right| < \infty; \\ &\left|\frac{\partial m_1}{\partial T_N}\right| = \left|-(\gamma_2 + r_2 + \mu + \delta_2)\right| < \infty; \left|\frac{\partial m_1}{\partial T_D}\right| = 0 < \infty; \left|\frac{\partial m_1}{\partial R}\right| = 0 < \infty \end{aligned}\right\} \tag{71)}$$

The above partial derivatives exist, continuous, and are bounded. From equation (5), we obtained the following partial derivatives

$$\left.\begin{aligned} &\left|\frac{\partial m_1}{\partial S}\right| = 0 < \infty; \left|\frac{\partial m_1}{\partial E}\right| = 0 < \infty; \left|\frac{\partial m_1}{\partial I}\right| = 0 < \infty; \left|\frac{\partial m_1}{\partial T_N}\right| = \left|\gamma_2\right| < \infty; \\ &\left|\frac{\partial m_1}{\partial T_D}\right| = \left|-(+r_3 + \mu + \delta_3)\right| < \infty; \left|\frac{\partial m_1}{\partial R}\right| = 0 < \infty \end{aligned}\right\} \tag{72}$$

The above partial derivatives exist, continuous, and are bounded. From equation (6), we obtained the following partial derivatives

$$\left.\begin{aligned}\left|\frac{\partial m_1}{\partial S}\right| = 0 < \infty; \left|\frac{\partial m_1}{\partial E}\right| = |\alpha| < \infty; \left|\frac{\partial m_1}{\partial I}\right| = |r_1| < \infty; \\ \left|\frac{\partial m_1}{\partial T_N}\right| = |r_2| < \infty; \left|\frac{\partial m_1}{\partial T_D}\right| = |r_3| < \infty; \left|\frac{\partial m_1}{\partial R}\right| = |-(\sigma+\mu)| < \infty\end{aligned}\right\} \quad (73)$$

Since all the partial derivatives exist, bounded, and defined, then system of equations (1) – (6) exists and has solution in $\Re^6$.

Equilibrium Points of the Model

At equilibrium

$$\frac{dS}{dt} = \frac{dE}{dt} = \frac{dI}{dt} = \frac{dT_N}{dt} = \frac{dT_D}{dt} = \frac{dR}{dt} \quad (74)$$

$$\pi+\sigma R-\beta SI-\propto S=0 \quad (75)$$

$$\beta SI-(\propto+\alpha)E=0 \quad (76)$$

$$\alpha E-(\gamma_1+r_1+\propto+\delta_1)I=0 \quad (77)$$

$$\gamma_1 I-(\gamma_2+r_2+\propto+\delta_2)T_N=0 \quad (78)$$

$$\gamma_2 T_N-(r_3+\propto+\delta_3)T_D=0 \quad (79)$$

$$r_1 I+r_2 T_N+r_3 T_D-(\propto+\sigma)R=0 \quad (80)$$

From equation (77) we have

$$\alpha E=(\gamma_1+r_1+\propto+\delta_1)I \quad (81)$$

$$I = \frac{\alpha E}{(\gamma_1 + r_1 + \mu + \delta_1)} \quad (82)$$

Substitute equation (82) into equation (76)

$$\frac{\beta S\alpha E}{(\gamma_1 + r_1 + \mu + \delta_1)} - (\mu+\alpha)E = 0 \quad (83)$$

Cross multiplication

$$\beta S\alpha E=(\gamma_1+r_1+\propto+\delta_1)(\propto+\alpha)E=0 \quad (84)$$

$$[\beta S\alpha-(\gamma_1+r_1+\propto+\delta_1)(\propto+\alpha)]E=0 \quad (85)$$

$$E=0 \text{ or } \beta S\alpha-(\gamma_1+r_1+\propto+\delta_1)(\propto+\alpha)=0 \quad (86)$$

Suppose $E=0$ (87)

Substitute equation (87) into (77) we have

$$\alpha(0)-(\gamma_1+r_1+\propto+\delta_1)I=0 \tag{88}$$

Therefore

$$I=0 \tag{89}$$

Substitute equation (89) into equation (77), we have

$$\gamma_2(0)=(\gamma_2+r_2+\propto+\delta_2)T_N \tag{90}$$

Therefore

$$T_N=0 \tag{91}$$

Substitute equation (91) into equation (79)

$$\gamma_2(0)=(+r_{3+}\propto+\delta_3)T_D \tag{92}$$

Therefore

$$T_D=0 \tag{93}$$

Substitute equation (79), (91) and (93) into equation (80), we have

$$r_1(0)+r_2(0)+r_3(0)=(\propto+\sigma)R \tag{94}$$

Therefore,

$$R=0 \tag{95}$$

Substitute equation (89) and (95) into equation (75), we have

$$\pi+\sigma(0)-\beta S(0)=\propto S \tag{96}$$

$$\pi=\propto S \tag{97}$$

Therefore,

$$S=\frac{\pi}{\mu} \tag{98}$$

Disease-Free Equilibrium

The equilibrium state in the absence of infection is known as zero equilibrium state or disease-free equilibrium. Therefore, from equations (75) to (80), disease-free equilibrium is given as

$$E^0=\left(S^*,E^*,I^*,T_M^*,T_D^*,R^*\right)=\left(\frac{\pi}{\mu},0,0,0,0,0\right) \tag{99}$$

EFFECTIVE REPRODUCTION NUMBER

In epidemiology, the basic reproduction number (sometimes called basic reproductive rate, basic reproductive ratio and is denoted by R_0) of an infection can be thought of as the number of cases which generate on the average over the course of its infection period, in an otherwise uninfected population.

