GLOBAL STABILITY OF THE ENDEMIC EQUILIBRIUM OF A TUBERCULOSIS MODEL WITH IMMIGRATION AND TREATMENT

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ABSTRACT. Mathematical analysis is carried out for a tuberculosis (TB) model incorporating both latent and clinical stages, immigration and treatment. With immigration into the latent classes, we show that the model always has a unique endemic equilibrium and it is globally asymptotically stable. The global stability of the endemic equilibrium is proved using a global Lyapunov function.

1 Introduction. Tuberculosis (TB) is an airborne disease caused by infection of bacterium *Mycobacterium tuberculosis*. Though TB is preventable and curable, the current global TB incidence rate remains at a high level of 139 cases per 100,000 population, according to the 2009 WHO report [24], and there were 9.27 million new TB cases worldwide, with close to 1.77 million TB-related deaths in 2007. TB incidence rates are falling slowly in most WHO regions. However, the number of TB-related deaths and TB cases are still rising, largely due to population growth, emerging antibiotic resistance, increasing migration, and co-infection with HIV [24, 25].

Mathematical models have been developed to improve our understanding of the transmission dynamics of TB, to study the impact of drug-resistance, co-infection with HIV, re-infection and relapses, and to evaluate the effectiveness of various control and prevention strategies [2, 4, 5, 6, 7, 8, 14, 17, 18, 20, 21]. Ziv et al. [21] introduced a TB model with early and late latent stages to discuss effectiveness of treating TB patients at different stages, which has been used as a template for later TB models. In [18], a TB model with a single latent
stage was considered, and immigration was allowed to enter both latent and infective classes. Immigration into the infective class was first considered in a model for the HIV/AIDS [6]. It is known that in such a case, due to the constant influx of infectives, the models will no longer have a disease-free equilibrium, and the basic reproduction number also loses its original meaning. The disease will always be endemic, and a unique endemic equilibrium is expected to be globally stable. In the present paper, we propose and investigate a TB model with both early latent and late latent stages, and immigration into the susceptible and both latent stages. Most of the developed countries have TB screening policies for new immigrants. However, immigrants with early or late latent TB are usually not detected by the TB screening, and TB cases from immigrants or foreign-borns contribute an increasingly significant proportion of the national TB incidence of industrial countries [22, 23]. We also incorporate into the model reinfection and relapses due to treatment failure. So that our model can also be applied to study impact of migration among different regions in high TB incidence countries. Our model is more general than those in [12, 21] in that immigrations are allowed into the latent stages, and it generalizes a class of models in [18] to include two latent stages.

We prove that, with immigration into the latent classes, the TB is always endemic in the population, and a unique endemic equilibrium is globally asymptotically stable. The global stability is established with a global Lyapunov function. In the next section, we will formulate the model. In Section 3, we establish the uniqueness of the endemic equilibrium. In Section 4, we prove the main global-stability result. In Section 5, impacts of immigrate levels on equilibrium curves are explored by two figures feathering disease eradication and persistence.

2 Model formulation The TB bacteria can spread in the air from a person with active TB disease to others when they are in close contact. When first infected with TB bacteria, a person typically goes through a latent and asymptomatic period. There are two distinct time periods during the latent TB infection. Within the first two years after infection, the risk of developing active disease is much higher, whereas at the later years of infection, the progression to active disease is much slower. This process is the so-called fast and slow dynamics of TB [4].

