

**ANALYSIS OF TRANSMISSION DYNAMICS OF TUBERCULOSIS (TB) USING
DIFFERENTIAL EQUATIONS: A CASE STUDY OF AMANSIE WEST DISTRICT,
GHANA**

ABSTRACT

In this paper, a Susceptible - Exposed - Infected - Recovered (SEIR) epidemiological model is formulated to determine the transmission of tuberculosis. The equilibrium points of the model are found and their stability is investigated. By analyzing the model, a threshold parameter R_0 was found which is the basic reproductive number. It is noted that when $R_0 < 1$ the disease will fail to spread and when $R_0 > 1$ the disease will persist in the population and become an endemic. The model has two non – negative equilibria namely the disease – free equilibrium and the endemic equilibrium. Using the stability theory and the computer simulation, it was observed that the number of immunized individuals in the population will increase the level of immunity. The graphical solutions of the differential equations were developed using Matlab as well as the computer simulations.

Keywords: differential equations, exposed and infected, simulation, transmission dynamics, tuberculosis

Introduction

Tuberculosis, MTB, or TB (short for tubercle bacillus) is a common, and in many cases lethal, infectious disease caused by various strains of mycobacteria, usually *Mycobacterium tuberculosis* (Kumar *et al*, 2007). Tuberculosis typically attacks the lungs, but can also affect other parts of the body. It is spread through the air when people who have an active TB infection cough, sneeze, or otherwise transmit their saliva through the air (Konstantinos, 2010). Most infections are asymptomatic and latent, but about one in ten latent infections eventually progresses to active disease which, if left untreated, kills more than 50% of those infected.

Tuberculosis (TB) describes an infectious disease that has plagued humans since the Neolithic times. Two organisms cause tuberculosis; *Mycobacterium tuberculosis* and *Mycobacterium*

bovis. Consumption, phthisis, scrofula, Pott's disease, and the White Plague are all terms used to refer to tuberculosis throughout history (Wikipedia/ History of tuberculosis, 2012).

Physicians in ancient Greece called this illness phthisis to reflect its wasting character. During the 17th and 18th centuries, TB caused up to 25% of all deaths in Europe. In more recent times, tuberculosis has been called consumption. It was not clear how TB was transmitted until Robert Koch's brilliant discovery of the tubercle bacillus in 1882 and established TB as an infectious disease. (www.emedicinehealth.com/Tuberculosis, 2012).

Tuberculosis is caused by mycobacterium, usually *Mycobacterium tuberculosis*. The bacterium is transmitted from an infected host to a new host through respiratory mist. When people with active pulmonary TB cough, sneeze, speak, sing, or spit, they expel infectious aerosol droplets 0.5 to 5.0 μm in diameter. A single sneeze can release up to 40,000 droplets (Cole and Cook, 1998). Each one of these droplets may transmit the disease, since the infectious dose of tuberculosis is very low (the inhalation of fewer than 10 bacteria may cause an infection) (Nicas *et.al*, 2005).

People with prolonged, frequent, or close contact with people with TB are at particularly high risk of becoming infected, with an estimated 22% infection rate (Ahmed and Hasnain, 2011). A person with active but untreated tuberculosis may infect 10–15 (or more) other people per year (TB Fact sheet. WHO, 2011). Transmission occur from people with active TB, those with latent infection are not thought to be contagious (Kumar *et al*, 2007).

Once inhaled, the mycobacteria enter the lungs. When they reach the pulmonary alveoli, they encounter macrophages, which are white blood cells that surround and digest pathogens. Sometimes, the immune system can destroy the mycobacteria, but if not, the mycobacteria begin multiplying within the macrophages. The macrophages are then used as transportation to nearby lymph nodes. Once in the lymph nodes, the mycobacteria can spread throughout the body. (Kumar *et al*, 2007 and Herrmann and Lagrange, 2005).

Because mycobacterium tuberculosis is a slow-growing bacterium, the immune system, if not able to destroy it, may be able to keep it from spreading enough to cause symptoms. This is

called a latent tuberculosis infection, and it accounts for 90% of TB infections (Skolnik, 2011). While the organism might be present in the body for years, there is only a 10% chance that it will ever progress to an active infection (Arch and Claire, 2009). People with latent infections cannot spread TB to others.

Tuberculosis may infect any part of the body, but most commonly occurs in the lungs (known as pulmonary tuberculosis) (Mandell *et al*, 2010). Extrapulmonary TB occurs when tuberculosis develops outside of the lungs. Extrapulmonary TB may coexist with pulmonary TB as well. General signs and symptoms include fever, chills, night sweats, loss of appetite, weight loss, and fatigue, and significant finger clubbing may also occur (Abramson *et al*, 2005). One may not notice any symptoms of illness until the disease is quite advanced. Even the symptoms might be blamed on other disease.

A number of factors make people more susceptible to TB infections. The most important risk factor globally is HIV; 13% of all TB cases are infected by the virus (WHO, 2011). This is a particular problem in sub-Saharan Africa, where rates of HIV are high (W.H.O., 2006 and Chaisson and Martinson, 2008).

Tuberculosis is closely linked to both overcrowding and malnutrition, making it one of the principal diseases of poverty (Lawn and Zumla, 2011). Those at high risk thus include: people who inject illicit drugs, inhabitants and employees of locales where vulnerable people gather (e.g. prisons and homeless shelters), medically underprivileged and resource-poor communities, high-risk ethnic minorities, children in close contact with high-risk category patients and health care providers serving these clients (Griffith and Kerr, 1996).

Tuberculosis is diagnosed by finding *Mycobacterium tuberculosis* bacteria in a clinical specimen taken from the patient. While other investigations may strongly suggest tuberculosis as the diagnosis, they cannot confirm it. A complete medical evaluation for tuberculosis (TB) must include a medical history, a physical examination, a chest X-ray and microbiological examination (of sputum or some other appropriate sample). It may also include a tuberculin skin test, other scans and X-rays, surgical biopsy (Kumar *et al*, 2007).

Tuberculosis prevention and control efforts primarily rely on the vaccination of infants and the detection and appropriate treatment of active cases. The World Health Organisation (WHO) has achieved some success with improved treatment regimens, and a small decrease in case numbers (Lawn and Zumla, 2011).

The only currently available vaccine as of 2011 is *Bacillus Calmette–Guérin* (BCG) which, while it is effective against disseminated disease in childhood, confers inconsistent protection against contracting pulmonary TB (McShane, 2011). Nevertheless, it is the most widely used vaccine worldwide, with more than 90% of all children being vaccinated (Lawn and Zumla, 2011). However, the immunity it induces decreases after about ten years. BCG is only administered to people at high risk. Part of the reasoning arguing against the use of the vaccine is that it makes the tuberculin skin test falsely positive, and therefore, of no use in screening (Teo and Shiggadia, 2006). A number of new vaccines are currently in development (Lawn and Zumla, 2011).

Despite the availability of highly efficacious treatment for decades, TB remains a major global health problem. In 1993, the World Health Organization (WHO) declared TB a global public health emergency, at a time when an estimated 7–8 million cases and 1.3–1.6 million deaths occurred each year (WHO, 1993).

Although TB is currently well-controlled in most countries, recent data indicate that the overall global incidence of TB is rising as a result of resurgence of the disease in Africa and parts of Eastern Europe and Asia (Dye, 2006). In these regions, the emergence of drug-resistant TB and the convergence of the HIV (human immunodeficiency virus) and TB epidemics have created substantial new challenges for disease control.

