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Simulating Deterministic and Stochastic Models of Tuberculosis (TB) Transmission Dynamics

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ABSTRACT

In this paper, a stochastic differential equation model as a version of a deterministic model of tuberculosis transmission dynamics considering treatment rate and population density as controls is formulated. The objective of this study is to compare the solutions of both versions for varying areas. The two models were solved numerically using Runge-Kutta method of order four. The sample paths show different trends of TB disease spread and thus ensemble the variability inherent in the outcomes of the spread of disease observed in practice unlike the trajectory of the deterministic model that shows one outcome. This partly explains variability in global distribution of tuberculosis prevalence in communities with similar demographic and environmental factors. The findings of this study show that the role of chance effects on the spread of tuberculosis is significant.

Keywords: Tuberculosis, infection, stochastic model, deterministic model, chance effects

INTRODUCTION

Tuberculosis (TB) is a global health threat. It causes ill-health among millions of people each year and ranks alongside the human immunodeficiency virus (HIV) as a leading cause of death worldwide. In 2014, there were an estimated 9.6 million new TB cases: 5.4 million among men, 3.2 million among women and 1.0 million among children. There were also 1.5 million TB deaths (1.1 million among HIV-negative people and 0.4 million among HIV-positive people), of which approximately 890 000 were men, 480 000 were women and 140 000 were children (WHO, 2015). As shown in Hattaf *et al;* (2009), about one third of the world human population constitutes a reservoir of TB infection.

Mycobacterium tuberculosis is the causative agent of TB. The tubercle bacilli live in the lungs of infected hosts. They spread in the air when infectious individuals sneeze, cough, speak or sing. A susceptible individual may become infected with TB if he or she inhales bacilli from the air. The particles containing Mycobacterium tuberculosis are so small that normal air currents keep them airborne and transport them throughout rooms or buildings. Hence, individuals who regularly share space with those with active TB (the infectious stage of the disease) have a much higher risk of becoming infected. These bacilli become established in the alveoli of the lungs from where they spread throughout the body if not suppressed by the immune system. The hosts' immune responses usually limit bacilli multiplication and, consequently, the spread that follows primary infections. The general symptoms of TB disease include feelings of sickness or weakness, weight loss, fever, and night sweats. The symptoms of TB disease of the lungs also include coughing, chest pain, and the coughing up of blood. Symptoms of TB disease in other parts of the body depend on the area affected [Castillo-Chavez and Song, (2004); CDC, (2011); WHO, (2013)]. About 10% of infected individuals eventually develop active TB. Most infected individuals remain as latently infected carriers for their entire lives. The average length of the latent period (noninfectious stage) ranges from months to decades. However, the risk of progression toward active TB increases markedly in the presence of co-infections that debilitate the immune system. Most forms of TB can be treated. Effective and widespread treatment for active and latently infected individuals has been available for about five decades. Streptomycin is still used today to treat TB but in combination with pyrazinamide (Castillo-Chavez and Song, 2004; WHO, 2013).

Mathematical models have been used for several decades to study the transmission dynamics of TB. As reported in Castillo-Chavez and Song (2004), Waaler was the first that built a model for the transmission dynamics of TB in 1962. Since then manifold models have been ensuing.

The list cannot be exhausted, and we do not try to be encyclopedic. For a survey of mathematical models of TB, see Castillo-Chavez and Song (2004). For some pioneer works in this area, see Castillo-Chavez and Feng (1997); Kirschner (1999); Feng *et al;* (2000); Song *et al;* (2001); Caminero *et al;* (2001); Song *et al;* (2002); Murphy *et al* (2003); Aparicio and Hernandez *(2006).*

Models incorporating vaccination, treatment or both as control strategies for TB disease abound. See, for example, Ssemtimba *et al* (2005), Adetunde (2007), Adetunde (2008), Koriko and Yusuf (2008) and Hattaf *et al;* (2009).

In this study a mathematical model for the dynamics of tuberculosis in density-dependent populations studied in Ssemtimba *et al;* (2005) is revisited. This model was also applied by Adetunde (2007). Unlike in Ssemtimba (2005), a stochastic version of the model is formulated. Mathematical models that display the role of chance effects on disease transmissions can be seen in Allen (2003) and Allen (2008).

The plan of this paper is as follows. We first formulate a stochastic differential equation model as a version of the deterministic model proposed by Ssemtimba (2005) *et al;* next we perform numerical simulations and present the results. Conclusion remarks finally follow.

