A Model of Tuberculosis and Diabetes Co-Infection with Optimal Control

Original Research Article

Abstract

Aims/ objectives: Tuberculosis and diabetes co-infection is a complex health issue, thus, effective management requires understanding disease dynamics and interactions. This paper expands the existing model to incorporate the co-infection of diabetes and tuberculosis to understand disease complications better.

Methodology: The study employs the next-generation matrix to calculate $\mathcal{R}_C$ and utilizes LaSalle's invariance principle. It demonstrates that the model achieves global asymptotic stability at the disease-free equilibrium (DFE) when $\mathcal{R}_C \leq 1$. The Volterra-Lyapunov matrix is then employed to establish global asymptotic stability of the endemic equilibrium when $\mathcal{R}_C > 1$. Based on the Jacobian matrix, local stability analysis suggests the potential for epidemic eradication when $\mathcal{R}_C \leq 1$, while $\mathcal{R}_C \geq 1$ indicates a risk of epidemic spread. Numerical solutions using ODE45 in Matlab R2021b are employed for the analysis.

Results: The sensitivity analysis highlighted the significant impact of TB transmission coefficient β and diabetes acquisition rate α_1 on $\mathcal{R}_C$, emphasizing the need for optimal control measures targeting these factors.

Conclusion: A decrease in TB transmission coefficient led to a reduction in $\mathcal{R}_C$ from 1.0863 to 0.1845, suggesting the potential effectiveness of control strategies. The study also recommends exploring models considering different diabetes types in future research.

Keywords: Mathematical model; non-standard finite difference; Tuberculosis; Diabetes
2010 Mathematics Subject Classification: 53C25; 83C05; 57N16

1 Introduction

Tuberculosis is an ailment that affects both human and animal population. It is caused by mycobacterium tuberculosis complex (MTBC), which includes seven TB-causing mycobacterium [37, 50]. It is an airborne disease and is transmitted through fluid particles called droplet nuclei of 1-5 microns in diameter generated from the respiratory system of TB-infected individuals when they cough, sneeze, speak, sing or spit [33, 54]. These droplet nuclei can be suspended in the air for several hours. The World health organization posits that TB is one of the top ten causes of death in the world [15]. 10.4 million People were exposed to TB in 2016 and 1.7 million died that year [6]. In 2019, it was estimated that 10 million people got infected while 1.4 million people died [18].

Kenya is a high TB burden country ranked 13^{th} amongst the 22 countries, contributing 80 percent of the global caseload [47]. Diabetes Mellitus, on the other hand, is a syndrome of disordered metabolism that occurs when the pancreas does not produce enough insulin or the body does not effectively use the insulin produced. Insulin which is made by the beta cells of the pancreas regulates the blood sugar. If not well regulated, one develops hyperglycemia (high sugar levels), which seriously damages various body systems, especially the nerves, blood vessels, eyes, and kidneys [55]. The global prevalence of diabetes over the past few decades has shown a trend of rapid increase and, therefore raising a significant concern. Two individuals develop diabetes every 10 seconds, and two individuals die of diabetes every 10 seconds as per the International Diabetes Federation (IDF) statistics [3].

Diabetes is one of the risk factors of tuberculosis due to its immune-compromising effect. It is known to affect the natural course of TB by making individuals have a lifetime risk of getting TB infection activated from the latent stage of infection, getting more severe symptoms, treatment failure, more lapses as well as more prone to death [51]. There is also a likelihood for misdiagnosis of patients with TB who have diabetes because these patients show typical imaging changes and lesion distribution in the lower lobe instead of the upper lobe, which TB infected patient shows [23]. This has a serious clinical implication because a lesion in the lower lobe is easily misdiagnosed as a tumor or community-acquired pneumonia. The misdiagnosis may delay early TB treatment, increasing the spread and affecting the control of transmission [31]. It is therefore, very crucial to study TB-diabetes co-infection in order to comply with the WHO's end TB blueprint, aiming at reducing TB incidences by 80 percent and deaths by 90 percent by 2030.

Contribution

Tuberculosis and diabetes co-infection is a complex health issue. Effective management requires understanding disease dynamics and interactions. The study extends earlier models to include diabetes and tuberculosis co-infection in order to enhance understanding of the complexities associated with disease complications. Stability analysis is performed using $\mathcal{R}_C$ for disease-free and endemic equilibrium in order to assess the potential epidemic eradication conditions. Sensitivity analysis also assesses the parameters most significantly impact $\mathcal{R}_C$. Suggested optimal control measures based on the most sensitive parameter to $\mathcal{R}_C$ to suggest the potential effectiveness of control strategies for TB-diabetes coinfection.

2 Methods

2.1 Model formulation

- S: The model description that represents the dynamics of tuberculosis and diabetes co-infection is divided into compartments where the compartment S are healthy individuals, and is increased by Λ, the recruitment of individuals by birth. It is decreased by λS (individuals getting TB), $\alpha_1 S$ (Individuals acquiring Diabetes), and by μS (natural deaths).
- L_f: The compartment L_f (individuals with fast propagating TB) is increased by $p\lambda S$ (proportion of susceptible individuals developing a fast propagating TB) and πL_s (individuals with slow propagating TB developing fast propagating TB), and is decreased by μ (natural death), $\sigma_1 L_f$ (individuals with fast propagating TB becoming infectious).
- L_s: The compartment L_s (individuals with slow propagating TB) is increased by $(1-p)\lambda S$ (susceptible individuals developing slow propagating TB) and $\rho_1 I_T$ (those infectious and treated individual getting a slow propagation TB) and is decreased by μL_s (natural deaths), λL_f (individuals with slow propagating TB developing fast propagating TB), $\sigma_2 L_s$ (individuals with slow propagating TB becoming infectious), $\alpha_2 L_s$ (individuals with slow propagating TB acquiring diabetes) and $\delta_1 L_s$ (TB induced deaths).
- I_T: The compartment I_T (TB infectious individuals) is increased by $\sigma_2 L_s$ (individuals with slow propagating TB becoming infectious) and $\sigma_1 L_f$ (individuals with fast propagating TB becoming infectious) and is decreases by $\rho_1 I_T$ (those infectious and treated gets a slow propagation TB) , μI_T (natural deaths) and $\delta_2 I_T$ (TB induced deaths).
- D_T: The compartment D_T (individuals with TB and diabetes) and is increased by $\alpha_2 L_s$ (individuals with slow propagating TB acquiring diabetes), ηD (individuals with diabetes getting TB) and $\rho_2 I_{DT}$ individuals with diabetes but treated of TB becomes exposed to TB. The class is decreased by μD_T (natural death) and $\sigma_3 D_T$ (individuals becomes infectious of TB).
- I_{DT}: The compartment I_{DT} (individuals with diabetes and infectious of TB) is increased by $\sigma_3 D_T$ (individuals become infectious of TB) and $\omega_2 C_{DT}$ (proportion of individuals with diabetes complications due to TB). The class is decreased by $\rho_2 I_{DT}$ (individuals with diabetes but treated of TB become exposed to TB), μ (natural death rate), $\delta_2 I_{DT}$ (disease-induced deaths) and $\theta_2 I_{DT}$ (proportion of individuals progressing to individual with diabetes complications due to TB).
- C_{DT}: The compartment C_{DT} (individuals with diabetes complications due to TB) and is increased by $\theta_2 I_{DT}$ (individuals infectious with TB and has Diabetes developing complications) and decreases by $\omega_2 C_{DT}$ (individuals receiving treatment of the complications), μC_{DT} (natural death) and $\delta_3 C_{DT}$ (TB induced deaths due to complications).
- D: The compartment D (individuals with diabetes) is increased by $\alpha_1 S$ (susceptible individuals acquiring diabetes) and $\omega_1 C$ (individuals with diabetes complications getting treatment of the complications) and is decreased by μD (natural deaths), $\theta_1 D$ (diabetic individuals getting diabetes complications) and λD (individuals with diabetes getting TB).
- C: The compartment C(diabetic individuals with complications) is increased by $\theta_1 D$ (diabetic individuals getting diabetes complications) and is decreased by μC (natural deaths), $\delta_3 C$ (induced deaths due to diabetes complications) and $\omega_1 C$ (individuals with diabetes complications getting treatment of the complications).

Following the description given in the flow diagram, the model system is described by the first-order differential equations given in (2.1).

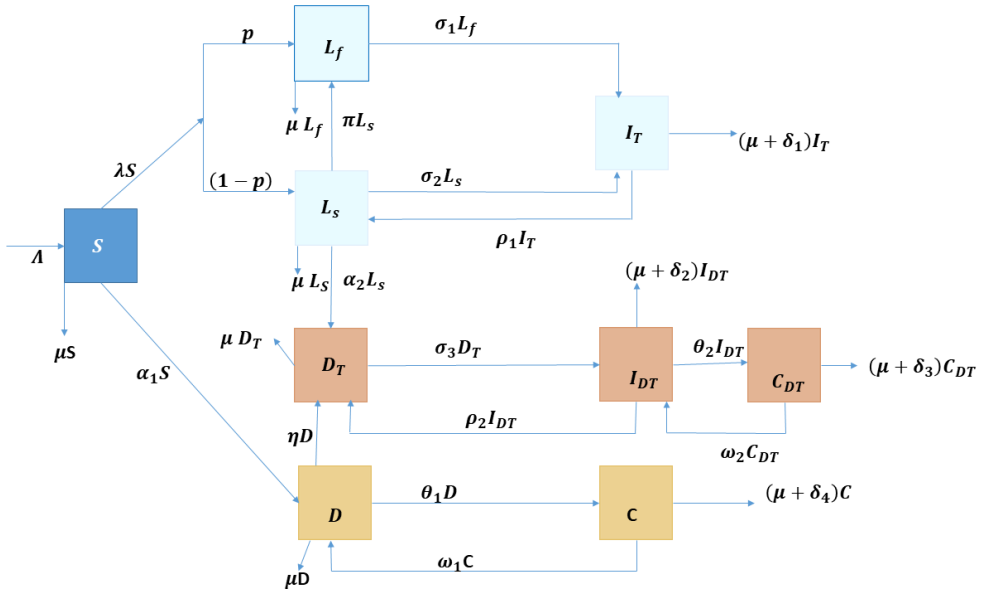

Fig. 1: TB-Diabetes model

$$
\left.
\begin{aligned}
\frac{dS}{dt} &= \overbrace{\Lambda}^{\text{recruitment}} - \overbrace{\beta I S}^{L_f L_s \text{ transmission}} - \overbrace{\alpha_1 S}^{D \text{ transmission}} - \overbrace{\mu S}^{\text{natural deaths}}, \\
\frac{dL_f}{dt} &= \overbrace{p\beta I S}^{S \text{ becomes } L_f} + \overbrace{\pi L_s}^{L_s \text{ becoming } L_f} - \overbrace{\sigma_1 L_f}^{L_f \text{ becoming } I_T} - \overbrace{\mu L_f}^{\text{natural deaths}}, \\
\frac{dL_s}{dt} &= \overbrace{(1-p)\beta I S}^{\text{S becoming } L_s} + \overbrace{\rho_1 I_T}^{I_T \text{ transforming to } L_s} - \overbrace{\pi L_s}^{L_s \text{ becoming } L_f} - \overbrace{\sigma_2 L_s}^{I_T \text{ becoming } L_s} - \overbrace{\alpha_2 L_s}^{L_s \text{ becoming } D_T} - \overbrace{\mu L_s}^{\text{natural deaths}}, \\
\frac{dI_T}{dt} &= \overbrace{\sigma_2 L_s}^{L_s \text{ becomes infectious}} + \overbrace{\sigma_1 L_f}^{L_f \text{ becomes infectious}} - \overbrace{\rho_1 I_T}^{I_T \text{ becomes } L_s} - \overbrace{\delta_1 I_T}^{\text{disease induced death}} - \overbrace{\mu I_T}^{\text{natural deaths}}, \\
\frac{dD_T}{dt} &= \overbrace{\alpha_2 L_s}^{L_s \text{ become diabetic}} + \overbrace{\eta D}^{D \text{ acquires TB}} + \overbrace{\rho_2 I_{DT}}^{I_{DT} \text{ exposed to TB}} - \overbrace{\sigma_3 D_T}^{D_T \text{ become infectious}} - \overbrace{\mu D_T}^{\text{natural deaths}}, \\
\frac{dI_{DT}}{dt} &= \overbrace{\sigma_3 D_T}^{D_T \text{ become infectious}} + \overbrace{\omega_2 C_{DT}}^{C_{DT} \text{ becomes } I_{DT} \text{ due to TB}} - \overbrace{\rho_2 I_{DT}}^{I_{DT} \text{ is exposed to TB}} - \\
&\quad \overbrace{\theta_2 I_{DT}}^{I_{DT} \text{ gets complication due to TB}} - \overbrace{\delta_2 I_{DT}}^{\text{disease induced death}} - \overbrace{\mu I_{DT}}^{\text{natural deaths}}, \\
\frac{dC_{DT}}{dt} &= \overbrace{\theta_2 I_{DT}}^{I_{DT} \text{ gets complication due to TB}} - \overbrace{\omega_2 C_{DT}}^{C_{DT} \text{ becomes } I_{DT} \text{ due to TB}} - \overbrace{\delta_3 C_{DT}}^{\text{disease induced death}} - \overbrace{\mu C_{DT}}^{\text{natural deaths}}, \\
\frac{dD}{dt} &= \overbrace{\alpha_1 S}^{S \text{ acquires diabetes}} + \overbrace{\omega_1 C}^{\text{treated } C} - \overbrace{\eta D}^{D \text{ gets TB}} - \overbrace{\theta_1 D}^{D \text{ getting complications}} - \overbrace{\mu D}^{\text{natural deaths}}, \\
\frac{dC}{dt} &= \overbrace{\theta_1 D}^{D \text{ getting complications}} - \overbrace{\omega_1 C}^{C \text{ getting treatment}} - \overbrace{\delta_4 C}^{\text{disease induced deaths}} - \overbrace{\mu C}^{\text{natural deaths}},
\end{aligned}
\right\} \tag{2.1}
$$

where $\lambda = \beta I$ and $I = I_T + I_{DT}$, subject to the initial conditions in (2.2).

