IOSR Journal of Mathematics (IOSR-JM)
e-ISSN: 2278-5728, p-ISSN:2319-765X. Volume 10, Issue 2 Ver. I (Mar-Apr. 2014), PP 26-50
www.iosrjournals.org

Modelling the Effect of DOTS and Isolation on TB Transmission Dynamics

S. O. Adewale[1], I. A. Olopade[2], S. Garba[3] and P. O. Olanrewaju[4]
[1](Department of P/A Mathematics, Ladoke Akintola University of Technology, LAUTECH Ogbomoso, Nigeria.)
[2](Department of P/A Mathematics, Ladoke Akintola University of Technology, LAUTECH Ogbomoso, Nigeria.)
[3](Department of Mathematics, University of Pretoria, South Africa.)
[4](Department of Mathematical Science Oduduwa University, Ipetumodu, Nigeria.)

Abstract: *A deterministic model for the transmission dynamics of Tuberculosis (TB) under Direct Observation Therapy Strategy (DOTS) and Isolation in Nigeria is developed and rigorously analysed. The model, consisting of mutually-exclusive epidemiological compartments representing the number of undetected, detected and isolated individuals who are treated under DOTS programme and those who developed Multi-drug resistance. The model has a disease free equilibrium (DFE), which is locally asymptotically stable, whenever the maximum of the associated reproduction numbers of the model (denoted by R_c) is less than unity. Furthermore, the model undergoes a backward bifurcation, where the disease-free equilibrium co-exists with a stable endemic equilibrium. Numerical simulations, using epidemiological and demographic data relevant to Nigeria obtained from WHO and USAID [35,36,38], shows that provided the rate at which the undetected individuals with active TB recovered exceeded a critical values, then DOTS, the STOP TB initiative programme of WHO can lead to effective elimination of TB in Nigeria. This suggest that the detection rate plays significant role in the elimination of TB. Furthermore, it is shown that if the progress or rate of individuals who are susceptible to TB is low, it can also lead to elimination of the disease in Nigeria. The results also shows that if the effective contact rate (β) for TB infection remains below certain critical value (0.187), the disease can be eliminated.*

Keywords: *Bifurcation, Case Detection Rate (CDR), DOTS, Dynamical system, Reproduction number, Tuberculosis.*

I. Introduction

Tuberculosis (TB), an airborne-transmitted disease caused by the bacterium Mycobacterium tuberculosis, remains one of the most important public health challenges for decades. In addition to affecting at least one-third of the human population (2 billion people), TB is the second greatest contributor of adult mortality amongst infectious disease (causing at least 2 million death a year globally) [1, 15, 35, 36, 37]. Owing to the rising deaths and infection rates (especially in developing countries), the World Health Organization (WHO) declared TB as a global public health emergence in 1993 [14, 21]. Over 80% of all TB patients live in 22 countries, mostly in sub-saharan Africa and Asia.

Over the years, a number of global initiatives, spearheaded by WHO, were embarked upon with the hope of minimizing the burden of TB worldwide (in particular, to achieve the Millennium Development Goal of halting ang beginning to reverse the incidence of TB by 2015). These include the "Stop TB Partnership", "International Standards of Tuberculosis care and patient's care" and the "Global Plan to Stop TB" [1]. A notable medical contribution in TB control was the introduction of antibiotics, which resulted in significant decrease in mortality (for instance, a 70% reduction in TB-related mortality was recorded in the USA between 1945 to 1955 [3,13,23]). TB-infected people can be effectively treated using multiple drugs via the Direct Observation Therapy Strategy (DOTS) [40]. However, if not strictly complied to or administered wrongly, such therapy may lead to the evolution and development of multi-drug resistant TB (MDR-TB) [8].

Numerous modelling studies have been carried out to gain insights into the transmission dynamics and control of TB spread in human population (see, for instance [3, 10, 15, 17, 22, 23, 29, 33]). The purpose of the current study is to provide a rigorous mathematical analysis of a model for TB spread in the presence of DOTS and isolation of infectious INDIVIDUALS. The model to be designed is an extension of many of the models in the aforementioned studies.

The paper is organized as follows. The model is formulated in section 2, and is qualitatively analysed in section 3. Some numerical simulation results are provided in section 4. In particular, a case study, for TB dynamics in Nigeria is considered.

II. Model Formulation

The total homogeneously-mixing population at time t, denoted by N (t), is subdivided into mutually-exclusive compartments of, susceptible (S (t)),exposed (E(t)), undetected infectious (T_U(t)), detected infectious (T_D(t)), isolated (J (t)), treated (H (t)) and those who failed treatment (F(t)) individuals, so that

$$N(t) = S(t) + E(t) + T_U(t) + T_D(t) + J(t) + H(t) + F(t)$$

The susceptible population is increased by recruitment (either by birth or immigration) into the population (all recruited individuals are assumed to be susceptible) at a rate II. This population is decreased by infection, which can be acquired following effective contact with infectious individuals in the undetected (T_U), detected (T_D), isolated (J), treated (H) or failed treatment (F) category, at a rate given by:

$$\lambda = \frac{\beta(T_U + \eta_D T_D + \eta_J J + \eta_F F + \eta_H H}{N} \qquad (1)$$

In (1), β represents the effective contact rate (i.e., contact capable of leading to infection), η_D is a modification parameter comparing the transmissibility of detected infectious individuals in relationship to undetected infectious individuals. Since detected individuals are offered treatment and/or isolation, it is intuitive to assume that $\eta_D \leq 1$. Similarly, η_J, η_F and η_H are modification parameters comparing the transmissibility of infectious individuals in the isolated, failed treatment and treated classes, respectively, with those in the undetected infectious class. Here, $\eta_J \leq 1$ (since isolated individuals have reduced contact and are offered treatment during isolation), $\eta_H \leq 1$ (since treatment reduces transmissibility) and $\eta_F \leq 1$. Finally, this population decreases by natural death at a rate . Thus, the rate of change of the susceptible population is given by

$$\frac{dS}{dt} = \prod - \lambda S - \mu S \qquad (2)$$

A fraction, ξ , of new infected individuals move to the exposed class (E), while the remaining fraction, (1-ξ), move to the infectious undetected class (fast progressors) T_U. The population of exposed individuals is further increased by the natural recovery rate of undetected individuals (at the rate υ), by the reversion of individual s who failed treatment (at a rate $\theta_1 \rho$, where $\theta_1 < 1$) and by individuals who are successfully treated (at a rate rα , with r < 1 representing the fraction of treated individuals). This population is decreased by progression to active TB (at a rate κ), exogenous re-infection (at a rate $\psi\lambda$, where ψ < 1 accounts for the assumption that exposed individuals have reduced infection rate in comparison to wholly susceptible individuals) and natural death (at the rate μ). Thus,

$$\frac{dE}{dt} = \xi\lambda S + \upsilon T_U + \theta_1 \rho F + r\alpha H - (\kappa + \psi\lambda + \mu)E \qquad (3)$$

The population of undetected infectious individuals is increased by the new infection of fast progressors (at the rate (1-ξ)λ) and the development of symptoms by exposed individuals (at the rate $(1-\omega_1)\kappa$, where ω_1 is the fraction of exposed individuals who develop symptoms and are detected), exogenous re-infection of exposed individuals (at the rate $(1-\omega_2)\psi\lambda$, where ω_2 is the fraction of re-infected individuals who are detected) and by individuals who failed treatment (at the rate $\theta_2\rho$). This population is decreased by natural recovery (at the rate *v*), detection (at a rate γU), natural death (at the rate μ) and disease-induced death (at a rate δ_U). Hence,

$$\frac{dT_U}{dt} = (1-\xi)\lambda S + (1-\omega_1)\kappa E + (1-\omega_2)\psi\lambda E + \theta_2\rho F - (\upsilon + \gamma U + \mu + \delta_U)T_U \qquad (4)$$

The population of detected individuals increases by the detection of exposed individuals (at the rates $\omega_1\kappa$ and $\omega_2\psi\lambda$), undetected individuals (at the rate γU)and failed treated individuals (at a rate $[1-(\theta_1+\theta_2)]\rho$) . The population is decreased by isolation (at the rate σ), treatment (at a rate τ_1), natural death (at the rate μ) and disease-induced death (at a rate $\delta_D < \delta_U$). This gives

$$\frac{dT_D}{dt} = \omega_1\kappa E + \omega_2\psi\lambda E + \gamma_U T_U + [1-(\theta_1+\theta_2)]\rho F - (\sigma + \tau_1 + \mu + \delta_D)T_D \qquad (5)$$

The population of isolated individuals is generated by the isolation of detected individuals (at the rate σ). It diminishes due to treatment (at a rate τ_2), natural death (at the rate μ) and disease-induced death (at a rate $\delta_J < \delta_U$). Hence,

$$\frac{dJ}{dt} = \sigma T_D - (\tau_2 + \mu + \delta_J)J \tag{6}$$

Individuals in the F class are those in whom treatment has failed. This (treatment failure) could be due to a number of reasons such as incomplete compliance to the specified treatment regimen, development of resistance etc. This population is generated by the failure of treatment in detected individuals (at the rate $(1-q_1)\tau_1)$, isolated individuals (at the rate $(1-q_2)\tau_2)$ and treated individuals (at a rate $1-r)\alpha)$. In addition to natural death (at the rate μ) and disease-induced mortality (at the rate δF), individuals can leave this class and move to the exposed class (at the rate $\theta_1\rho$), undetected class (at the rate $\theta_2\rho$) and detected class (at the rate $[1-(\theta_1+\theta_2)]\rho)$). In other words, it is assumed that individuals in whom treatment has failed can eventually become latent naturally (i.e., move to the E class) or remain infectious (and join either T_U or T_D class). It should be noted that the fractions θ_1 and θ_2 are such that $\theta_1 + \theta_2 \leq 1$. Thus,

$$\frac{dF}{dt} = (1-q_1)\tau_1 T_D + (1-q_2)\tau_2 J + (1-r)\alpha H - (\rho + \mu + \delta_F)F \tag{7}$$

The population of treated individuals is increased by the treatment of detected individuals (at the rate $q_1\tau_1$) and isolated individuals (at the rate $q_2\tau_2$). Since there is no cure for TB, successfully-treated individual as eventually move to the exposed class (at the rate α). This population is further decreased by natural death (at the rate μ) and disease-induced death (at a rate $\delta_H < \delta_D$). Hence

$$\frac{dH}{dt} = q_1\tau_1 T_D + q_2\tau_2 J - (\alpha + \mu + \delta_H)H \tag{8}$$

Thus, in summary, the TB treatment and isolation model is given by the following system of non-linear differential equations (a flow diagram is depicted in figure 3; the associated variables and parameters are described in Tables 2 and 3).

$$\begin{aligned}
\frac{dS}{dt} &= \prod -\lambda S - \mu S \\
\frac{dE}{dt} &= \xi\lambda S + \upsilon T_U + \theta_1\rho F + r\alpha H - (\kappa + \psi\lambda + \mu)E \\
\frac{dT_U}{dt} &= (1-\xi)\lambda S + (1-\omega_1)\kappa E + (1-\omega_2)\psi\lambda E + \theta_2\rho F - (\upsilon + \gamma_u + \mu + \delta_U)T_U \\
\frac{dT_D}{dt} &= \omega_1\kappa E + \omega_2\psi\lambda E + \gamma_U T_U + [1-(\theta_1+\theta_2)]\rho F - (\sigma + \tau_1 + \mu + \delta_D)T_D \\
\frac{dJ}{dt} &= \sigma T_D - (\tau_2 + \mu + \delta_J)J \\
\frac{dF}{dt} &= (1-q_1)\tau_1 T_D + (1-q_2)\tau_2 J + (1-r)\alpha H - (\rho + \mu + \delta_F)F \\
\frac{dH}{dt} &= q_1\tau_1 T_D + q_2\tau_2 J - (\alpha + \mu + \delta_H)H
\end{aligned} \tag{9}$$

The essential features of the model (9) are:

(i) allows for infection by individuals in all infected classes (T_U; T_D; J; F; H) with exception of those in the exposed class;

(ii) allows for exogenous re-infection (at the rate $\psi\lambda$) and endogenous re-activation (at the rate κ);

(iii) allows for slow progression (at the rate $\xi\lambda$) and fast progression (at the rate $\xi\lambda$ to disease;

(iv) treatment and isolation of infected individuals, and allowing for the possibility of treatment failure. Individuals who failed treatment are distributed into the exposed or infectious classes for detected and undetected individuals;

(v) exposed individuals who develop symptoms (either due to re-activation or reinfection) are distributed into the undetected and detected classes.

The model extends some of the earlier models, such as those in [1, 8, 23], by including;

(a) the isolated class (J),
(b) the failed treatment class (F),
(c) slow and fast progression aspect of TB disease(ξ), and
(d) screening and detection of undetected infectious individuals (at the rate λU).

Using a set of demographic and epidemiological data relevant to Nigeria (given in Table 1), the model (9) gives a reasonable fit of the observed TB burden data from Nigeria for the period 2000-2007 [36, 37] as depicted in Figure 4. This shows that the model can be used to gain insights into TB transmission dynamics in a population such as Nigeria.

III. Analysis Of The Model

Lemma 1: The closed set $D=\left\{(S,E,T_u,T_d,J,F,H)\in\Re_+^7 : N\le\frac{\prod}{\mu}\right\}$ is positively-invariant and attracting with respect to model (9).

