UNIVERSITY OF GHANA

MODELING TUBERCULOSIS TRANSMISSION DYNAMICS IN THE ASHANTI REGION OF GHANA

BY

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THIS THESIS IS SUBMITTED TO THE UNIVERSITY OF GHANA,

LEGON IN PARTIAL FULFILIMENT OF THE REQUIREMENT

FOR THE AWARD OF MPHIL STATISTICS DEGREE

JULY, 2019

DECLARATION

Candidate's Declaration

I Prince Osei Affi certify that this research was done independently in the Department of Statistics and Actuarial Science, University of Ghana as part of the demand for the award of MPhil in Statistics.

…….. ……

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Supervisors' Declaration

We hereby attest that this piece of research was conducted by the candidate himself and supervised in accordance with guidelines on supervision of thesis laid down by the University of Ghana.

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ABSTRACT

In attempt to model tuberculosis epidemic in the Ashanti Region of Ghana, SIR and SEIR deterministic and stochastic epidemiological models with demographic characteristics were employed. Both models showed success in modeling the infection dynamics of tuberculosis in the region. These models equilibrium points were established and their stability investigated through the Routh - Hurwitz stability criterion. The models predicted tuberculosis dying out in the entire region (Disease free equilibrium point stable) and an outbreak in Obuasi municipal and Amansie West district (endemic equilibrium point stable). It was revealed that SEIR model is the ideal model for modeling tuberculosis epidemic in the region since it characterized the infection dynamics of tuberculosis; the initial condition of the exposed compartment has influence on tuberculosis infection dynamics. Also, the branching process approximation of the epidemic revealed that there is a probability of one (1) for TB to be extinct or die out in the entire region. This was confirmed by the values of the thresholds: Malthusian parameter and the average number of offspring in a single generation. Sensitivity analysis was performed to investigate the impact of the model parameters on the reproduction number and it brought to light that increasing the infection and exposed rates increases the reproduction number while increasing the recovery/removal rate decreases the reproduction number. Finally, numerical simulations were done to validate the empirical results obtained and it revealed that all empirical estimates are good approximations for studying TB infection dynamics in the region.

DEDICATION

The thesis is dedicated to the late Esther Affih my mum. May her soul rest well.

ACKNOWLEDGEMENT

Much appreciation goes to the Supreme God for through his support and will that the work has been a successful one.

I show my heartfelt regards to my supervisors: Dr. Felix O. Mettle for his time, support, patience, spur and gigantic knowledge towards the writing of this thesis and Dr. Perpetual S. Andam for her support. I appreciate the immense contribution by Clement Twumasi towards this thesis and I say God bless you.

Clearly, I owe a debt of gratitude to Irene Oppong and the rest of my family for their prayers, help and cheering during the program and I say the good God bless them all.

Lastly, I say thank you to all loved once who gave their quota in several ways to my success in this program.

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List of Abbreviations

ANC	Antenatal Clinic
ART	Antiretroviral Therapy
BCG	Bacille Calmette - Geurin
CDC	Center for Disease Control
CTMC	Continuous Time Markov Chain
DFEP	Disease Free Equilibrium Point
DOT	Detection Observed Treatment
EEP	Endemic Equilibrium Point
GHS	Ghana Health Service
HIV	Human Immunodeficiency Virus
HBsAg	Hepatitis B
IGRA	Interferon – Gamma Release Assays
OPD	Out Patient Department
ODE	Ordinary Differential Equation
PNG	Papua New Guinea
R_o	Basic Reproduction Number
SIR	Susceptible Infected Recovered/Removed
SEIR	Susceptible Exposed Infected Recovered/Removed
SDE	Stochastic Differential Equation
TB	Tuberculosis
WHO	World Health Organization

CHAPTER 1

INTRODUCTION

1.1 Background of study

The study shows the relevance of deterministic and stochastic models. Models employed to study the transmission of communicable diseases are termed dynamic epidemiological models since they study the development of infectious disease over time. The huge spread of communicable diseases in living organisms have increased the need for mathematical epidemiology research in the world by building models to help foretell the spread of communicable disease for development of strategies to help prevent their occurrence. Using deterministic model in studying epidemiology of communicable disease has a very long history. These models have been utilized enormously in studying communicable diseases like: influenza, chicken pox, measles and many more in various contexts (Feng et al., 2000).

Deterministic models provide theoretical results like the basic reproduction number (R_0), thresholds, replacement and contact numbers. In terms of infectious disease, it helps countries, regions and communities to design proper remedies to lessen the infection rate of the disease pathogens (Hethcote, 2000).

Through the application of deterministic models in the transmission of infectious disease among human and animal population the infection dynamics are understood, the direction the epidemic will take when there is an outbreak is predicted, the termination time and the effectiveness of the control measures are evaluated. The accuracy of model developed determines the variability and reliability of the remedies suggested to curb the disease (Trottier and Philippe, 2001).

Stochastic model on the other hand estimates the likelihood distributions of possible outcomes by permitting random variation in one or more input over time. This relies on variation in risk exposure, other diseases as well as the disease itself. It is often employed when random change remains significant (Jacob, 2010).

Deterministic modeling has a limitation of the fact that; the researcher presumed that every individual contact every other individual at the same rate which maybe false for an infectious disease (tuberculosis) because the time for exposure maybe different. It is against this backdrop that the deployment of stochastic model is particularly relevant. Tough the deterministic model has certain challenges or drawbacks for which the stochastic model seeks to address but in all stochastic models average the outcomes of the deterministic mathematical model (Murray et al., 1986 and Murray, 1989).

In this study, the focus is on stochastic branching process for tuberculosis epidemic and developing some stochastic threshold such as the Malthusian parameter. This parameter measures the intrinsic growth rate of the epidemic (branching process). Branching process conjecture will help determine the likelihood of disease (tuberculosis) disappearance in Ashanti region even at the being of the study. Get et al. (2006) has extensively used this type of modeling approach to learn the infection dynamics of measles and smallpox.

1.2 Tuberculosis

This is a communicable disease that affects living organisms. The causative organism is the Mycobacterium tuberculosis organism. This organism looks rod-like in shape and grows at a slow pace. The organism possess' highly acidic cell wall content hence hydrophobic and

resistant to oral fluid. Millions of people over the world are being killed by tuberculosis. Roughly, one-third of the world's population is infected by tuberculosis (WHO, 2011). Figure 1.1 below displays the mycobacterium tuberculosis under a microscope.

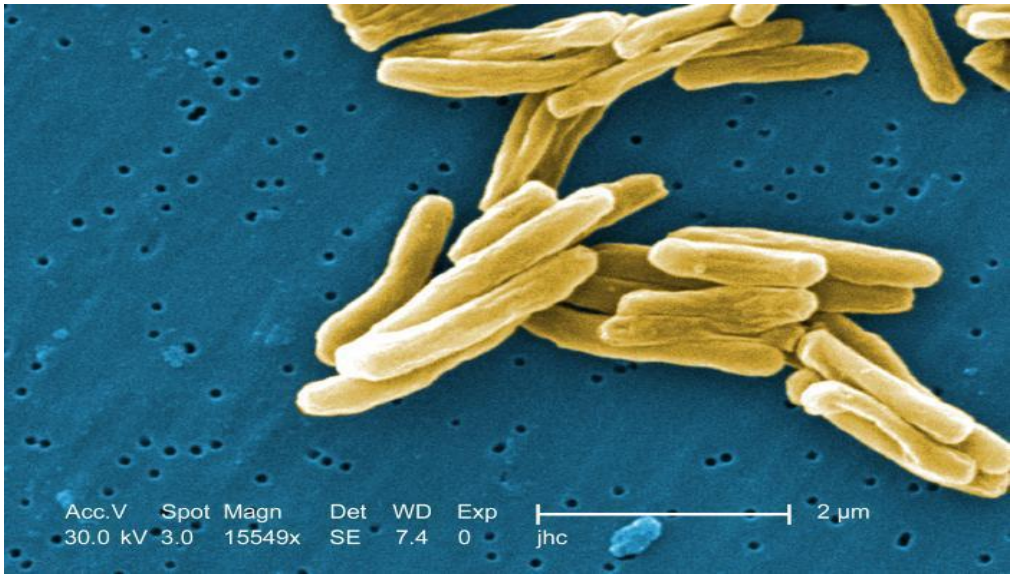


Figure 1.1 Mycobacterium tuberculosis under a microscope

1.2.1 Aetiology and Clinical Manifestation of Tuberculosis

The Mycobacterium tuberculosis is transmitted from one individual to another when the individual inhaled a droplet of saliva or mucus released into the air by an infected person through sneezing, talking or coughing. Macrophage covers the tuberculosis bacteria when the infected particles get into the alveoli of another cell. The bacteria then move to the lymphatic system as well as other organs of the human body. Tuberculosis bacteria increase under oxygen pressure. HIV infections, low socioeconomic status, migration, alcoholisms, crowded living condition, HBsAg are some of the risk factors of tuberculosis disease. One is prone to tuberculosis if the individual has any conditions that enfeeble the immune system.

The initial stage of tuberculosis is asymptomatic in most instances, unless the disease has progress into active tuberculosis. Loss of appetite and chills, fever, diaphoresis at night, fatigue, unexplained or intended weight loss, cough for prolong duration, this for more than three weeks are all common symptoms of tuberculosis. Though, having these signs does not guarantee one to have tuberculosis. There are other several symptoms, in such instances one needs to undergo tests to be sure to have tuberculosis. Mostly, the individual's lungs are infected. Some of the clinical manifestations of tuberculosis of the lungs are: haemoptisis, chest pain and coughing. Active TB infection may sometimes differ depending on the organ affected, usually in it's signs and symptoms.

Other organs that are infected are: lymph nodes, adventitia, genitourinary nodes, and bone and joint sites (WHO, 1993).

1.2.2 Testing for Tuberculosis Infection

A tuberculosis infection bacterium is detected by two main types of test: tuberculosis blood test and the tuberculin skin test. Either test showing positive results simply means the individual has tuberculosis infection. Further test like x-ray of the chest and sample sputum are mostly done to determine the extent of the infection (WHO, 2006).

1.2.2.1 Test for Tuberculosis in the Blood

Interferon-gamma release assays (IGRA) is the name given to the Test for Tuberculosis in the blood. This measures how the individual's immunity response to the Mycobacterium TB. This

test can be done at the medical laboratory by taking blood sample for the IGRA test (WHO, 2006).

1.2.2.2 The Tuberculin Skin Test

This type of test is done by the introduction of tuberculin into the skin in the lower arm. The manifestation of the presence of Mycobacterium tuberculosis is observed after two to three hours by health professional. The size of the portion where reaction took place determines the extent of the tuberculosis infection progression (WHO, 2006).

1.2.3 Treatment of Tuberculosis

Health workers usually treat an individual infected with tuberculosis by prescribing antibiotics for 6 to 12 months. Special medications are used in the treatment of tuberculosis. Bacille Calmette-Geurin (BCG) vaccine is also used to prevent tuberculosis in newly born individuals (WHO, 2000b). This vaccine was obtained from strain of Mycobacterium bovis. The antibiotics used for the treatment have their own side effects since they are taken for a longer period. With all these medication there is still the chance of some infected individuals dying.

According to CDC (2007), between 4 to 6 out of every 10 infected individual under treatment die. Also there is a possibility of an infected individual getting cured totally when the individual co-operate fully in the treatment program. Tuberculosis infection can be treated either at the incubation stage or infectious stage with the antibiotics remedy. When individuals fail to co-operate fully with the treatment program and default taking the full dose of the medication then the treatment program will have to be started all over again.

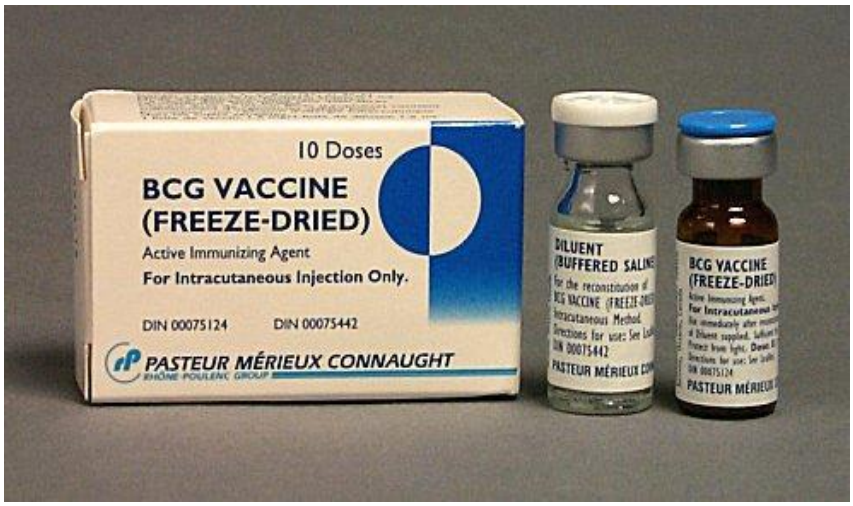


Figure 1.2 BCG Vaccine

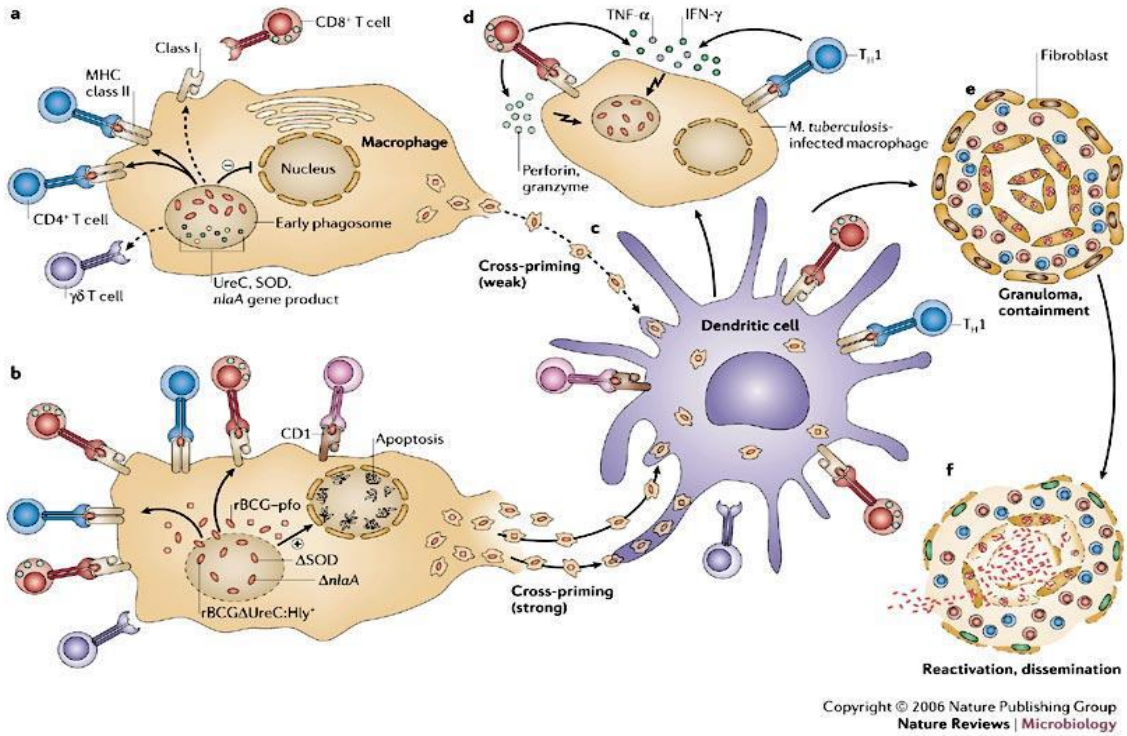


Figure 1.3 Immune responds to Mycobacterium tuberculosis infection

1.3 Problem Statement

Tuberculosis continues to remain as one of the major global health problems despite the highly efficacy treatment availability over the years. For instance in 1993, World Health Organization made it known to the global world that TB infection is a public health emergency. WHO (2011), indicated that 1.2 – 1.5 million individuals died out of 8.5 – 9.2 million tuberculosis cases.

In Ghana, it is reported that over 46,000 new cases are recorded annually (WHO, 2016). Though in July, 1954 a body was established to be supporting and supplementing the effort made by the government to help curb tuberculosis in Ghana (GHS – Stop TB Prog., 2012). Despite the effort by the government and the body established tuberculosis still remains a public health problem causing more deaths in Ghana (CDC, 2017). The current records published on tuberculosis indicates that 11,738 (6.25%) of the total deaths are as a results of tuberculosis infection and that tuberculosis is ranked among the top ten causes of deaths in Ghana (CDC, 2017).

Ashanti region is the most densely populated region in Ghana recording 4,780,380 individuals out of the 26million people (Ghana Population Census, 2010). Hence there is therefore the need for epidemiology research in Ghana specifically in the Ashanti region to study the infection dynamics of tuberculosis and suggest appropriate recommendations to help control the spread of tuberculosis base on conclusions from the epidemiology research.

1.4 The Study Objectives

The principal study objective is to model tuberculosis epidemiology in the Ashanti region of Ghana. Specifically, this study seeks to:

- Fit both the SIR and SEIR deterministic and stochastic epidemiological models with demography.
- Investigate into the steady state stability of the equilibrium points of both models.
- Study the relationship between the basic reproduction number and some stochastic thresholds.
- Derive the probability of tuberculosis extinction.
- Validate the empirical results by numerical simulation.

1.5 Methodology

The study used administrative data compiled by Ashanti regional health directorate. The data contained the screening report on tuberculosis in the Ashanti region of Ghana for the year 2017. Deterministic and stochastic models will be formulated using differential equations based on epidemiological compartment modeling. R statistical software package will be use to solve the differential equations and perform the numerical (sensitivity) analysis.

1.6 Significance of study

The mathematical epidemic models (SIR and SEIR) formulated will give an in-depth examination of the inherent dynamics of tuberculosis epidemiology and its spread over a given period of time. With the Galton – Watson branching process approximation, tuberculosis epidemic prediction will become apparent. Several studies have been done on tuberculosis epidemiology in Ghana specifically in the Ashanti region but none of them employed SIR and SEIR epidemic model with demography. As a result, the study will therefore be of importance by helping policy makers to make good intervention in controlling TB infection in the Ashanti region.

1.7 Organization of study

The study is organized in 5 chapters. Chapter 1 comprise of background of tuberculosis, problem statement, study aims, methodology and significance of study. Chapter 2 focuses on the review of other studies related to the topic under study. Chapter 3 presents the review of the methodology. Thus the mathematical models and statistical tools relevant to the study are looked at. The SIR and SEIR deterministic model, their stochastic equivalent and the Galton - Watson branching process are the mathematical and statistical models highlighted under the Chapter 3. Chapter 4 also displays the analysis and discussion of the study findings. Chapters 5 consist of summary of study outcomes, conclusions and recommendations. Finally the study ends with References and Appendices which provide support to the investigator in the investigation.

CHAPTER 2

LITERATURE REVIEW

This section reviews related works by several authors with regards to tuberculosis infection. In modeling infectious disease (tuberculosis) stochastic and deterministic models are very useful hence the empirical works and authors' opinions are looked at. The review focuses on the following:

- Application of Epidemic models other than the SIR or SEIR model
- Application of SEIR(S) Deterministic models
- Description of SIR and SEIR Deterministic models
- Application of Stochastic SIR or SEIR models
- Branching Processes

2.1 Application of Epidemic models other than the SIR or SEIR(S) Model

Blower, et al. (1995) in their study investigated into the reasons why tuberculosis epidemic rises and why it falls dramatically in advance countries before effective therapy. They did this by building two mathematical models one simple and one complex or detailed. They formulated the susceptible (X), latent infected (L) and the infectious (T) deterministic model for the simple model. This was done by dividing the population into three groups. They assumed that an individual develop Tuberculosis either by endogenous reactivation or direct progression. Their detailed model was a build up on the simple one with the detailed model including a situation where tuberculosis will be cured without treatment, a case where the individuals in the recovery group can relapse and finally only a section of cases are taken to be contagious. Latin hypercube

was the sampling method they employed in the sensitivity analysis to estimate R_o (basic reproduction number) and its distribution function.

They found that out of the three proposed factors responsible for the tuberculosis infection dynamics prior to treatment, population growth result in the population size exceeding the threshold and hence lead to $R_o > 1$. Also the reaming proposed factors urbanization and industrialization also increases the transmission coefficient and reduced the threshold population size necessary to initiate epidemic. According to them these factors simultaneously influence the sudden rise in the population size of the threshold population. From their simulations they found out that R_o (basic reproduction number) was high hence the rise of tuberculosis prior to effective therapy.

Castillo and Feng (1998) looked into the global stability of an age – ordered model built to study infection dynamics of tuberculosis subjected to vaccination scheme. With the formation of the age – structure model, they developed a deterministic model by grouping the population into five (susceptible, vaccination, exposed, infectious and treated) categories. They assumed that the population is proportionate mixed as in the case of Hethcote and Yorke (1984), Dietz and Schenzle (1985), May and Anderson (1984) and Castillo et al. (1989).

In achieving the aim of their study they proved that the disease-free equilibrium point (DFEP) was globally stable once the R_o is less than one and also endemic steady state exist if R_o in the existence of vaccine is greater than unity. They then used the conceptual outcomes to formulate policies to obtain optimal age or ages where the individual will have to be vaccinated.

In the study by Thomas, et al. (2010) the motivation of their study was to study the infection dynamics of tuberculosis in the presence of drug resistance as well as HIV. The study was rooted on data from Papua New Guinea (PNG) western provinces in order to provide recommendation guide to policy makers in Papua New Guinea and Australia since there is a high likely cross border spread linking PNG western province and Australia Torres – strait Islands. Thomas, et al. (2010) developed two deterministic models like what Blower, et al. (1995) did one simple and the other detailed for TB in the PNG western provinces. The detailed model included drug resistance and HIV. The simple model unlike Blower, et al. (1995) added a fourth class called the non – infectious. That is the susceptible (X), latent infected (L), infectious (T_1) and then non – infectious (T_N). To develop the detailed model they expanded the simple model by adding the influence of HIV infection and drug resistance strains of tuberculosis. The population was first grouped into two that is HIV positive and negative. For those with TB the individuals were classified as drug – sensitive TB (DSTB) and multidrug – resistance TB (MDRTB). The HIV negative population was classified as susceptible (X_N), latent infected with drug sensitive TB (L_N), infectious DSTB (T_{N1}), non – infectious DSTB (T_{NN}), latently infected with MDRTB (L_{NM}), infectious MDRTB (T_{NM1}) and Non infectious with MDRTB (T_{NMN}). They then did the same classification for HIV positive population with the first subscript N in the above replaced by H.

The analysis focused on TB prevalence and population size from 1895 to 2019. The results from both models were quantitatively the same but vary in the detailed model. The prevalence of TB moves rapidly with the simple model than as with the detailed model and peaks two decades before. But after the detection observed treatment (DOTS) program in 1997 the

prevalence with the simple model reduce slightly than that of the detailed model such that TB prevalence indicated by the detailed model is 13% less than for the simple model by 2020.