$$\left.\begin{aligned} &S(0) = S_0,\ \ L_s(0) = L_{s0},\ \ I_T(0) = I_{T0},\ \ L_f(0) = L_{f0},\ \ I_{DT} = I_{0DT}, \\ &C_{DT} = C_{0DT},\ \ D_T(0) = D_{T0},\ \ D(0) = D_0,\ \ C(0) = C_0. \end{aligned}\right\} \tag{2.2}$$

The model (2.1) is an extension of some earlier mentioned modeling studies such as:

1. [28] by including diabetes complications and tuberculosis complications due to diabetes.
2. [28, 41, 31] by incorporating the non-standard finite difference method to carry out the numerical simulation of the model.

2.1.1 Assumptions

The following assumptions were made when developing the model:

1. Recruitment is by birth only.
2. Individuals in the infectious class are treated and develop latent slow TB, which can also become infectious.
3. No permanent immunity upon treatment.
4. Individuals with TB complications due to diabetes, even when treated, are still infectious from TB.

2.2 Well-posedness of the model

For the TB-Diabetes model in (2.1) to be epidemiologically meaningful, it must be proven that all solutions with non–negative initial data will remain non-negative for all time.

Theorem 2.1. *If initial values* $S(0), L_f(0), L_s(0), I_T(0), D_T(0), I_{DT}(0), C_{DT}(0), D(0), C(0)$ *are non-negative, then the solution* $(S(t), L_f(t), L_s(t), I_T(t), D_T(t), I_{DT}(t), C_{DT}(t), D(t), C(t))$ *of system* (2.1) *is non-negative for all* $t \geq 0$.

Proof. We use the Theorem by Birkhoff and Rota on differential inequality [9], we have

$$\lim_{x \to \infty} \sup N \leq \frac{\Lambda}{\mu} \tag{2.3}$$

Suppose, $N(0) \leq \frac{\Lambda}{\mu}$, then $N(t) \leq \frac{\Lambda}{\mu}$, then the system represented by (2.1) is biologically feasible in the region given by

$$\Omega = \left\{ (S, L_f, L_s, I_T, D_T, I_{DT}, C_{DT}, D, C) \in \mathbb{R}^9_+ : N \leq \frac{\Lambda}{\mu} \right\}$$

Thus, the set Ω is positively invariant, i.e. all the solutions in Ω remain in $\Omega\ \forall\ t \geq 0$.
The system (2.1) is supplemented by the initial conditions (2.2) with initial conditions can be expressed as: $\frac{dX}{dt} = f(X), X(0) = X_0$, where $X = (S, L_f, L_s, I_T, D_T, I_{DT}, C_{DT}, D, C)$ is a vector in $\mathbb{R}^9$, and $f(X) = \Big(f_1(X), f_2(X), f_3(X), f_4(X), f_5(X), f_6(X), f_7(X), f_8(X), f_9(X)\Big)^T$ is a vector field in $\mathbb{R}^9$ such that $f_1(X) - f_9(X)$ are defined by

$$
\begin{aligned}
f_1(X) &= \tfrac{dS}{dt} &&= \Lambda - \beta IS - \alpha_1 S - \mu S,\\
f_2(X) &= \tfrac{dL_f}{dt} &&= p\beta IS + \pi L_s - \sigma_1 L_f - \mu L_f,\\
f_3(X) &= \tfrac{dL_s}{dt} &&= (1-p)\beta IS + \rho_1 I_T - \pi L_s - \sigma_2 L_s - \alpha_2 L_s - \mu L_s,\\
f_4(X) &= \tfrac{dI_T}{dt} &&= \sigma_2 L_s + \sigma_1 L_f - \rho_1 I_T - \delta_1 I_T - \mu I_T,\\
f_5(X) &= \tfrac{dD_T}{dt} &&= \alpha_2 L_s + \eta D + \rho_2 I_{DT} - \sigma_3 D_T - \mu D_T,\\
f_6(X) &= \tfrac{dI_{DT}}{dt} &&= \sigma_3 D_T + \omega_2 C_{DT} - \rho_2 I_{DT} - \theta_2 I_{DT} - \delta_2 I_{DT} - \mu I_{DT},\\
f_7(X) &= \tfrac{dC_{DT}}{dt} &&= \theta_2 I_{DT} - \omega_2 C_{DT} - \delta_3 C_{DT} - \mu C_{DT},\\
f_8(X) &= \tfrac{dD}{dt} &&= \alpha_1 S + \omega_1 C - \eta D - \theta_1 D - \mu D,\\
f_9(X) &= \tfrac{dC}{dt} &&= \theta_1 D - \omega_1 C - \delta_4 C - \mu C,
\end{aligned}
\tag{2.4}
$$

It is easy, using the standard dynamical system in Theorem 2.1.3 [46, p. 102] to see that f is differentiable, hence, locally Lipschitz, thus there exists a unique local solution of (2.1) based on some open ball containing $X(0)$. Thus, unique solution exists in some open ball containing $X(0)$. Suppose we have $X(0) = (S_0, L_{f_0}, L_{s_0}, I_{T_0}, D_{T_0}, I_{DT_0}, C_{DT_0}, D_0, C_0) \geq 0$. From (2.1), $S^{'}(t) = \Lambda \geq 0$, whenever $S = 0$, $L_f^{'} = p\beta IS + \pi L_s \geq 0$, whenever $L_f = 0$, $L_s^{'} = (1-p)\beta IS + \rho_1 I_T \geq 0$, whenever $L_s = 0$, $I_T^{'} = \sigma_2 L_s + \sigma_1 L_f \geq 0$, whenever $I_T = 0$, $D_T^{'} = \alpha_2 L_s + \eta D + \rho_2 I_{DT} \geq 0$, whenever $D_T = 0$, $I_{DT}^{'} = \sigma_3 D_T + \omega_2 C_{DT} \geq 0$, whenever $I_{DT} = 0$, $C_{DT}^{'} = \theta_2 I_{DT} \geq 0$, whenever $C_{DT} = 0$, $D^{'} = \alpha_1 S + \omega_1 C \geq 0$, whenever $D = 0$ and $C^{'} = theta_1 D \geq 0$ whenever $C = 0$
Using Proposition $B.7$ of [44], the solution of the system (2.1) is non-negative. We can now proceed to verify the dissipation condition as follows:

$$
\begin{aligned}
F(X).X &= (f_1, f_2, f_3, f_4, f_5, f_6, f_7, f_8, f_9).(S, L_f, L_s, I_T, D_T, I_{DT}, C_{DT}, D, C)\\
&= f_1 S + f_2 L_f + f_3 L_s + f_4 I_T + f_5 D_T + f_6 I_{DT} + f_7 C_{DT} + f_8 D + f_9 C\\
&= D(C\omega_1 - Dm_8 + S\alpha_1) - C_D T(C_D T m_7 - I_D T\theta_2)\\
&-L_s(L_s m_3 - I_T\rho_1 + L_s\pi + S\beta(p-1)(I_D T + I_T)) - C(Cm_9 - D\theta_1)\\
&+D_T(D\eta + L_s\alpha_2 - D_T m_5 + I_D T\rho_2) + I_D T(C_D T\omega_2 - I_D T m_6 + D_T\sigma_3)\\
&+I_T(L_f\sigma_1 - I_T m_4 + L_s\sigma_2) + L_f(L_s\pi - L_f m_2 + S\beta p(I_D T + I_T))\\
&-S(Sm_1 - \Lambda + S\beta(I_D T + I_T))\\
&= (m_1 + m_2 + m_3 + m_4 + m_5 + m_6 + m_7 + m_8 + m_9)(S^2 + L_f^2 + L_s^2 + I_T^2 + D_T^2 + I_{DT}^2 + C_{DT}^2 + D^2 + C^2)\\
&= +D(C\omega_1 + S\alpha_1) - C_D T(-I_D T\theta_2) - L_s(-I_T\rho_1 + L_s\pi + S\beta(p-1)(I_D T + I_T)) - C - D\theta_1)\\
&+D_T(D\eta + L_s\alpha_2 + I_D T\rho_2) + I_D T(C_D T\omega_2 + D_T\sigma_3) + I_T(L_f\sigma_1 + L_s\sigma_2) + L_f(L_s\pi + S\beta p(I_D T + I_T))\\
&\leq a|X|^2 + q
\end{aligned}
\tag{2.5}
$$

where, a and q represent constants whose magnitudes are positive, and $m_1 = (\alpha_1 + \mu)m_2 = (\mu + \sigma_1), m_3 = (\sigma_2 + \mu + \alpha_2), m_4 = (\rho_1 + \mu + \delta_1), m_5 = (\mu + \sigma_3), m_6 = (\rho_2 + \theta_2 + \mu + \delta_2), m_7 = (\omega_2 + \mu + \delta_3)m_8 = (\eta + \mu + \theta_1), m_9 = (\omega_1 + \delta_4 + \mu)$;. Therefore, $X(t)$ of the system (2.1) is well defined in time. Hence, $S(t) \leq N, L_f(t) \leq N, L_s(t) \leq N, I_T(t) \leq N, D_T(t) \leq N, I_{DT}(t) \leq N, C_{DT}(t) \leq N, D(t) \leq N, C(t) \leq N; \forall t \geq 0$. Thus, X is bounded. □

3 Disease Free Equilibrium

3.1 The DFE

The disease-free equilibrium (DFE) is the state where there in no infection in the population, that is, $I_T = I_{DT} = 0$. Using the S equation, we obtain,

$$
S_0^* = \frac{\Lambda}{m_1}. \tag{3.1}
$$

We use (3.1) with L_s to obtain

$$L^*_{s_0} = 0. \tag{3.2}$$

Similarly, we use (3.1) and (3.2) with L_f to obtain

$$L^*_{f_0} = 0. \tag{3.3}$$

We use (3.3) and (3.2) to to obtain

$$D^*_{T_0} = \frac{\eta}{m_5}. \tag{3.4}$$

Factorizing the values of $I^*_{T_0} = I^*_{DT_0} = 0$ in C_{DT} we obtain $C^*_{DT_0} = 0$, from where we obtain

$$D^*_0 = \frac{\alpha_1 S^*_0 + \omega_1 C^*_0}{m_7}. \tag{3.5}$$

We use C to get

$$C^*_0 = \frac{\theta_1 D^*_0}{m_9}. \tag{3.6}$$

We use (3.6) in (3.5) and manipulate algebraically to obtain

$$\begin{aligned} D^*_0 &= \tfrac{m_9\alpha_1 S^*_0}{\Pi_1} \\ C^*_0 &= \tfrac{\theta_1\alpha_1 S^*_0}{\Pi_1}, \end{aligned} \tag{3.7}$$

where $\Pi_1 = m_9 m_7 - \omega_1\theta_1$. Therefore, the dfe of the system (2.1) is given by

$$\left(S^*_0, L^*_{f_0}, L^*_{s_0}, I^*_{T_0}, D^*_{T_0}, I^*_{DT_0}, C^*_{DT_0}, D^*_0, C^*_0\right) = \left(S^*_0, 0, 0, 0, \frac{\eta}{m_5}, 0, 0, \frac{m_9\alpha_1 S^*_0}{\Pi_1}, \frac{\theta_1\alpha_1 S^*_0}{\Pi_1}\right), \tag{3.8}$$

where S^*_0 is given by (3.1).