MATERIALS AND METHODS

In this paper, we formulate a stochastic version of a mathematical model of tuberculosis transmission dynamics of a one-strain model of tuberculosis by Ssemtimba *et al;* (2005). We carry out the numerical simulations of both model versions.

Formulation of the Model

Ssemtimba *et al;* (2005) proposed the dynamics of a one-strain model of tuberculosis as follows.

Deterministic Model

$$\frac{dS}{dt} = \lambda - \mu S - \beta_1 c S\frac{I}{A} \quad (2.1)$$

$$\frac{dL}{dt} = \beta_1 c S\frac{I}{A} - (\mu + k + \gamma_1)L + \beta_2 c T\frac{I}{A} \quad (2.2)$$

$$\frac{dI}{dt} = kL - (\mu + d + \gamma_2)I \quad (2.3)$$

$$\frac{dT}{dt} = \gamma_1 L + \gamma_2 I - \mu T - \beta_2 c T\frac{I}{A} \quad (2.4)$$

$N(t) = S(t) + L(t) + I(t) + T(t)$ is the total population size.

The variables and parameters of the above model are described as follows.

Table 1: Variables and Parameters of the model

$S(t)$ =the number of susceptible individuals at time t
$L(t)$ =the number of latently infected individuals at time t
$I(t)$ =the number of infectious individuals at time t
$T(t)$ =the number of recovered/treated individuals at time t
A =the total area occupied by the population
λ =recruitment rate
μ =the per capita natural mortality rate
d =the tuberculosis-induced mortality rate
β_1 =the probability that a susceptible individual becomes infected by one infectious individual per contact per unit
β_2 = the probability that a treated individual becomes infected by one infectious individual per contact per unit
k =the rate of progression to active tuberculosis
γ_1 =recovery rate of the latent class
γ_2 =recovery rate of the infectious class
c =the per capita contact rate

Stochastic Model

We first determine the various transitions and probabilities for the system of equations (2.1) − (2.4) as follows.

Table 2:

The compartmental changes in small time period Δt	
Transition	**Probability**
$(\Delta X)_1 = [1, 0, 0, 0]^{\top}$	$p_1 = \lambda \Delta t$
$(\Delta X)_2 = [-1, 0, 0, 0]^{\top}$	$p_2 = \mu X_1 \Delta t$

$(\Delta X)_3 =$ [-1, 1,0, 0] $^\top$	$p_3 = \beta_1 c X_1 X_3 \Delta t$
$(\Delta X)_4 =$ [0, 1, 0, -1] $^\top$	$p_4 = \frac{\beta_2 c X_3 X_4}{A} \Delta t$
$(\Delta X)_5 =$ [0, -1, 0, 0] $^\top$	$p_5 = \mu X_2 \Delta t$
$(\Delta X)_6 =$ [0, -1, 1, 0] $^\top$	$p_6 = k X_2 \Delta t$
$(\Delta X)_7 =$ [0, -1, 0, 1] $^\top$	$p_7 = r_2 X_2 \Delta t$
$(\Delta X)_8 =$ [0, 0, -1, 0] $^\top$	$p_8 = (d + \mu) X_3 \Delta t$
$(\Delta X)_9 =$ [0, -1, 0, 1] $^\top$	$p_9 = r_1 X_3 \Delta t$
$(\Delta X)_{10} =$ [0, 0, 0, -1] $^\top$	$p_{10} = \mu X_4 \Delta t$
$(\Delta X)_{11} =$ [0, 0, 0, 0] $^\top$	$1 - (p_1 + p_2 + p_3 + p_4 + p_5 + \cdots + p_{10})$

Let $X = (X_1, X_2, X_3, X_4)$ be a random vector, where, $X_1, X_2, X_3, and\ X_4$ are the numbers of the susceptible, latent, infectious and treated individuals respectively. To form the stochastic differential equation (SDEs) using the procedure developed by Allen (2008), the expectation and the covariance need to be computed.
The system of stochastic differential equations (SDEs) takes the form:

$$\Delta X(t) = F(t, X)dt + B(t, X)dw(t) \qquad (2.5),$$

$$F(t, X) = E(\Delta X) = \begin{pmatrix} \lambda - \mu S - \beta_1 c X_1 \frac{X_3}{A} \\ \beta_1 c X_1 \frac{X_3}{A} - (\mu + k + \gamma_1) X_2 + \beta_2 c X_4 \frac{X_3}{A} \\ k X_2 - (\mu + d + \gamma_2) X_3 \\ \gamma_1 X_2 + \gamma_2 X_3 - \mu X_4 - \beta_2 c X_4 \frac{X_3}{A} \end{pmatrix} \Delta t$$