In an attempt to study how the misgivings in the output of tuberculosis epidemiological model can be apportioned to different sources of uncertainty in its input in Papua New Guinea, Hickson, et al. (2011) constructed a simple model in relation to Thomas, et al. (2010). Their model included aspects important to explore the DOTS intervention recommended by the WHO. They divided the population into six compartments with four describing the different stages of the disease that is susceptible, latently infected, extra pulmonary and pulmonary and the remaining two were from the DOTS intervention program (detection and treatment). But the first four stages can also be further grouped into three as in the case of Blower et al.(1995), as susceptible, latently infected and infectious hence SEI model.

Hickson, et al. (2011) also used Latin hypercube sampling method used previously by Blower, et al. (1995) to determine the parameter space. Their findings showed that the most relevant parameter for TB infection in PNG was the rate of advancement from incubation to active TB clinically. The most important intervention parameter was the detection parameter for the DOTS program, hence they suggested that the DOTS program should be increased in coverage and the rate of advancement from incubation to infectious period should be concentrated upon.

Feng, et al. (2000) also looked at the impact of exogenous re-infections on the spared of tuberculosis. Castillo and Feng (1998b) model was the basis of their model to study the influence of exogenous re-infection on the transmission dynamic of tuberculosis. They were of the notion that only small section of the population progresses to active TB following the primary infection

but most individuals at the latent phase are at risk of developing active TB as a result of the impact of exogenous re-infection of latent bacilli. The population was splitted into four classes (susceptible, exposed, infectious and effective treatment) that is the SEIT model with a term to model the exogenous re-infection rate.

They found out that exogenous re-infection has drastic impact on the qualitative dynamics of TB. They also recommended that decreasing R_o may not be enough to get rid of the infection but an extra decreasing in the re-infection rate may be required. To them this might elaborate the recently observed re-emergence of TB.

In the research of Chen Junjie and Liu Xiangguan (2006), the aim of their study was to investigate into SEIS epidemic model equilibrium point stability with continual recruitment and a varying total population size. Their work considered infectious drive at the incubation stage and a population dependent contact rate. Their model was based on Meng, et al. (2001) and Genik, et al. (1998). The model as usual with deterministic mathematical models was constructed by dividing the population into three groups (susceptible (S), exposed (E) and infectious (I)). The model with infectious drive at the incubation stage and continual recruitment was analyzed quantitatively. The model showed two equilibria that is disease free equilibrium and unique endemic equilibrium. The DFEP is globally asymptotically stable once the threshold (R_o) is lower than one and EEP stable if and only if the threshold (R_o) is more than one.

Sarkodie (2014) modified the SEIS model by Castillo (1989b) with varying population size to a non-varying population size to fore tell the spread of tuberculosis in the central region of Ghana. The population was divided into three groups. Individuals will either belong to a susceptible class, exposed or infectious class. He assumed that an infectious individual may die

from the disease or recover with no acquired immunity to the disease and become susceptible again. Disease - free and endemic equilibrium points were the two equilibrium points of his model. After the stability analysis, it was revealed that the endemic equilibrium point was stable while disease – free was not. The R_o was equal to two hence TB will persist in the region. The sensitivity analysis he performed also revealed that the most sensitive parameter that controls the transmission of TB in the central region was the initial infection rate of susceptible.

In conclusion deterministic mathematical model related to the study of tuberculosis transmission dynamics in several nations have been there for long. Several mathematical models have been developed to study the spread of tuberculosis. Very few or no study have been done on the use of SEIR and SIR models with demography on the transmission of TB in Ashanti region.

2.2 Application of SEIR(S) Deterministic Models

In epidemiological study with deterministic approach when the population is grouped into four that is susceptible (S), Latent (E), infectious (I) and recovery (R), susceptible individual may be considered to first move through the latent period after contact with infectious individual before entering the infectious stage. The model types are SEIR or SEIRS respectively depending on the acquisition of immunity after recovery whether perennial or not. Several researchers have explored this area.

Li, et al. (1995) investigated the global stability for the SEIR model with a non-sequential occurrence rate. The equilibrium point stability was investigated and it was revealed that the

endemic equilibrium point was stable when ever R_0 is bigger than one and Disease-free stable when R_0 is lesser than one.

Li, et al. (1999) again considered the global dynamics of SEIR model with varying population size. The force of infection was considered to be proportionate mixing. A threshold was identified and used in studying the stability behavior of the disease – free and the endemic equlibria globally. When the defined threshold ɗ ≤ 1 then the disease – free equilibrium was stable globally and when ɗ > 1, then the endemic equilibrium was also stable.

Li, et al. (2001) continued the study on the global dynamics of an SEIR model but this time with vertical transmission for the spread of infectious disease like tuberculosis. Transmission of the infection can be horizontal and vertical with a portion "p" of newborns from the latent compartment and a section "q" also of newborns from the infectious group considered to be infected at birth. R_o (p, q) was defined as the sensitive threshold to determine the global dynamics of their model. It was revealed in their model that if their basic reproduction number R_o (p, q) ≤ 1 then the disease – free equilibrium was globally stable in the search space but when R_o (p, q) > 1 then unique endemic exist and globally stable in the search space. Their study outcome gave a generalize picture on the global stability study by Li, et al. (1995) where no vertical transmission was considered. The endemic equilibrium global stability analysis was shown using the procedure by Li, et al. (1996).

Li, et al. (2005) looked into the global stability of an SEIR epidemiological model but with infectious drive at the incubation, infectious and immune stage. The R_o was obtained and the stability analysis of the two identified equilibria was performed. Similar results shown in Li

et al. (2001) were revealed. That is the disease – free was globally asymptotically stable when $R_0 \leq 1$ but endemic equilibrium was stable otherwise

Cooke and Driessch (1996) also looked into the analysis of SEIRS model with two delays. They formulated this type of epidemiological model with exponential demographic structure. Any newborn was considered to be susceptible. The host population was presumed to be variable but the latent and immune periods were considered constant. Their model was made up of set of integro – differential equation. The disease – free and endemic equilibrium stability analysis was done, it was revealed that when their important threshold parameter "Ɵ" was identified to be higher than unity, the disease will not fade away but persist and endemic equilibrium point stable. But if identified to be less than one, then the disease dies out and the disease – free equilibrium point becomes stable.

An SEIR model was analyzed with a limiting treatment resource (Sarah A. Al – Sheikh, 2012). The treatment rate was considered directly proportional to the number of patients so far as this number is not up to a certain capacity but becomes constant if the number of patients exceeds this capacity (I_o). It was revealed that the potent performance of the model can be known by its R_o value. The stability analysis showed that the disease – free equilibrium was globally asymptotically stable when $R_o < 1$ that is the disease dies out but on the other hand disease – free equilibrium will become unstable when $R_o > 1$ and Endemic equilibrium set in here. This result on the stability analysis was similar to that of Li, et al. (2006), Driessche and Watmough (2002) and Brauer, et al. (2008). The treatment rate also resulted in the existence of multiple endemic equilibria. She found out that endemic equilibrium exist if and only if $1< R_o \leq P_o$ which will be globally asymptotically stable. Where $P_o = 1 + \beta \frac{I_0}{u}$ and β is the infectious rate and u is the natural death rate.

The model SEIRS was analyzed with saturated incidence rate (Adebimpe et al., 2013). The model as usual with epidemic deterministic models showed two equilibria that is the disease – free equilibrium and the endemic equilibrium. R_0 was identified and used in the analysis of the stability of the equilibria. It was found out that the globally asymptotically stability exist at the disease – free equilibrium whenever the R_o is less than unity and endemic equilibrium was also asymptotically stable when R_o is greater than unity.

Agrawal (2014) also considered an SEIRS model with new modulated saturated occurrence rate. The behavior of the SEIRS model was investigated globally and then R_0 was determined. The stability analysis results were similar to Li, et al. (1995) who studied the global stability for the SEIR model with non-sequential occurrence rate. There exist stability at disease – free equilibrium globally when the basic reproduction number was less than one and endemic stable when otherwise.

In the study of Appoh (2013), the SEIR model was developed to explore the transmission of tuberculosis in Amansie west a district in the Ashanti region. He performed the usual stability analysis of the two equlibria after he has found the R_o. The results of his study were almost the same as most of the already reviewed studies (Agrawal, 2014; Li, et al., 1995; Adebimpe, et al., 2013) and others.

Globally very little study has been done on the infection dynamics of tuberculosis with the SEIR model in relation to the SIR, SEI and SEIS models. Li who have really explore the SEIR model did not regard the effect of treatment being introduced at the latent (exposed) class and the effect of the initial condition of the latent class. They have only considered the introduction of infectious force in the latent (exposed) class (Li, et al., 2005). Chen Junje and Liu

Xiangguan (2006) have also explored the latent class in the same way when investigating into the stability of the SEIS model.

In Ghana, specifically Ashanti region, the only study on the transmission dynamics of tuberculosis which fitted an SEIR model was by Appoh (2013). The study by Appoh (2013) did not consider the effect of the initial condition of the exposed compartment on the infection transmission dynamics and also the effect of introducing treatment at the latent class. Hence this study seeks to modify the SEIR model by introducing treatment at the exposed stage. This is to investigate into the effect the treatment will have on the infection dynamics of tuberculosis. Also the initial condition of the exposed compartment impact on the infection dynamics will be investigated. Numerical analysis will be performed to study effect of the SEIR model parameters on the reproduction number.

2.3 Description of Deterministic models

This section describes the mathematical formation and the operation of the two deterministic models: SIR and SEIR models used in the study.

2.3.1 Description of SIR Deterministic model

This is one of the standard epidemic models well studied for the spread of communicable disease in a fixed population medium. The SIR model is an appropriate model for infections that have lifelong or permanent immunity at the recovery state. SIR model is used to model infections that do not undergo incubation, for example mumps and measles.

According to Mckendrick (1926), SIR model is formulated by dividing the total population into three: susceptible (S), Infectious (I) and Recovery/Remove (R). When a susceptible individual comes into contact with an infectious, the new infected individual moves straight to the infectious compartment and later recovers/remove with permanent immunity. The Figure 2.1 presents the generalized SIR model.

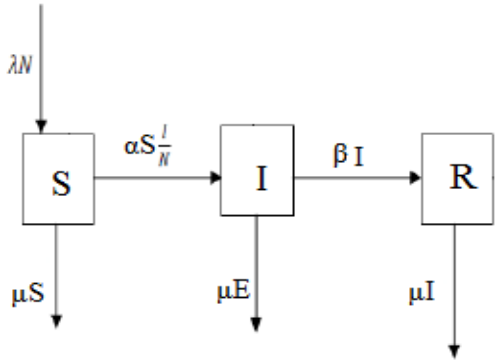


Figure 2.1: Generalized SIR model

The ordinary differential equations below indicate the changes that occur in each of the compartment.

$$\frac{dS}{dt} = \lambda N - \alpha\left(\frac{S}{N}\right)I - \mu S$$

$$\frac{dI}{dt} = \alpha\left(\frac{S}{N}\right)I - (\beta + \mu)I \qquad (2.1)$$

$$\frac{dR}{dt} = \beta I - \mu R$$

$$N(t) = S(t) + I(t) + R(t)$$

$$S(0) > 0, I(0) > 0, R(0) \geq 0$$

Where λ= is the birth rate, μ= death rate, β= recovery rate and α=infection rate

2.3.2 Description of SEIR Deterministic model

SEIR epidemiological model is one of the models developed by Kermack – Mckendrick to study the spread of infectious diseases (Mckendrick, 1926). This model is an expansion of the standard SIR. The model is built as systems of ordinary differential equations (ODE). Almost all the above reviews were developed from the original model by Kermack – Mckendrick. For example Hethcote (2000) and Li, et al. (1995) studied several mathematical models whose groups and interactions were subset of the SEIRS model. Building the SEIR model the host population is split into four groups or class at each point in time.

Susceptible (S), exposed (E), infectious (I) and recovery/remove (R) are the four groups. Susceptible class is made up of individual who do not have any form of immunity to the disease that is they can be infected upon coming into contact with infectious persons. When there is enough contact a susceptible individual proceed to the incubation class. That is what is normally referred to as the incubation period. Individuals in the incubation class are not yet infectious. After the end of this, the incubated individual then invades the infectious class. Any individual who finds him or herself in this class is capable of transmitting the disease. That is they can infect new individuals. When infectious period is over the infected individual now enter into the recovery class. At the recovery class the individual is anticipated to attain permanent immunity after recovery. That is a recovered individual cannot be infected again. This SEIR model has been extensively used by: Li, et al. (1999), Li, et al. (1995), Li, et al. (2001), Hethcote (1976), Andersson and Britton (2000), Cooke and Driessch (1996) and Sarah A. Al – Sheikh, (2011).

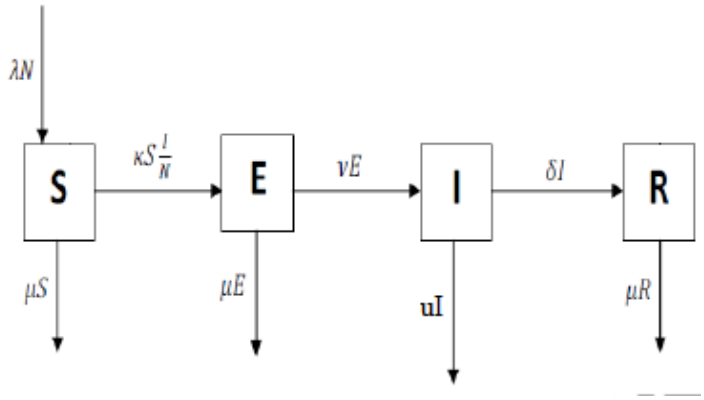


Figure 2.2: Generalized SEIR deterministic model

The corresponding change in each class of the SEIR model is giving by the following systems of ordinary differential equations.

$$\frac{dS}{dt} = \lambda N - K\left(\frac{S}{N}\right)I - \mu S$$

$$\frac{dE}{dt} = K\left(\frac{S}{N}\right)I - (v + \mu)E \qquad (2.2)$$

$$\frac{dI}{dt} = vE - (\delta + \mu)I$$

$$\frac{dR}{dt} = \delta I - \mu R$$

$$N(t) = S(t) + E(t) + I(t) + R(t)$$

$$S(0) > 0, E(0) > 0, I(0) > 0, R(0) \geq 0$$

Where λ= is the birth rate, μ= death rate, δ = recovery rate, ν = exposed rate and α=infection rate

The SEIR model which will be formulated in this thesis is a particular case of the SI, SIR, SEI, models. When $v \to \infty$, then the exposed class moves away and hence SIR model is formed. When $\delta = 0$ then there is a lifelong infective which results in the SEI model. Finally, if $v \to \infty$ and $\delta = 0$ then the exposed class moves away and we have lifelong infective which also result to SI model.

2.4 Application of Stochastic SIR or SEIR models

Stochastic models are seldomly used to study the spared of contagious disease. Few works has been done on infection dynamics of contagious disease with stochastic SIR and SEIR compartment models.

Mudassar, et al. (2013) compared a deterministic and stochastic model for the study of hepatitis C with segregation stage. They developed the compartment epidemic SIR model with severe chronic and segregation class. They then analyzed the influence of the segregated class on the infection dynamics of the Hepatitis C. With the help of Ro they perform the stability analysis that is when $R_o \leq 1$ disease dies out and when $R_o > 1$ disease persist. It was also realized that increasing the rate of segregation of chronically infected persons minimized the spread of the disease.

They then formulated the stochastic model equivalent of the deterministic model with continuous time markov chain (CTMC). This model also showed to a large extent the same behavior as the compartment model with the exception that there was a positive chance of disease extinction regardless of the value of the reproduction number (R_o).

Mbaya and Ondami (2016) formulated the stochastic version of the SEI model. The stochastic model was developed base on Allen (2008). The transition probabilities were obtained. They then performed some numerical simulations to verify the validity of their theoretical results. Mbaya and Dimi (2016) considered an individual modeling for tuberculosis set in environmental noise. SEI deterministic model was the framework of their individual (stochastic) model hence its equivalent stochastic model was formulated. They showed for the existence of the global stability and stochastic stability using the lyapounov function.

Pertsev, et al. (2014) used stochastic model to analyzed the spread of tuberculosis with regards to reproduction and seasonal immigration of individuals. They observed that both reproduction and seasonal migration affect the spread of tuberculosis.

The probability that polio will die out in a given period of time *t* was studied by Eichner and Dietz (1996). They simulated a continuous time markov process with the inclusion of vaccination. They realized that the size of the vaccination compartment included in the SIR model has effect on the spread of polio.

Allen (2017) developed a primer on stochastic epidemic models. Allen's intention was to provide introduction to newcomers to the field of epidemiology modeling using stochastic model. The SIR deterministic model was the basis for the development of the stochastic model. Two stochastic settings were employed in building the stochastic models Allen introduced: the CTMC and SDES. Gillespie algorithm and Euler – Maryam numerical method are described for the two individual processes. Allen also introduces freshers in the field to some systematic methods from a single type branching processes that are related to CTMC models example to approximate the chance of an outbreak and extinction of an infectious disease.

This study will develop the stochastic model equivalent of the SIR and SEIR deterministic models to explore the extinction and outbreak probability of tuberculosis using the continuous – time discrete state Galton – Watson branching process.

2.5 Branching Processes

One of the main features of biological population is the fact that individuals undergo birth and death processes and carry information passed on from their parents at birth. This phenomenon is a random process since the number of births an individual gives rise to is not deterministic but random. This phenomenon can be model by branching processes by making some simple assumptions.

Branching process is an individual process that uses markov process to model a population in which each individual in generation n gives rise to some random number of individual in generation n+1, according to a fixed probability distribution that does not change from an individual to the other. This process is used to model reproduction and other systems with similar dynamics for example the transmission of infectious disease in a community. Watson and Galton (1875) described a family tree from the perspective of generation. But the real time of development of the number of infective individuals is more interested in the statistical epidemiology.

Mode (1971) used Galton and Watson branching processes in discrete time to model the survival of surnames and from there onwards Jagers (1975) also had many biological applications with it. At time t = 0, i initial ancestors begin their lifetimes. The ancestor in each of their lifetimes gives birth to offspring at time points following poisson process with rate k, and

these offspring start their own life and also give birth to their offspring. Let I(t) be the number of individual that are living in the branching process at time t then the total birth occurs at rate kI(t).

CHAPTER 3

METHODOLOGY

This section center on how the research was conducted. It also shows the theoretical aspects of both mathematical and statistical models and tests used in the thesis.

3.1 Description of data and variables

The study employed administrative data compiled by Ashanti regional health directorate. The data contained the screening report on tuberculosis in the Ashanti region of Ghana for the year 2017. The data was structured in such a way that it presents the screening report on tuberculosis for some twelve (12) districts in the Ashanti region regarded as the high burden districts of tuberculosis by the Ghana health service though the region is made up of twenty seven (27) districts. The remaining fifteen (15) districts were regarded to produce routine cases of tuberculosis which plays insignificant role in the spread of tuberculosis in the region. In the twelve (12) high burden districts of tuberculosis the screening was done in the following units at the various hospitals and health centers located in the districts: General OPD, ART clinics, Reproductive health (ANC), Diabetic clinic, Household contact investigation, pediatric clinic or ward, Female and Male wards.

The variables captured in the data were attendance, number tested for tuberculosis, number diagnosed of tuberculosis, number referred, number initiated on tuberculosis treatment and finally number recovered or died. For this study the needed variables are number diagnosed of tuberculosis (the infectious individual), number recovered or died and number susceptible (number tested for tuberculosis – number diagnosed of tuberculosis).

3.2 Data Analysis

The infection dynamics of tuberculosis in each of the 12 high burdened districts are studied and compared to that of the entire region. Epidemiological models are employed to study the infection dynamics. Infected individual recover from tuberculosis with permanent immunity and also when there is infectious contact it is assumed that the individual goes through the latent (incubation or exposed) period before becoming infectious. The appropriate epidemic model that characterized the infection dynamics of tuberculosis is the SEIR model (Susceptible - Exposed Infected - Recovery model). The data on the exposed or latent individual was not captured better still very difficult to obtain in Ghana because there is no mechanism to detect an individual in the exposed (incubation) period in Ghana. The reduced form of the SEIR model is employed. This model forms the basis of most of the standard epidemic models which is SIR (Susceptible Infected Recovery) model. This model is modified by including demography and excluding the latent compartment (Kermack and Mckendrick, 1933).

Sensitivity analysis is performed on the SEIR model to study the influence of the initial condition of the exposed compartment on tuberculosis infection dynamics in Ashanti region. The influence of SEIR model parameters on the transmission dynamics of tuberculosis is also investigated with the sensitivity analysis. Also the outcome of introducing treatment at the incubation stage of TB transmission is looked at. This sensitivity analysis is done by performing numerical analysis (varying the values of the parameters used in the SEIR models and the initial population size of the exposed class).

For SIR and SEIR models with demography both deterministic and individual modeling approach is employed. With the deterministic modeling the basic reproduction number (R_0) is

obtained using the next generation matrix. The R_0 obtain is use to analyze the equilibrium point of the disease transmission. With the individual (stochastic) modeling the branching process approximation is used. The stochastic threshold: Malthusian parameter (ρ) and $f^{|}(1)$ (the mean number of infections produce by an infectious individual in a single generation) are computed to confirm the outcome of the stability analysis of the equilibrium point. With the help of the branching process approximation, the probability of tuberculosis extinction is deduced. Numerical simulation is done to validate the empirical thresholds obtained.

Finally, the poission distribution is assumed for the birth and death process spanning 52 weeks (one year). All graphical procedures together with all the analysis are carried out in R statistical software package.

3.3 Mathematical formation of the SIR model with Demography

Below are assumptions employed in the formation of deterministic SIR model with natural birth and death:

- An individual can be infected by physical contact with an infected person.
- The disease transmission is in a closed system hence the size of the population remains the same (demography: birth rate "λ" equal to death rate "μ" $\Leftrightarrow \lambda = \mu$)
- Infectious individual recover with permanent immunity.

3.3.1 The Deterministic SIR model with Demography

This type of deterministic or compartment model is developed by splitting the host population into three categories that is: Susceptible (S), Infectious (I) and Remove/Recovery (R)

($N = S+I+R$) where N is the host population.

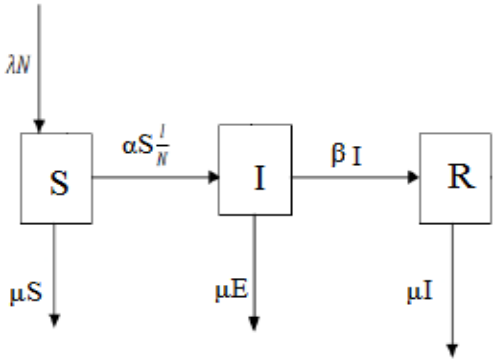


Figure 3.1 Illustration of the SIR model.

