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A Mathematical Model on the Transmission Dynamics of Tuberculosis

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Abstract
This study explores a mathematical model to analyze the transmission dynamics of tuberculosis (TB), focusing on Drug-Sensitive TB (DS-TB) and Drug-Resistant TB (DR-TB). The study adopted a deterministic (SEIR) model where each compartment represents a distinct stage of the epidemic and the population's members are assigned to them (the immunized, susceptible, latently infected, infectious, and recovered compartments). Parameters such as transmission rates, treatment efficiencies, and vaccination coverage are incorporated into the model. Equilibrium analysis identifies a Disease-Free Equilibrium (DFE), and solutions are shown to be biologically feasible, bounded, and unique. Findings indicate that improved treatment efficiency and higher vaccination coverage lower the basic reproduction number (R_0) and mitigate TB spread. It is recommended that the government strengthen vaccination programs to maintain high coverage, particularly for newborns, and enhance treatment strategies to improve recovery rates.

Keywords: Mathematical Model, Transmission, Dynamics, Tuberculosis

Introduction

Through quantitative analysis and abstract thinking, mathematics is a foundational science that investigates relationships, structures, and patterns. A strong tool for critical thinking and problem-solving is mathematics. Mathematics, according to Nwuke, & Anaekwe (2023), is the systematic and abstract study of numbers, amounts, forms, structures, and patterns, as well as their characteristics and manipulation. Models might have a mathematical, computational, or conceptual basis. A collection of differential equations that characterize the rate of change of each of these variables over time can be used to mathematically construct a model to identify patterns, relationships, and the behavior of mechanisms. WHO (2021) defined a model as a simplified representation of a system or phenomenon that is used to understand, predict, or control behaviour. Analysis is the methodical inspection and assessment of data or systems, frequently with the aid of statistical or mathematical techniques (Centers for Disease Control and Prevention, 2018).

In epidemiology, mathematical modeling is a vital tool that sheds light on the mechanisms underlying disease transmission and the possible outcomes of public health initiatives. Understanding the transmission dynamics of tuberculosis (TB) is crucial for developing effective control strategies and mitigating its spread within populations (Pai & Schito, 2019). TB is primarily transmitted through the inhalation of respiratory droplets containing Mycobacterium tuberculosis (Mtb) expelled by individuals with infectious pulmonary TB during coughing, sneezing, or speaking (Pai & Schito, 2019). These droplets can remain suspended in the air for prolonged periods, potentially infecting others who inhale them (Pai & Schito, 2019). Individuals with active pulmonary TB disease are the most infectious (Pai & Schito, 2019). However, not everyone exposed to Mtb becomes ill. Many individuals develop latent TB infection (LTBI), where the bacteria are present in the body but are not actively multiplying or causing symptoms (Cohen et al., 2019). Latently infected individuals are not contagious but have the potential to develop active TB disease in the future (Cohen et al., 2019). Factors such as compromised immune function or other illnesses can lead to the reactivation of latent TB infection, resulting in the development of active TB disease (Cohen et al., 2019). Active TB is characterized by symptoms such as cough, fever, weight loss, and night sweats, and individuals with active TB can transmit the infection to others (Cohen et al., 2019). Several factors increase the risk of TB transmission and progression from latent infection to active disease, including close and prolonged contact with infectious individuals, overcrowded living conditions, poor ventilation, malnutrition, and comorbidities such as HIV infection (Dowdy et al., 2019).

Tuberculosis (TB), an infectious disease primarily caused by the bacterium called Mycobacterium tuberculosis, continues to be a global public health issue, particularly in low- and middle-income countries. Despite

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significant advances in control measures, TB remains a leading cause of morbidity and mortality worldwide, with millions of new cases reported annually (WHO, 2021). According to Khan et al. (2019) Tuberculosis (TB) is a contagious bacterial infection that is caused by a bacillus mycobacterium TB (MTB). TB is still a first-class public health challenge and remains the major cause of deaths at the global level, especially in low and middle income countries. Due to its high rate of mortality, this infection is listed in the 10 most causes of deaths in the world. Despite advancements in diagnosis and treatment, TB continues to pose a major global health challenge Drug-sensitive TB (DS-TB) refers to TB strains that respond effectively to first-line anti-TB medications, such as isoniazid and rifampicin. These treatments, typically administered over a 6-month regimen, have high success rates if adhered to correctly. DS-TB remains the most common form of TB and is usually curable with proper diagnosis and adherence to treatment. Drug-resistant TB (DR-TB) occurs when TB bacteria develop resistance to one or more anti-TB drugs. This is often due to improper use of antibiotics, incomplete treatment, or transmission of resistant strains. Types of DR-TB include: Mono-Resistance, Poly-Resistance etc.

Tuberculosis (TB) remains a significant global health burden despite advancements in diagnosis and treatment. Challenges persist in addressing drug sensitive TB (DS-TB) and drug-resistant TB (DR-TB). Numerous control methods, including vaccination, public health campaigns, and standard treatment protocols, have struggled to stop the spread of TB, owing to intricate factors influencing its dynamics. Mathematical modeling of TB transmission dynamics is a valuable tool for gaining deeper insights into these mechanisms and can lead to more effective TB control strategies and ultimately reduce global TB incidence. The aim of this study is to use a mathematical model to analyse the transmission dynamics of tuberculosis (TB) in a populations and identify the parameters that will facilitate the spread and those that will impede the spread of tuberculosis TB

Model Formulation

The study adopted a deterministic model where each compartment represents a distinct stage of the epidemic and the population's members are assigned to them. The Susceptible-Exposed-Infected-Recovered (SEIR) model, which takes into account newborns who are passively immune will be considered in this study.

Table 1 Description of Model variables with passive immunity, drug-sensitive TB and drug resistant TB.

Variables	Description
$M(t)$	the number of individuals who are immunized against TB through vaccination at time *t.*
$S(t)$	the number of susceptible individuals at time *t.*
$E_s(t)$	the number of latently infected individuals with Drug-Sensitive TB at time *t.*
$E_R(t)$	the number of latently infected individuals with Drug-Resistant at time *t.*
$I_s(t)$	the number of infectious individuals with Drug-Sensitive TB at time *t*
$I_R(t)$	the number of infectious individuals with Drug-Resistant TB at time *t*
$R_s(t)$	the number of recovered individuals with Drug-Sensitive TB at time *t*
$R_R(t)$	the number of recovered individuals with Drug- Resistant TB at time *t*

Table 2: Description of Model Parameters with passive immunity, drug-sensitive TB and drug resistant TB.

β_S	the transmission rate of Drug-Sensitive TB
β_R	the transmission rate of Drug-Resistant TB
π	the recruitment rate
$r1$	the treatment efficiency of Drug-Sensitive TB
$r2$	the treatment efficiency of Drug-Resistant TB
σ	proportion of new births that have been immunized through vaccination
θ	the rate of expiration of vaccine efficacy
R	the probability of Drug-Resistant TB emerging during treatment
μ	natural mortality rate

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υ	progression rate from latent TB to active TB for both DS-TB and DR-TB cases
μT	mortality rate due to TB
ρS	the proportion of new infections that produce active TB for DS-TB Cases
ρR	the proportion of new infections that produce active TB for DR-TB Case

The following model proposed by Momoh, et'al (2019). is considered in this study of TB transmission dynamics.

Model Equations

$$\frac{dM}{dt} = \sigma\pi - (\theta + \mu)M, \qquad M(0) = M_O \qquad (3)$$

$$\frac{dS}{dt} = (1-\sigma)\pi + \theta M - (\beta_s I_s + \beta_R I_R + \mu)S, \qquad S(0) = S_O \qquad (4)$$

$$\frac{dE_s}{dt} = (1-\rho_S)\,\beta_s I_s - (\nu + \mu)E_s, \qquad E_S(0) = E_{So} \qquad (5)$$

$$\frac{dE_R}{dt} = (1-\rho_R)\,\beta_R I_R S - (\nu + \mu)E_R, \qquad E_R(0) = E_{Ro} \qquad (6)$$

$$\frac{dI_s}{dt} = \rho_S\beta_s I_s S_s + \upsilon E_s - (\mu + \mu_T + \mu_2)I_S, \qquad I_S(0) = I_{So} \qquad (7)$$

$$\frac{dI_R}{dt} = \rho_R\beta_R I_R S_R + \upsilon E_R + r_2 r I_s - (\mu + \mu_T + r_1)I_{R,} \qquad I_R(0) = I_{Ro} \qquad (8)$$

$$\frac{dR_S}{dt} = r_2(1-r)I_s - \mu R_S, \qquad R_s(0) = R_{so} \qquad (9)$$

$$\frac{dR_R}{dt} = r_1 I_R - \mu R_R, \qquad R_R(0) = R_{Ro} \qquad (10)$$

Model Analysis

In this section, the conditions for the existence of equilibria of the system was explored.