and $B = \sqrt{V}$, where,

$$V = \begin{pmatrix} \lambda + \mu S + \beta_1 c X_1 \frac{X_3}{A} & -\beta_1 c X_1 \frac{X_3}{A} & 0 & 0 \\ -\beta_1 c X_1 \frac{X_3}{A} & \beta_1 c X_1 \frac{X_3}{A} + \beta_2 c X_4 \frac{X_3}{A} + (\mu + k + \gamma_1) X_2 & -k X_2 & -(\beta_2 c X_4 \frac{X_3}{A} + \gamma_1 X_2) \\ 0 & -k X_2 & k X_2 + (\mu + d + \gamma_2) X_3 & -\gamma_2 X_3 \\ 0 & -(\beta_2 c X_4 \frac{X_3}{A} + \gamma_1 X_2) & -\gamma_2 X_3 & \beta_2 c X_4 \frac{X_3}{A} - (\gamma_2 + d + \mu) X_4 \end{pmatrix}$$

Numerical Simulation

Numerical simulations are performed using the parameter values in Table 3.

Table 3

Variable/parameter	***Value***	Source
$S(0) = X_1$	5000	assumed
$L(0) = X_2$	0	assumed
$I(0) = X_3$	5	assumed
$T(0) = X_4$	0	assumed
λ	1500	Ssemtimba *et al.* (2005)
μ	0.0185	Ssemtimba *et al.* (2005).
c	2	Ssemtimba *et al.* (2005)
β_1	2	Ssemtimba *et al.* (2005)
β_2	2	Ssemtimba *et al.* (2005)
γ_1	1.5	Ssemtimba *et al.* (2005)
γ_2	1.5	Ssemtimba *et al.* (2005)
k	0.00396	Ssemtimba *et al.* (2005)
d	0.365	Ssemtimba *et al.* (2005)
A	$0.2 - 2000$	Ssemtimba *et al.* (2005)

The results of the numerical simulations for varying areas are shown in Figures 1 through 8. All other parameter values are fixed as in Table 3.

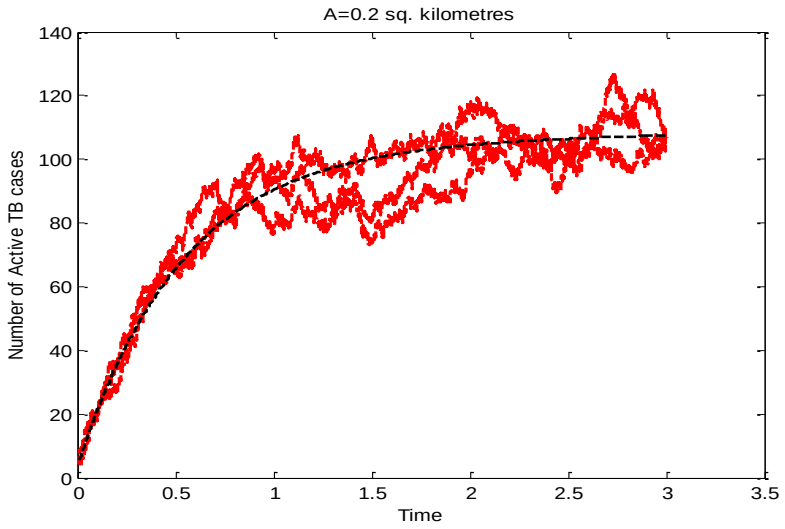

Figure 1: Red curves represent the sample paths and the dotted black curve represents the deterministic solution