Proof 1: Consider the biologically-feasible region, $D=\left\{(S,E,T_u,T_d,J,F,H)\in\Re_+^7 : N\le\frac{\prod}{\mu}\right\}$

We shall show that D is positive invariance (i.e; all solutions in D remain in D for all time t > 0). The rate of change of the total population, obtained by adding all the equations in model (9), is given by:

$$\frac{dN}{dt}=\prod-\mu N-\delta_U T_U-\delta_D T_D-\delta_J J-\delta_F F \qquad (10)$$

It follows that $\frac{dN}{dt}<0$ whenever $N>\frac{\prod}{\mu}$. Note that $\frac{dN}{dt}$ is bounded by $\prod-\mu N$, and a standard comparison theorem [32] can be sued to show that $N(t)\le N(0)e^{-\mu t}+\frac{\prod}{\mu}(1-e^{-\mu t})$. In particular $N(t)\le\frac{\prod}{\mu}$, if $N(0)\le\frac{\prod}{\mu}$,. Therefore, all solution of the model with initial conditions in D remains there for t>0 (i.e. the w-limits sets of the system (9) are contained in D). This implies that D is positively-invariant and attracting. In this region, the model can be considered as been epidemiologically and mathematically well-posed [19].

3.1 DISEASE FREE EQUILIBRIUM (DFE)

The model (9) has a disease free equilibrium (DFE) given by

$$C_0=\left(S^*,E^*,T_U^*,T_D^*,J^*,F^*,H^*\right)=\left(\frac{\prod}{\mu},0,0,0,0,0,0\right) \qquad (11)$$

Using the next generation matrix (see[25])/ The non-negative matrix F (of the new infection terms) and the non-singular matrix V are given, respectively by:

$$F=\begin{bmatrix}F_1 & F_2\\ 0 & 0\end{bmatrix}$$

Where,

$$F_1=\begin{bmatrix}0 & \xi\beta & \xi\beta\eta\rho\\ 0 & (1-\xi)\beta & (1-\xi)\beta\eta\rho\\ 0 & 0 & 0\end{bmatrix},\qquad F_2=\begin{bmatrix}\xi\beta\eta_J & \xi\beta\eta_F & \xi\beta\eta_H\\ (1-\xi)\beta\eta_J & (1-\xi)\beta\eta_F & (1-\xi)\beta\eta_H\\ 0 & 0 & 0\end{bmatrix}$$

$$V=\begin{bmatrix}V_1 & V_2\\ V_3 & V_4\end{bmatrix}$$

Where

$$V_1 = \begin{bmatrix} K_1 & -\nu & 0 \\ -(1-\omega_1)\kappa & K_2 & 0 \\ -\omega_1\kappa & -\gamma\upsilon & K_3 \end{bmatrix}, V_2 = \begin{bmatrix} 0 & -\rho\theta_1 & -r\alpha \\ 0 & -\rho\theta_2 & 0 \\ 0 & -(1-\theta_1+\theta_2))\rho & 0 \end{bmatrix}$$

$$V_3 = \begin{bmatrix} 0 & 0 & -\sigma \\ 0 & 0 & (1-q_1)\tau_1 \\ 0 & 0 & q_1\tau_1 \end{bmatrix}, \qquad V_4 = \begin{bmatrix} K_4 & 0 & 0 \\ -(1-q_2)\tau_2 & K_5 & -(1-\tau)\alpha \\ -q_2\tau_2 & 0 & K_0 \end{bmatrix}$$

and, $K_1 = \kappa + \mu,\ K_2 = \upsilon + \gamma U + \mu,\ K_3 = \sigma + \tau_1 + \mu + \delta_D,\ K_4 = \tau_2 + \mu + \delta_J$

$K_5 = \rho + \mu + \delta_F,\ K_6 = \alpha + \mu + \delta_H$

Define,

$$R_1 = \frac{\beta(1-\xi)(K_1K_3 + \eta D\gamma UK_1 + \eta D\kappa\upsilon\omega_1) + (1-\omega_1)(\xi\kappa K_3 + \xi\kappa\eta D\gamma\upsilon) + \xi\kappa\eta D\omega_1 K_2]}{K_3[K_1K_2 + \upsilon\kappa(\omega_1 - 1)]} \tag{12}$$

$$R_2 = \frac{\beta(1-\xi)\eta_F K_1K_3 + (1-q_2)\xi\eta_F\tau_2K_{61} + (1-\tau)\xi\eta_F\tau_2\alpha q_2 + \xi\eta_J K_5K_6 + \xi\eta_H\alpha q_2K_5]}{K_4K_5K_6}$$

It follows that the basic reproduction number, denoted by Rc, is given $R_C = \sigma(FV^{-1}) = \max\{\Re_1, \Re_2\}$ where σ denotes the spectral radius (dominant eigenvalue magnitude) of the next generation matrix F V^{-1}. Hence, using Theorem (2) of [25], we have established the following result.

Lemma 2: The DFE of the model (9), given by (10), is locally asymptotically stable (LAS) if Rc < 1, and unstable if Rc > 1.

The threshold quantity, Rc, is the reproduction number for the model. It measures the average number of new TB infections generated by a single TB-infected individual in a population where a certain fraction of infected individuals are treated and/or isolated. The epidemiological implication of Lemma 2 is that TB can be controlled in the community (when Rc < 1) if the initial sizes of the sub-populations of the model are in the basin of attraction of c_0. Since TB models are often shown to exhibit the phenomenon of backward bifurcation [23], where the stable DFE co-exists with a stable endemic equilibrium when the associated reproduction threshold (Rc) is less than unit, it is instructive to determine whether or not the TB dynamics model (9) exhibits this feature. This is investigated below,

Theorem 1: The model (9) undergoes a backward bifurcation at R_c=1 if

$$a = \frac{2\beta\mu}{\pi}(\xi\upsilon_3(\omega_2 + \omega_{23} + \omega_1 + \omega_5 + \omega_6 + \omega_7) + \upsilon_1(\omega_2 + \omega_{23} + \omega_1 + \omega_5 + \omega_6 + \omega_7) +$$

$$\omega_2\psi(1-\omega_2)\upsilon_3 + \upsilon_4\omega_2 - \upsilon_2) - \xi\upsilon_2(\omega_2 + \omega_{23} + \omega_1 + \omega_5 + \omega_6 + \omega_7) - \upsilon_3((\omega_2 + \omega_{23} + \omega_1$$

$$+ \omega_5 + \omega_6 + \omega_7))((\eta_H\omega_3 + \eta_F\omega_{43} + \omega_5 + \eta_D\omega_6 + \eta_J\omega_7)\ \textit{is positive}$$

The proof, based on the centre Manifold theory, is given in Appendix A.

3.2: GLOBAL STABILITY OF THE DFE

Here, the global asymptotic stability (GAS) property of the DFE of the model (9) will be explored for the case $\psi = 0$ (i.e, in the absence of re-infection). By letting $\psi = \delta_U = \delta_D = \delta_J = \delta_F = \delta_H = 0$ in the model (9), it follows that $S = N^* - E - T_u - T_d - J - F - H$ at steady state. Hence, the global stability of ε_0 can be established by considering the following mass action equivalent of the model (9).

$$\frac{dE}{dt} = \xi\lambda(N^* - E - T_U - T_D - J - F - H) + \upsilon T_U + \rho\theta_1 F + r\alpha H - K_{11}E.$$
$$\frac{T_U}{dt} = (1-\xi)\lambda(N^* - E - T_U - T_D - J - F - H) + (1-\omega_1)\kappa E + \rho\theta_2 F - K_{12}T_U$$
$$\frac{T_D}{dt} = \omega_1\kappa E + \gamma_U T_U + [1-(\theta_1 + \theta_2)]\rho F - K_{13}T_D$$
$$\frac{dJ}{dt} = \sigma T_D - K_{14}J \qquad (13)$$
$$\frac{dF}{dt} = (1-q_1)\tau_1 T_D + (1-q_2)\tau_2 J + (1-r)\alpha H - K_{15}F.$$
$$\frac{dH}{dt} = q_1\tau_1 T_D + q_2\tau_2 J - K_{16}H$$

Where now

$$\lambda = \frac{\beta(T_U + \eta_D T_D + \eta_J J + \eta_F F + \eta_H H)}{N^*}$$

and,

$$K_{11} = \kappa + \mu,\ K_{12} = \upsilon + \gamma U + \mu,\ K_{15} = \rho + \mu,\ \ K_{16} = \alpha + \mu\ \ K_{13} = \sigma + \tau_1 + \mu,\ K_{14} = \tau_2 + \mu$$

Here, the invariance region is given by

$$D^* = \{(E, T_U, T_D, J, F, H) \in \Re_+^6 : E + T_U + T_D + J + F + H \le N^*\} \qquad (14)$$

For the model (13), the associated reproduction number, denoted by R_0, is given by $R_0 = \max\{R_{01}, R_{02}\}$, where

$$\Re_{01} = \frac{\beta(1-\xi)(K_{11}K_{13} + \eta D\gamma U K_{11} + \eta D\kappa\upsilon\omega_1) + (1-\omega_1)(\xi\kappa K_{13} + \xi\kappa\eta D\gamma\upsilon) + \xi\kappa\eta D\omega_1 K_{12}]}{K_{13}[K_{11}K_{12} + \upsilon\kappa(\omega_1 - 1)]} \qquad (15)$$
$$\Re_{02} = \frac{\beta(1-\xi)\eta_F K_{11}K_{13} + (1-q_2)\xi\eta_F\tau_2 K_{\ 16} + (1-\tau)\xi\eta_F\tau_2\alpha q_2 + \xi\eta_J K_{15}K_{16} + \xi\eta_H\alpha q_2 K_{15}]}{K_{14}K_{15}K_{16}}$$

Theorem 2: The DFE of the model (13), given by (11), is GAS in D^* if $R_0<1$.

Proof: The equations in (13) can be re-written as:

$$\begin{pmatrix} \frac{dE}{dt} \\ \frac{dT_U}{dt} \\ \frac{dT_D}{dt} \\ \frac{dJ}{dt} \\ \frac{dF}{dt} \\ \frac{dH}{dt} \end{pmatrix} = (G_1 - G_2 - G_3) \begin{pmatrix} E \\ T_U \\ T_D \\ J \\ F \\ H \end{pmatrix} \qquad (16)$$

Where the matrices G_1, G_2, and G_3, are given by

$$G_1 = \begin{bmatrix} 0 & \xi\beta & \xi\beta\eta\rho & \xi\beta\eta_J & \xi\beta\eta_F & \xi\beta\eta_H \\ 0 & (1-\xi)\beta & (1-\xi)\beta\eta_D & (1-\xi)\beta\eta_J & (1-\xi)\beta\eta_F & (1-\xi)\beta\eta_H \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \end{bmatrix}$$

$$G_2 = \begin{bmatrix} K_1 & -\upsilon & 0 & 0 & -\rho\theta_1 & -r\alpha \\ -(1-\omega_1)\kappa & K_2 & 0 & 0 & -\rho\theta_2 & 0 \\ -\omega_1\kappa & -\gamma U & K_3 & 0 & -(1-(\theta_1+\theta_2))\rho & 0 \\ 0 & 0 & -\sigma & K_4 & 0 & 0 \\ 0 & 0 & -(1-q_1)\tau_1 & -(1-q_2)\tau_2 & K_5 & -(1-r)\alpha \\ 0 & 0 & -q_1 r_1 & -q_2 r_2 & 0 & K_6 \end{bmatrix}$$

And

$$G_1 = \begin{bmatrix} 0 & \xi\lambda & \xi\lambda & \xi\lambda & \xi\lambda & \xi\lambda \\ (1-\xi)\lambda & (1-\xi)\lambda & (1-\xi)\lambda & (1-\xi)\lambda & ((1-\xi)\lambda & (1-\xi)\lambda \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \end{bmatrix}$$

Since matrix G_3 is non-negative, thus,

$$\begin{pmatrix} \frac{dE}{dt} \\ \frac{dT_U}{dt} \\ \frac{dT_D}{dt} \\ \frac{dJ}{dt} \\ \frac{dF}{dt} \\ \frac{dH}{dt} \end{pmatrix} \leq (G_1 - G_2) \begin{pmatrix} E \\ T_U \\ T_D \\ J \\ F \\ H \end{pmatrix} \qquad (17)$$

If $R_0 < 1$, then $\rho(G_1 G_2^{-1}) \prec 1$ (from the local stability result given in lemma 2, which is equivalent to G_1-G_2 having all its eigenvalues in the left-half plane [32]. It follows that the linearized differential inequality system (13) is stable whenever $R_0 < 1$. Consequently, by comparison theorem [32], it follows that (E; T_U; T_D; J; F; H) $\rightarrow$ (0; 0; 0; 0; 0; 0). Hence, since D is positively-invariant, it follows that DFE is GAS in D^* *if* $R_0 < 1$

3.3: Existence of Endemic Equilibrium Point (EEP)

For a special case of model (9) when $q_1=q_2=1$ and υ and α are very small (negligible), then the model (9) becomes

$$\frac{dS}{dt} = \prod -\lambda S - \mu S$$

$$\frac{dE}{dt} = \xi\lambda S + K_{11}E$$

$$\frac{dT_U}{dt} = (1-\xi)\lambda S + (1-\omega_1)\kappa E - K_{22}T_U$$
$$\frac{dT_D}{dt} = \omega_1\kappa E + \gamma_U T_U - K_{13}T_D \qquad (18)$$
$$\frac{dJ}{dt} = \sigma T_D - K_{14}J$$
$$\frac{dH}{dt} = \tau_1 T_D + \tau_2 J - K_{26}H$$

and, $K_{11} = \kappa + \mu,\ K_{22} = \gamma_U + \mu,\ K_{13} = \sigma + \tau_1 + \mu,\ K_{14} = \tau_2 + \mu^*,\ K_{26} = \mu^*$

