MODELING THE IMPACT OF DRUG RESISTANCE AND SENSITIVITY ON TRANSMISSION DYNAMICS OF TUBERCULOSIS INCORPORATING CASE DETECTION

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Abstract

In this paper, an epidemiology model of tuberculosis with case detection is developed and analysed. The total population is compartmentazed into eight (8) classes namely: Vaccinated, Susceptible Latently infected with drug-resistance TB, Latently infected with drug sensitive-TB, Infectious with drug resistance-TB, Infectious with drug sensitive-TB, Recovered with drug resistance-TB and Recovered with drug sensitive-TB. We prove the positivity of the solution and boundedness of the model which shows that the model is mathematically and biologically well posed. The disease free equilibrium, endemic equilibrium, reproduction number where established. The local and global stability analysis were established and found to be stable if $R_0 < 1$ *and otherwise if* $R_0 > 1$. *Finally, we solve the model equations numerically to study the impact of case detection, transmission probability, vaccination and treatment of infected individuals on the transmission dynamics of tuberculosis. The results show that the tested parameters are vital if tuberculosis must be brought under control.*

1.0 Introduction

Tuberculosis (TB) is a highly infectious airborne disease. Its causative agent is Mycobacterium Tuberculosis [1]. The majority of tuberculosis deaths occur in low and middle-income countries. Tuberculosis affects one-third of the world's population, either latently or actively [2]. It is an ancient disease, with proof of its presence discovered in the eighteenth century (18th century) in relics from Ancient Egypt, India and China. This disease wreaked havoc on Western Europe, with mortality rates as high as nine hundred deaths per one hundred thousand. Bad ventilation, overcrowding, primitive sanitation, and malnutrition were among the risk factors that contributed to the outbreak [3]. When an exposed or susceptible person inhales the TB germs that are released into the air when infected people cough, sneeze, spit, or speak, he or she becomes

infected with the disease. Tuberculosis (TB) cannot be transmitted by handshakes, sharing toilet seats, or sharing dishes or utensils with someone who has the disease [4].

In developing countries, TB is the second leading cause of death from infectious disease (after HIV/AIDS). Despite the fact that the disease is treatable and curable, complete eradication is not feasible due to the difficulty of producing an effective vaccine, the costly and time-consuming diagnosis procedure, and the need for months of care, but we can monitor the disease's transmission level [2]. In 2016, an estimated 1.3 million HIV-negative people died of tuberculosis (down from 1.7 million in 2000), with an additional 374, 000 HIV positive people dying. In 2016, an estimated 10.4 million people were ill with tuberculosis: 90% were adults, 65% were men, and 10% were HIV-positive (74 percent in Africa) and 65% were in five countries: India, Indonesia, China, the Philippines, and Pakistan [5] (WHO, 2017).

In 2016, 600,000 new cases of drug-resistant tuberculosis (RR-TB), the most effective first-line drug, were recorded, with 490,000 of those having multi-drug resistance TB (MDR-TB). Almost half of these cases (47%) occurred in India, China, and the Russian Federation. The global TB mortality rate is decreasing at a rate of about 3% per year. To meet the first (2020) targets of the end TB strategy, TB incidence is dropping at about 2% per year, and 16 percent of TB cases die from the disease; by 2020, these figures would rise to 4-5 percent per year and 10%, respectively [5].

Nigeria has the highest TB burden in Africa and is ranked fourth in the world, according to the World Health Organization (WHO, 2016 global TB report). It ranks sixth among the countries with 60 percent of the global TB burden. They also discovered that Nigeria and India were responsible for 48 percent of global TB deaths among HIV-negative people and 43 percent of total TB deaths among HIV-positive and HIV-negative people. Nigeria accounts for 77% of the global gap in TB case findings, according to the survey. In 2016, Nigeria recorded less than 20% of the total TB cases expected for the year, implying that more than 80% of TB cases in the country remain undiagnosed (undetected) TB cases in the community which serve as a reservoir for continuing transmission of TB [5].

The amount of psycho-socio trauma that societies experience is immense. This entails contemplating the loss of loved ones as well as the financial implications of caring for the ill, especially among the poor. These have an effect not only on individuals, but also on the country's economic growth. The mortality rate of tuberculosis has risen by 45 percent in the last 25 years, owing in large part to inadequate diagnosis and treatment [6].

However, the world is still a long way from eradicating the disease; by 2025, a total of $8 billion US dollars will be needed to fully respond to the global epidemic in low and middle income countries, with a funding gap of 2.3 billion US dollars per year. This figure did not include research and development costs, which were projected to be about 2 billion dollars a year [5]. People who are malnourished as a result of their diet, substance abuse, or hunger are often at risk of contracting tuberculosis. People who walk close to or live close to a person with active tuberculosis, such as health care staff, people who live in cramped living spaces, or people who work in enclosed areas like schools or jails, are often at risk of contracting tuberculosis [7].

The severity and occurrence of tuberculosis are affected by factors related to the bacteria, the human host, environmental growth and urbanization, as well as population movement and migration. When it comes to the climate and urbanization, the prevalence of tuberculosis is typically lower in prime urban areas than in rural areas, as adequate medical treatment is more difficult to ascertain in rural areas than in urban areas. The settlers are mostly migrant workers from rural villages, and they tend to settle mostly in poor, overcrowded houses, commonly referred to as slums, with little to no proper sanitation, which leads to increased exposure of the population to Mycobacterium tuberculosis bacteria (MTB), and thus a possibility of the disease amplification to epidemic proportions due to a lack of effective treatments [8].

Tuberculosis is curable if diagnosed early and treated properly, it can take anywhere from six months to two years for active tuberculosis to clear [9]. Vaccination is the process of administering weak antigens to induce disease immunity. Screening services and vaccination, commonly with the Bacillus Calmete Guerin (BCG) vaccine, are used to prevent tuberculosis. While the vaccine protects against serious forms of TB in children (TB meningitis and Military TB), a vaccine that is effective in preventing TB in adults remains elusive. In the meantime, vaccinations may be rendered ineffective due to inadequate administration and environmental factors. Radiology (commonly a chest X-ray), a tuberculin skin test, a blood test, as well as microscopic analysis and micro biological culture of body fluids such as sputum, are all used to diagnose tuberculosis. TB is most often associated with the lungs, but it may also affect the spine, central nervous system, and even the skin [10].

Antibiotics are used to treat tuberculosis, although it takes a longer period of time (around 6-24 months) to fully remove the micro bacterium from the body. The internationally recommended techniques for TB management and cure is the directly Observed Treatment Shorts (DOTS)) technique, which ensures free diagnosis and medicines for tuberculosis patients, assisting in tuberculosis control and management and it helps in controlling drug resistance cases. [5].

Multi-drug resistant (MDR) tuberculosis, which is characterized as tuberculosis resistant to both of the most effective first-line antibiotic treatments for active tuberculosis, ionized (INH) and Rifampicin (RIF), is becoming more difficult and costly to treat. It is currently a major health problem for medical workers and researchers, and MDR tuberculosis can be contracted from either spending time with an MDR patient or inhaling the MDR tuberculosis is much more difficult to treat, and the mortality rate of people with this TB is higher if the second line of antibiotic treatment is not initiated promptly [11].

In 2016, an estimated 480, 000 new cases of multidrug-resistant tuberculosis (MDR-TB) were diagnosed, with an additional 10,000 people with Rifampicin-Resistant tuberculosis (RR-TB) being eligible for MDR-TB care. The federation of India, China, and Russia accounted for 45 percent of the total of 580, 000 cases [5].

2. Model Formulation

In this paper, we studied a model of impact of drug resistance and sensitivity on transmission dynamics of tuberculosis by incorporating case detection. Based on the $VSL_RL_SI_RI_SR_RR_S$ model, the total population is divided into eight compartmental models namely; the vaccinated compartment at time t $V(t)$, the susceptible class at time t, $S(t)$, the latently infected class with drug resistance at time t, $L_R(t)$,the latently infected individuals with drug sensitivity at time t, $L_S(t)$, the infected class with drug resistance at time t, $I_R(t)$, the infected class with drug sensitivity at time t, $I_S(t)$, the recovered class with drug resistance at time t, $R_R(t)$ and the recovered class with drug sensitivity at time t, $R_S(t)$.

The vaccinated class increases due to the recruitment of the vaccinated newborn babies at the proportion $\delta\Lambda$. The class also increases due to the incoming of the individuals recruited at susceptible class not vaccinated at the rate cS, the vaccinated class reduces to the susceptible class due to the waning of the vaccine efficacy at the rate, ωV.

The susceptible class increases due to the incoming of the newborn babies not vaccinated against TB infections into the population at the rate $(1-\delta)\Lambda$ and as a result of waning of the vaccine efficacy at the rate ωV. The susceptible class decreases as a result of progression of individuals into the latently infectious individuals with drug resistance at the slow rate $(1-\rho_r)\left(\alpha_{r_1}\eta+\alpha_{r_2}(1-\eta)\right)$, the progression of individuals into the latently infected class with drug sensitivity at the slow rate $(1-\rho_s)\left(\alpha_{s_1}\eta+\alpha_{s_2}(1-\eta)\right)$, progression of infected class with drug resistance at fast progression $\rho_r\left(\alpha_{r_1}\eta+\alpha_{r_2}(1-\eta)\right)$, progression of infected class with drug

sensitivity at fast progression rate $\rho_s\left(\alpha_{s_1}\eta+\alpha_{s_2}\left(1-\eta\right)\right)$, and reduces to the immunized class at the rate cS.

The population in latently infected class with drug resistance grows as a result of progression of individuals from susceptible class at the rate $\left(1-\rho_r\right)\left(\alpha_{r_1}\eta+\alpha_{r_2}\left(1-\eta\right)\right)$. This class reduces to infectious individuals with drug resistance and recovered class at the rate θ_r and ν_{r_1} respectively.The population of infectious individuals with drug resistance grows as a result of progression of latent class to infected class with drug resistance at the rate θ_r and as a result of progression of susceptible class at the rate, $\rho_r\left(\alpha_{r_1}\eta+\alpha_{r_2}\left(1-\eta\right)\right)$. The infectious class with drug resistance reduces to recovered class with drug resistance due to successful treatment at the rate $\nu_{r_2}\eta$ and disease induced death d_r.

The infected class with drug sensitivity reduces to recovered class with drug sensitivity at the rate $\nu_{s_2}\eta$ and disease induced death, d_s. The recovered class with drug resistance increases due to successful treatment of latently infectious individuals to recovered class with drug resistance at the rate, ν_{r_1}. The recovered class with drug sensitivity increases as a result of successful treatment of latently infectious individuals to recovered class with drug sensitivity at the rate, ν_{s_1}. All the eight compartments reduces as a result of natural death d

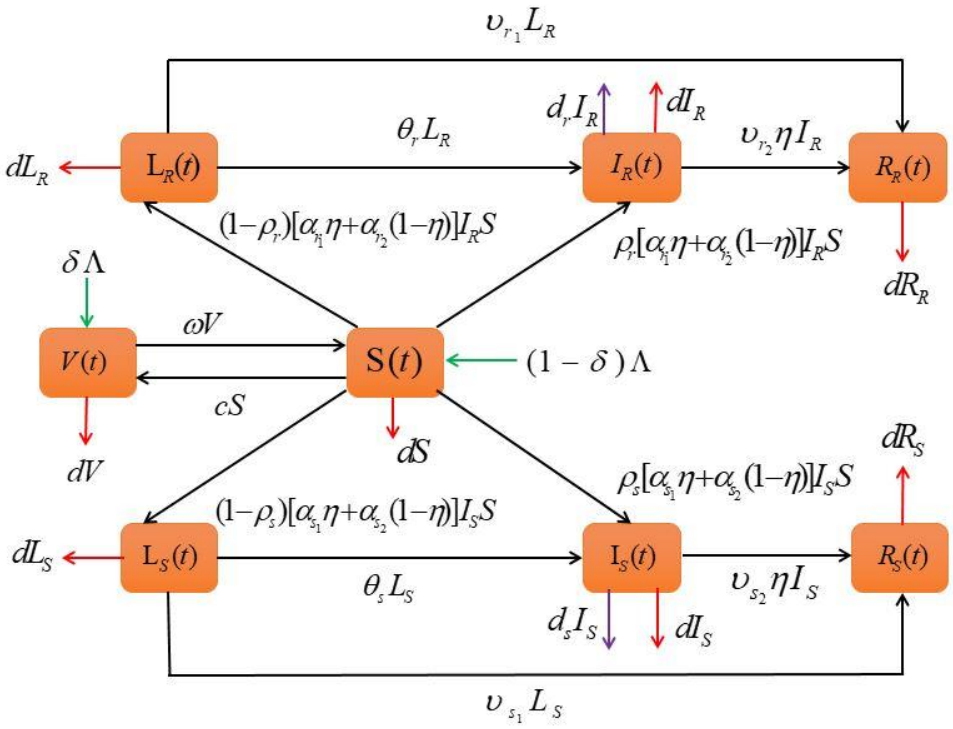


Figure1. Schematic diagram of model with drug resistance and drug sensitivity

The governing equations of the model with drug resistance and drug sensitivity are

$$\frac{dV}{dt} = \delta\Lambda + cS - (\omega + d)V \tag{1}$$

$$\frac{dS}{dt} = (1-\delta)\Lambda + \omega V - (c+d)S - (\alpha_{r_1}\eta + \alpha_{r_2}(1-\eta))I_R S - (\alpha_{s_1}\eta + \alpha_{s_2}(1-\eta))I_S S \tag{2}$$

$$\frac{dL_R}{dt} = (1-\rho_r)\left(\alpha_{r_1}\eta + \alpha_{r_2}(1-\eta)\right)I_R S - \left(\nu_{r_1} + \theta_r + d\right)L_R \tag{3}$$

$$\frac{dL_S}{dt} = (1-\rho_s)\left(\alpha_{s_1}\eta + \alpha_{s_2}(1-\eta)\right)I_S S - \left(\nu_{s_1} + \theta_s + d\right)L_S \tag{4}$$

$$\frac{dI_R}{dt} = \rho_r\left(\alpha_{r_1}\eta + \alpha_{r_2}(1-\eta)\right)I_R S + \theta_r L_R - \left(\nu_{r_2}\eta + d_r + d\right)I_R \tag{5}$$

$$\frac{dI_S}{dt} = \rho_s\left(\alpha_{s_1}\eta + \alpha_{s_2}(1-\eta)\right)I_S S + \theta_s L_S - \left(\nu_{s_2}\eta + d_s + d\right)I_S \tag{6}$$

$$\frac{dR_R}{dt} = \nu_{r_2}\eta I_R + \nu_{r_1} L_R - dR_R \tag{7}$$

$$\frac{dR_S}{dt} = \nu_{s_2}\eta I_S + \nu_{s_1} L_S - dR_S \tag{8}$$

$$V = V_0, S = S_0, \ L_R = L_{R0}, L_S = L_{S0}, I_R = I_{R0}, I_S = I_{S0}, R_R = R_{R0}, R_S = R_{S0} \tag{9}$$

3. Analysis of impact of drug resistance and sensitivity

3.1 Positivity of the solution

Theorem 1: Let the initial solution set $\{V > 0, S > 0, L_R > 0, L_S > 0, I_R > 0, I_S > 0, R_R > 0, R_S > 0\} \in R_+^8$, Then the solution set $\{V(t), S(t), L_R(t), L_S(t), I_R, I_S(t), R_R(t), R_S(t)\}$ is positive for all time t.