3.2 Control Reproduction Number

We use the method described in [52, 1] to rewrite our main system in the following form:

$$\begin{aligned} \dot{x_i} &= \mathcal{F}(x,y) - \mathcal{V}_{\mathbf{\Gamma}i}(x,y) \\ \dot{y_j} &= g(x,y) \end{aligned} \tag{3.9}$$

with

$$\begin{aligned} x &= (L_s, I_T, D_T, I_{DT}, C_{DT})^\top \\ y &= (S, L_f, D, C)^\top. \end{aligned}$$

Let $F = \nabla\mathcal{F}|_{(S^*,V^*,0)}$, and $V = \nabla\mathcal{V}|_{(S^*,V^*,0)}$, be the Jacobian matrices of maps $\mathcal{F}$ and $\mathcal{V}$ evaluated at the DFE.

$$\mathcal{F} = \begin{pmatrix} (1-p)\beta IS \\ \sigma_1 L_f \\ \eta D \\ 0 \\ 0 \end{pmatrix}, \quad \mathcal{V} = \mathcal{V}^- - \mathcal{V}^+ = \begin{pmatrix} m_3 L_s - \rho_1 I_T \\ m_4 I_T - \sigma_2 L_s \\ m_5 D_T - \alpha_2 L_s \\ m_6 I_{DT} - \omega_2 C_{DT} - \alpha_3 D_T \\ m_7 C_{DT} - \theta_2 I_{DT} \end{pmatrix}. \tag{3.10}$$

Vector $\mathcal{F}$ represents the rate of new infections in compartment i, vector $\mathcal{V}^+$ represents the rate of new infections in compartment i by other means and vector $\mathcal{V}^-$ is the rate of transfer of individuals out of

compartment i. Jacobian matrices for $\mathcal{F}$ and $\mathcal{V}$ at dfe are given by matrices F and $\mathcal{V}$ respectively and are defined as follows:

$$F = \frac{\partial \mathcal{F}}{\partial X}$$

and

$$\mathcal{V} = \frac{\partial \mathcal{V}}{\partial X}.$$

F and its corresponding value at dfe,

$$F = \begin{pmatrix} 0 & \frac{\Lambda}{m_1}\beta(1-p) & 0 & \frac{\Lambda}{m_1}\beta(1-p) & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{pmatrix}; V = \begin{pmatrix} m_3 & -\rho_1 & 0 & 0 & 0 \\ -\sigma_2 & m_4 & 0 & 0 & 0 \\ -\alpha_2 & 0 & m_5 & 0 & 0 \\ 0 & 0 & -\sigma_3 & m_6 & -\omega_2 \\ 0 & 0 & 0 & -\theta_2 & m_7 \end{pmatrix}.$$

The next-generation matrix of the system of the model is given by $F\mathcal{V}^{-1}$. The control reproduction number is given by the spectral radius of $F\mathcal{V}^{-1}$, meaning $F\mathcal{V}^{-1} = \mathcal{R}_C$ or the largest eigenvalues of $F\mathcal{V}^{-1}$. Thus,

$$\mathcal{R}_C = \left(\frac{\Lambda}{m_1}\right)\left(\frac{\beta(1-p)}{m_5}\right)\left(\frac{\alpha_2 m_4 m_7 \sigma_3 + m_5 m_6 m_7 \sigma_2 - m_5 \omega_2 \sigma_2 \theta_2}{(m_6 m_7 - \omega_2 \theta_2)(m_3 m_4 - \rho_1 \sigma_2)}\right). \tag{3.11}$$

Equation (3.11) indicates that one case of secondary infection of tuberculosis and diabetes co-infections in a susceptible population can cause spread in the entire population.

4 Stability Analysis

4.1 Local Stability of DFE

Theorem 4.1. *The DFE,* $X_0 = \left(S_0^*, 0, 0, 0, \frac{\eta}{m_5}, 0, 0, \frac{m_9\alpha_1 S_0^*}{\Pi_1}, \frac{\theta_1\alpha_1 S_0^*}{\Pi_1}\right)$ *for the system* (2.1)*,* X_0 *is locally asymptotically stable if* $\mathcal{R}_C < 1$ *and unstable if* $\mathcal{R}_C > 1$ *where* $\mathcal{R}_C$ *is defined by* (3.11)*.*

Proof. See proof of Theorem 4.1 in [52] □

4.2 Global Stability of DFE

Theorem 4.2. *If* $\mathcal{R}_0 \leq 1$*, then the DFE of system* (2.1) *is globally asymptotically stable in* $\Omega = \{X = (S, L_f, L_s, I_T, D_T, I_{DT}, C_{DT}, D, C) \in \mathbb{R}^9 : S+L_f+L_s+I_T+D_T+I_{DT}+C_{DT}+D+C \leq N$ *and it is unstable if* $\mathcal{R}_C > 1$*.*

Proof. We use matrix-theoretic method as suggested by [1, 37, 38, 43, 48, 52]. Let $x = (L_s, I_T, D_T, I_{DT}, C_{DT})^T$ and $y = (S, L_f, D, C)$. We consider F, V, $\mathcal{F}$ and $\mathcal{V}$ as defined in Section 3.2. If the disease compartments for the system are given by

$$\frac{dx}{dt} = \mathcal{F}(x, y) - \mathcal{V}(x, y)$$

and dynamics of infected compartments is given by

$$\frac{dx}{dt} = (F - V)x - f(x, y).$$

Thus, we can obtain $f(x,y)$ as follows;

$$\begin{aligned} f(x,y) &= (F-\mathcal{V})x - \mathcal{F}(x,y) + \mathcal{V}(x,y) \\ &= \begin{pmatrix} \frac{\beta(Sm_1-\Lambda)(p-1)(D_T\sigma_3+I_Tm_6m_7-I_T\omega_2\theta_2)}{m_1(m_6m_7-\omega_2\theta_2)} \\ -L_f\sigma_1 \\ -D\eta \\ 0 \\ 0 \end{pmatrix} \end{aligned} \tag{4.1}$$

while

$$V^{-1}F = \begin{pmatrix} 0 & \frac{\Lambda\beta m_4(1-p)}{m_1(m_3m_4-\rho_1\sigma_2)} & 0 & -\frac{\Lambda\beta m_4(p-1)}{m_1(m_3m_4-\rho_1\sigma_2)} & 0 \\ 0 & \frac{\Lambda\beta\sigma_2(1-p)}{m_1(m_3m_4-\rho_1\sigma_2)} & 0 & \frac{\Lambda\beta\sigma_2(1-p)}{m_1(m_3m_4-\rho_1\sigma_2)} & 0 \\ 0 & \frac{\Lambda\alpha_2\beta m_4(1-p)}{\Gamma_1} & 0 & \frac{\Lambda\alpha_2\beta m_4(1-p))}{\Gamma_1} & 0 \\ 0 & \frac{\Lambda\alpha_2\beta m_4m_7\sigma_3(1-p))}{\Gamma_1} & 0 & \frac{\Lambda\alpha_2\beta m_4m_7\sigma_3(1-p)}{\Gamma_1} & 0 \\ 0 & \frac{\Lambda\alpha_2\beta m_4\sigma_3\theta_2(1-p)}{\Gamma_1} & 0 & \frac{\Lambda\alpha_2\beta m_4\sigma_3\theta_2(1-p)}{\Gamma_1} & 0 \end{pmatrix}.$$

where

$$\Gamma_1 = m_1(m_3m_4m_5m_6m_7 - m_3m_4m_5\omega_2\theta_2 - m_5m_6m_7\rho_1\sigma_2 + m_5\omega_2\rho_1\sigma_2\theta_2)$$

We see that $F \geq 0$, $V^{-1} \geq 0$, $f(x,y) \geq 0$ in $\Omega \subset \mathbb{R}^9_+$; thus $V^{-1}F$ is reducible. We can therefore construct Lyapunov function based on Theorem 2.1 and 2.2 as stated by [43]. We denote the left eigenvectors of $V^{-1}F$ corresponding to the eigenvalue of $\mathcal{R}_C$ by $\{v_1, v_2, v_3v_4, v_5\}$.
Then

$$(v_1, v_2, v_3v_4, v_5)\, V^{-1}F = \mathcal{R}_C\, (v_1, v_2, v_3, v_4, v_5)$$

or

$$(v_1, v_2, v_3, v_4, v_5)\, V^{-1}F = \begin{pmatrix} 0 & \frac{\Lambda\beta(1-p)}{m_1}\left(\frac{\Gamma_4v_4}{\Gamma_1} + \frac{m_4v_1}{\Gamma_2} + \frac{\sigma_2v_2}{\Gamma_2} + \frac{\alpha_2m_4v_3}{\Gamma_3}\right) & 0 & \frac{\Lambda\beta(1-p)}{m_1}\left(\frac{\Gamma_4v_4}{\Gamma_1} + \frac{m_4v_1}{\Gamma_2} + \frac{\sigma_2v_2}{\Gamma_2} + \frac{\alpha_2m_4v_3}{\Gamma_3}\right) & 0 \end{pmatrix} \tag{4.2}$$

where $\Gamma_2 = m_3m_4 - \rho_1\sigma_2$, $\Gamma_3 = m_5\Gamma_2$, $\Gamma_4 = \alpha_2m_4m_7\sigma_3$
and

$$\mathcal{R}_C\, (v_1, v_2, v_3, v_4, v_5) = \left\{ \overbrace{\left(\frac{\Lambda}{m_1}\right)\left(\frac{\beta(1-p)}{m_5}\right)\left(\frac{\alpha_2m_4m_7\sigma_3 + m_5m_6m_7\sigma_2 - m_5\omega_2\sigma_2\theta_2}{\Gamma_6\Gamma_2}\right)}^{\mathcal{R}_C} \right\} (v_1, v_2, v_3, v_4, v_5)\,, \tag{4.3}$$

where $\Gamma_6 = m_6m_7 - \omega_2\theta_2$. We use equations (4.2) and (4.3) to derive a possible solution as $v_1 = 0$, $v_3 = 0$, $v_5 = 0$ and to allow workability, let $v_4 = \psi_t$, where ψ_t is a random parameter and v_2 is given by

$$v_2 = \left(\frac{m_1\mathcal{R}_C}{\Lambda\beta(1-p)} - \frac{\Gamma_4\psi_t}{\Gamma_1}\right)\left(\frac{\Gamma_1}{\sigma_2}\right). \tag{4.4}$$

Suppose we let $\psi_t = 1$, then

$$v_2 = \left(\frac{m_1\mathcal{R}_C}{\Lambda\beta(1-p)} - \frac{\Gamma_4}{\Gamma_1}\right)\left(\frac{\Gamma_1}{\sigma_2}\right). \tag{4.5}$$

Therefore, $\Pi^T = (0, v_2, 0, 1, 0)$. Thus, by Theorem 2.1 of [43], we have $\mathcal{Q} = \Pi^TV^{-1}x$ as the Lyapunov function of the model given by;

$$\begin{aligned} \mathcal{Q} &= \Pi^TV^{-1}x \\ &= I_T\left(\frac{m_3v_2}{\Gamma_2} + \frac{\alpha_2m_7\rho_1\sigma_3}{\Gamma_1}\right) + L_s\left(\frac{\sigma_2v_2}{\Gamma_2} + \frac{\Gamma_4}{\Gamma_1}\right) + \frac{C_DT\omega_2}{\Gamma_6} + \frac{I_Dm_7}{\Gamma_6} + \frac{D_Tm_7\sigma_3}{m_5m_6m_7 - m_5\omega_2\theta_2} \end{aligned} \tag{4.6}$$

We differentiate $\mathcal{Q}$ at DFE to get

$$\begin{aligned}\mathcal{Q}|'_{DFE} &= (\mathcal{R}_C - 1)\,\Pi^T x - \Pi^T V^{-1} f(x,y) \\ &= 0.\end{aligned} \tag{4.7}$$

