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Age - Structured Continuous - Time Markov Chan Tuberculosis Model

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ABSTRACT

Tuberculosis (TB), records an average of 4500 mortality cases daily, and is listed amongst the world's infectious killer-diseases. Given that TB transmission is often impacted by fluctuations including spatial effects, human behavior and other real life factors, deterministic models alone may not fully capture the inherent fluctuations, thus, this study develops and analyzes a stochastic age-structured model for understanding tuberculosis (TB) transmission incorporating exogenous reinfection and heterogeneous mixing between children and adults. The model is formulated as a continuous-time Markov chain (CTMC) with six epidemiological compartments. We derive the Kolmogorov forward equations, and rigorously prove the equivalence between the stochastic mean dynamics of the system. Numerical simulations illustrate the impact of transmission and recovery parameters on disease dynamics.

1. Introduction

Tuberculosis (TB), which claims an average of about 4500 lives each day, is listed amongst the world's leading infectious killers with data showing that the epidemic trend is rising (WHO, 2018). About 10% of the first strain infected persons are able to transmit the disease in their life time, with a disease reproduction rate of about 10 to 15 new cases every year each. Where appropriate care is lacking, and co-infection with other disease exist, this proportion increases. Unfortunately, the worst hit are people from poor and disadvantaged regions with little or no access to adequate healthcare and appropriate medication; mostly young adults within their most productive years (WHO, 2017). With TB being linked to densely populated and poverty-stricken areas, countries like India and Nigeria are at the fore. These have failed many deadlines and/or targets, with challenges in improving access to diagnosis and care. Prior to 2020, the rate of TB induced mortality and incidence, were declining at 3% and 2% per annum respectively, but the goal was to further reach a decline rate of 4-5% per year, with a drop in TB related death to 10% by year 2020; but with the passing of this deadline, a large gap in the detection and effective treatment rates yet exists hence new goals have been projected with the sole aim of eradicating this life threatening disease by the year 2035 (WHO, 2017 & 2020).

Nigeria, who ranks 1st in TB-burdened locations in Africa, 4th among global 22 High burden nations, accounts for nearly two-thirds of global burden alongside five other countries; jointly recorded 48% of global TB-HIV coinfection mortality counts with India, and 77% of the global gap in TB case finding with about 80% non-notified TB cases (WHO, 2017) thus, serving as a base for continued TB spread. The emergence of multidrug-resistant TB (MDR TB)

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and an increase in pediatric TB cases are issues on the front burner in Nigeria's struggle against this menace (NSP-TB, 2018).

TB also poses the gravest threat to the world youngest inhabitants. More than 1 million children annually become sick from this disease. Although children under the age of 15 are among those most vulnerable, most diagnostic tests for TB are unable to identify their disease; most available treatments are ineffective for younger victims; and an estimated 20 percent of all children with TB disease will die.

Mathematical modeling serves as an indispensable tool for elucidating transmission dynamics when direct observation is constrained by ethical, logistical, or methodological limitations. Models can disentangle complex interactions between multiple biotic and abiotic factors, forecast outbreak trajectories, identify effective control points, and inform research priorities (Abundo, 2024). Among modeling approaches, stochastic formulations have gained increasing prominence for their ability to capture the inherent randomness in disease transmission, particularly in small populations and for rare events such as spillover infections. Unlike deterministic models that produce single predicted trajectories, stochastic models generate distributions of possible outcomes, enabling realistic risk assessment and uncertainty quantification (Rasmussen et al., 2025).

Based on the work of Nyabadza & Kgosimore (2012), this study provides a CTMC approach to examining age structure influence on the dynamics of TB in Nigeria in the presence of exogeneous reinfection. The mean functions are derived from the moment generating functions; and simulations of some disease pathways are provided.

2. Methods

Nyabadza & Kgosimore (2012) developed a deterministic mathematical model for TB dynamics in children and adults. They established the key model properties and derived the reproduction numbers for the children and adult population. A continuous-time Markov chain (CTMC) model based on this is formulated. The possibility of exogenous re-infection in an age structured (adults vs children) population in tuberculosis dynamics is explored. The model assumed:

(a) a heterogeneous population which can be split into homogeneous subgroups according to their disease state;

(b) the size of a disease state is differentiable with time and the epidemic dynamics is stochastic;

(c) the population mixes heterogeneously according to their age structure but all age specific susceptible individuals experience homogeneous mixing;

(d) individuals return to the exposed class at a known rate due to loss of immunity;

(e) uniform natural death rate; and

(f) entrance into the population is by birth while exit is through natural or TB-related deaths.

2.1 Model Formulation:
Let $X_i(t)\ \ i = 1,2,\dots,6$ represent the random size of the population in compartment i at an elapsed time t so that

$$X(t) = [X_1(t), X_2(t), \dots, X_6(t)]'$$

$$= [S_c(t), E_c(t)I_c(t), S_a(t), E_a(t), I_a(t)]'$$

The jump intensities are as follows: (1) Birth into the susceptible children (S_c) at rate πN; (2) Linear migration from Susceptible children (S_c) class to Latently infected children class (E_c) at a rate $K_{12}X_1$, where $K_{12} = (1-p)\beta_c I_c/N$, and (3) from susceptible children class (S_c) to infectious children class, (I_c) at rate $K_{13}X_1$, where $K_{13} = p\beta_c I_c/N$; (4) also from susceptible, (S_c) (or exposed, (E_c)) children class to susceptible (S_a) (or exposed, (E_a)) adult class at rate $K_{14}X_1(K_{25}X_2)$; $K_{14}, K_{25} = f$. (5) From exposed children class, (E_c) to Infectious children class, (I_c) (2 to 3) at rate $K_{23}X_2$ where $K_{23} = r_c + \theta\beta_c I_c/N$, θ is the proportion of those with a second strain of TB infection $(0 < \theta < 1)$. (6) From Infectious children back to Exposed children class due to recovery either naturally or from treatment at rate $K_{32}X_3$; $K_{32} = \sigma_c$. (7) From Susceptible adult class, (S_a) to Latently infected adult class, (E_a) $K_{45}X_4$, where $K_{45} =$