Where λ= birth rate, μ = death rate, α = infection rate and β = remove/recovery rate of the infected person.

Above stated assumptions and Figure 3.1 lead to the system of ordinary differential equations presented in equation (3.1) to indicate the rate of change from one class to the other.

$$\frac{ds}{dt} = \lambda N - \mu S - \alpha S\frac{I}{N}$$

$$\frac{dI}{dt} = \alpha S\frac{I}{N} - (\beta + \mu)I \qquad (3.1)$$

$$\frac{dR}{dt} = \beta I - \mu R$$

We re-scale the equation above by representing $s = \frac{S}{N}, i = \frac{I}{N}$ $and\, r = \frac{R}{N}$ where s = susceptible proportion of the population, i = infectious proportion and r = recovery proportion (Affi, 2018). The scaled equations are given in equation (3.2):

$$\frac{ds}{dt} = \lambda - \mu s - \alpha s i$$

$$\frac{di}{dt} = \alpha s i - (\beta + \mu) i \qquad (3.2)$$

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

where $s + i + r = 1$.

From the relation above we make "r" the subject to get $r = 1 - s - i$; hence it is enough to study the system in equation (3.3) instead of equation (3.2) (Britton, 2017).

$$\frac{ds}{dt} = \lambda - \mu s - \alpha s i$$

$$\frac{di}{dt} = \alpha s i - (\beta + \mu) i \qquad (3.3)$$

3.3.1.1 Computation of the Basic Reproduction Number of SIR model

According to Roy and Robert (1991), Diekmann and Heesterbek (1990), basic reproduction number (R_0) is the mean number of secondary infections produce by one infective individual in a completely susceptible population at the DFEP. That is:

R_0 = (Rate of secondary infections) × (Infectious period).

It is presumed that "s" is close the disease – free equilibrium hence we linearlized the ODE's in equation (3.3) about the DFE since infectious class "*i*" only contains the infection (Affi, 2018).

We denote the rate of secondary infections as "α" and the rate of removal/recovery as β hence the average infectious period (duration) is $\frac{1}{\beta}$. Similarly if "*u*" is the natural death rate then the life expectancy is $\frac{1}{\mu}$ (Junjie and Xiangguan, 2006). Base on the condition above, the mean infectious period from equation (3.3) is $\frac{1}{\beta+\mu}$.

$$\Rightarrow R_0 = \alpha \times \frac{1}{\beta+\mu} = \frac{\alpha}{\beta+\mu} \qquad (3.4)$$

3.3.1.2 The Equilibrium Point of the SIR model

For this study two equilibrium point are considered that is: the disease – free equilibrium point (DFEP) where $i = 0$ and the endemic equilibrium (EEP) also $i \neq 0$. To achieve this, system in equation (3.3) are set to zero and then the values of "*s*", and "*i*" are solve for.

$$\frac{ds}{dt} = 0 \Rightarrow \lambda - \mu s - \alpha si = 0$$

$$\frac{di}{dt} = 0 \Rightarrow \alpha si - (\beta + \mu)i = 0 \qquad (3.5)$$

3.3.1.2.1 Disease – Free Equilibrium Point

At the disease – free equilibrium point it is presumed that there is no infection in the system hence $i = 0$. This results in the following from equation (3.5):

$\lambda - \mu s - \alpha s(0) = 0$

$\alpha s(0) - (\beta + \mu)(0) = 0$

These equations at the DFE reduces to

$\lambda - \mu s = 0$

$\lambda = \mu s \Rightarrow s = \frac{\lambda}{\mu}$

Therefore at the DFE $(s, i) = \left\{\frac{\lambda}{\mu}, 0\right\} = \{1,0\}$ since the host population is constant ($\lambda = \mu$).

3.3.1.2.2 The Endemic Equilibrium point

The endemic equilibrium point shows that the disease will persist in the system at the steady state. Here we solve the equations (3.5) to obtain "*s*" and "*i*". But for easy identification "*s*" and "*i*" are represented by (s^*, i^*) at the steady state of the endemic respectively.

From $\alpha si - (\beta + \mu)i = 0 \Rightarrow \alpha si = (\beta + \mu)i$

$s = \frac{(\beta + \mu)i}{\alpha i} \Rightarrow s^* = \frac{\beta + \mu}{\alpha}$

Also from $\lambda - \mu s - \alpha si = 0 \Rightarrow \lambda - \mu s = \alpha si$

$i = \frac{\lambda - \mu s}{\alpha s}$ and $s = \frac{\beta + \mu}{\alpha}$ hence substituting "s" into "*i*" gives

$$\Rightarrow i = \frac{\lambda - \left(\frac{\beta + \mu}{\alpha}\right)\mu}{\alpha\left(\frac{\beta + \mu}{\alpha}\right)} = \frac{\lambda - \left(\frac{\beta + \mu}{\alpha}\right)\mu}{\beta + \mu}$$

$$i = \frac{\frac{\lambda\alpha - \mu(\beta+\mu)}{\alpha}}{\beta+\mu} = \frac{\lambda\alpha - \mu(\beta+\mu)}{\alpha} \times \frac{1}{\beta+\mu}$$

$$i^* = \frac{\lambda\alpha - \mu(\beta+\mu)}{\alpha(\beta+\mu)}$$

Hence at the endemic equilibrium point we have:

$$(s^*, i^*) = \left(\frac{\beta+\mu}{\alpha}, \frac{\lambda\alpha - \mu(\beta+\mu)}{\alpha(\beta+\mu)}\right)$$

3.3.1.2.3 Stability of the Equilibrium Points

To study the stability of the equilibrium points obtained above with the Routh – Hurwitz stability criterion we considered the linearization of the system of equation (3.3) about the DFE by taking the Jacobian of them (Britton, 2017).

3.3.1.2.4 Routh-Hurwitz Stability Criterion

This criterion is a procedure that can be used to confirm the stability of a system without solving its characteristics equation (Hurwitz, 1964). Taking the characteristics equation below into consideration

$\lambda^n + a_1\lambda^{n-1} + \ldots\ldots\ldots + a_{n-1}\lambda + a_n = 0$, where a_i are real constants, $i = 1,2,\ldots\ldots,n$ and using the a_i the n Hurwitz matrices are define as: $H_1 = (a_1)$, $H_2 = \begin{pmatrix} a_1 & a_3 \\ 1 & a_2 \end{pmatrix}$,

$$H_3 = \begin{pmatrix} a_1 & a_3 & a_5 \\ 1 & a_2 & a_4 \\ 0 & a_1 & a_3 \end{pmatrix}, \text{ and } H_n = \begin{pmatrix} a_1 & a_3 & a_5 & & 0 \\ 1 & a_2 & a_4 & \cdots & 0 \\ 0 & a_1 & a_3 & & 0 \\ & \vdots & & \ddots & \vdots \\ 0 & 0 & 0 & \cdots & a_n \end{pmatrix}$$

where $a_j = 0 \; if \; j > n$. Also all the roots of the characteristic equation above will have negative real part if the determinant of all the Hurwitz matrices listed above are positive that is

$|H_j| \geq 0, j = 1,2,3, \ldots, n$ but when $n = 2$ (the degree of the characteristic equation) the Routh-Hurwitz criterion simplifies to $H_1 = a_1 > 0 \; and \; |H_2| = \begin{vmatrix} a_1 & a_3 \\ 1 & a_2 \end{vmatrix} = a_1 a_2 - a_3 > 0$

The summary of the Routh-Hurwitz criteria are presented below for a characteristic equation with degrees $n = 2,3,4$

When $n = 2$: $a_1 > 0, and \; a_2 > 0$

When $n = 3$: $a_1 > 0, and \; a_3 > 0 \; and \; a_1 a_2 > a_3$

And finally when $n = 4$: $a_1 > 0, a_3 > 0, a_4 > 0 \; and \; a_1 a_2 a_3 > a_3^2 + a_1^2 a_4$

Macher (1964) proved the Routh – Hurwitz criterion above in a case where the degree of the characteristic equation is two ($n = 2$). That is $\lambda^2 + a_1 \lambda + a_2 = 0$

The root (eigen values) of the characteristics equation satisfy this relation $\lambda_{1,2} = \frac{-a_1 \pm \sqrt{a_1^2 - 4a_2}}{2}$

Assuming $a_1 \; and \; a_2$ are positive then the roots are real and both negative but if they are complex conjugates then they have real part. Also if they are either negative or have negative real part then $a_1 > 0$ and if root are complex conjugate $0 < a_1^2 < 4a_2$ then it implies a_2 is also positive.

3.3.1.2.5 Stability of the endemic equilibrium point

An epidemic occurs if the number of infected individual is greater than zero that is:

$$\alpha si - (\beta + \mu)i > 0$$

$$\alpha si > (\beta + \mu)i \Rightarrow \frac{\alpha si}{(\beta + \mu)i} > \frac{(\beta + \mu)i}{(\beta + \mu)i}$$

$$\frac{\alpha s}{(\beta + \mu)} > 1$$

But at the beginning of an epidemic nearly every one with the exception of the index case is susceptible hence the susceptible proportion $s \simeq 1$. Putting $s = 1$ into the relation $\frac{\alpha s}{(\beta+\mu)} > 1$ result in the inequality

$\frac{\alpha}{(\beta+\mu)} > 1 \Rightarrow R_0 > 1$ which leads to the Theorem 3.1.

Theorem 3.1: The endemic equilibrium point of system (3.3) is asymptotically stable when $R_0 > 1$ and unstable when $R_0 < 1$.

Proof:

At the endemic equilibrium point we have showed that:

$$(s^*, i^*) = \left(\frac{\beta + \mu}{\alpha}, \frac{\lambda\alpha - \mu(\beta + \mu)}{\alpha(\beta + \mu)}\right)$$

Hence the Jacobian matrix at the endemic equilibrium point is:

$$J(s^*, i^*) = \begin{pmatrix} -\mu - \alpha i^* & -\alpha s^* \\ \alpha i^* & \alpha s^* - (\beta + \mu) \end{pmatrix}$$

We let $J(s^*, i^*)_{EEP}$ be the Jacobian matrix at the endemic equilibrium point and then solved for the characteristics equation of $J(s^*, i^*)_{EEP} - \lambda I$ and then set the result to zero. Here "I" is a two by two identity matrix hence $I = \begin{pmatrix} 1 & 0 \\ 0 & 1 \end{pmatrix}$ and $\lambda I = \begin{pmatrix} \lambda & 0 \\ 0 & \lambda \end{pmatrix}$

$$J(s^*, i^*)_{EEP} - \lambda I = \begin{pmatrix} -(\mu + \alpha i^* + \lambda) & -\alpha s^* \\ \alpha i^* & \alpha s^* - (\beta + \mu) - \lambda \end{pmatrix}$$

From this we obtained characteristics equation by finding the determinant of the above matrix and equate it to zero.

$$|J(s^*, i^*)_{EEP} - \lambda I| = \begin{vmatrix} -(\mu + \alpha i^* + \lambda) & -\alpha s^* \\ \alpha i^* & \alpha s^* - (\beta + \mu) - \lambda \end{vmatrix}$$

$$= (\mu + \alpha i^* + \lambda)(\alpha s^* - (\beta + \mu) - \lambda) + \alpha i^*(\alpha s^*)$$

$$= -[\mu\alpha s^* - \mu(\beta + \mu) - \mu\lambda + \alpha i^*\alpha s^* - \alpha i^*(\beta + \mu) - \lambda\alpha i^* + \lambda\alpha s^* - \lambda(\beta + \mu) - \lambda^2]$$
$$+ \alpha^2 i^* s^*$$

$$= \lambda^2 + [(\beta + \mu) - \alpha s^* + \alpha i^* + \mu]\lambda + \mu(\beta + \mu) - \mu\alpha s^* + \alpha i^*(\beta + \mu)$$

Equating the equation above to zero gives :

$$\lambda^2 + [(\beta + \mu) - \alpha s^* + \alpha i^* + \mu]\lambda + \mu(\beta + \mu) - \mu\alpha s^* + \alpha i^*(\beta + \mu) = 0$$

We let Y and Z represent the coefficient of λ and the constant term respectively in the quadratic equation above:

$Y = (\beta + \mu) - \alpha s^* + \alpha i^* + \mu$ and

$Z = \mu(\beta + \mu) - \mu\alpha s^* + \alpha i^*(\beta + \mu)$

The characteristic equation (quadratic) above becomes $\lambda^2 + Y\lambda + Z = 0$. Using the Routh – Hurwitz stability analysis if the condition $Z > 0$ and Y > 0 or YZ > 0 holds then all the zeros of the characteristic equation are negative and hence the endemic equilibrium point is stable and unstable otherwise. To show this is in line with Theorem 3.1 we show that the inequality $Z > 0$ is equivalent to $R_0 > 1$. That is:

$$Z > 0 \Rightarrow \mu(\beta + \mu) - \mu\alpha s^* + \alpha i^*(\beta + \mu) > 0$$

$$\mu(\beta + \mu) - \mu\alpha\left(\frac{\beta + \mu}{\alpha}\right) + \alpha\left(\frac{\lambda\alpha - \mu(\beta + \mu)}{\alpha(\beta + \mu)}\right)(\beta + \mu) > 0$$

$$\lambda\alpha - \mu(\beta + \mu) > 0$$

$\lambda\alpha > \mu(\beta + \mu)$, dividing both sides by $\mu(\beta + \mu)$ becomes

$\frac{\lambda\alpha}{\mu(\beta+\mu)} > 1$, since λ=μ then $\frac{\alpha}{(\beta+\mu)} > 1 \Rightarrow R_0 > 1$

□

3.3.1.2.6 Stability of the Disease – free Equilibrium Point

Unlike the endemic equilibrium point disease – free occurs when $\frac{di}{dt} \leq 0$. This result in $R_0 \leq 0$ and leads to the Theorem 3.2.

Theorem 3.2: The disease – free equilibrium point of the system (3.3) is asymptotically stable if and only if $R_0 \leq 1$and unstable if $R_0 > 1$.

Proof:

At the DFE we obtained the Jacobian matrix about the point (*s*, *i*) = (1,0). This yields the matrix

$$J(s,i) = \begin{pmatrix} -\mu & -\alpha \\ 0 & \alpha - (\beta + \mu) \end{pmatrix}$$

We let $J(s,i)_{DFEP} = J(s,i)$ be the Jacobian matrix at the disease – free equilibrium and solve the characteristics equation of $J(s,i)_{DFE}$. This can be achieved by solving the relation:

$J(s,i)_{DFEP} - I\lambda$ where "I" is the $2x2$ identity matrix, i.e.

$$I = \begin{pmatrix} 1 & 0 \\ 0 & 1 \end{pmatrix} \; and \; \lambda I = \begin{pmatrix} \lambda & 0 \\ 0 & \lambda \end{pmatrix}$$

$$J(s,i)_{DFEP} - \lambda I = \begin{pmatrix} -(\mu + \lambda) & -\alpha \\ 0 & \alpha - (\beta + \mu) - \lambda \end{pmatrix}$$

The determinant of the matrix $J(s,i)_{EEP} - \lambda I$ above gives the characteristics equation hence:

$$|J(s,i)_{DFEP} - \lambda I| = \begin{vmatrix} -(\mu + \lambda) & -\alpha \\ 0 & \alpha - (\beta + \mu) - \lambda \end{vmatrix}$$

$$= -(\mu + \lambda)(\alpha - (\beta + \mu) - \lambda)$$

Expanding this and setting it to zero gives: $\lambda^2 + [(\beta + \mu) - \alpha + \mu]\lambda + \mu(\beta + \mu) - \alpha\mu = 0$

We let Z be the coefficients of λ and A be the constant term hence:

$$Z = (\beta + \mu) - \alpha + \mu$$

$$A = \mu(\beta + \mu) - \alpha\mu$$

And the characteristic equation becomes: $\lambda^2 + Z\lambda + A$.

From Routh-Hurwitz Stability criterion analysis if $A > 0 \; and \; Z > 0 \;\; or \; ZA > O$ holds, then all the roots of the characteristic equation are negative and hence the equilibrium (Disease free

equilibrium) point is stable but unstable otherwise. To show this is in line with Theorem 3.2 we show that the inequality $A > 0$ is equivalent to $R_0 < 1$. That is:

$$A > 0 \Rightarrow \mu(\beta + \mu) - \alpha\mu > 0$$

$$-\alpha\mu > -\mu(\beta + \mu) \Rightarrow \alpha\mu < \mu(\beta + \mu)$$

Dividing both sides of the equation by $\mu(\beta + \mu)$ becomes;

$$\frac{\alpha\mu}{\mu(\beta + \mu)} < 1 \Rightarrow R_0 < 1$$

□

3.3.2 The Stochastic SIR Model

The stochastic model equivalent of the SIR deterministic model is developed in this section. The stochastic equivalent is developed using the Continuous Time Markov Chains (CTMC). This model takes into account the random effect of birth and death processes (demographic variability). Stochastic process also known as random process is defined as the probability that different event occur in a small time interval Δt.

3.3.2.1 The SIR Continuous Time Markov Chain

In this CTMC the time variable is continuous $t \in [0, T)$ but the state variable is discrete. The discrete random variables *S(t), I(t)* and *R(t)* represent Susceptible, Infectious and Recovered individuals respectively. *S(t), I(t), R(t)* $\in \{0,1,2, \ldots \ldots, k\}$ where *k* is the maximum population size. Initially when $t = 0$ the host population is made up of *n* susceptible individuals and tuberculosis is introduced by infecting one individual, the infected individual stay in the

infectious class for an exponential time with rate β unless he or she dies out. But after this period the individuals from the infectious class recover to attain permanent immunity to remain in the recovery class unless he or she dies.

During the infectious period the infective has infectious contact randomly in time according to homogeneous poisson process with rate α, each time with a uniformly selected random individual. The contacted individual if susceptible moves to the infectious class else the contact has no influence. For the CTMC stochastic model the transition from one state to a new state occurs at any time and the transition probabilities and population component are presented in Table 1.

TABLE 1: State transitions and rates of the CTMC SIR Stochastic model with Demographic Characteristics

Event	**Population Component at t**	**Population Component at $\Delta t + t$**	**Transition probabilities**
Birth	*(S,I,R)*	*(S+1,I,R)*	$\lambda \Delta t$
Susceptible Death	*(S,I,R)*	*(S-1,I,R)*	$\mu s \Delta t$
Susceptible Infection	*(S,I,R)*	*(S-1,I+1,R)*	$\alpha s \left(\frac{I}{N}\right) \Delta t$
Infectious Death	*(S,I,R)*	*(S,I-1,R)*	$\mu I \Delta t$
Recovery	*(S,I,R)*	*(S,I-1,R+1)*	$\beta I \Delta t$
Death of recovered	*(S,I,R)*	*(S,I,R-1)*	$\mu R \Delta t$

3.3.2.2 Branching Process Approximation of the SIR Model

We employed the single-type Galton-Watson branching process in the approximation. The single – type was use because the individuals are of the same kind. This type of branching process is a Continuous Time Markov Chain process as described above. It is a Markov chain because of the fact that it makes use of the Markov property where the population size at generation *n+1* depends on only the population size at generation *n*.

At the initial stage of the epidemic the infection rate is small. The infectious class at any time *{I(t)}* is fed with a rate $\alpha I(t)S(t)/N(t)$ and is being reduced by the rate $(\beta + \mu)I(t)$. At the initial stage the host population *N(t)* is almost the same as the susceptible population *S(t)* hence the ratio of the two is approximately one ($S(t)/N(t) \simeq 1$). Hence the infectious class turns to be increased by the rate $\alpha I(t)$ instead of $\alpha I(t)S(t)/N(t)$. We let $I_n(t)$ be the number of infected individual at time *t* where *n* is the number of infections. From the above relation $I_n(t)$ can be approximated by the branching process according to the Theorem 3.3 below.

Theorem 3.3: if $I_n(t)$ is epidemic process and $I_\infty(t)$ be the branching process then $I_n(t)$ converges weakly to $I_\infty(t)$, $n \to \infty$ on any finite interval $[0, t_1]$.

Proof. See (Diekmann et al., 2013, p.54) for the proof. This approximation is possible due to the fact that when "*I"* hits zero it stays in the state zero. This means *"I"* has reached the absorbing state and the disease transmission stops that is $I(t) \to 0 \; as \; t \to \infty$ (Allen, 2017). The approximation of the stochastic SIR process is near the disease – free equilibrium where there is no disease in the system. This is so because when the initial infectious are few the branching process will either grows exponentially or hit zero. The branching process is a birth and death

process for the infectious *(I)* where αI is the infection rate (birth) and βI is the recovery (death) rate. The approximation was possible based on the following assumption:

- The susceptible population is sufficiently large.
- Every infectious individual has the same chance of recovery and same chance of transferring an infection.
- Every infectious individual lives independent from other infectious individuals.

3.3.2.3 Computation of the stochastic Thresholds of the SIR model

In this subsection we deduced the thresholds R_0 (basic reproduction number) and ρ(Malthusian parameter) and $f^{|}(1)$ (the average number of infections produce by an infectious individual in a single generation) for the stochastic process (branching process) I_∞.

Malthusian parameter is the intrinsic exponential growth rate of the epidemic branching process (I_∞). We denote it by ρ hence:

$$\int_0^\infty e^{-\rho t} g(t)dt = 1 \qquad (3.6)$$

Where $g(t)$ is the average rate at which an individual gives birth (infectious contact) at time *t* (Jagers, 1975).

Theorem 3.4: The Malthusian parameter of the epidemic is given by: $\alpha - (\mu + \beta)$

Proof:

In the SIR model, the contact rate during the infectious period is α. It follows that:

$$g(t) = \alpha e^{-\mu t} \int_0^t e^{-\beta(t-s)} ds = \alpha e^{-(\mu+\beta)t} \int_0^t e^{\beta s}\, ds$$

Upon integrating with respect to *s* and applying the limit gives

$$g(t) = \begin{cases} \frac{\alpha}{\beta}\left(e^{-\mu t} - e^{-(\beta+\mu)t}\right), if\ \alpha \neq \beta \\ e^{-\mu t} - e^{-(\mu+\mu)t}, if\ \alpha = \beta \end{cases}$$

Putting this equation above into equation (3.6), and solving for the value of ρ gives:

$$\int_0^\infty e^{-\rho t}\left[\frac{\alpha}{\beta}\left\{e^{-\mu t} - e^{-(\mu+\beta)}\right\}\right] dt = 1 \Rightarrow \frac{\alpha}{\beta}\left[\int_0^\infty e^{-(\rho+\mu)t} - e^{-(\rho+\mu+\beta)t}\right] = 1$$

$$\text{Then, } \rho = \begin{cases} \alpha - (\mu+\beta), if\ \alpha \neq \beta \\ \alpha - \mu, if\ \alpha = \beta \end{cases}$$

Considering a situation where $\neq \beta \implies \rho = \alpha - (\mu + \beta)$.