When
R_0<1The infection will die out in the long run, but if
R_0>1 The infection will be able to spread in a population
In this model, the spectral radius of the equation is given as largest Eigen value given as Equation (90).

$$R_0=\rho k\rightarrow fv^{-1} \tag{100}$$

From equation (1) to equation (6), we have

$$F_i=\begin{pmatrix}\beta SI\\ \alpha E\\ \gamma_1 I\\ \gamma_2 T_N\end{pmatrix} \tag{101}$$

$$V_i=\begin{pmatrix}-(\mu+\alpha)E\\ -(\gamma_1+r_1+\mu+\delta_1)I\\ -(\gamma_2+r_2+\mu+\delta_2)T_M\\ -(r_3+\mu+\delta_3)T_D\end{pmatrix} \tag{102}$$

$$F=\begin{pmatrix}0 & \frac{\beta\pi}{\mu} & 0 & 0\\ \alpha & 0 & 0 & 0\\ 0 & \gamma_1 & 0 & 0\\ 0 & 0 & \gamma_2 & 0\end{pmatrix} \tag{103}$$

$$V=\begin{pmatrix}-(\mu+\alpha) & 0 & 0 & 0\\ 0 & -(\gamma_1+r_1+\mu+\delta_1) & 0 & 0\\ 0 & 0 & -(\gamma_2+r_2+\mu+\delta_2) & 0\\ 0 & 0 & 0 & -(r_3+\mu+\delta_3)\end{pmatrix} \tag{104}$$

Therefore, the inverse

$$V^{-1}=\frac{adjo\,\mathrm{int}}{\det er\,\min ant} \tag{105}$$

$$V^{-1}=\begin{pmatrix}-\frac{1}{(\mu+\alpha)} & 0 & 0 & 0\\ 0 & -\frac{1}{(\gamma_1+r_1+\mu+\delta_1)} & 0 & 0\\ 0 & 0 & -\frac{1}{(\gamma_2+r_2+\mu+\delta_2)} & 0\\ 0 & 0 & 0 & -\frac{1}{(r_3+\mu+\delta_3)}\end{pmatrix} \tag{106}$$

$$FV^{-1}=\begin{pmatrix} 0 & \frac{\beta\pi}{\mu} & 0 & 0 \\ \alpha & 0 & 0 & 0 \\ 0 & \gamma_1 & 0 & 0 \\ 0 & 0 & \gamma_2 & 0 \end{pmatrix}$$

$$\begin{pmatrix} -\frac{1}{(\mu+\alpha)} & 0 & 0 & 0 \\ 0 & -\frac{1}{(\gamma_1+r_1+\mu+\delta_1)} & 0 & 0 \\ 0 & 0 & -\frac{1}{(\gamma_2+r_2+\mu+\delta_2)} & 0 \\ 0 & 0 & 0 & -\frac{1}{(r_3+\mu+\delta_3)} \end{pmatrix} \tag{107}$$

$$FV^{-1}=\begin{pmatrix} 0 & -\frac{\beta\pi}{\mu(\gamma_1+r_1+\mu+\delta_1)} & 0 & 0 \\ -\frac{\alpha}{(\mu+\alpha)} & 0 & 0 & 0 \\ 0 & -\frac{\gamma_1}{(\gamma_1+r_1+\mu+\delta_1)} & 0 & 0 \\ 0 & 0 & -\frac{\gamma_2}{(\gamma_2+r_2+\mu+\delta_2)} & 0 \end{pmatrix} \tag{108}$$

To compute, the Eigen values

$$FV^{-1}=\begin{pmatrix} \lambda & -\frac{\beta\pi}{\mu(\gamma_1+r_1+\mu+\delta_1)} & 0 & 0 \\ -\frac{\alpha}{(\mu+\alpha)} & \lambda & 0 & 0 \\ 0 & -\frac{\gamma_1}{(\gamma_1+r_1+\mu+\delta_1)} & \lambda & 0 \\ 0 & 0 & -\frac{\gamma_2}{(\gamma_2+r_2+\mu+\delta_2)} & \lambda \end{pmatrix}=0 \tag{109}$$

The characteristics equation given as equation (110) to equation (111)

$$\lambda=0 \tag{110}$$

$$\lambda=\frac{\sqrt{\mu\left(\mu^2+\mu\alpha+\mu r_1+\mu\delta_1+\mu\gamma_1+\alpha r_1+\alpha\delta_1+\alpha\gamma_1\right)\pi\alpha\beta}}{\mu\left(\mu^2+\mu\alpha+\mu r_1+\mu\delta_1+\mu\gamma_1+\alpha r_1+\alpha\delta_1+\alpha\gamma_1\right)}$$

and

$$\lambda=-\frac{\sqrt{\mu\left(\mu^2+\mu\alpha+\mu r_1+\mu\delta_1+\mu\gamma_1+\alpha r_1+\alpha\delta_1+\alpha\gamma_1\right)\pi\alpha\beta}}{\mu\left(\mu^2+\mu\alpha+\mu r_1+\mu\delta_1+\mu\gamma_1+\alpha r_1+\alpha\delta_1+\alpha\gamma_1\right)} \tag{111}$$

Then,

$$R_0 = \frac{\sqrt{\mu\left(\mu^2 + \mu\alpha + \mu r_1 + \mu\delta_1 + \mu\gamma_1 + \alpha r_1 + \alpha\delta_1 + \alpha\gamma_1\right)\pi\alpha\beta}}{\mu\left(\mu^2 + \mu\alpha + \mu r_1 + \mu\delta_1 + \mu\gamma_1 + \alpha r_1 + \alpha\delta_1 + \alpha\gamma_1\right)} \tag{112}$$