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$(1-q)\beta_a I_a/N$. (8) From susceptible adult class, (S_a) to infectious adult class, (I_a) at rate $K_{46}X_4$ where $K_{46} = \frac{q\beta_a I_a}{N}$. (9) From Exposed adult class, (E_a) to Infectious adult class, (I_a) at rate $K_{56}X_5$ where $K_{56} = r_a + \theta\beta_a I_a/N$. (10) From Infectious adult class, (I_a) back to Exposed adult class, (E_a) due to recovery either naturally or from treatment at rate $K_{65}X_6$; $K_{65} = \sigma_a$. (11) Death in subgroups could occur: $due\ to\ natural\ causes\ at\ \mu X_i,\ i = 0,1,2,3,4,5,6$ and $TB\ related\ causes$ at a rate $\mu_T X_i \ , \ i = 3,6$

Table 1: Parameters and variables of the model

Variables	Description
$S_c(t);\ S_a(t)$	Susceptible children at time; Susceptible adult at time
$E_c(t);\ E_a(t)$	latently infected children at time; latently infected adults at time
$I_c(t);\ I_a(t)$	Infectious children at time; Infectious adults at time
p	Proportion of children who develop active TB in the first year after primary infection
q	Proportion of adults who develop active TB in the first year after primary infection
β_a	Effective transmission rate of TB among children
β_c	Effective transmission rate of TB among adults
π	Recruitment rate
r_c	Progression rate from latent TB to active TB for children
r_a	Progression rate from latent TB to active TB for adults
θ	Rate of exogenous reinfection (second strain of TB) where $0 \le \theta \le 1$
σ_a	Recovery rate among adults either natural or with treatment with individuals going back to the latently infected class
μ	Natural mortality rate
σ_c	Recovery rate among children either natural or with treatment with individuals going back to the latently infected class
μ_T	Mortality rate due to TB
f	Rate at which children join adult classes (either as susceptible or latently infected)

Given the multivariate states dynamics, following Matis & Hartley (1971), the Kolmogorov equations describing the model dynamics is obtained as the probability of an event taking place given the transition rates or jump intensities described above. This may be written as shown below:

$$P_{x_1x_2x_3x_4x_5x_6}(t+\Delta t) = P_{x_1-1,x_2,x_3,x_4x_5x_6}(t)\,\pi N\Delta t + P_{x_1+1,x_2,x_3,x_4,x_5x_6}(t)\,\mu(x_1+1)\Delta t$$

$$+ P_{x_1+1,x_2-1,x_3,x_4x_5x_6}(t)\,K_{12}(x_1+1)\Delta t + P_{x_1,x_2-1,x_3+1x_4,x_5x_6}(t)\,K_{32}(x_3+1)\Delta t$$

$$+ P_{x_1,x_2+1,x_3-1,x_4x_5x_6}(t)\,K_{23}(x_2+1)\Delta t + P_{x_1,x_2-1,x_3+1x_4,x_5x_6}(t)\,K_{32}(x_3+1)\Delta t$$

$$+ P_{x_1+1,x_2,x_3,x_4-1x_5x_6}(t)\,K_{14}(x_1+1)\Delta t + P_{x_1,x_2+1,x_3,x_4,x_5-1x_6}(t)\,K_{25}(x_2+1)\Delta t$$

$$+ P_{x_1+1,x_2,x_3,x_4-1x_5x_6}(t)\,\mu(x_1+1)\Delta t + P_{x_1,x_2,x_3,x_4+1,x_5-1x_6}(t)\,K_{45}(x_4+1)\Delta t$$

$$+ P_{x_1,x_2,x_3,x_4+1x_5x_6-1}(t)\,K_{46}(x_4+1)\Delta t + P_{x_1,x_2,x_3,x_4,x_5+1x_6}(t)\,\mu(x_5+1)\Delta t$$

$$s + P_{x_1+1,x_2,x_3,x_4x_5+1x_6-1}(t)\,K_{56}(x_5+1)\Delta t + P_{x_1,x_2,x_3,x_4,x_5x_6+1}(t)\,(\mu+\mu_T)(x_6+1)\Delta t$$

$$+ P_{x_1+1,x_2,x_3,x_4x_5-1x_6+1}(t)\,K_{65}(x_6+1)\Delta t$$

$$+ P_{x_1,x_2,x_3,x_4x_5x_6}(t)(1-\pi N-(\mu+K_{12}+K_{13}+K_{14})(x_1+1)-(\mu+K_{23}+K_{25})(x_2+1)$$

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$$-(\mu+\mu_T+K_{32})(x_3+1)-(\mu+K_{45}+K_{46})(x_4+1)-(\mu+K_{56})(x_5+1)$$
$$-(\mu+\mu_T+K_{65})(x_6+1))\Delta t+o(\Delta t) \quad (1)$$

Subtracting $P_{x_1x_2x_3x_4x_5x_6}(t)$ and dividing through by Δt and then taking the limit as $t \to 0$