Theorem 3.5: The basic reproduction number of the branching process is

$$R_0 = \frac{\alpha}{(\mu+\beta)}$$

Proof:

We denote "*X*" to be the number of infectious contact that an individual has during the infection period. Hence,

$$p(X = 0) = \frac{\beta + \mu}{\alpha + \beta + \mu} \qquad (3.7)$$

Which follows a zero - modified geometric distribution and for all positive integer *r* we have:

$$p(X = r) = \left(\frac{r}{\alpha + \beta + \mu}\right)^r \frac{\beta + \mu}{\alpha + \beta + \mu} \qquad (3.8)$$

If the number of infectious contact before a secondary infection is produced follows a geometric distribution then it has a parameter $a = \frac{\beta+u}{\alpha+\beta+\mu}$ (Jagers, 2005). Then the expectation of *"X"* having a zero modified geometric distribution is:

$$E(X) = \frac{1-a}{a} = \left(\frac{1 - \frac{\beta + \mu}{\alpha + \beta + \mu}}{\frac{\beta + \mu}{\alpha + \mathrm{d} + \mu}}\right)$$

$$= \left(\frac{\frac{\alpha + \beta + \mu - (\beta + \mu)}{\alpha + \beta + \mu}}{\frac{\beta + \mu}{\alpha + \beta + \mu}}\right) = \frac{\alpha}{\alpha + \beta + \mu}\frac{\alpha + \beta + \mu}{\beta + \mu}$$

Hence the basic reproduction number $(R_0) = E(X) = \frac{\alpha}{(\mu+\beta)}$ (3.9)

3.3.2.4 The relationship between the stochastic thresholds of the SIR model

We consider the instances where the intrinsic growth rate of the epidemic is greater than zero. That is:

$$\rho > 0 \Rightarrow \alpha - (\mu + \beta) > 0, \text{ then } \alpha > \mu + \beta$$

Dividing both sides of the inequality above by $\mu + \beta \Rightarrow \frac{\alpha}{\mu+\beta} > \frac{\mu+\beta}{\mu+\beta}$ gives $R_0 > 1$. This confirms the sign relation sign $(\rho) = sign(R_0 - 1)$ (Diekman, 1990).

3.3.2.5 The Probability of Disease (Tuberculosis) Extinction

In this section we derive the chance of extinction using the branching process approximation. The probabilities of extinction of the epidemic when started with one infectious individual will be derived. We will also derive the probability of extinction of the epidemic when it starts with *"n"* infectious individuals. To derive this we assumed geometric offspring probability generating function (Lloyd, 2007).

$$f(z) = \sum_{r=0}^{\infty} p(X = r)z^r \qquad z \in [0,1] \qquad (3.10)$$

Where $p(X = r)$ is the probability of *"X"* individual generating *"r"* new individuals of the same type. Expanding equation (3.10) results in:

$$f(z) = \frac{\beta+u}{\beta+\alpha+u} + \frac{\alpha}{\beta+\alpha+u}z^2, \ z \in [0,1] \qquad (3.11)$$

$\frac{\beta+u}{\beta+\alpha+u}$ term in the equation (3.10) above is the chance that an individual recovers or die and $\frac{\alpha}{\beta+\alpha+u}$ which is the coefficient of the second term in (3.11) represent the probability that an infectious individual infect another individual. The index of *"z"* represents the number of infectious individual generated from one infectious individual. "z^0" means the individual recovers or die out hence no new infectious are generated and "z^2" also means the infection is transferred to another two individuals and hence there are now two individuals infectious. This offspring probability generating function is different from the discrete-time branching process where the parent will die and the child represents the parent in the next generation. The difference is due to the fact that the time interval is small and also the continuous - time process upon which this stochastic process is built, the infectious individual that infect another individual

is still counted as infectious hence the number of infectious individual are two. Also differentiating the offspring probability generating function in equation (3.11) and evaluating the derivative obtained at 1(one) gives: $\frac{2\alpha}{\alpha+\beta+\mu}$

But $f^{|}(1)$ is not the same as R_0, $f^{|}(1)$ is the mean number of infections produce by an infectious individual in a single generation. This is also another stochastic threshold parameter similar to R_0 but $f^{|}(1) > 1$ only when $R_0 > 1$.

To derive the probability for extinction we solved for the roots of the relation $f(z) = z$ for $z\epsilon[0,1]$. This is done below:

$$\frac{\beta+u}{\beta+\alpha+u} + \frac{\alpha}{\beta+\alpha+u}z^2 = z$$

$$\frac{\alpha}{\beta+\alpha+u}z^2 - z + \frac{\beta+u}{\beta+\alpha+u} = 0$$

Factorizing the quadratic equation above for the values of "z" gives the probabilities of minor outbreak whose stability is condition on the value of R_0. Multiplying the equation above by $\beta+\alpha+u$ gives:

$$\alpha z^2 - (\beta+\alpha+u)z + (\beta+u) = 0 \Rightarrow (\alpha z^2 - \alpha z) - \{(\beta+\mu)z + (\beta+\mu)\} = 0$$

$$\{\alpha z - (\beta+\mu)\}\{z-1\} = 0 \Rightarrow z = \frac{\beta+\mu}{\alpha} = \frac{1}{R_0} \; and \; z = 1.$$

We summarized the results below for when the system start with one infectious.

$$P(minor\ outbreak) = \pi_0 = \begin{cases} 1, R_0 \leq 1 \\ \frac{1}{R_0}, R_0 > 1 \end{cases}$$

$$P(major\ outbreak) = 1 - \pi_0 = \begin{cases} 0, R_0 \leq 1 \\ 1 - \frac{1}{R_0}, R_0 > 1 \end{cases}$$

We also presented the probability of both major and minor outbreak when the system starts with "*n*" infectious individual below:

$$P(minor\ outbreak) = \pi = \begin{cases} 1, R_0 \leq 1 \\ \left(\frac{1}{R_0}\right)^n, R_0 > 1 \end{cases}$$

$$P(major\ outbreak) = 1 - \pi = \begin{cases} 0, R_0 \leq 1 \\ 1 - \left(\frac{1}{R_0}\right)^n, R_0 > 1 \end{cases}$$

The Galton-Watson branching process is termed supercritical if $R_0 > 1$, critical if $R_0 = 1$ and subcritical when $R_0 < 1$. If the process is subcritical then there is a certain probability of extinction (minor outbreak) but if supercritical then there is a positive probability $1 - \left(\frac{1}{R_0}\right)^n$ that the epidemic will survive (major outbreak).

3.4 Mathematical formation of the SEIR model with Demography

The presumption below together with that of the SIR model was made when fitting the SEIR model. That is the latently infected (exposed) are not infectious hence they cannot transmit the bacteria.

3.4.1 The Deterministic SEIR model with Demography

This type of deterministic or compartment model is formulated by dividing the host population into four classes that is: Susceptible *(S)*, Exposed *(E)*, Infectious *(I)* and Recovery *(R)*. That is in mathematical terms: $N = S + E + I + R$.

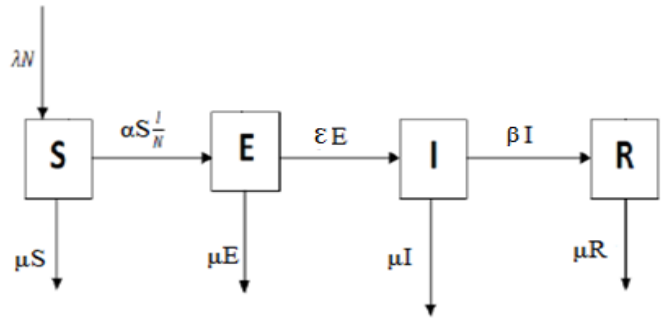


Figure 3.2 Illustration of the SEIR model.

Where λ= birth rate, μ = death rate, α = infection rate, Ɛ = rate at which an individual moves from the exposed class to the infection class and β = recovery rate of the infectious individual.

The above stated assumptions together with Figure 3.2 lead to the following system of ordinary differential equations to indicate the rate of change from one class to the other.

$$\frac{ds}{dt} = \lambda N - \mu S - \alpha S \frac{I}{N}$$

$$\frac{dE}{dt} = \alpha S \frac{I}{N} - (\mu + \varepsilon)E \qquad (3.12)$$

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

$$\frac{dR}{dt} = \beta I - \mu R$$

Rescaling the equation above by representing $s = \frac{S}{N}$, $e = \frac{E}{N}$, $i = \frac{I}{N}$ and $r = \frac{R}{N}$ where

s = susceptible proportion of the population, e= exposed proportion, i= infectious proportion and r = recovery proportion. The scaled equations are given below:

$$\frac{ds}{dt} = \lambda - \mu s - \alpha si$$

$$\frac{de}{dt} = \alpha si - (\mu + \text{Ɛ})e \qquad (3.13)$$

$$\frac{di}{dt} = \text{Ɛ}e - (\mu + \beta)i$$

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

Here $s + e + i + r = 1$

But from the relation above we make "r" the subject $r = 1 - s - e - i$; hence it is enough to study the system below instead of equation (3.13).

$$\frac{ds}{dt} = \lambda - \mu s - \alpha si$$

$$\frac{de}{dt} = \alpha si - (\mu + \text{Ɛ})e \qquad (3.14)$$

$$\frac{di}{dt} = \text{Ɛ}e - (\mu + \beta)i$$

3.4.1.1 Computation of the Basic Reproduction Number using Next Generation Matrix

According to Roy and Robert (1991), Odo and Heesterbek (2000), basic reproduction number (R_0) is the mean number of secondary infections produce by one infective individual in a completely susceptible population at the disease – free equilibrium point. That is:

R_0 = (Rate of secondary infections) (Duration of infection)

It is assumed that *"s"* is near the disease – free equilibrium hence we lineralized the ODE's in equation (3.3) about the DFE for exposed and infectious class which yield the matrix from the next generation matrix approach (Driessche and Watmough, 2002).

$$H - K = \begin{bmatrix} 0 & \alpha \\ 0 & 0 \end{bmatrix} - \begin{bmatrix} (\mu + \varepsilon) & 0 \\ -\varepsilon & (\mu + \beta) \end{bmatrix}$$

Where H = matrix of infection rates and K = matrix of transition rates

$$H = \begin{bmatrix} 0 & \alpha \\ 0 & 0 \end{bmatrix} \text{ and } K = \begin{bmatrix} (\mu + \varepsilon) & 0 \\ -\varepsilon & (\mu + \beta) \end{bmatrix}$$

$$\text{But } |K| = (\mu + \varepsilon)(\mu + \beta) + 0 \Rightarrow |K| = (\mu + \varepsilon)(\mu + \beta)$$

$$K^{-1} = \frac{1}{(\mu + \varepsilon)(\mu + \beta)} \begin{bmatrix} (\mu + \beta) & 0 \\ \varepsilon & (\mu + \varepsilon) \end{bmatrix}$$

$$\text{Hence } K^{-1} = \begin{bmatrix} \frac{1}{(\mu+\varepsilon)} & 0 \\ \frac{\varepsilon}{(\mu+\varepsilon)(\mu+\beta)} & \frac{1}{(\mu+\beta)} \end{bmatrix}$$

Multiplying the inverse of *"K"* above by the matrix *"H"* result in

$$HK^{-1} = \begin{bmatrix} 0 & \alpha \\ 0 & 0 \end{bmatrix} \begin{bmatrix} \frac{1}{(\mu + \varepsilon)} & 0 \\ \frac{\varepsilon}{(\mu + \varepsilon)(\mu + \beta)} & \frac{1}{(\mu + \beta)} \end{bmatrix} = \begin{bmatrix} \frac{\alpha\varepsilon}{(\mu + \varepsilon)(\mu + \beta)} & \frac{\alpha}{(\mu + \beta)} \\ 0 & 0 \end{bmatrix}$$

Basic reproduction number(R_0) is defined as the spectral radius of HK^{-1} (Driessche and Watmough, 2002). We denote this by $\rho(HK^{-1})$ hence

$$R_0 = \rho(HK^{-1}) = \frac{\alpha\mathcal{E}}{(\mu + \mathcal{E})(\mu + \beta)}$$

3.4.1.2 The Equilibrium Point of the SEIR model

For the purpose of this study we shall consider two equilibrium states that is: the disease – free equilibrium (DFEP) when $i = 0$ and the endemic equilibrium (EEP) when $i \neq 0$. To achieve this we set the system of differential equations in (3.14) to zero and then solve for the values of *s*, *e* and *i*.

$$\frac{ds}{dt} = 0 \Rightarrow \lambda - \mu s - \alpha si = 0$$

$$\frac{de}{dt} = 0 \Rightarrow \alpha si - (\mu + \mathcal{E}) = 0 \qquad (3.15)$$

$$\frac{di}{dt} = 0 \Rightarrow \mathcal{E}e - (\mu + \beta)i = 0$$

3.4.1.2.1 Disease – Free Equilibrium Point

At the disease – free equilibrium point it is presumed that there is no infection or disease in the system hence $i = 0 \; and \; e = 0$. This results in the following from equation (3.14):

$$\lambda - \mu s - \alpha s(0) = 0$$

$$\alpha s(0) - (\mu + \mathcal{E})(0) = 0$$

$$\mathcal{E}(0) - (\mu + \beta)(0) = 0$$

These equations at the DFE reduce to

$$\lambda - \mu s = 0$$

$$\lambda = \mu s \Rightarrow s = \frac{\lambda}{\mu}$$

Therefore at the DFE $(s, e, i) = \left({}^{\lambda}/_{\mu}, 0,0\right) = (1,0,0)$ since the host population is constant and $\lambda = \mu$.

3.4.1.2.2 The Endemic Equilibrium point

The endemic equilibrium point shows that disease will persist in the system in the steady state. Here we solve equations (3.15) to obtain *s*, *e* and *i*. But for easy identification *s*, *e*, *i* are represented by (s^*, e^*, i^*) at the steady state of the endemic respectively.

From $\varepsilon e - (\mu + \beta)i = 0 \Rightarrow i = \frac{\varepsilon e}{u+\beta}$

Similarly from $\alpha s i - (\mu + \varepsilon)e = 0 \Rightarrow s = \frac{(\mu+\varepsilon)}{\alpha i}$

Putting *i* above into s above gives $s = \frac{(\mu+\varepsilon)e}{\alpha\left(\frac{\varepsilon e}{u+\beta}\right)} = \frac{(u+\varepsilon)(\mu+\beta)e}{\alpha\varepsilon e}$

The e will cancel out to give $s^* = \frac{(\mu+\varepsilon)(\mu+\beta)}{\alpha\varepsilon}$

Also from $\alpha s i - (\mu + \varepsilon)e = 0$ *we have* $\alpha s i = (\mu + \varepsilon)e$ and putting this into

$$\lambda - \mu s - \alpha s i = 0 \text{ yields } \lambda - \mu s - (\mu + \varepsilon)e = 0$$

$$\lambda - \mu s - (\mu + \varepsilon)e = 0$$

$$\lambda - \mu s + (-\mu - \varepsilon)e = 0$$

$$(-\mu - \mathcal{E})e = -\lambda + \mu s$$

But since $s = \frac{(\mu+\mathcal{E})(\mu+\beta)}{\alpha\mathcal{E}}$

$$-(\mu + \mathcal{E})e = -(\lambda - \mu s) \Rightarrow -(\mu + \mathcal{E})e = -\left\{\lambda - \mu\frac{(\mu + \mathcal{E})(\mu + \beta)}{\alpha\mathcal{E}}\right\}$$

Dividing both sides by $-(\mu + \mathcal{E})$ gives $e^* = \frac{\lambda\alpha\mathcal{E}-\mu(\mu+\mathcal{E})(\mu+\beta)}{\alpha\mathcal{E}(\mu+\mathcal{E})}$

Also since $i = \frac{\mathcal{E}e}{\mu+\beta}$ and e^* as given above, $i = \frac{\mathcal{E}}{(\mu+\beta)}\left(\frac{\lambda\alpha\mathcal{E}-\mu(\mu+\mathcal{E})(\mu+\beta)}{\alpha\mathcal{E}(\mu+\mathcal{E})}\right)$ $\mathcal{E}$ and $(\mu + \beta)$ will cancel out to result in $i^* = \frac{\lambda\alpha\mathcal{E}-\mu(\mu+\mathcal{E})}{\alpha(\mu+\mathcal{E})}$. Hence at the endemic equilibrium point we have:

$$(s^*, e^*, i^*) = \left(\frac{(\mu + \mathcal{E})(\mu + \beta)}{\alpha\mathcal{E}}, \frac{\lambda\alpha\mathcal{E} - \mu(\mu + \mathcal{E})(\mu + \beta)}{\alpha\mathcal{E}(\mu + \mathcal{E})}, \frac{\lambda\alpha\mathcal{E} - \mu(\mu + \mathcal{E})}{\alpha(\mu + \mathcal{E})}\right)$$

3.4.1.2.3 Stability of the Disease – free Equilibrium Point

The stability of disease – free equilibrium point is obtained based on the theorem 3.6.

Theorem 3.6: The disease – free equilibrium point of the system (3.14) is asymptotically stable if and only if $R_0 \leq 1$ and unstable if $R_0 > 1$.

Proof:

At the DFE we obtained the Jacobian matrix about the point *(s, e, i)* = (1, 0, 0). This yields the matrix:

$$J(s, e, i) = \begin{bmatrix} -\mu & 0 & -\alpha \\ 0 & -(\mu + \mathcal{E}) & \alpha \\ 0 & \mathcal{E} & -(\mu + \beta) \end{bmatrix}$$

We let $J(s,e,i)_{DFE} = J(s,e,i)$ the Jacobian matrix at the disease – free equilibrium and solve the characteristics equation of $J(s,e,i)_{DFE}$. This can be achieved by solving the relation: $J(s,e,i)_{DFE} - I\lambda$ where *"I"* is the identity $3x3$ matrix.

$$I\lambda = \lambda\begin{bmatrix}1 & 0 & 0\\ 0 & 1 & 0\\ 0 & 0 & 1\end{bmatrix} = \begin{bmatrix}\lambda & 0 & 0\\ 0 & \lambda & 0\\ 0 & 0 & \lambda\end{bmatrix}$$

$$J(s,e,i)_{DFE} - I\lambda = \begin{bmatrix}-\mu & 0 & -\alpha\\ 0 & -(\mu+\mathcal{E}) & \alpha\\ 0 & \mathcal{E} & -(\mu+\beta)\end{bmatrix} - \begin{bmatrix}\lambda & 0 & 0\\ 0 & \lambda & 0\\ 0 & 0 & \lambda\end{bmatrix}$$

$$= \begin{bmatrix}-(\mu+\lambda) & 0 & -\alpha\\ 0 & -\{(\mu+\mathcal{E})+\lambda\} & \alpha\\ 0 & \mathcal{E} & -\{(\mu+\beta)+\lambda\}\end{bmatrix}$$

From this we obtained characteristics equation by finding the determinant of the above matrix and equate it to zero.

$$|J(s,e,i)_{DFE} - I\lambda| = \begin{vmatrix}-(\mu+\lambda) & 0 & -\alpha\\ 0 & -\{(\mu+\mathcal{E})+\lambda\} & \alpha\\ 0 & \mathcal{E} & -\{(\mu+\beta)+\lambda\}\end{vmatrix}$$

$$= -(\mu+\lambda)\begin{vmatrix}-(\mu+\mathcal{E}+\lambda) & \alpha\\ \mathcal{E} & -(\mu+\beta+\lambda)\end{vmatrix} - 0\begin{vmatrix}0 & \alpha\\ 0 & -(\mu+\beta+\lambda)\end{vmatrix} - \alpha\begin{vmatrix}0 & -(\mu+\mathcal{E}+\lambda\\ 0 & \mathcal{E}\end{vmatrix}$$

$$= -(\mu+\lambda)[(\mu+\mathcal{E}+\lambda)(\mu+\beta+\lambda) - \alpha\mathcal{E}]$$

For $|J(s,e,i)_{DFE} - I\lambda| = 0$ we get

$-(\mu+\lambda)[(\mu+\mathcal{E}+\lambda)(\mu+\beta+\lambda) - \alpha\mathcal{E}] = 0$ Expanding the relation results in:

$$-(\mu+\lambda)[\mu^2 + \mu\beta + \mu\lambda + \mu\mathcal{E} + \mathcal{E}\beta + \mathcal{E}\lambda + \lambda\mu + \lambda\beta + \lambda^2 - \alpha\mathcal{E}] = 0$$

Expanding the above equation again and grouping like terms gives:

$$\lambda^3 + (3\mu + \mathcal{E} + \beta)\lambda^2 + (3\mu^2 + 2\mu\beta + 2\mathcal{E}\mu + \mathcal{E}\beta - \alpha\mathcal{E})\lambda + (\mu^3 + \mu^2\beta + \mu^2\mathcal{E} + \mu\mathcal{E}\beta - \mu\alpha\mathcal{E}) = 0$$

We let Y, Z be the coefficients of λ^2, λ and A the constant term hence

$$Y = 3\mu + \mathcal{E} + \beta$$

$$\text{Z}= 3\mu^2 + 2\mu\beta + 2\mathcal{E}\mu + \mathcal{E}\beta - \alpha\mathcal{E}$$

$$\text{A}= \mu^3 + \mu^2\beta + \mu^2\mathcal{E} + \mu\mathcal{E}\beta - \mu\alpha\mathcal{E}$$

The characteristic equation becomes: $\lambda^3 + Y\lambda^2 + Z\lambda + A$

From Routh-Hurwitz Stability criterion analysis if $A > 0, Z > 0$ and $YZ - A > 0$ holds then all the roots of the characteristic equation has negative real part and hence the equilibrium point (DFE) point is stable but unstable otherwise. To show this is in line with Theorem 3.6 we show that the inequality $A > 0$ is equivalent to $R_0 < 1$. That is:

$$A > 0 \Rightarrow \mu^3 + \mu^2\beta + \mu^2\mathcal{E} + \mu\mathcal{E}\beta - \mu\alpha\mathcal{E} > 0$$

$$\mu\alpha\mathcal{E} < \mu^3 + \mu^2\beta + \mu^2\mathcal{E} + \mu\mathcal{E}\beta$$

$$\mu\alpha\mathcal{E} < \mu(\mu^2 + \mu\beta + \mu\mathcal{E} + \mathcal{E}\beta)$$

$$\mu\alpha\mathcal{E} < \mu(\mu + \varepsilon)(\mu + \beta)$$

Dividing both sides by $\mu(\mu + \varepsilon)(\mu + \beta)$ result in:

$$\frac{\alpha\mathcal{E}}{(\mu+\varepsilon)(\mu+\beta)} < 1 \Rightarrow R_0 < 1$$

□

3.4.1.2.4 Stability of the Endemic Equilibrium Point

The Theorem 3.7 below was employ when determining the stability of the endemic equilibrium.

Theorem 3.7: The endemic equilibrium of system (3.14) is also asymptotically stable when $R_0 > 1$ and unstable when $R_0 \leq 1$.