For the model (18), the associated reproduction number, denoted by R_0^1 is given by $R_0^1 = \max\{R_1^1.R_2^1\}$, where

$$R_1^1 = \frac{\beta(1-\xi)(K_{11}K_{13} + \eta_D\gamma_U K_{11}) + (1-\omega_1)(\xi\kappa K_{13} + \xi\kappa\eta_D\gamma\upsilon) + \xi\kappa\eta_D\omega_1 K_{22}]}{K_{13}K_{11}K_{12}}$$

$$R_2^1 = \frac{\beta\xi\eta_J}{K_{14}}$$

Let $\varepsilon_1 = (S^*, E^*, T_U^*, T_D^*, J^*, H^*)$ represents any arbitrary endemic equilibrium of the model (18). Solving the equations of the model at steady-state gives

$$S^{**} = \frac{\Pi}{\lambda^{**} + \mu}$$
$$E^{**} = \frac{\xi\lambda^{**}S^{**}}{K_{11}}$$
$$T_U^{**} = \frac{(1-\xi)\lambda^{**}S^{**} + (1-\omega_1)\kappa E^{**}}{K_{22}}$$
$$T_D^{**} = \frac{\omega_1\kappa E^{**} + \gamma_U T_U^{**}}{K_{13}} \qquad (19)$$
$$J^{**} = \frac{\sigma T_D^{**}}{K_{14}}$$
$$H^{**} = \frac{q_1\tau_1 T_D^{**} + q_2\tau_2 J^{**}}{K_{26}}$$

The expression for λ at the endemic steady-state, denoted by λ ** is given by

$$\lambda^{**} = \frac{\beta[T_U^{**} + \eta_D T_D^{**} + \eta_j J^{**} + \eta_H H^{**}]}{N^{**}} \qquad (20)$$

Fro computational convenience, we re-write expressions (19) in terms of $\lambda^{**}S^{**}$ as below:

$$E^{**} = \frac{\xi\lambda^{**}S^{**}}{K_{11}}$$

$$T_U^{**} = \frac{(1-\xi)\lambda^{**}S^{**}}{K_{22}} + \frac{(1-\omega_1)\xi\kappa\lambda^{**}S^{**}}{K_{11}K_{22}} = P_1\lambda^{**}S^{**}$$

$$T_D^{**} = \frac{\omega_1 \kappa \xi \lambda^{**} S^{**}}{K_{13}} + \frac{\gamma_U P_1 \lambda^{**} S^{**}}{K_{11} K_{22}} = P_2 \lambda^{**} S^{**} \quad (21)$$

$$J^{**} = \frac{\sigma}{K_{14}} \left[\frac{\omega_1 \kappa \xi \lambda^{**} S^{**}}{K_{11} K_{13}} + \frac{\gamma_U P_1 \lambda^{**} S^{**}}{K_{13}} \right] = P_3 \lambda^{**} S^{**}$$

$$H^{**} = \frac{\tau_1}{K_{26}} P_2 \lambda^{**} S^{**} + \frac{\tau_2}{K_{26}} P_3 \lambda^{**} S^{**} = P_4 \lambda^{**} S^{**}$$

Where

$$P_1 = \frac{(1-\xi)}{K_{22}} + \frac{(1-\omega_1)\xi\kappa}{K_{11}K_{22}}$$

$$P_2 = \frac{\omega_1 \kappa \xi}{K_{11} K_{13}} + \frac{\gamma_\upsilon}{K_{13}} \left[\frac{(1-\xi)}{K_{22}} + \frac{(1-\omega_1)\xi\kappa}{K_{11}K_{12}} \right]$$

$$P_3 = \frac{\sigma}{K_{14}} \left[\frac{\omega_1 \kappa \xi}{K_{11} K_{13}} + \frac{\gamma_u}{K_{13}} \left[\frac{(1-\xi)}{K_{22}} + \frac{(1-\omega_1)\xi\kappa}{K_{11}K_{12}} \right] \right]$$

$$P_4 = \frac{\tau_1}{K_{26}} \left[\frac{\omega_1 \kappa \xi}{K_{11} K_{13}} + \frac{\gamma_\upsilon}{K_{13}} \left[\frac{(1-\xi)}{K_{22}} + \frac{(1-\omega_1)\xi\kappa}{K_{11}K_{22}} \right] \right] + \frac{\tau_2}{K_{26}} \left[\frac{\sigma}{K_{14}} \left[\frac{\omega_1 \kappa \xi}{K_{11} K_{13}} + \frac{\gamma_\upsilon}{K_{13}} \left(\frac{(1-\xi)}{K_{22}} + \frac{(1-\omega_1)\xi\kappa}{K_{11}K_{22}} \right) \right] \right]$$

Substituting the expressions in (21) into (20) gives

$$\lambda^{**}[S^{**} + \frac{\xi \lambda^{**} S^{**}}{K_{11}} + P_1 \lambda^{**} S^{**} + P_2 \lambda^{**} S^{**} + P_3 \lambda^{**} S^{**} + P_4 \lambda^{**} S^{**}] = \beta \lambda^{**} S^{**} [P_1 + \eta_D P_2 + \eta_J P_3 + \eta_H P_4] \quad (22)$$

Dividing each term in (22) by $\lambda^{**} S^{**}$ (noting that, at the endemic steady-state, $\lambda^{**} S^{**} \neq 0$ gives

$$1 + P_5 \lambda^{**} = \beta [P_1 + \eta_D P_2 + \eta_J P_3 + \eta_H P_4]$$

Where

$$P_5 = \frac{\xi}{K_{11}} + P_1 + P_2 + P_3 + P_4 \geq 0$$

So that,

$$1 + P_5 \lambda^{**} = \frac{\beta}{K_{11}K_{22}K_{13}K_{14}K_{16}} [(1-\xi)K_{11}K_{13}K_{14}K_{26} + (1-\omega_1)\xi\kappa K_{13}K_{14}K_{16} + \eta_D \omega_1 \xi \kappa K_{22}K_{14}K_{26} + \eta_D \gamma_\upsilon$$
$$(1-\xi)K_{11}K_{14}K_{26} + \eta_D \gamma_\upsilon (1-\omega_1)\xi\kappa K_{14}K_{26} + \eta_J \sigma \omega_1 \xi \kappa K_{22}K_{26} + \eta_J \sigma \gamma_\upsilon (1-\xi)K_{11}K_{26} + \eta_J \sigma \gamma_U (1-\omega_1)\xi\kappa K_{26}$$
$$+\eta_H \tau_1 \omega_1 \xi \kappa K_{22}K_{14} + \eta_H \tau_1 \gamma_U (1-\xi)K_{11}K_{14} + \eta_H \tau_1 \sigma \gamma_U (1-\omega_1)\xi\kappa K_{14} + \eta_H \tau_2 \sigma \omega_1 \xi \kappa K_{22} + \eta_H \tau_2 \sigma \gamma_U (1-\xi)K_{11}$$
$$+\eta_H \tau_2 \sigma \gamma_U (1-\omega_1)\xi\kappa] = R_1^1 + Q$$

Where

$$Q = \frac{\beta}{K_{11}K_{22}K_{13}K_{14}K_{16}} [\eta_J \omega_1 \xi \kappa K_{22}K_{24} + \eta_J \gamma \upsilon K_{26}[(1-\xi)K_{11} + (1-\omega_1)\xi\kappa] + \eta_H \tau_1 \omega_1 \xi \kappa K_{22}K_{14} +$$
$$\eta_H \tau_1 \gamma_U K_{14}[(1-\xi)K_{11} + (1-\omega_1)\xi\kappa] + \eta_H \tau_2 \sigma \omega_1 \xi \kappa K_{22} + \eta_H \tau_2 \sigma \gamma_U [(1-\xi)K_{11} + (1-\omega_1)\xi\kappa]$$

Therefore, $1 + P_5 \lambda^{**} = R_1^1 + Q$

So that, $\lambda^{**} = \frac{R_1^1 + Q - 1}{P_5} > 0$ whenever $R_1^1 > 1$

3.4 LOCAL STABILITY OF THE ENDEMIC EQUILIBRIA POINT (EEP)

Define $D_0 = \{(S, E, T_U, T_D, J, H) \in D : E = T_U = T_D = J = H = 0\}$, as the stable manifold of the DFE (ε_0). To prove the local stability of the EEP of the model (18), we consider the case where N=N** (i.e. the total population is at an endemic equilibrium). Using this definition $(S = N^{**} - E - T_U - T_D - J - H)$ in (18) gives the following systems:

$$\frac{dE}{dt} = \frac{\xi\beta(T_U + \eta_D T_D + \eta_J J + \eta_H H)(N^{**} - E - T_U - T_D - J - H)}{N^{**}} - K_{11}E$$

$$\frac{dT_U}{dt} = \frac{(1-\xi)\beta(T_U + \eta_D T_D + \eta_J J + \eta_H H)(N^{**} - E - T_U - T_D - J - H)}{N^{**}} + (1-\omega_1)\kappa E - K_{22}T_U$$

$$\frac{dT_D}{dt} = \omega_1\kappa E + \gamma_U T_U - K_{13}T_D \qquad (23)$$

$$\frac{dJ}{dt} = \sigma T_D - K_{14}J$$

$$\frac{dH}{dt} = \tau_1 T_D + \tau_2 J - K_{26}H$$

Let $\varepsilon_1^1 = (E^{**}, T_U^{**}, T_D^{**}, J^{**}, H^{**})$ denotes any arbitrary equilibrium of model (23). We claim the following:

Theorem 3: The unique endemic equilibrium, ε_1^1, of the model (23) is LAS in *D/D₀* whenever $R_1^1 > 1$.

Proof: We will follow the method given in Thieme [44] (see also [42,43]), which is based on using a Krasnoselskii sub-linearity approach. The approach essentially entails showing that the linearization of the system (23), around the equilibrium ε_1^1, has solutions of the form

$$\bar{Z}(t) = \bar{Z}_0 e^{\pi} \qquad (24)$$

With $\bar{Z}_0 = (Z_1, Z_2, Z_3, Z_4, Z_5), Z_i \in C$ and Re $\tau \geq 0$. The consequence of this is that the eigenvalues of the characteristics polynomial associated with the linearized method will have negative real part; in which case, the equilibrium ε_1^1 is LAS.

Linearizing the model (23) around the endemic equilibrium ε_1^1, gives

$$\frac{dE}{dt} = (-P_{11} - K_{11})E + (p_{12} - p_{11})T_U + (\eta_D P_{12} - P_{11})T_D + (\eta_J P_{12} - P_{11})J + (\eta_H P_{12} - P_{11})H$$

$$\frac{dT_U}{dt} = ((1-\omega_1)\kappa - P_{13})E + (P_{14} - P_{13} - K_{22})T_U + (\eta_D P_{14} - P_{13})T_D + (\eta_J P_{14} - P_{13})J + (\eta_H P_{14} - P_{13})H$$

$$\frac{dT_D}{dt} = \omega_1\kappa E + \gamma_U T_U - K_{13}T_D \qquad (25)$$

$$\frac{dJ}{dt} = \sigma T_D - K_{14}J$$

$$\frac{dH}{dt} = \tau_1 T_D + \tau_2 J - K_{26}H$$

Where

$$P_{11} = \frac{\xi\beta}{N^{**}}\left(T_U^{**} + \eta_D T_D^{**} + \eta_J J^{**} + \eta_H H^{**}\right),\ P_{12} = \frac{\xi\beta}{N^{**}}S^{**}, P_{13} = \frac{(1-\xi)\beta}{N^{**}}\left(T_U^{**} + \eta_D T_D^{**} + \eta_J J^{**} + \eta_H H^{**}\right)$$

$$and\ \ P_{14} = \frac{(1-\xi)\beta}{N^{**}}S^{**}$$

Substituting a solution of the forms (24) into the linearized system (23) around ε_1^1 gives the following system of linear equations

$$\tau Z_1 = (-P_{11} - K_{11})Z_1 + (p_{12} - p_{11})Z_2 + (\eta_D P_{12} - P_{11})Z_3 + (\eta_J P_{12} - P_{11})Z_4 + (\eta_H P_{12} - P_{11})Z_5$$
$$\tau Z_2 = (1-\omega_1)\kappa - P_{13})Z_1 + (P_{14} - P_{13} - K_{22})Z_2 + (\eta_D P_{14} - P_{13})Z_3 + (\eta_J P_{14} - P_{13})Z_4 + (\eta_H P_{14} - P_{13})Z_5$$

$$\begin{aligned} \tau Z_3 &= \omega_1 \kappa Z_1 + \gamma_U Z_2 - K_{13} Z_3 \\ \tau Z_4 &= \sigma Z_3 - K_{14} Z_4 \\ \tau Z_5 &= \tau_1 Z_3 + \tau_2 Z_4 - K_{16} Z_5 \end{aligned} \qquad (26)$$

Solving for Z_3; Z_4 and Z_5 from the third, fourth and fifth equations respectively of (26) in term of Z_1 and Z_2 each, and then after substituting the values of Z_3; Z_4 and Z_5 into the remaining equations of (26) adding the first two equations and simplifying, gives the equivalent system

$$\begin{aligned} Z_1[1 + F_1(\tau)] + [1 + F_2\tau)]Z_2 &= (M\bar{Z})_1 + (M\bar{Z})_2 \\ [1 + F_3\tau)]Z_3 &= (M\bar{Z})_3 \\ [1 + F_4\tau)]Z_4 &= (M\bar{Z})_4 \\ [1 + F_5\tau)]Z_5 &= (M\bar{Z})_5 \end{aligned} \qquad (27)$$

Where,

$$\begin{aligned} F_1(\tau) &= \frac{\tau + P_{11}}{K_{11}} + \frac{P_{13}}{K_{22} - P_{12}} + \left(\frac{P_{11}}{K_{11}} + \frac{P_{13}}{K_{22} - P_{12}} \right) A_1 \\ F_2(\tau) &= \frac{P_{11}}{K_{11}} + \frac{\tau + P_{13}}{K_{22} - P_{12}} + \left(\frac{P_{11}}{K_{11}} + \frac{P_{13}}{K_{22} - P_{12}} \right) A_2 \\ F_3(\tau) &= \frac{\tau}{K_{13}},\ F_4(\tau) = \frac{\tau}{K_{14}},\ F_5(\tau) = \frac{\tau}{K_{26}} \end{aligned} \qquad (28)$$