Using a compartmental approach, the total host population is partitioned into four compartments: susceptible individuals (X), early latent (E) and late latent (L) individuals, and individuals with active
pulmonary TB disease (T). Let \( X(t) \), \( E(t) \), \( L(t) \) and \( T(t) \) denote the density of populations in the four corresponding compartments at time \( t \). Only individuals in compartment \( T \) are infectious, and new infections result from contacts between a susceptible and an infectious individual, with an incidence rate \( \beta X(t)T(t) \). Once infected, individuals progress through the early latent stage with an average rate \( \omega \). A fraction \( 0 < p < 1 \) of these individuals progress directly to the active TB stage, and the remaining \( 1 - p \) fraction progress to the late latent stage. Once there, the rate of progression to active disease is at a lower rate \( \nu \). The immigration input to the whole population is assumed to be a constant \( \pi \), with a fraction \( q_1 \) moving into the early latent compartment, \( q_2 \) into the late latent compartment, and the remaining fraction \( (1 - q_1 - q_2) \) into the susceptible compartment. Due to strict border screening policies in developed countries for immigrants, we assume that there are no immigrants with active TB can gain entry. The current WHO DOTS plan has a target treatment rate of 85% [24]. However, this target rate is difficult to achieve in most regions with high TB prevalence, partially due to treatment failure or relapse after therapy. We assume that TB patients in compartment \( T \) can revert to the susceptible compartment \( X \) with a rate \( \delta \) due to complete treatment, and they can revert to the early latent compartment \( E \) with rate \( \gamma \), mostly due to incomplete treatment. The removal rates for the four compartments are \( d_X \), \( d_E \), \( d_L \) and \( d_T \), respectively. The disease induced death rate is \( \alpha \). The dynamical transfer among the four compartments is depicted in the following transfer diagram. Here, all parameters are assumed to be positive. Based on the assumptions and the transfer diagram, the model can be described by

\[ \begin{align*}
&\text{FIGURE 1: Transfer diagram of model (1).}
\end{align*} \]
the following four ordinary differential equations:

\[
\begin{align*}
X' &= (1 - q_1 - q_2)\pi - \beta X T - d_X X + \delta T, \\
E' &= q_1 \pi + \beta X T + \gamma T - (d_E + \omega)E, \\
L' &= q_2 \pi + (1 - p)\omega E - (d_L + \nu) L, \\
T' &= p\omega E + \nu L - (d_T + \alpha + \delta + \gamma) T.
\end{align*}
\]

(1)

Here, we assume that \(0 < q_1 + q_2 < 1\). When \(q_1 = q_2 = 0\) and \(\delta = \gamma = 0\), model (1) reduces to the one in [12], and its global dynamics was completely established using a global Lyapunov function. When \(p \to 1\), model (1) has only one latent stage and structurally is similar to one model studied in [18], in which the proportionate incidence is used. Our model allows for different removal rates for all compartments where earlier models typically use equal removal rates. We will establish the global dynamics of model (1) using a global Lyapunov function motivated by those in [1, 12, 15]. Lyapunov functions of this type have been used effectively for other biological and epidemic models [3, 9, 10, 13, 19].

3 Equilibrium and its uniqueness

From (1), in absence of disease, we have

\[X' \leq (1 - q_1 - q_2)\pi - d_X X,\]

and thus \(\limsup_{t \to \infty} X(t) \leq (1 - q_1 - q_2)\pi / d_X\) along each solution to (1). Let \(N(t) = X(t) + E(t) + L(t) + T(t)\). Then using (1) we have

\[N' \leq \pi - d_X X - d_E E - d_L L - d_T T - \alpha T \leq \pi - d N,\]

where \(d = \min\{d_X, d_E, d_L, d_T + \alpha\}\). This implies \(\limsup_{t \to \infty} N(t) \leq \pi / d\). The model can be studied in the feasible region \(\Gamma\) defined as

\[\Gamma = \left\{ (X, E, L, T) \in \mathbb{R}_+^4 \left| 0 \leq X \leq \frac{(1 - q_1 - q_2)\pi}{d_X}, \quad 0 \leq X + E + L + T \leq \frac{\pi}{d} \right. \right\}.\]

It can be verified that the closed set \(\Gamma\) is positively invariant with respect to (1). We denote by \(\text{Int} \Gamma\) the interior of \(\Gamma\) in \(\mathbb{R}_+^4\). Next we establish the existence of endemic equilibrium in the feasible region \(\Gamma\).
For simplification, we use the following notations:

\[ \Pi = (1 - q_1 - q_2)\pi, \]
\[ d_2 = d_E + \omega, \]
\[ d_3 = d_L + \nu, \]
\[ d_4 = d_T + \alpha + \delta + \gamma. \]