Therefore

$$\frac{\sqrt{\mu\left(\mu^2 + \mu\alpha + \mu r_1 + \mu\delta_1 + \mu\gamma_1 + \alpha r_1 + \alpha\delta_1 + \alpha\gamma_1\right)\pi\alpha\beta}}{\mu\left(\mu^2 + \mu\alpha + \mu r_1 + \mu\delta_1 + \mu\gamma_1 + \alpha r_1 + \alpha\delta_1 + \alpha\gamma_1\right)} < 1 \tag{113}$$

LOCAL STABILITY OF DISEASE-FREE EQUILIBRIUM POINT

To analyze local stability at the disease-free equilibrium point, the Jacobian matrix of the system of equations (1) to (6) at DFE is evaluated. Then, the stability is determined based on the sign of the Eigen values of the Jacobian matrix.

Theorem 7.1

The disease-free equilibrium point is said to be locally asymptotically stable, if all the Eigen values of the Jacobian matrix at DFE are negative or unstable otherwise.

Proof:
The Jacobian matrix of the system of equations is;

$$J = \begin{pmatrix} -\mu & 0 & -\frac{\beta\pi}{\mu} & 0 & 0 & \sigma \\ 0 & -(\mu+\alpha) & \frac{\beta\pi}{\mu} & 0 & 0 & 0 \\ 0 & \alpha & -(\gamma_1 + r_1 + \mu + \delta_1) & 0 & 0 & 0 \\ 0 & 0 & \gamma_1 & -(\gamma_2 + r_2 + \mu + \delta_2) & 0 & 0 \\ 0 & 0 & 0 & \gamma_2 & -(r_3 + \mu + \delta_3) & 0 \\ 0 & 0 & r_1 & r_2 & r_3 & -(\mu+\sigma) \end{pmatrix} \tag{114}$$

Reducing equation (116) to upper triangular matrix,

$$J = \begin{pmatrix} -\mu & 0 & -\frac{\beta\pi}{\mu} & 0 & 0 & \sigma \\ 0 & -(\mu+\alpha) & \frac{\beta\pi}{\mu} & 0 & 0 & 0 \\ 0 & 0 & -\frac{\mu\left(\pi\beta\alpha + \mu^2 + \mu\alpha + \mu r_1 + \mu\delta_1 + \mu\gamma_1 + \alpha r_1 + \alpha\delta_1 + \alpha\gamma_1\right)}{\mu(\mu+\alpha)} & 0 & 0 & 0 \\ 0 & 0 & 0 & -(\gamma_2 + r_2 + \mu + \delta_2) & 0 & 0 \\ 0 & 0 & 0 & 0 & -(r_3 + \mu + \delta_3) & 0 \\ 0 & 0 & 0 & 0 & 0 & -(\mu+\sigma) \end{pmatrix}$$

(115)

The characteristics equation is;

$$\left|J\left(E^0\right)-\lambda I\right| =$$

$$\begin{pmatrix} -\mu-\lambda & 0 & -\frac{\beta\pi}{\mu} & 0 & 0 & \sigma \\ 0 & -(\mu+\alpha)-\lambda & \frac{\beta\pi}{\mu} & 0 & 0 & 0 \\ 0 & 0 & -\frac{\mu\left(\begin{matrix}\pi\beta\alpha+\mu^2+\mu\alpha+\mu r_1+\mu\delta_1 \\ +\mu\gamma_1+\alpha r_1+\alpha\delta_1+\alpha\gamma_1\end{matrix}\right)}{\mu(\mu+\alpha)}-\lambda & 0 & 0 & 0 \\ 0 & 0 & 0 & -(\gamma_2+r_2+\mu+\delta_2)-\lambda & 0 & 0 \\ 0 & 0 & 0 & 0 & -(r_3+\mu+\delta_3)-\lambda & 0 \\ 0 & 0 & 0 & 0 & 0 & -(\mu+\sigma)-\lambda \end{pmatrix} = 0$$

(116)

The determinates give;

$$\begin{bmatrix} (-\mu-\lambda_1)(-(\mu+\alpha)-\lambda_2)\left(-\frac{\mu\left(\pi\beta\alpha+\mu^2+\mu\alpha+\mu r_1+\mu\delta_1+\mu\gamma_1+\alpha r_1+\alpha\delta_1+\alpha\gamma_1\right)}{\mu(\mu+\alpha)}-\lambda_3\right) \\ (-(\gamma_2+r_2+\mu+\delta_2)-\lambda_4)(-(r_3+\mu+\delta_3)-\lambda_5)(-(\mu+\sigma)-\lambda_6)=0 \end{bmatrix}$$

(117)

Either

$-\infty-\lambda=0$ or $-(\infty+\alpha)-\lambda_2=0$ or $-\frac{\mu\left(\pi\beta\alpha+\mu^2+\mu\alpha+\mu r_1+\mu\delta_1+\mu\gamma_1+\alpha r_1+\alpha\delta_1+\alpha\gamma_1\right)}{\mu(\mu+\alpha)}-\lambda_3=0$ or $-(\gamma_2+r_2+\infty+\delta_2)-\lambda_4=0$ or $-(r_3+\infty+\delta_3)-\lambda_5=0$ or $-(\infty+\sigma)-\lambda_6=0$ (118)