Proof:

Recall equation (1) we have

$$\frac{dV}{dt} = \delta\Lambda + cS - (\omega + d)V$$

By comparison theorem, equation (3.5) becomes

$$\frac{dV(t)}{dt} \geq -(\omega + d)V \tag{10}$$

Solving by the method of separation of variables we have

$$\frac{dV(t)}{V} \geq -(\omega + d)\,dt \tag{11}$$

Integrating both sides of the equation (4.2) we have

$$\ln(V) \geq \int -(\omega + d)\,dt + c \tag{12}$$

Taking the exponential of both sides of (4.3) we have

$$V(t) \geq e^{\int -(\omega+d)dt + c} \tag{13}$$

$$V(t) \geq C_1\, e^{\int -(\omega+d)dt} \tag{14}$$

where $C_1 = e^c$

Applying the initial condition $t = 0$ on (14) we get

$$V(0) \geq C_1 \tag{15}$$

Substituting (15) into (14) we have

$$\mathrm{V}(t) \geq V_0 e^{\int -(\omega+d)dt} > 0 \qquad (16)$$

Applying the same approach to the other variables, $S(t), \mathrm{L}_R(t), \mathrm{L}_S(t), \mathrm{I}_R, \mathrm{I}_S(t), R_R(t), \mathrm{R}_S(t)$ shows that the solution is positive for all time t.

3.2 Invariant region

The model equations (1) to (8) will be analyzed in a biologically feasible region.

Theorem 2: The solutions to the system (1) to (8) with initial conditions in theorem 1 satisfy $V > 0, S > 0, \mathrm{L}_R > 0, \mathrm{L}_S > 0, I_R > 0, \mathrm{I}_S > 0, R_R > 0, \mathrm{R}_S > 0$ for all $t > 0$.

The region $\Omega^* \in \mathbb{R}^8_+$ is positively invariant and attracting with respect to system (1) to (8).

$N = V + S + L_R + L_S + I_R + I_S + R_R + R_S$ such that $\Omega = \Omega^* \subset R^8_+$ with

$$\Omega^* = \left\{ (\mathrm{V}, S, L_R, \mathrm{L}_S, I_R, \mathrm{I}_S, R_R, \mathrm{R}_S) \in \mathbb{R}^8_+ ; V + S + L_R + L_S + I_R + I_S + R_R + R_S \leq \frac{\Lambda}{d} \right\} \qquad (17)$$

Proof:

The total population in the model is given by

$$\frac{dN}{dt} = \frac{d}{dt}\left(V + S + L_R + L_S + I_R + I_S + R_R + R_S\right)$$

$$= \frac{dV}{dt} + \frac{dS}{dt} + \frac{dL_R}{dt} + \frac{dL_S}{dt} + \frac{dI_R}{dt} + \frac{dI_S}{dt} + \frac{dR_R}{dt} + \frac{dR_S}{dt} \qquad (18)$$

Substituting (1) to (8) in (18) and solving we have

$$\frac{dN}{dt} = \Lambda - (V + S + L_R + L_S + I_R + I_S + R_R + R_S)d - d_r I_r - d_s I_S \qquad (19)$$

Thus, by comparison theory, equation (19) can be rewritten as

$$\frac{dN}{dt} = \Lambda - (V + S + L_R + L_S + I_R + I_S + R_R + R_S)d \qquad (20)$$

$$\frac{dN}{dt} \leq \Lambda - dN \qquad (21)$$

By separation of variables we get

$$\frac{d}{\Lambda - dN} N \leq dt \tag{22}$$

Integrating both side of (22)

$$\int \frac{d}{\Lambda - dN} N = \int dt \tag{23}$$

$$-\frac{1}{d}\ln(z) \geq \mathrm{t} + c \tag{24}$$

where $z = \Lambda - dN$

$$e^{\ln(z)} \geq e^{-(t+c)} \tag{25}$$

$$z \geq e^{-dt}.e^{-dc} \tag{26}$$

$$z(t) \geq C_1 e^{-dt} \tag{27}$$

where $C_1 = e^{-dc}$

At $t = 0$ equation (27) becomes

$$z(0) \geq c_1 \tag{28}$$

$$N(t) \geq \frac{1}{d}(\Lambda - z(t))e^{-dt} \tag{29}$$

As $t \to \infty$ in (29) the population size $N \to \frac{\Lambda}{d}$ which implies that (29) is $0 \leq N \leq \frac{\Lambda}{d}$.

Thus, the feasible solution set of the system of the model (1) to (8) is positively-invariant in the region Ω.

3.3 Drug Resistance Only Model

3.3.1 Disease free equilibrium of drug resistance only model

In this section, we analyze the disease free equilibrium, endemic equilibrium, reproduction number, local stability and global stability for the case of drug resistance TB only model.

Recall equations (1) to (8) and set

$L_S = 0, I_S = 0, R_S = 0$ 30

$$\left.\begin{aligned}
\frac{dV}{dt} &= \delta\Lambda + cS - (\omega + d)V \\
\frac{dS}{dt} &= (1-\delta)\Lambda + \omega V - (c+d)S - (\alpha_{r_1}\eta + \alpha_{r_2}(1-\eta))I_R S - (\alpha_{s_1}\eta + \alpha_{s_2}(1-\eta))I_S S \\
\frac{dL_R}{dt} &= (1-\rho_r)\left(\alpha_{r_1}\eta + \alpha_{r_2}(1-\eta)\right)I_R S - \left(\nu_{r_1} + \theta_r + d\right)L_R \\
\frac{dI_R}{dt} &= \rho_r\left(\alpha_{r_1}\eta + \alpha_{r_2}(1-\eta)\right)I_R S + \theta_r L_R - \left(\nu_{r_2}\eta + d_r + d\right)I_R \\
\frac{dR_R}{dt} &= \nu_{r_2}\eta I_R + \nu_{r_1} L_R - dR_R
\end{aligned}\right\}$$

(31)

At equilibrium

$$\frac{dV}{dt} = \frac{dS}{dt} = \frac{dL_R}{dt} = \frac{dI_R}{dt} = \frac{dR_R}{dt} = 0$$

$$\delta\Lambda + cS - (\omega + d)V = 0 \tag{32}$$

$$(1-\delta)\Lambda + \omega V - (c+d)S - (\alpha_{r_1} + \alpha_{r_2}(1-\eta)I_R S = 0 \tag{33}$$

$$(1-\rho_r)\left(\alpha_{r_1}\eta + \alpha_{r_2}(1-\eta)\right)I_R S - \left(\nu_{r_1} + \theta_r + d\right)L_R = 0 \tag{34}$$

$$\rho_r\left(\alpha_{r_1}\eta + \alpha_{r_2}(1-\eta)\right)I_R S + \theta_r L_R - \left(\nu_{r_2}\eta + d_r + d\right)I_R = 0 \tag{35}$$

$$\nu_{r_2}\eta I_R + \nu_{r_1} L_R - dR_R = 0 \tag{36}$$

From equation (32) we have

$$V = \frac{\delta\Lambda + cS}{k_1} \tag{37}$$

Substituting (37) into (33) at disease free we have

$$S^0 = \frac{(1-\delta)\Lambda k_1 + \omega\delta\Lambda}{k_1 k_2 - \omega c} \tag{38}$$

Substituting (38) into (37) we have

$$V^0 = \frac{\delta\Lambda}{k_1} + \frac{c((1-\delta)\Lambda k_1 + \omega\delta\Lambda)}{k_1 k_2 - \omega c} \tag{39}$$

Therefore the disease free equilibrium state for drug resistance only model is

$$E_0^R = \left(V^0, S^0, L_R^0, I_R^0, R_R^0\right) = \left(\frac{\delta\Lambda}{k_1} + \frac{c((1-\delta)\Lambda k_1 + \omega\delta\Lambda)}{k_1 k_2 - \omega c}, \frac{(1-\delta)\Lambda k_1 + \omega\delta\Lambda}{k_1 k_2 - \omega c}, 0, 0, 0 \right)$$

(40)

where $k_1 = (\omega + d)$

$k_2 = (c + d)$

3.3.2 Endemic equilibrium state for drug resistance

The endemic equilibrium state is a state at which the disease persists in a population under consideration.

Hence, the Endemic Equilibrium Points of the Model with drug resistance only $(V^*, S^*, L_R^*, I_R^*, R_R^*)$ is expressed as follows:

$$\left.\begin{aligned}
V^* &= \frac{1}{k_1}(\delta\Lambda + c(\frac{(1-\delta)\Lambda k_1 + \omega\delta\Lambda)}{m_1 k_1 I_R^* + k_1 k_2 - \omega c}) \\
S^* &= \frac{(1-\delta)\Lambda k_1 + \omega\delta\Lambda}{m_1 k_1 I_R^* + k_1 k_2 - \omega c} \\
L_R^* &= \frac{(1-\rho_r) m_1 I_R^* ((1-\delta)\Lambda k_1 + \omega\delta\Lambda)}{k_3 (m_1 k_1 I_R^* + k_1 k_2 - \omega c)} \\
I_R^* &= \frac{+\theta_r ((1-\rho_r) m_1 I_R^* (1-\delta)\Lambda k_1 + \omega\delta\Lambda)(m_1 k_1 I_R^* + k_1 k_2 - \omega c))}{k_3 (m_1 k_1 I_R^* + k_1 k_2 - \omega c)((m_1 k_1 I_R^* + k_1 k_2 - \omega c) k_4 - \rho_r m_1 ((1-\delta)\Lambda k_1 + \omega\delta\Lambda))} \\
R_R^* &= \nu_{r_2} \eta I_R^* + \frac{\nu_{r_1} ((1-\rho_r) m_1 I_R^* ((1-\delta)\Lambda k_1 + \omega\delta\Lambda)}{k_3 (m_1 k_1 I_R^* + k_1 k_2 - \omega c)}
\end{aligned}\right\}$$

(41)

where $m_1 = \left(\alpha_{r_1}\eta + \alpha_{r_2}(1-\eta)\right)$

$k_3 = (\nu_{r_1} + \theta_r + d)$

$k_4 = \nu_{r_2}\eta + d_r + d$

3.3.3 Reproduction number for drug-resistant TB

We apply the next generation matrix technique by [12] to obtain the basic reproduction number for drug-resistant, R_0^R by considering the infected compartments of the system (31) of this work. That is equation (4) and (6).

Let F_i be the rate of appearance of new infection in the i compartment and V_i be the rate of transfer of individuals out of i, given the disease free equilibrium, then R_0^R is the spectral radius (largest Eigen values) of the next generation matrix denoted by $G = FV^{-1}$.

By applying next generation matrix technique, we have the reproduction number for drug resistance TB model only as.

$$R_0^R = \frac{\left(\theta_r\left(1-\rho_r\right)+\rho_r(\nu_{r_1}+\theta_r+d)(\alpha_{r_1}\eta+\alpha_{r_2}(1-\eta)\right)(1-\delta)\Lambda(\omega+d)+\omega\delta\Lambda)}{(\nu_{r_1}+\theta_r+d)(\nu_{r_2}\eta+d_r+d)(\mathrm{k}_1 k_2+\omega c)} \tag{42}$$

3.3.4 Local stability of disease free equilibrium point with drug-resistant TB

Theorem 3: The disease free equilibrium point, E_0^R is locally asymptotically stable if $R_0^R < 1$ and unstable if $R_0^R > 1$.