With

$$M = \begin{pmatrix} 0 & \frac{\xi\beta S^{**}}{N^{**}K_{aa}} & \frac{\eta_d \xi\beta\theta S^{**}}{N^{**}K_{aa}} & \frac{\eta_j \xi\beta\theta S^{**}}{N^{**}K_{aa}} & \frac{\eta_h \xi\beta\theta S^{**}}{N^{**}K_{aa}} \\ \frac{(1-\omega_1)\kappa}{K_{22}-P_{14}} & 0 & \frac{(\eta_d(1-\xi)\beta\theta S^{**}}{N^{**}(K_{22}-P_{14})} & \frac{(\eta_j(1-\xi)\beta\theta S^{**}}{N^{**}(K_{22}-P_{14})} & \frac{(\eta_h(1-\xi)\beta\theta S^{**}}{N^{**}(K_{22}-P_{14})} \\ \frac{\omega_1\kappa}{K_{13}} & \frac{\gamma_u}{K_{13}} & 0 & 0 & 0 \\ 0 & 0 & \frac{\sigma}{K_{14}} & 0 & 0 \\ 0 & 0 & \frac{\tau_1}{K_{213}} & \frac{\tau_2}{K_{23}} & 0 \end{pmatrix}$$

$$A_1 = \frac{\omega_1\kappa}{\tau + K_{13}} + \frac{\sigma\omega_1\kappa}{(\tau + K_{14})(\tau + K_{13})} + \left(\tau_1 + \frac{\tau_2\sigma}{\tau + K_{14}} \right) \frac{\omega_1\kappa}{\tau + K_{13}},$$

And

$$A_2 = \frac{\gamma_\mu}{\tau + K_{13}} + \frac{\sigma\gamma_\mu}{(\tau + K_{14})(\tau + K_{13})} + \left(\tau_1 + \frac{\tau_2\sigma}{\tau + K_{14}} \right) \frac{\gamma_\mu}{\tau + K_{13}}$$

where, the notation $M(Z)_i$ (with i = 1; 2; 3; 4; 5) denotes the ith coordinate of the vector M ($\bar{Z}$). It should further be noted that the matrix M has non-negative entries provided $k_{22} - p_4 > 0$ and the equilibrium ε_1^1 satisfies $\varepsilon_1^1 = M\varepsilon_1^1$. Furthermore, since the coordinates of ε_1^1 are all positive, it follows then that if $\bar{Z}$ is a solution of (27), then it is possible to find a minimal positive real number s such that

$$\left| \bar{Z} \right| \le s\varepsilon_1^1 \qquad (29)$$

Where, $\left|\bar{Z}\right| = (|Z_1|,|Z_2|,|Z_3|,|Z_4|,|Z_5|)$ with the lexicographic order, and $|\ |$ is a norm in C.

The main goal is to show that $\mathrm{Re}\,\tau < 0$. Assume the contrary (i.e. $\mathrm{Re}\,\tau \geq 0$, consider two cases: $\tau = 0$ *and* $\tau \neq 0$. Assume the first case τ =0. Then, (26) is a homogenous linear system in the various Z_i(i=1,2,3,4,5). The determinant of this system corresponds to that of the Jacobian of system (23) evaluated at ε_1^1, which is given by

$$\Delta = -\frac{E^{**} + T_U^{**} + \eta_D T_D^{**} + \eta_J J^{**} + \eta_H H^{**}}{N^{**}} B_1 - K_{11}K_{22}K_{13}K_{14}K_{26}\left(1 - \frac{S^{**}}{N^{**}} R_1^1\right) + \frac{S^{**}}{N^{**}} B_2, \qquad (30)$$

$$= -\frac{E^{**} + T_U^{**} + \eta_D T_D^{**} + \eta_J J^{**} + \eta_H H^{**}}{N^{**}} B_1 - K_{11}K_{22}K_{13}K_{14}K_{26}\left(1 - \frac{S^{**}}{N^{**}} R_1^1 - \frac{S^{**}}{N^{**}} \frac{B_2}{K_{11}K_{22}K_{13}K_{14}K_{26}}\right)$$

w

here

$$B_1 = (\tau_1 K_{14} + \sigma K_{26} + K_{14}K_{26} + \sigma\tau_2)\left[(1-\xi)K_{11}\gamma_\mu + (1-\omega_1)\xi\kappa\gamma_\mu + \omega_1\kappa\xi K_{22}\right]$$
$$+K_{13}K_{14}K_{26}\left[(1-\xi)K_{11} + (1-\omega_1)\xi\kappa + \xi K_{22}\right]$$
$$B_2 = (\sigma\eta_J K_{26} + \sigma\eta_H\tau_2 + \tau_1\eta_H K_{14})\left[(1-\xi)K_{11}\gamma_\mu + (1-\omega_1)\xi\kappa\gamma_\mu + \omega_1\kappa\xi K_{22}\right]$$

Solving (25) at the endemic steady-state (ε_1^1) and then from the first equation of (26) it can be shown that, $\Delta < 0$. Consequently, the system (26) can only have the trivial solution $\bar{Z} = \bar{0}$ Z=0 (which corresponds to the DFE, ε_0).

Now we consider the case $\tau \neq 0$. In this case, $\mathrm{Re}\,F_i(\tau) \geq 0 (i = 1,2,3,4,5)$ since, by assumption, $\mathrm{Re}\,\tau \geq 0$. It is easy to see that this implies $|1 + F_i(\tau)| > 1$, for all *i*. Now, define $F(\tau) = \min|1 + F_i(\tau)| > 1,\ i = 1,2,3,4,5.$ Then $F_i(\tau) > 1$, and therefore, $\frac{s}{F(\tau)} < s$. The minimality of s implies that $\left|\bar{Z}\right| > \frac{s}{F(\tau)}\varepsilon_1^1$. But, on the other hand, taking norms on both sides of the second equation of (26), and using the fact that M is non-negative, we obtain

$$F(\tau)|Z_3| \leq M(|Z|)_3 \leq s(M|\varepsilon_1^1|)_3 \leq sT_U^{**} \qquad (31)$$

Then, it follows from the above inequality that $|Z_3| \leq \frac{s}{F(\tau)} T_U^{**}$ which is a contradiction. Hence, $\mathrm{Re}\,\tau < 0$, which implies that ε_1^1 is LAS, if $R_1^1 > 1$.

The epidemiological implication of Theorem 3 is that the disease would persists in the community if the basic reproduction threshold $R_1^1 > 1$ if the initial sizes of the sub-populations of the model are in the basic of attraction of the endemic equilibrium point ε_1^1.

Appendix A

To explore the possibility of a backward bifurcation in the model (9), we re-label the variables by $S = x_1, E, E = x_2, T_U = x_3, T_D = x_4, J = x_5, F = x_6$ *and* $H = x_7$,so that $N = x_1 + x_2 + x_3 + x_4 + x_5 + x_6 + x_7$.Further by introducing the vector notation $X = (x_1 + x_2 + x_3 + x_4 + x_5 + x_6 + x_7)^T$. the model (9) can be written in the form $\frac{dX}{dt} = F(x)$, where $F = (f_1, f_2, f_3, f_4, f_5, f_6, f_7)^T$ as follows

$$\frac{dx_1}{dt} = f_1 = \prod - \frac{\beta(x_7\eta_H + x_6\eta_F + x_3 + x_4\eta_D + x_5\eta_J)}{(x_1 + x_2 + x_3 + x_4 + x_5 + x_6 + x_7)} x_1 - \mu x_1$$

$$\frac{dx_2}{dt} = f_2 = \frac{\beta(x_7\eta_H + x_6\eta_F + x_3 + x_4\eta_D + x_5\eta_J)}{(x_1 + x_2 + x_3 + x_4 + x_5 + x_6 + x_7)} x_1 - \upsilon x_3 + \rho\theta_1 x_6 + \tau\alpha x_7 -$$

$$(\kappa + \mu + \frac{\psi\beta(x_7\eta_H + x_6\eta_F + x_3 + x_4\eta_D + x_5\eta_J)}{(x_1 + x_2 + x_3 + x_4 + x_5 + x_6 + x_7)} x_2$$

$$\frac{dx_3}{dt} = f_3 = \frac{(1-\xi)\beta(x_7\eta_H + x_6\eta_F + x_3 + x_4\eta_D + x_5\eta_J)}{x_1 + x_2 + x_3 + x_4 + x_5 + x_6 + x_7} x_1 + (1-\omega_1)\kappa x_2 + \rho\theta_2 x_6 +$$

$$\frac{(1-\omega_2)\psi\beta(x_7\eta_H + x_6\eta_F + x_3 + x_4\eta_D + x_5\eta_J)}{x_1 + x_2 + x_3 + x_4 + x_5 + x_6 + x_7} x_2 - (\upsilon + \gamma_U + \mu + \delta_U)x_3, \qquad (32)$$

$$\frac{dx_4}{dt} = f_4 = \omega_1\kappa x_2 + \frac{\omega_2\psi\beta(x_7\eta_H + x_6\eta_F + x_3 + x_4\eta_D + x_5\eta_J)}{x_1 + x_2 + x_3 + x_4 + x_5 + x_6 + x_7} x_2 + \gamma_U x_3 + (1-\theta_1-\theta_2)\rho x_6 -$$

$$(\sigma + \tau_1 + \mu + \delta_D)x_4,$$

$$\frac{dx_5}{dt} = f_5 = \sigma x_4 - (\tau_2 + \mu + \delta_J)x_5$$

$$\frac{dx_6}{dt} = f_6 = (1-q_1)\tau_1 x_4 + (1-q_2)\tau_2 x_5 + (1-r)\alpha x_7 - (\rho + \mu + \delta_F)x_6$$

$$\frac{dx_7}{dt} = f_7 = q_1\tau_1 x_4 + q_2\tau_2 x_5 - (\alpha + \mu + \delta_H)x_7,$$

The Jacobian of the system (18), at the DFE is given by

$$J = \begin{bmatrix} -\mu & 0 & -\beta & -\beta\eta_D & -\beta\eta_J & -\beta\eta_F & -\beta\eta_H \\ 0 & -K_1 & \xi\beta + \upsilon & \xi\beta\eta_D & \xi\beta\eta_J & \xi\beta\eta_F + \rho\theta_1 & \xi\beta\eta_H + r\alpha \\ 0 & (1-\omega_1)\kappa & (1-\xi)\beta - K_2 & (1-\xi)\beta\eta_D & (1-\xi)\beta\eta_J & (1-\xi)\beta\eta_F + \rho\theta_2 & (1-\xi)\beta\eta_H \\ 0 & \omega_1\kappa & \gamma_U & -K_3 & 0 & 1-\theta_1-\theta_2\rho & 0 \\ 0 & 0 & 0 & \sigma & -K_4 & 0 & 0 \\ 0 & 0 & 0 & (1-q_1)\tau_1 & (1-q_2)\tau_2 & -K_5 & (1-r)\alpha \\ 0 & 0 & 0 & q_1\tau_1 & q_2\tau_2 & 0 & -K_6 \end{bmatrix}$$

From which it can be shown that $R_c = \rho(FV^{-1}) =, \max\{R_1, R_2\}$, where

$K_1 = \kappa + \mu, K_2 = \upsilon + \gamma_U + \mu + \delta_U, K_3 = \sigma + \tau_1 + \mu + \delta_D, K_4 = \tau_2 + \mu + \delta_J, K_5 = \rho + \mu + \delta_F$ and $K_6 = \alpha + \mu + \delta_H$.

We choose β as our bifurcation parameter. Using the following theorem ([3]), we will determine whether or not the system (18) undergoes a backward bifurcation at R_c=1

Theorem 4: Consider the following general system of ordinary differential equations with a parameter ϕ.

$$\frac{dx}{dt} = f(x,\phi),\ f: R^n \times R \to R^n \ \ and \ \ f \in C^2(R^n \times R),$$

Where

0 is an equilibrium point of the system (that is, $f(0,\phi) \equiv 0$ for all ϕ) and

A1. $A = D_x f(0,0) = \frac{\partial f_i}{\partial x_j}(0,0)$ is the linearization matrix of the system around the equilibrium 0 with ϕ evaluated at 0;

A2. Zero is a simple eigenvalue of A and all other eigenvlaues of A have negative real parts;
A3. Matrix A has a right eigenvector w and a left eigenvector v corresponding to the zero eigenvalue.
Let f_k be the k^{th} component of *f* and

$$a = \sum_{k,i,j=1}^{n} v_k w_i w_j \frac{\partial^2 f_k}{\partial x_i \partial x_j}(0,0) \qquad (3.3)$$

$$b = \sum_{k,i,=1}^{n} v_k w_i \frac{\partial^2 f_k}{\partial x_i \partial \phi}(0,0)$$

Then the local dynamics of the system around the equilibrium point 0 is totally determined by the signs of a and b. particularly, if a>0 and b>0, then a backward bifurcation occurs at ϕ =0.