Therefore,

$$\lambda_1=-\mu \quad \text{or} \quad \lambda_2=-(\mu+\alpha) \quad \text{or} \quad \lambda_3=-\frac{\mu\left(\pi\beta\alpha+\mu^2+\mu\alpha+\mu r_1+\mu\delta_1+\mu\gamma_1+\alpha r_1+\alpha\delta_1+\alpha\gamma_1\right)}{\mu(\mu+\alpha)} \quad \text{or}$$

$$\lambda_4=-(\gamma_2+r_2+\mu+\delta_2) \quad \text{or} \quad \lambda_5=-(r_3+\mu+\delta_3) \quad \text{or} \quad \lambda_6=-(\mu+\sigma) \tag{119}$$

From equation (119)

$\lambda_1, \lambda_2, \lambda_3, \lambda_4, \lambda_5, \lambda_6<0$ (120)

Hence, the disease-free equilibrium point is locally asymptotically stable.

GLOBAL STABILITY OF DISEASE-FREE EQUILIBRIUM

Theorem 3.9.1

The disease-free equilibrium of equations (45) to (50) is globally asymptotically stable provided $R_0<1$ and unstable if $R_0>1$

Proof: Referring to Castillo–Chaves *et al.* (2004)[11], the system of equations (45) to (50) can be written

as,

$$\frac{dx(t)}{dt} = F(x,y), \quad \frac{dy(t)}{dt} = G(x,y) \tag{55}$$

Where $x = (S, E, I, T_N, T_D, R) \in \Re_+^6$ denote the different compartments of uninfected humans, $y = (E, I, T_N, T_D) \in \Re_+^4$ denote the different compartments of infected humans.

The disease free equilibrium (DFE)=(x_0, 0), where $x_0 = \left(\frac{\pi}{\mu}, 0\right)$ (56)

We are required to proof that,

$\frac{dx(t)}{dt} = F(x,0)$, x_0 is globally asymptotically stable, and $G(x,y) = Cy - \hat{G}(x,y)$, $\hat{G}(x,y) \geq 0$ for $(x,y) \in \Omega$ (57)

Case 1: Consider the uninfected subsystem,

$$\frac{dx(t)}{dt} = F(x,y) = \begin{pmatrix} \pi + \sigma R - \beta SI - \mu S \\ r_1 I + r_2 T_N + r_3 T_D - (\mu + \sigma) R \end{pmatrix} \tag{58}$$

When $y = 0$ that is $E = I = T_N = T_D = 0$

Then, equation (58) becomes,

$$F(x,0) = \begin{pmatrix} \pi - \mu S \\ 0 \end{pmatrix} \tag{60}$$

Solving equation (60), gives

$$\frac{dS(t)}{dt} = \pi - \mu S \tag{61}$$

$$\frac{dS(t)}{dt} + \mu S = \pi \tag{62}$$

Multiply equation (62) by its integrating factor $(\ell^{\mu t})$, gives

$$\frac{dS(t)}{dt}\ \ell^{\mu t} + \mu S \ell^{\mu t} = \Lambda \ell^{\mu t} \tag{63}$$

$$\frac{d}{dt}\ \left[S\ell^{-\mu t}\right] = \pi \ell^{\mu t} \tag{64}$$

Integrate equation (65), gives

$$\int \frac{d}{dt}\left[S\ell^{\mu t}\right] = \int \pi \ell^{\mu t} \tag{66}$$

$$S\ell^{(1+\mu)t} = \left(\frac{\Lambda}{(1+\mu)}\right)\ell^{(1+\mu)t} + c \tag{68}$$

Divide equation (68) by $\ell^{\propto t}$

$$S(t) = \left(\frac{\Lambda_d}{(1+\mu)}\right) + c\ell^{-(1+\mu)t} \tag{69}$$

When t=0, equation (69) becomes,

$$c = S(0) - \left(\frac{\pi}{\mu}\right) \tag{70}$$

Substitute equation (70) into equation (69) gives,

$$S(t) = \left(\frac{\pi}{\mu}\right) - \left(\frac{\pi}{\mu}\right)\ell^{-\mu t} + S(0)\ell^{-\mu t} \tag{71}$$

As $t\to\infty$, $S \to \frac{\pi}{\mu}, R \to 0$ regardless of the value of $S(0)$, $R(0)$

Therefore,

$x_0 = \left(\frac{\pi}{\mu}, 0\right)$ is globally asymptotically stable.

Case 2: Consider an infected subsystem

$$y' = G(x,y) = \begin{pmatrix} \beta SI - (\mu+\alpha)E \\ \alpha E - (\gamma_1 + r_1 + \mu + \delta_1)I \\ \gamma_1 I - (\gamma_2 + r_2 + \mu + \delta_2)T_N \\ \gamma_2 T_N - (r_3 + \mu + \delta_3)T_D \end{pmatrix} \tag{72}$$

Given that,

$$G(x,y) = Cy - \hat{G}(x,y) \tag{73}$$

Then,

$$\hat{G}(x,y) = Cy - G(x,y) \tag{74}$$

Where $C = \frac{\partial G(x,0)}{\partial t}$

$$C=\begin{bmatrix} -(\mu+\alpha) & \beta S & 0 & 0 \\ \alpha & -(\gamma_1+r_1+\mu+\delta_1) & 0 & 0 \\ 0 & \gamma_1 & -(\gamma_2+r_2+\mu+\delta_2) & 0 \\ 0 & 0 & \gamma_2 & -(r_3+\mu+\delta_3) \end{bmatrix} \tag{75}$$

$$Cy=\begin{bmatrix} -(\mu+\alpha) & \beta S & 0 & 0 \\ \alpha & -(\gamma_1+r_1+\mu+\delta_1) & 0 & 0 \\ 0 & \gamma_1 & -(\gamma_2+r_2+\mu+\delta_2) & 0 \\ 0 & 0 & \gamma_2 & -(r_3+\mu+\delta_3) \end{bmatrix} \begin{bmatrix} E \\ I \\ T_N \\ T_D \end{bmatrix} \tag{76}$$