From equation (31) we let

$$F_1 = \delta\Lambda + cS - (\omega + d)V \tag{43}$$

$$F_2 = \left(1-\delta\right)\Lambda + \omega V - (c+d)S - (\alpha_{r_1}\eta + \alpha_{r_2}(1-\eta))\,\mathrm{I}_R\, S \tag{44}$$

$$F_3 = \left(1-\rho_r\right)\left(\alpha_{r_1}\eta + \alpha_{r_2}\left(1-\eta\right)\right)I_R S - \left(\nu_{r_1}+\theta_r+d\right)L_R \tag{45}$$

$$F_4 = \rho_r\left(\alpha_{r_1}\eta + \alpha_{r_2}\left(1-\eta\right)\right)I_R S + \theta_r L_R - \left(\nu_{r_2}\eta + d_r + d\right)I_R \tag{46}$$

$$F_5 = \nu_{r_2}\eta I_R + \nu_{r_1} L_R - dR_R \tag{47}$$

Thus, the Jacobean matrix J for the equations (43) to (47) and evaluating at the disease free equilibrium is

$$J(E_0) = \begin{bmatrix} -k_1 & c & 0 & 0 & 0 \\ \omega & -k_2 & 0 & -m_1 S^0 & 0 \\ 0 & 0 & -k_3 & \left(1-\rho_r\right)m_1 S^0 & 0 \\ 0 & 0 & \theta_r & \rho_r m_1 S^0 - k_4 & 0 \\ 0 & 0 & \nu_{r_1} & \nu_{r_2}\eta & -d \end{bmatrix} \tag{48}$$

Given

$$\left|J\left(E_O\right) - \lambda I\right| = 0 \tag{49}$$

Substituting equation (48) into equation (49), we obtain

$$\begin{vmatrix} -k_1-\lambda & c & 0 & 0 & 0 \\ \omega & -k_2-\lambda & 0 & -m_1S^0 & 0 \\ 0 & 0 & -k_3-\lambda & (1-\rho_r)m_1S^0 & 0 \\ 0 & 0 & \theta_r & (\rho_r m_1 S^0 - k_4)-\lambda & 0 \\ 0 & 0 & \nu_{r_1} & \nu_{r_2}\eta & -d-\lambda \end{vmatrix} = 0 \quad (50)$$

From equation (50), $\lambda_1 = -d$, thus equation (50) reduces to

$$\begin{vmatrix} -k_1-\lambda & c & 0 & 0 \\ \omega & -k_2-\lambda & 0 & -m_1S^0 \\ 0 & 0 & -k_3-\lambda & A_1S^0 \\ 0 & 0 & \theta_r & (\mathrm{A}_2 S^0 - k_4)-\lambda \end{vmatrix} = 0 \quad (51)$$

where

$\mathrm{A}_1 = (1-\rho_r)m_1$, $A_2 = \rho_r m_1$

The characteristic polynomial is

$$D_1\lambda^4 + D_2\lambda^3 + D_3\lambda^2 + D_4\lambda + D_0 = 0 \quad (52)$$

where

$D_1 = 1$

$D_2 = (k_1 + k_2 + k_3 - A_2S^0)$

$D_3 = (k_3(k_1+k_2) + k_1k_2 - c\omega - A_2s^0(k_1+k_2+k_3) - \theta_r A_1S^0)$

$D_4 = \theta_r A_1k_3S^0 - A_2S^0(k_3(k_1+k_2) - c\omega + k_1k_2) - k_3(c\omega - k_1k_2) - \theta_r A_1k_3S^0(k_1+k_2+k_3))$

$D_0 = (A_2k_3S^0(c\omega - k_1k_2) - \theta_r A_1k_3^2S^0 - \theta_r A_1S^0(k_3(k_1+k_2) - c\omega + k_1k_2) + \theta_r A_1k_3S^0(k_1+k_2+k_3))$

by applying Routh Hurwitz criterion which state that all roots of polynomial (52) have negative real part iff the coefficients a_i are positive and the determinant of the matrices $H_i > 0$ for $i = 1, 2, 3, 4$. Therefore, all the Eigen values of the polynomial (52) have negative real parts. Since all the values of $\lambda_i < 0$, for when $R_0^R < 1$, we conclude that the disease-free equilibrium point is locally asymptotically stable.

3.3.5 Global stability of disease free equilibrium point with drug- resistant TB

We used the method of [13] to obtain the global stability of the disease equilibrium point. Two conditions which guarantee the global stability of the disease- free state were considered. Therefore, our systems of equations (31) are re-write in the following form;

$$\left.\begin{aligned}\frac{dX}{dt} &= F\left(X,Z\right)\\ \frac{dZ}{dt} &= G\left(X,Z\right), G\left(X,0\right)=0\end{aligned}\right\} \tag{4.66}$$

Where $X=\left(V,\mathrm{S},R_R\right)$ denotes the number of uninfected individuals and $X\in R^3$, while $Z=\left(L_R,\mathrm{I}_R\right)$ denotes the number of infected individuals and $Z\in R^2$. We represent the disease-free state by $E^0=\left(X^0,0\right)$.

Lemma 1: The point $K^0=\left(X^0,0\right)$ is called stable global asymptotic equilibrium point, if in addition $R_0<1$ and the conditions H_1 and H_2 holds. The following theorem is formed:

Theorem 4: Let $R_0<1$. Then the disease free equilibrium is globally asymptotically stable if

$$R_0<1 \text{ and otherwise if } R_0>1$$

Proof:

Let $X=\left(V,\mathrm{S},R_R\right)$, $Z=\left(L_R,I_R\right)$ and $K^0=\left(X^0,0\right)$ where

$$X^0=(V^0,S^0,L_R^0,I_R^0,R_R^0)=(\frac{\delta\Lambda}{k_1}+\frac{c((1-\delta)\Lambda k_1+\omega\delta\Lambda)}{k_1k_2-\omega c},\frac{(1-\delta)\Lambda k_1+\omega\delta\Lambda}{k_1k_2-\omega c},0,0,0) \tag{53}$$

$$\left.\begin{aligned}X&\in R^3\\ \frac{dV}{dt}&=\delta\Lambda+cS-(\omega+d)V\\ \frac{dS}{dt}&=(1-\delta)+\omega V-(c+d)S-m_1I_RS\\ \frac{dR_R}{dt}&=\nu_{r_2}\eta+\nu_{r_1}L_R-dR_R\end{aligned}\right\} \tag{54}$$

$$F\left(X,0\right)=\begin{pmatrix}\delta\Lambda-(\omega+d)V\\ (1-\delta)-\left[(c+d)+m_1I_R\right]S\\ 0\end{pmatrix} \tag{55}$$

$$Z \in R^2$$

$$\left.\begin{aligned} \frac{dL_R}{dt} &= (1-\rho_r)m_1 I_R S - k_3 L_R \\ \frac{dI_R}{dt} &= \rho_r m_1 I_R S + \theta_r L_R - k_4 I_R \end{aligned}\right\} \tag{4.70}$$

$$C = \begin{pmatrix} -k_3 & A_1 S \\ \theta_r & A_2 S - k_4 \end{pmatrix} \tag{56}$$

$$CZ = \begin{pmatrix} -k_3 & A_1 S \\ \theta_r & A_2 S - k_4 \end{pmatrix}\begin{pmatrix} L_R \\ I_R \end{pmatrix} \tag{57}$$

$$\hat{G}(X,Z) = C\,\mathrm{Z} - \mathrm{G(X,Z)}$$

(4.73)

$$\hat{G}(X,Z) = \begin{pmatrix} -k_1 L_R + A_1 I_R S^0 \\ \theta_r L_R + A_2 I_R S^0 - k_4 I_R \end{pmatrix} - \begin{pmatrix} A_1 I_R S - k_3 L_R \\ A_2 I_R S + \theta_r L_R - k_4 I_R \end{pmatrix}$$

$$\hat{G}(X,Z) = \begin{pmatrix} \hat{G}(X,Z) \\ \hat{G}(X,Z) \end{pmatrix} = \begin{pmatrix} (1-\rho_r)m_1 I_R \left(S^0 - S\right) \\ \rho_r m_1 I_R \left(S^0 - S\right) \end{pmatrix} \tag{58}$$

Therefore, since $S \le S^0$ we have $\hat{G}_1(X,Z), \hat{G}_2(X,Z) \ge 0$ the global stability of $X^0 = (\mathrm{V}^0, S^0, 0, 0, 0)$. The system of $\frac{dX}{dt} = F(X^0, 0)$ is easy to verify. Therefore X^0 is globally asymptotically stable if $R_0 < 1$. This completes the proof

3.4 Drug Sensitivity Only Model

In this section, we analyze the disease free equilibrium, endemic equilibrium, reproduction number, local stability and global stability for the case of drug sensitive TB only model

For the case of drug sensitivity only model, we set

$$L_R = 0, I_R = 0, R_R = 0 \tag{58}$$

$$\left.\begin{aligned}
\frac{dV}{dt} &= \delta\Lambda + cS - (\omega + d)V \\
\frac{dS}{dt} &= (1-\delta)\Lambda + \omega V - (c+d)S - (\alpha_{r_1}\eta + \alpha_{r_2}(1-\eta))I_R S - (\alpha_{s_1}\eta + \alpha_{s_2}(1-\eta))I_S S \\
\frac{dL_S}{dt} &= (1-\rho_s)\left(\alpha_{s_1}\eta + \alpha_{s_2}(1-\eta)\right)I_S S - \left(\nu_{s_1} + \theta_s + d\right)L_S \\
\frac{dI_S}{dt} &= \rho_s\left(\alpha_{s_1}\eta + \alpha_{s_2}(1-\eta)\right)I_S S + \theta_s L_S - \left(\nu_{s_2}\eta + d_s + d\right)I_S \\
\frac{dR_S}{dt} &= \nu_{s_2}\eta I_S + \nu_{s_1} L_S - dR_S
\end{aligned}\right\}$$

(59)

3.4.1 Disease free equilibrium for only drug sensitivity TB

At disease free equilibrium state for drug sensitivity only model we have

$$E_0 = (V^0, S^0, L_S^0, I_S^0, R_S^0) = \left(\frac{\delta\Lambda}{k_1} + \frac{c((1-\delta)\Lambda k_1 + \omega\delta\Lambda)}{k_1 k_2 - \omega c}, \frac{(1-\delta)\Lambda k_1 + \omega\delta\Lambda}{k_1 k_2 - \omega c}, 0, 0, 0\right) \quad (60)$$

3.4.2 Endemic equilibrium state for drug sensitivity model

The Endemic Equilibrium Points of the Model with drug sensitivity only $\left(V^*, S^*, L_S^*, I_S^*, R_S^*\right)$ is expressed as follows

$$\left.\begin{aligned}
V^{**} &= \frac{1}{k_1}\left(\delta\Lambda + c\left(\frac{(1-\delta)\Lambda k_1 + \omega\delta\Lambda)}{m_2 k_1 I_S^* + k_1 k_2 - \omega c}\right)\right. \\
S^{**} &= \frac{(1-\delta)\Lambda k_1 + \omega\delta\Lambda}{m_2 k_1 I_S^* + k_1 k_2 - \omega c} \\
L_S^{**} &= \frac{(1-\rho_s)m_2 I_S^*((1-\delta)\Lambda k_1 + \omega\delta\Lambda)}{k_5(m_2 k_1 I_S^* + k_1 k_2 - \omega c)} \\
I_S^{**} &= \frac{+\theta_s((1-\rho_s)m_2 I_S^*(1-\delta)\Lambda k_1 + \omega\delta\Lambda)(m_2 k_1 I_S^* + k_1 k_2 - \omega c))}{k_5(m_2 k_1 I_S^* + k_1 k_2 - \omega c)((m_2 k_1 I_S^* + k_1 k_2 - \omega c)k_6 - \rho_s m_2((1-\delta)\Lambda k_1 + \omega\delta\Lambda))} \\
R_S^{**} &= \nu_{s_2}\eta I_S^* + \frac{\nu_{s_1}((1-\rho_s)m_2 I_S^*((1-\delta)\Lambda k_1 + \omega\delta\Lambda)}{k_5(m_2 k_1 I_S^* + k_1 k_2 - \omega c)}
\end{aligned}\right\}$$

(61)

where $m_2 = \left(\alpha_{s_1}\eta + \alpha_{s_2}(1-\eta)\right)$

$$k_5 = (\nu_{s_1} + \theta_s + d)$$

$$k_6 = (\nu_{s_2}\eta + d_s + d)$$

3.4.3 Reproduction number for drug-sensitivity TB

Applying the next generation matrix technique by [12] we obtained the basic reproduction number for drug-sensitivity, R_0^S

$$R_0^S = \frac{(\theta_s(1-\rho)(\alpha_{s_1}\eta + \alpha_{s_2}(1-\alpha\eta) + \rho_s(\alpha_{s_1}\eta - \alpha_{s_2}(1-\eta)(\nu_{s_1} + \theta_s + \mathrm{d}))}{(\nu_{s_1} + \theta_s + d)(\nu_{s_2}\eta + d_s + dk_6)} \tag{62}$$

3.4.4 Local stability of disease free equilibrium point with drug sensitivity TB

Theorem 5*:*The disease free equilibrium point, E_0^S is locally asymptotically stable if $R_0^S < 1$ and unstable if $R_0^S > 1$.