Case 1: $R_1>R_2$: Consider a situation where $R_1>R_2$, so that the basic reproduction number Rc=1 gives 1. $R_1 > R_2$. Since β is our chosen bifurcation parameter, solving for β from R_c =1 gives

$$\beta = \beta^* = \frac{K_3(K_1K_2 + \upsilon\kappa(\omega_1 - 1)}{[(1-\xi)(K_1K_3 + \eta_D\gamma_U K_1 + \eta_D\kappa\upsilon\omega_1) + (1-\omega_1)(\xi\kappa K_3 + \xi\kappa\eta_D\gamma_U) + \xi\kappa\eta_D\omega_1 K_2]}$$

Case 2: $R_2>R_1$: Consider a situation where $R_2>R_1$, so that the basic reproduction number Rc=1 gives 1. $R_2 > R_1$. Since β is our chosen bifurcation parameter, solving for β from R_c =1 gives

$$\beta = \beta^* = \frac{K_4K_5K_6}{[(1-\xi)\eta_F K_4K_6 + (1-q_2)\xi\eta_F\tau_2 K_6 + (1-r)\xi\eta_F\tau_2\alpha q_2 + \xi\eta_J K_5K_6 + \xi\eta_H\alpha q_2 K_5]}$$

For our convenience, we denote the value of J when $\beta = \beta^*$ by J_{β^*}

Eigenvectors of J_{β^*}

Secondly, the following computations are carried out.

Eigenvectors of $J(\varepsilon_0)\big|_{\beta=\beta^*}$

It can be shown that the Jacobian of the system (33) at $\beta = \beta^*$ denoted by $J(\varepsilon_0)\big|_{\beta=\beta^*} = J_{\beta^*}$ has a right eigenvector (corresponding to the zero eigenvalue) given by

$$w = (\omega_1, \omega_2, \omega_3, \omega_4, \omega_5, \omega_6)^T,$$

Where $\omega_1 = \dfrac{-(\beta\eta_H\omega_7 + \beta\eta_F\omega_6 + \beta\omega_3 + \beta\eta_D\omega_4 + \beta\eta_J\omega_5)}{\mu}$

$\omega_2 = free$

$\omega_3 = free$

$\omega_4 = \dfrac{\gamma_U\omega_3 + (1-\theta_1-\theta_2)\rho\omega_6 + \kappa\omega_1\omega_2}{K_3}$

$\omega_5 = \dfrac{\sigma\omega_4}{K_4}$

$\omega_6 = free$

$\omega_7 = \dfrac{q_1\tau_1\omega_4 + q_2\tau_2\omega_5}{K_6}$

Furthermore, the Jacobian J_{β^*} has left eigenvectors (associated with the zero eigenvalue) given by $v = (\upsilon_1, \upsilon_2, \upsilon_3, \upsilon_4, \upsilon_5, \upsilon_6, \upsilon_7)$ where

$$\upsilon_1 = 0$$
$$\upsilon_2 = free$$
$$\upsilon_3 = \frac{(\xi\beta + \upsilon)\upsilon_2 + \gamma_U\upsilon_4}{(K_2 - (1-\xi)\beta)}$$
$$\upsilon_4 = free$$
$$\upsilon_5 = \frac{\xi\beta\eta_J\upsilon_2 + (1-\xi)\beta\eta_J\upsilon_3 + (1-q_2)\tau_2\upsilon_6 + q_2\tau_2\upsilon_7}{K_4}$$
$$\upsilon_6 = \frac{(\xi\beta\eta_F + \rho\theta_1)\upsilon_2 + (1-\xi)\beta\eta_F + \rho\theta_2)\upsilon_3 + (1-\theta_1-\theta_2)\rho\upsilon_4}{K_5}$$
$$\upsilon_7 = \frac{(\xi\beta\eta_H + r\alpha)\upsilon_2 + (1-\xi)\beta\eta_H\upsilon_3 + (1-r)\alpha\upsilon_6}{K_6}$$

COMPUTATIONS OF A AND B

FOR the system (18), the associated non-zero second partial derivatives of F (at the DFE) are given by:

$$\frac{\partial^2 f_2}{\partial x_2\partial x_3} = \frac{-\beta\mu(\xi+\upsilon)}{\prod}, \frac{\partial^2 f_2}{\partial x_2\partial x_4} = \frac{-\beta\eta_D\mu(\xi+\psi)}{\prod}, \frac{\partial^2 f_2}{\partial x_2\partial x_5} = \frac{-\beta\eta_J\mu(\xi+\psi)}{\prod}, \frac{\partial^2 f_2}{\partial x_2\partial x_6} = \frac{-\beta\eta_F\mu(\xi+\psi)}{\prod},$$
$$\frac{\partial^2 f_2}{\partial x_2\partial x_7} = \frac{-\beta\eta_H\mu(\xi+\psi)}{\prod}, \frac{\partial^2 f_2}{\partial x_4\partial x_3} = \frac{-\xi\beta\mu(\eta_D+1)}{\prod}, \frac{\partial^2 f_2}{\partial x_4\partial x_4} = \frac{-2\xi\beta\eta_D\mu}{\prod}, \frac{\partial^2 f_2}{\partial x_4\partial x_5} = \frac{-\xi\beta\mu(\eta_D+\eta_J)}{\prod},$$
$$\frac{\partial^2 f_2}{\partial x_4\partial x_6} = \frac{-\xi\beta\mu(\eta_F+\eta_D)}{\prod}, \frac{\partial^2 f_2}{\partial x_4\partial x_7} = \frac{-\xi\beta\mu(\eta_H+\eta_D)}{\prod}, \frac{\partial^2 f_2}{\partial x_5\partial x_5} = \frac{-2\xi\beta\mu\eta_J}{\prod}, \frac{\partial^2 f_2}{\partial x_5\partial x_6} = \frac{-\xi\beta\mu(\eta_F+\eta_J)}{\prod},$$
$$\frac{\partial^2 f_2}{\partial x_5\partial x_7} = \frac{-\xi\beta\mu(\eta_H+\eta_J)}{\prod}, \frac{\partial^2 f_2}{\partial x_6\partial x_6} = \frac{-2\xi\beta\mu\eta_F}{\prod}, \frac{\partial^2 f_2}{\partial x_2\partial x_3} = \frac{-(1-\xi-\psi+\psi\omega_2)\beta\mu}{\prod},$$
$$\frac{\partial^2 f_2}{\partial x_6\partial x_7} = \frac{-\xi\beta\mu(\eta_F+\eta_H)}{\prod}, \frac{\partial^2 f_2}{\partial x_7\partial x_7} = \frac{-2\xi\beta\mu\eta_H}{\prod}, \frac{\partial^2 f_2}{\partial x_2\partial x_4} = \frac{-(1-\xi-\psi+\psi\omega_2)\eta_D\beta\mu}{\prod}$$

$$\frac{\partial^2 f_3}{\partial x_2\partial x_5} = \frac{-(1-\xi-\psi+\psi\omega_2)\eta_H\beta\mu}{\prod}, \frac{\partial^2 f_3}{\partial x_3\partial x_3} = \frac{-2(1-\xi)\beta\mu}{\prod}, \frac{\partial^2 f_3}{\partial x_3\partial x_4} = \frac{(-1+\xi)\beta\mu(1+\eta_D)}{\prod},$$
$$\frac{\partial^2 f_3}{\partial x_3\partial x_5} = \frac{(-1+\xi)\beta\mu(1+\eta_J)}{\prod}, \frac{\partial^2 f_3}{\partial x_3\partial x_6} = \frac{(-1+\xi)\beta\mu(1+\eta_F)}{\prod}, \frac{\partial^2 f_3}{\partial x_3\partial x_7} = \frac{(-1+\xi)\beta\mu(1+\eta_H)}{\prod}$$
$$\frac{\partial^2 f_3}{\partial x_4\partial x_4} = \frac{2(-1+\xi)\beta\mu\eta_D}{\prod}, \frac{\partial^2 f_3}{\partial x_4\partial x_5} = \frac{(-1+\xi)\beta\mu(\eta_D+\eta_J)}{\prod}, \frac{\partial^2 f_3}{\partial x_4\partial x_6} = \frac{(-1+\xi)\beta\mu(\eta_D+\eta_F)}{\prod},$$
$$\frac{\partial^2 f_3}{\partial x_4\partial x_7} = \frac{(-1+\xi)\beta\mu(\eta_D+\eta_H)}{\prod}, \frac{\partial^2 f_3}{\partial x_5\partial x_5} = \frac{-2(-1+\xi)\beta\mu\eta_J}{\prod}, \frac{\partial^2 f_3}{\partial x_5\partial x_6} = \frac{(-1+\xi)\beta\mu(\eta_J+\eta_F)}{\prod},$$
$$\frac{\partial^2 f_3}{\partial x_5\partial x_7} = \frac{(-1+\xi)\beta\mu(\eta_J+\eta_H)}{\prod}, \frac{\partial^2 f_3}{\partial x_6\partial x_6} = \frac{-2(-1+\xi)\beta\mu\eta_F}{\prod}, \frac{\partial^2 f_3}{\partial x_6\partial x_7} = \frac{(-1+\xi)\beta\mu(\eta_H+\eta_F)}{\prod},$$
$$\frac{\partial^2 f_3}{\partial x_7\partial x_7} = \frac{2(-1+\xi)\beta\mu\eta_H}{\prod}, \frac{\partial^2 f_4}{\partial x_2\partial x_3} = \frac{\omega_2\psi\beta\mu}{\prod}, \frac{\partial^2 f_4}{\partial x_2\partial x_4} = \frac{\omega_2\psi\beta\mu\eta_D}{\prod}, \frac{\partial^2 f_4}{\partial x_2\partial x_5} = \frac{\omega_2\psi\beta\mu\eta_J}{\prod},$$
$$\frac{\partial^2 f_4}{\partial x_2\partial x_6} = \frac{\omega_2\psi\beta\mu\eta_F}{\prod}, \frac{\partial^2 f_4}{\partial x_2\partial x_7} = \frac{\omega_2\psi\beta\mu\eta_H}{\prod}$$

It follows from the above expressions that

$$a = \sum_{i,j=1}^{7}\upsilon_k\omega_i\omega_j\frac{\partial^2 f_k}{\partial x_i\partial x_j} = \frac{2\beta\mu}{\pi}(\xi\upsilon_3(\omega_2+\omega_3+\omega_4+\omega_5+\omega_6+\omega_7)+$$
$$\upsilon_1(\omega_2+\omega_3+\omega_4+\omega_5+\omega_6+\omega_7)+\omega_2\psi(1-\omega_2)\upsilon_3+\upsilon_4\omega_2-\upsilon_2)-$$
$$\xi\upsilon_2(\omega_2+\omega_3+\omega_4+\omega_5+\omega_6+\omega_7)-\upsilon_3(\omega_2+\omega_3+\omega_4+\omega_5+\omega_6+\omega_7))$$
$$(\eta_H\omega_3+\eta_F\omega_4+\omega_5+\eta_D\omega_6+\eta_J\omega_7)$$

From which it can be showed that a>0 iff

$$(\xi\upsilon_3+\upsilon_1)(\omega_2+\omega_3+\omega_4+\omega_5+\omega_6+\omega_7)+\omega_2\psi(1-\omega_2)\upsilon_3+\upsilon_4\omega_2-\upsilon_2)>$$

$$(\xi\upsilon_2+\upsilon_3)(\omega_2+\omega_3+\omega_4+\omega_5+\omega_6+\omega_7)$$

For the sign of b, it can be shown that the associated non-vanishing derivatives of F are

$$\frac{\partial^2 f_2}{\partial x_3\partial\beta^*}=\xi\frac{\partial^2 f_2}{\partial x_4\partial\beta^*}=\xi\eta_D,\frac{\partial^2 f_2}{\partial x_5\partial\beta^*}=\xi\eta_J,\frac{\partial^2 f_2}{\partial x_6\partial\beta^*}=\xi\eta_F,\frac{\partial^2 f_2}{\partial x_7\partial\beta^*}=\xi\eta_H$$

$$\frac{\partial^2 f_3}{\partial x_3\partial\beta^*}=(1-\xi),\frac{\partial^2 f_3}{\partial x_4\partial\beta^*}=(1-\xi)\eta_D,\frac{\partial^2 f_3}{\partial x_5\partial\beta^*}=(1-\xi)\eta_J,\frac{\partial^2 f_3}{\partial x_6\partial\beta^*}=(1-\xi)\eta_F,$$

$$\frac{\partial^2 f_3}{\partial x_7\partial\beta^*}=(1-\xi)\eta_H$$

So that,

$$b=\sum_{i,=1}^{7}\upsilon_k\omega_i\frac{\partial^2 f_k}{\partial x_i\partial\beta^*}$$

$$=(\xi(\upsilon_2-\upsilon_3)+\upsilon_3-\upsilon_1)(\omega_1+\omega_2+\omega_3+\omega_4+\omega_5+\omega_6+\omega_7)(\eta_H\omega_3+\eta_F\omega_4+\omega_5+\eta_D\omega_6+\eta_J\omega_7)>0$$

Thus we have established the following results.