In 2010, there were an estimated 8.5–9.2 million cases and 1.2–1.5 million deaths (including deaths from TB among HIV-positive people) (WHO, 2011). TB is the second leading cause of death from an infectious disease worldwide (after HIV, which caused an estimated 1.8 million deaths in 2008) (Mandell *et al*, 2010). In 2009 there were 9.4 million new cases of TB and 1.7 million deaths, including 380,000 deaths from TB among people with HIV (WHO, 2011). The vast majority of deaths from TB are in the developing world.

Tuberculosis (TB), a preventable disease linked to poverty, was declared an emergency in Africa in 2005. Each year it claims the lives of half a million Africans, many young and in their most

productive years. In the past 15 years, overall rates have doubled in Africa and tripled in high HIV areas. Africa has the highest per capital incidence of TB in the world (28%), with most of the worst affected countries located in sub-Saharan Africa. Those most at risk include the urban poor, migrants and refugees, who are forced to live in overcrowded conditions (AMREF, 2012).

Africa is also the only continent where TB rates are increasing, with 1,500 TB deaths every day. Tragically and avoidably, 10% of these are children. TB is also a leading killer of HIV-positive people with weakened immune systems. About 200,000 people living with HIV/AIDS die from TB every year, most of them in Africa. Completing a particularly vicious circle, HIV itself has been the single most important factor in the rising incidence of TB in Africa since 1990. Treating co-infected people is hard as the drug therapies for each are hard to safely combine (AMREF, 2012).

One-third of the world's population is currently infected with the TB bacilli with nearly 2 million deaths each year. Of those infected, over 1.5 million cases occur annually in sub-Saharan Africa (WHO, 2005).

Tuberculosis in Ghana started way back in the pre-independence era when the then colonial government recognized the need to combat the disease due to the threat it posed to the larger society. In July 1954, the Ghana Society for the Prevention of Tuberculosis was established to support and supplement government's efforts at combating the disease (GHS – Stop TB Prog., 2012).

Over 46,000 new cases of TB annually are estimated by the World Health Organization (WHO) in Ghana (WHO, 2006). However, in reality, less than a third of the estimated number of cases is officially reported each year by health facilities in the country. For instance, in 2008, only 14,022 TB cases of all forms were reported, the highest cases ever recorded officially in the country (National Tuberculosis Programme Annual Report – GHS / MoH, 2008).

The first mathematical model of TB was presented by Waaler *et al.* (1962). Following this, there were several numerical studies, primarily focusing on cost-effectiveness of different interventions (Brogger, 1967; Revelle *et al.*, 1969). Revelle *et al.* (1969) used a model with one progression rate and various latent classes representing different treatment and control strategies,

and argued that vaccination was cost-effective in countries with high TB burdens. Waaler continued his work in 1968 and 1970, Waaler and Piot (1969), and Waaler and Piot (1970). After the 1970's, little work on models of tuberculosis appeared in the literature until the mid - 1990's.

The Amansie West District is one of the 27 districts in the Ashanti region of Ghana. It was carved out of the Amansie East District of the Ashanti Region in 1989, as part of the Government's Decentralization Policy. Manso-Nkwanta is the district capital. The district is located in the south-western part of the Ashanti Region. It shares common boundary on its Western part with the Atwima Mponua District. On its northern part can be found the Atwima Nwabiagya and the Bosomtwe – Atwima - Kwanhuma Districts, while a regional boundary separates it from Western and Central Region on its southern part. The predominant occupation is subsistence farming and illegal small scale mining popularly known as Galamsey. Due to the activities of the illegal mining, the district is faced with the problem of immigration making the district exposed to infectious diseases with tuberculosis being prevalent.

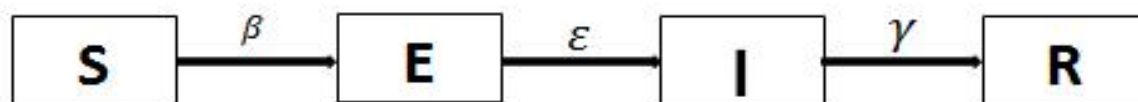
Materials and Methods

The mathematical model will be formulated using differential equations based on the epidemiological compartment modelling. The computer software package that will be used to solve the differential equation model numerically is Matrix Laboratory (Matlab R2010a). Analysis and numerical simulations of the model will be conducted. Records showing the trend of tuberculosis cases recorded annually were obtained from the Amansie West District Health Directorate, from 2002 - 2011.

The Model

We consider the standard SEIR model where the individuals in the population are divided into four compartments. The susceptibles (S) which refers to the healthy individuals that has not yet come into contact with TB bacterium. The exposed (E) are people who have come into contact with the disease but are not yet infective or infectious. The infective (I) are those who have become infected with TB and are able to transmit the disease and the recovered (R) are

173 individuals who have recovered from TB. The proportions of the individuals in the compartment



174 of the population, i.e. S, E, I and R, at time t is denoted as $S(t)$, $E(t)$, $I(t)$ and $R(t)$ respectively.

175 **Figure 1: Flow chart showing the SEIR model**

176

177 **Model Assumptions**

- 178 1. Age, sex, social status, race coupled with climatic conditions in the district does not
179 affect the probability of an individual being infected.
- 180 2. The death rate of all individuals is balanced by a birth rate (birth and deaths occurs at
181 equal rates).
- 182 3. We assume that once an individual is infected, he or she become exposed to the
183 environment before becoming infectious.
- 184 4. The disease is transmitted in a closed environment. There is no emigration or
185 immigration and there is neither birth nor death in the population. Hence the total
186 population, N of individuals in the district remains constant.

187 **Model Equations**

188 Applying the assumption here, the total population, N is at full capacity (it value is between 0
189 and N).

190 Also, the individuals are likely to be infected by the infectious individuals in case of contact
191 except those who are immune. Those who are undetected or late detected infectious are the ones
192 contributing to the disease transmission and spread. Those detected are isolated to the hospital
193 for immediate treatment and education.

194 Furthermore, those that are recovered become immune and are educated about the transmission
195 of the disease. The transmission of the disease within the sanatorium is neglected.

196 Lastly, we assume that there is no treatment failure in the sanatorium and therefore a patient will
197 recover or die.

198 The birth and death rate is μ . Hence μN will be the rate at which individuals are born into the
199 susceptible class without any immunity and μS is the rate at which they leave it through death.

200 The rate at which the susceptible class changes is equal to the rate at which infections occur. This
201 occurs when the disease is passed from an infective individual to a susceptible one. The number
202 of susceptible – infective contacts is proportional to the product of $S(t)$ and $I(t)$.

203 Hence the rate of change in the susceptible individuals is

$$204 \quad \frac{dS}{dt} = \mu N - \mu S - \frac{\beta SI}{N}, \text{ where } \beta SI \text{ is rate of infection.}$$

205 The term $\frac{\beta SI}{N}$ is negative because the number of susceptible individuals decreases. The rate at
206 which individuals leave the susceptible population is equal to the rate at which they enter the
207 exposed population.

208 The number of individuals in the exposed class increases since those in the susceptible class
209 becomes exposed to the disease.