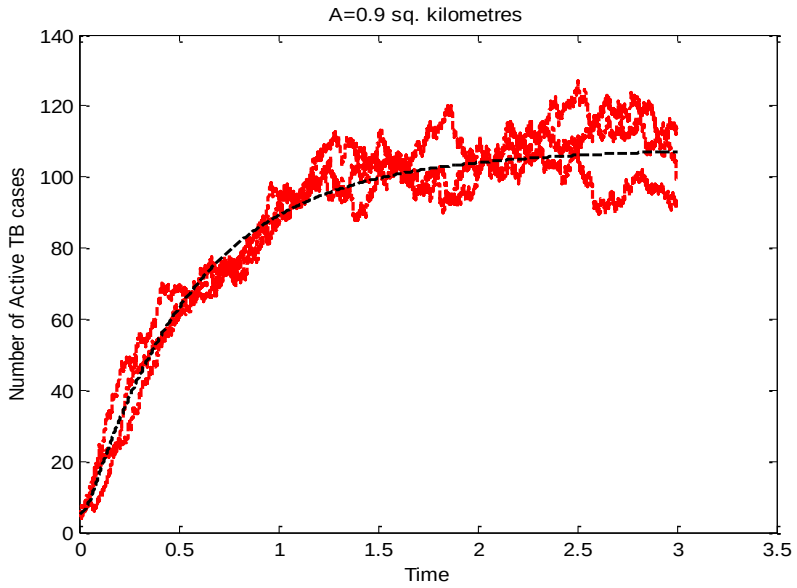

Figure 2: Red curves represent the sample paths and the dotted black curve represents the deterministic solution

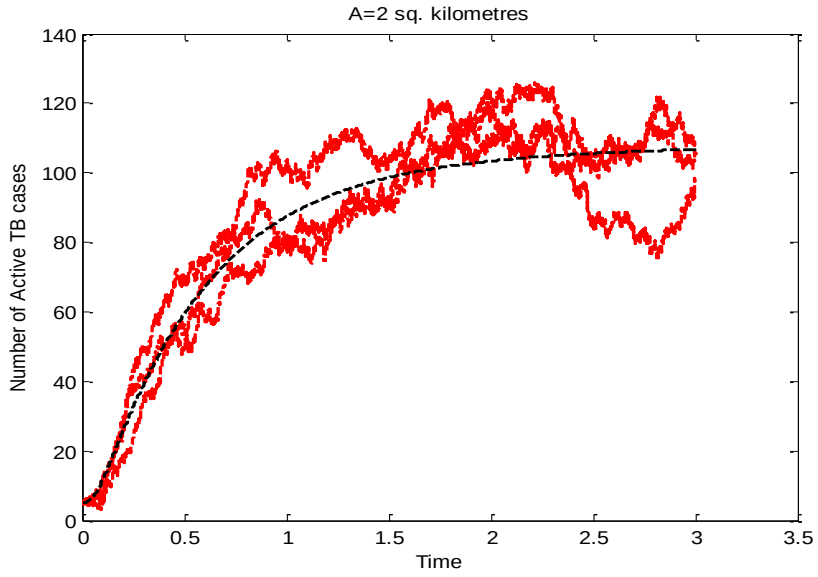

Figure 3: Red curves represent the sample paths and the dotted black curve represents the deterministic solution

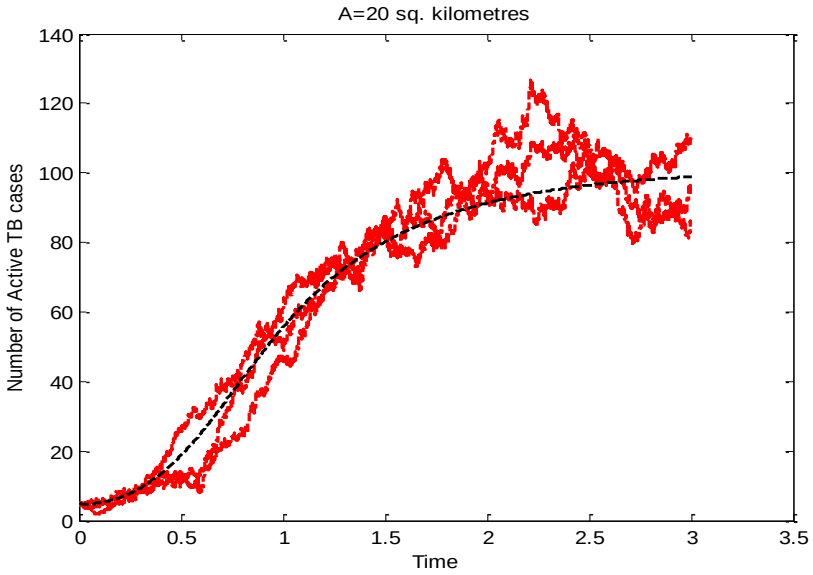

Figure 4: Red curves represent the sample paths and the dotted black curve represents the deterministic solution