Let

$$F_1 = \delta\Lambda + cS - (\omega + d)V$$

$$F_6 = (1-\delta)\Lambda + \omega V - (c+d)S - (\alpha_{s_1}\eta - \alpha_{s_2}(1-\eta))I_S S \tag{63}$$

$$F_7 = (1-\rho_s)\left(\alpha_{s_1}\eta + \alpha_{s_2}(1-\eta)\right)I_S S - \left(\nu_{s_1} + \theta_s + d\right)L_S \tag{64}$$

$$F_8 = \rho_s\left(\alpha_{s_1}\eta + \alpha_{s_2}(1-\eta)\right)I_S S + \theta_s L_S - \left(\nu_{s_2}\eta + d_s + d\right)I_S \tag{65}$$

$$F_9 = \nu_{s_2}\eta I_S + \nu_{s_1} L_S - dR_S \tag{66}$$

Evaluating the Jacobean matrix J for the system (63) to (66) at the disease free equilibrium, we obtain

$$J(E_0) = \begin{bmatrix} -k_1 & c & 0 & 0 & 0 \\ \omega & -k_2 & 0 & -m_2 S^0 & 0 \\ 0 & 0 & -k_5 & (1-\rho_s)m_2 S^0 & 0 \\ 0 & 0 & \theta_r & \rho_s m_2 S^0 - k_6 & 0 \\ 0 & 0 & \nu_{s_1} & \nu_{s_2}\eta & -d \end{bmatrix} \tag{67}$$

Given

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

$$\begin{vmatrix} -k_1-\lambda & c & 0 & 0 & 0 \\ \omega & -k_2-\lambda & 0 & -m_2S^0 & 0 \\ 0 & 0 & -k_5-\lambda & (1-\rho_s)m_2S^0 & 0 \\ 0 & 0 & \theta_s & (\rho_s m_2S^0-k_6)-\lambda & 0 \\ 0 & 0 & \nu_{s_1} & \nu_{s_2}\eta & -d-\lambda \end{vmatrix} = 0 \quad (68)$$

From equation (68), $\lambda_1 = d_1$ thus equation (68) reduces to

$$\begin{vmatrix} -k_1-\lambda & c & 0 & 0 \\ \omega & -k_2-\lambda & 0 & -m_2 \\ 0 & 0 & -k_5-\lambda & (1-\rho_s)m_2S^0 \\ 0 & 0 & \theta_s & \rho_s m_2S^0-\lambda \end{vmatrix} = 0 \quad (69)$$

The characteristic polynomial is

$$U_1\lambda^4 + U_2\lambda^3 + U_3\lambda^2 + U_4\lambda + U_0 \quad (70)$$

where

$U_1 = 1$

$U_2 = (k_1 + k_2 + k_5 - A_4S^0)$

$U_3 = (k_5(k_1+k_2) + k_1k_2 - c\omega - A_4s^0(k_1+k_2+k_5) - \theta_r A_3S^0)$

$U_4 = \theta_s A_3k_5S^0 - A_4S^0(k_5(k_1+k_2) - c\omega + k_1k_2) - k_5(c\omega - k_1k_2) - \theta_s A_3k_5S^0(k_1+k_2+k_5))$

$U_0 = (A_4k_5S^0(c\omega - k_1k_2) + \theta_s A_3k_5S^0(k_1+k_2+k_5) - \theta_s A_3k_3^2S^0 - \theta_r A_3S^0(k_5(k_1+k_2) - c\omega + k_1k_2))$

We apply Routh-Hurwitz criterion which states that all roots of the polynomial (70) have negative real part iff the coefficients a_i, are positive and the determinant of the matrices $H_i > 0$ for $i = 0,1,2,3,4.$ we conclude that the disease-free equilibrium point is locally asymptotically stable.

3.4.5 Global stability of disease free equilibrium point with drug-sensitive TB

We used the method of [13] to obtain the global stability of the disease equilibrium point. Two conditions which guarantee the global stability of the disease- free state were considered. Therefore, our systems of the model equations are re-write in the following form;

$$\left.\begin{aligned}\frac{dX}{dt} &= F\left(X,Z\right)\\ \frac{dZ}{dt} &= G\left(X,Z\right), G\left(X,0\right)=0\end{aligned}\right\}$$

Where $X=\left(V,\mathrm{S},R_S\right)$ denotes the number of uninfected individuals and $X\in R^3$, while $Z=\left(L_S,\mathrm{I}_S\right)$ denotes the number of infected individuals and $Z\in R^2$. We represent the disease-free state by $E^0=\left(X^0,0\right)$.

Lemma 1: The point $K^0=\left(X^0,0\right)$ is called stable global asymptotic equilibrium point, if in addition $R_0<1$ and the conditions H_1 and H_2 holds. The following theorem is formed:

Theorem 6: Let $R_0<1$. Then the disease free equilibrium is globally asymptotically stable.

Proof:

Let $X=\left(S,V,R_S\right)$, $Z=\left(L_S,I_S\right)$ and $K^0=\left(X^0,0\right)$ where

$$X^0=(V^0,S^0,L_S^0,I_S^0,R_S^0)=(\frac{\delta\Lambda}{k_1}+\frac{c((1-\delta)\Lambda k_1+\omega\delta\Lambda)}{k_1k_2-\omega c},\frac{(1-\delta)\Lambda k_1+\omega\delta\Lambda}{k_1k_2-\omega c},0,0,0) \quad (71)$$

Recall (3.5) to (3.12)

$X\in R^3$

$$\left.\begin{aligned}\frac{dV}{dt} &= \delta\Lambda+cS-(\omega+d)V\\ \frac{dS}{dt} &= (1-\delta)+\omega V-(c+d)S-m_2I_SS\\ \frac{dR_S}{dt} &= \nu_{s_2}\eta+\nu_{s_1}L_S-dS_S\end{aligned}\right\} \quad (72)$$

$$F\left(X,0\right)=\begin{pmatrix}\delta\Lambda-(\omega+d)V\\ (1-\delta)-\left[(c+d)+m_1I_S\right]S\\ 0\end{pmatrix} \quad (73)$$

$$Z \in R^2$$

$$\left.\begin{aligned} \frac{dL_S}{dt} &= (1-\rho_s)m_2 I_S S - k_5 L_S \\ \frac{dI_S}{dt} &= \rho_s m_2 I_S S + \theta_s L_s - k_6 I_S \end{aligned}\right\} \tag{74}$$

$$C_2 = \begin{pmatrix} -k_5 & A_3 S \\ \theta_s & A_4 S - k_6 \end{pmatrix} \tag{75}$$

$$C_2 Z = \begin{pmatrix} -k_5 & A_3 S \\ \theta_s & A_4 S - k_6 \end{pmatrix} \begin{pmatrix} L_S \\ I_S \end{pmatrix} \tag{76}$$

$$\hat{G}(X,Z) = C_2 Z - G(X,Z) \tag{77}$$

$$\hat{G}(X,Z) \quad = \begin{pmatrix} -k_1 L_S + A_3 I_S S^0 \\ \theta_s L_S + A_4 I_S S^0 \end{pmatrix} - \begin{pmatrix} A_3 I_S S - k_5 L_S \\ A_4 I_S S - \theta_s L_S - k_6 I_S \end{pmatrix}$$

$$\hat{G}(X,Z) = \begin{pmatrix} \hat{G}(X,Z) \\ \hat{G}(X,Z) \end{pmatrix} = \begin{pmatrix} (1-\rho_s)(\alpha_{s_1}\eta - \alpha_{s_2}(1-\eta) I_S \left(S^0 - S\right) \\ \rho_s(\alpha_{s_1}\eta - \alpha_{s_2}(1-\eta) I_S \left(S^0 - S\right) \end{pmatrix} \tag{78}$$

Therefore, since $S \le S^0$ we have $\hat{G}_1(X,Z), \hat{G}_2(X,Z) \ge 0$ the global stability of $X^0 = (\mathrm{V}^0, S^0, 0, 0, 0)$. The system of $\frac{dX}{dt} = F(X^0, 0)$ is easy to verify. Therefore X^0 is globally asymptotically stable if $R_0 < 1$. This completes the proof.

4.0 Drug resistance and drug sensitivity model

In this section, we analyze the DFE, EE, and reproduction number, local and global stability for the case of DR-TB and DS-TB model

4.1 *Disease free equilibrium state*

For both drug resistance and drug sensitive model, the equilibrium state for the model was obtained by setting the model equations to zero (0)

At equilibrium the disease free equilibrium state for drug resistance and drug sensitivity model is

$$E_0^{RS} = \left(V^0, S^0, L_R^0, L_S^0, I_R^0, I_S^0, R_R^0, R_S^0\right) = \left(\frac{\delta\Lambda}{k_1} + \frac{c((1-\delta)\Lambda k_1 + \omega\delta\Lambda)}{k_1 k_2 - \omega c}, \frac{(1-\delta)\Lambda k_1 + \omega\delta\Lambda}{k_1 k_2 - \omega c}, 0, 0, 0, 0, 0, 0\right)$$

(79)

4.2 Endemic equilibrium for drug resistance and drug sensitivity model

The Endemic Equilibrium Point of the Model with drug resistance and drug sensitive model $(V^*, S^*, L_R^*, L_S^*, I_R^*, I_S^*, R_R^*, R_S^*)$ is expressed as follows:

$$\left.\begin{aligned}
V^{***} &= \frac{\delta\Lambda}{k_1} + \frac{c\left((1-\delta)\,\mathrm{k}_1 + \omega\delta\Lambda\right)}{k_1\left((m_1 I_R^* + m_2 I_S^*) + \mathrm{k}_2)k_1 - c\omega\right)} \\
S^{***} &= \frac{(1-\delta)\Lambda k_1 + \omega\delta\Lambda}{(m_1 I_R^* + m_2 I_S^*) + k_1 k_2 - c\omega} \\
L_R^{***} &= \frac{(1-\rho_r) m_1 I_R^* (1-\delta)\Lambda k_1 + \omega\delta\Lambda}{\left((m_1 I_R^* + m_2 I_S^*)k_3 + k_2\right)k_1 - c\omega} \\
L_S^{***} &= \frac{(1-\rho_s) m_1 I_S^* (1-\delta)\Lambda k_1 + \omega\delta\Lambda}{\left((m_1 I_R^* + m_2 I_S^*)k_5 + k_2\right)k_1 - c\omega} \\
I_R^{***} &= \frac{\theta_r (1-\rho_r) m_1 I_R^* (1-\delta)\Lambda k_1 + \omega\delta\Lambda}{(m_1 I_R^* + m_2 I_S^*)\,\mathrm{k}_3 + k_2)k_1 - c\omega)(k_4 - \rho_r m_1 S^*)} \\
I_S^{***} &= \frac{\theta_s (1-\rho_s) m_2 I_S^* (1-\delta)\Lambda k_1 + \omega\delta\Lambda}{(m_1 I_R^* + m_2 I_S^*)\,\mathrm{k}_5 + k_2)k_1 - c\omega)(k_6 - \rho_s m_2 S^*)} \\
R_R^{***} &= \nu_{r_2}\eta I_R^* + \frac{\nu_{r_1}\left((1-\rho_r) m_1 I_R^* (1-\delta)\Lambda k_1 + \omega\delta\Lambda\right)}{\left((m_1 I_R^* + m_2 I_S^*)k_5 + k_2)k_1 - c\omega\right)d} \\
R_S^{***} &= \nu_{s_2}\eta I_S^* + \frac{\nu_{s_1}\left((1-\rho_s) m_2 I_S^* (1-\delta)\Lambda k_1 + \omega\delta\Lambda\right)}{\left((m_1 I_R^* + m_2 I_S^*)k_5 + k_2)k_1 - c\omega\right)d}
\end{aligned}\right\} \quad (80)$$

4.3 Reproduction number for drug sensitive and drug-resistant TB

We apply the next generation matrix technique by [12] to obtain the basic reproduction number, R_0^{RS}. by considering the infected compartments of the system (1) to (8) of this work.

$$R_0^S = \frac{(\theta_s(1-\rho)(\alpha_{s_1}\eta + \alpha_{s_2}(1-\alpha\eta) + \rho_s(\alpha_{s_1}\eta = \alpha_{s_2}(1-\eta)(\nu_{s_1} + \theta_s + \mathrm{d}))}{(\nu_{s_1} + \theta_s + d)(\nu_{s_2}\eta + d_s + dk_6)} \tag{81}$$

The reproduction number for both drug sensitive and drug resistant is given as $R_0^{RS} = \max\left\{R_0^R, R_0^S\right\}$, where R_0^R and R_0^S are reproduction numbers for drug sensitive TB strain and drug resistant TB strain respectively.

4.4.4 Local stability of the disease free equilibrium point with both drug resistant TB and drug sensitivity TB

Theorem 7: The disease free equilibrium point, E_O is locally asymptotically stable if $R_0 < 1$ and unstable if $R_0 > 1$.