210 Let εE the rate which an exposed individual becomes infectious. Then the rate of change of the
211 exposed population is given by

$$212 \quad \frac{dE}{dt} = \frac{\beta SI}{N} - (\mu + \varepsilon)E$$

213 Let γI be the rate at which an infected individual may recover. The rate of change of the
214 infective individuals will be

$$215 \quad \frac{dI}{dt} = \varepsilon E - (\mu + \gamma)I$$

216 The rate of change of the recovered is given by

$$217 \quad \frac{dR}{dt} = \gamma I - \mu R$$

218 This leads to the following formulations of the SEIR model from the description, assumptions
219 and compartmental diagram and was given as follows;

$$220 \quad \frac{dS}{dt} = \mu N - \mu S - \frac{\beta SI}{N} \quad (1)$$

$$221 \quad \frac{dE}{dt} = \frac{\beta SI}{N} - (\mu + \varepsilon)E \quad (2)$$

$$222 \quad \frac{dI}{dt} = \varepsilon E - (\mu + \gamma)I \quad (3)$$

$$223 \quad \frac{dR}{dt} = \gamma I - \mu R$$

224 (4)

225 The nonlinear system of differential equations formulated above has initial conditions
226 $S(0) = S_0 > 0, E(0) = E_0 > 0, I(0) = I_0 > 0$ and $R(0) = R_0 > 0$.

227 Also, the rate of contact, the rate of infection, the recovery rate and the birth and death rate are
228 all non-negative ($\beta > 0, \varepsilon > 0, \gamma > 0$ and $\mu > 0$ respectively).

229 Hence $N(t) = S(t) + E + I(t) + R(t)$ and

$$230 \quad \frac{dS}{dt} + \frac{dE}{dt} + \frac{dI}{dt} + \frac{dR}{dt} = 0 \quad (5)$$

231 Since $\frac{dN}{dt} = 0$ and thus $N = S + E + I + R$ is a constant.

$$232 \quad \text{If we let } \left. \frac{S(t)}{N} = s(t), \frac{E(t)}{N} = e(t), \frac{I(t)}{N} = i(t), \text{ and } \frac{R(t)}{N} = r(t) \right\} \quad (6)$$

233 Where $s(t), e(t), i(t)$ and $r(t)$ are the respective fractions of the population for susceptible,
234 exposed, infective and recovered individuals.

235 Then $s(t) + e(t) + i(t) + r(t) = 1$

Variable	Definition
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$S(t)$	The number of Susceptible individuals in the population at time, t
$E(t)$	The number of Exposed individuals in the population at time, t
$I(t)$	The number of Infected individuals in the population at time, t
$R(t)$	The number of Recovered individuals in the population at time, t
N	Total population

Table 1: Variables and definitions.

Parameter	Definition
β	The rate of contact. It is defined as the average number of effective contacts with other individuals (susceptible) per infective unit time.
ε	The rate at which the exposed individuals become infective or infectious.
γ	The rate at which the infectious individuals recover per unit time.
μ	The birth and death rate

Table 2: Parameters and their definitions.

The SEIR model is similar to the SIR endemic model except that it has an additional compartment E or the exposed class. This compartment reflects an inclusion of incubation period. Individuals in this class are infected but not infectious.

We divide equations (1) and (2) by N and then substitute equation (6) into equations (1) – (4) respectively to obtain

$$\frac{ds}{dt} = \mu - (\mu + \beta i)s$$

(7)

$$\frac{de}{dt} = \beta si - (\mu + \varepsilon)e$$

(8)

$$\frac{di}{dt} = \varepsilon e - (\mu + \gamma)i$$

(9)

$$\frac{dr}{dt} = \gamma i - \mu r$$

(10)

With initial conditions $s(0) = s_0 \geq 0, e(0) = e_0 \geq 0, i(0) = i_0 \geq 0, r(0) = r_0 \geq 0$

Basic Reproductive Number, R_0

In epidemiology, the basic reproductive number (sometimes basic reproduction rate or ratio) of an infection is the number of cases one case generates on the average over the course of its infectious period.

The Basic Reproduction number R_0 is the threshold for many epidemiological models. When $R_0 < 1$, the infection dies out in the long run (i.e. each infected individual produces one average less than one new infected individual). On the other hand, if $R_0 > 1$, the infection will

264 be able to spread in a population (i.e. each infected individual produces more than one new
265 infected individual).

266 For the purpose of our model, we use the approach by Ottar Bjørnstad (2005) to determine the
267 basic reproductive number for this thesis and is given by

$$268 \quad R_0 = \frac{\beta \varepsilon}{(\mu + \varepsilon)(\mu + \gamma)} \quad (11)$$

269 Also, the number of contacts between susceptible and infective is given by

$$270 \quad \sigma = \frac{\beta}{\gamma} \quad (12)$$

271 The SEIR model always has at least one solution given by $s = I$, and $e = i = r = 0$. If the
272 threshold quantity is greater than one then there is a unique endemic equilibrium solution in D
273 where $D = \{(e, i, r) | e \geq 0, i \geq 0, r \geq 0, e + i + r \leq 1\}$, (Hethcote, 2000).

274 **The Herd Immunity Threshold, H_I**

275 The herd immunity threshold (H_I) is the percentage of the population that needs to be immunized
276 to control the transmission of the disease. The endemicity of a disease depends on the basic
277 reproduction number, R_0 . This threshold value can predict whether the disease will approach and
278 spread through the population or not.

279 The equation (given by Diekmann and Heesterbeek, 2000) for estimating the herd immunity
280 threshold is given as

$$281 \quad H_1 = 1 - \frac{1}{R_0} \quad (13)$$

282

283 **Analysis of the Model**

284 In this section, we present the results of stability analysis of the equilibrium points.

285 **Equilibrium of the Model**

The system of equations of the model (Equations 7 - 10) has two non-negative equilibrium points, namely, the disease-free equilibrium, where $i = 0$ and endemic equilibrium, where $i \neq 0$. The equilibrium point for the disease – free equilibrium is given as:

$$(s^*, e^*, i^*) = (1, 0, 0) \quad (14)$$

The endemic equilibrium points for the respective states are as follows:

$$(s_e, e_e, i_e) = \left(\frac{1}{R_0}, \frac{\mu(R_0 - 1)}{(\mu + \varepsilon)R_0}, \frac{\mu(R_0 - 1)}{\beta} \right) \quad (15)$$

Stability of the Equilibria

To determine the stability of the system, we will consider linearizing the systems of equations (7) – (9) about the equilibrium points by taking the Jacobian of them.

The Jacobian matrix is given by

$$J(s, e, i) = \begin{bmatrix} -\mu - \beta i & 0 & -\beta s \\ \beta i & -\mu - \varepsilon & \beta s \\ 0 & \varepsilon & -\mu - \gamma \end{bmatrix} \quad (16)$$

For the disease-free equilibrium, we evaluate the Jacobian matrix at the equilibrium points

$(s^*, e^*, i^*) = (1.0, 0)$ and hence we get

$$J(s^*, e^*, i^*) = \begin{bmatrix} -\mu & 0 & -\beta \\ 0 & -\mu - \varepsilon & \beta \\ 0 & \varepsilon & -\mu - \gamma \end{bmatrix} \quad (17)$$

Solving for roots of the characteristic polynomial (with real coefficient) given in the Jacobian matrix leads to the characteristic equation given as:

$$\lambda^3 + a_1\lambda^2 + a_2\lambda + a_3 = 0 \quad (18)$$

Where

$$\left. \begin{aligned} a_1 &= (3\mu + \varepsilon + \gamma) \\ a_2 &= [(\mu + \varepsilon)(\mu + \gamma) - \beta\varepsilon + \mu(2\mu + \varepsilon + \gamma)] \\ a_3 &= \mu[(\mu + \varepsilon)(\mu + \gamma) - \beta\varepsilon] \end{aligned} \right\}$$

(19)

Using the Routh – Hurwitz stability criterion analysis we talked about earlier, the conditions $a_1 > 0$, $a_3 > 0$ and $a_1a_2 - a_3 > 0$ must hold. If these conditions are true, then all roots of the characteristic polynomial equation have negative real part, which concludes that there is a stable equilibrium.