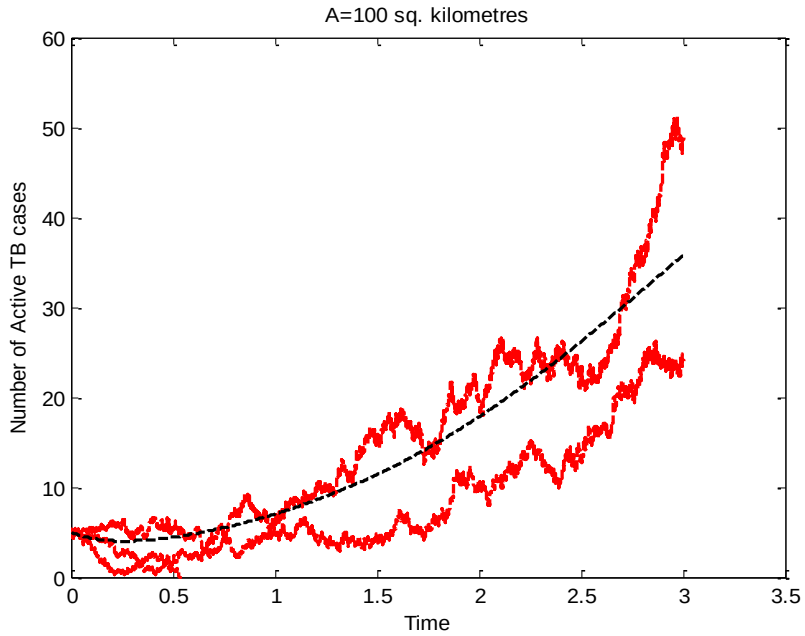

Figure 5: Red curves represent the sample paths and the dotted black curve represents the deterministic solution

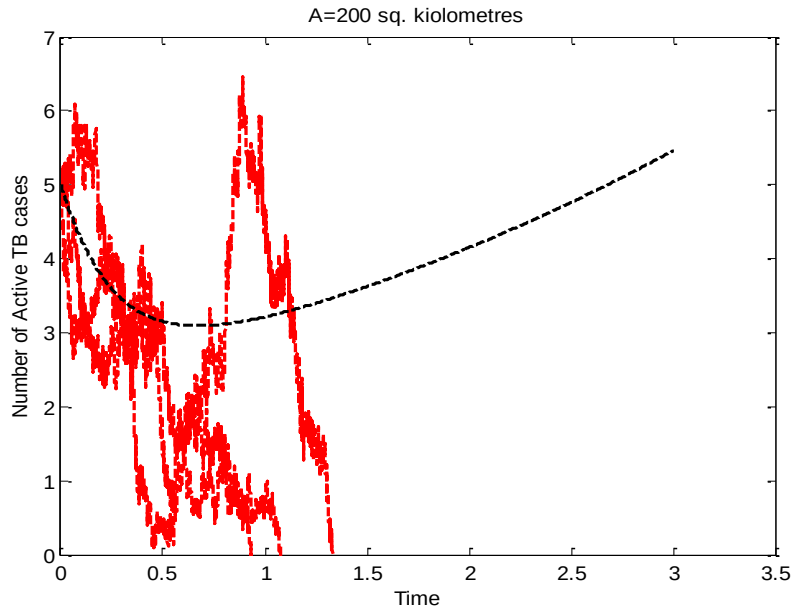

Figure 6: Red curves represent the sample paths and the dotted black curve represents the deterministic solution