From (1) to (8) we let

$$F_1 = \delta\Lambda + cS - (\omega + d)V$$

$$F_9 = (1-\delta)\Lambda + \omega V - (c+d)S - (\alpha_{r_1}\eta - \alpha_{r_2}(1-\eta))I_R S - (\alpha_{s_1}\eta + \alpha_{s_2}(1-\eta))I_S S$$

$$F_3 = (1-\rho_r)\left(\alpha_{r_1}\eta + \alpha_{r_2}(1-\eta)\right)I_R S - \left(\nu_{r_1} + \theta_r + d\right)L_R$$

$$F_4 = (1-\rho_s)\left(\alpha_{s_1}\eta + \alpha_{s_2}(1-\eta)\right)I_S S - \left(\nu_{s_1} + \theta_s + d\right)L_S$$

$$F_5 = \rho_r\left(\alpha_{r_1}\eta + \alpha_{r_2}(1-\eta)\right)I_R S + \theta_r L_R - \left(\nu_{r_2} + d_r + d\right)I_R$$

$$F_6 = \rho_s\left(\alpha_{s_1}\eta + \alpha_{s_2}(1-\eta)\right)I_s S + \theta_s L_S - \left(\nu_{s_2}\eta + d_s + d\right)I_S$$

$$F_7 = \nu_{r_2}\eta I_R + \nu_{r_1} L_R - dR_R$$

$$F_8 = \nu_{s_2}\eta I_S + \nu_{s_1} L_S - dR_S$$

Thus, the Jacobean matrix J for the system evaluating at the disease free equilibrium is

$$J(E_O) = \begin{bmatrix} -k_1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ \omega & -k_2 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & -k_3 & 0 & A_1 S^0 & 0 & 0 & 0 \\ 0 & 0 & 0 & -k_5 & 0 & A_3 s^0 & 0 & 0 \\ 0 & 0 & \theta_r & 0 & A_2 S^0 - k_4 & 0 & 0 & 0 \\ 0 & 0 & 0 & \theta_s & 0 & A_4 S^0 - k_6 & 0 & 0 \\ 0 & 0 & \nu_{r_1} & 0 & \nu_{r_2}\eta & 0 & -d & 0 \\ 0 & 0 & 0 & \nu_{s_1} & 0 & \nu_{s_{2\eta}} & 0 & -d \end{bmatrix} \tag{82}$$

Given $\left|J\left(E_O\right)-\lambda I\right|=0$ we obtain

$$\begin{vmatrix} -k_1-\lambda & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ \omega & -k_2-\lambda & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & -k_3-\lambda & 0 & A_1S^0 & 0 & 0 & 0 \\ 0 & 0 & 0 & -k_5-\lambda & 0 & A_3s^0 & 0 & 0 \\ 0 & 0 & \theta_r & 0 & \left(A_2S^0-k_4\right)-\lambda & 0 & 0 & 0 \\ 0 & 0 & 0 & \theta_s & 0 & \left(A_4S^0-k_6\right)-\lambda & 0 & 0 \\ 0 & 0 & \nu_{r_1} & 0 & \nu_{r_2}\eta & 0 & -d-\lambda & 0 \\ 0 & 0 & 0 & \nu_{s_1} & 0 & \nu_{s_{2\eta}} & 0 & -d-\lambda \end{vmatrix}=0 \quad (83)$$

equation (83) can be reduced to

$$\begin{bmatrix} -k_1-\lambda & c & 0 & 0 & 0 & 0 \\ \omega & -k_2-\lambda & 0 & 0 & 0 & 0 \\ 0 & 0 & -k_3-\lambda & 0 & A_1S^0 & 0 \\ 0 & 0 & 0 & -k_5-\lambda & 0 & A_3S^0 \\ 0 & 0 & \theta_r & 0 & (A_2S^0-k_4)-\lambda & 0 \\ 0 & 0 & 0 & \theta_s & 0 & (A_4S^0-\mathrm{k}_6)-\lambda \end{bmatrix} \quad (84)$$

Therefore, solving (84) yields the characteristics polynomial

$$b_1\lambda^6+b_2\lambda^5+b_3\lambda^4+b_4\lambda^3+b_5\lambda^2+b_6\lambda+b_0=0 \quad (85)$$

where

$b_1=1$

$b_2=k_1+k_2+k_3+k_5+k_6-(A_4+A_2)$

$b_3=((A_4-k_6)(c\omega-k_3(k_1+k_2)+\theta_rA_1-k_1k_2-k_5(k_1+k_2+k_3)+A_2(k_1+k_2+k_3+k_5))$

$+\mathrm{k}_5(k_3(k_1+k_2)-c\omega+k_1k_2)+\theta_rA_1k_3\theta_sA_3k_5-A_2(k_3(k_1+k_2)-c\omega+k_1k_2+k_5(k_1+k_2+k_3)$

$-k_3(c\omega-k_1k_2)-\theta_sA_3(k_1+A_2+k_2+k_3+k_5)-\theta_rA_1(k_1+A_2+k_2+k_3+k_5)$

$b_4=((A_4-k_6(\mathrm{A}_2(\mathrm{k}_5(\mathrm{k}_3(\mathrm{k}_1+\mathrm{k}_2)-\mathrm{c}\,\omega+\mathrm{k}_1+\mathrm{k}_2)-\mathrm{k}_3(c\omega-k_1k_2+\chi\theta_rA_1k_3^2+\theta_rA_1k_3^3+$

$\theta_r(A_4-k_6)(c\omega-k_3(k_1+k_2)+\theta_rA_1-k_1k_2-k_5(k_1+k_2+k_3)+A_2(k_1+k_2+k_3+k_5))$

$+\mathrm{k}_5(k_3(k_1+k_2)-c\omega+k_1k_2)+\theta_rA_1k_3\theta_sA_3k_5-A_2(k_3(k_1+k_2)-c\omega+k_1k_2+k_5(k_1+k_2+k_3)$

$-k_3(c\omega-k_1k_2)-\theta_sA_3(k_1+A_2+k_2+k_3+k_5)-\theta_rA_1(k_1+A_2+k_2+k_3+k_5)$

$$b_5 = ((A_4 - k_6)(A_2(k_3(k_1 + k_2) + \theta_s A_3 k_5(k_1 - a_2 + k_2 + k_3 + k_5) + \theta_r \mathrm{A}_1(k_1 + k_2 + k_3 + \mathrm{k}_5) + k_3(c\omega + k_1 k_2)$$
$$+\theta_r A_1 k_3(k_1 + k_2 + k_3 + k_5)) - \theta_r A_1 k_3) - \mathrm{A}_2(k_5(k_3(k_1 + k_2) + \theta_s A_3(c\omega - k_3(k_1 + k_2) + \theta_r A_1$$
$$+A_2(k_1 + k_2 + \mathrm{k}_3 + \mathrm{k}_5)) - \theta_r A_1 k_3^2 - \theta_s A_3 k_5^2 - \theta_r A_1(k_3(k_1 + k_2) - \mathrm{c}\,\omega + k_1 k_2 + k_5(k_1 + k_2 + k_3))$$
$$-kl3k_5(c\omega - k_1 k_2) + \theta_s A_3 k_5(k_1 - a_2 + k_2 + k_3 + k_5) - \mathrm{c}\,\omega + k_1 k_2) - K_3(c\omega - k_1 k_2)) - \theta_r A_1 k_3^2 - \theta_s A_3 k_5^2$$
$$-\theta_r A_1(k_3(k_1 + k_2) - \mathrm{c}\,\omega + k_1 k_2 - k_5(k_1 + k_2 + k_3) - k_3 k_5(c\omega - k_1 k_2) + \theta_s - k_1 k_2 - k_5(k_1 + k_2 + k_3)$$
$$-A_1 k_3(k_1 + k_2 + k_3 + k_5))$$
$$b_6 = ((A_4 + \mathrm{k}_1 + \mathrm{k}_2) - \mathrm{k}_3(c\omega - k_1 k_2 + \theta_r A_1 k_3^2 + \theta_r A_1 k_3^3 + \theta_r(A_4 - k_6)(c\omega - k_3(k_1 + k_2) + \theta_r A_1 - k_1 k_2$$
$$-k_5(k_1 + k_2 + k_3) + A_2(k_1 + k_2 + k_3 + k_5)) + \mathrm{k}_5(k_3(k_1 + k_2) - c\omega + k_1 k_2) + \theta_r A_1 k_3 \theta_s A_3 k_5$$
$$-A_2(k_3(k_1 + k_2) - -k_3(c\omega - k_1 k_2) - \theta_s A_3(k_1 + A_2 + k_2 + k_3 + k_5)$$
$$-\theta_r A_1(k_1 + A_2 + k_2 + k_3 + k_5)((A_4 - k_6)(A_2(k_3(k_1 + k_2) - c\omega + k_1 k_2 + k_5(k_1 + k_2 + k_3)) - \mathrm{k}_5(k_3(k_1 + k_2)$$
$$-\mathrm{c}\,\omega + k_1 k_2) + k_3(c\omega + k_1 k_2) + \theta_r\,\mathrm{A}_1(k_1 + k_2 + k_3 + \mathrm{k}_5) - \theta_r A_1 k_3)$$
$$+\theta_r A_1 - k_1 k_2 - k_5(k_1 + k_2 + k_3) + A_2(k_1 + k_2 + \mathrm{k}_3 + \mathrm{k}_5)) - \theta_r A_1 k_3^2 - \theta_s A_3 k_5^2 - \theta_r A_1(k_3(k_1 + k_2) - \mathrm{c}\,\omega + k_1 k_2$$
$$+k_5(k_1 + k_2 + k_3)) - k_3 k_5(c\omega - k_1 k_2) + \theta_s A_3 k_5(k_1 - a_2 + k_2 + k_3 + k_5) + \theta_r A_1 k_3(k_1 + k_2 + k_3 + k_5))$$
$$b_0 = \theta_s A_3 A_2(k_5(k_3(k_1 + k_2) + \theta_r A_1 k_3^2 + \theta_r A_1(k_1 + k_2) - \mathrm{c}\,\omega + \mathrm{k}_1\, k_2 \theta_r A_1(k_1 + A_2 + k_2 + k_3 + k_5)$$
$$+k_5(k_1 + k_2 + k_3 + k_5))(\theta_r A_1 k_3^3 b_4 + ((A_4 - k_6(\mathrm{A}_2(\mathrm{k}_5(\mathrm{k}_3(\mathrm{k}_1 + \mathrm{k}_2) - \mathrm{c}\,\omega + \mathrm{k}_1 + \mathrm{k}_2) k_5(k_1 + k_2 + k_3) +$$
$$A_2(k_1 + k_2 + k_3 + k_5)) + \mathrm{k}_5(k_3(k_1 + k_2) - c\omega + k_1 k_2) + \theta_r A_1 k_3 \theta_s A_3 k_5 c\omega + k_1 k_2 + k_5(k_1 + k_2 + k_3)$$
$$-\mathrm{k}_3(c\omega - k_1 k_2 + \chi\theta_r A_1 k_3^2 + \theta_r A_1 k_3^3 + \theta_r(A_4 - k_6)(c\omega - k_3(k_1 + k_2) + \theta_r A_1 - k_1 k_2 - k_5(k_1 + k_2 + k_3) +$$
$$A_2(k_1 + k_2 + k_3 + k_5)) + \mathrm{k}_5(k_3(k_1 + k_2) - c\omega + k_1 k_2) + \theta_r A_1 k_3 \theta_s A_3 k_5 - A_2(k_3(k_1 + k_2) - c\omega + k_1 k_2 +$$
$$k_5(k_1 + k_2 + k_3) - k_3(c\omega - k_1 k_2) - \theta_s A_3(k_1 + A_2 + k_2 + k_3 + k_5) - c\omega + k_1 k_2) - k_3(c\omega - k_1 k_2))$$
$$-\theta_s A_3 k_5^4 - (A_4 - k_6) - \mathrm{A}_2(k_5(k_3(k_1 + k_2) - k_6(\mathrm{A}_2(\mathrm{k}_5(\mathrm{k}_3(\mathrm{k}_1 + \mathrm{k}_2) - \mathrm{c}\,\omega - \mathrm{c}\,\omega + k_1 k_2) - k_3(c\omega - k_1 k_2))$$
$$+\theta_s A_3(c\omega - k_3(k_1 + k_2)$$

We apply Routh-Hurwitz criterion which states that all roots of the polynomial (85) have negative real part iff the coefficients m_i, are positive and the determinant of the matrices $H_i > 0$ for $i = 0,1,2,3,4,5,6.$ therefore,

$$\begin{pmatrix} P_5 & P_3 & P_1 & P_{-1} & P_{-3} & P_{-5} \\ P_6 & P_4 & P_2 & P_0 & P_{-2} & P_{-4} \\ 0 & P_5 & P_3 & P_1 & P_{-1} & P_{-3} \\ 0 & P_6 & P_4 & P_2 & P_0 & P_{-2} \\ 0 & 0 & P_5 & P_3 & P_1 & P_{-1} \\ 0 & 0 & P_6 & P_4 & P_2 & P_0 \end{pmatrix} > 0$$

$$H_1 = a_3 = b_2 + b_3 + b_4 + b_5 > 0$$

$$H_2 = \begin{vmatrix} b_2 & b_4 \\ 1 & b_3 \end{vmatrix} = b_2 b_3 - b_4 > 0, \text{ iff } \; b_2 b_3 > b_4$$

$$H_3 = \begin{vmatrix} b_2 & b_4 & b_6 \\ b_1 & b_3 & b_5 \\ 0 & b_5 & b_4 \end{vmatrix} = b_2 \begin{vmatrix} b_3 & b_5 \\ b_5 & b_4 \end{vmatrix} - b_1 \begin{vmatrix} 1 & b_0 \\ 0 & 1 \end{vmatrix} = b_2 B_3 > b_0 b_3^2$$

$$b_1 b_2 b_3 - b_0 b_3^{\,2} - b_1^{\,2} = b_1 b_2 b_3 - (\mathrm{b}_0\, b_3^{\,2} + b_1^{\,2}) > 0 \text{ iff } b_1 b_2 b_3 > b_0 b_3^2 + b_1^3$$

$$H_4 = \begin{vmatrix} b_3 & b_1 & 0 & 0 \\ 1 & b_2 & b_0 & 0 \\ 0 & b_3 & b_1 & 0 \\ 0 & 1 & b_2 & b_0 \end{vmatrix} = b_3 \begin{vmatrix} b_2 & b_0 & 0 \\ b_3 & b_1 & 0 \\ 1 & b_2 & b_0 \end{vmatrix} - b_1 \begin{vmatrix} 1 & b_0 & 0 \\ 0 & b_1 & 0 \\ 0 & b_2 & b_0 \end{vmatrix}$$

$$= b_3 \left\{ b_2 \begin{vmatrix} b_1 & 0 \\ b_2 & b_0 \end{vmatrix} - b_0 \begin{vmatrix} b_3 & 0 \\ 1 & b_0 \end{vmatrix} \right\} - b_1 \left\{ 1 \begin{vmatrix} b_1 & 0 \\ b_2 & b_0 \end{vmatrix} - b_0 \begin{vmatrix} 0 & 0 \\ 0 & b_0 \end{vmatrix} \right\}$$

$$b_3 \left[b_0 b_1 b_2 - b_0 b_3) \right] - b_1 \left[b_0 b_1 \right]$$

$$b_0 b_1 b_2 b_3 - (\mathrm{b}_0\, b_1^{\,2} + b_0^{\,2} b_3^{\,2}) > 0 \text{ iff } b_0 b_1 b_2 b_3 > (\mathrm{b}_0\, b_1^{\,2} + b_0^{\,2} b_3^{\,2})$$

Therefore, all the Eigen values of the polynomial (85) have negative real parts, implying that $\lambda_7 < 0$ and $\lambda_8 < 0$. Since all the values of $\lambda_i < 0, \text{ for } i = 1,2,3,4,5,6,7,8. \text{when } R_0 < 1,$ we conclude that the disease-free equilibrium point is locally asymptotically stable.