This implies that $x = 0$ and $f(x,y) = 0$ or $y = (S, L_f, D, C)^\top = \left(S_0^*, 0, \frac{m_9\alpha_1 S_0^*}{\Pi_1}, \frac{\theta_1\alpha_1 S_0^*}{\Pi_1}\right)^\top$. Therefore, $\left(S_0^*, 0, 0, 0, \frac{\eta}{m_5}, 0, 0, \frac{m_9\alpha_1 S_0^*}{\Pi_1}, \frac{\theta_1\alpha_1 S_0^*}{\Pi_1}\right)$ is the only invariant set in Ω where $\mathcal{Q}' = 0$. Thus, by LaSalle's invariance principle [2], the DFE, and is globally asymptotically stable in Ω and $\mathcal{R}_C \leq 1$. □

We use LaSalle's invariance principle [7] to prove global stability of DFE as follows; if $\mathcal{Q} = 0$,

$$(\mathcal{R}_C - 1)\,\Pi^T x = I_T\,(\mathcal{R}_C + 1) + \frac{D_T\sigma_3\,(\mathcal{R}_C + 1)}{\Gamma_6}, \tag{4.8}$$

Equation (4.8) is only feasible when $\mathcal{R}_C < 1$ or $\mathcal{R}_C > 1$. Thus, $\left(S_0^*, 0, 0, 0, \frac{\eta}{m_5}, 0, 0, \frac{m_9\alpha_1 S_0^*}{\Pi_1}, \frac{\theta_1\alpha_1 S_0^*}{\Pi_1}\right)$ is the only invariant set in Ω which satisfies $\mathcal{Q}' = 0$ when $R_C < 1$. Therefore, by LaSalle's invariance principle, the DFE is globally asymptotically in Ω when $\mathcal{R}_C < 1$. Therefore, by continuity $\mathcal{Q}'$ remains positive in a small neighbourhood of X_0.

4.3 Endemic Equilibrium

4.3.1 Endemic Equilibrium Points

Using (3.11) and simplifying the constants yields

$$\begin{aligned}\mathcal{R}_C &= \left(\tfrac{\Lambda}{m_1}\right)\left(\tfrac{\beta(1-p)}{m_5}\right) K_B, \\ \rightarrow \quad \Lambda &= \tfrac{\mathcal{R}_C m_1 m_5}{\beta(1-p)K_R},\end{aligned} \tag{4.9}$$

where $K_R = \left(\frac{\alpha_2 m_4 m_7\sigma_3 + m_5 m_6 m_7\sigma_2 - m_5\omega_2\sigma_2\theta_2}{(m_6 m_7 - \omega_2\theta_2)(m_3 m_4 - \rho_1\sigma_2)}\right)$. Using S and simplifying yields,

$$\begin{aligned}S^* &= \tfrac{\Lambda}{\beta I^* + m_1}, \\ &\text{Substituting } \Lambda \text{ from (4.9)}, \\ \rightarrow S^* &= \tfrac{\mathcal{R}_C m_1 m_5}{(\beta I^* + m_1)(\beta(1-p)K_R)}, \\ &= \tfrac{\mathcal{R}_C K_B}{\beta I^* + m_1},\end{aligned} \tag{4.10}$$

where $K_B = \frac{m_1 m_5}{\beta(1-p)K_R}$. Re-writing (4.10) to find explicit value of I^* yields

$$I^* = \frac{\mathcal{R}_C K_B}{S^*\beta} - \frac{m_1}{\beta}. \tag{4.11}$$

Using L_f yields

$$L_f^* = \frac{p\beta I^* S^* + \pi L_s^*}{m_2}. \tag{4.12}$$

Using L_s yields

$$L_s^* = \frac{(1-p)\beta I^* S^* + \rho_1 I_T^*}{m_3}. \tag{4.13}$$

Using I_T yields

$$I_T^* = \frac{\sigma_2 L_s^* + \sigma_1 L_f^*}{m_4}. \tag{4.14}$$

Using D_T yields

$$D_T^* = \frac{\alpha_2 L_s^* + \eta D^* + \rho_2 I_{DT}^*}{m_5}. \tag{4.15}$$

Using I_{DT} yields

$$I_{DT}^* = \frac{\sigma_3 D_T^* + \omega C_{DT}^*}{m_6}. \tag{4.16}$$

Using C_{DT} yields

$$C_{DT}^* = \frac{\theta_2 I_{DT}^*}{m_7}. \tag{4.17}$$

Using D yields

$$D^* = \frac{\alpha_1 S^* + \omega_1 C^*}{m_8}. \tag{4.18}$$

Using C yields

$$C^* = \frac{\theta_1 D^*}{m_9} \tag{4.19}$$

Substituting (4.19) into (4.18) and simplifying yields

$$D^* = \frac{\alpha_1 S^* m_1}{K_M}, \tag{4.20}$$

where $K_M = m_1 m_8 - \omega_1 \theta_1$. Using (4.17) with (4.16) yields

$$I_{DT}^* = \frac{\sigma_3 m_7 D_T^*}{\Gamma_6}. \tag{4.21}$$

Substituting (4.21) and (4.20) into (4.15) yields

$$D_T^* = \frac{L_S^* \Phi_1 + \Phi_2 S^*}{K_D}, \tag{4.22}$$

where $\Phi_1 = \alpha_2 K_M \Gamma_2$, $\Phi_2 = \eta \alpha_1 m_1 \Gamma_6$ and $K_D = m_5 \Gamma_6 - \rho_2 \sigma_3 m_7 K_M$. Substituting (4.14) into (4.13) yields,

$$L_s^* = \frac{\Phi_3 I^* S^* + \rho_1 \sigma_1 L_f^*}{\Gamma_2}, \tag{4.23}$$

where $\Phi_3 = (1-p)\beta m_4$. Substituting (4.23) into (4.12) yields

$$L_f^* = \frac{I^* S^* \Phi_5}{\Phi_4}, \tag{4.24}$$

where $\Phi_4 = m_2 \Gamma_2 - \rho_1 \sigma_2 \pi$ and $\Phi_5 = \Gamma_2 p \beta + \pi \Phi_3$. Substituting (4.11) into (4.24) yields

$$L_f^* = \frac{\mathcal{R}_C K_B - S^* m_1 \Phi_5}{\beta \Phi_4}. \tag{4.25}$$

Substituting (4.25) and (4.11) into (4.23) yields

$$L_s^* = \frac{\mathcal{R}_C K_B \Phi_6 - S^* m_1 \Phi_7}{\beta \Phi_4 \Gamma_2} \tag{4.26}$$

where $\Phi_6 = \Phi_4 \Phi_3 + \rho_1 \sigma_1$ and $\Phi_7 = \Phi_3 \Phi_4 + \rho_1 \sigma_1 \Phi_5$. Using (4.26) into (4.22) results to

$$D_T^* = \frac{\mathcal{R}_C\Phi_8 + (\Phi_9 - m_1\Phi_7)\, S^*}{K_D\beta\Phi_4\Gamma_2}, \tag{4.27}$$

where $\Phi_8 = \Phi_1 K_B \Phi_6$ and $\Phi_9 = \beta\Phi_4\Gamma_2\Phi_2$. Substituting (4.27) into (4.21) yields

$$I_{DT}^* = \frac{\mathcal{R}_C\Phi_{11} + \sigma_3 m_7\Phi_{12}S^*}{\Phi_{10}}, \tag{4.28}$$

where $\Phi_{10} = \Gamma_6 K_D\beta\Phi_4\Gamma_2$, $\Phi_{11} = \sigma_3 m_7\Phi_8$ and $\Phi_{12} = \Phi_9 - m_1\Phi_7$. Using (4.28) into (4.17) yields

$$C_{DT}^* = \frac{\Phi_{12}\Phi_{11}\mathcal{R}_C + \Phi_{13}S^*}{m_7\Phi_{10}}, \tag{4.29}$$

where $\Phi_{13} = \sigma_3 m_7\Phi_{12}\Phi_2$. Substituting (4.20) into (4.19) yields

$$C^* = \frac{\theta_1\alpha_1 m_1 S^*}{m_9 K_M}. \tag{4.30}$$

Using (4.25) and (4.26) in (4.14) yields

$$I_T^* = \frac{\mathcal{R}_C K_B\Phi_{14} - \Phi_{15}S^* m_1}{\beta\Phi_4\Gamma_2}, \tag{4.31}$$

where $\Phi_{14} = \sigma_2\Phi_6 + \sigma_1\Gamma_2$ and $\Phi_{15} = \sigma_2\Phi_2 + \sigma_2\Phi_5\Gamma_2$. Using (4.30) and (4.28), I^* can be written explicitly as

$$I^* = \frac{\Phi_{21}\mathcal{R}_C + \Phi_{22}S^*}{\Phi_{20}} \tag{4.32}$$

where $\Phi_{16} = \Phi_{10}K_B\Phi_{14}$, $\Phi_{17} = \beta\Phi_4\Gamma_2\Phi_{11}$, $\Phi_{18} = \beta\Phi_4\Gamma_2\sigma_3 m_7\Phi_{12}$, $\Phi_{19} = \Phi_{10}\Phi_{15}m_1$, $\Phi_{20} = \beta\Phi_4\Gamma_2\Phi_{10}$, $\Phi_{21} = \Phi_{16} + \Phi_{17}$ and $\Phi_{22} = \Phi_{18} - \Phi_{19}$. Substitute (4.32) into (4.10) and simplifying yields

$$\Phi_{22}S^* + (\beta\Phi_{21}\mathcal{R}_C + m_1\Phi_{20})\, S^* - \mathcal{R}_C K_B\Phi_{20} = 0. \tag{4.33}$$

The endemic equilibrium point of the system (2.1) is given by (4.34)

$$\begin{aligned}
&S^* \\
&L_f^* = \left(\tfrac{\mathcal{R}_C K_B - S^* m_1\Phi_5}{\beta\Phi_4}\right) \\
&L_s^* = \left(\tfrac{\mathcal{R}_C K_B\Phi_6 - S^* m_1\Phi_7}{\beta\Phi_4\Gamma_2}\right) \\
&I_T^* = \left(\tfrac{\mathcal{R}_C K_B\Phi_{14} - \Phi_{15}S^* m_1}{\beta\Phi_4\Gamma_2}\right) \\
&D_T^* = \left(\tfrac{\mathcal{R}_C\Phi_8 + (\Phi_9 - m_1\Phi_7)S^*}{K_D\beta\Phi_4\Gamma_2}\right) \\
&I_{DT}^* = \left(\tfrac{\mathcal{R}_C\Phi_{11} + \sigma_3 m_7\Phi_{12}S^*}{\Phi_{10}}\right) \\
&C_{DT}^* = \left(\tfrac{\Phi_{12}\Phi_{11}\mathcal{R}_C + \Phi_{13}S^*}{m_7\Phi_{10}}\right) \\
&D^* = \left(\tfrac{\alpha_1 S^* m_1}{K_M}\right) \\
&C^* = \left(\tfrac{\theta_1\alpha_1 m_1 S^*}{m_9 K_M}\right)
\end{aligned} \tag{4.34}$$

4.3.2 Global Stability of endemic equilibrium

Lemma 4.1. *When $\mathcal{R}_C > 1$, there exists a unique endemic equilibrium X^* given by $S^* = \frac{-b \pm \sqrt{b^2-4ac}}{2a}$, where $a = \Phi_{22}$, $b = (\beta\Phi_{21}\mathcal{R}_C + m_1\Phi_{20})$ and $c = -\mathcal{R}_C K_B \Phi_{20}$. When $\mathcal{R}_0 \leq 1$, there is no endemic equilibrium.*

Proof. From (4.34), S^* can be simplified as

$$0 = aS^{*2} + bS^* + c, \tag{4.35}$$

where

$$a = \Phi_{22} \tag{4.36a}$$
$$b = (\beta\Phi_{21}\mathcal{R}_C + m_1\Phi_{20}) \tag{4.36b}$$
$$c = -\mathcal{R}_C K_B \Phi_{20} \tag{4.36c}$$

Equation (4.35) suggests that there are two endemic equilibria as

$$S_1^* = \frac{-b+\sqrt{b^2-4ac}}{2a} \quad S_2^* = \frac{-b-\sqrt{b^2-4ac}}{2a}. \tag{4.37}$$

Equation (4.37) indicates that the following cases are feasible;

1. When $\mathcal{R}_C > 1$, then
   S_1^* exists iff $\left(\sqrt{b^2+4ac}\right) > b$.
   S_2^* will not exist. Thus a possibility of the existence of only one real root.
2. When $\mathcal{R}_C = 1$, then
   S_1^* exists iff $\left(\sqrt{b^2+4ac}\right) > b$.
   S_2^* will not exist. Thus a possibility of the existence of only one real root.
3. When $\mathcal{R}_C < 1$:
   S_1^* exist iff $b^2 > 4ac$ and $\left(\sqrt{b^2+4ac}\right) > b$.
   S_2^* will not exist. Thus a possibility of the existence of only one real root

Table 1 summarizes the analytical solution of (4.35) based on $\mathcal{R}_C$.