Existence of invariant region

From the model equations (3.3) – (3.10), the total population is given by

N= M + S + E_S + E_R+ I_S+ I_R + R_S + R_R

$$that\ is\ \frac{dN}{dt} = \frac{dM}{dt} + \frac{dS}{dt} + \frac{dE_S}{dt} + \frac{dE_R}{dt} + \frac{dI_S}{dt} + \frac{dI_R}{dt} + \frac{dR_S}{dt} + \frac{dR_R}{dt}$$

Therefore, adding the differential equations, we have

$$\frac{dN}{dt} = \pi - \mu(\mathrm{M} + \mathrm{S} + E_S + E_R + I_S + I_R + R_S + R_R) - \mu_r(I_S + I_R)$$

$$\frac{dN}{dt} = \pi - \mu N - \mu_r(I_S + I_R)$$

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

By using of integrating factor, it is given that

$$N(t) \leq N(0)e^{-\mu t} + \frac{\pi}{\mu}(1 - e^{-\mu t})$$

$$N(t) \leq \frac{\pi}{\mu} + (N(0) - \frac{\pi}{\mu})e^{-\mu t}$$

$$\lim_{i\to\infty} N(t) \leq \frac{\pi}{\mu}$$

$$As \lim_{i\to\infty} e^{-\mu t}$$

So that at $i \to \infty, N(t) \leq \frac{\pi}{\mu}$

The region in which the model makes biological sense is given by

$$\Omega = \left\{\mathrm{M}, \mathrm{S}, E_S, E_R, I_S, I_R, R_S, R_R \epsilon \mathrm{i}^8{}_+ : \mathrm{M} + \mathrm{S} + E_S + E_R + I_S + I_R + R_S + R_R \leq \frac{\pi}{\mu}\right\}$$

This means that every solution with initial condition in Ω remains in Ω for all t ≥0. Therefore, the region Ω, the model is biologically feasible, mathematically well posed and positively invariant.

Disease Free equilibrium state

At equilibrium, setting equations (3) – (10) to zero gives

$$\sigma\pi - (\theta + \mu)M = 0 \qquad (11)$$

$$(1-\sigma)\,\pi + \theta M - (\beta_s I_s + \beta_R I_R + \mu)S = 0 \qquad (12)$$

$$(1-\rho_s)\,\beta_s I_s S - (\upsilon + \mu)E_s = 0 \qquad (13)$$

$$(1-p_R)\,\beta_R I_R S - (\upsilon + \mu)E_R = 0 \qquad (14)$$

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$p_S\beta_s I_s S + \upsilon E_s - (\mu + \mu_r + \mu_1)I_s = 0$ (15)
$p_R\beta_R I_R S + \upsilon E_R + r_2 r I_{s-}(\mu + \mu_r + \mu_1)I_R = 0$ (16)
$r_2(1-r)rI_s - \mu R_s = 0$ (17)
$r_1 I_R - \mu R_R = 0$ (18)

Following equations (11) – (18) the disease – free equilibrium is given as

state:$E_0 = \left(\frac{\sigma\pi}{\theta+\mu}, \frac{\pi(\theta+\mu-\mu\sigma)}{\mu(\theta+\mu)}\ 0,0,0,0,0,0\right)$

Positivity and Boundedness of solutions

Lemma 3.1 The zeros of the system of equations $(3)-(10)$ {M , S , E_S , E_R, I_S, I_R , R_S , and R_R} with initial condition $\{M_{10}, S_{10}, E_{s_{10}}, E_{R_{10}}, I_{s_{10}}, I_{R_{10}}, R_{S_{10}}, R_{R_{10}} \geq 0\}\epsilon\ A$ will remain positive ∀ time $t \geq 0$.

Proof. From equation (3),

$\frac{dM}{dt} = \sigma\pi - (\theta+\mu)M$
$\leq -[(\theta+\mu)]M$
$\Rightarrow M \geq SM_{10}e^{-\int[(\theta+\mu)]dt} \geq 0 \qquad \forall\ t > 0$

Similarly, equations (4) – (10) show that ∀ $t > 0$,
$S \geq S_{10}e^{-\int(\beta_s I_s + \beta_R I_R + \mu)dt} \geq 0$, $E_s \geq E_{s_{10}}e^{-\int[(\nu+\mu)]dt} \geq 0$, $E_R \geq E_{R_{10}}e^{-\int((\nu+\mu)dt} \geq 0$, $I_s \geq I_{s_{10}}e^{\int[(P_S\beta_s S_{S)}-(\mu+\mu_T+\mu_2)]dt} \geq 0$, $I_R \geq I_{R_{10}}e^{\int[(P_R\beta_R S_R)-(\mu+\mu_T+r_1)]dt} \geq 0$ and
$R_S \geq R_{S_{10}}e^{-\int\mu dt} \geq 0$, $R_R \geq 0$, $R_{R_{10}}e^{-\int\mu dt}$

Existence and Uniqueness of Solution To determine the conditions for the existence and uniqueness of solution for the model equations (3) – (10), let

$h_1(t,m) = \sigma\pi - (\theta+\mu)M$ (19)
$h_2(t,m) = (1-\sigma)\pi + \theta M - (\beta_s I_s + \beta_R I_R + \mu)S,$ (20)
$h_3(t,x) = (1-\rho_S)\,\beta_s I_s - (\nu+\mu)E_s,$ (21)
$h_4(t,m) = (1-\rho_R)\,\beta_s I_s - (\nu+\mu)E_R,$ (22)
$h_5(t,m) = \rho_S\beta_s I_s S_s + \upsilon E_s - (\mu+\mu_T+\mu_2)I_S.$ (23)
$h_6(t,m) = \rho_R\beta_R I_R S_R + \upsilon E_R + r_2 r I_s - (\mu+\mu_T+r_1)I_R$ (24)
$h_7(t,m) = r_2(1-r)I_s - \mu R_S$ (25)
$h_8(t,m) = r_1 I_R - \mu R_R$ (26)

Such that

$\frac{dm}{dt} = h(t,m) = h(m).$ (27)

Theorem 3.1 Let A represent the region
$|t-t_0| \leq k_1,\ \|m-m_0\| \leq k_2$, and $m = (m_1, m_2, \dots, m_n) = (m_{10}, m_{20,} \dots, m_{n0})$ (28)
with $h(t,m)$ satisfying the Lipschitz condition

$\|h(t,m_1) - h(t_1,m_2)\| \leq k\|m_1 - m_2\|$ (29)

for (t,m_1) and (t_1,m_2) in A and $k > 0$. Then, there exists a constant $\delta > 0$ such that a unique continuous vector solution $\bar{m}(t)$ of equations (19) – (26) exists in $|t-t_0| \leq \delta$.
$\frac{\partial h_i}{\partial m_j},\ i,j = 1,2,\dots,n$ is continuous and bounded in A and fulfilled the condition in equation (30)

Lemma 3.2. If $h(t,m)$ is continuous and has partial derivative $\frac{\partial h_i}{\partial m_j}$ on a bounded closed convex domain $\mathbb{R}$, then it satisfies a Lipschitz condition in $\mathbb{R}$.

The region of interest is given by

$1 \leq \epsilon \leq \mathbb{R}$ (31)

and bounded solution of the form below is sought for:

$0 < \mathbb{R} < \infty$ (32)

Below is the proof of the existence theorem:

Theorem 3.2: If A represents the region defined in (29) such that (28) and (31) hold, then ∃ a solution of the model equations (19) – (26) bounded in the region A.