The endemic steady state has equilibrium point given by

$$(s_e, e_e, i_e) = \left(\frac{1}{R_0}, \frac{\mu(R_0 - 1)}{(\mu + \varepsilon)R_0}, \frac{\mu(R_0 - 1)}{\beta} \right)$$

The Jacobian matrix of this equilibrium point is evaluated to obtain

$$J(s_e, e_e, i_e) = \begin{bmatrix} -\mu R_0 & 0 & \frac{-(\mu + \varepsilon)(\mu + \gamma)}{\varepsilon} \\ \mu(R_0 - 1) & -(\mu + \varepsilon) & \frac{(\mu + \varepsilon)(\mu + \gamma)}{\varepsilon} \\ 0 & \varepsilon & -(\mu + \gamma) \end{bmatrix} \quad (20)$$

Solving for the roots of the polynomial in the Jacobian matrix leads to the characteristic equation

$$\lambda^3 + b_1\lambda^2 + b_2\lambda + b_3 = 0 \quad (21)$$

Where

$$\left. \begin{aligned} b_1 &= \varepsilon + \gamma + \mu(2 + R_0) \\ b_2 &= \mu R_0(2\mu + \varepsilon + \gamma) \\ b_3 &= \mu(R_0 - 1)[\mu^2 + \mu(\varepsilon + \gamma) + \varepsilon\gamma] \end{aligned} \right\}$$

(22)

From the Routh – Hurwitz stability criterion, we need to determine the stability of the characteristic equation above. From the theorem, if the conditions $b_1 > 0$, $b_3 > 0$ and $b_1 b_2 - b_3 > 0$ are true, then all the roots of the characteristic equation have negative real part, which means a stable equilibrium.

From equation (3.41), the conditions are true for $R_0 > 1$ since $b_1 > 0$, $b_3 > 0$ and $b_1 b_2 - b_3 > 0$ (all non-negative), for all the values of the parameter and $R_0 > 1$, hence it is also true. In conclusion, by the Routh – Hurwitz stability criteria, the endemic steady state is stable when $R_0 > 1$.

Numerical Analysis and Results

Records obtained from the Amansie West district Health Directorate shows that tuberculosis is an endemic in the district. For instances, from 2007 to 2011, there has been an increase in the number of cases recorded. In 2007, 34 cases were diagnosed, 2008 (62 cases), 2009 (59 cases), 2010 (62 cases) and 2011 (70 cases). Figure 2 shows the trend of tuberculosis cases recorded in the district from 2002 – 2011.

AMANSIE WEST DISTRICT HEALTH DIRECTORATE
TUBERCULOSIS (TB) CASES DETECTED AND RECORDED

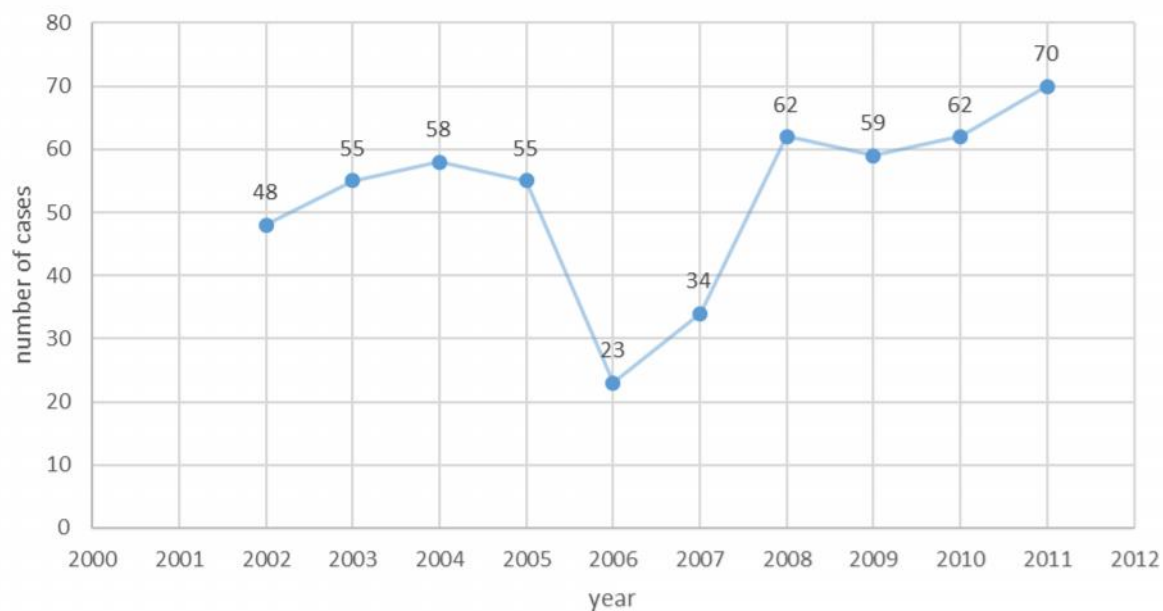


Figure 2. Trend of Tuberculosis cases in the Amansie West District from 2002 – 2011.

The table below shows the estimates of the parameters used in the model.

PARAMETER	SYMBOL	VALUE
Death rate	μ	0.00875
Transmission rate	β	0.5853
Infectious rate	ε	0.1666
Recovery rate	γ	0.5000

Table 3: Parameters and their estimated values used in the model.

The values of the parameter estimates from Table 3 are substituted into equations (7) – (10) to obtain

$$\frac{ds}{dt} = 0.00875 - (0.00875 + 0.5853i)s$$

(23)

$$\frac{de}{dt} = 0.5853i - 0.17535e$$

(24)

$$\frac{di}{dt} = 0.1666e - 0.50875i$$

(25)

$$\frac{dr}{dt} = 0.5i - 0.00875r$$

(26)

Estimation of the Basic Reproductive Number, R_0

From equation (11), the basic reproduction number for the SEIR model is given by

$$R_0 = \frac{\beta\varepsilon}{(\mu + \varepsilon)(\mu + \gamma)} = \frac{0.5853 \times 0.1666}{(0.00875 + 0.1666)(0.00875 + 0.5)} = 1.09305 > 1$$

Since $R_0 > 1$, the prevalence of Tuberculosis will result in an epidemic. This is due to the fact that rate of transmission is greater than the recovery rate.

The number of contacts between susceptible individuals and the infective ones is calculated from equation (12) and is given by

$$\sigma = \frac{\beta}{\gamma} = \frac{0.5853}{0.5000} = 1.1706$$

This shows that an average of one tuberculosis patient contacts 1.1706 susceptible individuals during an infectious period.

Estimation of the Herd Immunity Threshold, H_1

From equation (13), the herd immunity threshold is given as

$$H_1 = 1 - \frac{1}{1.09305} = 0.0851$$

Therefore, to control an epidemic, about 8.51% of the population has to be immunized when there is an outbreak.