Evaluating equation (76), we have

$$Cy=\begin{pmatrix} \beta SI-(\mu+\alpha)E \\ \alpha E-(\gamma_1+r_1+\mu+\delta_1)I \\ \gamma_1 I-(\gamma_2+r_2+\mu+\delta_2)T_N \\ \gamma_2 T_N-(r_3+\mu+\delta_3)T_D \end{pmatrix} \tag{77}$$

Substituting equation (77) and equation (72) into equation (74), gives

$$\hat{G}(x,y)=\begin{pmatrix} \beta SI-(\mu+\alpha)E \\ \alpha E-(\gamma_1+r_1+\mu+\delta_1)I \\ \gamma_1 I-(\gamma_2+r_2+\mu+\delta_2)T_N \\ \gamma_2 T_N-(r_3+\mu+\delta_3)T_D \end{pmatrix} - \begin{pmatrix} \beta SI-(\mu+\alpha)E \\ \alpha E-(\gamma_1+r_1+\mu+\delta_1)I \\ \gamma_1 I-(\gamma_2+r_2+\mu+\delta_2)T_N \\ \gamma_2 T_N-(r_3+\mu+\delta_3)T_D \end{pmatrix} \tag{78}$$

$$\hat{G}(x,y)=\begin{pmatrix} \hat{G}_1(x,y) \\ \hat{G}_2(x,y) \\ \hat{G}_3(x,y) \\ \hat{G}_4(x,y) \end{pmatrix} = \begin{pmatrix} 0 \\ 0 \\ 0 \\ 0 \end{pmatrix} \tag{79}$$

Then, $\hat{G}(x,y)=0$.

Therefore, the disease-free equilibrium point is globally asymptotically stable when $R_0<1$

ANALYTICAL SOLUTION OF EQUATION (4.4.1) USING HOMOTOPY PERTURBATION

Method

The system of equation

$$\begin{cases} \frac{dS}{dt}+\mu S+\beta SI-\sigma R-\pi=0 \\ \frac{dE}{dt}+(\mu+\alpha)E-\beta SI=0 \\ \frac{dI}{dt}+(\gamma_1+r_1+\mu+\delta_1)I-\alpha E=0 \\ \frac{dT_N}{dt}+(\gamma_2+r_2+\mu+\delta_2)T_N-\gamma_1 I=0 \\ \frac{dT_D}{dt}+(r_3+\mu+\delta_3)T_D-\gamma_2 T_N=0 \\ \frac{dR}{dt}+(\mu+\sigma)R-r_3T_D-r_2T_N-r_1I=0 \end{cases}$$

Conditions for the differential equation above
We construct a homotopy:

$$\begin{cases} (1-h)\frac{dS}{dt}+h\left[\frac{dS}{dt}+\mu S+\beta SI-\sigma R-\pi\right]=0 \\ (1-h)\frac{dE}{dt}+h\left[\frac{dE}{dt}+(\mu+\alpha)E-\beta SI\right]=0 \\ (1-h)\frac{dI}{dt}+h\left[\frac{dI}{dt}+(\gamma_1+r_1+\mu+\delta_1)I-\alpha E\right]=0 \\ (1-h)\frac{dT_N}{dt}+h\left[\frac{dT_N}{dt}+(\gamma_2+r_2+\mu+\delta_2)T_N-\gamma_1 I\right]=0 \\ (1-h)\frac{dT_D}{dt}+h\left[\frac{dT_D}{dt}+(r_3+\mu+\delta_3)T_D-\gamma_2 T_N\right]=0 \\ (1-h)\frac{dR}{dt}+h\left[\frac{dR}{dt}+(\mu+\sigma)R-r_3T_D-r_2T_N-r_1I\right]=0 \end{cases}$$

The basic assumption is that the solution of equation (1) can be written as a series in powers of p

$$\begin{cases} S(t)=a_0+ha_1+h^2a_2+... \\ E(t)=b_0+hb_1+h^2b_2+... \\ I(t)=c_0+hc_1+h^2c_2+... \\ T_N(t)=d_0+hd_1+h^2d_2+... \\ T_D(t)=e_0+he_1+h^2e_2+... \\ R(t)=f_0+hf_1+h^2f_2+... \end{cases}$$