Proof. Considering equations $(19)-(26)$,

It will be shown that the continuity of $\frac{\partial h_i}{\partial m}, i = j = 1,2,3,4,5,6,7,8$ exists. Differentiating h_i partially with respect to M , S , E_S , E_R, I_S, I_R , R_S , and R_R, give:

$\frac{\partial h_i}{\partial m} = -(\theta+\mu),$ $\left|\frac{\partial h_i}{\partial m}\right| = -|(\theta+\mu)| < \infty$ (33)
$\frac{\partial h_i}{\partial s} = 0,$ $\left|\frac{\partial h_i}{\partial s}\right| = |0| < \infty$ (34)
$\frac{\partial h_i}{\partial Es} = 0,$ $\left|\frac{\partial h_i}{\partial Es}\right| = |0| < \infty$ (35)

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$\frac{\partial h_i}{\partial E_R} = 0,$ $\left|\frac{\partial h_i}{\partial E_R}\right| = |0| < \infty$ (36)

$\frac{\partial h_i}{\partial I_S} = 0,$ $\left|\frac{\partial h_i}{\partial E_R}\right| = |0| < \infty$ (37)

$\frac{\partial h_i}{\partial I_R} = 0,$ $\left|\frac{\partial h_i}{\partial I_R}\right| = |0| < \infty$ (38)

$\frac{\partial h_i}{\partial R_S} = 0,$ $\left|\frac{\partial h_i}{\partial R_S}\right| = |0| < \infty$ (39)

$\frac{\partial h_i}{\partial R_R} = 0,$ $\left|\frac{\partial h_i}{\partial R_R}\right| = |0| < \infty$ (40)

Also,

$\frac{\partial h_2}{\partial M} = \theta,$ $\left|\frac{\partial h_2}{\partial M}\right| = |\theta| < \infty$ (41)

$\frac{\partial h_2}{\partial S} = -(\beta_S I_S + \beta_R I_R + \mu),$ $\left|\frac{\partial h_2}{\partial S}\right| = |\beta_S I_S + \beta_R I_R + \mu| < \infty$ (42)

$\frac{\partial h_2}{\partial E_S} = 0,$ $\left|\frac{\partial h_2}{\partial E_S}\right| = |0| < \infty$ (43)

$\frac{\partial h_2}{\partial E_R} = 0,$ $\left|\frac{\partial h_2}{\partial E_R}\right| = |0| < \infty$ (44)

$\frac{\partial h_2}{\partial I_S} = -(\beta_S I_S + \beta_R + \mu)\, S,$ $\left|\frac{\partial h_2}{\partial I_S}\right| = |(\beta_S + \beta_R I_R + \mu)S| < \infty$ (45)

$\frac{\partial h_2}{\partial I_R} = -(\beta_S I_S + \beta_R + \mu)\, S,$ $\left|\frac{\partial h_2}{\partial I_R}\right| = |-(\beta_S I_S + \beta_R + \mu)S| < \infty$ (46)

$\frac{\partial h_2}{\partial R_S} = 0,$ $\left|\frac{\partial h_2}{\partial R_S}\right| = |0| < \infty$ (47)

$\frac{\partial h_2}{\partial R_R} = 0,$ $\left|\frac{\partial h_2}{\partial R_R}\right| = |0| < \infty$ (48)

Similarly,

$\frac{\partial h_3}{\partial M} = 0,$ $\left|\frac{\partial h_3}{\partial M}\right| = |0| < \infty$ (49)

$\frac{\partial h_3}{\partial S} = (1 - \rho_s)\beta_s I_s\ ,$ $\left|\frac{\partial h_3}{\partial S}\right| = |[(1 - \rho_s)\beta_s I_s]| < \infty$ (50)

$\frac{\partial h_3}{\partial E_S} = -(V + \mu)\ ,$ $\left|\frac{\partial h_3}{\partial E_S}\right| = |-(V + \mu)| < \infty$ (51)

$\frac{\partial h_3}{\partial E_R} = 0\ ,$ $\left|\frac{\partial h_3}{\partial E_R}\right| = |0| < \infty$ (52)

$\frac{\partial h_3}{\partial I_S} = 0\ ,$ $\left|\frac{\partial h_3}{\partial I_S}\right| = |0| < \infty$ (35)

$\frac{\partial h_3}{\partial I_R} = 0\ ,$ $\left|\frac{\partial h_3}{\partial I_R}\right| = |0| < \infty$ (54)

$\frac{\partial h_3}{\partial R_S} = 0\ ,$ $\left|\frac{\partial h_3}{\partial R_S}\right| = |0| < \infty$ (55)

$\frac{\partial h_3}{\partial R_R} = 0\ ,$ $\left|\frac{\partial h_3}{\partial R_R}\right| = |0| < \infty$ (56)

Furthermore,

$\frac{\partial h_4}{\partial M} = 0,$ $\left|\frac{\partial h_4}{\partial M}\right| = |0| < \infty$ (57)

$\frac{\partial h_4}{\partial S} = -(1 - \rho_R)\ \beta_R I_R\ ,$ $\left|\frac{\partial h_4}{\partial S}\right| = |(1 - \rho_R)\ \beta_R I_R| < \infty$ (58)

$\frac{\partial h_4}{\partial E_S} = 0\ ,$ $\left|\frac{\partial h_4}{\partial E_S}\right| = |0| < \infty$ (59)

$\frac{\partial h_4}{\partial E_R} = -(V + \mu),$ $\left|\frac{\partial h_4}{\partial E_R}\right| = -|(V + \mu)| < \infty$ (60)

$\frac{\partial h_4}{\partial I_S} = 0\ ,$ $\left|\frac{\partial h_4}{\partial I_S}\right| = |0| < \infty$ (61)

$\frac{\partial h_4}{\partial I_R} = (1 - \rho_R)\ \beta_R S\ ,$ $\left|\frac{\partial h_4}{\partial I_R}\right| = |(1 - \rho_R)\ \beta_R S| < \infty$ (62)

$\frac{\partial h_4}{\partial R_S} = 0\ ,$ $\left|\frac{\partial h_4}{\partial R_S}\right| = |0| < \infty$ (63)

$\frac{\partial h_4}{\partial R_R} = 0\ ,$ $\left|\frac{\partial h_4}{\partial R_R}\right| = |0| < \infty$ (64)

Likewise,

$\frac{\partial h_5}{\partial M} = 0,$ $\left|\frac{\partial h_5}{\partial M}\right| = |0| < \infty$ (65)

$\frac{\partial h_5}{\partial S} = \rho_s\ \beta_s I_s\ ,$ $\left|\frac{\partial h_5}{\partial S}\right| = |\rho_s\ \beta_s I_s\ | < \infty$ (66)

$\frac{\partial h_5}{\partial E_S} = V\ ,$ $\left|\frac{\partial h_5}{\partial E_S}\right| = |V| < \infty$ (67)

$\frac{\partial h_5}{\partial E_R} = 0\ ,$ $\left|\frac{\partial h_5}{\partial E_R}\right| = |0| < \infty$ (68)

$\frac{\partial h_5}{\partial I_S} = \rho_s\ \beta_s S - (\mu + \mu_R + r_2)I_s\ ,$ $\left|\frac{\partial h_5}{\partial I_S}\right| = |[\rho_s\ \beta_s S - (\mu + \mu_R + r_2)I_s]| < \infty$ (69)

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$\frac{\partial h_5}{\partial I_R} = 0$, $\left|\frac{\partial h_5}{\partial I_R}\right| = |0| < \infty$ (70)

$\frac{\partial h_5}{\partial R_S} = 0$, $\left|\frac{\partial h_5}{\partial R_S}\right| = |0| < \infty$ (71)

$\frac{\partial h_5}{\partial R_R} = 0$, $\left|\frac{\partial h_5}{\partial R_R}\right| = |0| < \infty$ (72)

Analogously,

$\frac{\partial h_6}{\partial M} = 0,$ $\left|\frac{\partial h_6}{\partial M}\right| = |0| < \infty$ (73)

$\frac{\partial h_6}{\partial S} = \rho_R \beta_R I_R$, $\left|\frac{\partial h_6}{\partial S}\right| = |\rho_R \beta_R I_R| < \infty$ (74)

$\frac{\partial h_6}{\partial E_S} = 0$, $\left|\frac{\partial h_6}{\partial E_S}\right| = |0| < \infty$ (75)

$\frac{\partial h_6}{\partial E_R} = \upsilon$, $\left|\frac{\partial h_6}{\partial E_R}\right| = |\upsilon| < \infty$ (76)

$\frac{\partial h_6}{\partial I_S} = r_2 r,$ $\left|\frac{\partial h_6}{\partial I_S}\right| = |r_2 r| < \infty$ (77)

$\frac{\partial h_6}{\partial I_R} = \rho_R \beta_R S - (\mu + \mu_r + r_1),$ $\left|\frac{\partial h_6}{\partial I_R}\right| = |[\rho_R \beta_R S - (\mu + \mu_r + r_1)]| < \infty$ (78)

$\frac{\partial h_6}{\partial R_S} = 0$, $\left|\frac{\partial h_6}{\partial R_S}\right| = |0| < \infty$ (79)

$\frac{\partial h_6}{\partial R_R} = 0$, $\left|\frac{\partial h_6}{\partial R_R}\right| = |0| < \infty$ (80)