An equilibrium \((X, E, L, T)\) of (1) satisfies following equations

\[ \begin{cases} 
\Pi = \beta X T + d_X X - \delta T, \\
 d_2 E = q_1 \pi + \beta X T + \gamma T, \\
 d_3 L = q_2 \pi + (1 - p)\omega E, \\
 d_4 T = p\omega E + \nu L. 
\end{cases} \]

Combining the last two equations of (3) to cancel the \(L\) term, we get

\[ \nu q_2 \pi + \frac{pd_3 + (1 - p)\nu}{d_2} \omega [q_1 \pi + \beta X T + \gamma T] + \nu q_2 \pi = d_3 d_4 T. \]

Let

\[ a_1 = \frac{pd_3 + (1 - p)\nu}{d_2} \omega. \]

Then (5) becomes

\[ a_1 q_1 \pi + \nu q_2 \pi = (d_3 d_4 - a_1 \gamma - a_1 \beta X) T. \]

From the first equation of (3), we have \(X = \frac{\Pi + \delta T}{\delta T + d_2}\). Substituting \(X\) equation into (7), we obtain a quadratic equation on \(T\)

\[ f(T) = AT^2 + BT + C = 0, \]

where

\[ A = d_3 d_4 - a_1 (\gamma + \delta), \]
\[B = d_X(d_3 d_4 - a_1 \gamma) - \beta(a_1 q_1 \pi + \nu q_2 \pi + a_1 \Pi),\]
\[C = -d_X(a_1 q_1 \pi + \nu q_2 \pi).\]

We see that coefficient \(C < 0\) if \(q_1^2 + q_2^2 \neq 0\). Also
\[
A = d_3 d_4 - a_1 (\gamma + \delta)
\]
\[
= (d_L + \nu)(d_T + \alpha + \delta + \gamma) - \frac{[pd_3 + (1 - p)\nu] \omega}{d_2} (\delta + \gamma)
\]
\[
= ((d_E + \omega)(d_L + \nu)(d_T + \alpha + \delta + \gamma)
- [pd_3 + (1 - p)\nu] \omega (\delta + \gamma)) / d_2
\]
\[
\geq \frac{[\omega (d_L + \nu)(\delta + \gamma) - [pd_3 + (1 - p)\nu] \omega (\delta + \gamma)]}{d_2}
\]
\[
= (\delta + \gamma) \omega [(d_L + \nu) - (pd_3 + (1 - p)\nu)] / d_2
\]
\[
> 0, \quad \text{since } 0 < p < 1.
\]

Therefore, the quadratic equation (8) has a unique positive solution \(T^*\).

Accordingly, from (3), we know that system (1) always has a unique positive equilibrium \(P^* = (X^*, E^*, L^*, T^*)\) with \(X^* > 0\), \(E^* > 0\), \(L^* > 0\) and \(T^* > 0\). It can also be concluded that \(\beta X^* - \delta > 0\) from the first equation of (3), since \(X^* \leq \Pi / d_X\).

**Proposition 1.** Suppose that \(0 < q_1 + q_2 < 0\). Then system (1) has a unique endemic equilibrium \(P^* = (X^*, E^*, L^*, T^*)\), \(X^* > 0\), \(E^* > 0\), \(L^* > 0\) and \(T^* > 0\).

Proposition 1 implies that system (1) has no disease-free equilibrium and the TB is always endemic in the population due to the influx of latent TB. In the next section, we show that the TB incidence stabilizes at the endemic equilibrium \(P^*\).

### 4 Global stability of the endemic equilibrium

**Theorem 2.** Suppose that \(0 < q_1 + q_2 < 0\). Then the unique endemic equilibrium \(P^*\) is globally asymptotically stable in the feasible region \(\Gamma\).