If p → 1, we recall the solution of the series
Substituting equation (4) into equation (3), we will have;

$$\begin{cases}
\left(a'_0+ha'_1+h^2a'_2+\ldots\right)+h\left[\begin{array}{l}\beta\left(a_0+ha_1+h^2a_2+\ldots\right)\left(c_0+hc_1+h^2c_2+\ldots\right)+\\ \mu\left(a_0+ha_1+h^2a_2+\ldots\right)-\sigma\left(f_0+hf_1+h^2f_2+\ldots\right)-\pi\end{array}\right]=0\\
\left(b'_0+hb'_1+h^2b'_2+\ldots\right)+h\left[\begin{array}{l}(\mu+\alpha)\left(b_0+hb_1+h^2b_2+\ldots\right)-\beta\left(a_0+ha_1+h^2a_2+\ldots\right)\\ \left(c_0+hc_1+h^2c_2+\ldots\right)\end{array}\right]=0\\
\left(c'_0+hc'_1+h^2c'_2+\ldots\right)+h\left[\begin{array}{l}(\gamma_1+r_1+\mu+\delta_1)\left(c_0+hc_1+h^2b_2+\ldots\right)-\\ \alpha\left(b_0+hb_1+h^2b_2+\ldots\right)\end{array}\right]=0\\
\left(d'_0+hd'_1+h^2d'_2+\ldots\right)+h\left[\begin{array}{l}(\gamma_2+r_2+\mu+\delta_2)\left(d_0+hd_1+h^2d_2+\ldots\right)-\\ \gamma_1\left(c_0+hc_1+h^2c_2+\ldots\right)\end{array}\right]=0\\
\left(e'_0+he'_1+h^2e'_2+\ldots\right)+h\left[\begin{array}{l}(r_3+\mu+\delta_3)\left(e_0+he_1+h^2e_2+\ldots\right)-\\ \gamma_2\left(d_0+hd_1+h^2d_2+\ldots\right)\end{array}\right]=0\\
\left(f'_0+hf'_1+h^2f'_2+\ldots\right)+h\left[\begin{array}{l}(\mu+\sigma)\left(f_0+hf_1+h^2f_2+\ldots\right)-r_3\left(e_0+he_1+h^2e_2+\ldots\right)\\ r_2\left(d_0+hd_1+h^2d_2+\ldots\right)-r_1\left(c_0+hc_1+h^2c_2+\ldots\right)\end{array}\right]=0
\end{cases}$$

We now compare the identical powers of p as follow:

$$\begin{cases}
S(t)=S_0+\left(\pi+\sigma R_0-\beta S_0I_0-\mu S_0\right)t+\\
\left(\begin{array}{l}\sigma\left(r_1I_0+r_2T_{N0}+r_3T_{D0}-(\mu+\sigma)R_0\right)-\beta\left(\begin{array}{l}\left(\pi+\sigma R_0-\beta S_0I_0-\mu S_0\right)I_0+\\ S_0\left(\alpha E_0-(\gamma_1+r_1+\mu+\delta_1)I_0\right)\end{array}\right)\\ -\mu\left(\pi+\sigma R_0-\beta S_0I_0-\mu S_0\right)\end{array}\right)\frac{t^2}{2}\\
E(t)=E_0+\left(\beta S_0I_0-(\mu+\alpha)E_0\right)t+\\
\left(\begin{array}{l}\beta\left(\left(\pi+\sigma R_0-\beta S_0I_0-\mu S_0\right)I_0+S_0\left(\alpha E_0-(\gamma_1+r_1+\mu+\delta_1)I_0\right)\right)\\ -(\mu+\alpha)\left(\beta S_0I_0-(\mu+\alpha)E_0\right)\end{array}\right)\frac{t^2}{2}\\
I(t)=I_0+\left(\alpha E_0-(\gamma_1+r_1+\mu+\delta_1)I_0\right)t+\left(\begin{array}{l}\alpha\left(\beta S_0I_0-(\mu+\alpha)E_0\right)-(\gamma_1+r_1+\mu+\delta_1)\\ \left(\alpha E_0-(\gamma_1+r_1+\mu+\delta_1)I_0\right)\end{array}\right)\frac{t^2}{2}\\
T_N(t)=T_{N0}+\left(\gamma_1I_0-(\gamma_2+r_2+\mu+\delta_2)T_{N0}\right)t+\left(\begin{array}{l}\gamma_1\left(\alpha E_0-(\gamma_1+r_1+\mu+\delta_1)I_0\right)-\\ (\gamma_2+r_2+\mu+\delta_2)\left(\gamma_1I_0-(\gamma_2+r_2+\mu+\delta_2)T_{N0}\right)\end{array}\right)\frac{t^2}{2}\\
T_D(t)=T_{D0}+\left(\gamma_2T_{N0}-(r_3+\mu+\delta_3)T_{D0}\right)t+\left(\begin{array}{l}\gamma_2\left(\gamma_1I_0-(\gamma_2+r_2+\mu+\delta_2)T_{N0}\right)-\\ (r_3+\mu+\delta_3)\left(\gamma_2T_{N0}-(r_3+\mu+\delta_3)T_{D0}\right)\end{array}\right)\frac{t^2}{2}\\
R(t)=R_0+\left(r_1I_0+r_2T_{N0}+r_3T_{D0}-(\mu+\sigma)R_0\right)t+\\
\left(\begin{array}{l}r_1\left(\alpha E_0-(\gamma_1+r_1+\mu+\delta_1)I_0\right)-r_2\left(\gamma_1I_0-(\gamma_2+r_2+\mu+\delta_2)T_{N0}\right)-\\ r_3\left(\gamma_2T_{N0}-(r_3+\mu+\delta_3)T_{D0}\right)+(\mu+\sigma)\left(r_1I_0+r_2T_{N0}+r_3T_{D0}-(\mu+\sigma)R_0\right)\end{array}\right)\frac{t^2}{2}
\end{cases}$$

NUMERICAL SIMULATION AND RESULTS

In this chapter, the model will be analyzed using the parameter values as well as estimated initial values of the susceptible, exposed, infected, recovered, and vaccinated individuals. The results obtained will be discussed. MATLAB was used to get the numerical solution of the model using ode45.
Table 1 shows the Notation and definition of variables and parameter used in the paper.
Table 2 parameter and estimated values for initial conditions for the $SEIT_NT_DR$ models