$$\frac{\partial P_{x_1x_2x_3x_4x_5x_6}(t)}{\partial t} = P_{x_1-1,x_2,x_3,x_4x_5x_6}(t)\,\pi N + P_{x_1+1,x_2,x_3,x_4,x_5x_6}(t)\,\mu(x_1+1)$$
$$+ P_{x_1+1,x_2-1,x_3,x_4x_5x_6}(t)\,K_{12}(x_1+1) + P_{x_1,x_2-1,x_3+1x_4,x_5x_6}(t)\,K_{32}(x_3+1)$$
$$+ P_{x_1,x_2+1,x_3-1,x_4x_5x_6}(t)\,K_{23}(x_2+1)$$
$$+ P_{x_1+1,x_2,x_3,x_4-1x_5x_6}(t)\,K_{14}(x_1+1) + P_{x_1,x_2+1,x_3,x_4,x_5-1x_6}(t)\,K_{25}(x_2+1)$$
$$+ P_{x_1+1,x_2,x_3,x_4-1x_5x_6}(t)\,\mu(x_1+1) + P_{x_1,x_2,x_3,x_4+1,x_5-1x_6}(t)\,K_{45}(x_4+1)$$
$$+ P_{x_1,x_2,x_3,x_4+1x_5x_6-1}(t)\,K_{46}(x_4+1) + P_{x_1,x_2,x_3,x_4,x_5+1x_6}(t)\,\mu(x_5+1)$$
$$+ P_{x_1+1,x_2,x_3,x_4x_5+1x_6-1}(t)\,K_{56}(x_5+1) + P_{x_1,x_2,x_3,x_4,x_5x_6+1}(t)\,(\mu+\mu_T)(x_6+1)$$
$$+ P_{x_1+1,x_2,x_3,x_4x_5-1x_6+1}(t)\,K_{65}(x_6+1)$$
$$-P_{x_1,x_2,x_3,x_4x_5x_6}(t)(\pi N-(\mu+K_{12}+K_{13}+K_{14})(x_1+1)-(\mu+K_{23}+K_{25})(x_2+1)$$
$$-(\mu+\mu_T+K_{32})(x_3+1)-(\mu+K_{45}+K_{46})(x_4+1)-(\mu+K_{56})(x_5+1)$$
$$-(\mu+\mu_T+K_{65})(x_6+1)) \quad (2)$$

One can transform the above into partial differential equations satisfying generating functions using the "Random Variable technique" developed by Bailey (1964) as

$$\frac{\partial P}{\partial t} = \sum_{ijk\ldots l}\left(S_1^i S_2^j S_3^k \ldots S_6^l - 1\right) f_{ijk\ldots l}\left(S_1\frac{\partial}{\partial S_1}, S_2\frac{\partial}{\partial S_2}, S_3\frac{\partial}{\partial S_3}, \ldots S_8\frac{\partial}{\partial S_6}\right) P(S_1, S_2, S_3, \ldots S_6, t) \quad (3)$$

$$\frac{\partial M}{\partial t} = \sum_{ijk\ldots l}\left(e^{i\theta_1+j\theta_2+k\theta_3+\cdots+l\theta_6} - 1\right) f_{ijkl}\left(\frac{\partial}{\partial\theta_1}, \frac{\partial}{\partial\theta_2}, \frac{\partial}{\partial\theta_3}, \ldots \frac{\partial}{\partial\theta_6}\right) M(\theta_1, \theta_2, \theta_3, \ldots \theta_6, t) \quad (4)$$

Using (3) and (4) above in (2), the partial differential equations of the probability, moment and cumulant generating functions will be of the forms below:

$$\frac{\partial P}{\partial t} = (S_1-1)\pi N\frac{\partial P}{\partial S_1} + (1-S_1)\mu_1\frac{\partial P}{\partial S_1} + (S_2-S_1)K_{12}\frac{\partial P}{\partial S_1} + (S_3-S_1)K_{13}\frac{\partial P}{\partial S_1} + (S_4-S_1)K_{14}\frac{\partial P}{\partial S_1}$$
$$+ (1-S_2)\mu_2\frac{\partial P}{\partial S_2} + (S_3-S_2)K_{23}\frac{\partial P}{\partial S_2} + (S_5-S_2)K_{25}\frac{\partial P}{\partial S_2} + (1-S_3)\mu_3\frac{\partial P}{\partial S_3} + (S_2-S_3)K_{32}\frac{\partial P}{\partial S_3}$$
$$+ (1-S_4)\mu_4\frac{\partial P}{\partial S_4} + (S_5-S_4)K_{45}\frac{\partial P}{\partial S_4} + (S_6-S_4)K_{46}\frac{\partial P}{\partial S_4} + (S_6-S_5)K_{56}\frac{\partial P}{\partial S_5} + (1-S_5)\mu_5\frac{\partial P}{\partial S_5}$$
$$+ (S_5-S_6)K_{65}\frac{\partial P}{\partial S_6}$$
$$+ (1-S_6)\mu_6\frac{\partial P}{\partial S_6} \quad (5)$$

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$$\frac{\partial M}{\partial t} = \left(e^{\theta_1}-1\right)\pi N\frac{\partial M}{\partial \theta_1}+\left(e^{-\theta_1}-1\right)\mu_1\frac{\partial M}{\partial \theta_1}+\left(e^{\theta_2-\theta_1}-1\right)K_{12}\frac{\partial M}{\partial \theta_1}+\left(e^{\theta_3-\theta_1}-1\right)K_{13}\frac{\partial M}{\partial \theta_1}$$
$$+\left(e^{\theta_4-\theta_1}-1\right)K_{14}\frac{\partial M}{\partial \theta_1}+\left(e^{-\theta_2}-1\right)\mu_2\frac{\partial M}{\partial \theta_2}+\left(e^{\theta_3-\theta_2}-1\right)K_{23}\frac{\partial M}{\partial \theta_2}+\left(e^{\theta_5-\theta_2}-1\right)K_{25}\frac{\partial M}{\partial \theta_2}$$
$$+\left(e^{-\theta_3}-1\right)\mu_3\frac{\partial M}{\partial \theta_3}+\left(e^{\theta_2-\theta_3}-1\right)K_{32}\frac{\partial M}{\partial \theta_3}+\left(e^{-\theta_4}-1\right)\mu_4\frac{\partial M}{\partial \theta_4}+\left(e^{\theta_5-\theta_4}-1\right)K_{45}\frac{\partial M}{\partial \theta_4}$$
$$+\left(e^{\theta_6-\theta_4}-1\right)K_{46}\frac{\partial M}{\partial \theta_4}+\left(e^{\theta_6-\theta_5}-1\right)K_{56}\frac{\partial M}{\partial \theta_5}+\left(e^{-\theta_5}-1\right)\mu_5\frac{\partial M}{\partial \theta_5}+\left(e^{-\theta_6}-1\right)\mu_6\frac{\partial M}{\partial \theta_6}$$
$$+\left(e^{\theta_5-\theta_6}-1\right)K_{65}\frac{\partial M}{\partial \theta_6} \qquad (6)$$