**Remark.** When \(q_1 = q_2 = 0\), there is no immigration into the latent classes. Model (1) in this case reduces to a model in [11], and the
global dynamics exhibit classical threshold phenomenon: there is a basic reproduction number

\[ R_0 = \frac{\beta \omega (pd_L + \nu)}{d_X (d_L + \nu)(d_E + \omega)(dT + \alpha + \delta + \gamma) - \gamma \omega (pd_L + \nu)}, \]

such that

(i) If \( R_0 \leq 1 \), then the disease-free equilibrium \( P_0 = (\pi/d_X, 0, 0, 0) \) is globally asymptotically stable in the feasible region.

(ii) If \( R_0 > 1 \), then \( P_0 \) is unstable, and a unique endemic equilibrium \( P^* \) is globally asymptotically stable in the interior of the feasible region.

We refer the reader to [11] for proofs of these results.

Proof of Theorem 2. Denote \( x(t) = (X(t), E(t), L(t), T(t)) \in \Gamma \subset \mathbb{R}_+^4 \).

Consider a Lyapunov function

\[ V(x) = (a_0 + a_1) \left( X - X^* - X^* \ln \frac{X}{X^*} \right) \]

\[ + a_1 \left( E - E^* - E^* \ln \frac{E}{E^*} \right) \]

\[ + a_2 \left( L - L^* - L^* \ln \frac{L}{L^*} \right) \]

\[ + a_3 \left( T - T^* - T^* \ln \frac{T}{T^*} \right), \]

where

\[ a_0 = \frac{a_1 \delta}{\beta X^* - \delta}, \quad a_1 = \frac{(1-p)a_2 + pd_L}{d_2} \omega, \quad a_2 = \nu, \quad a_3 = d_3 \]

are positive constants and \( P^* = (X^*, E^*, L^*, T^*) \) is the endemic equilibrium. Constant \( a_1 \) is same as in (6). We note that \( V(x) \) is positive definite with respect to \( x = P^* \). The derivative of \( V(t) \) along a solution of (1) is

\[ V' = (a_0 + a_1) \left( 1 - \frac{X^*}{X} \right) X' + a_1 \left( 1 - \frac{E^*}{E} \right) E' \]
Using the first equation of (3) and the $X$ equation in (1) we obtain

\begin{equation}
X' = \Pi - d_X X - \beta X T + \delta T
\end{equation}

\begin{align*}
&= \Pi - d_X X - \beta T (X - X^*) - \beta X^* (T - T^*) \\
&\quad + d_X X^* - \Pi + \delta (T - T^*) \\
&= -d_X (X - X^*) - \beta T (X - X^*) \\
&\quad - \beta X^* (T - T^*) + \delta (T - T^*) \\
&= -(d_X + \beta T) (X - X^*) - (\beta X^* - \delta) (T - T^*).
\end{align*}

It follows that

\begin{equation}
a_0 \frac{X - X^*}{X} X' = -a_0 (d_X + \beta T) \frac{(X - X^*)^2}{X}
\end{equation}

\begin{align*}
&\quad - a_0 (\beta X^* - \delta) (T - T^*) \frac{(X - X^*)}{X} \\
&= -a_0 (d_X + \beta T) \frac{(X - X^*)^2}{X} \\
&\quad - a_1 \delta (T - T^*) \frac{(X - X^*)}{X}.
\end{align*}

It follows from (1) and the first equation of (3) that

\begin{equation}
\left(1 - \frac{X^*}{X}\right) X' = \Pi - \beta X T - d_X X + \delta T - \Pi \frac{X^*}{X}
\end{equation}

\begin{align*}
&\quad + \beta X^* T + d_X X^* - \delta T \frac{X^*}{X} \\
&= (\beta X^* T + d_X X^* - \delta T \frac{X^*}{X}) \left(1 - \frac{X^*}{X}\right) \\
&\quad - \beta X T - d_X X + \beta X^* T \\
&\quad + d_X X^* + \delta T \left(1 - \frac{X^*}{X}\right) \\
&= d_X X^* \left(2 - \frac{X}{X^*} - \frac{X^*}{X}\right) + \beta X^* T
\end{align*}
\[- \beta XT + \beta X^* T^* \left(1 - \frac{X^*}{X}\right) \]
\[+ \delta(T - T^*) \left(1 - \frac{X^*}{X}\right).\]