Correspondingly,

$\frac{\partial h_7}{\partial M} = 0,$ $\left|\frac{\partial h_7}{\partial M}\right| = |0| < \infty$ (81)

$\frac{\partial h_7}{\partial S} = 0$, $\left|\frac{\partial h_7}{\partial S}\right| = |0| < \infty$ (82)

$\frac{\partial h_7}{\partial E_S} = 0$, $\left|\frac{\partial h_7}{\partial E_S}\right| = |0| < \infty$ (83)

$\frac{\partial h_7}{\partial E_R} = 0$, $\left|\frac{\partial h_7}{\partial E_R}\right| = |0| < \infty$ (84)

$\frac{\partial h_7}{\partial I_S} = r_2(1 - r)$ $\left|\frac{\partial h_7}{\partial I_S}\right| = |r_2(1 - r)| < \infty$ (85)

$\frac{\partial h_7}{\partial I_R} = 0$, $\left|\frac{\partial h_7}{\partial I_R}\right| = |0| < \infty$ (86)

$\frac{\partial h_7}{\partial R_S} = -\mu$, $\left|\frac{\partial h_7}{\partial R_S}\right| = -|\mu| < \infty$ (87)

$\frac{\partial h_7}{\partial R_R} = 0$, $\left|\frac{\partial h_7}{\partial R_R}\right| = |0| < \infty$ (88)

Finally,

$\frac{\partial h_8}{\partial M} = 0,$ $\left|\frac{\partial h_8}{\partial M}\right| = |0| < \infty$ (89)

$\frac{\partial h_8}{\partial S} = 0$, $\left|\frac{\partial h_8}{\partial S}\right| = |0| < \infty$ (90)

$\frac{\partial h_8}{\partial E_S} = 0$, $\left|\frac{\partial h_8}{\partial E_S}\right| = |0| < \infty$ (91)

$\frac{\partial h_8}{\partial E_R} = 0$, $\left|\frac{\partial h_8}{\partial E_R}\right| = |0| < \infty$ (92)

$\frac{\partial h_8}{\partial I_S} = 0,$ $\left|\frac{\partial h_8}{\partial I_S}\right| = |0| < \infty$ (93)

$\frac{\partial h_8}{\partial I_R} = r_1$, $\left|\frac{\partial h_8}{\partial I_R}\right| = |r_1| < \infty$ (94)

$\frac{\partial h_8}{\partial R_S} = 0$, $\left|\frac{\partial h_8}{\partial R_S}\right| = |0| < \infty$ (95)

$\frac{\partial h_8}{\partial R_R} = -\mu$, $\left|\frac{\partial h_8}{\partial R_R}\right| = -|\mu| < \infty$ (96)

The partial derivatives (33) – (96) of the right hand side of (3) – (10) with respect M , S , E_S , E_R, I_S, I_R , R_S , and $R_R$are continuously differentiable and bounded. Hence, by Theorem 2, it is locally Lipschitz, therefore, M(t), S(t) , $E_S(t)$, $E_R(t)$, $I_S(t)$, $I_R(t)$, $R_S(t)$, and $R_R(t)$ is a unique solution to the system of equations (3) – (10) with the initial conditions $M_{10}, S_{10}, E_{s_{10}}, E_{R_{10}}, I_{s_{10}}, I_{R_{10}}, R_{S_{10}}, R_{R_{10}}$ in the region A.

Basic reproduction number

The basic reproduction number for both drug sensitive TB and drug-resistant TB is denoted byR_{os} and R_{oR} respectively. It is defined as the average number of secondary infections infected by an infective individual during an infective period provided that all members of the population are susceptible.

The next generation matrix technique by Diekman and Heesterbeck (2002) was applied to obtain the basic reproduction numbers, R_{os} and R_{oR} by considering the drug sensitive infected compartments of the system (3) to (10). That in equations (5), (6), (7) and (8).

Reproduction number for drug – sensitive TB

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From equation (5) and (7) it is given that

$$\frac{dE_S}{dt} = (1-\rho_s)\beta_s I_s S - (\upsilon+\mu)E_s$$

$$\frac{dI_S}{dt} = \rho_S\beta_s I_s S + \upsilon E_s - (\mu+\mu_r+\mu_1)I_s$$

Evaluating F and V, which are the Jacobian matrices of F and V, respectively at disease free equilibrium E_0 gives

$$F = \begin{bmatrix} 0 & \frac{(1-\rho_S)\beta_s\pi(\theta+\mu-\mu\theta)}{\mu(\theta+\mu)} \\ 0 & \frac{\rho_S\beta_s\pi(\theta+\mu-\mu\theta)}{\mu(\theta+\mu)} \end{bmatrix}, \quad V = \begin{bmatrix} (\upsilon+\mu) & 0 \\ -\upsilon & (\mu+\mu_r+\mu_2) \end{bmatrix}$$

The spectral radius $\rho(FV^{-1})$, which is defined as the largest eigenvalue of FV^{-1} is obtained. Thus the basic reproduction number for drug sensitive TB, R_{os} is

$$R_{os} = \frac{\upsilon(1-\rho_S)\beta_s\pi(\theta+\mu-\mu\sigma)}{\mu(\theta+\mu)(\upsilon+\mu)(\mu+\mu_T+r_2)} + \frac{\rho_S\beta_s\pi(\theta+\mu-\mu\sigma)}{\mu(\theta+\mu)(\mu+\mu_T+r_2)}$$

Reproduction number for drug-resistance TB

From equations (5) and (7) we have

$$\frac{dE_S}{dt} = (1-\rho_R)\beta_R I_R S - (\upsilon+\mu)E_R$$

$$\frac{dI_R}{dt} = \rho_R\beta_R I_R S + \upsilon E_R + r_2 r l_s - (\mu+\mu_T+\mu_1)I_R$$

We evaluated F and V are evaluated, which are the Jacobian matrices of F and V, respectively at disease free equilibrium E_0 to get

$$F = \begin{bmatrix} 0 & \frac{(1-\rho_S)\beta_R\pi(\theta+\mu-\mu\theta)}{\mu(\theta+\mu)} \\ 0 & \frac{\rho_S\beta_R\pi(\theta+\mu-\mu\theta)}{\mu(\theta+\mu)} \end{bmatrix} \text{ and } V = \begin{bmatrix} (\upsilon+\mu) & 0 \\ -\upsilon & (\mu+\mu_T+\mu_1) \end{bmatrix}$$

The spectral radius $\rho(FV^{-1})$ is obtained and the basic reproduction number for drug resistant TB, R_{0R} is

$$R_{oR} = \frac{\upsilon(1-\rho_R)\beta_R\pi(\theta+\mu-\mu\sigma)}{\mu(\theta+\mu)(\upsilon+\mu)(\mu+\mu_T+r_1)} + \frac{\rho_R\beta_R\pi(\theta+\mu-\mu\sigma)}{\mu(\theta+\mu)(\mu+\mu_T+r_1)}$$

Table3.3: Variables and parameters values used for computational results

Variable / Parameter	Values	Source(s)
β_s	0.0290	Jung, E., Lenhart, S., & Feng, Z. (2002)
β_R	0.0290	Jung, E., Lenhart, S., & Feng, Z. (2002)
Π	200	Jung, E., Lenhart, S., & Feng, Z. (2002)
μ	0.02	Bhunu, C. P., et. al., (2012)
μ_T	0.3	Bhunu, C. P., et. al., (2012)
ν	0.0013	Bhunu, C. P., et. al., (2012)
ρ_S	0.1	Bhunu, C. P., et. al., (2012)
ρ_R	0.1	Bhunu, C. P., et. al., (2012)
r_1	0.2	Bhunu, C. P., et. al., (2012)
r_2	0.3	Bhunu, C. P., et. al., (2012)
θ	0.7	Bhunu, C. P., et. al., (2012)
r	0.9	Assumed
σ	0.10	Cagri, O., et. al., (2012)
$\mathrm{M}(0)$	950	Assumed
$\mathrm{S}(0)$	3800	Cagri, O., et. al., (2012)
$E_S(0)$	1800	Cagri, O., et. al., (2012)
$E_R(0)$	100	Cagri, O., et. al., (2012)
$I_S(0)$	200	Cagri, O., et. al., (2012)
$I_R(0)$	50	Cagri, O., et. al., (2012)
$R_S(0)$	30	Assumed
$R_R(0)$	20	Assumed

Sensitivity analysis: sensitivity analysis illuminates the path through the uncertainties, helping you understand how variations in model parameters affect disease transmission dynamics. The process involves identifying which parameters significantly influence the spread of disease for better prioritization, management of risks,

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decision-making, and model validation. It is a method used to determine how different values of an independent variable.