DISCUSSION OF RESULTS

Figure 2: Is the graph of susceptible human against time for different of rate at which the susceptible

Table 1: Notation and definition of variables and parameter

Symbol	Description
$S(t)$	Susceptible at time t
$E(t)$	Exposed at time t
$I(t)$	Infected at time t
$T_N(t)$	First Line Treatment t
$T_D(t)$	Second Line Treatment t
$R(t)$	Recovered t
π	Recruitment rate
σ	Lose their immunity at the rate
β	Rate at which the susceptible become exposed to Mtb
α	Infection rate
γ_1	First line treatment class
γ_2	Second line treatment class
$r_1, r_2 r_3$	Reduces at rate of treatment class
$\propto$	Rate of natural death
δ_1	Disease induced death rate
δ_2	Disease induced death rate
δ_3	Disease induced death rate

Table 2: Variables and model parameters values

Parameters and State Variables	Value	Source
β	0.00003	Assumed
σ	0.470104	Assumed
μ	0.019896	Assumed
α	0.01	Assumed
S	85,000	Assumed
E	32,000	Assumed
I	1800	Assumed
T_N	2300	Assumed
T_D	1500	Assumed
R	1700	Assumed
r_1	0.3	Assumed
r_2	0.3	Assumed
r_3	0.2	Assumed
γ_1	0.5	Assumed
γ_2	0.2	Assumed
δ_1	0.01	Assumed
δ_2	0.01	Assumed
δ_3	0.01	Assumed
π	0.03	Assumed

become exposed to Mtb. It is observed that the population susceptible human decreases as the rate at which the susceptible become exposed to Mtb increases.

Figure 3: Is the graph of exposed individual against time for different of contact rate for human. It is observed that the population exposed individual increases as the rate at which the susceptible become exposed to Mtb increases.

Figure 4: Is the graph of first line treatment individuals against time for different of first line treatment class. It is observed that the population first line treatment decreases as the first line treatment class increases.

Figure 5: Is the graph of second line treatment individuals against time for different of second line treatment class. It is observed that the population second line treatment decreases as the second line treatment class increases.

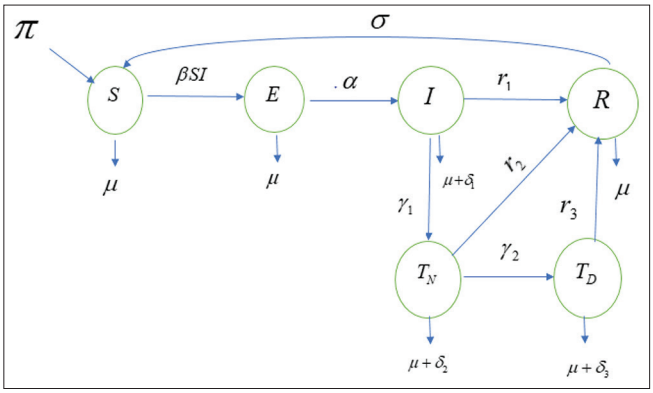

Figure 1: Schematic diagram of the model

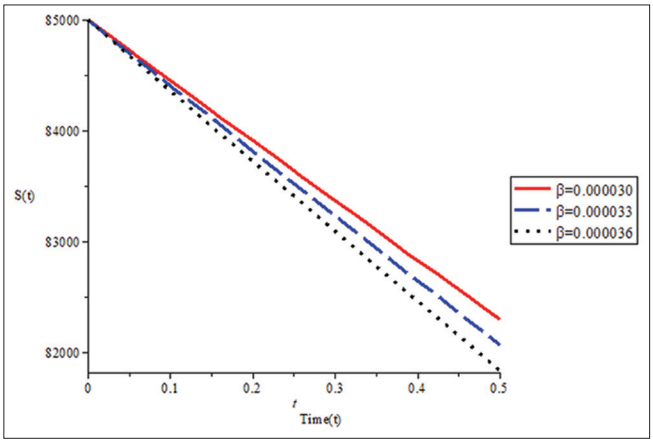

Figure 2: Graph of Susceptible individuals against time for different of Rate at which the susceptible become exposed to Mtb

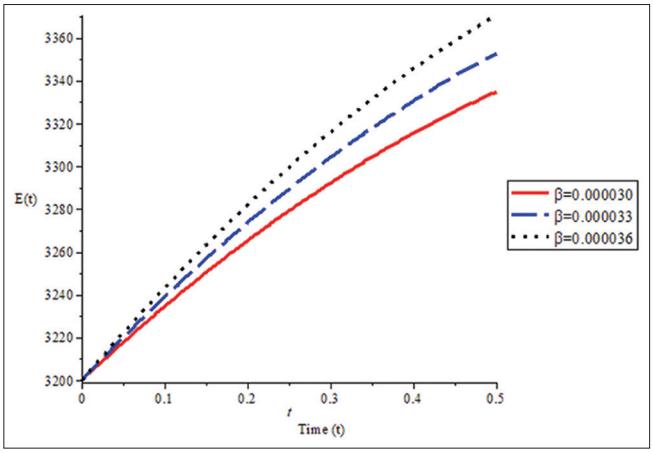

Figure 3: Graph of Exposed individuals against time for different of Rate at which the susceptible become exposed to Mtb

Figure 6: Is the graph of infected individuals against time for different of first line treatment class. It is observed that the population infected decreases as the first line treatment class increases.
Figure 7: Is the graph of recovered individuals against time for different of reduces at rate of treatment class. It is observed that the population of recovered increases as reduces at rate of treatment class increases.