Table 1: Analytic solution of (4.35).

$\mathcal{R}_\mathbf{C}$	$\mathbf{c}$	$\mathbf{4ac}$	$\mathbf{b}$	$\mathbf{b^2-4ac}$	$\mathbf{-b+\sqrt{b^2-4ac}}$	$\mathbf{-b-\sqrt{b^2-4ac}}$	Comment
>1	<0	<0	>0	>0	>0	<0	1 EE
$=1$	<0	<0	>0	>0	>0	<0	1 EE
<1	>0	>0	>0	>0 iff $b^2>4ac$	>0 iff $b^2>4ac$	<0	No EE

Table 1 shows that when $\mathcal{R}_C < 1$, there is no endemic equilibrium, but if $\mathcal{R}_C > 1$, a unique endemic equilibrium is obtained when

$$S^* = S_1^* = \frac{-b+\sqrt{b^2-4ac}}{2a}$$

□

Theorem 4.3. *If $\mathcal{R}_C > 1$, the unique equilibrium is globally asymptotically stable in Ω.*

Proof. The proof is based on Volterra-Lyapunov stable matrices according to [25]. The Lyapunov function is defined as follows;

$$\begin{aligned} L \quad &= \varpi_1(S-S^*)^2 + \varpi_2(L_f - L_f^*)^2 + \varpi_3(L_s - L_s^*)^2 + \varpi_4(I_T - I_T^*)^2 + \varpi_5(D_T - D_T^*)^2 + \varpi_6(I_{DT} - I_{DT}^*)^2 \\ &+\varpi_7(C_{DT} - C_{DT}^*)^2 + \varpi_8(D-D^*)^2 + \varpi_9(C-C^*)^2 \end{aligned} \tag{4.38}$$

where ϖ_i are positive constants. $\frac{\partial L}{\partial x_i}$ yields

$$\begin{aligned} L^{'} \quad &= -2\varpi_1 \left(S-S^*\right)^2 (\beta + m_1) - 2\varpi_1(S-S^*)(I_T - I_T^*)(\beta S^*) - 2\varpi_1(S-S^*)(I_{DT} - I_{TD}^*)(\beta S^*) \\ &-2\varpi_2 \left(L_f - L_f^*\right)^2 (m_2) + 2\varpi_2 \left(L_f - L_f^*\right)(S-S^*)\left(p\beta(I_T^* + I_{DT}^*)\right) + 2\varpi_2 \left(L_f - L_f^*\right)(L_s - L_s^*)(\pi) \\ &+2\varpi_2 \left(L_f - L_f^*\right)(I_T - I_T^*)(p\beta S^*) + 2\varpi_2 \left(L_f - L_f^*\right)(I_{DT} - I_{DT}^*)(p\beta S^*) \\ &+2\varpi_3 \left(L_s - L_s^*\right)^2 (-m_3) + 2\varpi_3 \left(L_s - L_s^*\right)(S-S^*)\left((1-p)\beta I^*\right) \\ &+2\varpi_3 \left(L_s - L_s^*\right)(I_T - I_T^*)\left((1-p)\beta I_{DT}^*\right) + 2\varpi_3 \left(L_s - L_s^*\right)(I_{DT} - I_{DT}^*)\left((1-p)\beta I_T^*\right) \\ &-2\varpi_4 \left(I_T - I_T^*\right)^2 (m_4) + 2\varpi_4 \left(I_T - I_T^*\right)\left(L_f - L_f^*\right)(\sigma_1) + 2\varpi_4 \left(I_T - I_T^*\right)(L_s - L_s^*)(\sigma_2) \\ &-2\varpi_5 \left(D_T - D_T^*\right)^2 (m_5) + 2\varpi_4 \left(D_T - D_T^*\right)(L_s - L_s^*)(\alpha_2) + 2\varpi_5 \left(D_T - D_T^*\right)(D-D^*)(\eta) \\ &-2\varpi_6 \left(I_{DT} - I_{DT}^*\right)^2 (m_6) + 2\varpi_6 \left(I_{DT} - I_{DT}^*\right)(D_T - D_T^*)(\sigma_3) + 2\varpi_6 \left(I_{DT} - I_{DT}^*\right)(C_{DT} - C_{DT}^*)(\omega_2) \\ &-2\varpi_7 \left(C_{DT} - C_{DT}^*\right)^2 (m_7) + 2\varpi_7 \left(C_{DT} - C_{DT}^*\right)(I_{DT} - I_{DT}^*)(\theta_2) \\ &-2\varpi_8 \left(D-D^*\right)^2 (m_8) + 2\varpi_8 \left(D-D^*\right)(S-S^*)(\alpha_1) + 2\varpi_8 \left(D-D^*\right)(C-C^*)(\omega_1) \\ &-2\varpi_9 \left(C-C^*\right)^2 (m_9) + 2\varpi_9 \left(C-C^*\right)(D-D^*)(\theta_1) \\ &= Y(MA + A^T M^T)Y^T \end{aligned} \tag{4.39}$$

where $Y = \left(S-S^*, L_f - L_f^*, L_s - L_s^*, I_T - I_T^*, D_T - D_T^*, I_{DT} - I_{DT}^*, C_{DT} - C_{DT}^*, D-D^*, C-C^*\right)$, $M =$ diag $(m_1, m_2, m_3, m_4, m_5, m_6, m_7, m_8, m_9)$ and

$$A = \begin{pmatrix} -(\beta I^* + m_1) & 0 & 0 & -\beta S^* & 0 & -\beta S^* & 0 & 0 & 0 \\ p\beta I^* & -m_2 & \pi & p\beta S^* & 0 & p\beta S^* & 0 & 0 & 0 \\ (1-p)\beta I^* & 0 & -m_3 & (1-p)\beta I_{DT}^* & 0 & (1-p)\beta I_T^* & 0 & 0 & 0 \\ 0 & \sigma_1 & \sigma_2 & -m_4 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & \alpha_2 & 0 & -m_5 & 0 & 0 & \eta & 0 \\ 0 & 0 & 0 & 0 & \sigma_3 & -m_6 & \omega_2 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & \theta_2 & -m_7 & 0 & 0 \\ \alpha_1 & 0 & 0 & 0 & 0 & 0 & 0 & -m_8 & \omega_1 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & \theta_1 & -m_9 \end{pmatrix} \tag{4.40}$$

Evaluating the $det(A)$ at X_{x_t} gives

$$\begin{aligned} det(A) = &\left(m_7\omega_1\theta_1 - m_7 m_8 m_9\right) m_1 m_2 m_3 m_4 m_5 m_6 + \left(m_8 m_9 \omega_2 \theta_2 - \omega_1\omega_2\theta_1\theta_2\right) m_1 m_2 m_3 m_4 m_5 \\ &+ \left(\Lambda\beta m_7 m_8 m_9 p\sigma_1 - \Lambda\beta m_7\omega_1 p\sigma_1\theta_1\right) m_3 m_5 m_6 + \left(\Lambda\beta\omega_1\omega_2 p\sigma_1\theta_1\theta_2 - \Lambda\beta m_8 m_9\omega_2 p\sigma_1\theta_2\right) m_3 m_5 \\ &- \frac{1}{m_1}\left(\Lambda\alpha_1\beta\eta m_7 m_9\sigma_3\right) m_2 m_3 m_4 \end{aligned} \tag{4.41}$$

$$\frac{dS}{dt} = \Lambda - \beta I^* S - m_1 S^* = 0, \tag{4.42}$$

$$\frac{dL_f}{dt} = p\beta I^* S^* + \pi L_s^* - m_2 L_f^* = 0, \tag{4.43}$$

$$\frac{dL_s}{dt} = (1-p)\beta I^* S^* + \rho_1 I_T^* - m_3 L_s^* = 0, \tag{4.44}$$

$$\frac{dI_T}{dt} = \sigma_2 L_s^* + \sigma_1 L_f^* - m_4 I_T^* = 0, \tag{4.45}$$

$$\frac{dI_{DT}}{dt} = \sigma_3 D_T^* + \omega_2 C_{DT}^* - m_6 I_{DT}^* = 0, \tag{4.46}$$

$$\frac{dC_{DT}}{dt} = \theta_2 I_{DT}^* - m_7 C_{DT}^* = 0 \tag{4.47}$$

In order to prove that $det(A) > 0$, then all then $S^* > 0, L_f^* > 0, L_s^* > 0, I_T^* > 0, I_{DT}^* > 0, C_{DT}^* > 0, D_T^* > 0$. Suppose $S^* \geq 0$ and $S^* = 0$, then (4.42) reduces to

$$\Lambda = 0. \tag{4.48}$$

Equation (4.48) is not feasible, since $\Lambda \neq 0$, hence, $S^* > 0$. Suppose $L_s^* \geq 0$ and $L_s = 0$, then (4.43) and (4.44) reduces to

$$\begin{aligned} p\beta I^* S^* - m_2 L_f^* &= 0, \\ &\rightarrow L_f^* = \tfrac{p\beta I^* S^*}{m_2}, \\ (1-p)\beta I^* S^* + \rho_1 I_T^* &= 0, \\ &\rightarrow I_T^* = \tfrac{(p-1)\beta I^* S^*}{\rho_1}. \end{aligned} \tag{4.49}$$

Equation (4.45) yields

$$\begin{aligned} \sigma_2 L_s^* + \sigma_1 L_f^* - m_4 I_T^* &= 0 \\ &\rightarrow I_T^* = \tfrac{\sigma_1 p \beta I^* S^*}{m_2 m_4} \end{aligned} \tag{4.50}$$

Equating (4.49) and (4.50) yields

$$\begin{aligned} \tfrac{(p-1)\beta I^* S^*}{\rho_1} &= \tfrac{\sigma_1 p \beta I^* S^*}{m_2 m_4} \\ \rightarrow \tfrac{(p-1)}{\rho_1} &= \tfrac{\sigma_1 p}{m_2 m_4} \end{aligned} \tag{4.51}$$

Equation (4.51) is not feasible since $\frac{(p-1)}{\rho_1} \neq \frac{\sigma_1 p}{m_2 m_4}$. Hence, $L_s^* > 0, \implies det(A) > 0$. Therefore, $M(-A) + [M(-A)]^T > 0$ which implies that the matrix A is Volterra-Lyapunov stable and M is a constant matrix. Thus, when $\mathcal{R}_C > 1$, the endemic equilibrium of the system is globally asymptotically stable in Ω.

□

5 Numerical Simulation

5.1 Sensitivity analysis of parameters

The parameter values listed in Table 2 to perform a sensitivity analysis of parameters in control reproduction number $\mathcal{R}_C$ in (3.11). The results will inform the strength of the disease control.

5.1.1 Parameter estimation

The estimated birth rate in Kenya was 27.67 births per year for 1000 births in 2022, according to the World Bank collection of development indicators [53]. Thus, $\Lambda = \frac{8.06}{1000} \times 53 \times 10^6$ per year. The mortality rate in Kenya was estimated to 8.06 deaths per 1000 people. The rest of the estimation for the parameters used in the model diagram are outlined Table 2.