Eqn. (6) is re-expressed as

$$\frac{\partial M}{\partial t} = \left[\left(e^{\theta_1}-1\right)\pi N+\left(e^{-\theta_1}-1\right)\mu_1+\left(e^{\theta_2-\theta_1}-1\right)K_{12}+\left(e^{\theta_3-\theta_1}-1\right)K_{13}+\left(e^{\theta_4-\theta_1}-1\right)K_{14}\right]\frac{\partial M}{\partial \theta_1}$$
$$+\left[\left(e^{-\theta_2}-1\right)\mu_2+\left(e^{\theta_3-\theta_2}-1\right)K_{23}+\left(e^{\theta_5-\theta_2}-1\right)K_{25}\right]\frac{\partial M}{\partial \theta_2}$$
$$+\left[\left(e^{-\theta_3}-1\right)\mu_3+\left(e^{\theta_2-\theta_3}-1\right)K_{32}\right]\frac{\partial M}{\partial \theta_3}$$
$$+\left[\left(e^{-\theta_4}-1\right)\mu_4+\left(e^{\theta_5-\theta_4}-1\right)K_{45}+\left(e^{\theta_6-\theta_4}-1\right)K_{46}\right]\frac{\partial M}{\partial \theta_4}$$
$$+\left[\left(e^{\theta_6-\theta_5}-1\right)K_{56}+\left(e^{-\theta_5}-1\right)\mu_5\right]\frac{\partial M}{\partial \theta_5}+\left(e^{-\theta_6}-1\right)\mu_6\frac{\partial M}{\partial \theta_6}$$
$$+\left(e^{\theta_5-\theta_6}-1\right)K_{65}\frac{\partial M}{\partial \theta_6} \qquad (7)$$

The initial conditions are as stated below: $X_i(0) = N_i(0) \qquad i = 1,2,3,4,5,6$

$$K(\theta_1,\theta_2,\dots,\theta_m,0) = \sum_{i=1}^{m} N_i\theta_i$$

All coefficients of M and its derivatives in the PDE (7) are constraints in t, as such, is linear and homogeneous with time-independent generator $A(\theta,\partial_\theta)$. The equation (7) can be re-expressed in compact form as

$$\frac{\partial}{\partial t}M(\theta,t) = \sum_{i=1}^{6} a_i(\theta)\, M_i \qquad (8)$$

Where each $a_i(\theta)$ is the bracket in front of $\partial M/\partial\theta_i$ in Eqn (7).

The mean and variance functions follow from the derivatives of M at $\theta = 0$; where

$$m_i(t) = E[X_i(t)] = M_i(0,t); \quad E[X_i^2(t)] = M_{ii}(0,t); \quad Var\left(X_i(t)\right) = M_{ii}(0,t) - [M_i(0,t)]^2$$

Differentiating both sides of (8) $w.r.t\ \theta_k$:

$$\frac{\partial M_k}{\partial t} = \sum_{i=1}^{6}\left(a_{i,k}M_i + a_iM_{ik}\right) \qquad (9)$$

where $a_{i,k} = \partial a_i/\partial\theta_k$

Setting $\theta = 0$; $a_i(0) = 0\ \forall\ i$ since every factor $\left(e^{\theta_j-\theta_i}-1\right)\ or\ \left(e^{\theta_j}-1\right)$ vanishes at $\theta = 0$. The term with a_iM_{ik} disappear and only the derivatives $a_{i,k}(0)$ remains;

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$$\frac{d}{dt}M_k(0,t) = \sum_{i=1}^{6} a_{i,k}(0)\, M_i(0,t)$$

But $M_k(0,t) = m_k(t)$ and $M_i(0,t) = m_i(t)$, thus,

$\frac{dm_k(t)}{dt} = \sum_{i=1}^{6} a_{i,k}(0)\, m_i(t)$ (10)

The coefficients of $M_i(i = 1,2,3,4,5,6)$, that is, $a_i(\theta)$ from the PDE in (7) are as follows:

$a_1 = \left(e^{\theta_1} - 1\right)\pi N + \left(e^{\theta_2-\theta_1} - 1\right)K_{12} + \left(e^{\theta_3-\theta_1} - 1\right)K_{13} + \left(e^{\theta_4-\theta_1} - 1\right)K_{14} + \left(e^{-\theta_1} - 1\right)\mu_1$

$a_2 = \left(e^{\theta_3-\theta_2} - 1\right)K_{23} + \left(e^{\theta_5-\theta_2} - 1\right)K_{25} + \left(e^{-\theta_2} - 1\right)\mu_2$

$a_3 = \left(e^{\theta_2-\theta_3} - 1\right)K_{32} + \left(e^{-\theta_3} - 1\right)\mu_3$; $a_4 = \left(e^{\theta_5-\theta_4} - 1\right)K_{45} + \left(e^{\theta_6-\theta_4} - 1\right)K_{46} + \left(e^{-\theta_4} - 1\right)\mu_4$

$a_5 = \left(e^{\theta_6-\theta_5} - 1\right)K_{56} + \left(e^{-\theta_5} - 1\right)\mu_5$; $a_6 = \left(e^{\theta_5-\theta_6} - 1\right)K_{65} + \left(e^{-\theta_6} - 1\right)\mu_6$

Differentiating these $w.r.t\ every\ \theta_k$ and evaluating at $\theta = 0$ to compute $a_{i,k}(0)$, gives the non-zero derivatives as follows:

$a_{1,1}(0) = \pi N - K_{12} - K_{13} - K_{14} - \mu_1$; $a_{1,2}(0) = K_{12}$; $a_{1,3}(0) = K_{13}$; $a_{1,4}(0) = K_{14}$