Proof:

At the endemic equilibrium we have showed that: $s^* = \frac{(\mu+\mathcal{E})(\mu+\beta)}{\alpha\mathcal{E}}$, $e^* = \frac{\lambda\alpha\mathcal{E}-\mu(\mu+\mathcal{E})(\mu+\beta)}{\alpha\mathcal{E}(\mu+\mathcal{E})}$ and $i^* = \frac{\lambda\alpha\mathcal{E}-\mu(\mu+\mathcal{E})}{\alpha(\mu+\mathcal{E})}$ hence the Jacobian matrix at the endemic equilibrium point is

$$J(s^*, e^*, i^*) = \begin{bmatrix} -\mu - \alpha i^* & 0 & -\alpha s^* \\ \alpha i^* & -(\mu+\mathcal{E}) & \alpha s^* \\ 0 & \mathcal{E} & -(\mu+\beta) \end{bmatrix}$$

$J(s^*, e^*, i^*)EE$ is the Jacobian matrix at the endemic equilibrium point. We solved for the characteristic equation of $J(s^*, e^*, i^*)EE$ by finding the determinant of $J(s^*, e^*, i^*)EE - \lambda I$ and setting the results to zero. I is a three by three unit matrix hence $I = \begin{bmatrix} 1 & 0 & 0 \\ 0 & 1 & 0 \\ 0 & 0 & 1 \end{bmatrix}$ and

$$I\lambda = \lambda \begin{bmatrix} 1 & 0 & 0 \\ 0 & 1 & 0 \\ 0 & 0 & 1 \end{bmatrix} = \begin{bmatrix} \lambda & 0 & 0 \\ 0 & \lambda & 0 \\ 0 & 0 & \lambda \end{bmatrix}$$

$$J(s^*, e^*, i^*)EE - \lambda I = \begin{bmatrix} -\mu - \alpha i^* & 0 & -\alpha s^* \\ \alpha i^* & -(\mu + \varepsilon) & \alpha s^* \\ 0 & \varepsilon & -(\mu + \beta) \end{bmatrix} - \begin{bmatrix} \lambda & 0 & 0 \\ 0 & \lambda & 0 \\ 0 & 0 & \lambda \end{bmatrix}$$

$$= \begin{bmatrix} -(\mu + \alpha i^* + \lambda) & 0 & -\alpha s^* \\ \alpha i^* & -(\mu + \beta + \lambda) & \alpha s^* \\ 0 & \beta & -(\mu + \text{d} + \lambda) \end{bmatrix}$$

$$|J(s^*, e^*, i^*)EE - \lambda I| = \begin{vmatrix} -(\mu + \alpha i^* + \lambda) & 0 & -\alpha s^* \\ \alpha i^* & -(\mu + \varepsilon + \lambda) & \alpha s^* \\ 0 & \varepsilon & -(\mu + \beta + \lambda) \end{vmatrix}$$

$$= -(\mu + \alpha i^* + \lambda) \begin{vmatrix} -(\mu + \varepsilon + \lambda) & \alpha s^* \\ \varepsilon & -(\mu + \beta + \lambda) \end{vmatrix} - 0 \begin{vmatrix} \alpha i^* & \alpha s^* \\ 0 & -(\mu + \beta + \lambda) \end{vmatrix}$$

$$- \alpha s^* \begin{vmatrix} \alpha i^* & -(\mu + \varepsilon + \lambda) \\ 0 & \varepsilon \end{vmatrix}$$

$$= -(\mu + \alpha i^* + \lambda)[(\mu + \varepsilon + \lambda)(\mu + \beta + \lambda) - \varepsilon \alpha s^*] - \alpha s^* \varepsilon \alpha i^*$$

Expanding the equation above and setting it to zero gives:

$$\lambda^3 + (3\mu + \alpha i^* + \varepsilon + \beta)\lambda^2 + (2\mu^2 + 2\mu\varepsilon + \mu\beta + 2\alpha i^* \mu + \alpha i^* \varepsilon + \alpha i^* \beta + \varepsilon\beta - \varepsilon \alpha s^*)\lambda + \mu^3$$
$$+ \varepsilon\mu^2 + \mu\varepsilon\beta - \mu\varepsilon\alpha s^* + \alpha i^* \mu^2 + \alpha i^* \varepsilon\mu + \alpha i^* \varepsilon\beta = 0$$

We let Y, Z represents the coefficient of λ^2 *and* λ respectively and A be the constant term in the polynomial above.

$$\text{Then } Y = 3\mu + \alpha i^* + \varepsilon + \beta$$

$$Z = 2\mu^2 + 2\mu\varepsilon + \mu\beta + 2\alpha i^* \mu + \alpha i^* \varepsilon + \alpha i^* \beta + \varepsilon\beta - \varepsilon \alpha s^*$$

$$A = \mu^3 + \varepsilon\mu^2 + \mu\varepsilon\beta - \mu\varepsilon\alpha s^* + \alpha i^* \mu^2 + \alpha i^* \varepsilon\mu + \alpha i^* \varepsilon\beta$$

The polynomial (characteristics equation) above then becomes $\lambda^3 + Y\lambda^2 + Z\lambda + A = 0$

Using the Routh-Hurwitz stability analysis if the conditions $A > 0, Y > 0$ and $YZ - A > 0$ hold, all the zeros of the characteristics equation have negative real part and hence the equilibrium (endemic) point is stable but unstable otherwise. To show this is in line with Theorem 3.7 we show that the inequality $A > 0$ is equivalent to $R_0 > 1$. That is:

$$A > 0 \Rightarrow \mu^3 + \text{Ɛ}\mu^2 + \mu\text{Ɛ}\beta - \mu\text{Ɛ}\alpha s^* + \alpha i^*\mu^2 + \alpha i^*\text{Ɛ}\mu + \alpha i^*\text{Ɛ}\beta > 0$$

Substituting the expressions for s^*, e^*, i^* and grouping like terms results in:

$$\lambda\alpha\varepsilon > \mu(\mu + \varepsilon)(\mu + \beta)$$

$$\text{Since } \lambda = \mu \Rightarrow \mu\alpha\varepsilon > \mu(\mu + \varepsilon)(\mu + \beta)$$

Dividing both sides by $\mu(\mu + \varepsilon)(\mu + \beta)$ result in:

$$\frac{\alpha\varepsilon}{(\mu + \varepsilon)(\mu + \beta)} > 1 \Rightarrow R_0 > 1$$

□

3.4.2.1 The SEIR Continuous Time Markov Chain Model

With the Continuous Time Markov Chain **(**CTMC) for SEIR the time variable and the state variable both show the same behavior as that of the SIR model. But the discrete state variables are four instead of the three for the SIR model. They are *S(t), E(t), I(t)* and *R(t)* representing Susceptible, Exposed ,Infectious and Recovered individuals respectively. *S(t), E(t), I(t), R(t)* $\in \{0,1,2, \ldots\ldots, k\}$ where *k* is the highest population size. Initially when *t=0* the host population consist of *n* susceptible individuals and the infectious disease (tuberculosis) is introduced by infecting one individual, the infected individual stay in the exposed class for an exponential time with rate Ɛ. After this period the infected individual becomes infectious unless he or she dies out.

The infectious individual now stays in the infectious class also for exponential time with rate β unless he or she dies out. But after this period the individuals from the infectious class recover to attain permanent immunity to remain in the recovery class unless he or she dies. During the infectious period the infective has infectious contact randomly in time according to homogeneous poisson process with rate α, each time with a uniformly selected random individual. The contacted individual if susceptible moves to exposed class if not the contact has no influence. For the CTMC stochastic model the transition from one state to a new state occurs at any time and the transition probabilities and population component are presented in Table 2.

TABLE 2 :Transitional state and rates of the CTMC SEIR Stochastic model with Demographic Characteristics

Event	**Population Component at t**	**Population Component at $\Delta t + t$**	**Transition Probabilities**
Birth	(S,E,I,R)	(S+1,E,I,R)	$\lambda \Delta t$
Susceptible death	(S,E,I,R)	(S-1,E,I,R)	$\mu s \Delta t$
Susceptible Infection	(S,E,I,R)	(S-1,E+1,I,R)	$\alpha s \left(\frac{I}{N}\right) \Delta t$
Death of exposed	(S,E,I,R)	(S,E-1,I,R)	$\mu E \Delta t$
End of exposed	(S,E,I,R)	(S,E-1,I+1,R)	$\varepsilon E \Delta t$
Death of infectious	(S,E,I,R)	(S,E,I-1,R)	$\mu I \Delta t$
Recovery	(S,E,I,R)	(S,E,I-1,R+1)	$\beta I \Delta t$
Death of recovered	(S,E,I,R)	(S,E,I,R-1)	$\mu R \Delta t$

3.4.2.2 Branching Process Approximation of the SEIR model

In the early stage of the epidemics the infection rate is small. The exposed class at any time *{E(t)}* is fed with a rate $\alpha I(t)S(t)/N(t)$ and is being reduced by the rate $(\mathcal{E}+\mu)E(t)$. The infectious class population on the other hand is increased by the rate $\mathcal{E}E(t)$ and reduced by $(\beta+\mu)I(t)$. At the initial stage the host population *N(t)* is almost the same as the susceptible population *S(t)* hence the ratio of the two is approximately one ($S(t)/N(t) \simeq 1$); hence the exposed class turns to be increased by the rate $\alpha I(t)$ instead of $\alpha I(t)S(t)/N(t)$.

We let $T_n(t) = E_n(t) + I_n(t)$ denote the number of infected individual at time *t*. From this relation, $T_n(t)$ is approximated by the branching process.

For the approximation from the Theorem (3.3) $T_\infty(t) = E_\infty(t) + I_\infty(t)$ having two stages that is the childhood (exposed) E_∞ and the adulthood (infectious) I_∞ (Diekmann et al., 2013). At the initial stage of the process that is $t = 0$ $(E_\infty(0), I_\infty(0)) = (1,0)$, $E_\infty(t)$ is increase by $\alpha I_\infty(t)$ and reduced by rate $(\mu+\mathcal{E})E_\infty(t)$. $I_\infty(t)$ is increase by $\mathcal{E}E_\infty(t)$ (end of childhood) and reduce by $(\mu+\beta)I_\infty(t)$ (end of adulthood). But when state $I(t)$ reaches the absorbing state the disease (TB) transmission stops.

3.4.2.3 Computation of the stochastic Thresholds of the SEIR model

In this subsection we derive the same thresholds we derived for the SIR model but with the inclusion of the exposed compartment: R_0 (basic reproduction number) and ρ (Malthusian parameter) for the stochastic process (branching process) T_∞.

Malthusian parameter is the intrinsic exponential growth rate of the epidemic branching process (T_∞). We denote it by ρ hence:

$$\int_0^\infty e^{-\rho t} g(t)dt = 1 \qquad (3.16)$$

Where $g(t)$ represent the average rate at which an individual gives birth (infectious contact) at time t (Jagers, 1975).

Theorem 3.8: The Malthusian parameter of the epidemic is given as:

$$\rho = -\left\{\mu + \frac{\varepsilon + \beta}{2}\right\} + \sqrt{\frac{(\varepsilon - \beta)^2}{4} + \alpha\varepsilon}$$

Proof:

At where the exposed period comes to an end there is no contact but α contact rate at the infectious period gives:

$$g(t) = \alpha e^{-\mu t} \int_0^t \varepsilon e^{-\varepsilon s} e^{-\beta(t-s)} ds \Rightarrow g(t) = \alpha\varepsilon e^{-(\mu+\beta)t} \int_0^t e^{-(\varepsilon-\beta)s} ds$$

Upon integrating with respect to *s* and applying the limit gives

$$g(t) = \begin{cases} \frac{\alpha\varepsilon}{\varepsilon - \beta}\left(e^{-(\mu+\beta)t} - e^{-(\varepsilon+\mu)t}\right), if\ \varepsilon \neq \beta \\ \alpha\varepsilon t e^{-(\mu+\beta)t}, if\ \varepsilon = \beta \end{cases}$$

Substituting $g(t)$ obtained above into (3.16) gives:

$$= \begin{cases} -\left(\mu + \frac{\varepsilon+\beta}{2}\right) + \sqrt{\frac{(\varepsilon-\beta)^2}{4} + \alpha\varepsilon}, if\ \varepsilon \neq \beta \\ \sqrt{\alpha\varepsilon} - (\mu + \beta), if\ \varepsilon = \text{ɗ} \end{cases}$$

But since we considering a situation where $\mathcal{E} \neq \beta$ then

$$\rho = -\left\{\mu + \frac{\mathcal{E}+\beta}{2}\right\} + \sqrt{\frac{(\mathcal{E}-\beta)^2}{4} + \alpha\mathcal{E}}$$

Theorem 3.9: The basic reproduction number of the branching process is given as

$$R_0 = \frac{\alpha\mathcal{E}}{(\mu+\mathcal{E})(\mu+\beta)}$$

Proof:

Denoting *"X"* as the number of infectious contact an individual has during the infection period. Then

$$p(X=0) = \frac{\mu}{\mu+\mathcal{E}} + \frac{\mathcal{E}}{\mu+\mathcal{E}}\frac{\beta+\mu}{\alpha+\beta+\mu} \qquad (3.17)$$

Which follows a geometric distribution and for all positive integer *r*

$$p(X=r) = \frac{\mathcal{E}}{\mu+\mathcal{E}}\left(\frac{r}{\alpha+\beta+\mu}\right)^r \frac{\beta+\mu}{\alpha+\beta+\mu} \qquad (3.18)$$

If the number of infectious contact before a secondary infection is produced follows a geometric distribution then it has a parameter $a = \frac{\beta+u}{\alpha+\beta+\mu}$ (Jagers, 2005).

Then the expectation of *"X"* having a zero modified geometric distribution is

$$E(X) = \frac{\mathcal{E}}{\mu+\mathcal{E}}\frac{1-a}{a} = \frac{\mathcal{E}}{\mu+\mathcal{E}}\left(\frac{1-\frac{\beta+\mu}{\alpha+\beta+\mu}}{\frac{\beta+\mu}{\alpha+\beta+\mu}}\right)$$

$$= \frac{\mathcal{E}}{\mu+\mathcal{E}} \frac{\alpha}{\alpha+\beta+\mu} \frac{\alpha+\beta+\mu}{\beta+\mu}$$

Hence $R_0 = E(X) = \frac{\alpha\mathcal{E}}{(\mu+\mathcal{E})(\mu+\beta)}$

3.4.2.4 The Relationship between the Stochastic Thresholds for the SEIR Model

Considering the instances of which the intrinsic growth rate for the epidemic is greater than zero. That is $\rho > 0$, we have

$-\left\{\mu + \frac{\mathcal{E}+\beta}{2}\right\} + \sqrt{\frac{(\mathcal{E}-\beta)^2}{4} + \alpha\mathcal{E}} > 0$ which gives us $\frac{(\mathcal{E}-\beta)^2}{4} + \alpha\mathcal{E} > \left(\mu + \frac{\mathcal{E}+\beta}{2}\right)^2$

$$4\alpha\mathcal{E} > (2\mu + \mathcal{E} + \beta)^2 - (\mathcal{E} - \beta)^2$$

$$4\alpha\mathcal{E} > 2(2\mu + 2\mathcal{E})(2\mu + 2\beta)$$

$$\alpha\mathcal{E} > (\mu + \mathcal{E})(\mu + \beta)$$

Dividing through by $(\mu + \mathcal{E})(\mu + \beta)$ results in $\frac{\alpha\mathcal{E}}{(\mu+\mathcal{E})(\mu+\beta)} > 1 \; which \; denote \; R_0 > 1$

This confirms the sign relation sign $(\rho) = sign(R_0 - 1)$ (Diekman, 1990).

3.4.2.5 The Probability of Disease (Tuberculosis) Extinction

In this section the probability of extinction is derived using the branching process approximation of the SEIR model with demography. Both the probabilities of extinction of the epidemic when started with one latent $\pi(1,0)$ and when started with one infectious $\pi(0,1)$ individual will be derive as two points. We will also derive the probability of extinction of the epidemic when it starts with *"n"* latent and *"z"* infectious individuals using the two points $\pi(1,0) and \; \pi(0,1)$. To

derive these two points we assumed geometric offspring probability generating function (Lloyd, 2007). We let "π" be the smallest positive solution of the equation $q = f(q)$ when begins with one incubated individual. *f* is the probability generating function of *X*.

$$f(q) = \sum_{r=0}^{\infty} P(X = r)q^r \qquad (3.19)$$

$$= \frac{\mu}{\mu + \varepsilon} + \frac{\varepsilon}{\mu + \varepsilon}\frac{\beta + \mu}{\alpha + \beta + \mu} + \sum_{r=1}^{\infty} \frac{\varepsilon}{\mu + \varepsilon}\frac{\beta + \mu}{\alpha + \beta + \mu}\left(\frac{r}{\alpha + \beta + \mu}\right)^r q^r$$

$$= A + \frac{(1-A)B}{1-(1-B)U} \text{ where } A = \frac{\mu}{\mu+\varepsilon} and\ B = \frac{\beta+\mu}{\alpha+\beta+\mu}$$

Then, "π" is the smallest solution in the range [0, 1] of the equation (3.20):

$$q = A + \frac{(1 - A)B}{1 - (1 - B)\mu} \qquad (3.20)$$

The equation (3.20) has two solutions: $q_0 = 1\ and\ q_1 = A + \frac{B}{1-B}$

$$q_1 = \frac{\mu}{\mu + \varepsilon} + \frac{\varepsilon}{\mu + \varepsilon}\frac{\beta + \mu}{\alpha} = \frac{\mu}{\mu + \varepsilon} + \frac{\varepsilon}{\mu + \varepsilon}\frac{1}{R_0}$$

This yields the two points:

$$\pi(1,0) = \begin{cases} 1 & if\ R_0 \le 1 \\ \dfrac{\mu}{\mu + \varepsilon} + \dfrac{\varepsilon}{\mu + \varepsilon}\dfrac{1}{R_0} & if\ R_0 > 1 \end{cases}$$

And

$$\pi(0,1) = \begin{cases} 1\ , if\ R_0 \le 1 \\ \dfrac{1}{R_0}, if R_0 > 1 \end{cases}$$

Therefore the probability of disease extinction in general is: $\pi(n,z) = [\pi(1,0)]^n[\pi(0,1)]^z$ since all the n+z independent epidemics must die out (Allen and Lahodny, 2012). This results in:

$$\pi(n,z) = \begin{cases} 1 & if\ R_0 \leq 1 \\ \left[\frac{\mu}{\mu+\varepsilon} + \frac{\varepsilon}{\mu+\varepsilon}\frac{1}{R_0}\right]^n \left[\frac{1}{R_0}\right]^z & ,if\ R_0 > 1 \end{cases}$$

3.4.2 Deterministic formation of the SEIR model with the introduction of treatment at the exposed stage

In the formation of the SEIR model with the introduction of treatment at the exposed (incubation) stage, the following assumptions together with the assumptions employed in the formation of the SIR model were made:

- The exposed individual are not infectious
- The exposed individual receives treatment.
- The exposed individuals may either recover back to the susceptible compartment, may die or becomes infectious.

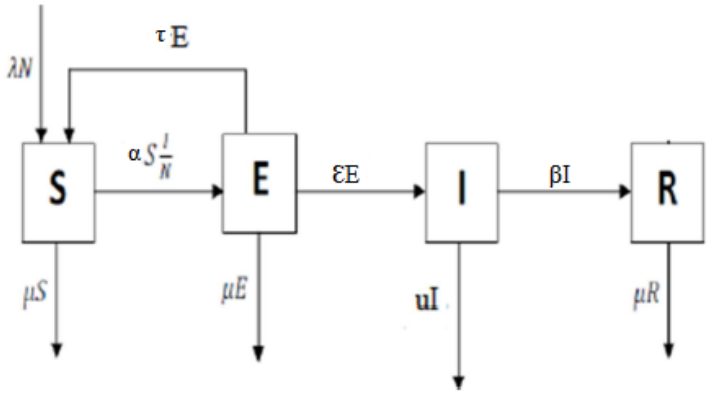


Figure 3.3 Illustration of the SEIR model with the introduction of treatment at the exposed stage.

λ= birth rate, μ = death rate, α = is the infection rate, Ɛ = the rate at which an individual moves

from the exposed class to the infection class, τ = treatment rate introduced at the exposed stage and β = recovery rate of the infectious individual.

3.4.2.1 Mathematical formation of the SEIR model with the introduction of treatment at the exposed stage.

This model as usual with SEIR model has the host population divided into four compartments. That is Susceptible (*S),* Exposed (*E*), Infected (*I*) and Recovery (*R*). Figure 3.3 together with assumptions made resulted in the following ordinary differential equation representing the model equations below:

$$\frac{ds}{dt} = \lambda N - \mu S - \alpha S\frac{I}{N} + \tau E$$
$$\frac{dE}{dt} = \alpha S\frac{I}{N} - (\tau + \mu + \mathcal{E})E \qquad (3.14.1)$$
$$\frac{dI}{dt} = \mathcal{E}E - (\mu + \beta)I$$
$$\frac{dR}{dt} = \beta I - \mu R$$

Rescaling equation (3.14.1) above we represent $s = \frac{S}{N}$, $e = \frac{E}{N}$, $i = \frac{I}{N}$ *and* $r = \frac{R}{N}$ where *"s", "e", "i", and "r"* represent the susceptible, exposed, infectious and recovery/removal population proportions respectively. Substituting the proportions into the equation (3.14.1) results in the following equations:

$$\frac{ds}{dt} = \lambda - \mu s - \alpha si + \tau e$$
$$\frac{de}{dt} = \alpha si - (\tau + \mu + \mathcal{E})e \qquad (3.14.2)$$
$$\frac{di}{dt} = \mathcal{E}e - (\mu + \beta)i$$
$$\frac{dr}{dt} = \beta i - \mu r$$

Here $s+e+i+r=1 \Rightarrow r=s+e+i$. Hence according to Affi (2018) and Tom (2017) it is enough to study the system below:

$$\frac{ds}{dt} = \lambda - \mu s - \alpha s i + \tau e$$
$$\frac{de}{dt} = \alpha s i - (\tau + \mu + \mathcal{E})e \qquad (3.14.3)$$
$$\frac{di}{dt} = \mathcal{E}e - (\mu + \beta)i$$

3.4.2.2 Computation of the Basic Reproduction Number of the SEIR model with Treatment at the exposed stage

R_0 = (Rate of secondary infections) × (Duration of infection) hence linearlizing equation (3.14.3) leads to the next generation matrix.

$$H - K = \begin{bmatrix} 0 & \alpha \\ 0 & 0 \end{bmatrix} - \begin{bmatrix} (\tau + \mu + \mathcal{E}) & 0 \\ -\mathcal{E} & (\mu + \beta) \end{bmatrix}$$

H = matrix of infection rates and K = matrix transition rates

$$H = \begin{bmatrix} 0 & \alpha \\ 0 & 0 \end{bmatrix} \text{ and } K = \begin{bmatrix} (\tau + \mu + \mathcal{E}) & 0 \\ -\mathcal{E} & (\mu + \beta) \end{bmatrix}$$

$$|K| = (\tau + \mu + \mathcal{E})(\mu + \beta) + 0 \Rightarrow |K| = (\tau + \mu + \mathcal{E})(\mu + \beta)$$

$$K^{-1} = \frac{1}{(\tau + \mu + \mathcal{E})(\mu + \beta)} \begin{bmatrix} (\mu + \beta) & 0 \\ \mathcal{E} & (\tau + \mu + \mathcal{E}) \end{bmatrix}$$

$$\text{Hence } K^{-1} = \begin{bmatrix} \frac{1}{(\tau+\mu+\mathcal{E})} & 0 \\ \frac{\mathcal{E}}{(\tau+\mu+\mathcal{E})(\mu+\beta)} & \frac{1}{(\mu+\beta)} \end{bmatrix}$$

$$HK^{-1} = \begin{bmatrix} 0 & \alpha \\ 0 & 0 \end{bmatrix} \begin{bmatrix} \frac{1}{(\tau+\mu+\varepsilon)} & 0 \\ \frac{\varepsilon}{(\tau+\mu+\varepsilon)(\mu+\beta)} & \frac{1}{(\mu+\beta)} \end{bmatrix} = \begin{bmatrix} \frac{\alpha\varepsilon}{(\tau+\mu+\varepsilon)(\mu+\beta)} & \frac{\alpha}{(\mu+\beta)} \\ 0 & 0 \end{bmatrix}$$

Since the basic reproduction number(R_0) is defined as the spectral radius of HK^{-1} (Driessche and Watmough, 2002).

$$\text{Hence } R_0 = \rho(HK^{-1}) = \frac{\alpha\mathcal{E}}{(\tau+\mu+\mathcal{E})(\mu+\beta)}$$

CHAPTER 4

DATA ANALYSIS AND DISCUSSION OF RESULTS

The chapter presents the data analysis and discussion of results from the secondary data obtained from the Ashanti region health directorate by using diverse mathematical/statistical tools and methods described in Chapter 3. Tuberculosis epidemiology is modeled using SIR and SEIR epidemic models for the individual districts and the entire region: the basic reproduction number is estimated and the various equilibrium points are investigated. Also the stochastic thresholds: Malthusian parameter and the mean number of offspring in a single generation are estimated. The probability of tuberculosis extinction is estimated using the branching process approximation.