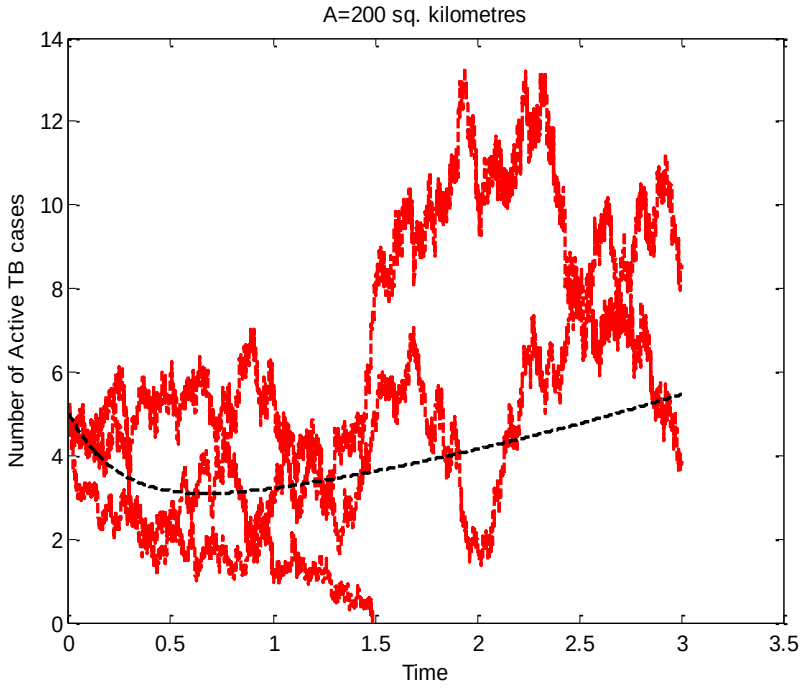

Figure 7: Red curves represent the sample paths and the dotted black curve represents the deterministic solution

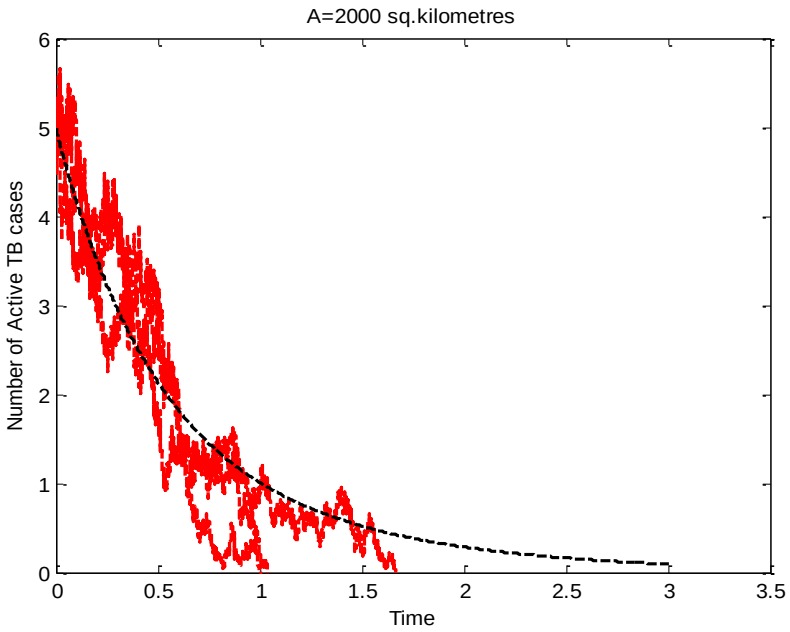

Figure 8: Red curves represent the sample paths and the dotted black curve represents the deterministic solution

RESULTS AND DISCUSSION

Ssemtimba *et al;* (2005) studied the effect of population density on the dynamics of tuberculosis. They pointed out that population density determines the level of respiratory contact in a community and this level directly determines the infection rate of airborne diseases like tuberculosis. Thus, their study focused on the impact of the population density on the spread of tuberculosis among internally displaced persons in Uganda as a case study. In this research we formulated a system of stochastic differential equations as a version of the model proposed by Ssemtimba *et al;* (2005) and studied the role of chance effects on the spread of tuberculosis. The main results of the study are shown in Figures 1 through 8. The figures show the sample paths and the trajectory for the SDEs and the deterministic model for varying area sizes ranging from 0.2 to 2000 square kilometers. Stochastic effects have played a major role in the transmission of tuberculosis. Sample paths show that the numbers of active TB cases fluctuate over time at varying magnitudes while the trajectory of the deterministic model shows a

definite outcome. This can be observed in Figures 1 through 8. The sample paths also show a possibility of disease eradication in a population (see Figures 5, 6 and 7) even though the trajectory of the deterministic model shows persistence of disease. Another feature observed in the results is possibility of eradication at varying times because of chance effects. See Figures 5, 6, 7 and 8.

CONCLUSION

In this paper, a system of stochastic differential equations as a version of a deterministic model of tuberculosis (TB) transmission dynamics is proposed. The deterministic and the stochastic models can be seen in equations (2.1) through (2.5). Both model versions were solved numerically using Runge-Kutta method of order four. The main results are in Figures 1 through 8. A factor of interest in this study is chance effect or stochastic noise. The findings of the study have shown that stochastic has a significant effect on TB transmission dynamics in terms of the magnitude of the number of cases, persistence or eradication of disease or timing of disease eradication.

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