$a_{2,1}(0) = \mu_2$; $a_{2,2}(0) = -(\mu_2 + K_{23} + K_{25})$; $a_{2,3}(0) = K_{23}$; $a_{2,5}(0) = K_{25}$ $a_{3,2}(0) = K_{32}$;

$a_{3,3}(0) = -(\mu_3 + K_{32})$; $a_{4,4}(0) = \mu_4 - (K_{45} + K_{46})$; $a_{4,5}(0) = K_{45}$; $a_{4,6}(0) = K_{46}$

$a_{5,5}(0) = -(\mu_5 + K_{56})$; $a_{5,6}(0) = K_{56}$ $a_{6,5}(0) = K_{65}$; $a_{6,6}(0) = -(\mu_6 + K_{65})$

Thus, the mean vector $m(t) = (m_1, \dots, m_6)^T$ solves the matrix ODE

$\frac{d\boldsymbol{m}}{dt} = B\boldsymbol{m}$ (11)

Where $B = (b_{kl})$ $with\ b_{kl} = a_{l,k}(0)$; $B\ is\ a\ 6\ by\ 6\ dimensional\ matrix$

Thus, the equations for each mean are:

$$\frac{d\boldsymbol{m_1}}{dt} = (\pi N - K_{12} - K_{13} - K_{14} - \mu_1)m_1 + m_2\mu_2$$

$$\frac{d\boldsymbol{m_2}}{dt} = K_{12}m_1 - (\mu_2 + K_{23} + K_{25})m_2 + K_{32}m_3$$

$$\frac{d\boldsymbol{m_3}}{dt} = K_{13}m_1 + K_{23}m_2 - (\mu_3 + K_{32})m_3$$

$$\frac{d\boldsymbol{m_4}}{dt} = (\mu_4 - K_{45} - K_{46})m_4$$

$$\frac{d\boldsymbol{m_5}}{dt} = K_{25}m_2 + K_{45}m_4 - (\mu_5 + K_{56})m_5 + K_{65}m_6$$

$$\frac{d\boldsymbol{m_6}}{dt} = K_{46}m_4 + K_{56}m_5 - (\mu_6 + K_{65})m_6$$

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From (8), that is, $\frac{\partial}{\partial t}M(\theta,t) = \sum_{i=1}^{6} a_i(\theta)\, M_i$, the variance and covariance functions are obtained by differentiating both sides $w.r.t\ every\ \theta_k\ and\ \theta_l$,

$$\frac{\partial^2 M}{\partial t \partial \theta_k} = \sum_{i=1}^{6} (a_{i,kl}\, M_i + a_{i,k} M_{il} + a_{i,l} M_{ik} + a_i M_{ikl}) \tag{12}$$

Where $a_{i,k} = \partial a_i / \partial \theta_k \quad and \quad a_{i,kl} = \partial^2 a_i / \partial \theta_k \partial \theta_l$

Evaluating at $\theta = 0;\ a_i(0) = 0\ \forall i$, also, terms with $a_i M_{ikl}$ vanish; we need second derivatives $a_{i,kl}(0)$; thus,

$$\frac{\partial}{\partial t} M_{kl}(0,t) = \sum_{i=1}^{6} (a_{i,kl}(0)\, M_i(0,t) + a_{i,k}(0) M_{il}(0,t) + a_{i,l}(0) M_{ik}(0,t)) \tag{13}$$

Since $M_{kl}(0,t) = M_{lk}(0,t)$ (symmetry) and $M_i(0,t) = m_i(t)$, and $M_{ik}(0,t) = M_{ki}(0,t)$

$$\frac{d}{dt} M_{kl}(0,t) = \sum_{i=1}^{6} a_{i,kl}(0)\, M_i(t) + \sum_{i=1}^{6} a_{i,k}(0) M_{il}(0,t) + \sum_{i=1}^{6} a_{i,l}(0) M_{ik}(0,t) \tag{14}$$

Expressing in terms of second moments, $M_{kl}(0,t) = \sigma_{kl}(t)$ denote the second moment, then

$$\frac{d}{dt} M_{kl}(0,t) = \sum_{i=1}^{6} a_{i,kl}(0)\, m_i(t) + \sum_{i=1}^{6} a_{i,k}(0) \sigma_{il}(t) + \sum_{i=1}^{6} a_{i,l}(0) \sigma_{ik}(t) \tag{15}$$

From the expressions for $a_i(\theta)$, the non-zero derivatives are:

For $\boldsymbol{a_1}$: $a_{1,11}(0) = \pi N + K_{12} + K_{13} + K_{14} + \mu_1\ ;\quad a_{1,22}(0) = K_{12};\quad a_{1,33}(0) = K_{13};\quad a_{1,44}(0) = K_{14}$

$a_{1,12}(0) = -K_{12}\ ;\quad a_{1,13}(0) = -K_{13};\ a_{1,14}(0) = -K_{14};$

For a_2: $a_{2,22}(0) = K_{23} + K_{25} + K_{46} + \mu_2\ ;\ a_{2,33}(0) = K_{23};\quad a_{2,55}(0) = K_{25};\quad a_{2,23}(0) = -K_{23};$

$a_{2,25}(0) = -K_{25}\ ;$

For a_3: $a_{3,22}(0) = K_{32}\ ;\quad a_{3,33}(0) = K_{32} + \mu_3;\qquad a_{3,23}(0) = -K_{32};$

For a_4: $a_{4,44}(0) = K_{45} + K_{46} + \mu_4;\quad a_{4,55}(0) = K_{45};\quad a_{4,66}(0) = K_{46};\quad a_{4,45}(0) = -K_{45}$

$a_{4,46}(0) = -K_{46}\ ;$

For a_5: $a_{5,55}(0) = K_{56} + \mu_5;\quad a_{5,66}(0) = K_{56};\quad a_{5,56}(0) = -K_{56};$

For a_6: $a_{6,55}(0) = K_{65}\ \ a_{6,66}(0) = K_{65} + \mu_6;\quad a_{6,56}(0) = -K_{65};$