374

375 Estimation of the Equilibrium Points

From equation (14), the equilibrium point of the disease – free steady state was determined to be

$$(s^*, e^*, i^*) = (1, 0, 0)$$

The estimates of the endemic steady state equilibrium were determined from equation (15) and is given by

$$\begin{aligned} (s_e, e_e, i_e) &= \left(\frac{1}{R_0}, \frac{\mu(R_0 - 1)}{(\mu + \varepsilon)R_0}, \frac{\mu(R_0 - 1)}{\beta} \right) \\ &= \left(\frac{1}{1.09305}, \frac{0.00875(1.09305 - 1)}{(0.00875 + 0.1666) \times 1.09305}, \frac{0.00875(1.09305 - 1)}{0.5853} \right) \\ &= (0.914871, 0.00042479, 0.00139106) \end{aligned}$$

383

384 Stability Analysis of the Equilibrium Points

The disease – free equilibrium point for the model was determined as $(s^*, e^*, i^*) = (1, 0, 0)$. We therefore determine the stability of the equilibrium point using the Jacobian matrix from equation (17). Hence, we obtain

$$J(s^*, e^*, i^*) = \begin{bmatrix} -0.00875 & 0 & -0.5853 \\ 0 & -0.17535 & 0.5853 \\ 0 & 0.1666 & -0.50875 \end{bmatrix}$$

We determine the roots of the character polynomial equation from the equation (18), as given in the Jacobian matrix as follows:

$$a_1 = [(3 \times 0.00875) + 0.1666 + 0.5] = 0.69285$$

$$a_2 = [(0.00875 + 0.1666)(0.00875 + 0.5) - (0.5853 \times 0.1666) + 0.00875((2 \times 0.00875) + 0.1666 + 0.5)] = -2.3158 \times 10^{-3}$$

393

$$a_3 = 0.00875[(0.00875 + 0.1666)(0.00875 + 0.5) - (0.5853 \times 0.1666)] = -7.2639 \times 10^{-5}$$

394

395 Note:

$$a_1 a_2 - a_3 = \left[(0.69285 \times -2.3158 \times 10^{-3}) - (-7.2639 \times 10^{-5}) \right] = -1.5318 \times 10^{-3}$$

396 Therefore, the characteristic equation is given by

397 $\lambda^3 + 0.69285\lambda^2 - 2.3158 \times 10^{-3}\lambda - 7.2639 \times 10^{-5} = 0$

398 (27)

399 The results indicates that $a_1 > 0$, $a_2 < 0$, and $a_1 a_2 - a_3 < 0$. From the Routh – Hurwitz stability
 400 criterion, these conditions does not hold. Hence, the disease – free equilibrium is an unstable
 401 steady state. This means that when an individual infected with mycobacterium tuberculosis is
 402 present in a susceptible population, it will eventually result in an outbreak of the disease.

403 From equation (4.08), the endemic equilibrium point was given as

404 $(s_e, e_e, i_e) = (0.914871, 0.00042479, 0.00139106)$. We therefore determine the Jacobian matrix
 405 corresponding to the endemic equilibrium point from equation (20) and we obtain

406
$$J(s_e, e_e, i_e) = \begin{bmatrix} 9.56141875 \times 10^{-3} & 0 & -0.53547 \\ 8.141875 \times 10^{-4} & -0.17535 & 0.53547 \\ 0 & 0.1666 & -0.50875 \end{bmatrix}$$

407 The roots of the characteristic polynomial equation given in equation (21) are obtained as
 408 follows

409 $b_1 = [0.1666 + 0.5 + 0.00875(2 + 1.09305)] = 0.69366$

410 $b_2 = [0.00875 \times 1.09305(2 \times 0.00875 + 0.1666 + 0.5)] = 6.5429 \times 10^{-3}$

411 $b_3 = 0.00875(1.09305 - 1)[0.00875^2 + 0.00875(0.1666 + 0.5) + (0.1666 \times 0.5)] = 7.2633 \times 10^{-5}$

412 Note: $b_1 b_2 - b_3 = 0.69366 \times (6.5429 \times 10^{-3}) - (7.2633 \times 10^{-5}) = 4.4660 \times 10^{-3}$

413 The characteristic equation is given by

414 $\lambda^3 + 0.69366\lambda^2 + 6.5429 \times 10^{-3}\lambda + 7.2633 \times 10^{-5} = 0.$ (28)

415 The values of the roots of the characteristic polynomial equation satisfy the Routh – Hurwitz
 416 stability criterion. This is because $b_1 > 0$, $b_2 > 0$, and $b_1 b_2 - b_3 > 0$. Therefore, the endemic
 417 steady state is asymptotically stable.

418 Sensitivity Analysis

419 Sensitivity analysis deals with the study of how the uncertainty in the output of a mathematical
420 model or system (numerical or otherwise) can be apportioned to different sources of uncertainty
421 in its inputs (Saltelli *et. al.*, 2008).

422 We analyse the effect on the reproduction number, R_0 and the stability of the disease – free
423 equilibrium. This will be done when the value of the parameter β changes whilst μ , ε and γ
424 remain the same and also, when γ changes whilst μ , β and ε are maintained.

425 1. If β is increased and γ is maintained, i.e. $\beta = 0.6853$ and $\gamma = 0.5$,

$$\left. \begin{aligned} &\Rightarrow R_0 = 1.2798 > 1 \\ &a_1 = 0.69285 > 0 \\ 426 \quad &a_2 = -0.018975 < 0 \\ &a_3 = -0.000218 < 0 \\ &a_1 a_2 - a_3 = -0.012928 < 0 \end{aligned} \right\}$$

427 From these results, the disease-free equilibrium is unstable.

428 2. If β is reduced and γ is maintained. i.e. $\beta = 0.4853$ and $\gamma = 0.5$,

$$\left. \begin{aligned} &\Rightarrow R_0 = 0.9063 < 1 \\ &a_1 = 0.69285 > 0 \\ 429 \quad &a_2 = 0.014344 > 0 \\ &a_3 = 0.000731 > 0 \\ &a_1 a_2 - a_3 = 0.009207 > 0 \end{aligned} \right\}$$

430 Hence, we have a stable disease – free equilibrium.

431 From the above results, as the transmission rate increases or the recovery rate decreases, $R_0 > 1$
432 and the disease – free equilibrium is unstable. This indicates that, the disease will spread when
433 there is an outbreak. Apparently, as the transmission rate decreases or the recovery rate increases,
434 $R_0 < 1$ and hence the disease – free equilibrium will be stable. This therefore means that the
435 disease will not spread.

436 We used the same scenarios as we did for the disease – free equilibrium.

437 1. If β increases and γ remains the same. i.e. $\beta = 0.6853$ and $\gamma = 0.5$,

$$\left. \begin{aligned} \Rightarrow R_0 &= 1.2798 > 1 \\ b_1 &= 0.69529 > 0 \\ b_2 &= 0.00766 > 0 \\ b_3 &= 0.000218 > 0 \\ b_1 b_2 - b_3 &= 0.005108 > 0 \end{aligned} \right\}$$

The endemic equilibrium is stable.

2. If the β is reduced and γ remains the same. i.e. $\beta = 0.4853$ and $\gamma = 0.5$,

$$\left. \begin{aligned} \Rightarrow R_0 &= 0.9063 < 1 \\ b_1 &= 0.69203 > 0 \\ b_2 &= 0.005424 > 0 \\ b_3 &= -0.0000755 < 0 \\ b_1 b_2 - b_3 &= 0.00382 > 0 \end{aligned} \right\}$$

Hence, the endemic equilibrium is unstable.