4.4.5 Global stability of the disease free equilibrium point with both drug resistant TB *and* drug resistant TB

We used the method of [13] to obtain the global stability of the disease equilibrium point. Two conditions which guarantee the global stability of the disease- free state were considered.

Therefore, we recall lemma 1 and theorem 4. The system of equations (1) to (8) is re-write in the following form;

$$\left.\begin{aligned}\frac{dX}{dt} &= F(X,Z)\\ \frac{dZ}{dt} &= G(X,Z), G(X,0)=0\end{aligned}\right\} \tag{86}$$

Where $X=(V,\mathrm{S},R_R,R_S)$ denotes the number of uninfected individuals and $X\in R^3$, while $Z=(L_R\,\mathrm{L}_S,\mathrm{I}_R\,I_S)$ denotes the number of infected individuals and $Z\in R^4$. We represent the *disease*-free state by $E^0=(X^0,0)$.

Lemma 1: The point $K^0=(X^0,0)$ is called stable global asymptotic equilibrium point, if in addition $R_0<1$ and the conditions H_1 and H_2 holds. The following theorem is formed:

Theorem 8: Let $R_0<1$. Then the disease free equilibrium is globally asymptotically stable.

Proof:

Let $X=(S,V,R_R,R_S)$, $Z=(L_R,L_S,I_R,I_S)$ and $K^0=(X^0,0)$ where

$$X^0=(V^0,S^0,\mathrm{L}_R,L_S^0,\mathrm{I}_R\,I_S^0,\mathrm{R}_R^0\,R_S^0)=(\frac{\delta\Lambda}{k_1}+\frac{c((1-\delta)\Lambda k_1+\omega\delta\Lambda)}{k_1k_2-\omega c},\frac{(1-\delta)\Lambda k_1+\omega\delta\Lambda}{k_1k_2-\omega c},0,0,0,0,0,0) \tag{87}$$

$$X\in R^4$$

$$\left.\begin{aligned}&\delta\Lambda+cS-(\omega+d)V\\ &(1-\delta)\Lambda+\omega V-(c+d)S-(\alpha_{r_1}\eta-\alpha_{r_2}(1-\eta))I_RS-(\alpha_{s_1}\eta+\alpha_{s_2}(1-\eta))I_SS\\ &\nu_{r_2}\eta I_R+\nu_{r_1}L_R-dR_R\\ &\nu_{s_2}\eta I_S+\nu_{s_1}L_S-dR_S\end{aligned}\right\} \tag{88}$$

$$F\left(X,0\right)=\begin{pmatrix}\delta\Lambda-(\omega+d)V\\(1-\delta)-\left[(c+d)+m_1I_R\right]S-m_2I_SS\\0\\0\end{pmatrix} \tag{89}$$

Considering the following equations (3) to (6)

$Z\in R^4$

$$\left.\begin{aligned}\frac{dL_R}{dt}&=\left(1-\rho_r\right)\left(\alpha_{r_1}\eta+\alpha_{r_2}\left(1-\eta\right)\right)I_RS-\left(\nu_{r_1}+\theta_r+d\right)L_R\\\frac{dL_S}{dt}&=\left(1-\rho_s\right)\left(\alpha_{s_1}\eta+\alpha_{s_2}\left(1-\eta\right)\right)I_SS-\left(\nu_{s_1}+\theta_s+d\right)L_S\\\frac{dI_R}{dt}&=\rho_r\left(\alpha_{r_1}\eta+\alpha_{r_2}\left(1-\eta\right)\right)I_RS+\theta_rL_R-\left(\nu_{r_2}\eta+d_r+d\right)I_R\\\frac{dI_S}{dt}&=\rho_s\left(\alpha_{s_1}\eta+\alpha_{s_2}\left(1-\eta\right)\right)I_sS+\theta_sL_S-\left(\nu_{s_2}\eta+d_s+d\right)I_S\end{aligned}\right\} \tag{90}$$

$$A=\begin{bmatrix}-k_3&0&A_1S^0&0\\0&-k_5&0&A_3S^0\\\theta_r&0&A_2S^0-k_4&0\\0&\theta_s&0&A_4S^0-k_6\end{bmatrix} \tag{91}$$

$$AZ=\begin{bmatrix}-k_3&0&A_1S^0&0\\0&-k_5&0&A_3S^0\\\theta_r&0&A_2S^0-k_4&0\\0&\theta_s&0&A_4S^0-k_6\end{bmatrix}\begin{bmatrix}L_R\\L_S\\I_R\\I_S\end{bmatrix} \tag{92}$$

$$AZ=\begin{bmatrix}-k_3L_R+A_1S^0I_R&0\\0&-k_5L_S+A_2S^0I_S\\\theta_rL_R+(A_3S^0-k_4)I_R&0\\0&\theta_sL_S+(A_4S^0-k_6)I_S\end{bmatrix} \tag{93}$$

$$\hat{G}(X,Z)=AZ-G(X,Z) \tag{94}$$

$$\hat{G}(\mathrm{X},Z)=\begin{bmatrix} -k_3L_R+A_1S^0I_R & 0 \\ 0 & -k_5L_S+A_2S^0I_S \\ \theta_rL_R+(A_3S^0-k_4)I_R & 0 \\ 0 & \theta_sL_S+(A_4S^0-k_6)I_S \end{bmatrix}-\begin{bmatrix} A_1I_RS-k_3L_R \\ A_2I_SS-k_5L_S \\ A_3I_RS+\theta_rL_R-k_4I_R \\ A_4I_SS+\theta_sL_S-k_6I_S \end{bmatrix}$$

$$\hat{G}(X,Z)=\begin{pmatrix} \hat{G}_1(X,Z) \\ \hat{G}_2(X,Z) \\ \hat{G}_3(X,Z) \\ \hat{G}_4(X,Z) \end{pmatrix}=\begin{pmatrix} (1-\rho_r)(\alpha_{r_1}\eta+\alpha_{r_2}(1-\eta))L_R\left(S^0-S\right) \\ (1-\rho_s)(\alpha_{s_1}\eta+\alpha_{s_2}(1-\eta))L_S\left(S^0-S\right) \\ \rho_r(\alpha_{r_1}\eta+\alpha_{r_2}(1-\eta))I_R\left(S^0-S\right) \\ \rho_s(\alpha_{s_1}\eta+\alpha_{s_2}(1-\eta))I_S\left(S^0-S\right) \end{pmatrix} \quad (95)$$

Therefore, since $S\le S^0$ we have $\hat{G}_1(X,Z),\hat{G}_2(X,Z),\hat{G}_3(X,Z),\hat{G}(X,Z)\ge 0$ the global stability of $X^0=(\mathrm{V}^0,S^0,0,0,0)$. The system of $\frac{dX}{dt}=F(X^0,0)$ is easy to verify. Therefore X^0 is globally asymptotically stable if $R_0<1$. This completes the proof.

5.0 Numerical Results

We present the numerical simulation for the TB model with drug resistance and sensitivity incorporating case detection. The graphs are generated using Table 1 and the results presented in Figures 4.1 to 4.32. We implemented the numerical results for four (4) cases namely: Dynamics of the compartments with respect to time; variation of case detection; variation of transmission rate and variation of treatment rate.

Table 1: Variables and parameters values used for computational results

Variable/Parameter	Values	Reference
V	900	[14]
S	3800	[14]
L_R	1800	Assumed
L_S	100	Assumed
I_R	50	[14]
I_S	200	[14]
R_R	20	[14]
R_S	30	[14]

ρ_S	0.1	[14]
ρ_R	0.1	[14]
νr_1	0.8	[14]
νr_2	0.8	[14]
θ_r	0.7	[14]
θ_s	0.7	[14]
ω	0.67	Assumed
δ	0.10	[14]
c	0.715	Assumed
d	0.075	[15]
d_r	0.32	[14]
d_s	0.32	[15]
η	0.57	[15]
Λ	18	[15]
θ_r	0.7	[16]
θ_s	0.7	[16]
α_{r_1}	0.01	[15]
α_{r_2}	0.03	[15]