The second moment matrix $B\Sigma + \Sigma B^T + D$ where B is the matrix from the equations ($b_{kl} = a_{l,k}(0)$) and D is a 6 by 6 diagonal matrix with:

$$D_{kk} = \sum_{i=1}^{6} a_{i.kk}(0)\, m_i(t) \tag{16}$$

The elements of D are

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$$D_{11} = a_{1,11}(0)m_1 = (\pi N + K_{12} + K_{13} + K_{14} + \mu_1)m_1$$

$$D_{22} = a_{1,22}(0)m_1 + a_{2,22}(0)m_2 + a_{3,22}(0)m_3 = K_{12}m_1 + (K_{23} + K_{25} + \mu_2)m_2 + K_{32}m_3$$

$$D_{33} = a_{1,33}(0)m_1 + a_{2,33}(0)m_2 + a_{3,33}(0)m_3 = K_{13}m_1 + K_{23}m_2 + (K_{32} + \mu_3)m_3$$

$$D_{44} = a_{4,44}(0)m_4 = (K_{45} + K_{46} + \mu_4)m_4$$

$$D_{55} = a_{2,55}(0)m_2 + a_{4,55}(0)m_4 + a_{5,55}(0)m_5 + a_{6,55}(0)m_6 = K_{25}m_2 + K_{45}m_4 + (K_{56} + \mu_5)m_5 + K_{65}m_6$$

The variance is

$$Var\big(X_k(t)\big) = \sigma_{kk}(t) - m_k^2(t) \tag{17}$$

Therefore,

$$\frac{d}{dt}Var(X_t) = \frac{d\sigma_{kk}}{dt} - 2m_k\frac{dm_k}{dt} \tag{18}$$

From the equations derived above, the complete system of equations for variances and covariances can be obtained.

3. Results

For model with pediatric and adult Tuberculosis with exogenous reinfection, initial values were drawn from literature as shown in table 2 below. The life expectancy ratio of individuals in Nigeria www.indexmundi.org 2024 is 60.87years (≈ 61years). It also suggests that the death rate equals the inverse of the life expectancy ratio. Thus,

$$Death\ rate, \mu = \frac{1}{61} = 0.0164 \approx 0.02yr^{-1}$$

Furthermore, Central Intelligence Agency (www.cia.gov) as at April 2024, says 44% of the population are less than 15years (regarded in this study as children) while 56% are 15years and above. World Health Organization suggests that about a third of the world's population are affected with TB. An estimate of the start off values for the disease compartments are as follows:

a) Passively Immuned, $M(0) = 9500$ (Assumed)
b) Susceptible, $S(0) = \frac{2}{3} * \frac{1}{3} * N(= 199916496) = 44425888$
c) Exposed/ Latently Infected, $E(0) = \frac{1}{3} * \frac{1}{3} * N(= 199916496) = 22212944$
d) Infectious individuals, $I(0) = 470628$ (total count of infectives from data collected)

The initial values of the passively immuned, susceptible and latently infected individuals for adult and children were 56% and 44% of the above values respectively. For the infectious class, literature shows that about 10% of all incidence TB cases are children. This was used in this study. Numerical realizations of the model dynamics were obtained using the stochastic simulation algorithm and the Kolmogorov differential equation in equation 2. The "adaptivetau" package in R version 3.3.3 was adopted.

Table 2: Model Parameters

Parameters	Values	Source
$\beta_a;\beta_c$	0.005,0.0290	Jung et al. (2002)
p, q	(0,1)	Range
r_a, r_c	0.5	Nelson & Wells (2004)
f	0.175	Assumed

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σ_a, σ_c	0.035; 0.025,	Bhunu et al (2008)
π	0.9	Assumed
$\mu; \mu_T$	0.02;0.3	Estimated; Bhunu *et. al* (2008)
ρ	0.3	Bhunu *et. al* (2008)

Numerical simulations of model with vaccination, passively immune infants, exposed and infectious individual therapy and exogenous reinfection in a population was carried out. Key parameters were varied to investigate their impact on the transmission dynamics. Figures 1 to 12 are graphical realizations of the disease dynamics.

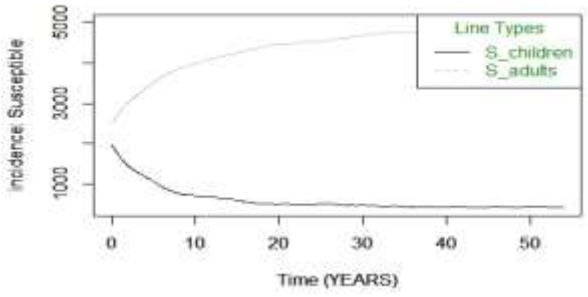

Figure 1: Plots of the dynamics of susceptible adult and children's populations at initial values

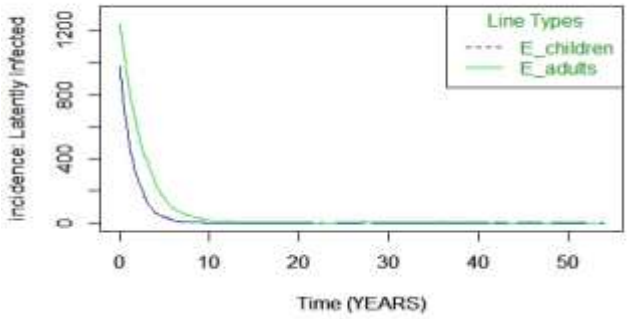

Figure 2: Plots of the dynamics of Latently infected (Exposed) adult and children populations at initial values of the model

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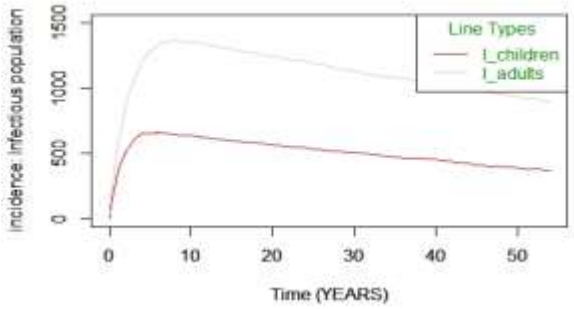