Similarly, using (1) and the remaining three equations in (3), we have

\[\left(1 - \frac{E^*}{E}\right) E' = q_1 \pi + \beta XT + \gamma T - d_2 E \]
\[- q_1 \pi \frac{E^*}{E} - \beta X^* T^* \frac{X T E^*}{X^* T^* E} \]
\[- \gamma T^* \frac{T E^*}{T^* E} + (q_1 \pi + \beta X^* T^* + \gamma T^*),\]

\[\left(1 - \frac{L^*}{L}\right) L' = q_2 \pi + (1 - p) \omega E - d_3 L \]
\[- q_2 \pi \frac{L^*}{L} - (1 - p) \omega E^* \frac{E L^*}{E^* L} \]
\[+ (q_2 \pi + (1 - p) \omega E^*),\]

\[\left(1 - \frac{T^*}{T}\right) T' = p \omega E + \nu L - d_4 T \]
\[- p \omega E^* \frac{E T^*}{E^* T} - \nu L \frac{L T^*}{L^* T} + (p \omega E^* + \nu L^*).\]

Substituting (14), (15) and (16) into (12) and using (11), we obtain

\[V' = a_1 d_X X^* \left(2 - \frac{X}{X^*} - \frac{X^*}{X}\right) - a_0 \left(d_X + \beta T\right) \frac{(X - X^*)^2}{X} \]
\[+ a_1 \beta X^* T^* \left(2 - \frac{X^*}{X} - \frac{X T E^*}{X^* T^* E}\right) \]
\[+ a_2 q_1 \pi \left(2 - \frac{E^*}{E}\right) + a_1 \gamma T^* \left(1 - \frac{T E^*}{T^* E}\right) \]
\[+ a_2 q_2 \pi \left(2 - \frac{L^*}{L}\right) + a_2 (1 - p) \omega E^* \left(1 - \frac{E L^*}{E^* L}\right) \]
\[+ a_3 \omega E^* \left(1 - \frac{E T^*}{E^* T}\right) \]
\[+ a_3 \omega E^* \left(1 - \frac{L T^*}{L^* T}\right) + T[a_1 \beta X^* - a_3 d_4 + a_1 \gamma].\]
Note that from (7)

\[(a_1x + a_4d_4) + \frac{a_1q_1\pi + a_2q_2\pi}{T^*} = 0.\]

Substituting (18) into (17) gives

\[
V = a_1dXX^* \left(2 - \frac{X}{X^*} - \frac{X^*}{X} \right) - a_0(\xi + \beta T) \frac{(X - X^*)^2}{X}
\]

\[+ a_1\beta X^* \left(2 - \frac{X}{X^*} - \frac{X^{TE^*}}{X^{TE^*}T^*} \right) + a_1q_1\pi \left(2 - \frac{E^*}{E} \frac{T}{T^*} \right) + a_1\gamma T^* \left(1 - \frac{TE^*}{T^*E} \right) + a_2q_2\pi \left(2 - \frac{L}{L^*} - \frac{T}{T^*} \right) + a_2(1 - p)\omega E^* \left(1 - \frac{EL^*}{E^*L} \right) + a_3p\omega E^* \left(1 - \frac{E^*T}{E^*T} \right) + a_3\nu L^* \left(1 - \frac{LT^*}{L^*T} \right)
\]

\[\leq V_1 + V_2.
\]

From the mean inequality

\[a_1 + a_2 + \cdots + a_n \geq n \sqrt[n]{a_1a_2\cdots a_n} \quad \text{for } a_i \geq 0, \quad i = 1, \cdots, n,
\]

it follows that

\[
V_1 = a_1dXX^* \left(2 - \frac{X}{X^*} - \frac{X^*}{X} \right) - a_0(dX + \beta T)^2 \frac{(X - X^*)^2}{X} \leq 0 \quad \text{for } T \geq 0.
\]