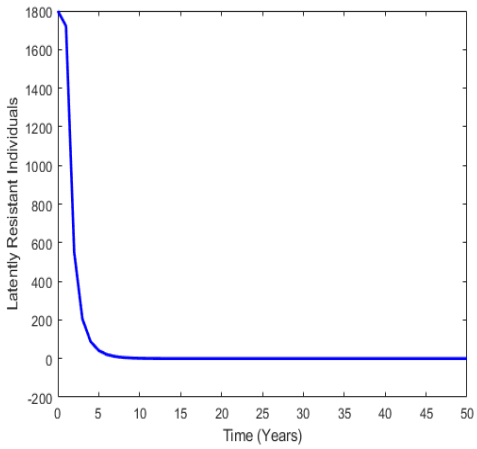


Fig.2 Dynamics of vaccinated individuals

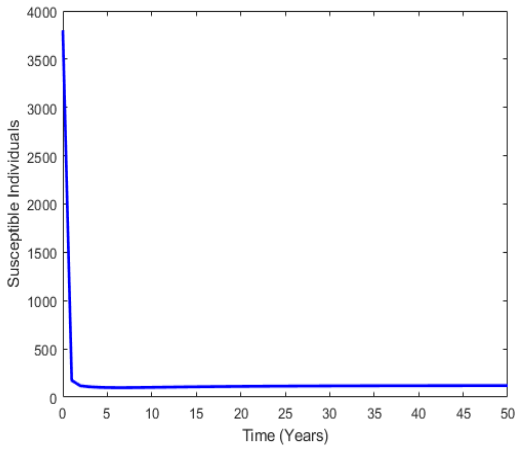


Fig.3 Dynamics of susceptible individuals

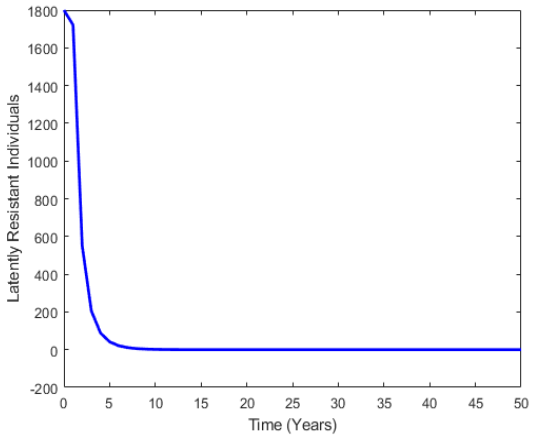


Fig.4 Dynamics of latently resistant persons

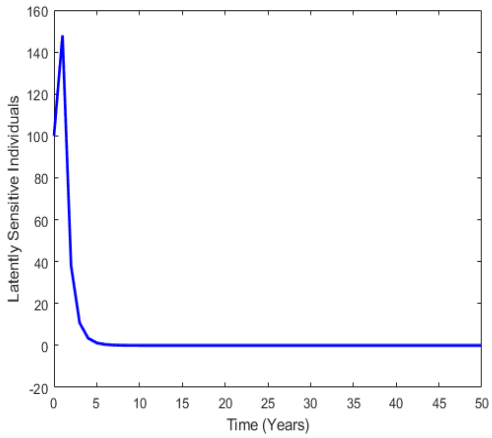


Fig.5 Dynamics of latently sensitive persons

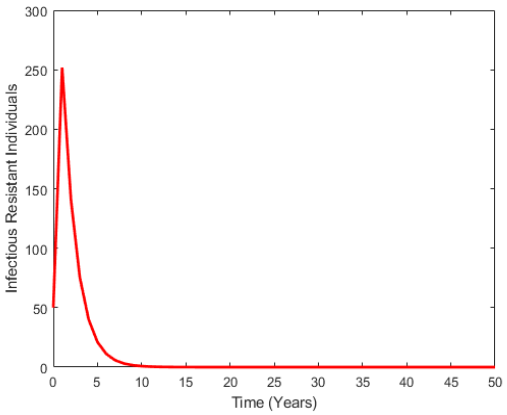


Fig.6: infectious resistant individuals

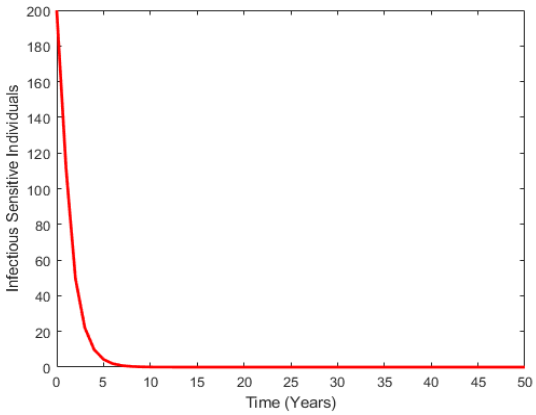


Fig.7: infectious sensitive individuals

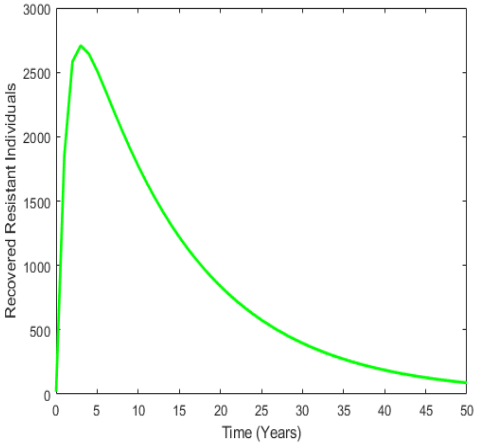


Fig.8: recovered resistant individuals

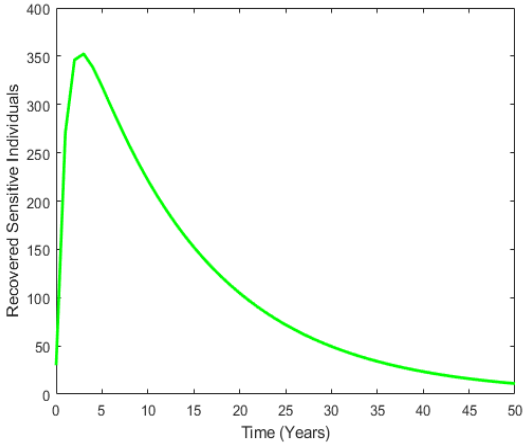
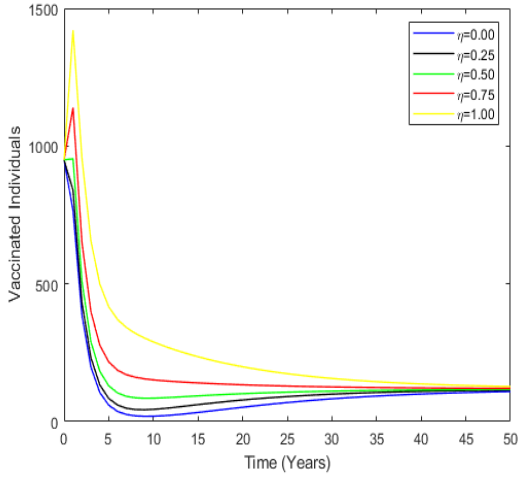


Fig.9: recovered sensitive individuals



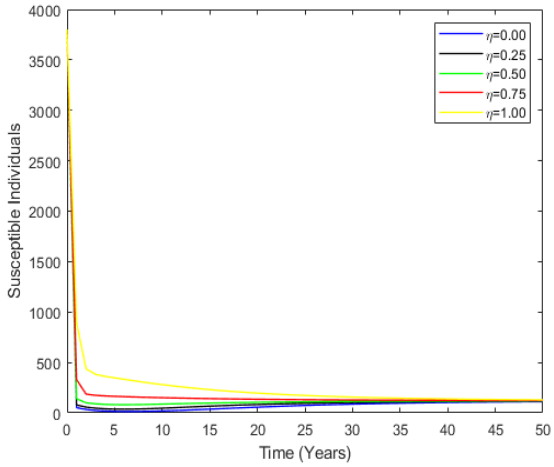
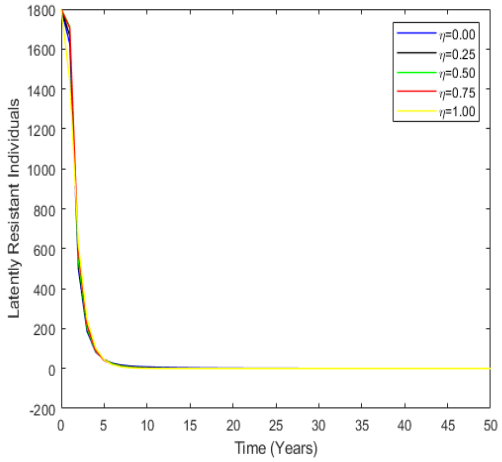


Fig.10 vaccinated when case detection is varied. Fig.11 susceptible when case is varied



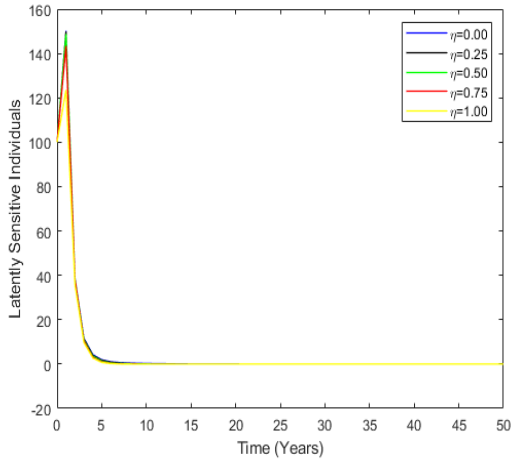


Fig.12: latently resistant when case is varied. Fig.13. latently sensitive when case is varied

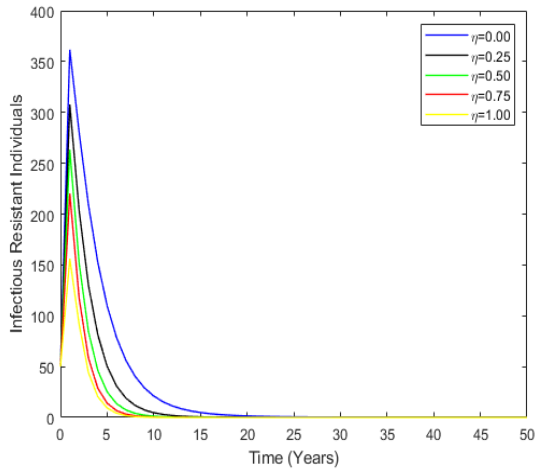


Fig.14: infectious resistant when case varied.

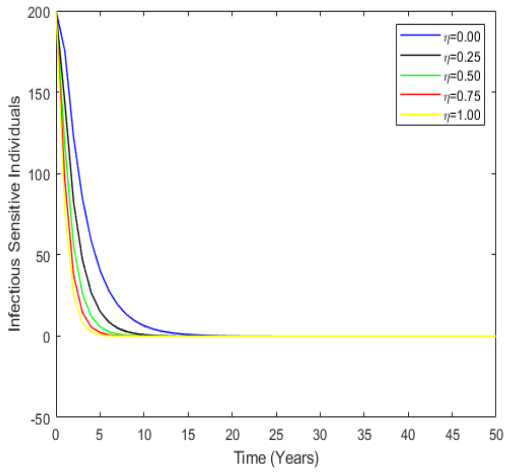


Fig.15: infectious sensitive when case varied

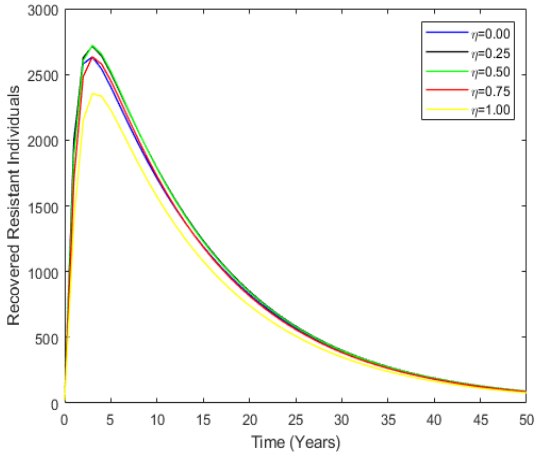


Fig.16 recovered resistant when case is varied.

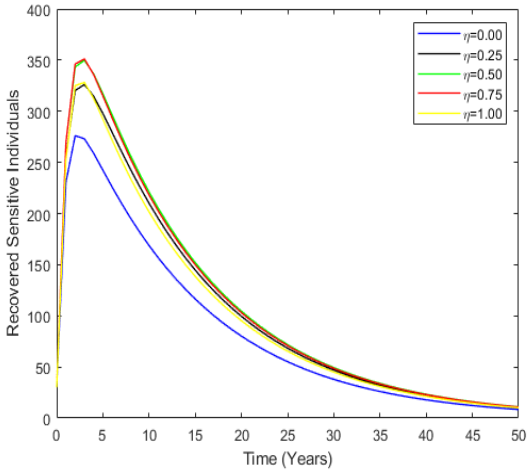
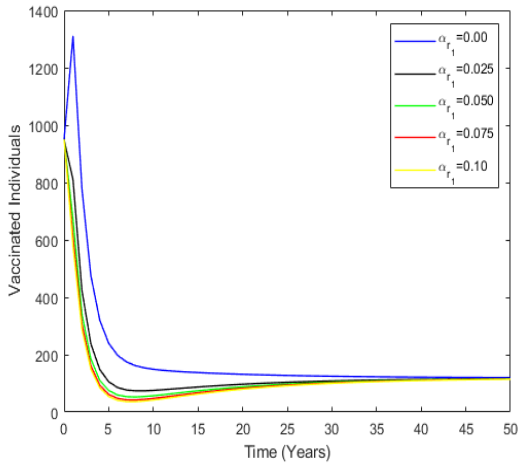


Fig.17 recovered sensitive when case is varied



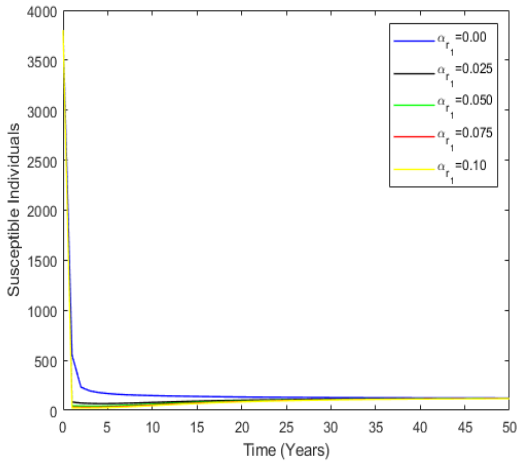
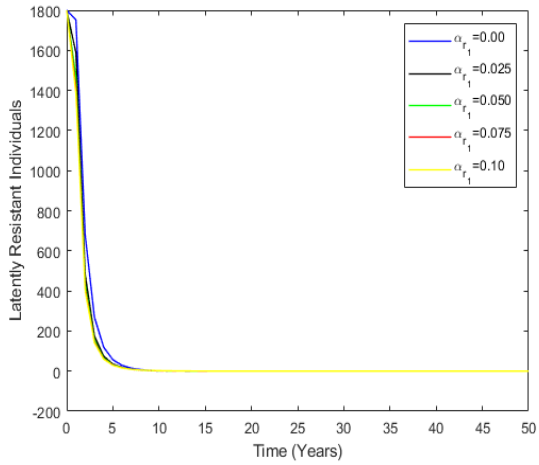


Fig.18: Vaccinated when cases is varied. Fig.19: Susceptible when cases are varied



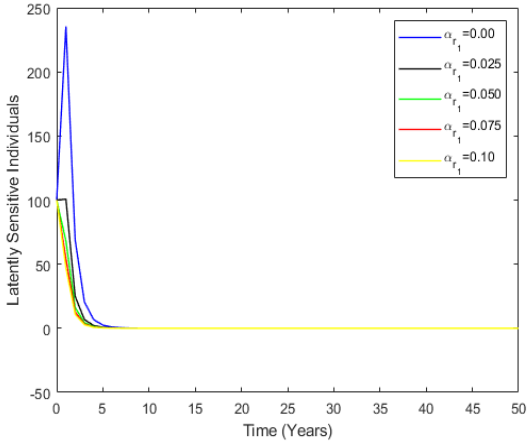


Fig.20: Latently resistant when cases is varied. Fig.21: Latently sensitive when cases is varied

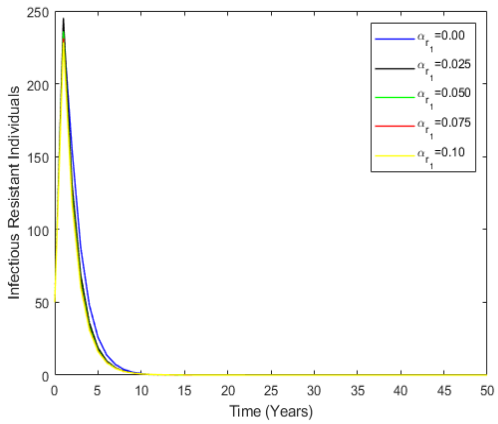


Fig.22: Infectious resistant when cases varied.

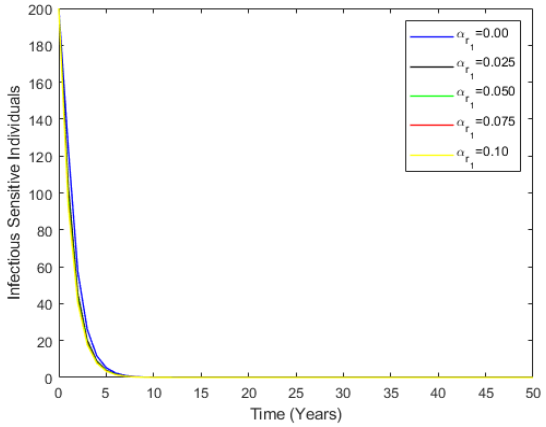


Fig.23: Infectious sensitive when cases varied

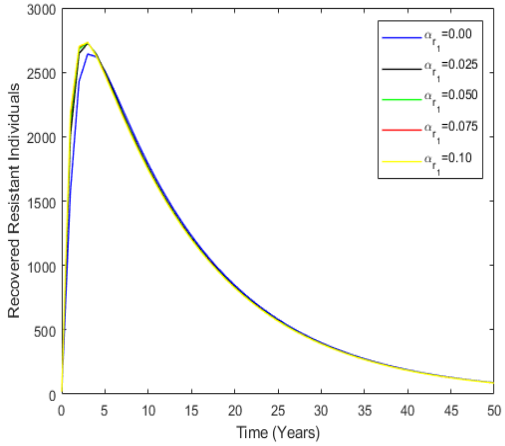


Fig.24:Recovered resistant when cases varied.