Figure 3: Plots of the dynamics of infectious adult and children populations at initial values of the model

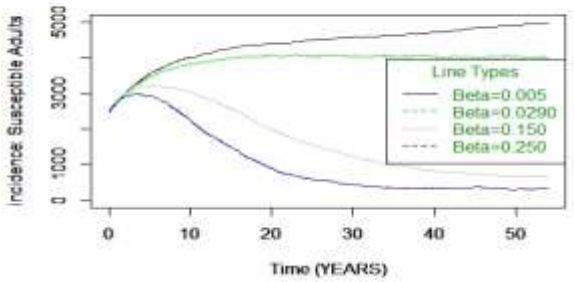

Figure 4: Plots of the dynamics of the Latently infected children population at initial values of the model when the transmission parameter beta vary from 0.005 – 0.250.

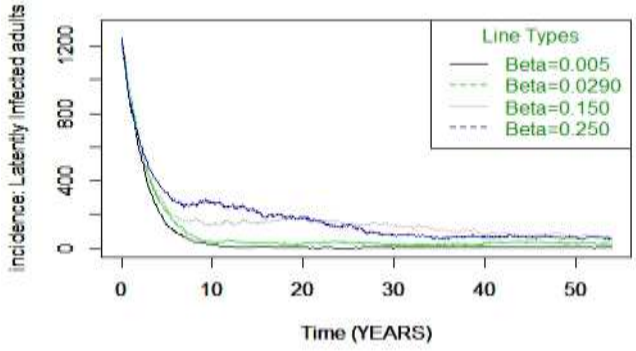

Figure 5: Plots of the dynamics of the latently infected adult population at initial values of the model when the transmission parameter beta from vary 0.005 – 0.250.

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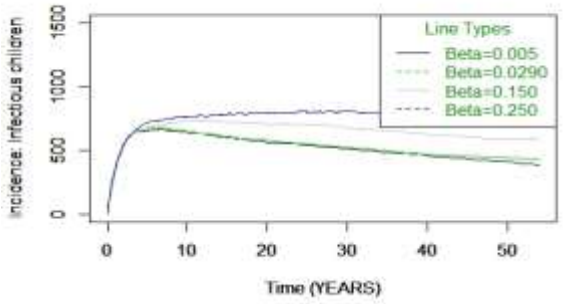

Figure 6: Plots of the dynamics of the Infectious children population at initial values of the model when the transmission parameter beta vary from 0.005 – 0.250.

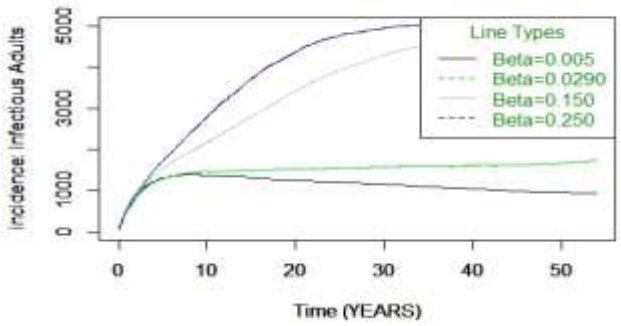

Figure 7: Plots of the dynamics of the infectious adult population (‘0000) at initial values of the model when the transmission parameter beta vary from 0.005 – 0.250.

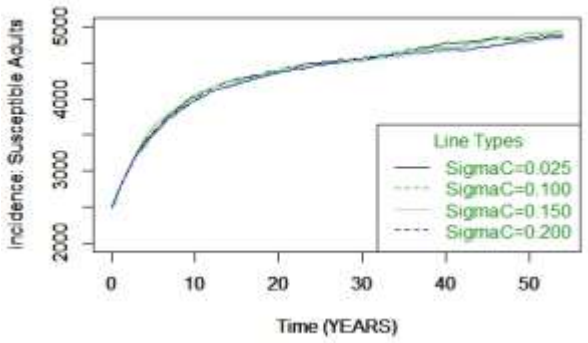

Figure 8: Plots of the dynamics of the susceptible adult population at initial values of the model when the recovery parameter sigma vary among children from 0.025 – 0.200

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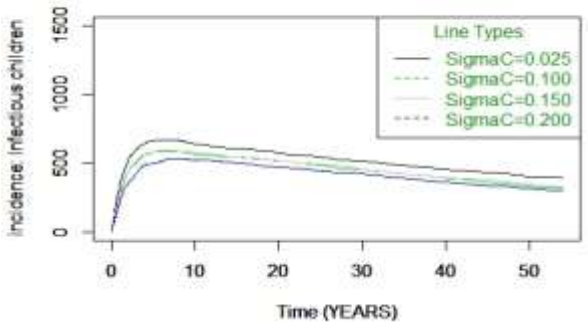

Figure 9: Plots of the dynamics of the infectious children population at initial values of the model when the recovery parameter sigma for children vary from 0.025 – 0.200.

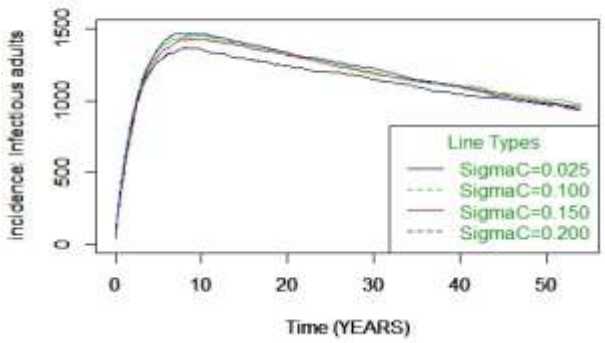

Figure 10: Plots of the dynamics of the infectious adult population at initial values of the model when the recovery parameter sigma for children vary from 0.025 – 0.200.