In conclusion, when the transmission rate is increases or the recovery rate decreases, $R_0 > 1$ and hence the endemic equilibrium is stable. This means that the disease will spread when there is an outbreak. On the other hand, as the transmission rate decreases or the recovery rate increases, $R_0 < 1$, and the endemic equilibrium is in an unstable state. This therefore means that the disease will not spread.

Sensitivity Analysis by Simulation

In this section, we perform numerical simulations on the SEIR model for tuberculosis using the data we have. We simulate our model using Matlab R2010a and the value of the parameters as found in Table 4.1. The Matlab codes are found in the appendix. We tried to look at the effects and the changes the will occur in the model when the values of each of the compartments of the model are altered .i.e. Susceptible(S), Exposed(E), Infected(I) and the Removed(R). We measured our time in months for a period of one year depending on the period of how tuberculosis prevalence occurs. We made some assumptions and graphing to see the effect of changes in each compartment of the model.

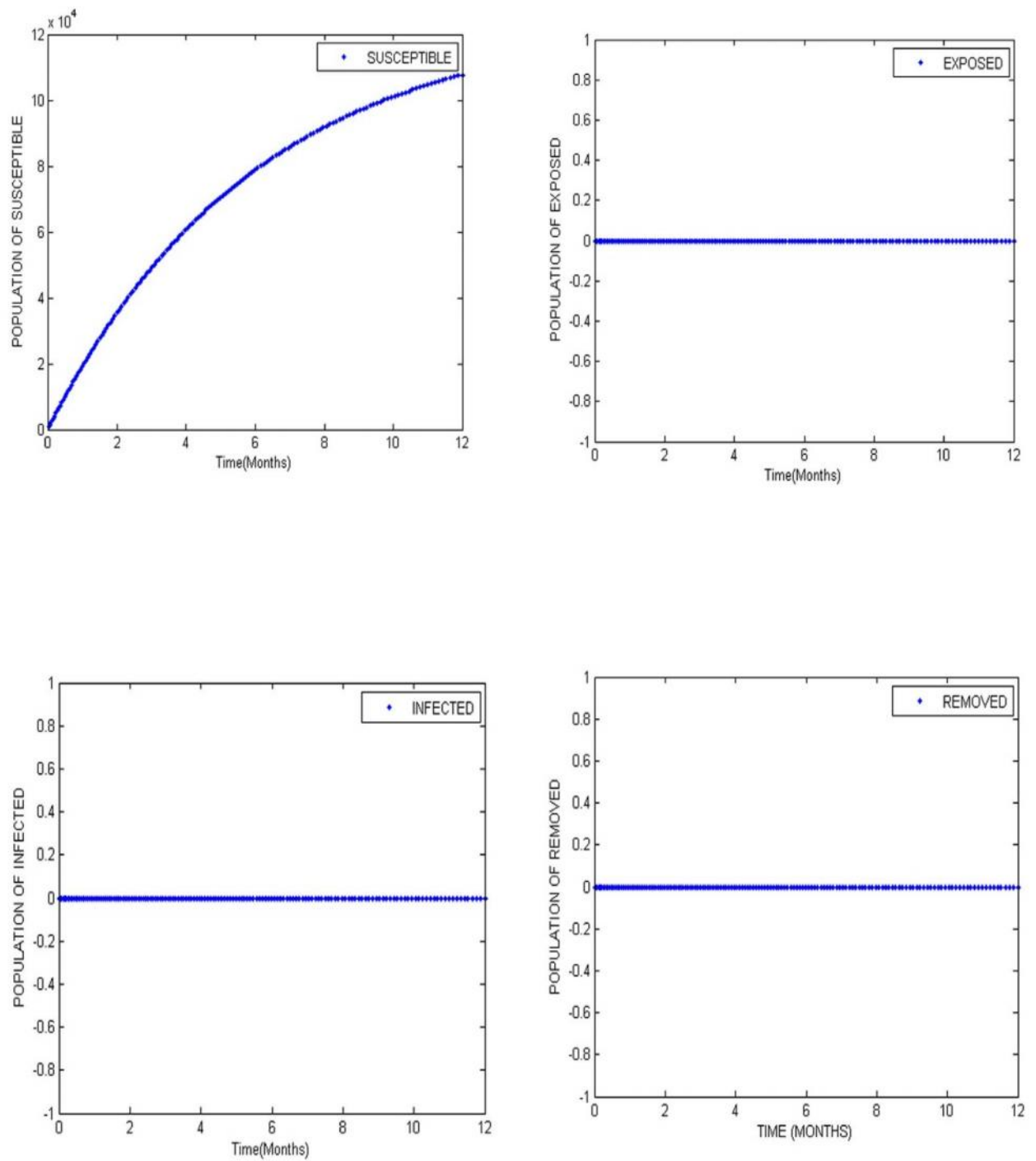
We first start with a total population of 500 individuals in which they all belong to the susceptible. This implies that there are no exposed, infected and recovered individuals in the population. The simulation gave the following graphs as shown in Figure 3.

It can be noticed from the graph that, the number of susceptibles is constant at 500 throughout the period of time under study while the number of exposed, infected and recovered are all at a constant number of zero during the entire period under study. This implies that there will be no effect on each compartment when all the population belong to the susceptible.