The equality in (20) holds if and only if \(X = X^*\). The next step is to prove \(V_2 \leq 0\). We note that \(pd_L + \nu = p(d_L + \nu) + (1 - p)\nu = pd_4 + (1 - p)a_2\) and define

\[
b_1 = \frac{pd_3}{pd_L + \nu}, \quad b_2 = \frac{(1 - p)a_2}{pd_L + \nu}, \quad b_1 + b_2 = 1, \quad b_1 > 0, b_2 > 0.
\]
We also define
\[ c_1 = \frac{q_1 \pi}{d_2 E^*}, \quad c_2 = \frac{\beta X^* T^*}{d_2 E^*}, \quad c_3 = \frac{\gamma T^*}{d_2 E^*}. \]

Then \( c_i > 0, \ i = 1, 2, 3, \) and \( \sum_{i=1}^{3} c_i = 1 \) from the second equation of (3). Canceling the \( E^* \) term from the second and third equations of (3), we get
\[ \nu d_3 L^* = \frac{(1 - p) \nu}{d_2} [q_1 \pi + \beta X^* T^* + \gamma T^*] + \nu q_2 \pi \]
\[ = \frac{(1 - p) a_2}{p d_L + \nu} \left( \frac{pd_L + \nu}{a_2} \omega \right) [q_1 \pi + \beta X^* T^* + \gamma T^* + a_2 q_2 \pi] \]
\[ = b_2 a_1 [q_1 \pi + \beta X^* T^* + \gamma T^*] + a_2 q_2 \pi. \]

Define
\[ \eta_1 = \frac{b_2 a_1 q_1 \pi}{a_2 d_3 L^*}, \quad \eta_2 = \frac{b_2 a_1 \beta X^* T^*}{a_2 d_3 L^*}, \quad \eta_3 = \frac{b_2 a_1 \gamma T^*}{a_2 d_3 L^*}, \quad \eta_4 = \frac{a_2 q_2 \pi}{a_2 d_3 L^*}. \]

We can show that \( \eta_i > 0 \) and \( \sum_{i=1}^{4} \eta_i = 1 \). Using (21)–(23), we can arrange \( V_2 \) as
\[ V_2 = (b_1 + b_2) a_1 \beta X^* T^* \left( 2 - \frac{X^*}{X} - \frac{X T E^*}{X T^* E} \right) \]
\[ + a_2 q_2 \pi \left( 2 - \frac{L^*}{L} - \frac{T}{T^*} \right) \]
\[ + (b_1 + b_2) a_1 \gamma T^* \left( 1 - \frac{T E^*}{T^* E} \right) \]
\[ + (c_1 + c_2 + c_3) a_2 (1 - p) \omega E^* \left( 1 - \frac{E L^*}{E^* L} \right) \]
\[ + (b_1 + b_2) a_1 q_1 \pi \left( 2 - \frac{E^*}{E} - \frac{T}{T^*} \right) \]
\[ + (c_1 + c_2 + c_3) a_3 p \omega E^* \left( 1 - \frac{E T^*}{E^* T} \right) \]
\[ + (\eta_1 + \eta_2 + \eta_3 + \eta_4) a_3 \nu L^* \left( 1 - \frac{L T^*}{L^* T} \right) \]
\begin{align*}
&= \left[ b_{2a_1} \beta X^* T^* \left( 2 - \frac{X^*}{X} - \frac{X T E^*}{X^* T^* E^*} \right) \\
&\quad + c_{2a_2} (1 - p) \omega E^* \left( 1 - \frac{EL^*}{E^* L} \right) \\
&\quad + \eta_{2a_3} \nu L^* \left( 1 - \frac{LT^*}{L^* T} \right) \right] \\
&\quad + \left[ b_{1a_1} \beta X^* T^* \left( 2 - \frac{X^*}{X} - \frac{X T E^*}{X^* T^* E^*} \right) \\
&\quad + c_{2a_3} \rho E^* \left( 1 - \frac{ET^*}{E^* T} \right) \right] \\
&\quad + \left[ b_{2a_1} \gamma T^* \left( 1 - \frac{TE^*}{T^* E} \right) + c_{3a_3} \rho E^* \left( 1 - \frac{E T^*}{E^* T} \right) \right] \\
&\quad + \left[ b_{2a_1} q_1 \pi \left( 2 - \frac{E^*}{E} - \frac{T}{T^*} \right) \right] \\
&\quad + \left[ c_{1a_2} (1 - p) \omega E^* \left( 1 - \frac{EL^*}{E^* L} \right) + \eta_{1a_3} \nu L^* \left( 1 - \frac{LT^*}{L^* T} \right) \right] \\
&\quad + \left[ b_{1a_1} q_1 \pi \left( 2 - \frac{E^*}{E} - \frac{T}{T^*} \right) + c_{1a_3} \rho E^* \left( 1 - \frac{ET^*}{E^* T} \right) \right] \\
&\quad + \left[ a_{2q_2} \pi \left( 2 - \frac{L^*}{L} - \frac{T}{T^*} \right) + \eta_{1a_3} \nu L^* \left( 1 - \frac{LT^*}{L^* T} \right) \right] \\
\equiv &\sum_{i=1}^{7} I_i.
\end{align*}