Secondly, sensitivity analysis on the initial condition of the exposed compartment for the SEIR model is carry out to determine the effect of the initial condition of the latent compartment on the infection dynamics of tuberculosis in the region. Also the effect of the various parameters of the SEIR epidemic model on the spread of TB is investigated. The effect of introducing treatment at the exposed stage of TB infection on the spread of TB is determined. Finally, empirical results are validated with numerical simulations.

4.1 Modeling Tuberculosis Epidemics

In this section we present the SIR and SEIR modeling of tuberculosis epidemiology in the Ashanti region of Ghana. Each model is fitted for both the individual districts and the entire region.

4.1.1 Modeling Tuberculosis Epidemiology with SIR Epidemic model

The SIR epidemiological model with demography is fitted for both the individual districts and the entire Ashanti region. The deterministic and stochastic forms of the SIR model are developed.

4.1.1.1 Infection Dynamics of Tuberculosis in the High Burdened Districts in Ashanti Region

To present the transmission dynamics of tuberculosis in each of the twelve high burden districts in the Ashanti region, we first present the parameter estimates for the SIR model with demography for each of the twelve high burden districts.

4.1.1.1.1 SIR Model parameter Estimation

The parameters used in the study were birth (λ) and death (μ) rates, the infection rate (α) and finally the recovery/removal rates (β). These parameters were estimated from different sources. Some were estimated from the data from the regional health directorate and others from the literature. Birth (λ) and death (μ) rates together with the recovery/removal rate (β) are estimated from the existing literature about the disease in contention (tuberculosis). The natural death rate in Ghana is estimated to be 7 deaths per 1000 individual (Index Mundi, 2018). But since we made assumption of closed system, the natural birth and death rates are taken to be same hence $\lambda = \mu = 0.007$. Also the average period of infection is the reversed of the removal/recovery rate (Jones, 2007). According to the World Health Organization (1993), Ghana Health Service (2012) and Sarkodie (2014) tuberculosis has an average infectious period of two (2) weeks hence:

Recovery/removal rate (β) = $\frac{1}{Infectious\ period} = \frac{1}{2} = 0.5$ per week

The infection rate (α) is estimated from the tuberculosis data obtained from the regional health directorate as follows:

Infection rate (α) = $\frac{effective\ contact}{total\ contact}$ (Wikipedia, Transmission risks and rates, 2009)

An effective contact in this case is the number of infected individuals while that of the total contact is made up of the sum of infected individual and susceptible individual (number who reported to be screen for tuberculosis). Table 3 shows the total contact, effective contact for each of the twelve high burdened districts with the corresponding estimates of the infection rates for the SIR model. Also the recovery rate, natural birth and death rates estimates are the same for all the twelve high burden districts.

Table 3: Estimates of the Infection Rate of each of the High Burden Districts

Number	District	Total Contact	Effective Contact	Infection Rate (α)
1	Adansi south	444	54	0.1216
2	Asanti Akim North Municipal	2150	948	0.4409
3	Amansie West	332	234	0.7048
4	Mampong Municipal	790	38	0.0481
5	Atwima Nwabiagye	440	115	0.2613
6	Bekwai Municipal	455	139	0.3055
7	Bosomtwe	570	57	0.1000
8	Ejusu – Juaben Municipal	774	63	0.0814
9	Obuasi Municipal	183	112	0.6120
10	Offinso Municipal	21	8	0.3810
11	Kumasi Metropolitan	3251	864	0.2658
12	Sekyere South	243	10	0.0412

4.1.1.1.2 Stability Analysis of the Equilibrium Point for each District using SIR model

Based on Theorem 3.1 and Theorem 3.2 the analysis of the stability of the equilibrium point of each of the high burden districts using the Routh – Hurwitz stability criterion analysis is presented. The basic reproduction number for the districts shows that in some of the districts transmission of tuberculosis will results in disease free equilibrium point while in others there will be endemic equilibrium point. The derived characteristics equation deduced in Chapter 3 for the disease free equilibrium point is: $\lambda^2 + Z\lambda + A$ while that for the endemic equilibrium point is: $\lambda^2 + Y\lambda + Z = 0$. Table 4 displays the values of the R_0, co-efficients 'Z', 'A' and their product "ZA" for disease free case.

Table 4: Estimates of the Basic Reproduction Number and Coefficient of Characteristics Equation for Disease Free Districts of SIR model

Disease Free Equilibrium Districts

District	R_0	Z	A	ZA
Adansi south	0.2398	0.2742	0.0019	0.000521
Asanti Akim North Municipal	0.8696	0.0731	0.0004	0.000029
Sekyere South	0.0813	0.4728	0.0033	0.001560
Mampong Municipal	0.0949	0.4659	0.0032	0.001491
Atwima Nwabiagye	0.5154	0.2527	0.0017	0.000430
Bekwai Municipal	0.6026	0.0070	0.0014	0.000010
Bosomtwe	0.1972	0.4140	0.0029	0.001201
Ejusu – Juaben Municipal	0.1606	0.4326	0.0030	0.001298
Kumasi Metropolitan	0.5243	0.2482	0.0017	0.000422
Offinso Municipal	0.7515	0.1330	0.0009	0.000120

Also Table 5 indicates the values of R_0, co-efficients *'Y', 'Z'* and their product *"YZ"* for the endemic equilibrium cases.

Table 5: Estimates of the Basic Reproductive Number and Coefficient of Characteristics Equation for Endemic Districts of SIR model

Endemic Equilibrium Districts				
District	R_0	Y	Z	YZ
Obuasi Municipal	1.2071	0.0085	0.0007	0.000006
Amansie West	1.3901	0.0097	0.0014	0.000014

From Tables 4 and 5 we realized that both equilibrium points (disease free and endemic) have their respective co-efficient of characteristic equations derived in chapter 3 greater than zero ($Z > 0, A > 0$ for disease free and $Y > 0, Z > 0$ for endemic) and their respective products greater than zero ($ZA > 0$ for disease free and $YZ > 0$ for endemic). According to Routh – Hurwitz stability criterion analysis for both disease free and endemic equilibrium points, districts characterized by disease free have their equilibrium point stable and those characterized by endemic also have their equilibrium point stable.

4.1.1.1.3 SIR Model Simulation for the two Endemic Districts

For all the twelve districts in the Ashanti region considered by the Ghana health service as the high burden districts of tuberculosis the SIR model based on the respective basic reproduction numbers revealed that only two districts (Obuasi Municipal and Amansie West) will have the disease persisting at the end of the study time as a result we present the graphical view (Figures 4.1 and 4.2) of these two districts. The simulation for the two endemic districts were done using the following parameter and initial conditions: for Obuasi municipal 71 susceptible, 112 infectious, zero recovered/removed individual, 0.5 recovery rate, 0.007 natural death and birth rates and 0.6120 infectious rate whiles for Amansie West 98 susceptible, 234 infectious, zero recovered individual, 0.5 recovery rate, 0.007 natural death and birth rates and 0.7048 infectious rate. Figure 4.1 presents the infection dynamics of tuberculosis in Obuasi Municipal. From

Figure 4.1 it can be observed that the number infected fell sharply until the 10th week and then remain close to a population proportion of almost 0.00 for the rest of the study period. The susceptible individuals in Obuasi Municipal also declined slightly to around a population proportion of 0.2 in the 5th week after which it begins to rise gradually for the rest of the study period. Finally, the recovered/removed individuals increased spotlessly to a population proportion of around 0.8 in the 10th week after which it begins to fall gradually for the rest of the study period. It could be deduced from Figure 4.1 that the infection dynamics of tuberculosis for Obuasi Municipal will actually occur within the first 10 weeks of the study period since there is a good number of infectious individual in the system within this period. Significant change is recognized in the various compartmental sizes. After the 10th week the population proportion of the infectious individuals is almost 0.00. There will be approximately no one in the infectious compartment to infect the susceptible individuals and also no one in the infectious compartment to recover/remove. This accounted for the gradual rise and decline of the population proportion for the susceptible and recovery/removal compartments size respectively for the rest of the study period.

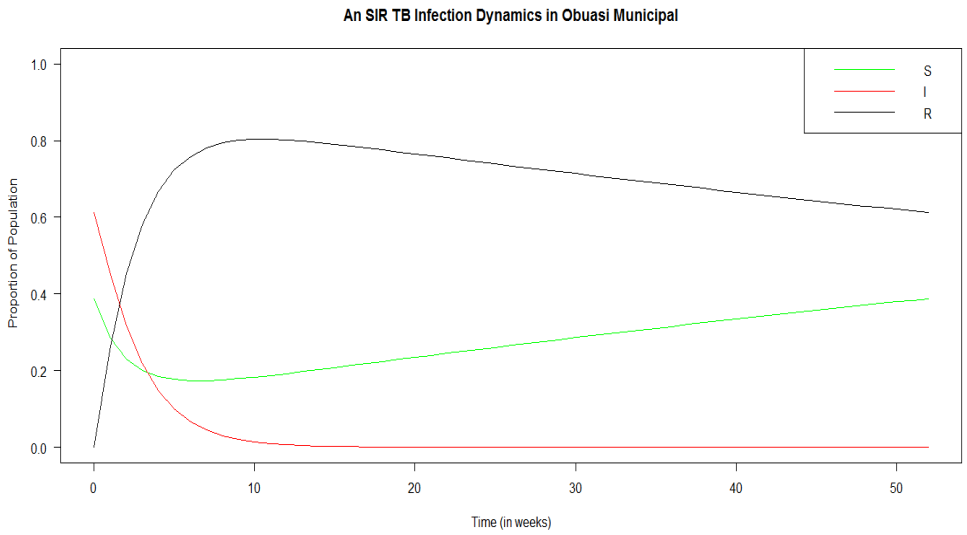


Figure 4.1: TB Infection Dynamics for Obuasi Municipal

Figure 4.2 presents the infection dynamics of tuberculosis in Amansie West district. In Figure 4.2 we observed similar trend of infection dynamics in relation to what occurred in Obuasi Municipal (Figure 4.1) for the same study period in Amansie West.

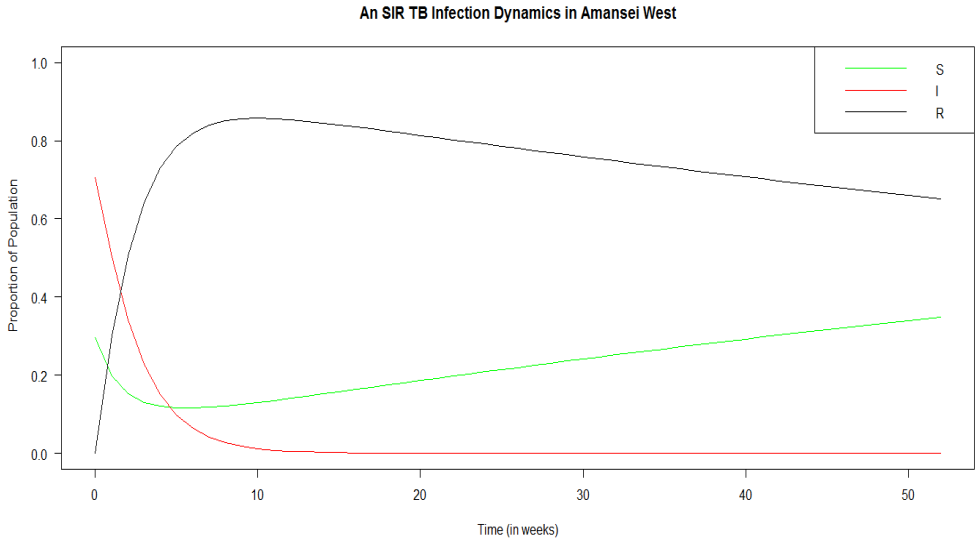


Figure 4.2 TB Infection Dynamics for Amansie West district

4.1.1.1.4 The Stochastic SIR model of Tuberculosis for the Twelve High Burdened Districts in Ashanti Region

In this subsection the values of the stochastic thresholds (Malthusian parameter (ρ) and the mean number of offspring in a single generation ($f^{|}(1)$)), the extinction (π) and outbreak (1-π) probabilities of tuberculosis for each of the 12 high burdened districts of tuberculosis in the Ashanti region are presented. Table 6 presents the values of the thresholds, extinction and outbreak probabilities.

Table 6: Estimates of Stochastic Thresholds, Extinction and Outbreak Probabilities for each District with SIR model

District	ρ	$f^{\mid}(1)$	Π	$1-\pi$
Adansi south	-0.3854	0.3869	1	0
Asanti Akim North Municipal	-0.0661	0.9303	1	0
Amansie West	0.1978	1.1630	0	1
Mampong Municipal	-0.4589	0.1733	1	0
Atwima Nwabiagye	-0.2457	0.6800	1	0
Bekwai Municipal	-0.2015	0.7520	1	0
Bosomtwe	-0.4070	0.3290	1	0
Ejusu – Juaben Municipal	-0.4256	0.2767	1	0
Obuasi Municipal	0.1050	1.0938	0	1
Offinso Municipal	-0.1260	0.8580	1	0
Kumasi Metropolitan	-0.2412	0.6879	1	0
Sekyere South	-0.4658	0.1503	1	0

From Table 6 it is revealed that the values of the stochastic threshold (ρ and $f^{\mid}(1)$) mirror the outcome of the deterministic model when analyzing the transmission dynamics of tuberculosis in the twelve high burden districts of tuberculosis in the Ashanti region. Just as the deterministic model ten (10) out of the 12 districts were found to exhibit disease – free equilibrium since their stochastic thresholds values are less than zero and one respectively whiles the remaining two exhibit endemic equilibrium. The disease will persist in these two districts (Amansie West and Obuasi Municipal) since their thresholds are greater than zero and one respectively.

4.1.1.2 Infection Dynamics of Tuberculosis in the entire Ashanti Region with the SIR model

In this subsection the empirical results of the SIR epidemic model with demography for tuberculosis infection in the whole of Ashanti region are discussed.

4.1.1.2.1 Estimation of the Basic Reproduction number with the SIR model for the entire region

To estimate the basic reproduction number (R_0) for the entire Ashanti region the parameter estimates for the SIR model are used. Birth and natural death rates λ= μ = 0.007 and the recovery/removal rate β = 0.5 have already been estimated when fitting the SIR model for the individual districts. Using 2017 as the base year, records available at the regional health directorate show that a total of 9663 individuals were screened for tuberculosis infection and out of this number 2643 were found to be diagnosed of tuberculosis in the entire region.

Hence infection rate (α) = $\frac{2643}{9663} = 0.2735$

From equation (3.4) in Chapter 3 it was deduced that the basic reproduction number for the SIR model is $R_0 = \frac{\alpha}{\beta+\mu} = \frac{0.2735}{0.5+0.007} = 0.5394$

Since $R_0 = 0.5394 < 1$, the prevalence of tuberculosis will not result in endemic but rather die out. That is tuberculosis will not persist in the region at the steady state. This is so because the rate at which individual recover in the region is greater than the infection rate.

4.1.1.2.2 Stability analysis of the equilibrium point of the SIR model for the entire region

From Theorem 3.1 we realized that based on R_0 which is less than one, the disease free equilibrium point of the system is stable. This is confirmed by the Routh – Hurwitz Stability criterion analysis using the parameter estimate of the SIR mode with demography (λ=μ=0.007, β=0.5 and α = 0.2735). From Chapter 3 the characteristics equation was deduced as: $\lambda^2 + Z\lambda + A$, where

$Z = (\beta + \mu) - \alpha + \mu \Rightarrow z = (0.5 + 0.007) - 0.2735 + 0.007 = 0.2405$

$A = \mu(\beta + \mu) - \alpha\mu \Rightarrow A = 0.007(0.5 + 0.007) - 0.2735(0.007) = 0.001635$

Since the value of Z = 0.2405 >0, A = 0.001635 >0 and their product ZA= 0.0003931 > 0 then by the Routh – Hurwitz stability criterion analysis the disease free equilibrium point for the entire region is stable.

4.1.1.2.3 SIR Model simulation for the Entire Ashanti Region

In this subsection, we present the empirical analysis of the deterministic compartment model. We carried out the analysis of the model using the 7020 susceptible , 2643 infectious individual and 10 recovered/removed individuals in the region with recovery rate of 0.5, infection rate of 0.2735 and natural death and birth rates of 0.007. Figure 4.3 present the infection dynamics of tuberculosis in the entire Ashanti region over a period of one year.

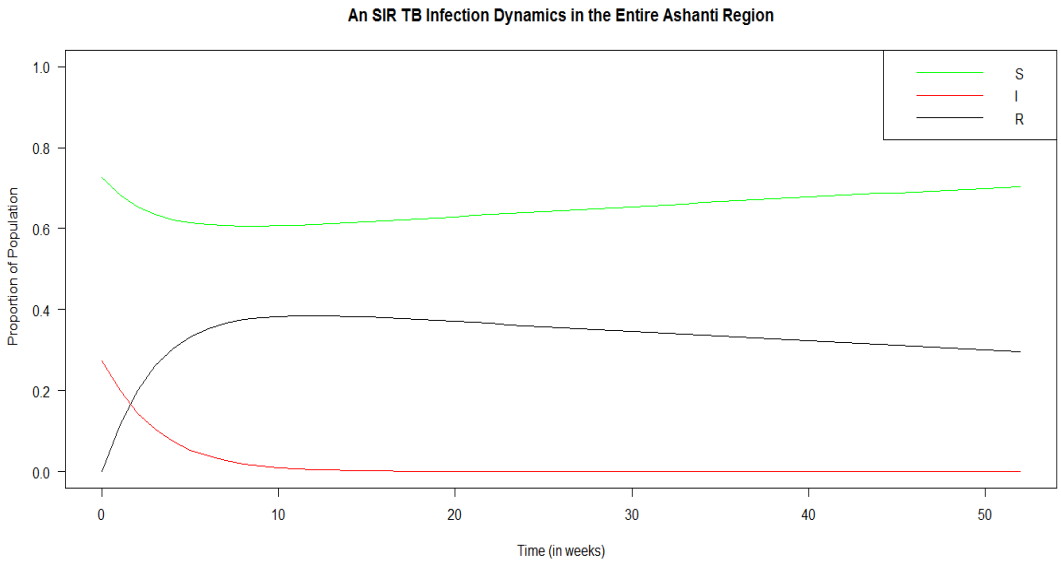


Figure 4.3: TB infection dynamics for the entire Ashanti region with SIR model

From Figure 4.3 it could be observed that the population of susceptible individuals declined slightly until around the 5th week when it began to rise again gradually. On the other hand the number of infected individuals fell rapidly until the 10th week, after which it remain close to an infected population of around zero individuals for the rest of the study period. The recovered/removed individuals also increased significantly until the 10th week and then began to

drop gradually for the remaining weeks. The population fractions at the end of the study time for each compartment are 0.7033, 0.000 and 0.2967 for susceptible exposed and recovered/removed respectively. It could be deduced from Figure 4.3 that tuberculosis actually dies out in Ashanti region after the 10^{th} week. It is deduced that the infection dynamics occurs within the first 10 weeks since there is a positive number of infectious individual in the system within this period. Infectious population declines to approximately zero after the 10^{th} week. This results in the gradual rise in the size of the susceptible compartment and that of the recovery decline since there is no infectious individual in the infectious compartment to infect the susceptible and also recover for the rest of the study period.

4.1.1.2.4 Stochastic SIR model with Demography for the entire Ashanti region

The stochastic individual contact model (SICM) is a member of the micro-simulation model. This model is developed to mirror the deterministic model but includes random variation in all components of the infection dynamics system from infection to recovery to demographics (births and deaths). The stochastic model is presented using the tuberculosis data from the regional health directorate that is 7020 susceptible, 2643 infectious individual and 10 recovered individuals in the region with recovery rate of 0.5, infection rate of 0.2735 and natural death and birth rate of 0.007. The R_0 of the stochastic model is the same as that of the deterministic model as shown in Chapter 3 equation (3.9). Hence $R_0 = 0.5394 < 1$ indicates that the disease is certain not to persist. The extinction probability of tuberculosis in the region is one. This is confirmed by two stochastic thresholds (Malthusian parameter (ρ) and the average number of offspring in a single generation $f^{|}(1)$). The Malthusian parameter $\rho = -0.2333$ has a relation with R_0 deduced in Chapter 3 that if $\rho > 0 \Rightarrow R_0 > 1$ and $\rho < 0 \Rightarrow R_0 < 1$. Hence $\rho = -0.2333$

$< 0 \Rightarrow R_0 = 0.5394 < 1$and $f^{|}(1)$ was deduce in Chapter 3 that $f^{|}(1) > 1$ only when $R_0 > 1$ and $f^{|}(1) < 1$ only when $R_0 < 1$. That is $f^{|}(1) = 0.6234 < 1 \Rightarrow R_0 = 0.5394 < 1$. These thresholds confirm tuberculosis extinction in the entire Ashanti region.