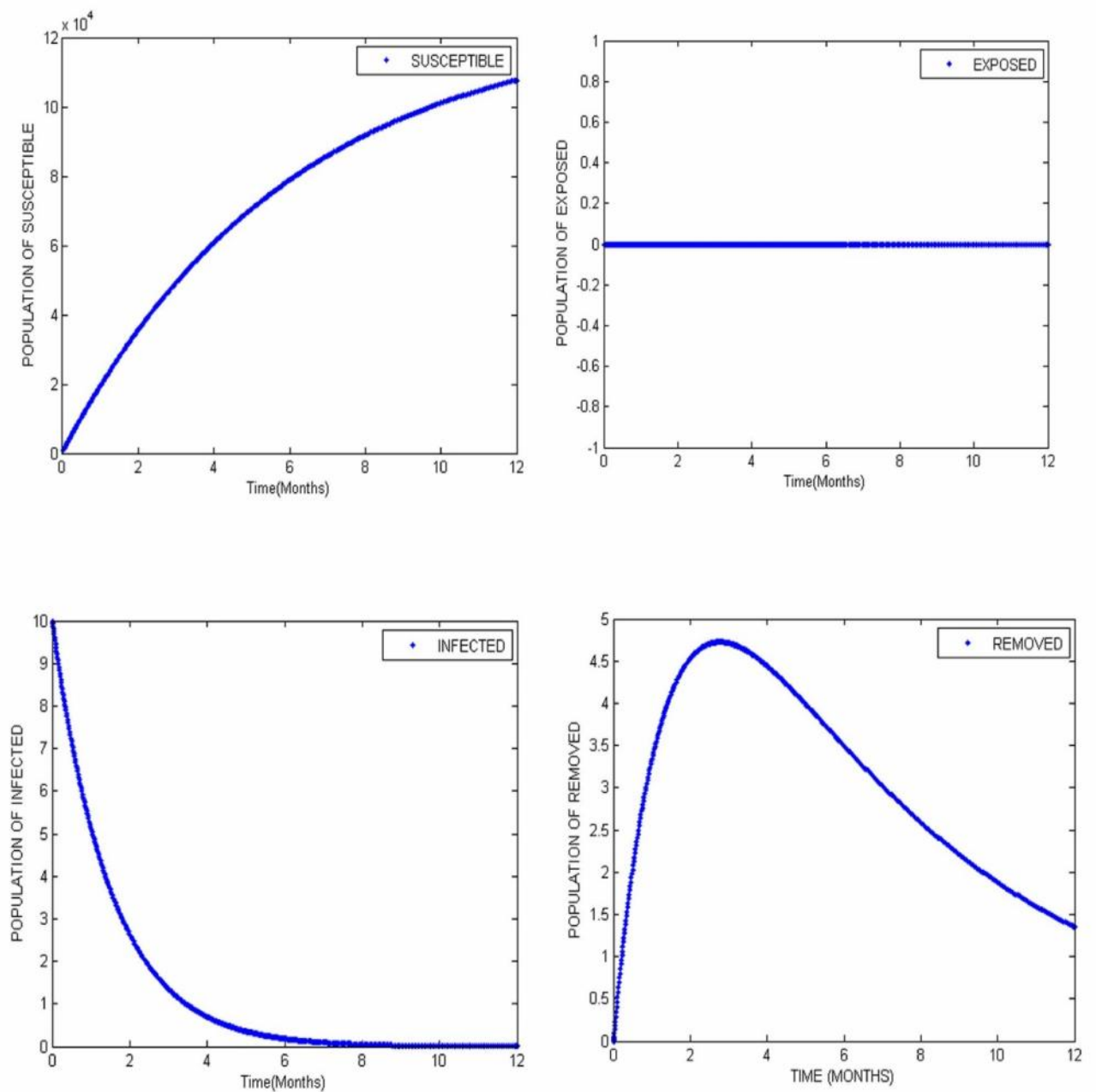
We make further adjustment of our system and analyse the results by introducing 10 infected, thereby reducing the susceptibles to 490, no exposed and no recovered individuals into the system.

It will be observed from Figure 4 that the number of susceptibles increased with time and became constant getting to the end of the period under study. There is also, no effect on the exposed individuals and the 10 infected reduced with time to zero. The 10 infected moves into the recovered compartment and no infection are recorded again. This may be due to early detection and probably seeking immunization. This will eventually cause the disease to die out anyway. By so doing, the recovered individuals begin to increase as the infected recovered and with time, they all move back to the susceptible compartment.

The final part of our simulation place emphasis on the exposed class. This will help put the disease under control in the district. With the introduction of some exposed individuals into our system, the number of infected tend to decrease but with time, they increase later. The susceptible class was stable at a point in time within the period of study but increase in number afterwards. When we introduce the infected into our system, with no exposed individuals, the disease failed to spread within some short period of time. The introduction of some exposed individuals will increase the infected after some period of time and hence the disease will spread again.



491 **Figure 3: $S = 500$, $E = 0$, $I = 0$, $R = 0$.**



492 **Figure 4: $S = 490$, $E = 0$, $I = 0$, $R = 0$**

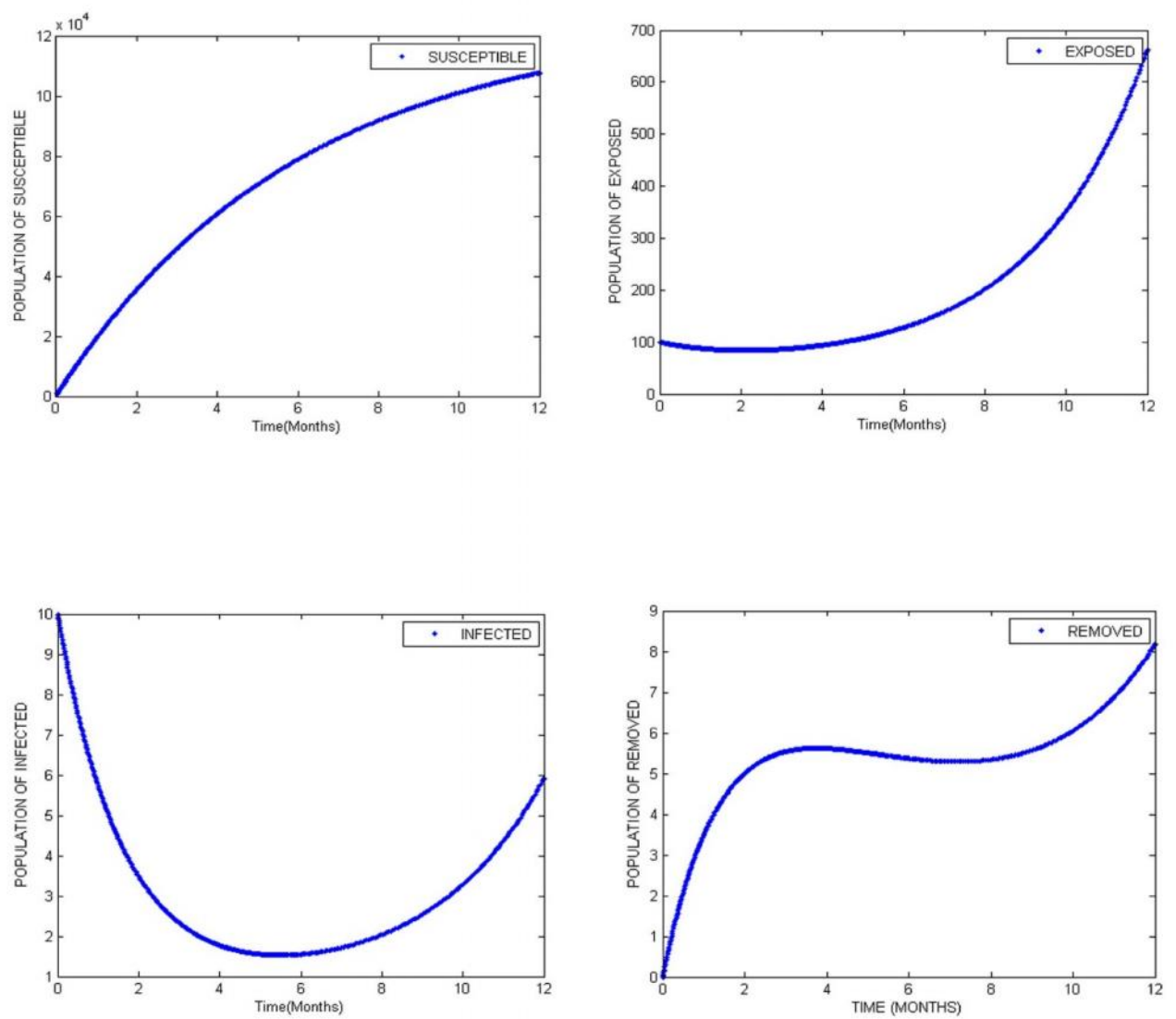


Figure 5: $S = 390$, $E = 100$, $I = 10$, $R = 0$

498 Discussion of Results

499 In this research, a mathematical model of the prevalence and transmission of tuberculosis in
 500 Amansie West district of the Ashanti Region is studied. We attempted to use the standard SEIR
 501 differential equation model to predict the transmission and spread of tuberculosis. By analyzing
 502 the model, we found a threshold parameter, R_0 , which is the basic reproductive number. It is
 503 noted that when $R_0 < 1$, then the epidemic will not spread and when $R_0 > 1$, the disease will
 504 persist in the population and hence become an endemic. The model has two non-negative
 505 equilibria, namely, the disease – free equilibrium and the endemic equilibrium. We discussed the
 506 existence and stability of the disease – free and endemic equilibria of the model and sensitivity
 507 analysis of the model were performed. The Herd immunity threshold, H_I , which shows the
 508 percentage or proportion of the population that needs to be immunized to control the
 509 transmission of the disease when there is an outbreak, was also considered.