FIGURES AND TABLE

Table1: Estimate of Epidemiological Burden of TB in Nigeria, 2007

All forms of TB (thousands of new cases per year)	460	123
All forms of TB (new cases per 10,000 pop/year)	311	83
New ss^+ cases (thousands of new cases per year)	195	43
New ss^+ cases (per 100,000 pop/year)	131	29
HIV^+ incident TB cases (% of all TB cases)	27	-
Prevalence	**All**	**In HIV^+ people**
All forms of TB (thousands of cases)	772	62
All forms of TB (cases per 10,000 pop)	521	42
2015 target for prevalence (cases per 1000,000 pop)	141	-
All forms of TB (thousands of cases)	138	59
All forms of TB (cases per 10,000 pop)	93	40
2015 target for prevalence (cases per 1000,000 pop)	18	-

	2000	**2001**	**2002**	**2003**	**2004**	**2005**	**2006**	**2007**
DOTs coverage (%)	47	55	55	60	65	65	75	91
Notification rate (new&relapse cases/100,000pop)	21	36	29	33	41	44	49	56
%notified (new&relapse cases under DOTS)	100	66	78	100	100	100	100	100
Notification rate (new ss^+ cases/100,000pop	14	18	17	21	24	25	28	30
% notified new ss^+ cases/100,000 pop	100	81	89	100	100	100	100	100
Cases detection rate (all new cases, %)	7.4	12	9.1	9.7	12	13	15	17
Cases detection rate (new ss^+ cases, %)	12	15	13	15	17	18	20	23
Treatment success (new ss^+ patients, %)	79	79	79	78	73	75	76	-
Re-treatment success (ss^+ patients, %)	71	71	73	-	73	66	77	-

Table 2: Description of variables of the model

Variable	**Description**
S(t)	Susceptible individuals
E(t)	Infected (exposed) individuals
$T_U(t)$	Undetected individuals with active TB
$T_D(t)$	Detected individuals with active TB
J(t)	Isolated individuals with active TB
F(t)	Individuals who failed treatment
H(t)	Treated individuals

Table 3: Description of parameters of the model

Parameter	Description
π	Recruitment rate into the population
μ	Per capita natural mortality rate
λ	Infection rate
β	Effective contact rate for TB infection
$\eta_D, \eta_J, \eta_F, \eta_H$	Modification parameters
σ	Isolation rate for detected individuals
ξ	Slow progressors
(1- ξ)	Fast progressors
ψ	Exogenous re-infection rate
κ	Progression rate of individuals in latent stage to active TB
ω_1	Endogenous reactivation rate
ω_2	Fraction of re-infected individuals that moves to detected class
γ_U	Detected rate for undetected individuals
υ	Natural recovery rate of undetected individuals
τ_1	Treatment rate for detected individuals
τ_2	Treatment rate for isolated individuals
q_1	Fraction of detected individuals who are successfully treated
q_2	Fraction of isolated individuals who are successfully treated
ρ	Rate at which individuals who failed treatment move to other classes
θ_1	Number of unsuccessfully treated individuals who move to the latent class
θ_2	Number of unsuccessfully treated individuals who move to the undetected class
$\delta_U, \delta_D, \delta_J, \delta_F, \delta_H$	Tuberculosis-induced mortality rate for classes, T_U, T_D, J, F, H respectively
α	Rate at which treated individuals lose their treatment-induced immunity
R	Fraction of treated individuals who move to exposed class after treatment wanes

Table 4: Parameters values

Parameter	Description	References
π	200(per 100000 population)	[]
μ	0.02	[8,23]
β	0.1	[38]
σ	0.20619	[44]
ξ	0.7	[23]
ψ	0.85	Assumed
κ	0.2522	[8]
ω_1	0.16	[8]
ω_2	0.7	[23]
γ_U	0.2	[38]
υ	0.2	[6,8]
τ_1, τ_2	Variable	
q_1	0.7	[38]
q_2	0.95	[38]
ρ	0.1	Assumed
θ_1, θ_2	Modification parameters	
$\delta_U, \delta_D, \delta_J, \delta_F, \delta_H$	0.3,0.1,0.1,0.3,0.01	[8]
$\eta_D, \eta_J, \eta_F, \eta_H$	0.001,0.001,0.001,0.001	[23]
α	5	[1]
R	0.8	Assumed

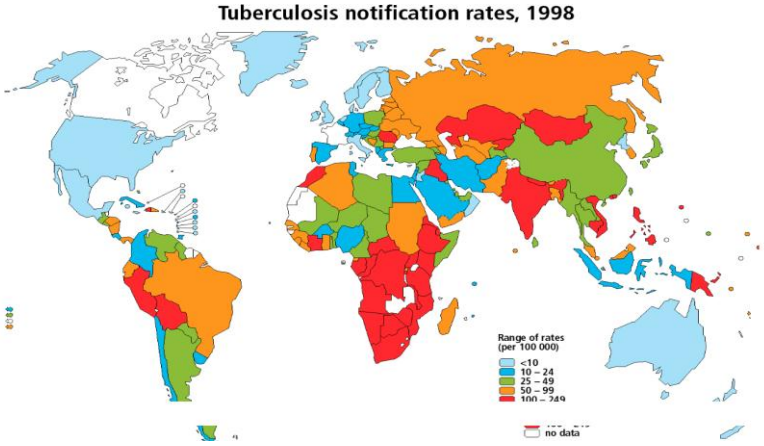


Figure 1

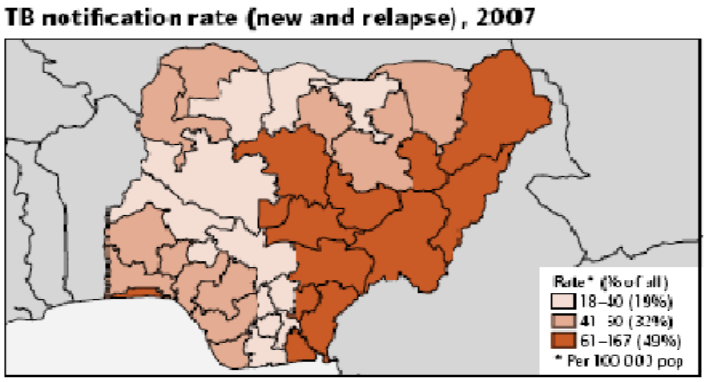


Figure 2

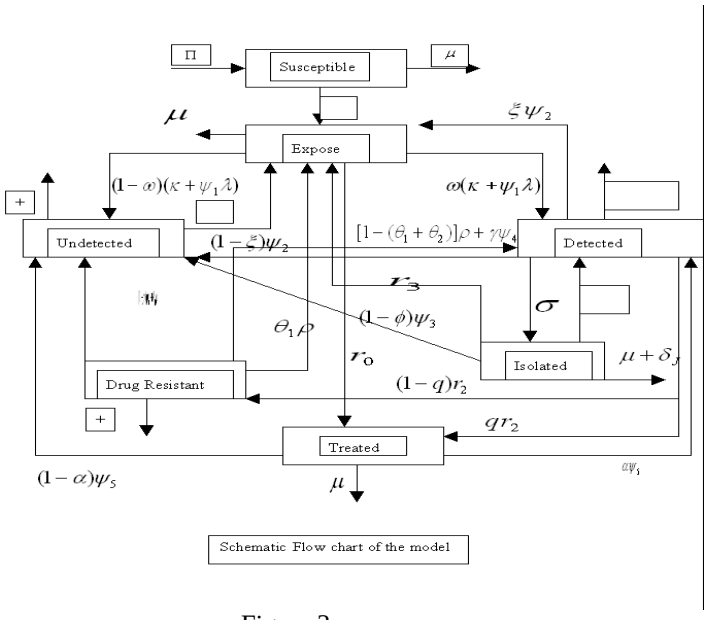


Figure 3

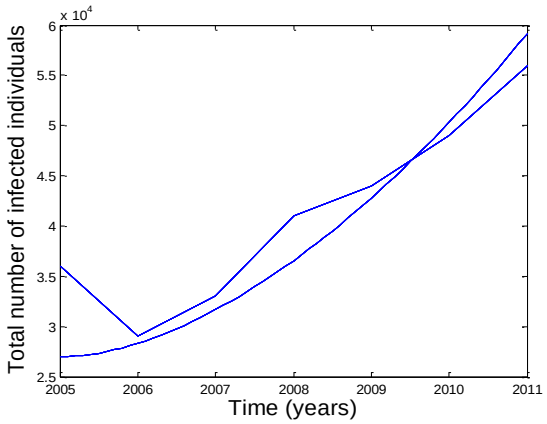
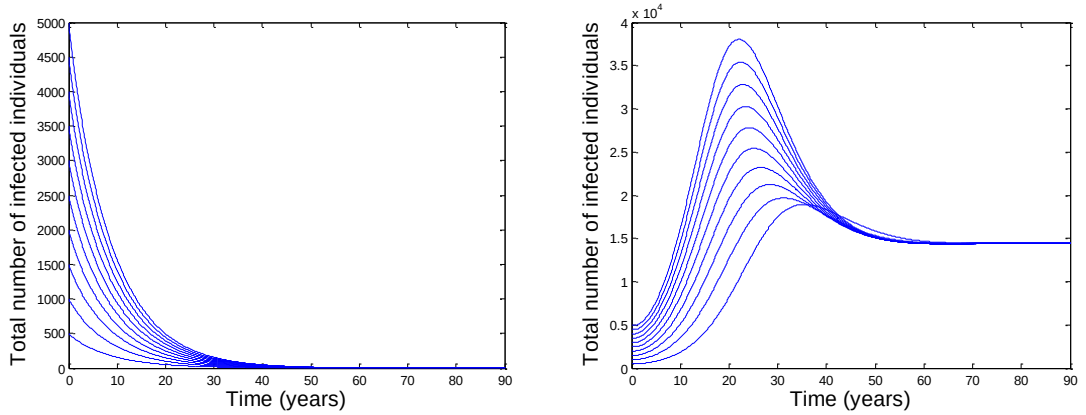


FIGURE 4: Comparison of observed TB data for Nigeria (Solid line) and model prediction (dotted line). Parameter values used are as given in Table 4, with $\beta = 0.2$

(A) (B)



(C)

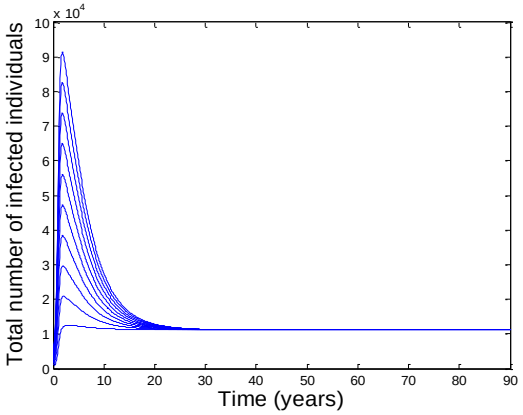


FIGURE 5: Simulation of the model (9) showing the total number of infected individuals (E+$T_U + T_D + J + F$) as a function of time, using the parameters in Table 4 with $\pi = 200, \mu = 0.02, \delta_U = 0.3, \delta_D = 0.1, \delta_J = 0.1,$ $\delta_F = 0.3, \gamma_U = 0.2 (A) \beta = 0.07 (R_1 = 0.1046). (B) \beta = 1 (R_1 = 1.4977). (C) \beta = 13 (R_1 = 19.4696).$

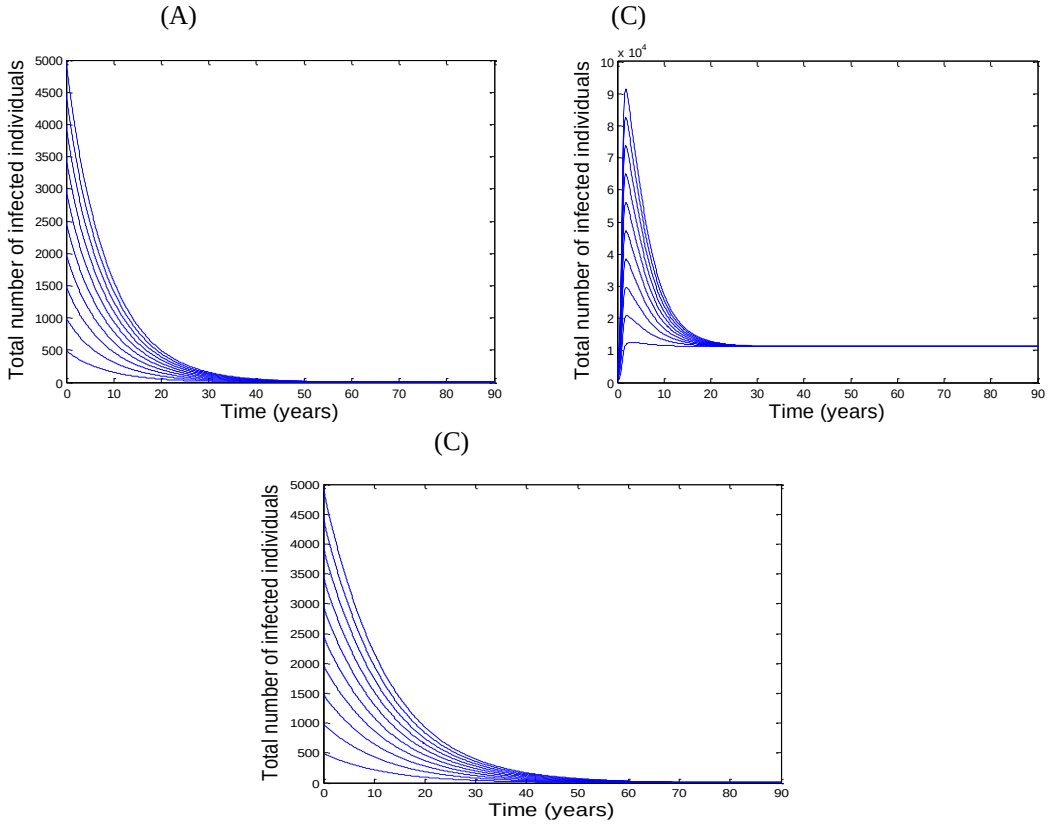


FIGURE 6: Simulation of the model (9) showing the total number of infected individuals (E+$T_U + T_D + J + F$) as a function of time, using the parameters in Table 4 with $\pi = 200, \mu = 0.02, \delta_U = 0.3, \delta_D = 0.1, \delta_J = 0.1, \delta_F = 0.3, \gamma_U = 0.2 (A) \beta = 0.07 (R_2 = 2.0042e^{-004}).(B) \beta = 1 (R_2 = 0.0029).(C) \beta = 13 (R_2 = 0.0372).$