For the coefficients in $I_1$, using (22), (23) and (11), we have

\[ c_{2a_2} (1 - p) \omega E^* = \beta X^* T^* - \frac{d_2}{2d_2 E^*-a_2 (1 - p) \omega E^*} \]

\[ = \beta X^* T^* \frac{(1 - p)a_2 (pd_L + \nu) \omega}{pd_L + \nu} - \frac{d_2}{2a_1 \beta X^* T^*}, \]
\[ \eta_2 a_3 \nu L^* = \frac{b_2 a_1 \beta X^* T^*}{a_2 d_3 L^*} a_3 \nu L^* = b_2 a_1 \beta X^* T^*. \]

By the mean inequality,

\[
I_1 = b_2 a_1 \beta X^* T^* \left( 4 - \frac{X^*}{X} \frac{X E^*}{X^* E^*} \frac{E L^*}{E^* L} \frac{L T^*}{L^* T} \right) \\ 
\leq b_2 a_1 \beta X^* T^* \left( 4 - 4 \left[ \frac{X^*}{X} \frac{X E^*}{X^* E^*} \frac{E L^*}{E^* L} \frac{L T^*}{L^* T} \right]^{1/4} \right) \\ 
= 0 \text{ for all } X > 0, E > 0, L > 0, T > 0.
\]

The equality in (25) holds if and only if

\[
X = X^*, \quad \frac{E^*}{E} = \frac{L^*}{L} = \frac{T^*}{T}.
\]

Similarly, using (21), (22), (23) and (11), we have the following relations regarding coefficients in \( I_2, \cdots, I_7 \):

\[
c_2 a_3 \nu E^* = \frac{\beta X^* T^*}{d_2 E^*} d_3 \nu E^* = \beta X^* T^* \frac{pd_4}{pd_L + \nu} \frac{(pd_L + \nu)\omega}{d_2} = b_1 a_1 \beta X^* T^*,
\]

\[
c_3 a_3 \nu E^* = \frac{\gamma T^*}{d_2 E^*} a_3 \nu E^* = \gamma T^* \frac{pd_4}{pd_L + \nu} \frac{(pd_L + \nu)\omega}{d_2} = b_1 a_1 \gamma T^*,
\]

\[
c_3 a_2 (1 - p) \nu E^* = \frac{\gamma T^*}{d_2 E^*} a_2 (1 - p) \nu E^* \\
= \gamma T^* \frac{(1 - p)a_2 (pd_L + \nu)\omega}{pd_L + \nu} = b_2 a_1 \gamma T^*,
\]

\[
\eta_3 a_3 \nu L^* = \frac{b_2 a_1 \gamma T^*}{a_2 d_3 L^*} a_3 \nu L^* = b_2 a_1 \gamma T^*,
\]

\[
c_1 a_2 (1 - p) \nu E^* = \frac{q_1 \pi}{d_2 E^*} a_2 (1 - p) \nu E^* = b_2 a_1 q_1 \pi,
\]

\[
\eta_1 a_3 \nu L^* = \frac{b_2 a_1 q_1 \pi}{a_2 d_3 L^*} a_3 \nu L^* = b_2 a_1 q_1 \pi,
\]