510 From the results, the basic reproductive number for the SEIR model was estimated as $R_0 =$
 511 1.09305. As indicated, $R_0 > 1$ and this means that, the disease will spread in case there is an
 512 outbreak. Incidentally, an average of one tuberculosis patient contacts 1.1706 susceptible
 513 individuals during an infectious period.

514 The steady states of the two non – negative equilibria were also found and analyzed. The disease
 515 – free equilibrium, $(s^*, e^*, i^*) = (1, 0, 0)$, was found to be unstable (saddle point) while the
 516 endemic equilibrium, $(s_e, e_e, i_e) = (0.914871, 0.00042479, 0.00139106)$, was also found to be
 517 asymptotically stable. These equilibrium points and analyses showed that the presence of an
 518 infected individual in a susceptible population will result in an outbreak of the disease.

519 In the sensitivity analysis, we tried to understand the relationship between the inputs and output
 520 variables of the model. By doing so, we were looking at how changes in the transmission rate (β)
 521 and the recovery rate (γ) affects the endemicity of the disease – free equilibrium and the endemic
 522 equilibrium. In this case, we used the basic reproductive number, R_0 .

523 It was seen that, an increase in the transmission rate or a decrease in the recovery rate will make
 524 $R_0 > 1$ and the disease – free equilibrium is unstable. This indicates that, the disease will spread
 525 when there is an outbreak. Apparently, as the transmission rate decreased or the recovery rate

526 increased, we had $R_0 < 1$ and hence the disease – free equilibrium is also asymptotically stable.
527 This therefore means that the disease will not spread.

528 Also, when the transmission rate was increased or the recovery rate decreased, we had $R_0 > 1$ and
529 hence the endemic equilibrium is stable. This means that the disease will spread when there is an
530 outbreak. On the other hand, as the transmission rate decreases or the recovery rate increases, R_0
531 < 1 , and the endemic equilibrium is in an unstable state. This therefore means that the disease
532 will not spread.

533 It was also found in our model that, increasing the number of infective individuals reduces the
534 number of susceptibles while the number of exposed individuals also increases. This concludes
535 that, if stakeholders fail to put in place proper measures to control and eradicate the disease, it
536 will spread. Hence, immunization programmes as well as education on tuberculosis must be
537 intensified throughout the communities and the country as a whole so that the disease can be
538 curbed down.

539 From our thesis, the herd immunity threshold was estimated to be 0.0851. This means that, about
540 8.51% of the population need to be immunized in order to control the spread of the disease. This
541 is can be effective when early detections are reported at tuberculosis clinics for appropriate
542 treatments. Children should also be vaccinated with Bacillus Calmette–Guérin (BCG) vaccines.
543 This will help effectively disseminate the disease in them. When the percentage of immunized
544 individuals exceed the herd immunity, the disease will fail to spread. Hence 8.51% shows the
545 minimum percentage of the population that must be screened and immunized on regular basis in
546 order for the disease not to spread in the district.

547 From the simulations, it was found out that, an increase in the number of immunized individuals
548 in the population will also increase the level of immunity. This is to say that, if immunization are
549 done on regular basis, especially among children will help increase the number of immunized
550 individuals thereby decreasing the spread of tuberculosis within the community. From this, we
551 can conclude that all children must be vaccinated to avoid making them exposed, because every
552 child that is not immunized increases the number of exposed individuals in the system and this
553 puts a threat in the district.

554

Conclusion

In search for the possible way of eradicating tuberculosis, there is the need to address the issue of the mechanism of the transmission and prevalence of the disease.

Many communicable diseases have been modeled using differential equations. The purpose of this thesis was to examine in detail, a mathematical models for the transmission and prevalence of tuberculosis and then to solve them using differential equations. The following assumptions were made before the model was formulated.

We assumed that the population has a constant size N , where birth and death occur at equal rates and that newborns are susceptible (no inherited immunity). Also, the population is homogeneously mixing, with no restriction of age, mobility or other social factors. We also assumed once infected with tuberculosis bacteria, you become exposed to the environment before becoming infectious.

Based on the assumptions above, which are also consistent with the conditions in Ghana, the tuberculosis model satisfies the SEIR epidemiological model, hence we adopted it to study the prevalence of tuberculosis by classifying the population as susceptible (S), exposed (E), infectious (I) and recovered (R). The model has shown success in attempting to predict the causes of transmission within a population. From the model, it was noticed that the spread of a disease largely depend on the contact rates with infected individuals within a population.

The model gave a basic reproductive number, $R_0 = 1.09305 > 1$. This means that the disease is endemic in the district and this is due to the high level of the transmission rate in the population.

From the model, the herd immunity threshold was found to be 8.51%. It was also realized that if the proportion of the population that is immune exceeds the herd immunity threshold for the disease, then the disease can no longer persist in the population. Thus if this level can be exceeded by mass screening and immunization, then the disease can be eliminated.

The model also pointed out that early detection has a positive impact on the reduction of tuberculosis transmission; that is there is a need to detect new cases as early as possible so as to provide early treatment for the disease. More people should be educated in order to create awareness to the disease transmission so that society will be aware of this deadly disease.

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586

587 **REFERENCE**

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655 APPENDIX

656 M-File for tuberculosis model

```
657 function dy=model(t,y,beta,gamma,mu,epsilon)
658 N= 124507;
659 dy=zeros(4,1);
660 dy(1)= mu*N-mu*y(1)-((beta*y(1)*y(3))/N);
661 dy(2)= ((beta*y(1)*y(2))/N)-(mu+epsilon)*y(2);
662 dy(3)= epsilon*y(2)-(mu+gamma)*y(3);
663 dy(4)= gamma*y(3)-mu*y(4);
664
```

665 Scripts Used in Calling the M-File for Tuberculosis Model

```
666 mu = 0.00875;
667 epsilon = 0.1666;
668 beta = 0.5853;
669 gamma = 0.5;
670 N= 124705;
671 options = odeset('RelTol',1e-9,'AbsTol',1e-9); [T,Y] = ode45(@emmaseir,[0 12],[390 100 10
672 0],options,beta,gamma,epsilon,mu);
673 figure(1)
674 plot(T,Y(:,1),'.')
675 legend('SUSCEPTIBLE')
676 xlabel('Time(Months)');ylabel('POPULATION OF SUSCEPTIBLE');
677 figure(2)
678 plot(T,Y(:,2),'.')
679 legend('EXPOSED')
680 xlabel('Time(Months)');ylabel('POPULATION OF EXPOSED');
681 figure(3)
682 plot(T,Y(:,3),'.')
683 legend('INFECTED')
684 xlabel('Time(Months)');ylabel('POPULATION OF INFECTED');
```

```
685 figure(4)
686 plot(T,Y(:,4),'.')
687 legend('REMOVED')
688 xlabel('TIME (MONTHS)');ylabel('POPULATION OF REMOVED');
689
```