4.1.2 Modeling Tuberculosis infection Dynamics with SEIR model

Under this subsection of the chapter, we present the outputs of deterministic and stochastic SEIR model with demography of tuberculosis in the individual high burdened districts in the region as well as the entire Ashanti region.

4.1.2.1 Modeling the Infection Dynamics of Tuberculosis in the High Burdened districts of Tuberculosis in Ashanti Region with the SEIR model

The infection dynamics of tuberculosis in all the twelve (12) high burden districts of tuberculosis is presented under this section.

4.1.2.1.1 SEIR Model parameter Estimation

The SEIR model with demography is an extension of the SIR model with demography. The difference is the inclusion of the exposed compartment and the rate at which individual proceed from the incubation class to the infectious class. Tuberculosis is said to have an average exposed period of six weeks. The exposed rate is estimated as:

$$\mathcal{E} = \frac{1}{Average\ exposed\ period} = \frac{1}{6} = 0.1667$$

The other parameters have already been estimated when fitting the SIR model as λ=μ= 0.007 and β= 0.5. The infection rate (α) is estimated as follows:

Infection rate (α) = $\frac{effective\ contact}{total\ contact}$ (Wikipedia, Transmission risks and rates, 2009)

The infection rate (α) is estimated based on the tuberculosis information obtained from the regional health directorate. Table 3 presents the estimates of the infection rate for each of the high burdened districts in the Ashanti region.

4.1.2.1.2 Stability Analysis of the Equilibrium Points of each High Burdened District

Using theorem 3.1, theorem 3.2 and the Routh – Hurwitz stability criterion, the stability analysis of the equilibrium points of the SEIR model with demography for each of the 12 high burdened districts in the Ashanti region are presented. The basic reproductive number for each of the districts indicated that some of the districts are characterized by disease free equilibrium point and others endemic equilibrium point. From the Routh – Hurwitz stability criterion for the disease free equilibrium point the characteristics equation was derive in Chapter 3 as: $\lambda^3 + Y\lambda^2 + Z\lambda + A$. Table 7 shows the basic reproduction number, co-efficient *Y*, *Z*, *A* and *YZ* – *A* for the disease free districts.

Table7: Estimates of Basic Reproduction Number and the Co-efficient of the Characteristics Equation for Disease free Equilibrium Point of the SEIR model

Districts	R_0	Y	Z	A	$YZ - A$
Adansi south	0.2308	0.6877	3.0725	0.00052	2.11291
Asanti Akim North Municipal	0.8346	0.6877	3.0192	0.00015	2.07615
Sekyere South	0.0779	0.6877	3.0859	0.00062	2.12156
Mampong Municipal	0.0910	0.6877	3.0847	0.00061	2.12074
Atwima Nwabiagye	0.4946	0.6877	3.0492	0.00036	2.09657
Bekwai Municipal	0.5783	0.6877	3.0418	0.00031	2.09154
Bosomtwe	0.1893	0.6877	3.0761	0.00055	2.11489
Ejusu – Juaben Municipal	0.1541	0.6877	3.0792	0.00057	2.11699
Kumasi Metropolitan	0.5031	0.6877	0.0484	0.00055	2.09580
Offinso Municipal	0.7212	0.6877	3.0292	0.00022	2.08295

Table 8 also present the basic reproduction number and the co-efficient of the characteristics equation for districts that resulted in endemic cases.

Table 8: Estimates of Basic Reproduction Number and the Co-efficient of the Characteristics Equation for Endemic Equilibrium Cases of the SEIR model

Districts	R_0	Y	Z	A	$YZ - A$
Obuasi Municipal	1.334	0.6877	6.356×10^{-3}	- 0.07870	0.08310
Amansie West	1.158	0.6877	5.5177×10^{-3}	-0.07996	0.08375

From Table 7 it is revealed that all the conditions for the stability of the disease free equilibrium point hold according to Routh – Hurwitz stability criterion: $Y > 0$, $A > 0$ and $YZ - A > 0$ hence, the equilibrium point of the districts characterized by disease free are stable. Similar to the

disease free cases, the endemic cases have the equilibrium point stable since from Table 8 the Routh – Hurwitz stability criterion conditions hold for all those districts.

4.1.2.2.1 Modeling Tuberculosis Infection Dynamics in the Entire Ashanti Region with the SEIR model

At this section we present the output of the deterministic and stochastic SEIR modeling of tuberculosis with demography for the whole region.

4.1.2.2.2 Estimation of the Basic Reproduction number with the SEIR model

In computing the basic reproduction number (R_0) for the entire Ashanti region with the SEIR model the parameter estimates for the SEIR model were used. Birth and natural death rates λ= μ = 0.007, exposed rate Ɛ= 0.1667 and the recovery/removal rate β = 0.5 and finally infection rate (α) = 0.2735. Using these parameter estimates and the derived formula in Chapter 3 R_0 for the entire region when SEIR model was fit is given by:

$$R_0 = \frac{\alpha\varepsilon}{(\mu+\varepsilon)(\mu+\beta)} = \frac{(0.2735\times0.1667)}{(0.007+0.1667)(0.007+0.5)} = 0.5177$$

$R_0 = 0.5177 < 1$ indicate that tuberculosis will not spread in the entire Ashanti region but rather die out.

4.1.2.2.3 Stability Analysis of the Equilibrium Point of the SEIR Model for the entire Ashanti region

The R_0 is less than one hence from Theorem 3.2, it is deduced that the disease free equilibrium point of the system is stable. By the Routh- Hurwitz stability analysis the characteristics equation deduced in Chapter 3 has the following co-efficients: *Y =0.6877, Z* = 3.04716, *A* = 0.0003461 and *YZ - A* = 2.095186. According to Routh- Hurwitz stability criterion when *Y > 0, Z > 0, A > 0*

and $YZ - A > 0$ then all the zeros of the characteristics equation have negative real part and since all these conditions holds, the disease free equilibrium point of the entire region is stable.

4.1.2.2.4 Stochastic SEIR Modeling of Tuberculosis for the entire Ashanti region

Stochastic or individual models are models mostly developed to mimic the deterministic models and also average the outcome of the deterministic model by including random variation in all components of the model. At this section of the study we estimated the stochastic thresholds called the Malthusian parameter (ρ), the average number of offspring in a single generation $f^{|}(1)$ and also the probability of tuberculosis extinction in Ashanti region using the branching process approximation. The thresholds are estimated to confirm the stability analysis of the equilibrium point. In Chapter 3 of the study it was deduced that when $R_0 < 1$, then ρ < 0, there is a probability of one for tuberculosis extinction. That is $R_0 = 0.5177 < 1$ implies ρ = -0.0695 < 0. $f^{|}(1)$ was deduce in Chapter 3 that $f^{|}(1) > 1$ only when $R_0 > 1$ and $f^{|}(1) < 1$ only when $R_0 < 1$.That is $f^{|}(1) = 0.5234 < 1 \Rightarrow R_0 = 0.5177 < 1$. The stochastic SEIR model based on the thresholds confirm that tuberculosis will go to extinction in the Ashanti region of Ghana.

4.2 Sensitivity Analysis of the SEIR model

In this subsection we present the sensitivity analysis of the SEIR model by varying the initial condition of the exposed compartment so as to study it effects on tuberculosis infection dynamics in the Ashanti region. We employed one-way sensitivity analysis. For one – way sensitivity analysis only the initial condition of the exposed compartment is varied at a time and others kept constant. The sensitivity analysis is performed using the initial conditions of the other compartments other than the exposed compartment of the entire region as a case study:

susceptible = 7020, exposed = unknown, infectious = 2643, recovery/remove = 10 and parameter estimate birth and natural death rates $\lambda = \mu = 0.007$, exposed rate $\varepsilon = 0.1667$, recovery/removal rate $\beta = 0.5$, infection rate $(\alpha) = 0.2735$.

Table 9 presents the initial size of the exposed class, population proportions at the end of the study time, probability of TB extinction (π) and outbreak ($1-\pi$) for the sensitivity analysis.

Table 9: the initial size of the Exposed class, Population Proportions at the end of the study time, Probability of TB Extinction and Outbreak

Initial size of the exposed class	**Population proportions at the end of the study time**				**π**	**$1-\pi$**
	Susceptible (S)	Exposed (E)	Infectious (I)	Recovery (R)		
0	0.7016	5.540×10^{-4}	2.596×10^{-4}	0.2976	1	0
1000	0.6210	1.514×10^{-3}	2.586×10^{-4}	0.3772	1	0
2000	0.5521	6.544×10^{-4}	2.456×10^{-4}	0.4470	1	0
3000	0.4899	4.828×10^{-4}	2.172×10^{-4}	0.5094	1	0

Figure 4.4 present the infection dynamics of tuberculosis for the sensitivity analysis.

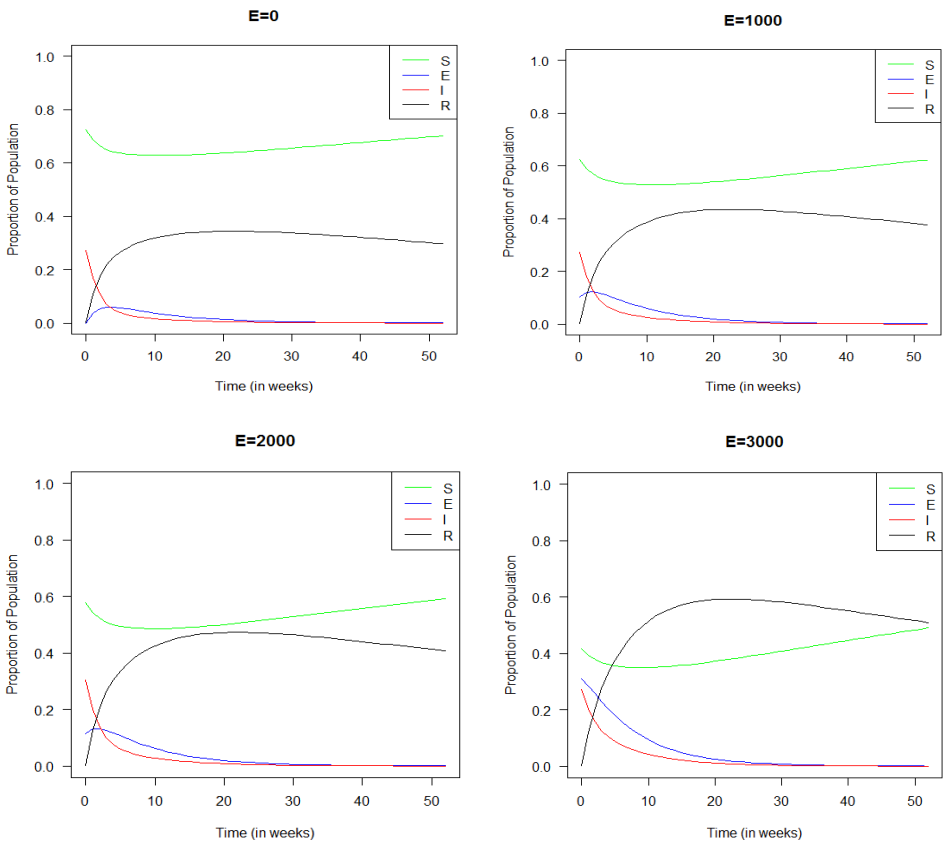


Figure 4.4: Infection dynamics of Tuberculosis when the initial condition of the exposed class is varied for the entire region

From the sensitivity analysis presented in Table 9 and Figure 4.4, it could be deduced that increasing the size of the initial condition of the exposed compartment decreases the size of the infectious and susceptible compartments but increases the size of the recovery/removal compartment at the end of the study period. There is a probability of one and zero for tuberculosis extinction and outbreak respectively in each case since the basic reproduction number was less than one. This confirms that, initial condition of the exposed compartment in the SEIR epidemic model has effect on the infection dynamics of tuberculosis in the Ashanti region hence cannot be neglected.

4.2.1 The Effect of the SEIR Model Parameters on the Basic Reproduction Number

At this subsection of the study we investigate into the effect each of the model parameters: infection rate (α), epsilon (Ɛ), and beta (β) has on the basic reproduction number (R_0). The results are presented in Figure 4.5.

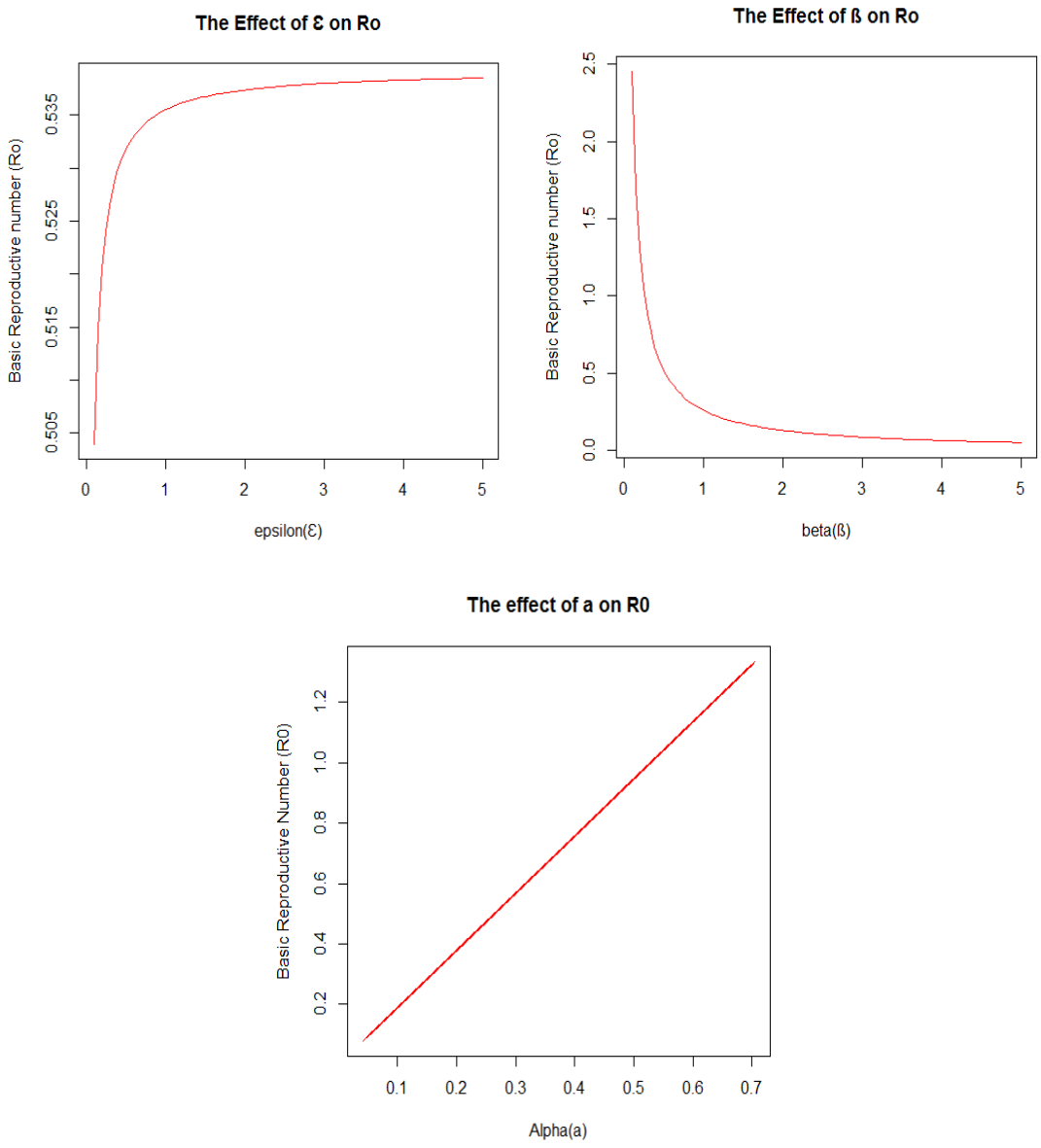


Figure 4.5: Effect of SEIR Model Parameters on Reproduction Number

Figure 4.5 revealed that the SEIR model parameters have effect on the R_0. Increasing the exposed rate (Ɛ) and the infection rate (α) increases R_0 whiles increasing the recovery/removal rate (β) also decreases the basic reproduction number (R_0)..

4.2.2 The Effect of Treatment Introduction at the Latent (Exposed) Period

At this subsection we looked into the effect of initiating treatment at the exposed stage of tuberculosis infection dynamics on the basic reproductive number (R_0). The result is displayed in Figure 4.6.

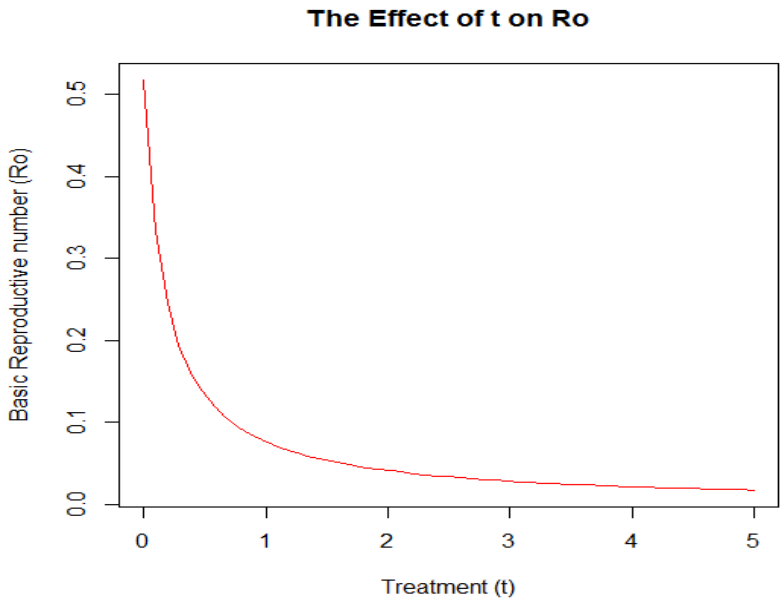


Figure 4.6: Effect of Treatment introduced at the exposed period on Reproduction number

The Figure 4.6 indicates that the initiation of treatment at the exposed stage has influence on R_0. Increasing the rate of treatment at the exposed stage decreases the R_0.

4.3 Numerical Simulation

The estimates of the various deterministic and stochastic thresholds are used in making decisive decisions in the infection dynamics of tuberculosis hence bad estimates can be misleading. In view of this numerical simulation is done to validate the empirical results of the various thresholds estimated in the study for the entire region. To improve on the various thresholds of the region beta distribution was fitted for the values of the infection rates (0.1216, 0.4409, 0.7048, 0.0481, 0.2613, 0.3055, 0.1, 0.0814, 0.6120, 0.3810, 0.2658, and 0.0412) for the various districts. It was revealed that the infection rates follow beta distribution with parameters scale1= 0.881 and scale 2 = 2.262. To compute the various thresholds 1000 data point for the infection rate (α) were generated from beta [0.881, 2.262].

For each of the 1000 infection rates generated given a fixed value for the birth and death rate (λ and μ), recovery/removal rate (β) and exposed rate (Ɛ) the thresholds were computed. Each of the thresholds (Basic reproduction number (R_0), Malthusian parameter (ρ) and the mean number of offspring in a single generation$f^{|}(1)$) is computed for each of the 1000 infection rates (see appendix for samples of each of the thresholds computed from the simulation). The basic reproduction number, Malthusian parameter and the mean number of offspring in a single generation for the entire region are the mean for each of the 1000 thresholds computed.

Table 10 presents the simulated estimates of the basic reproduction number, Malthusian parameter and the mean number of offspring in a single generation with their corresponding 95% confidence intervals for the entire region from the simulation of the 1000 infection rates from beta (0.881, 2.262). This was done for both (SIR and SEIR) model.

Table 10: Simulated Estimates of the Deterministic and Stochastic Thresholds with their corresponding 95% confidence interval

Model	R_0	95% confidence interval	ρ	95% confidence interval	$f^{\|}(1)$	95% confidence interval
SIR	0.5542	(0.5269, 0.5818)	-0.2260	(-0.2399, -0.2121)	0.6167	(0.5948, 0.6385)
SEIR	0.5319	(0.5057, 0.5581)	-0.0753	(-0.0794, -0.0712)	0.5442	(0.5169, 0.5718)

Table 11 present the empirical estimates of the various thresholds and the simulated estimates of the thresholds.

Table 11: Empirical estimate of thresholds against simulated estimate of thresholds

Model	Empirical R_0	Simulated R_0	Empirical ρ	Simulated ρ	Empirical $f^{\|}(1)$	Simulated $f^{\|}(1)$
SIR	0.5394	0.5542	-0.2333	-0.2260	0.6234	0.6167
SEIR	0.5177	0.5319	-0.0695	-0.0753	0.5234	0.5442

From Tables 10 and 11, it could be deduced that the empirical estimate of the thresholds are very close to the simulated estimates of the thresholds. The empirical estimates are found in the 95% confidence intervals computed for the simulated estimates of the thresholds. It is asserted that decisions made with simulated estimates of the thresholds are good since they are based on large sample approximation which increases the accuracy of the thresholds estimates. Specified 95% confidence interval for the simulated estimate of the thresholds gives a range of plausible values for the estimates of the thresholds and also measures the long term success rate of the thresholds. Thresholds found within the various intervals for the simulated estimates of the thresholds are good estimates and can be used to make decisions which are not misleading. This confirms that

the various empirical estimates of the thresholds computed in the study are good estimates since there is 95% chance that the intervals contained them.

4.4 Discussion of Results

The principal objective of the study is to model tuberculosis epidemiology in the entire Ashanti region and also the individual high burdened districts in the region. We attempted to fit the standard SEIR model with demography since it is the appropriate model that characterized the infection dynamics of tuberculosis. The reduced form of the SEIR model which exclude the exposed compartment was developed since records on the exposed individuals was not captured in the data from the regional health directorate. SIR model with demography by Kermack and Mckendrick (1933) is the reduced model fitted. Stochastic SIR model thresholds were compared with that of the deterministic thresholds. Sensitivity analysis was conducted on the SEIR model to investigate into the influence of the initial condition of the exposed compartment on the tuberculosis infection dynamics. The effect of the SEIR model parameters (infection rate (α), exposed rate (Ɛ) and recovery rate (β)) on the basic reproduction number (R_0) is investigated. Treatment was introduced at the latent stage of tuberculosis infection dynamics and its effect on the basic reproduction number was sort for. Numerical simulations were made to validate the empirical thresholds computed in the study.