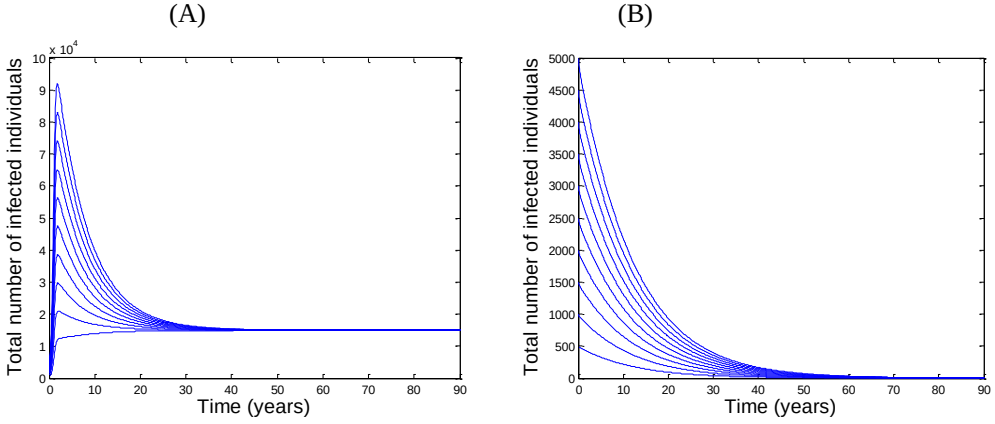


FIGURE 7: Simulation of the model (9) showing the total number of infected individuals (E+$T_U + T_D + J + F$) as a function of time, using the parameters in Table 4 with $\pi = 200, \mu = 0.02, \delta_U = 0.3, \delta_D = 0.1, \delta_J = 0.1, \delta_F = 0.3, \gamma_U = 0.2, \rho = 2\ (A) \beta = 0.07 (R_1 = 0.1048).(B) \beta = 13 (R_1 = 19.4696).$

(A) (B)

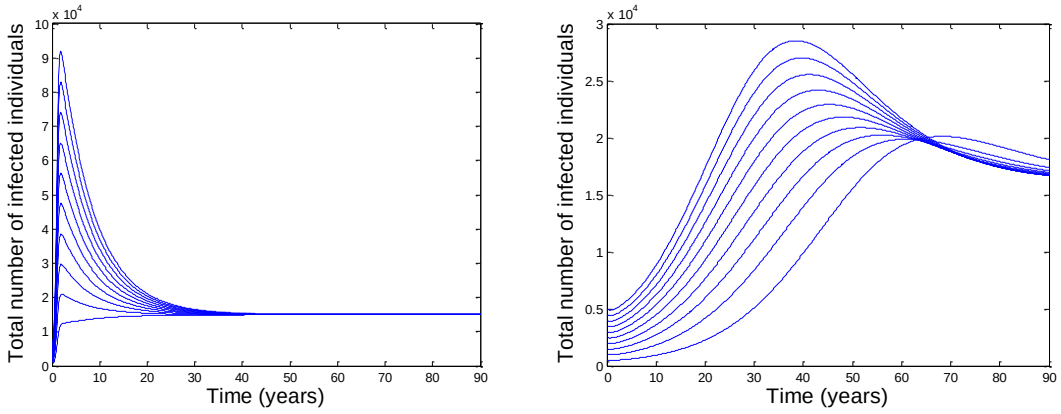


FIGURE 8: Simulation of the model (9) showing the total number of infected individuals (E+$T_U + T_D + J + F$) as a function of time, using the parameters in Table 4 with $\pi = 200, \mu = 0.02, \delta_U = 0.3, \delta_D = 0.1, \delta_J = 0.1,$ $\delta_F = 0.3, \gamma_U = 0.2, \rho = 2$ $(A)\beta = 0.07(R_2 = 1.0701e^{-004}).(B)\beta = 13(R_2 = 0.0199).$

(A) (B)

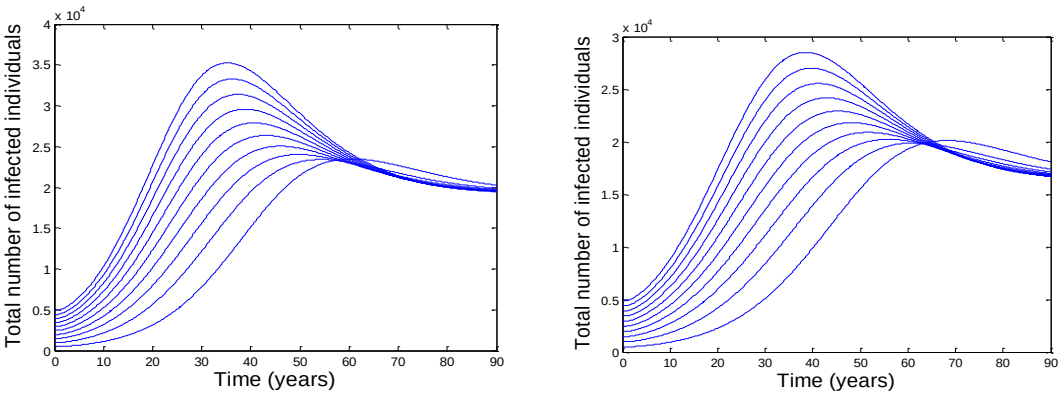


FIGURE 9: Simulation of the model (9) showing the total number of infected individuals (E+$T_U + T_D + J + F$) as a function of time, using the parameters in Table 4 with $\pi = 200, \mu = 0.02, \delta_U = 0.3, \delta_D = 0.1, \delta_J = 0.1,$ $\delta_F = 0.3, \gamma_U = 0.2, \rho = 2(A)\beta = 0.68(R_1 = 1.0184).(B)\beta = 0.7(R_1 = 1.0282).$

(A) (B)

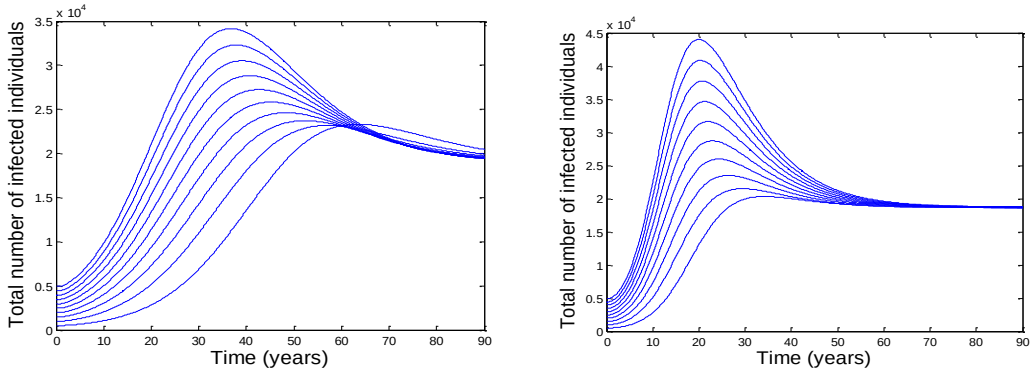


FIGURE 10:Simulation of the model (9) showing the total number of infected individuals (E+$T_U + T_D + J + F$) as a function of time, using the parameters in Table 4 with $\pi = 200, \mu = 0.02,$ $\delta_U = 0.3, \delta_D = 0.1, \delta_J = 0.1, \delta_F = 0.3, \gamma_U = 0.2, \rho = 2(A)\beta = 0.68(R_2 = 0.0010).(B)\beta = 0.7(R_2 = 0.010).$

(A) (B)

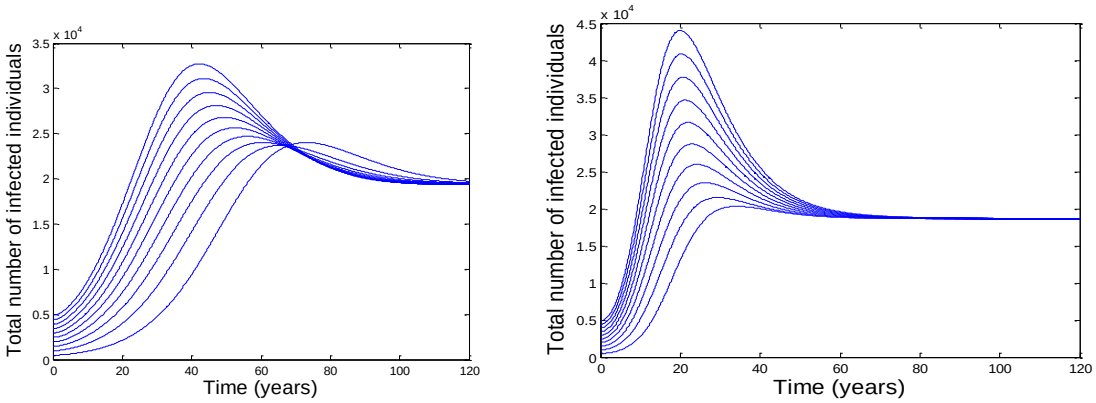


FIGURE 11: Simulation of the model (9) showing the total number of infected individuals $(E+T_U+T_D+J+F)$ as a function of time, using the parameters in Table 4 with $\pi = 200, \mu = 0.02, \delta_U = 0.3, \delta_D = 0.1, \delta_J = 0.1, \delta_F = 0.3, \gamma_U = 0.2, \xi = 0.067 (A) \beta = 0.68 (R_1 = 1.1989). (B) \beta = 0.7 (R_1 = 0.9743).$

(A) (B)

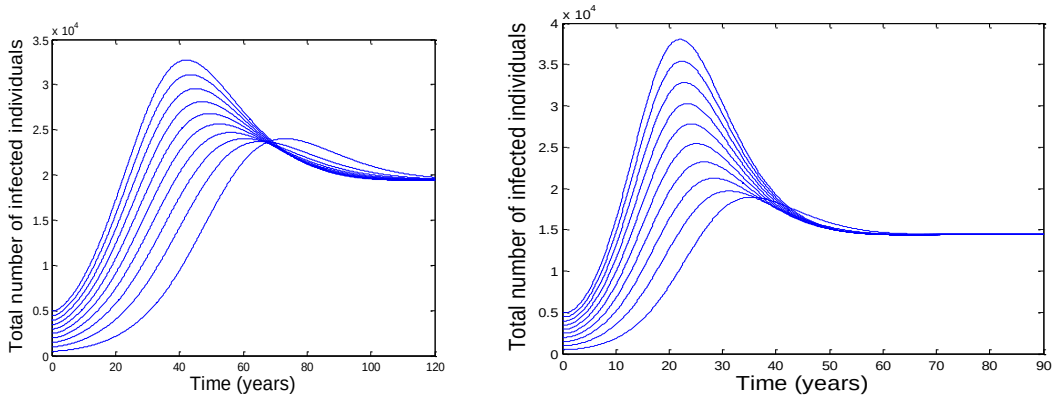
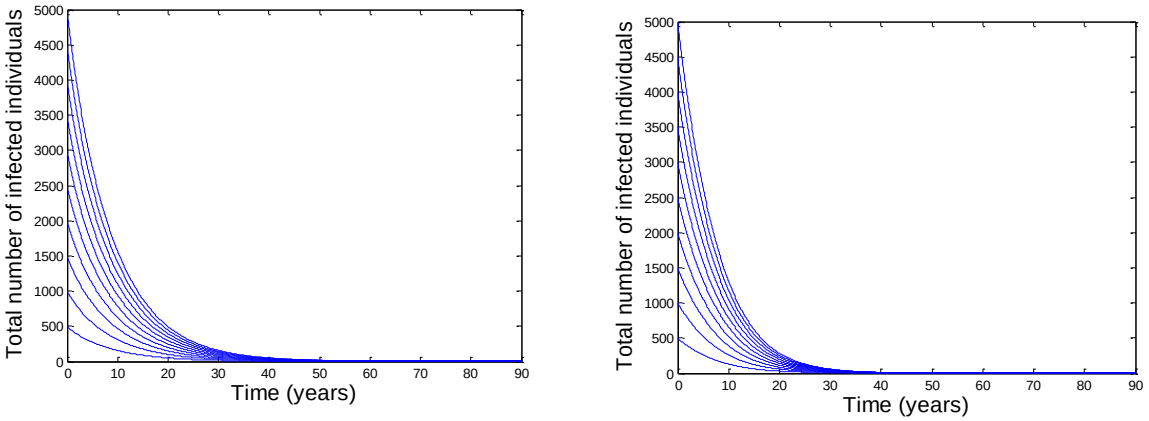


FIGURE 12: Simulation of the model (9) showing the total number of infected individuals $(E+T_U+T_D+J+F)$ as a function of time, using the parameters in Table 4 with $\pi = 200, \mu = 0.02, \delta_U = 0.3, \delta_D = 0.1, \delta_J = 0.1, \delta_F = 0.3, \gamma_U = 0.2, \xi = 0.09 (A) \beta = 0.68 (R_2 = 3.7522e^{-004}). (B) \beta = 0.7 (R_2 = 0.0013).$

(A) (B)



(C)

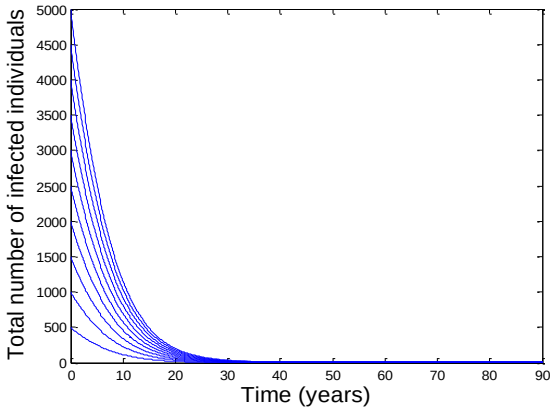


FIGURE 13: Simulation of the model (9) showing the total number of infected individuals (E+$T_U + T_D + J + F$) as a

function of time, using the parameters in Table 4 with $\pi = 200, \mu = 0.02, \delta_U = 0.3, \delta_D = 0.1, \delta_J = 0.1,$ $\delta_F = 0.3, \rho = 2$ $(A)\gamma_u = 0.2;$ $(B)\gamma_u = 0.5$ $(C)\gamma_u = 1.0$

IV. Discussion And Conclusions

A deterministic model for the transmission dynamics of tuberculosis (TB) in Nigeria under DOTS programme is designed. The model is rigorously analysed to gain insight into its dynamical features. Relevant demographics and biological data are used to simulate the model and explore the possibility of reducing the burden of the disease in the society. The study shows the following:

(1) The classical epidemiological requirement of having the maximum associated reproduction number Rc less than unity i.e one (1), while necessary, is not sufficient for the disease elimination due to the phenomenon of backward bifurcation, which the model exhibits.