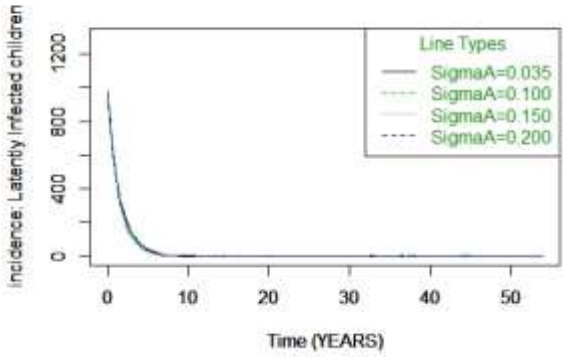

Figure 11: Plots of the dynamics of the latently infected (exposed) children population at initial values of the model when the recovery parameter sigma for adults vary from 0.035 – 0.200.

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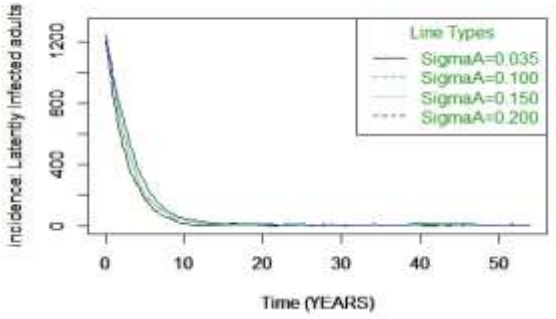

Figure 12: Plots of the dynamics of the latently infected (exposed) adult population at initial values of the model when the recovery parameter sigma for adults vary from 0.035 – 0.200.

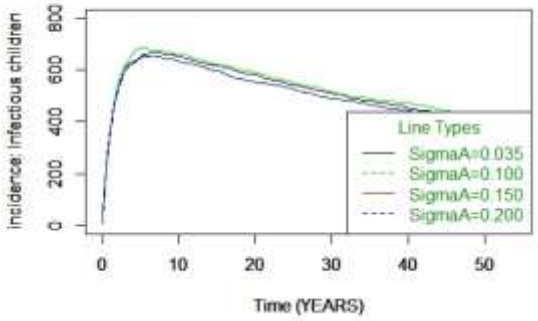

Figure 13: Plots of the dynamics of the infectious children population at initial values of the model when the recovery parameter sigma for adults vary from 0.035 – 0.200.

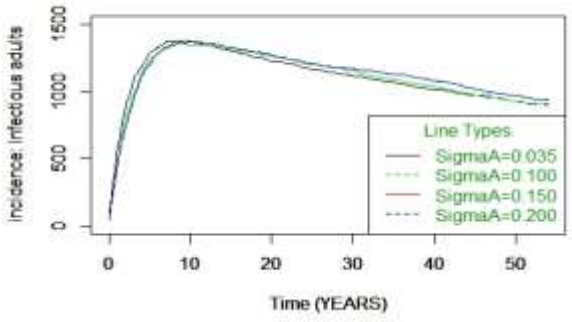

Figure 14: Plots of the dynamics of the infectious adult population at initial values of the model when the recovery parameter sigma for adults vary from 0.035 – 0.200.

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4. Discussion

From the numerical simulations plots, age structure can b observed to play a major role in the TB transmission dynamics. The susceptible populations of both children and adults gradually stabilize as demographic turnover and recovery processes balance disease transmission. This behavior is consistent with the report by Nyabadza and Kgosimore (2012), confirming that age-specific contact patterns substantially influence long-term disease persistence.

The trajectories of the exposed (latent) compartments indicate that latent tuberculosis infection constitutes the largest disease reservoir throughout the simulation period. This observation is consistent with the biological characteristics of Mycobacterium tuberculosis, where only a small proportion of infected individuals (10 – 15%) immediately progress to active disease while the majority remain latently infected for extended periods. The simulations further show that increasing the transmission coefficient produces substantial increases in both latent and infectious populations among children and adults. As the effective transmission rate increases from low to high values, disease prevalence rises rapidly, indicating that transmission intensity remains one of the dominant drivers of tuberculosis persistence.

An important finding concerns the influence of age structure. The model establishes that childhood TB contributes significantly to maintaining disease transmission despite lower observed notification rates. Because tuberculosis diagnosis among children remains challenging due to elusive symptoms confirmation, infected children may remain undetected for prolonged periods. As a result, the pediatric population become an important hidden reservoir that continuously replenishes infection within the adult population. This finding supports recent WHO recommendations emphasizing improved childhood TB surveillance and diagnosis.

Unlike deterministic formulations that generate only average epidemic trajectories, the CTMC formulation provides a probabilistic description of epidemic evolution. The derivation of the mean and variance equations enables simultaneous assessment of both expected disease behavior and the uncertainty surrounding epidemic outcomes. This stochastic information is particularly valuable during the early stages of outbreaks and in relatively small populations where random fluctuations strongly influence disease persistence or extinction.

5. Conclusion

In this paper, a continuous-time Markov chain model on TB transmission dynamics in children and adults is formulated following the deterministic version by Nyabadza & Kgosimore (2012). Our aim is to present the solution of the model via the probability generating and moment generating functions. The equation for the mean of each disease state is presented while equations from which the complete system of equations for the variances and covariances can be derived are also presented. Numerical realizations of the model dynamics are presented the stochastic simulation algorithm and the Kolmogorov differential equation in equation (2). The “adaptivetau” package in R version 3.3.3 was used. Overall, the study findings show that TB control efforts should combine reductions in transmission with improvements in treatment; especially enhanced detection of childhood infections. The stochastic age-structured framework developed in this study provides a mathematical tool for quantifying uncertainty while preserving the essential epidemiological mechanisms governing tuberculosis transmission. The model therefore represents a useful extension of existing deterministic age-structured TB models and provides a foundation for future investigations incorporating parameter estimation, optimal control, and real surveillance data.

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