Sensitivity Analysis: the sensitivity indices of the model parameter with respect to R_{0S} and R_{0R} are as follows

$$\times_{r_1}^{R_{0R}} = \frac{\partial R_{0R}}{\partial r_1} \times \frac{r_1}{R_{0R}} = \frac{V(1-\rho_R)\beta_{R\bar{\wedge}(\theta+\mu-\mu\sigma)}}{\mu(\theta+\mu)(V+\mu)(\mu+\mu_\tau+r_1)^2} - \frac{\rho_R\beta_{R\bar{\wedge}(\theta+\mu-\mu\sigma)}}{\mu(\theta+\mu)(\mu+\mu_\tau r_1)^2} \times \frac{r_1}{R_{0R}}$$

$$= \frac{\begin{matrix}V(1-\rho_R)\beta_{R\bar{\wedge}(\theta+\mu-\mu\delta)}\mu(\theta+\mu)(\mu+\mu_\tau+\gamma_1)^2+\rho_R)\\ \beta_{R\bar{\wedge}(\theta+\mu-\mu\sigma)}\mu(\theta+\mu)(V+\mu)(\mu+\mu_\tau+r_1)^2\end{matrix}}{\mu(\theta+\mu)(V+\mu)(\mu+\mu_\tau+r_1)^2\mu(\theta+\mu)(\mu+\mu_\tau+r_1)^2} \times \frac{\begin{matrix}r_1\mu(\theta+\mu)(V+\mu)(\mu+\mu_\tau+\gamma_1)\mu(\theta+\mu)(\mu+\mu_\tau+r_1)\\ V(1-\rho_R)\beta_{R\bar{\wedge}(\theta+\mu-\mu\sigma)}\mu(\theta+\mu)(\mu+\mu_\tau+r_1)+\rho_R\beta_{R\bar{\wedge}}\mu\\ (\theta+\mu_\tau)\mu(\theta+\mu)(V+\mu)(\mu+\mu_\tau+r_1)^2\end{matrix}}{}$$

$$= -\frac{(\mu+\mu_\tau+\gamma_1)\gamma_1}{(\mu+\mu_\tau+\gamma_1)^2} = -\frac{r_1}{\mu+\mu_\tau+\gamma_1} = -\frac{0.2}{0.02+0.3+0.2} = -0.3846$$

$$\times_{\beta_R}^{R_{0R}} = \frac{\partial R_{0R}}{\partial \beta_R} \times \frac{\beta_R}{R_{0R}} = \frac{V(1-\rho_R)\bar{\wedge}(\theta+\mu-\mu\sigma)}{\mu(\theta+\mu)(V+\mu)(\mu+\mu_\tau+\gamma_1)} + \frac{\rho_R\bar{\wedge}(\theta+\mu-\mu\sigma)}{\mu(\theta+\mu)(\mu+\mu_\tau+\gamma_1)} \times \frac{\beta_R}{R_{0R}}$$

$$= \frac{\begin{matrix}\mu(\theta+\mu)(\mu+\mu_\tau\gamma_1)V(1-\rho_R)\,\bar{\wedge}\,(\theta+\mu-\mu\sigma)\\ +\mu(\theta+\mu)(V+\mu)(\mu+\mu_\tau+\gamma_1)\rho_R\,\bar{\wedge}\,(\theta+\mu-\mu\sigma)\end{matrix}}{\mu(\theta+\mu)(V+\mu)(\mu+\mu_\tau+\gamma_1)\mu(\theta+\mu)(\mu+\mu_\tau+\gamma_1)} \times \frac{\begin{matrix}\beta_R\mu(\theta+\mu)(V+\mu)(\mu+\mu_\tau\gamma_1)\mu(\theta+\mu)(\mu+\mu_\tau\gamma_1)\\ V(1-\rho_R)\beta_{R\bar{\wedge}(\theta+\mu-\mu\sigma)}\mu(\theta+\mu)(\mu+\mu_\tau+\gamma_1)\\ +\rho_R\beta_{R\bar{\wedge}}\mu(\theta+\mu_\tau)\mu(\theta+\mu)(V+\mu)(\mu+\mu_\tau+\gamma_1)^2\end{matrix}}{}$$

$$= \frac{V(1-\rho_R)\,\bar{\wedge}\,(V+\mu)\rho_R\,\bar{\wedge}\times\beta_R)}{V(1-\rho_R)\beta_R\,\bar{\wedge}+\rho_R\beta_R\,\bar{\wedge}\,(V+\mu)} = \frac{V(1-\rho_R)(V+\mu)\rho_R\,\bar{\wedge}\times\beta_R)}{V(1-\rho_R)\beta_R\,\bar{\wedge}+\rho_R\beta_R\,\bar{\wedge}\,(V+\mu)} = 1$$

$$\times_{\bar{\wedge}}^{R_{0R}} = \frac{\partial R_{0R}}{\partial\,\bar{\wedge}} \times \frac{\bar{\wedge}}{R_{0R}} = \frac{V(1-\rho_R)(\theta+\mu-\mu\sigma)}{\mu(\theta+\mu)(V+\mu)(\mu+\mu_\tau+\gamma_1)} + \frac{\rho_R\beta_R(\theta+\mu-\mu\sigma)}{\mu(\theta+\mu)(\mu+\mu_\tau+\gamma_1)} \times \frac{\bar{\wedge}}{R_{0R}}$$

$$= \frac{\begin{matrix}\mu(\theta+\mu)(\mu+\mu_\tau+\gamma_1)V(1-\rho_R)\,\bar{\wedge}\,(\theta+\mu-\mu\sigma)\\ +\mu(\theta+\mu)(V+\mu)(\mu+\mu_\tau+\gamma_1)\rho_R\beta_R(\theta+\mu-\mu\sigma)\end{matrix}}{\mu(\theta+\mu)(V+\mu)(\mu+\mu_\tau+\gamma_1)\mu(\theta+\mu)(\mu+\mu_\tau+\gamma_1)} \times \frac{\begin{matrix}\bar{\wedge}\,\mu(\theta+\mu)(V+\mu)(\mu+\mu_\tau+\gamma_1)\mu(\theta+\mu)(\mu+\mu_\tau+\gamma_1)\\ V(1-\rho_R)\beta_{R\bar{\wedge}(\theta+\mu-\mu\sigma)}\mu(\theta+\mu)(\mu+\mu_\tau+\gamma_1)\\ +\rho_R\beta_{R\bar{\wedge}}(\theta+\mu-\mu_\tau)\mu(\theta+\mu)(V+\mu)(\mu+\mu_\tau+\gamma_1)\end{matrix}}{}$$

$$= \frac{V(1-\rho_R)(V+\mu)\rho_R\,\beta_R\,\bar{\wedge}}{V(1-\rho_R)\beta_R\,\bar{\wedge}+\rho_R\beta_R\,\bar{\wedge}\,(V+\mu)} = 1$$

$$\times_{\rho_R}^{R_{0R}} = \frac{\partial R_{0R}}{\partial \rho_R} \times \frac{\rho_R}{R_{0R}} = \frac{V\beta_R\,\bar{\wedge}\,(\theta+\mu-\mu\sigma)}{\mu(\theta+\mu)(V+\mu)(\mu+\mu_\tau+\gamma_1)} + \frac{\rho_R\beta_R(\theta+\mu-\mu\sigma)}{\mu(\theta+\mu)(\mu+\mu_\tau+\gamma_1)} \times \frac{\rho_R}{R_{0R}}$$

$$= \frac{\begin{matrix}\mu(\theta+\mu)(\mu+\mu_\tau+\gamma_1)V\beta_R\,\bar{\wedge}\,(\theta+\mu-\mu\sigma)\\ +\mu(\theta+\mu)(V+\mu)(\mu+\mu_\tau+\gamma_1)\beta_R\,\bar{\wedge}\,(\theta+\mu-\mu\sigma)\end{matrix}}{\mu(\theta+\mu)(V+\mu)(\mu+\mu_\tau+\gamma_1)\mu(\theta+\mu)(\mu+\mu_\tau+\gamma_1)} \times \frac{\begin{matrix}\rho_R\mu(\theta+\mu)(V+\mu)(\mu+\mu_\tau+\gamma_1)\mu(\theta+\mu)(\mu+\mu_\tau+\gamma_1)\\ V(1-\rho_R)\beta_{R\bar{\wedge}(\theta+\mu-\mu\sigma)}\mu(\theta+\mu)(\mu+\mu_\tau+\gamma_1)\\ +\rho_R\beta_{R\bar{\wedge}}(\theta+\mu-\mu_\tau)\mu(\theta+\mu)(V+\mu)(\mu+\mu_\tau+\gamma_1)\end{matrix}}{}$$