Table 2: Parameter description and estimation

Description	Symbol	Value/yr	Range	Source
TB transmission coefficient	β	$\frac{233}{100,000}$	$\frac{188 \text{ to } 266}{100,000}$	[13]
Recruitment rate	Λ	$\frac{8.06}{1000} \times 53 \times 10^6$	-	Assumed
TB induced mortality	δ_1	$\frac{50}{100,000}$	$\frac{9 \text{ to } 97}{}$	[19]
Diabetic-TB induced mortality	δ_2	$\frac{426}{100,000}$	$\frac{89 \text{ to } 616}{100,000}$	[24]
Diabetic complication induced mortality for diabetic individuals	δ_3	$\frac{10.9}{100,000}$	$\frac{7.2 \text{ to } 82.6}{100,000}$	[39, 42]
Diabetes induced mortality	δ_4	$\frac{20.9}{10000}$	$\frac{7.2-82.6}{10000}$	[47]
Rate of Latent fast TB individuals becoming infectious	σ_1	$\frac{558}{100,000}$	$\frac{455 \text{ to } 662}{100,000}$	[13]
Rate of latent slow TB individuals becomes infectious	σ_2	3.33%	2% - 5%	[16]
Rate of diabetes individuals becoming infectious of TB	σ_3	14.8%	7.1% - 23.8%	[45]
Rate of acquiring diabetes	α_1	2.2%	1.4% - 3.1%	[30]
Rate of acquiring diabetes when exposed to TB	α_2	2.16	1.19 - 3.93	[12]
Rate of treated TB individuals exposed to TB	ρ_1	80.1%	$78\% - 85$	[40]
Rate of treated TB-diabetes individuals exposed to TB	ρ_2	31%	$12\% - 44\%$	[29]
Rate of treatment of complications due to diabetes	ω_1	38%	25% - 45%	[35]
Rate of treatment of TB complications in diabetic	ω_2	0.5%	0.1% - 45%	[10]
Rate of developing Latent fast TB	p	6%	5%–10%	[17]
Natural mortality rate	μ	$\frac{8.06}{1000}$	$\frac{7.9-8.1}{1000}$	[4]
Rate of acquiring complicated diabetes	θ_1	3.2%	2.8% - 4.4%	[34]
Rate of acquiring complicated diabetes due to TB	θ_2	$\frac{1}{20}$	$\frac{1 \text{ to } 6}{20}$	[36]
Rate of latent slow individuals becoming latent fast	π	$\frac{1220}{10^6} \times 0.08$	$\frac{48 \text{ to } 1299}{10^6}$	[14]
Rate of diabetic individuals acquiring TB	η	$\frac{112}{1134}$	$\frac{90 \text{ to } 130}{1134}$	[36]

5.1.2 Elasticity Indices

The elasticity index ζ of parameter ν_i is given by $\frac{\nu_i \partial \mathcal{R}_C}{\mathcal{R}_C \partial \nu_i}$. ζ is a measure of the relative change in $\mathcal{R}_C$ to relative change in ν_i. ν_i with the largest absolute magnitude has a higher influence on $\mathcal{R}_C$ and affects the transmission dynamics of diabetes and TB co-infection. Table 3 shows elasticity indices of parameters computed based on the baseline given in Table 2 with an assumed N=1000. The table shows the indices arranged in descending order based on magnitude.
Table 3 indicates β (TB transmission coefficient) and α_1 (rate of acquiring diabetes) are the most elastic parameters. The least elastic parameter is δ_3 (Diabetic complication-induced mortality for diabetic individuals). The results align with the expectation that transmission and acquisition of the disease are often the most perceived elastic parameters [22].

5.2 Numerical solutions

The analysis of the model is presented using numerical simulations. The numerical simulations of (2.1) are presented in two cases based on the baseline values in Table 2: when $\mathcal{R}_C > 1$ (Figure 2) and when $\mathcal{R}_C < 1$ (Figure 3).
Figure 2 considers higher TB transmission coefficient $\beta = \frac{266}{10^5}$ which yields $\mathcal{R}_C = 1.0863$ with trajectories reaching unique equilibrium $S^* = 1.704 \times 10^3$, $L_f^* = 1.87795 \times 10^5$, $L_s^* = 2.3127 \times 10^4$, $I_T^* = 2.115 \times 10^3$, $D_T^* = 2.702 \times 10^3$, $I_{DT}^* = 9.307 \times 10^3$, $C_{DT}^* = 3.813 \times 10^3$, $D^* = 3.513660 \times 10^6$, and $C^* = 296$.

Table 3: Elasticity indices of parameters in $\mathcal{R}_C$

Parameter	Elasticity Index
β	1.0000
α_1	-1.0000
δ_2	-0.5598
σ_2	0.4343
α_2	-0.4306
ρ_1	-0.4050
δ_1	-0.0262
μ	-0.0081
p	-0.0060
ρ_2	-0.0041
θ_2	-6.3014×10^{-4}
σ_3	3.0747×10^{-5}
ω_1	2.5813×10^{-5}
δ_3	-2.4035×10^{-5}

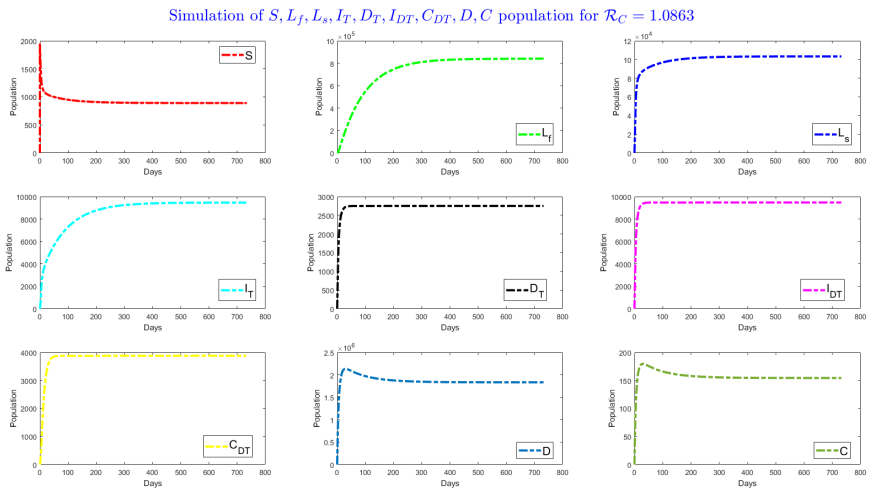

Fig. 2: Simulation of compartment population based on Table 2 with $S_0 = 1000; L_{f_0} = L_{s_0} = I_{T_0} = D_{T_0} = I_{DT_0} = C_{DT_0} = D_0 = C_0 = 0$ and $N = 1000$. $\beta = \frac{266}{10^5}$ resulting in approximated equilibrium values of $S^* = 1.704 \times 10^3$, $L_f^* = 1.87795 \times 10^5$, $L_s^* = 2.3127 \times 10^4$, $I_T^* = 2.115 \times 10^3$, $D_T^* = 2.702 \times 10^3$, $I_{DT}^* = 9.307 \times 10^3$, $C_{DT}^* = 3.813 \times 10^3$, $D^* = 3.513660 \times 10^6$, $C^* = 296$ and $\mathcal{R}_C = 1.0863$

.

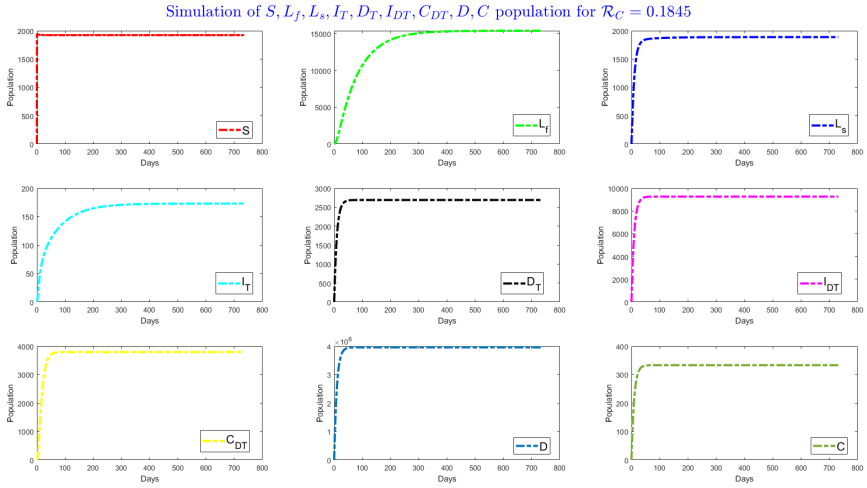

Fig. 3: Simulation of compartment population based on Table 2 with $S_0 = 1000; L_{f_0} = L_{s_0} = I_{T_0} = D_{T_0} = I_{DT_0} = C_{DT_0} = D_0 = C_0 = 0$ and $N = 1000$. $\beta = \frac{266}{10^5}$ resulting in approximated equilibrium values of $S^* = 192$, $L_f^* = 15342 \times 10^4$, $L_s^* = 1.888 \times 10^3$, $I_T^* = 172$, $D_T^* = 2.689 \times 10^3$, $I_{DT}^* = 9.262 \times 10^3$, $C_{DT}^* = 3.794 \times 10^3$, $D^* = 3.95913 \times 10^6$, $C^* = 334$ and $\mathcal{R}_C = 0.1845$

.

Figure 3 considers higher TB transmission coefficient $\beta = \frac{233}{10^5}$ which yields $\mathcal{R}_C = 0.1845$ with trajectories reaching unique equilibrium $S^* = 192$, $L_f^* = 15342 \times 10^4$, $L_s^* = 1.888 \times 10^3$, $I_T^* = 172$, $D_T^* = 2.689 \times 10^3$, $I_{DT}^* = 9.262 \times 10^3$, $C_{DT}^* = 3.794 \times 10^3$, $D^* = 3.95913 \times 10^6$, and $C^* = 334$. In both cases (Figure 2 and Figure 3), trajectories approach equilibrium, an indication of the stability of DFE in most cases of the state variables. A plot of different β values shows increasing the β values increases the population of infectious population (See Figure 4).

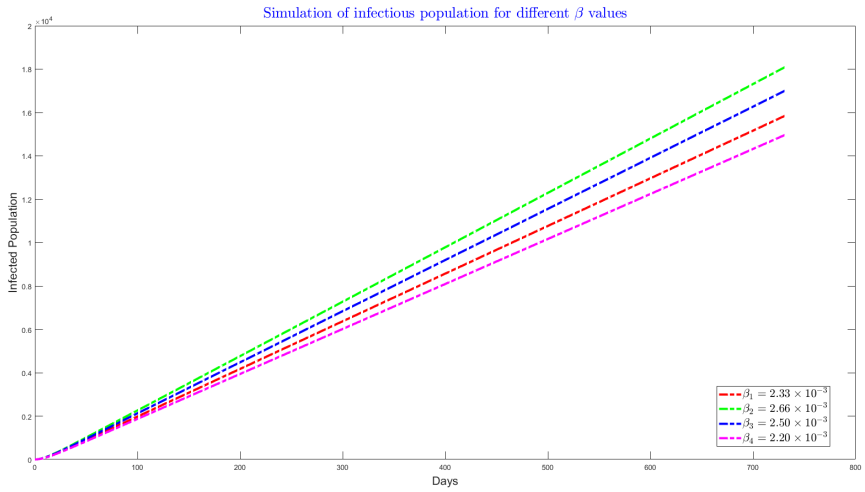

Fig. 4: Simulation of infectious population for different β values.

6 Optimal Control to Tuberculosis and Diabetes Co-Infection

Research has focused on incorporating optimal control strategies to manage the co-infection of tuberculosis and diabetes. Numerous studies have introduced optimal control models to investigate the influence of diabetes on tuberculosis (TB) infection and its treatment. These investigations have delved into the application of optimal control strategies for mitigating multidrug-resistant TB (MDR-TB) and extensively drug-resistant TB (XDR-TB) [32, 49]. Furthermore, analyses employing optimal control have been suggested for co-infection models, incorporating measures such as TB sensitization, dietary sensitization, and TB vaccination [11]. The studies underscore the significance of concurrently addressing TB and diabetes for effective outcomes, emphasizing the necessity for comprehensive strategies in managing co-infection scenarios [11, 5].

6.1 Introduction of controls

Table 3 shows the TB transmission coefficient β has the highest elasticity index followed by the rate of acquiring diabetes α_1. Thus, the control considers these two parameters: distancing (it will reduce TB transmission coefficient) and improvement in diet (since it will reduce the rate of diabetes among individuals).