\[
c_1 a_3 \nu E^* = \frac{q_1 \pi}{d_2 E^*} a_3 \nu E^* = b_1 a_1 q_1 \pi,
\]

\[
\eta_4 a_3 \nu L^* = \frac{a_2 q_2 \pi}{a_2 d_3 L^*} a_3 \nu L^* = a_2 q_2 \pi.
\]
By the mean inequality, we obtain
\begin{align*}
I_2 &= b_1 a_0 x^* T^* \left( 3 - \frac{X^*}{X} - \frac{X T E^*}{X T^* E} - \frac{E T^*}{E^* T} \right) \leq 0, \\
I_3 &= b_1 a_1 \gamma T^* \left( 2 - \frac{T E^*}{T^* E} - \frac{E T^*}{E^* T} \right) \leq 0, \\
I_4 &= b_2 a_1 \gamma T^* \left( 3 - \frac{T E^*}{T^* E} - \frac{E L^*}{E^* L} - \frac{L T^*}{L^* T} \right) \leq 0, \\
I_5 &= b_2 a_1 q_1 \pi \left( 4 - \frac{E^*}{E} - \frac{T}{T^*} - \frac{E L^*}{E^* L} - \frac{L T^*}{L^* T} \right) \leq 0, \\
I_6 &= b_1 a_1 q_1 \pi \left( 3 - \frac{E^*}{E} - \frac{T}{T^*} - \frac{E T^*}{E^* T} \right) \leq 0, \\
I_7 &= b_2 a_2 q_2 \pi \left( 3 - \frac{L^*}{L} - \frac{T}{T^*} - \frac{L T^*}{L^* T} \right) \leq 0.
\end{align*}
(27)

Substituting (19), (25) and (27) into (17), we conclude that $V' = V_1 + V_2 \leq 0$ for all $X > 0, E > 0, L > 0, T > 0$, and $V' = 0$ if and only if relations in (26) hold. To find the largest invariant set in the set where $V' = 0$, we use (26) and set $X = 0$ in the first equation of (1), and we see that $T = T^*$, and hence $E = E^*, L = L^*$. Namely, the largest invariant set where $V' = 0$ is the singleton \{P^*\}. By LaSalle’s Invariance Principle [16], $P^*$ is globally asymptotically stable with respect to $\Gamma$. This establishes Theorem 2.

5 Impact of immigration on endemic levels
In this section, we carry out simulations of our model (1) using data from [21] to investigate the effects of immigration level on active TB cases. We choose $\pi = 20000, d_X = d_E = d_L = d_T = 0.02, p = 0.05, \nu = 0.00256, \omega = 1.5, \alpha = 0.139$ and vary the levels of $q_1, q_2$. The effect of complete or partial treatment is studied numerically in [11], thus we let $\delta = \gamma = 0$. As a baseline case with $q_1 = q_2 = 0$, $\beta$ is set to $1 \times 10^{-6}$ and $2 \times 10^{-6}$, which correspond to $R_0 < 1$ and $R_0 > 1$, respectively. Initial condition is set as $(X_0, E_0, L_0, T_0) = (1000000, 0, 0, 1)$ with one infectious case is introduced into the susceptible population.

In Figure 2, when $q_1 = q_2$ varies from 0% (corresponding to $R_0 = 0.9794 < 1$) to 5%, the TB epidemic attains endemic state at different slopes. The higher of $q_1 = q_2$, the higher levels of endemic state. This shows that constant influx of latent TB can launch a TB epidemic itself irrespective of the initial conditions.
In Figure 3, we have chosen $\beta = 2 \times 10^{-6}$. When $q_1 = q_2 = 0$, this corresponds to $R_0 = 1.9588 > 1$. The TB incidence initially increases exponentially and then stabilizes to the endemic level. A higher level of latent immigrants will produce a higher level of TB incidence.

FIGURE 3: $\beta = 2 \times 10^{-6}$ and $q_1 = q_2 = 0\%, 1\%, 3\%, 5\%$, respectively.
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