$$= \frac{[V\beta_R\,\bar{\wedge}+(V+\mu)\beta_{R\bar{\wedge}}]}{V(1-\rho_R)\beta_{R\bar{\wedge}}+\rho_R\beta_{R\bar{\wedge}}(V+\mu)} = \left[\frac{V+(V+\mu)\rho_R}{V(1-\rho_R)+\rho_R(V+\mu)}\right] = \left[\frac{0.0013+(0.0013+0.02)0.1}{0.0013(1-0.1)+0.1(0.0013+0.02)}\right] = -0.2515$$

$$\times_{\sigma}^{R_{0R}} = \frac{\partial R_{0R}}{\partial \sigma} \times \frac{\sigma}{R_{0R}} = \frac{V(1-\rho_R)\beta_{R\bar{\wedge}}\mu}{\mu(\theta+\mu)(V+\mu)(\mu+\mu_\tau+\gamma_1)} - \frac{\rho_R\beta_{R\bar{\wedge}}\mu}{\mu(\theta+\mu)(\mu+\mu_\tau+\gamma_1)} \times \frac{\sigma}{R_{0R}}$$

$$= -\frac{\begin{matrix}\mu(\theta+\mu)(\mu+\mu_\tau+\gamma_1)V(1-\rho_R)\beta_{R\bar{\wedge}}\mu\\ +\mu(\theta+\mu)(V+\mu)(\mu+\mu_\tau+\gamma_1)\rho_R\beta_R\,\bar{\wedge}\,\mu\end{matrix}}{\mu(\theta+\mu)(V+\mu)(\mu+\mu_\tau+\gamma_1)\mu(\theta+\mu)(\mu+\mu_\tau\gamma_1)} \times \frac{\begin{matrix}\delta\mu(\theta+\mu)(V+\mu)(\mu+\mu_\tau\gamma_1)\mu(\theta+\mu)(\mu+\mu_\tau+\gamma_1)\\ V(1-\rho_R)\beta_{R\bar{\wedge}(\theta+\mu-\mu\sigma)}\mu(\theta+\mu)(\mu+\mu_\tau+\gamma_1)\\ +\rho_R\beta_{R\bar{\wedge}}(\theta+\mu-\mu_\tau)\mu(\theta+\mu)(V+\mu)(\mu+\mu_\tau+\gamma_1)\end{matrix}}{}$$

$$= -\frac{V(1-\rho_R)\mu+(V+\mu)\rho_R\mu)\times\delta}{V(1-\rho_R)(\theta+\mu-\mu\sigma)+\rho_R(\theta+\mu-\mu\sigma)(V+\mu)} = -\frac{\begin{matrix}0.0013(1-0.1)0.02+(0.0013+0.02)\\ 0.1x0.02)\times 0.10\\ 0.0013(1-0.1)(0.7+0.02-0.02x0.10)\\ +0.1(0.7+0.02-0.02x0.10)(0.0013+0.02)\end{matrix}}{}\frac{0.00002766}{0.0023694} = 0.0117$$

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$$\chi_{\beta_s}^{R_{0s}} = \frac{\partial R_{0s}}{\partial \beta_s} \times \frac{\beta_s}{R_{0s}} = \frac{V(1-\rho_s)\beta_{s\bar{\lambda}}(\theta+\mu-\mu\sigma)}{\mu(\theta+\mu)(V+\mu)(\mu+\mu_\tau+\gamma_2)} + \frac{\rho_s\beta_{s\bar{\lambda}}(\theta+\mu-\mu\sigma)}{\mu(\theta+\mu)(\mu+\mu_\tau+\gamma_2)} \times \frac{\beta_s}{\frac{V(1-\rho_s)\beta_{s\bar{\lambda}}(\theta+\mu-\mu\sigma)}{\mu(\theta+\mu)(\mu+\mu_\tau+\gamma_2)}} + \frac{\rho_s\beta_{s\bar{\lambda}}(\theta+\mu-\mu\sigma)}{\mu(\theta+\mu)(\mu+\mu_\tau+\gamma_2)} = 1$$

$$\chi_{\rho_s}^{R_{0s}} = \frac{\partial R_{0s}}{\partial \rho_s} \times \frac{\rho_s}{R_{0s}} - \frac{V\beta_{s\bar{\lambda}}(\theta+\mu-\mu\sigma)}{\mu(\theta+\mu)(V+\mu)(\mu+\mu_\tau+\gamma_2)} + \frac{\beta_{s\bar{\lambda}}(\theta+\mu-\mu\sigma)}{\mu(\theta+\mu)(\mu+\mu_\tau+\gamma_2)} \times \frac{\rho_s}{\frac{V(1-\rho_s)\beta_{s\bar{\lambda}}(\theta+\mu-\mu\sigma)}{\mu(\theta+\mu)(\mu+\mu_\tau+\gamma_2)}} + \frac{\rho_s\beta_{s\bar{\lambda}}(\theta+\mu-\mu\sigma)}{\mu(\theta+\mu)(\mu+\mu_\tau+\gamma_2)}$$

$$= -\frac{V\beta_{s\bar{\lambda}}(\theta+\mu-\mu\sigma)}{\mu(\theta+\mu)(V+\mu)(\mu+\mu_\tau+\gamma_2)} + \frac{\beta_{s\bar{\lambda}}(\theta+\mu-\mu\sigma)}{\mu(\theta+\mu)(\mu+\mu_\tau+\gamma_2)} \times \frac{\rho_s\mu(\theta+\mu)(V+\mu)(\mu+\mu_\tau+\gamma_2)\mu(\theta+\mu)(\mu+\mu_\tau+\gamma_2)}{\begin{matrix}V(1-\rho_s)\beta_{s\bar{\lambda}}(\theta+\mu-\mu\sigma)\mu(\theta+\mu)(\mu+\mu_\tau+\gamma_2) \\ +\mu(\theta+\mu)(V+\mu)(\mu+\mu_\tau+\gamma_2)\rho_s\beta_{s\bar{\lambda}}(\theta+\mu-\mu\sigma)\end{matrix}}$$

$$= -\frac{\begin{matrix}\mu(\theta+\mu)(\mu+\mu_\tau+\gamma_2)V\beta_{s\bar{\lambda}}(\theta+\mu-\mu\sigma) \\ -\mu(\theta+\mu)(\mu+\mu_\tau+\gamma_2)(V+\mu)\beta_{s\bar{\lambda}}(\theta+\mu-\mu\sigma)\end{matrix}}{\mu(\theta+\mu)(V+\mu)(\mu+\mu_\tau+\gamma_2)\mu(\theta+\mu)(\mu+\mu_\tau+\gamma_2)^2} \times \frac{\rho_s\mu(\theta+\mu)(V+\mu)(\mu+\mu_\tau+\gamma_2)\mu(\theta+\mu)(\mu+\mu_\tau+\gamma_2)}{\begin{matrix}V(1-\rho_s)\beta_{s\bar{\lambda}}(\theta+\mu-\mu\sigma)\mu(\theta+\mu)(\mu+\mu_\tau+\gamma_2) \\ \rho_s\beta_{s\bar{\lambda}} + \mu(\theta+\mu)(V+\mu)(\mu+\mu_\tau+\gamma_2)\rho_s\beta_{s\bar{\lambda}}(\theta+\mu-\mu\sigma)\end{matrix}}$$

$$= -\left[\frac{V-(V+\mu)\rho_s}{V(1-\rho_s)+\rho_s(V+\mu)}\right] = \left[\frac{0.0013-(0.0013+0.02)0.1}{0.0013(1-0.1)+0.1(0.0013+0.02)}\right] = -0.2515$$

$$\chi_{r_2}^{R_{0s}} = \frac{\partial R_{0s}}{\partial r_2} \times \frac{r_2}{R_{0s}} = -\left[\frac{V(1-\rho_s)\beta_{s\bar{\lambda}}(\theta+\mu-\mu\sigma)}{\mu(\theta+\mu)(V+\mu)(\mu+\mu_\tau+\gamma_2)^2} - \frac{\rho_s\beta_{s\bar{\lambda}}(\theta+\mu-\mu\sigma)}{\mu(\theta+\mu)(\mu+\mu_\tau+\gamma_2)^2}\right] \times \left[\frac{r_2}{\frac{V(1-\rho_s)\beta_{s\bar{\lambda}}(\theta+\mu-\mu\sigma)}{\mu(\theta+\mu)(V+\mu)(\mu+\mu_\tau+\gamma_2)} + \frac{\rho_s\beta_{s\bar{\lambda}}(\theta+\mu-\mu\sigma)}{\mu(\theta+\mu)(\mu+\mu_\tau+\gamma_2)}}\right]$$