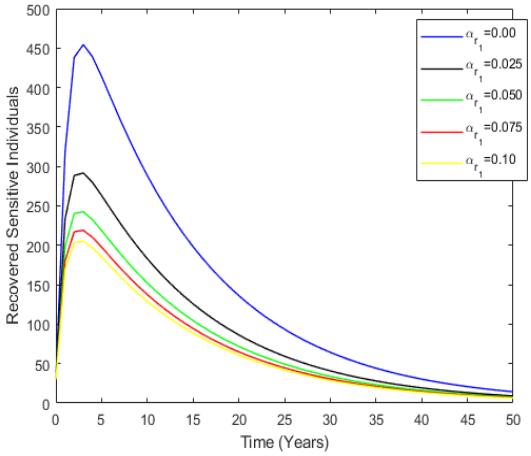
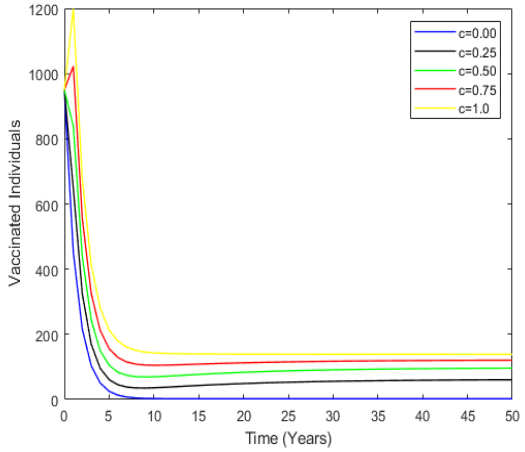


Fig.25 Recovered sensitive when cases varied



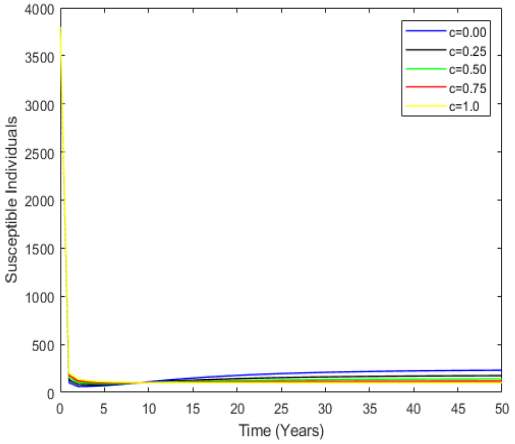
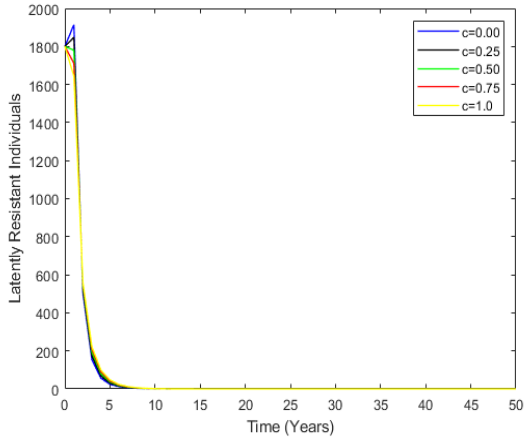


Fig.26: Vaccinated when vaccination varied. Fig.27: Susceptible when vaccination varied



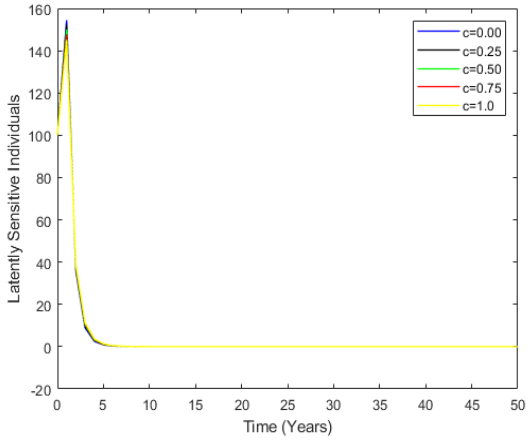
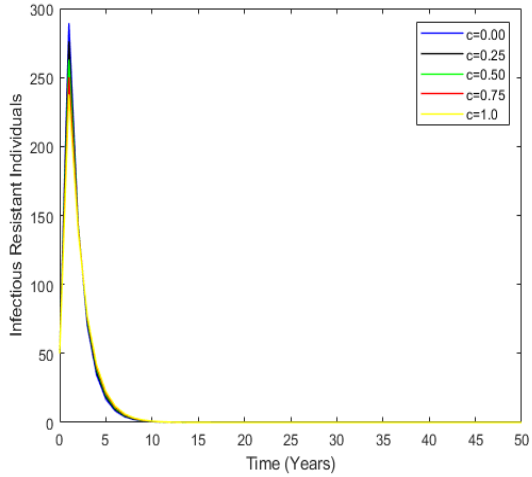


Fig.28:Latently resistant when vaccination varied Fig.29:Latently sensitive when vaccination varied



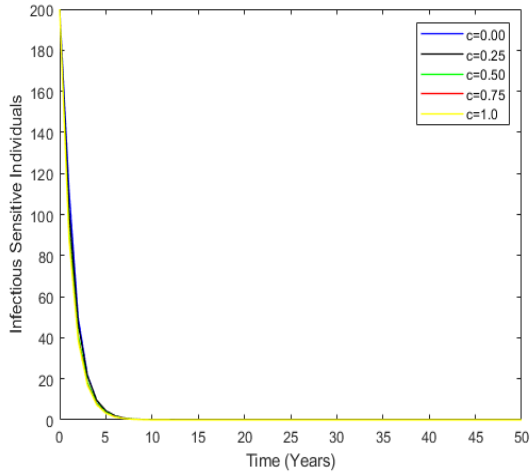
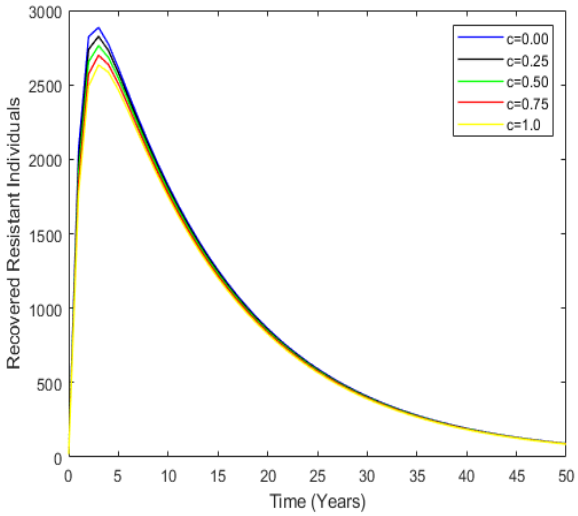


Fig.30: Infectious resistant when vaccination varied. Fig.31: Infectious sensitive when



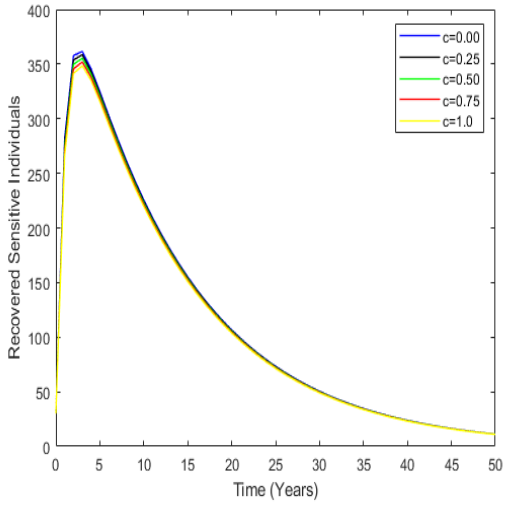


Fig.32: Recovered resistant when vaccination varied. Fig.33: Recovered sensitive when Vaccination rate is varied

6.0 Discussion of simulation results

6.1. Simulation results for models with the impact of drug resistant and drug sensitive *TB*

From figure (2), we observed that the population of vaccinated individuals decreases and later stabilizes to a certain level as a result of winning of vaccine. Figure (3) revealed that susceptible individuals drop sharply over time. This resulted from the fact that latently infected individuals with DS-TB, latently infected individuals with DR-TB, infectious individuals with DS-TB and infectious individuals with DS-TB influence the potentially ones thereby reducing the number of susceptible ones.

From Figure (4), we observed that the population of latently resistant infected individuals with drug resistance TB decreases slowly then sharply to a certain level. Latently infected individuals with drug sensitive TB rises gradually for year two, drops sharply and stabilises at year five and as depicted in Figure (5)

From Figure (6) we observe that the population of infectious individuals with drug resistant TB raised exponentially in the period of two years and later drops drastically to steady point. In Figure (7), it was observed that the population of infectious individuals with drug resistant TB decreases and stabilizes at year five.

We observed from Figure (8) that the population of recovered individuals with Drug resistant-TB increased exponentially over time and later decreases gradually over time. It was observed from Figure (9) that the population of recovered individuals with Drug sensitive TB increases over time before dropping drops down over a period of time

6.2 Simulation results when case detection is varied

In Figure (10) it was observed that there is a significant impact of case detection on the vaccinated individuals. This implies that as the rate of case detection increases in the population, Figure (10) shows that the vaccinated individuals rapidly increased due to case detection. Figure (11) shows no significant effect of case detection on the susceptible individuals. This implies that as the case detection rate increases over time, susceptible individuals reduces and later stabilizes.

In Figure (12) we observed that there is significant impact of case detection on the latently infected individuals with DR-TB individuals. This implies that as the case detection rate increases, latently infectious individuals with DR-TB decreases and stabilizes at a minimal point due to case detection. Similarly, Figures (13) revealed that as the rate of case detection increases, the latently infected individuals increases and later decreases sharply as there is a great impact of case detection as shown in Figure (13).

Figure (14) shows that as the rate of case detection increases, the infected individuals with DR-TB grows sharply, decreases over a time and later stabilizes over a period of time. Likewise Figure (15) revealed that as the rate of case detection increases, the infected individuals with DS-TB decreases as a result of case detection.

Figure (16) shows that as the rate of case detection increases, the recovered individuals with DR-TB increases over time and gradually decreases within a period of five years and

stabilized. Figure (17) shows that as the rate of case detection increases, the recovered individuals with DS-TB increases over time and gradually decreases within a period of five years and stabilizes

6.3 Simulation results when transmission rate with case detection is varied

Figure (18) we observed that as the transmission rate of detected cases increase, there is is an increase in number of vaccinated individuals. As the transmission rate of detected cases increases, susceptible individuals depicted sharply in Figure (19).

Figure (20) shows that as the transmission rate of detected cases increases, the latently infected individuals with DR-TB drops and later stabilizes. Figure (21) shows that as the transmission rate of detected cases increases, the latently infected individuals with DS-TB increases sharply. As the transmission rate of case detection rate increases, latently infected individual increases, and later stabilizes over a period of time.

Figure (22) has shown that as there is no transmission rate of detected cases, the latently infected individuals with DR-TB increase and later stabilized over a period of time. Figure (23) has shown that as transmission rate of detected cases increases, the latently infected individuals with DS-TB decrease and later stabilized over a period of time.

6.4 Simulation results when vaccination rate varied

Figure (26) has shown that as the vaccination rate increases, the number of vaccinated individual increases over a period of time. For the decrease in vaccination rate the number of vaccinated individuals also decreases.

From Figure (27) it was observed that as the number of vaccination rate increases or decreases it has no impact on susceptible individuals.

Figure (28) revealed that as the number of vaccination rate increases, the number of latently infected individuals with DR-TB decreases as a result of susceptible individuals been vaccinated. As the vaccination rate decreases individuals in a latently infected individuals with DR- TB increases. As the vaccination rate increases, the latently infected individuals with DR-TB increases exponentially and later dropped sharply over a period of time and then stabilized as revealed in Figure (29)

From Figure (30) it was shown that when the vaccination rate increases, the infected individuals with DR-TB increases and later decreases sharply over a period of time. As the vaccination rate increases, the infected individuals with DS-TB decreases over a period of time as shown in Figure (31)

From Figure (32) as the vaccination rate increases, the number of recovered individuals with DR-TB increases exponentially. It decreases over a period of time due to the winning of vaccine. Figure (33) has shown that the number of recovered individuals with DR-TB increases and later decreases gradually as a result of individuals coming into the susceptible class.

7.0 Conclusion

This paper presents a realistic deterministic model for the transmission dynamics of tuberculosis with case detection.. In contrast to many tuberculosis models in literature, we incorporate vaccine, fast and slow progression, case detection, drug resistant class and drug sensitive TB for tuberculosis into the existing model by [15].

Analytical study was carried out and the results shows that the disease free equilibrium points are locally asymptotically stable whenever $R_0 < 1$ and global asymptotically stable whenever $R_0 \leq 1$. The simulation carried out shows that case detection is vital in the eradication of TB in a population.

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