Distancing measures are crucial in reducing the transmission of TB, an infectious disease that spreads through the air when infected individuals cough, sneeze, or talk [20]. Social distancing, respiratory hygiene practices, proper ventilation, isolation of individuals with active TB infections, and public

awareness campaigns can help reduce the transmission coefficient of TB. These measures limit close contact, especially in crowded or enclosed spaces, and promote good respiratory hygiene practices. Diabetes is a chronic condition characterized by elevated blood glucose levels due to insufficient insulin production or ineffective insulin use. Lifestyle factors, including diet, play a crucial role in developing and managing diabetes [21]. A balanced diet focusing on whole grains, fruits, vegetables, lean proteins, and healthy fats helps regulate blood sugar levels. Maintaining a healthy weight and consuming fibre-rich foods can help stabilize blood sugar levels. Avoiding processed sugars and refined carbohydrates can prevent diabetes. Including healthy fats like avocados, nuts, and olive oil can improve insulin sensitivity and cardiovascular health. Regular monitoring and consulting with healthcare professionals can provide personalized guidance on dietary choices and lifestyle modifications.

6.1.1 Distancing

Let $d \in [0,1]$ (where d is an arbitrary letter used to indicate the control due to distancing) be a time-dependent and Lebesgue measurable control representing an improvement in distancing efforts that reduce TB transmission coefficient. Distancing includes respiratory hygiene practices, proper ventilation, isolation of individuals with active TB infections, and public awareness campaigns. The set of admissible distancing controls is

$$D = d(t) : [0,T] \longrightarrow [0,1] \text{ and is Lebesgue measurable.}$$

6.1.2 Healthy Diet

Let $h \in [0,1]$ (where h is an arbitrary letter used to indicate the control due to a healthy diet) be a time-dependent and Lebesgue measurable control representing an improvement in healthy diet efforts that reduces the rate of acquiring diabetes. The set of admissible healthy diet controls is

$$H = h(t) : [0,T] \longrightarrow [0,1] \text{ and is Lebesgue measurable.}$$

For simplicity, let denote the control $u = (d,h)$ and the set of admissible controls $U = D \times H$.

6.2 The extended mathematical model

Distancing reduces the TB transmission coefficient and is given by $d\beta$. Thus, $d\beta IS$ gives the portion practising distancing. The improved diet reduces the rate of acquiring diabetes and is given by $h\alpha_1$. Thus, $h\alpha_1 S$ gives the portion practising an improved diet. Therefore, the extended mathematical model of (2.1) is given as:

$$\begin{array}{ll}
\frac{dS}{dt} & = \Lambda - \Big([1-h]\alpha_1 + [1-d]\beta I + \mu\Big)S, \\
\frac{dL_f}{dt} & = pd\beta IS + \pi L_s - m_2 L_f, \\
\frac{dL_s}{dt} & = (1-p)(d\beta)IS + \rho_1 I_T - \pi L_s - m_3 L_s, \\
\frac{dI_T}{dt} & = \sigma_2 L_s + \sigma_1 L_f - m_4 I_T, \\
\frac{dD_T}{dt} & = \alpha_2 L_s + \eta D + \rho_2 I_{DT} - m_5 D_T, \\
\frac{dI_{DT}}{dt} & = \sigma_3 D_T + \omega_2 C_{DT} - m_6 I_{DT}, \\
\frac{dC_{DT}}{dt} & = \theta_2 I_{DT} - m_7 C_{DT}, \\
\frac{dD}{dt} & = h\alpha_1 S + \omega_1 C - m_8 D, \\
\frac{dC}{dt} & = \theta_1 D - m_9 C,
\end{array} \tag{6.1}$$

with the initial conditions given in (2.2).

Intervention needs to minimize the number of new cases and the cost of implementing controls. The cost may include improving distancing and diet. Thus, the control $u = (d, h)$ is considered optimal if it minimizes the objective function

$$J = \int_0^T \left(A_1 \left[\left([1-h]\alpha_1 + [1-d]\beta I \right) S \right] + A_2 d^2 + A_3 h^2 \right) dt \tag{6.2}$$

where A_1 is the unit cost of new infection per individual, $A_2 = A_3$ is the unit cost of implementing the controls per time unit. A_1, A_2 and A_3 balance coefficients that transform the integrand into cost per time unit, and $(1-h)\alpha_1 S$ represents the cost of new cases. Thus, we state the optimal control problem as follows:

$$\min_{u \in U} J(u) \tag{6.3}$$

subject to (6.1) and (2.2).

6.3 Existence of optimal control

Theorem 6.1. *There exists an optimal control u^* and the corresponding solution $(S^*, L_f^*, L_s^*, I_T^*, D_T^*, I_{DT}^*, C_{DT}^*, D^*, C^*)$ to the initial value problem given by (6.1) that minimizes the objective function given by (6.2) on U.*

Proof. The initial value problem (6.1) can be written as

$$X^{'} = f(t, X, u),$$
$$\text{with } X(0) = X_0.$$

We use the results of Theorem 4.1 in [8] to establish the existence of optimal control based on the following conditions:

1. There exist $\mathcal{C}_1$ and $\mathcal{C}_2$ such that
   (a) [a] $|f(t, X, u)| \leq \mathcal{C}_1(1 + X)$ and
   (b) [b] $|f(t, X_1, u)| - |f(t, X_2, u)| \leq \mathcal{C}_1 |X_1 - X_2|$,
   for all $t \geq 0$,
   $X_1, X_2 \in \left\{ \left(S, L_f, L_s, I_T, D_T, I_{DT}, C_{DT}, D, C \in \mathbb{R}_+^9 \middle| S + L_f + L_s + I_T + D_T + I_{DT} + C_{DT} + D + C = N, \right) \right.$
   and $u \in U$, where $U = \left\{ u = (d, h) : 0 :\leq d, h \leq 1 \right\}$
2. The set of controls and corresponding state variables is non-empty.
3. The control set U is convex and closed, $f(t, X, u) = \varphi_1(t, X) + \varphi_2(t, X)u$ and L is convex on U, where $L = A_1 \left[\left([1-h]\alpha_1 + [1-d]\beta I \right) S \right] + A_2 d(t)^2 + A_3 h(t)^2$ is the integrand in (6.2).
4. There exist $\mathcal{C}_3 > 0, \mathcal{C}_4 > 1$ and $\mathcal{C}_5 \geq 0$ such that

$$L(t, X, u) \geq \mathcal{C}_3 |u|^{\mathcal{C}_4} - \mathcal{C}_5. \tag{6.4}$$

Since f is $\mathcal{C}^1$, conditions 1a and 1b are implied by suitable bounds on partial derivatives of f and on $f(t, 0, 0)$. Since f is continuous and bounded on a finite time interval Theorem 9.2.1 of [27] guarantees the existence of at least one local solution. The set $U = \{(d, h) : d \in [0, 1]$ and $h \in [0, 1]$ is closed. By definition, the set $Q = \{d : d \in [0, 1]$ is Lebesgue measurable$\}$ is convex if $d_1, d_2 \in Q$ and $\gamma_1 \in [0, 1] \implies \left[1 - \gamma_1 d_1 + \gamma_1 d_2 \in D \right]$

$(1-\gamma_1)d_1 + \gamma_1 d_2 - 2 \geq 0$ since $\gamma_1, d_1, d_2 \in [0,1]$, and $(1-\gamma_1)d_1 + \gamma_1 d_2 \leq (1-\gamma_1) + \gamma_1$ since $d_1, d_2 \leq 1$.

Therefore, $(1-\gamma_1)d_1 + \gamma_1 d_2$ lies in D implies that Q is convex. Similarly, D is convex since, according to [26], the Cartesian of convex sets is convex; thus, $U = D \times H$ is a convex set. The function f is linear in each control variable d and h, hence can be written as $f(t,X,u) = \varphi_1(t,X) + \varphi_1(t,X)u$. L is convex on U since it is quadratic in u and the constants A_3 and A_5 are positive. Therefore,

$$\begin{aligned} L = & \quad A_1\left[\Big([1-h]\alpha_1 + [1-d]\beta I\Big)S\right] + A_2 d^2 + A_3 h^2 \\ \leq & \quad A_2 d^2 + A_3 h^2 + A_1\left[\Big([1-h]\alpha_1 + [1-d]\beta I\Big)S\right] \text{ since } d \geq 0, h \geq 0. \end{aligned} \tag{6.5}$$

Taking into consideration that

$$\begin{aligned} A_1\Big[\beta IS\Big] & \leq A_1\left[\Big([1-h]\alpha_1 + [1-d]\beta I\Big)S\right] \text{ since } d \leq 1 \; and \; h \leq 1 \\ & \leq A_1\left[\Big([1-h]\alpha_1 + [1-d]\beta I\Big)S\right] \text{ since } d\beta IS \leq IS. \\ & \leq A_1\Big[N^2\Big] \text{ since } S \leq N \text{ and } I = (I_T + T_{DT}) \leq N. \end{aligned} \tag{6.6}$$

Both sides of inequality are non-negative, thus,

$$A_1\left[\Big([1-h]\alpha_1 + [1-d]\beta I\Big)S\right] \geq -A_1\Big[\alpha_1 S + \beta IS\Big]. \tag{6.7}$$

We substitute (6.7) and (6.6) into (6.5) to have

$$\begin{aligned} L & \leq A_2 q(t)^2 + A_3 h(t)^2 - A_1\Big[\alpha_1 N + \beta N^2\Big] \\ & \geq \mathcal{C}_3 |u|^{\mathcal{C}_4} - \mathcal{C}_5 \end{aligned} \tag{6.8}$$

where $\mathcal{C}_3 = \min A_2, A_3$, $\mathcal{C}_4 = 2$ and $\mathcal{C}_5 = A_1\Big[\alpha_1 N + \beta N^2\Big]$.

□

6.4 Characterization of controls

We use Pontryagin's Maximum principle stated in Theorem 5.1 of [8] to find the best possible control for the system. Lets define the Hamiltonian H as follows;

$$
\begin{aligned}
H(X,u,p) &= f(t,X,u) + L(t,X,u) \\
&= p_1 f_1 + p_2 f_2 + p_3 f_3 + p_4 f_4 + p_5 f_5 + p_6 f_6 + p_7 f_7 + p_8 f_8 + p_9 f_9 + L \\
&= p_1 \Big[\Lambda - [1-d]\beta IS - ([1-h]\alpha_1 + \mu)\, S \Big] \\
&+ p_2 \Big[p[1-d]\beta IS + \pi L_s - m_2 L_f \Big] \\
&+ p_3 \Big[(1-p)[1-d]\beta IS + \rho_1 I_T - m_3 L_s \Big] \\
&+ p_4 \Big[\sigma_2 L_s + \sigma_1 L_f - m_4 I_T \Big] \\
&+ p_5 \Big[\alpha_2 L_s + \eta D + \rho_2 I_{DT} - m_5 D_T \Big] \\
&+ p_6 \Big[\sigma_3 D_T + \omega_2 C_{DT} - m_6 I_{DT} \Big] \\
&+ p_7 \Big[\theta_2 I_{DT} - m_7 C_{DT} \Big] \\
&+ p_8 \Big[[1-h]\alpha_1 S + \omega_1 C - m_8 D \Big] \\
&+ p_9 \Big[\theta_1 D - m_9 C \Big] \\
&+ \Big(A_1 \Big[\Big([1-h]\alpha_1 + [1-d]\beta I \Big) S \Big] + A_2 d^2 + A_3 h^2 \Big)
\end{aligned}
\tag{6.9}
$$

where $p = (p_1, p_2, p_3, p_4, p_5, p_6, p_7, p_8, p_9)$ and $p_1, p_2, p_3, p_4, p_5, p_6, p_7, p_8, p_9$ are adjoint variables for the state variable $S, L_s, L_s, I_T, D_T, I_{DT}, C_{DT}, D, C$.