$$= -\left[\frac{r_2}{\mu+\mu_\tau+\gamma_2}\right] = -\left[\frac{0.3}{0.02+0.3+0.3}\right] = -0.5$$

$$\chi_{\mu_\tau}^{R_{0s}} = \frac{\partial R_{0s}}{\partial \mu_\tau} \times \frac{\mu_\tau}{R_{0s}} = -\left[\frac{V(1-\rho_s)\beta_{s\bar{\lambda}}(\theta+\mu-\mu\sigma)}{\mu(\theta+\mu)(V+\mu)(\mu+\mu_\tau+\gamma_2)^2} - \frac{\rho_s\beta_{s\bar{\lambda}}(\theta+\mu-\mu\sigma)}{\mu(\theta+\mu)(\mu+\mu_\tau+\gamma_2)^2}\right] \times \frac{\mu_\tau}{R_{0s}}$$

$$= -\frac{\begin{matrix}\mu(\theta+\mu)(\mu+\mu_\tau+\gamma_2)^2V(1-\rho_s)\beta_{s\bar{\lambda}}(\theta+\mu-\mu\sigma) \\ +\mu(\theta+\mu)(\mu+\mu_\tau+\gamma_2)^2\rho_s\beta_{s\bar{\lambda}}(\theta+\mu-\mu\sigma)\end{matrix}}{\mu(\theta+\mu)(V+\mu)(\mu+\mu_\tau+\gamma_2)^2\mu(\theta+\mu)(\mu+\mu_\tau+\gamma_2)^2} \times \frac{\mu_\tau\mu(\theta+\mu)(V+\mu)(\mu+\mu_\tau+\gamma_2)\mu(\theta+\mu)(\mu+\mu_\tau+\gamma_2)}{\begin{matrix}V(1-\rho_s)\beta_{s\bar{\lambda}}(\theta+\mu-\mu\sigma)\mu(\theta+\mu)(\mu+\mu_\tau+\gamma_2) \\ \rho_s\beta_{s\bar{\lambda}} + \mu(\theta+\mu)(V+\mu)(\mu+\mu_\tau+\gamma_2)\end{matrix}} = -\left[\frac{\mu_\tau}{\mu+\mu_\tau+\gamma_2}\right] = -0.5$$

$$\chi_{V}^{R_{0s}} = \frac{\partial R_{0s}}{\partial V} \times \frac{V}{R_{0s}} = \left[\frac{(1-\rho_s)\beta_{s\bar{\lambda}}(\theta+\mu-\mu\sigma)\mu}{\mu(\theta+\mu)(\mu+\mu_\tau+\gamma_2)} + \frac{\rho_s\beta_{s\bar{\lambda}}(\theta+\mu-\mu\sigma)}{\mu(\theta+\mu)(\mu+\mu_\tau+\gamma_2)}\right] \times \frac{V\mu(\theta+\mu)(V+\mu)(\mu+\mu_\tau+\gamma_2)\mu(\theta+\mu)(\mu+\mu_\tau+\gamma_2)}{\begin{matrix}V(1-\rho_s)\beta_{s\bar{\lambda}}(\theta+\mu-\mu\sigma)\mu(\theta+\mu)(\mu+\mu_\tau+\gamma_2) \\ +\mu(\theta+\mu)(V+\mu)(\mu+\mu_\tau+\gamma_2)\rho_s\beta_{s\bar{\lambda}}(\theta+\mu-\mu\sigma)\end{matrix}}$$

$$= -\frac{\begin{matrix}\mu(\theta+\mu)(\mu+\mu_\tau+\gamma_2)(1-\rho_s)\beta_{s\bar{\lambda}}(\theta+\mu-\mu\sigma) \\ \mu+\mu(V+\mu)^2(\mu+\mu_\tau+\gamma_2)\rho_s\beta_{s\bar{\lambda}}(\theta+\mu-\mu\sigma)\end{matrix}}{\mu(\theta+\mu)(\mu+\mu_\tau+\gamma_2)\mu(\theta+\mu)(\mu+\mu_\tau+\gamma_2)} \times \frac{V\mu(\theta+\mu)(V+\mu)(\mu+\mu_\tau+\gamma_2)\mu(\theta+\mu)(\mu+\mu_\tau+\gamma_2)}{\begin{matrix}V(1-\rho_s)\beta_{s\bar{\lambda}}(\theta+\mu-\mu\sigma)\mu(\theta+\mu)(\mu+\mu_\tau+\gamma_2) \\ +\mu(\theta+\mu)(V+\mu)(\mu+\mu_\tau+\gamma_2)\rho_s\beta_{s\bar{\lambda}}(\theta+\mu-\mu\sigma)\end{matrix}}$$

$$-\frac{(1-\rho_s)\mu+(V+\mu)^2V(V+\mu)\rho_s}{V(1-\rho_s)+\rho_s} = -\frac{(1-0.1)0.02+(0.0013+0.02)^2 0.0013(0.0013+0.02)\ 0.1}{0.0013(1-0.1)+0.1}$$

$$-\frac{0.9\times0.02+0.00045369\times0.000002769}{0.00117+0.1} = -\frac{0.018+0.00000000125626761}{0.10117} = -0.0180$$

$$\chi_{\theta}^{R_{0s}} = \frac{\partial R_{0s}}{\partial \theta} \times \frac{\theta}{R_{0s}} = \left[\frac{V(1-\rho_s)\beta_{s\bar{\lambda}}\mu\sigma}{\mu(\theta+\mu)^2(V+\mu)(\mu+\mu_\tau+\gamma_2)} + \frac{\rho_s\beta_{s\bar{\lambda}}\mu\sigma}{\mu(\theta+\mu)^2(\mu+\mu_\tau+\gamma_2)}\right] \times \frac{\begin{matrix}\theta\mu(\theta+\mu)(V+\mu)(\mu+\mu_\tau+\gamma_2) \\ \mu(\theta+\mu)(\mu+\mu_\tau+\gamma_2)\end{matrix}}{\begin{matrix}V(1-\rho_s)\beta_{s\bar{\lambda}}\mu\sigma\,\mu(\theta+\mu)^2(\mu+\mu_\tau+\gamma_2) \\ +\rho_s\beta_{s\bar{\lambda}}\mu\sigma\,\mu(\theta+\mu)^2(V+\mu)(\mu+\mu_\tau+\gamma_2)\end{matrix}}$$

$$\frac{\begin{matrix}\mu(\theta+\mu)^2(\mu+\mu_\tau+\gamma_2)\mu(1-\rho_s)\beta_{s\bar{\lambda}}\mu\sigma \\ +\mu(\theta+\mu)^2(V+\mu)(\mu+\mu_\tau+\gamma_2)+\rho_s\beta_{s\bar{\lambda}}\mu\sigma\end{matrix}}{(\theta+\mu)^2(V+\mu)(\mu+\mu_\tau+\gamma_2)(\theta+\mu)^2(V+\mu)(\mu+\mu_\tau+\gamma_2)} \times \frac{\theta\mu(\theta+\mu)(V+\mu)(\mu+\mu_\tau+\gamma_2)\mu(\theta+\mu)(\mu+\mu_\tau+\gamma_2)}{\begin{matrix}V(1-\rho_s)\beta_{s\bar{\lambda}}\ (\theta+\mu-\mu\sigma)\mu(\theta+\mu)(\mu+\mu_\tau+\gamma_2) \\ +\mu(\theta+\mu)(V+\mu)(\mu+\mu_\tau+\gamma_2\rho_s\beta_{s\bar{\lambda}}\ (\theta+\mu-\mu\sigma)\end{matrix}}$$

$$\frac{(\theta+\mu)V(1-\rho_s)\mu\sigma+(\theta+\mu)(V+\mu)\rho_s\,\mu\sigma\theta}{(\theta+\mu)^2\,V(1-\rho_s)(\theta+\mu-\mu\sigma)+(V+\mu)\rho_s(\theta+\mu-\mu\sigma)} = \frac{\begin{matrix}(0.7+0.02)0.0013\ (1-0.1)0.02\times0.10+ \\ (0.7+0.02)(0.0013+0.02)0.1\times0.02\times0.10\times0.7\end{matrix}}{\begin{matrix}(0.7+0.02)^2\ 0.0013\ (1-01)(0.7+0.02-0.02\times0.10) \\ +(0.0013+0.02)\ 0.1(0.7+0.02-0.02\ \times0.10)\end{matrix}}$$

$$= \frac{0.72\times0.0013\times0.9\times0.02\times0.10+0.72\ \times0.0213\times0.00014}{0.5184\ \times0.0013\ \times0.9\times0.718+0.0213\ \times0.1\times0.715} = \frac{0.0000016848+0.00000214704}{0.000435487104+0.00152295} = \frac{0.00000383184}{0.001958437104} = 0.0019$$