(2) The model highlight the significant roles of the case detection rate (CDR) in reducing the burden of the disease in Nigeria.

(3) From the study, we also established that DOTS can lead to effective elimination of TB in Nigeria provided the rate at which the undetected individuals with active TB recovered exceeded a critical values, otherwise the disease will persist.

(4) The model also established that if the rate at which individuals who failed treatment (i.e people who developed multi-drug resistant) moves to other classes increases where they can be retreated under DOTS, then the burden of the disease will reduces.

(5) The study also shows that if the effective contact rate (β) for TB infection does not exceed certain critical value (0.187), the disease can be eliminated in Nigeria.

(6) The model predicts a substantial decline in TB incidence in the society provided the progressor rate (ξ) of individuals who are susceptible to TB is low.

(7) The occurrence of the backward bifurcation phenomenon necessarily requires the exogenous re-infection.

Numerical simulations of the model, using appropriate demographic and epidemiological data for Nigeria, show the following results:

(2) Using the data in Table 4, Figure 5 and 6 shows that when the effective contact rate is very low (β = 0.07, correspond to R_1= 0.1048 < 1 and R_2= 2.0042e^{-004} < 1) (see Fig.5A and 6A respectively) the model prediction shows that Nigeria would have maximum of 4800 per 100000 infected cases and in the next 50years years, the disease would have been eliminated completely in Nigeria. But when the effective contact rate is above the critical values for instance (β = 1.0, correspond to R_1= 1.4977 > 1 and R_2= 0.0029 < 1) (see Fig.5B and 6B respectively) it is shown that Nigeria will have maximum of 2.8 x 10^4 per 100000 infected individuals and in the next 80years, about 1.1 x 10^4per 100000 infected individuals would remain constant in the society. Further increase in effective contact rate (β = 13, correspond to R_1= 19.4696 > 1 and R_2= 0.0372 > 1) (see Fig.5C and 6C respectively) shows that Nigeria will have maximum of 5.7 x 10^4per 100000 infected individuals and in the next 45years, about 1.4 x 10^4per 100000 infected individuals would remain constant in the society.

(3) The simulation of the model using data in Table 4, with the rate at which those who developed multi-drug resistant (ρ) moves to other class for possible re treatment under DOTS increases (ρ = 2, β = 0.07; correspond to R_1= 0.1048 and R_2= $1.0701e^{-0.04}$and β = 13; correspond to R_1= 19.4696 and R_2= 0.0199) (see Fig.7A & 8A and 7B & 8B respectively) shows that when is increased, it increases the prospect of reducing the burden of TB in the society. The epidemiological implication of this is that when people who developed multi-drug resistant are moved to classes where they can be treated again at faster rate it can reduce the burden of TB in the society.

(4) In Figure 9 and 10, the results shows that $\beta = 0.68$ when the effective contact rate (β) is above the critical value (ρ = 2,;but less than unity, correspond to R_1= 1.0184 > 1 and R_2= 0.0010 < 1), the maximum number of infected individuals is about 25000 per 100000 (Fig.9A & 10A) and the disease cannot be totally eliminated in the society compared to (Fig.5A & 6A). But an increase in recovered rate of the undetected individuals (v) shows that (with ρ = 2, β = 0.7; correspond to R_1= 1.0282 > 1 and R_2 = 0.0010 < 1), in the early 40years the number of infected individuals in the society is insignificant, but gradually increases with time see (Fig.9B & 10B).

(5) The results of Figure 11 & 12 reveals that with low progressor (ξ = 0:067; correspond to R_1= 1.1989 > 1 and R_2= $3.7522e^{-004}$ < 1), reduces the burden of TB in the society to about 60years (Fig.11B & 12B) compare to about 80years and emergency resurface in between 90-110years when ξ = 0.09 (high progressor). R_1=0.9743<1 and R_2=0.0013.

(6) The results of Figure 13 A, B, C shows that as the case detection rate is increasing the numbers of years is decreasing. This implies that the case detection rate (CDR) plays a vital roles in the prospect of reducing (eliminating) TB burden in the society.

In summary, this study shows that the prospect of effectively reducing (or even eliminate) TB in Nigeria seems plausible provided the following measures are taken and/or improved upon:

(a) That concerted effort be made to keep the effective contact rate at minimum level. i.e below the critical value (0.187)

(b) The case detection rate is projected beyond the current target levels.

(c) All possibilities of developing Multi-drug resistant should be averted, e.g by employing trained personnel who will be able to administer drug to TB patients correctly. Also, the source of the drug must be reliable and the drug delivery should be regulated.

(d) DOTS should be promoted even in the rural areas in Nigeria.

References

[1] A.B. Gumel and B. Song(2008). Existence of Multiple-Stable Equilibria for a Multi-Drug-Resistant Model of Mycobacterium Tuberculosis. Mathematical Bio-sciences and Engineering. 5(3): 437-455.

[2] A. Ssematimba, J.Y.T. Migisha, and L.S. Luboobi (2005). Mathematical models for the dynamics of tuberculosis in density-dependent populations: The case of internally displaced peoples' camps (IDPCs) in uganda.Journal of Mathematics and Statistics. 1(3):217-224.

[3] C. Castillo-Chavez and B.Song (2004). Dynamical models of tuberculosis and their applications. Mathematical Biosciences and Engineering. 1(2):361-404.

[4] C. Dye, B.G. Williams(2000). Criteria for the control of drug-resistant tuberculosis.Proc. Natl. Acad. Sci. USA 97:8180-8185.

[5] C. Kribs-Zaleta and J. Valesco-Hernandez (2000). A simple vaccination model with multiple endemic states.Math Biosci. 164:183-201.

[6] C. Dye, G. P. Garnett, K. Sleeman, B. G. Williams (1998). Prospects for worldwide tuberculosis control under the WHO DOTS strategy. Directly observed shortcourse therapy. Lancet. 1998;352:1886-91 doi: 10.1016/S0140-6736(98)03199-7 pmid:

[7] C.Dye, C. J. Watt, D. M. Bleed, S. M Hosseini, M. C. Raviglione (2005). TEvolution of tuberculosis control and prospects for reducing tuberculosis incidence, prevalence, and deaths globally.JAMA. 2005;293:2767-75 doi:10.1001/jama.293.22.2767 pmid: 15941807.

[8] O. Daniel and K. Andrei (2007). Dynamics of tuberculosis: The effect of Direct Observation Therapy Strategy (DOTS) in Nigeria. Mathematical Modelling of Natural Phenomena. 2(1):101-113.

[9] D. W. Dowdy and R. E. Chaisson (2009). The persistence of tuberculosis in the age of DOTS: reassessing the effect of case detection. Bulletin of WHO. 2009(87):296-304.

[10] E.M. Chan and M.D. Iseman(2002). Current Medical treatment for tuberculosis.B.M.J., 325:1282-1286.

[11] B. Miller (1993). Preventive therapy for tuberculosis. Med. Clin. North Amer. 77:1263-1275.

[12] F. Brauer(2004). Backward bifurcation in a simple vaccination models. J.Math. Anal. and Appl.. 298(2):418-431.

[13] [13] Fort-forth World Health Assembly. Resolution WHA 44.8.Geneva: World Health Organization; 1991.

[14] [14] G. Magombedze, W. Garira, and E. Mwenje (2006). Modelling the Human Immune Response mechanisms to Mycobacterium tuberculosis infection in the lungs. Mathematical Biosciences and Engineering, 3,No 4:661-682.

[15] B. H. Singer and D. E. Kirschner(2004). Influence of backward bifurcation on interpretation of R_0 in a model of epidemic tuberculosis with reinfection. Math Bios. Engrg. 1(1):81-93.

[16] D.L.Cohn, B.J. Catlin, K.L. Peterson, F.N.Judson and J.A. Sbarbaro(1990). A.62-dose, 6-month therapy for pulmonary and extrpulmonary tuberculosis: A twiceweekly, directly observed, and cost-effective regimen. Ann. Intern. Med., 112:407-415.

[17] J.P. Aparicio and J.C. Hernandez (2006). Preventive treatment of Tuberculosis through contact tracing. Mathematical Studies on Human Disease Dynamics: Emerging paradigms and Challenges, AMS Contemporary Mathematics Series. Vol. 410.

[18] J. Dusho, W. Huang and C. Castillo-Chavez (1998). Backward bifurcations and catastrophe in simple models of fatal diseases.J. Math. Biol.. 36:227-248.
[19] J. Carr (1981). Application Centre Manifold Theory. Springer-Verlag, New York.
[20] O.K. Koriko and T. T. Yusuf (2008). Mathematical model to simulate tuberculosis disease population dynamics.Ame. Jour. of Applied Sci.. 5(4):301-306.
[21] L. Gammaitoni and M. C. Nucci (1997). Using a Mathematical model to evaluate the efficacy of TB control measures.Emergeging Infectious diseases, 3(3).
[22] M.W. Borgdor, K. Floyd, and J. F. Broekmans (2002). Interventions to reduce tuberculosis mortality and transmission in low and middle-income countries. Bull World Health Organ, 80:217-227.
[23] O. Sharomi, C. N. Podder, A. B. Gumel and B. Song (2008). Mathematical analysis of the transmission dynamics of HIV/TB co infection in the presence of treatment. Mathematical Biosciences and Engineering. 5(1):145-174.
[24] P. Rodrigues, M. G. Gomes, C. Rebelo (2007). Drug resistance in tuberculosis- a reinfection model. Theor.Pop. Biol. 71:196-212.
[25] P. Van den Driessche and J. Watmough (2002). Reproduction numbers and sub-threshold endemic equilibria for compartmental models of disease transmission. Math Bios. 180:29-48.
[26] P. C Hopewell (1994). Overview of clinical tuberculosis. In Bloom, B. R.(ed.),Tuberculosis, pathogenesis, protection, and Control, AMS, Washington, DC. pp:25-46.
[27] P. G. Smith and A. R. Moss (1994). Epidemiology of tuberculosis. In Bloom, B. R. (ed.),Tuberculosis: pathogenesis, protection, and Control, AMS, Washington, DC. pp:47-59.
[28] N.W. Schluger and W. N. Rom(1998). The host immune response to tuberculosis. Am. J. Respir. Crit. Care. Med., 157:679-691.
[29] M. G. M Gomes, A. O. Franco, M.C. Gomes, G. F. Medley (2004). The reinfection threshold promotes variability in tuberculosis epidemiology and vaccine efficacy. Proc. R. Soc. London B 271:617-623.
[30] S.M. Blower, T.Chou(2004). Modeling the emergence of the 'hot zones': tuberculosis and the amplication dynamics of drug resistance. Nature Med.. 10:1111-1116.
[31] T. Cohen, M. Murray (2004). Modeling epidemics of multi drug-resistant M. tuberculosis of heterogeneous fitness. Nature Med.. 10:1117-1121.
[32] V. Lakshmikantham, S. Leela, and A. A. Martynyuk(1989). Stability analysis of nonlinear systems. Marcel Dekker, Inc., New York and Basel.
[33] Z. Feng, C. Castillo-Chavez and A. F. Capurro (2000). A model for the tuberculosis with exogeneous reinfection. Theor.Pop. Biol.. 57:235-247.
[34] Z. Feng, W. Huang and C. Castillo-Chavez (2001). On the role of variable latent periods in mathematical models of tuberculosis.J. Dynam. Diff .Eqns. 13(2):425-452.
[35] D. Snider Jr., M. Raviglione and A. Kochi (1994). Global burden of tuberculosis. In Tuberculosis: pathogenesis, protection and control (B.Bloom ed.), Washininton D.C.,ASM Press, 1994.
[36] WHO. (2006). Global tuberculosis control: surveillance, planning, financing. WHO Report/WHO/HTM/TB/ 2006.362.
[37] WHO. (2008). WHO anti-tuberculosis drug resistance in the world report. WHO Report,2008.
[38] W. Wang (2006). Backward bifurcation of an epidemic model with treatment. Math Biosci. 201(1-2):58-71.
[39] USAID. (2008). Infectious disease. USAID Report, 2008.
[40] W.R. Bishai, N.M. Graham, S. Harrington, D.S. Pope, N. Hooper, J. Astemborski, L. Sheely, D. Vlahov, G.E. Glass, and R.E. Chaisson (1998). Molecular and Geographic patterns of Tuberculosis transmission after 15 years of directly observed therapy. J. Am. Med. Assoc., 208:1679-1684.
[41] B.A. Yanis, N. Bennett, S.Angad, S.Alyssa, and S.Neil (2008). Underreported Threat of Multi drug-Resistant Tuberculosis in African. Emergin Infectious Disease jour., 14(9).
[42] Esteva, L., Gumel, A.B. and Vargas de Le on, C. (2008). Qualitative study of transmission dynamics of drug-resistant malaria. Mathematical and Computer Modelling. To appear
[43] Esteva, L. and Vargas de Leon, C. (2000). Influence of vertical and mechanical transmission on the dynamics of dengue disease. Math. Biosci. 167: 51-64.
[44] Hethcote, H.W. and Thieme, H.R. (1985). Stability of the endemic equilibrium in epidemic models with subpopulations. Math. Biosci. 75: 205-227.
[45] G.Chowell, C. Castillo-Chavez, P. Fenimore, C. Kribs-Zaleta, L. Arriola and J. Hyma.