SUMMARY

TB is the most dreadful diseases that could be transmitted from human. To curb its spread, a mathematical model was proposed in this work so as to understand the transmission dynamics of the disease and to

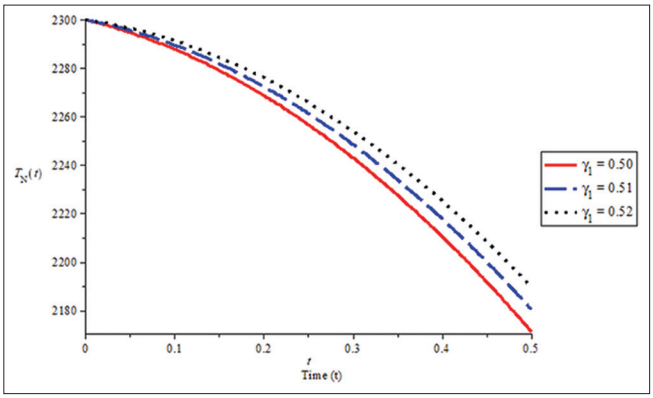

Figure 4: Graph of Frist Line Treatment individuals against time for different of first line treatment class

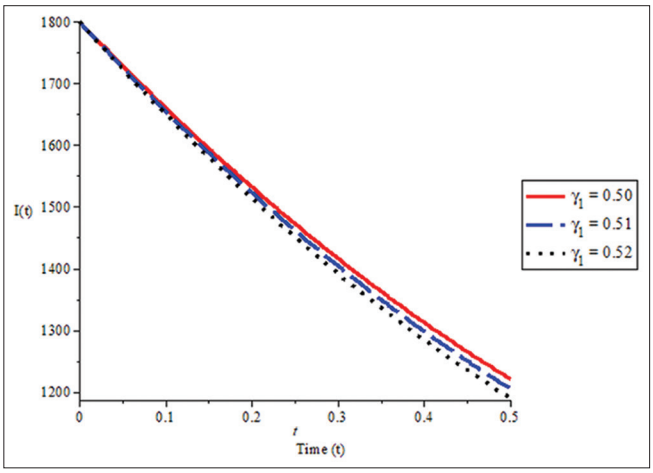

Figure 5: Graph of Second Line Treatment individuals against time for different of second line treatment class

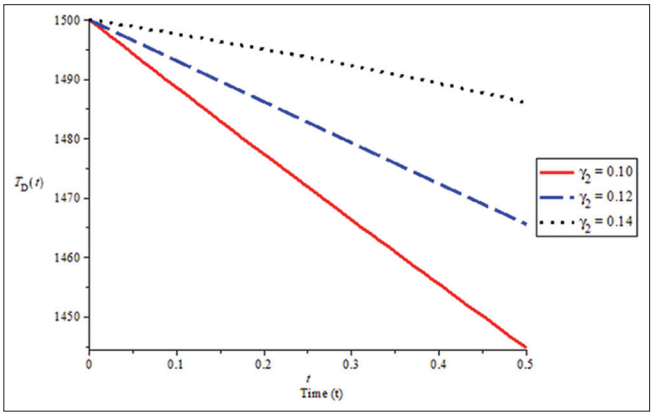

Figure 6: Graph of Infected individuals against time for different of first line treatment class

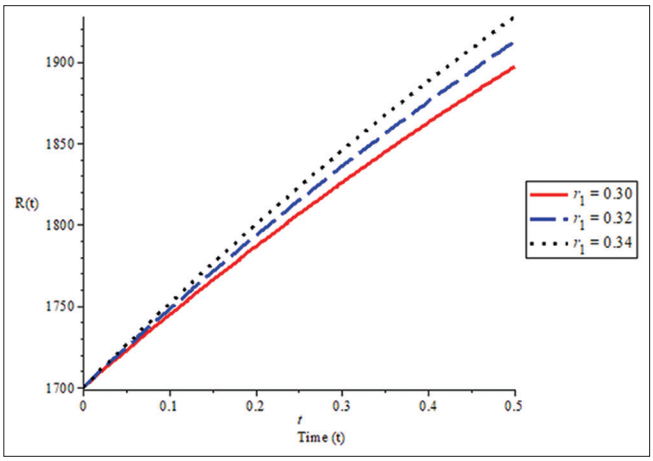

Figure 7: Graph of Recovered individuals against time for different of reduces at rate of treatment class

proffer solution by introducing vaccination to facilitate the prevention of the spread of the disease.
The population under consideration was a non-constant population. The SEIR and SEIV models were considered and the disease free points were obtained. Their basic reproduction number was obtained using the next generation matrix approach. The stability of the disease free points was analyzed. With estimated values for parameters and initial numbers of the population classes, MATLAB was used to get the numerical solution of the model using ode 45.

CONCLUSION

Mathematical model for TB disease was developed in this study. The disease-free state (DFE) was analyzed for stability, and it revealed that it is stable. The reproduction number was analyzed, and the result shows the stability of the disease, which implies that the disease would be reduced after the treatment used as a control parameter.
From the numerical simulation, we observe the different dynamics of the population from the graphical profiles of Figure 6 is it observed infected individuals decreases at first line treatment increases and from Figure 7, at rate of treatment class increases, its observed that the disease will be eradicated completely from the population.
The following findings are established:

1. Existence of the disease free state
2. Existence of the endemic state
3. Effective reproduction number shows the stability of the disease.

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