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$$X_{\mu}^{R_{oR}} = \frac{\partial R_{0R}}{\partial \mu} \times \frac{\mu}{R_{0R}} =$$

$$\frac{\begin{matrix}\mu(\theta+\mu)(v+\mu)(\mu+\mu_T+r_1)v(1-\rho_R)\beta_{R\pi} \\ (1-\sigma)-v(1-\rho_R)\beta_{R\pi}(\theta+\mu-\mu\sigma)[\mu(\theta+\mu) \\ (v+\mu)+\mu(\theta+\mu)(\mu+\mu_T+r_1)+\mu(v+\mu) \\ (\mu+\mu_T+r_1)+(\theta+\mu)(v+\mu)(\mu+\mu_T+r_1)\end{matrix}}{[\mu(\theta+\mu)(v+\mu)(\mu+\mu_T+r_1)]^2} + \frac{\begin{matrix}\mu(\theta+\mu)(\mu+\mu_T+r_1)\rho_R\beta_{R\pi}(1-\sigma)-\rho_R\beta_{R\pi} \\ (\theta+\mu-\mu\sigma)[\mu(\theta+\mu)(v+\mu)+\mu(\theta+\mu)(\mu+\mu_T+r_1) \\ +\mu(v+\mu)(\mu+\mu_T+r_1)+(\theta+\mu)(v+\mu)(\mu+\mu_T+r_1)\end{matrix}}{[\mu(\theta+\mu)(\mu+\mu_T+r_1)]^2} X \frac{\begin{matrix}\mu\mu^2(\theta+\mu)^2(v+\mu)(\mu+\mu_T+r_1)^2 \\ \mu(\theta+\mu)(\mu+\mu_T+r_1)v(1-\rho_R)\beta_{R\pi} \\ (\theta+\mu-\mu\sigma)+\mu(\theta+\mu)(v+\mu) \\ (\mu+\mu_T+r_1)\rho_R\beta_{R\pi}(\theta+\mu-\mu\sigma)\end{matrix}}{}$$

$$= \frac{\begin{matrix}\mu^2(\theta+\mu)^2(\mu+\mu_T+r_1)^2\mu(\theta+\mu)(v+\mu)(\mu+\mu_T+r_1)v(1-\rho_R)\beta_{R\pi}(1-\sigma) \\ -v(1-\rho_R)\beta_{R\pi}(\theta+\mu-\mu\sigma)\mu(\theta+\mu)(v+\mu)+\mu(\theta+\mu)(\mu+\mu_T+r_1)\mu(v+\mu) \\ (\mu+\mu_T+r_1)+(\theta+\mu)(v+\mu)(\mu+\mu_T+r_1)+\mu^2(\theta+\mu)^2(\mu+\mu_T+r_1)^2 \\ \mu(\theta+\mu)(\mu+\mu_T+r_1)\rho_R\beta_{R\pi}(1-\sigma)-\rho_R\beta_{R\pi}(\theta+\mu-\mu\sigma)\mu(\theta+\mu)(v+\mu)+ \\ \mu(\theta+\mu)(\mu+\mu_T+r_1)\mu(v+\mu)(\mu+\mu_T+r_1)+(\theta+\mu)(v+\mu)(\mu+\mu_T+r_1)\end{matrix}}{[\mu^2(\theta+\mu)^2(v+\mu)^2][\mu^2(\theta+\mu)^2(\mu+\mu_T+r_1)^2]} X \frac{\begin{matrix}\mu\mu^2(\theta+\mu)^2(v+\mu)(\mu+\mu_T+r_1)^2\mu(\theta+\mu)(\mu+\mu_T+r_1) \\ \rho_R\beta_{R\pi}(1-\sigma)-\rho_R\beta_{R\pi}(\theta+\mu-\mu\sigma)\mu(\theta+\mu)(v+\mu)+\mu(\theta+\mu) \\ (\mu+\mu_T+r_1)\mu(v+\mu)(\mu+\mu_T+r_1)+(\theta+\mu)(v+\mu)(\mu+\mu_T+r_1) \\ \mu(\theta+\mu)(\mu+\mu_T+r_1)v(1-\rho_R)\beta_{R\pi}(\theta+\mu-\mu\sigma) \\ +\mu(\theta+\mu)(v+\mu)(\mu+\mu_T+r_1)\rho_R\beta_{R\pi}(\theta+\mu-\mu\sigma)\end{matrix}}{}$$

$$= \frac{\begin{matrix}\mu^2(\theta+\mu)^2(\mu+\mu_T+r_1)(v+\mu)(\mu+\mu_T+r_1)v(1-\rho_R)\beta_{R\pi}(1-\sigma)-v(1-\rho_R)\mu(\theta+\mu)(v+\mu)\mu(\theta+\mu) \\ (\mu+\mu_T+r_1)+\mu(v+\mu)(\mu+\mu_T+r_1)+(\theta+\mu)(v+\mu)(\mu+\mu_T+r_1)+\mu^2(\theta+\mu)^2(\mu+\mu_T+r_1)^2\rho_R\beta_{R\pi}(1-\sigma)-\rho_R\mu \\ +(\theta+\mu)(v+\mu)+(\theta+\mu)(\mu+\mu_T+r_1)+\mu(v+\mu)(\mu+\mu_T+r_1)+(\theta+\mu)(v+\mu)(\mu+\mu_T+r_1)\times\mu\end{matrix}}{(v+\mu)^2\mu^2(\theta+\mu)^2(\mu+\mu_T+r_1)^2v(1-\rho_R)+(v+\mu)\rho_R}$$

$$= \frac{\begin{matrix}(0.02)^2(0.7+0.02)^2(0.02+0.3+0.2)(0.0013+0.02)0.0013(1-0.1)0.0290\times200 \\ (1-0.10)-0.0013(1-0.1)0.02(0.7+0.02)(0.0013+0.02)+0.02(0.7+0.02)(0.02+0.3+0.2)+0.02(0.0013+0.02)(0.02+0.3 \\ +0.2)+(0.7+0.02)(0.0013+0.02)(0.02+0.3+0.2)+(0.02)^2(0.7+0.02)^2(0.02+0.3+0.2)^2 \\ 0.1\times0.0290\times200(1-10)-0.1\times0.02(0.7+0.02)(0.02+0.3+0.2)+0.02(0.0013+0.02)(0.02+0.3+0.2)+(0.7+0.02) \\ (0.0013+0.02)(0.02+0.3+0.2)\times0.02\end{matrix}}{(0.0013+0.02)^2(0.02)^2(0.7+0.02)^2(0.02+0.3+0.2)^20.0013(1-0.1)+(0.0013+0.02)0.1} = 0.147$$

Summary of the sensitivity indices

Parameters	Sensitivity index
β_S	1
β_R	1
π	1
$r1$	-0.3846
$r2$	-0.5
σ	0.0117
θ	0.0019
μ	0.1473
υ	–0.0180
μ_T	–0.5
ρ_S	–0.2515
ρ_R	-0.2515

A positive index show that increasing the Parameter, increases Ro, whereby making the disease more transmissible. While A negative index indicates that an increase in the parameter, reduces Ro making the disease less transmissible. If >1 R_0 the infection will spread in the population; if R_0 =1, means the infection is steady but if R_0 <1 the infection is likely to die out

Effects of the Parameters on the Reproduction number

The rates of improved treatment efficiency (r_1 and r_2), higher vaccination coverage (σ), and reduced mortality (μ, μ_T) help lower basic reproduction number (R_0) Thereby reducing transmission rate; (r_1, r_2, μ, and μ_T) Which are the negative indexed number. Conversely, higher transmission rates (βS, βR, π) which are the positive index number increases R_0. Increasing these Parameter, will increase the value of the reproduction number and the disease will spread.

Conclusion

Parameters with negative indices are particularly significant because increasing these parameters will decrease R_0, thereby reducing disease transmission. In epidemiological models, parameters such as the rate of vaccination and the efficacy of treatment often exhibit negative sensitivity indices. Enhancing these parameters can lead to a decrease in R_0, contributing to better disease control. but if transmission rates, vaccination and treatment efforts are insufficient, R_0 will rise, leading to more widespread disease transmission.

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