Theorem 6.2. *Given an optimal solution* (X^*, u^*) *of the control problem* (6.3)*, there exists* $p_1, p_2, p_3, p_4, p_5, p_6, p_7, p_8, p_9$*, a solution set to the adjoint system*

$$
\begin{aligned}
\dot{p_1} &= -\tfrac{\partial H}{\partial S} &&= p_1[1-d]\beta I + p_1 m_1 - p_2 p[1-d]\beta I + p_3(1-p)[1-d]\beta I - p_8[1-h]\alpha_1 - A_1\Big([1-h]\alpha_1 + [1-d]\beta I\Big) \\
\dot{p_2} &= -\tfrac{\partial H}{\partial L_f} &&= p_2 m_2 - p_4\sigma_1 \\
\dot{p_3} &= -\tfrac{\partial H}{\partial L_s} &&= -p_2\pi + p_3 m_3 - p_4\alpha_2 - p_5\alpha_2 \\
\dot{p_4} &= -\tfrac{\partial H}{\partial I_T} &&= p_1[1-d]\beta S - p_2 p[1-d]\beta S - p_3(1-p)[1-d]\beta S - p_3\rho_1 + p_4 m_4 - A_1[1-d]\beta S \\
\dot{p_5} &= -\tfrac{\partial H}{\partial D_T} &&= p_5 m_5 - p_6\sigma_3 \\
\dot{p_6} &= -\tfrac{\partial H}{\partial I_{DT}} &&= p_1[1-d]\beta S - p_2 p[1-d]\beta S - p_3(1-p)[1-d]\beta S - p_5\rho_2 + p_6 m_6 - A_1[1-d]\beta S \\
\dot{p_7} &= -\tfrac{\partial H}{\partial C_{DT}} &&= -p_6\omega_2 + p_7 m_7 \\
\dot{p_8} &= -\tfrac{\partial H}{\partial D} &&= -p_5\eta + p_8 m_8 - p_9\theta_1 \\
\dot{p_9} &= -\tfrac{\partial H}{\partial C} &&= -p_8\omega_1 + p_9 m_9
\end{aligned}
\tag{6.10}
$$

with transversality condition

$$p_1(T) = 0,\ p_2(T) = 0,\ p_2(T) = 0,\ p_4(T) = 0,\ p_5(T) = 0,\ p_6(T) = 0,\ p_7(T) = 0,\ p_8(T) = 0,\ p_9(T) = 0,$$

such that $u^* = \min_{u \in U} H(X, p, u)$, $t \in [0, T]$. Furthermore, controls can be characterized as

$d^* = \min\left(1, \max\left(0, \frac{1}{2A_2}\left[\beta IS\Big(p_1 + p_2 p + p_3(1-p) + A_1\Big)\right]\right)\right)$ and

$h^* = \min\left(1, \max\left(0, \frac{1}{2A_3}\left[\alpha_1 S\Big(p_8 - p_1 + A_1\Big)\right]\right)\right)$.

Proof. The optimal control is derived from the optimality condition $\frac{\partial H}{\partial u}\Big|_{u^*} = 0$.

$$\begin{aligned} \frac{\partial H}{\partial d}\Big|_{d^*} &= -\beta IS\left(p_1 + p_2 p + p_3(1-p) + A_1\right) + 2A_2 d^* \\ \implies \quad d^* &= \frac{1}{2A_2}\left[\beta IS\Big(p_1 + p_2 p + p_3(1-p) + A_1\Big)\right] \end{aligned} \tag{6.11}$$

and

$$\begin{aligned} \frac{\partial H}{\partial h}\Big|_{h^*} &= p_1\alpha_1 S - p_8\alpha_1 S - A_1\alpha_1 S + 2A_3 h^* \\ \implies \quad h^* &= \frac{1}{2A_3}\Big[\alpha_1 S\left(p_8 - p_1 + A_1\right)\Big]. \end{aligned} \tag{6.12}$$

We consider the properties of the control space as

$$d^* = \begin{cases} 0, & \text{if } \frac{1}{2A_2}\left[\beta IS\Big(p_1 + p_2 p + p_3(1-p) + A_1\Big)\right] \geq 0, \\ \frac{1}{2A_2}\left[\beta IS\Big(p_1 + p_2 p + p_3(1-p) + A_1\Big)\right] & \text{if } 0 < \frac{1}{2A_2}\left[\beta IS\Big(p_1 + p_2 p + p_3(1-p) + A_1\Big)\right] < 1, \\ 1 & \text{if } \frac{1}{2A_2}\left[\beta IS\Big(p_1 + p_2 p + p_3(1-p) + A_1\Big)\right] \geq 1. \end{cases} \tag{6.13}$$

Thus, d^* can be characterized as

$$d^* = \min\left(1, \max\left(0, \frac{1}{2A_2}\left[\beta IS\Big(p_1 + p_2 p + p_3(1-p) + A_1\Big)\right]\right)\right).$$

Similarly, h^* can be characterized as

$$h^* = \min\left(1, \max\left(0, \frac{1}{2A_3}\Big[\alpha_1 S\left(p_8 - p_1 + A_1\right)\Big]\right)\right).$$

We also noted from (6.11) and (6.12) respectively that
$\frac{\partial^2 H}{\partial d^2}\Big|_{d^*} = 2A_2 > 0$ and $\frac{\partial^2 H}{\partial h^2}\Big|_{h^*} = 2A_3 > 0$. Since A_2 and A_3 are positive constants introduced in (6.2), this indicates that $u^* = (d^*, h^*)$ minimizes the Hamiltonian function $H(X, p, u)$. □

6.5 Numerical simulation for optimal control

The optimal problem (6.3) was solved numerically based on parameter values in Table 2. We compared numerical solutions with optimal control and without any intervention. The compartments are plotted side by side in the presence and absence of control measures $d \in [0, 1]$ and $h \in [0, 1]$ with $S_0 = L_{f_0} = L_{s_0} = I_{T_0} = D_{T_0} = I_{DT_0} = C_{DT_0} = D_0 = C_0 = 0$
A comparison of trajectories in the presence and absence of optimal control reveals that, as depicted in Figure 5, susceptible individuals increase in the presence of optimal control. This is because the improvement in the distancing and healthy diet reduced the population who could be in the components of diabetic-tuberculosis co-infection. The population of all other compartments reduces in the presence of optimal control. A plot of cost function is presented in Figure 6.
Figure 6 suggests that the minimum cost function is attained when $h \simeq .2$ and $d \simeq .6$. This indicate that optimal results are attained when the $h = .2$ and $d = .6$. These approximated values are used to generate the simulation results in Figure 5 and the estimated equilibrium results presented in Table 4.

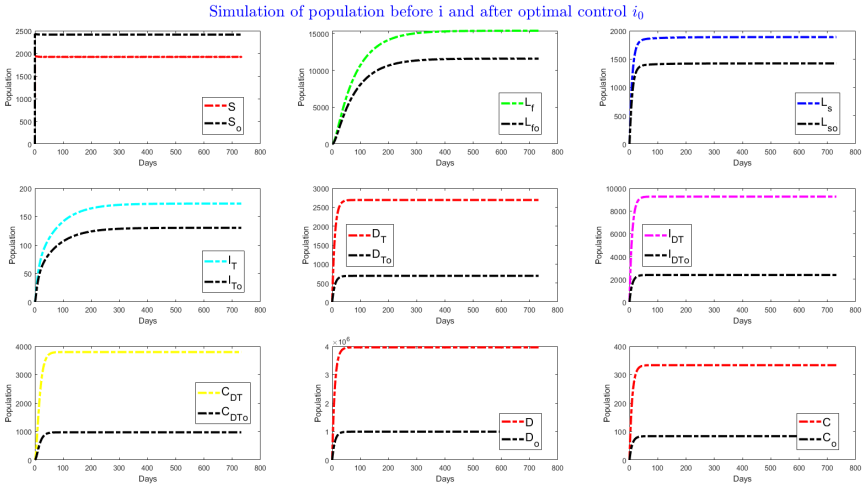

Fig. 5: Simulation of the population of individuals in each compartment in the absence and presence of optimal control $S(t), S_o(t)$; $L_f(t), L_{fo}(t)$; $I_T(t), I_{T_o}(t)$; $D_T(t), D_{To}$; $I_{DT}(t), I_{DTo}$; $C_{DT}(t), C_{DTo}$; $D(t), D_o(t)$ and $C(t), C_o(t)$ based on parameter values in Table 2.

Table 4: Comparison of compartment equilibrium values in the presence and absence of optimal control

Compartment	Without optimal (i)	With optimal (i_o)
S^*	1920	2424
L_f^*	15341	2896
L_s^*	1888	358
I_T^*	172	32
D_T^*	2689	677
I_{DT}^*	9263	2330
C_{DT}^*	3795	955
D^*	3.9591×10^6	9.9841×10^5
C^*	334	85

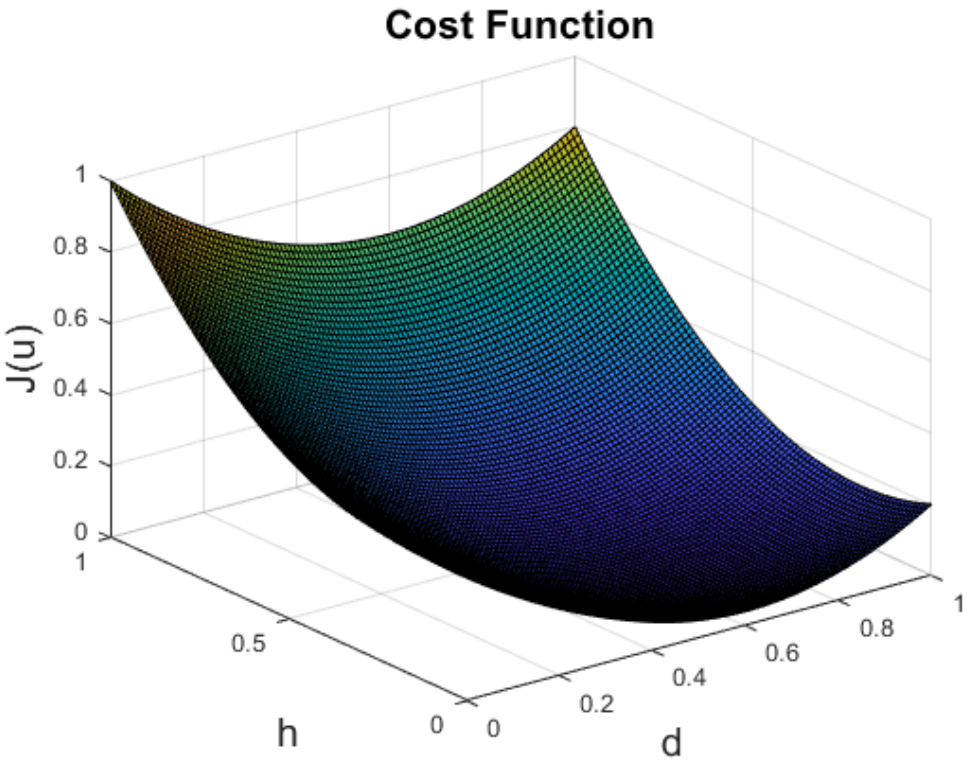

Fig. 6: Simulation of the cost function for values of $[d, h] \in [0, 1] \; \forall \; t = 732$ days.

7 Conclusion

Tuberculosis and diabetes co-infection is a complex health issues that require effective management. Understanding the dynamics and interactions between these two diseases is crucial for developing optimal control strategies. The co-infection is bidirectional, with each disease influencing the other's severity and progression. The immune dysregulation caused by diabetes compromises the host's ability to control TB infection, leading to higher TB and DM-related complications. Conversely, TB infection can exacerbate glucose control in patients with DM, worsening metabolic control. Understanding these intricate relationships allows for targeted interventions, such as pharmacological approaches, lifestyle modifications, and integrated treatment approaches, to manage TB and diabetes co-infection more effectively. These strategies can mitigate disease progression, improve patient outcomes, and inform future research and clinical practice. By implementing optimal control strategies, healthcare professionals can better address the complexity of tuberculosis and diabetes co-infection and improve patient outcomes.

In this paper, earlier models such as the one presented by [28] have been expanded to incorporate the co-infection of diabetes and tuberculosis. This extension aims to enhance our understanding of the complexities associated with disease complications. Through a stability analysis of the model using $\mathcal{R}_C$ for both disease-free and endemic equilibrium, it was observed that $\mathcal{R}_C \leq 1$ leads to potential epidemic eradication, while $\mathcal{R}_C \geq 1$ indicates a likelihood of the epidemic spreading in the population. The sensitivity analysis of parameters in $\mathcal{R}_C$ highlighted that the TB transmission coefficient β and the rate of acquiring diabetes α_1 significantly impact $\mathcal{R}_C$. Consequently, optimal control measures should focus on reducing the TB transmission coefficient and the rate of acquiring diabetes. A decrease in the TB transmission coefficient resulted in a reduction of $\mathcal{R}_C$ from 1.0863 to 0.1845, suggesting the promise of extending control strategies based on these findings.

An expanded model to encompass potential optimal control approaches, such as implementing increased distancing and enhancing dietary habits for better health. Graphical simulations have demonstrated a decrease in the number of infected individuals when controls are applied to reduce the transmission coefficient of TB and the rate of acquiring diabetes. This suggests that the optimal control measures were successful. In future research, it is essential to explore a model that considers various types of diabetes.

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