From the study, both the individual and deterministic SIR and SEIR models predict tuberculosis extinction in the entire Ashanti region. The SIR stochastic and deterministic empirical estimates of the thresholds were R_0= 0.5394, π = 1, ρ = -0.2333 and $f^{|}(1) = 0.6234$ for basic reproduction number, probability of tuberculosis extinction, Malthusian parameter and the mean number of offspring in a single generation respectively. That of the SEIR were R_0=

0.5177, π = 1, ρ = -0.0695 and $f^{|}(1) = 0.5234$ for basic reproduction number, probability of tuberculosis extinction, Malthusian parameter and the mean number of offspring in a single generation respectively. Tuberculosis was predicted to go on extinction in Ashanti region because the recovery rate of tuberculosis was higher than the infection rate of most of the districts in the region. The stability analysis of the equilibrium points from both models revealed that the disease free equilibrium point is stable for the entire Ashanti region. This result is consistent with the findings by Agrawal (2014), Li, et al. (1995), Adebimpe, et al. (2013) and Appoh (2013) when they were investigating the stability of the equilibrium point of the SEIR model with R_0 less than one. The population proportion for each compartment of the SIR model at the end of the study period (52 weeks) was: 0.7033, 0.00, and 0.2967 for susceptible, infectious and recovery/removed compartment respectively. This confirms the disease free equilibrium point stability of the SIR model.

The SIR and SEIR modeling of each of the 12 high burden districts revealed that ten (10) out of the twelve (12) districts are characterized by tuberculosis extinction. These districts have their basic reproduction numbers and the average number of offspring in a single generation less than one and the Malthusian parameter less than zero. These districts were: Adansi south, Asanti Akim North Municipal, Mampong Municipal, Atwima Nwabiagye, Bekwai Municipal, Bosomtwe, Ejusu – Juaben Municipal, Offinso Municipal, Kumasi Metropolitan and Sekyere South. The remaining two districts (Amansie West and Obuasi Municipal) will have persistent tuberculosis as predicted by their stochastic thresholds. This corresponds with the study by Affi (2018) and Appoh (2013). The two districts were revealed to have tuberculosis persisting because their infection rates were higher than the recovery rate.

The sensitivity analysis performed using the initial condition of the entire region as a case study indicated that the initial condition of the exposed compartment affect the tuberculosis infection dynamics and should not be ignored or assumed zero like what most researchers do. This is confirmed by the population proportions of the various compartments of the SEIR model at the end of the study period when the initial condition of the latent compartment was varied. This confirms the SEIR as the appropriate epidemiological model for modeling the infection dynamics of tuberculosis in the Ashanti region. Increasing the initial condition of the exposed compartment decreases the compartment size of the susceptible and the infectious but increase the size of the recovery/removal compartment at the end of the study time.

Using the parameters value for the SEIR model, we defined how different input parameters affect the basic reproduction number (R_0). Increasing the infection and exposed rates increases R_0 whiles increasing recovery rate reduces R_0. According to Mbogo (2018), increasing the infection rate means increasing the number of infectious individual and increasing the exposed rate also simply means decreasing the exposed or incubation period. Also increasing the recovery rate also means decreasing the infectious period.

Treatment rate introduced at the incubation period affect the basic reproduction number. This confirmed the study by Affi (2018). According to WHO and Ghana health services, every susceptible individual exposed to tuberculosis can be treated effectively at the incubation stage where infection is not active. Good medication can be use to increase or delay the latent period so as to reduce the rate at which the latent individuals proceed to the infectious class. Numerical simulations done to validate the empirical estimates of the stochastic and deterministic thresholds revealed that simulated estimates of the thresholds are the good estimates for the various threshold hence their corresponding 95% confidence interval contain plausible values for the

estimates of the thresholds since they are based on large samples. The various empirical estimates of the thresholds were all found in their respective simulated confidence intervals hence they are good estimates for the thresholds and can be used to make decision which are not misleading.

CHAPTER 5

SUMMARY, CONCLUSIONS AND RECOMMENDATIONS

In this section of the study, summary of major outcomes are presented and conclusions are build on the study outcomes. Recommendations are based on the conclusions.

5.1 Summary

This study primarily demonstrated success in modeling tuberculosis epidemics in the Ashanti region of Ghana with SIR and SEIR epidemic models. Both models predicted tuberculosis going to extinction in the entire region and some of the districts in the region base on their respective basic reproduction number. SIR and SEIR epidemic models revealed that empirical approximations of R_0 for the entire region were 0.5394 and 0.5177 respectively. The corresponding simulated 95% confidence intervals for both values were $0.5269 \leq \mathrm{R}_0 \leq 0.5818$ and $0.5057 \leq R_0 \leq 0.5581$ respectively. The branching process approximation for both models revealed that the probability for tuberculosis extinction in the region is one. Ten out of the twelve high burdened districts of tuberculosis were found to have tuberculosis going to extinction whiles the remaining two (Amansie West and Obuasi Municipal) have tuberculosis persisting at the end of the study time.

Sensitivity analysis brought to light that the initial condition of the exposed compartment affects the infection dynamics of tuberculosis. Increasing the initial condition of the exposed compartment decreases the susceptible and the infectious compartments size but increases the recovery/removal compartment size at the end of the study time.

Investigation through numerical analysis done to find out the influence of model parameters on the basic reproduction number revealed that increasing exposed and infection rates inflate the basic reproduction number whiles increasing recovery/removal rate drops the basic reproduction number. Also, introduction of treatment at the incubation (exposed) stage of tuberculosis infection dynamics decreases the basic reproduction number.

Finally, numerical simulation confirmed that the various thresholds approximations are good estimates for studying TB infection dynamics in the region.

5.2 Conclusion

The SEIR and SIR models both showed success in attempting to anticipate the growth of tuberculosis in the Ashanti region of Ghana. Each model predicted that on average every infectious person will infect less than one susceptible person with tuberculosis bacterial based on their respective basic reproductive number. Tuberculosis will not spared but die out in the entire Ashanti region with an extinction probability of one. Ten (10) out of the twelve (12) districts will have tuberculosis dyeing out and the remaining two persisting. These two districts are Amansie West and Obuasi Municipal.

The initial condition of the exposed compartment affect the tuberculosis infection dynamics hence the appropriate standard model for modeling tuberculosis infection dynamics in Ashanti region is the SEIR model. The 95% confidence intervals for SEIR model thresholds: basic reproduction number, Malthusian parameter and mean number of offspring in a single generation are (0.5057, 0.5581), (-0.0794, -0.0712) and (0.5169, 0.5718) respectively.

Increasing the exposed and infection rates increases the basic reproduction number whiles

increasing the recovery rate reduces the basic reproductive number. Introducing treatment together with increasing the mode of treatment at the exposed (latent) stage of the infection dynamics helps to prevent tuberculosis from spreading in the region.

5.3 Recommendations

The study outcomes and conclusions presented the following recommendations:

- Ghana Health Service should find a mechanism to detect individuals who are exposed to tuberculosis, since it is the appropriate stage to commence treatment for tuberculosis. Taken into consideration the side effect of the drug used for the treatment than to wait for them to become infectious.
- The SEIR epidemiological compartment model should be employed in studying and making decision about the infection dynamic of tuberculosis in the Ashanti region of Ghana.
- Infected persons of tuberculosis must have high adherence to proper medication and treatment practices since the pathogens of tuberculosis can be resistant to treatment over time if left unattended.
- In addition, public health education and other symposiums must be organized on the prevalence of tuberculosis in the Ashanti region most especially Amansie West district and Obuasi Municipal so as to create high level of awareness about the deadly nature of tuberculosis.
- Effort should be made by the Ghana Health Service to help lessen the infectious period but increase the exposed phase of tuberculosis transmission.

- Further study should be conducted on the use of SEIR model with the inclusion of tuberculosis fatality rate to examine the infection dynamics of TB in the region.

BIBLIOGRAPHY

Adebimpe, O., Waheed, A. A., and Gbadamosi, B. (2013). Modeling and analysis of an SEIRS epidemic model with saturated incidence. Int. Journal of Engineering Research and Application, 3(1), 1111-1116.

Affi, O.P. (2018). Global Stability Analysis of the SEIR Deterministic Model in the Presence of Treatment at the Latent Period. Mathematics Letters. Vol. 4, No. 4, 2018, pp. 67-73. doi: 10.11648/j.ml.20180404.12.

Affi, O. P. (2018). Sensitivity Analysis of the SEIR Epidemic Compartment Model. International Journal of Science and Research (IJSR). Volume 7 Issue 12, 352 – 357.

Allen, L.J.S. (2008). An introduction to stochastic epidemic models. In F. Brauer, P. van den Driessche, and J. Wu (Eds). Lecture notes in mathematics: Vol. 1945. Mathematics epidemiology (pp.81 – 130). Berlin: Springer. Ch. 3.

Allen, L. J.S (2017). A primer on stochastic epidemic models: Formulation, numerical simulation, and analysis" Infectious Disease Modeling 2(2017) 128 – 142.

Anderson, R. M. and May, R. M. (1991). Infectious diseases of humans. Oxford, UK: Oxford university press.

Agrawal, A. (2014). Global analysis of an SEIRS epidemic model with new modulated saturated incidence. Commun. Math. Biol. Neurosci. 2014:2.

Andersson, H., and Britton, T. (2000). Stochastic epidemic models and their statistical analysis. In Lecture notes in statistics, No. 151. New York: Springer - Verlag.

Blower, S. M., McLean, A. R., Porco, T. C., Small, P. M., Hopwell, P. C., Sanchez, M. A., and Ross, A. R.(1995). The intrinsic transmission dynamics of tuberculosis epidemics. Nature Medicine vol. 1, pp. 815 – 821.

Brauer, F., Van den Driessche, P., and Wu, J. (2008). Mathematical epidemiology, Springer.

Britton, T. and Ouedraogo, D. (2017). SEIRS epidemics with disease fatalities in growing populations. Mathematical Biosciences. Doi: 10.1016/j.mbs.2017.11.006.

Castillo-Chavez, C., and Feng, Z. (1998). Global stability of an age – structure model for TB and its applications to optimal vaccination strategies, Math. Biosci. 151. 135 – 154.

Castillo-Chavez, C., Hethcote, H. W., Andreason, V., Levin, S. A., and Liu, W. (1989). Epidemiological models with age structure, proportionate mixing and cross-immunity. J. Math. Biol. 27, 233 -258.

Centers for Disease Control and Prevention (CDC) (2017). Questions and answers about TB.

Cook, K. L., and Van den Driessche, P. (1996). Analysis of an SEIRS epidemic model with two delays. J. Math. Biol. 35:240.

Diekmann, O., Heesterbeek, J. A. and Metz, J. A. (1990). On the definition and the computation of the basic reproduction ratio (R_0) in models for infectious diseases in heterogeneous populations. Journal of Mathematical Biology, vol. 28, no. 4, pp. 365–382.

Diekmann, O., Heesterbeek, H. and Britton T. (2013). Mathematical Tools for understanding Infectious Disease Dynamics. Princeton University Press.

Dietz, K., and Schenzle, D. (1985). Proportionate mixing models for age-dependent infection transmission. J. Math. Biol. 22. 117 – 120.

Eichner, M. and Dietz, K. (1996). Eradication of poliomyelitis: When can one be sure that polio virus transmission has been terminated? American Journal of Epidemiology, 143: 816 – 822.

Thomas, G. E., Barrington, H. E., Lokuge, K. M., and Mercer, G. N. (2010). Modeling the spread of tuberculosis, including drug resistance and HIV: a case study in Papua New Guinea's western province. ANIAM J. 52(1), 26 – 45.

Feng, Z., Castillo-Chavez, C., and Capurro, A. F. (2000). A model for tuberculosis with exogenous reinfection. Theoretical Population Biology. 57: 235-247.

Felix O. Mettle, Prince Osei Affi, Emmanuel Aidoo and Shadrack Benn(2020). Stochastic modeling approach of infectious disease with SIR epidemiological compartment model. Communications in Mathematical Biology and Neuroscience, 2020:55

Genik, L., and Van Den Driessche, P.(1998). A model for diseases without immunity in a variable size population. Canadian Appl. Math. Quart, 6(1): 5 – 16.

Ghana Health Service (2012) – Stop TB Programme.

Haccou, P., Jagers, P. and Valutin, V. A. (2005). Branching Processes: Variation, Growth, and Extinction of Populations. Cambridge University Press, Cambridge.

Hethcote, H. (2000). The mathematics of infectious diseases. SIAM Review, 42(4): 599 – 653.

Hethcote, H. W., and Yorke, J.A. (1984). Gonorrhea transmission dynamics and control, Lect. Notes Biomath.,vol.56, springer, Berlin.

Hethcote, H. W. (2000). Qualitative analysis of communicable disease model. Math. Biosci., 28: 335 – 356.

Hickson, R. I., Mercer, G. N., and Lokuge, M. K. (2011). Sensitivity analysis of a model for tuberculosis. 19th International congress on modeling and simulation, Perth, Australia, 12 – 16.

Index mundi, (2017). http://www.indexmundi.com/ghana/death_rate.html.

Jacob, C. (2010). Branching processes: Their role in epidemiology. Int. J. Environ. Res. Public Health, 2010(7): 1186 – 1204.

Jagers, P. (1975). Branching Processes with Biological Applications. New York:Wiley

Jones, J. H., (2007). Notes on Reproductive Number.

Junjie, C. and Xiangguan, L. (2006). Stability of an SEIS epidemic model with constant recruitment and a varying total population size. Appl. Math.Chin.Univ. 21(1) : 1 - 8.

Kermack WO, McKendrick AG (1933). "Contributions to the Mathematical Theory of Epidemics. III. Further Studies of the Problem of Endemicity". Proc. R. Soc. Lond. A 141 (843): 94–122.

Li, M. Y., Smith, H. L., and Wang L. (2001). Global dynamics of an SEIR epidemic model with vertical transmission. SIAMJ Appl. Math. 62: 58 – 69.

Li, M. Y., and Muldowney, J. S. (1995). Global stability for the SEIR model in epidemiology. Math. Biosci. 125: 155 – 64.

Li, M. Y., Graef, J., Wand, L. and Karsai, J. (1999). Global dynamics of the SEIR model with

varying total population size. Mathematical Biosciences, 160: 191 – 215.

Li, G., and Zhen, J. (2005). Global stability of an SEIR epidemic model with infectious force in the latent, infected and immune period. Chaos, Solitions and Fractals, Elesvier, 25:1177-1184.

Li, J., Zhang, J, and Ma, Z. (2006). Global dynamic of an SEIR epidemic model with immigration of different compartments. Acta Mathematica Scientia, 26, 551-567.

Lloyd, A. L., Zhang, Z., and Morgan, R. A. (2007). Stochasticity and heterogeneity in host-vector models. Journal of the Royal Society Interface, 4, 851e863.

May, R. M., and Anderson, R. M. (1984). Spatial, temporal, and genetic heterogeneity in host populations and the design of immunization programmes, IMA J. Math. Appl. Med. Biol. 1: 233.

Mbaya, T. and Dimi, J. L. (2016). Analysis of stochastic model of tuberculosis transmission. Journal of Progressive Research in Mathematics (JPRM). ISSN: 2395 – 0218.

Mbaya, T., Dimi, J. L. and Ondami, B. (2016). Mathematical Analysis of Deterministic and Stochastic Model of Tuberculosis. International Journal of Scientific and Innovative Mathematical Research (IJSIMR). Vol. 4, Issue 1, pp 8 – 20.

Mbogo, W.R., Luboobi, S.L. and Odhiambo, W. J. (2018). A stochastic model for malaria transmission dynamics. Journal of applied mathematics. Volume 2018, Article ID 2439520, 13 pages.

Meng, F., Li, M. Y., and Wang Ke. (2001). Global stability of SEIS epidemic model with recruitment and a varying total population size. Math Biosci, 170: 199 – 208.

Mettle, F. O., Osei Affi, P., and Twumasi, C. (2020). Modelling the Transmission Dynamics of Tuberculosis in the Ashanti Region of Ghana. Interdisciplinary Perspectives on Infectious Diseases-Hindawi, 2020.

Mode, C. J. (1971). Multi – Type Branching Processes – Theory and Application. J American Elsevier Publishing Company, Inc.

Mudassar Imran, Muhammad Hassan, Muhammad Dur-E-Ahmad & Adnan Khan (2013) A

comparison of a deterministic and stochastic model for Hepatitis C with an isolation stage, Journal of Biological Dynamics, 7:1, 276-301, DOI: 10.1080/17513758.2013.859856.

Murray, J., Stanley, E., and Brown, D. (1986). On spatial spread of rabies among foxes. Proceedings of the Royal Society, London, 1255: 111- 150.

Murray, J. (1989). Mathematical Biology. Springer Verlag, Berln.

Pertsev, N. V. and Leononko, V. N. (2014). Analysis of stochastic model for the spread of tuberculosis with regard to reproduction and seasonal immigration of individuals. Sobolev Institute of Mathematics, Novosibirsk 630090 Russia. PP. 1 – 15 (2014).

Sarah, A. Al-Sheikh (2012). Modeling and analysis of an SEIR epidemic model with a limited resource for treatment. Global journal of Science Frontier Research Mathematics and Decision Sciences. 12: 1 – 11.

Sarkodie, E. (2014). Modeling the spread of tuberculosis in central region using the susceptible-exposed – infected - susceptible (SEIS) mathematical model. Department of mathematics, College of Science, KNUST, Ghana.

Trottier, H. and Philippe, P. (2001). Deterministic modeling of infectious diseases: Theory and methods. The International Journal of Infectious Diseases, 1(2).

Van den Driessche, P., and Watmough, J. (2002). Reproduction numbers and sub threshold endemic equilibria for compartmental models of disease transmission. Mathematical biosciences, 180, 29-48.

Watson, H. W. and Galton, F. (1875). On the probability of the extinction of families. Journal of the Anthropological Institute of Great Britain, 4:138-144.

Wikipedia (2018). http://www.wikipedia.com/Transmission risks and rates.

World Health Organization (1993). W.H.O. Calls Tuberculosis a Global Emergency, Los Angeles Times.

World Health Organization (2006). Global Tuberculosis Control Programme Report.

World Health Organization (2011).Tuberculosis Fact Sheet Number 104.

World Health Organization (2000b).Tuberculosis and BCG. Vaccines, Immunization and Bio.

Appendix 1: R Codes for Data Analysis

Appendix 1a: R codes for SIR epidemic deterministic model simulation

```
library(deSolve)
SIR_model= function(t, state_values, parameters)
 {
    # lambda=death rate
   #mu=birth rate
   #beta=recovery rate
   #alpha=infection rate

    # compute derivatives

#Rename the variables and parameters
  S = state_values[1]        # susceptibles
  I = state_values[2]        # infectious
  R = state_values[3]        # recovered

N=S+I+R

mu=parameters[1]
lambda=parameters[2]
beta=parameters[3]
alpha=parameters[4]

#Defining system of ODEs
      dS = lambda*N-mu*S-alpha*S*(I/N)
      dI = alpha*S*(I/N)-(mu+beta)*I
      dR = beta*I-mu*R

#Return the 3 values

return(list(c(dS,dI,dR)))
}
#Initial conditions
mu=0.007
lambda=0.007
beta=0.5
alpha=0.2735

SIR_par=c(mu,lambda,beta,alpha) #model parameters
SIR_init=c(7020,2642,10)# Initial condition for each class
SIR_t=seq(0, 52, by=1) #1 years

#Numerical solution
SIR_sol=lsoda(SIR_init,SIR_t,SIR_model,SIR_par)
head(SIR_sol)
Time=SIR_sol[,1]
S=SIR_sol[,2]
I=SIR_sol[,3]
```

```
R=SIR_sol[,4]


#Plotting the dynamics
N=S+I+R
plot(Time,S/N,main="TB Infection Dynamics",xlab="Time (in
weeks)",ylab="Proportion",col="green",las=1,type="l",ylim=c(0,1))
lines(Time,I/N,col="red")
lines(Time,R/N,col="black")
legend("topright",legend = c("Susceptibles (S)","Infecteds (I)", "Recovereds
(R)"),col=c("green","red",black"),
       lty = c(1,1,1,1))


#Calculating Ro for the SIR model
Reproductive_num=function(SIR_par){
    Ro=alpha/(mu+beta))
    return(Ro)
}
```

Appendix 1b: R codes for SEIR epidemic deterministic model simulation

```
library(deSolve)
SEIR_model= function(t, state_values, parameters)
 {
    # lambda=death rate
   #mu=birth rate
   #epsilon=exposed rate
   #beta=recovery rate
   #alpha=infection rate

    # compute derivatives

#Rename the variables and parameters
  S = state_values[1]        # susceptibles
  E = state_values[2]        # exposed
  I = state_values[3]        # infectious
  R = state_values[4]        # recovered

N=S+E+I+R
mu=parameters[1]
lambda=parameters[2]
epsilon=parameters[3]
beta=parameters[4]
alpha=parameters[5]

#Defining system of ODEs
      dS = lambda*N-mu*S-alpha*S*(I/N)
      dE = alpha*S*(I/N)-(mu+epsilon)*E
      dI = epsilon*E-(mu+beta)*I
      dR = beta*I-mu*R

#Return the 3 values
```

```
return(list(c(dS,dE,dI,dR)))
}
#Initial conditions
mu=0.007
lambda=0.007
epsilon=0.16667
beta=0.5
alpha=0.2737

SEIR_par=c(mu,lambda,epsilon,beta,alpha) #model parameters
SEIR_init=c(7011,0,2642,10)# Assuming there was no record of those exposed in
the entire region
SEIR_t=seq(0, 52, by=1) #1 years

#Numerical solution
SEIR_sol=lsoda(SEIR_init,SEIR_t,SEIR_model,SEIR_par)
head(SEIR_sol)

Time=SEIR_sol[,1]
S=SEIR_sol[,2]
E=SEIR_sol[,3]
I=SEIR_sol[,4]
R=SEIR_sol[,5]

#Plotting the dynamics
N=S+E+I+R
plot(Time,S/N,main="TB Infection Dynamics",xlab="Time (in
weeks)",ylab="Proportion",col="red",las=1,type="l",ylim=c(0,1))
lines(Time,E/N,col="blue")
lines(Time,I/N,col="green")
lines(Time,R/N,col="black")
legend("topright",legend = c("Susceptibles (S)","Exposed (E)","Infecteds
(I)", "Recovereds (R)"),col=c("red","blue","green","black"),
       lty = c(1,1,1,1))

#Calculating Ro for the SEIR model
Reproductive_num=function(SEIR_par){
    Ro=(alpha*epsilon)/((mu+epsilon)*(mu+beta))
    return(Ro)
}


#Efect of the SEIR model parameters on Ro

mu=0.007
lambda=0.007
epsilon=seq(0.16667,5,length.out=length(SEIR_t))
beta=seq(0.5,5,length.out=length(SEIR_t))
alpha=seq(0.2737,1,length.out=length(SEIR_t))

SEIR_par=c(mu,lambda,epsilon,beta,alpha)
Ro=Reproductive_num(SEIR_par)#Calculating Ro

plot(epsilon,Ro,type="l",xlab="Time",ylab="Reproductive number",col="red")
plot(beta,Ro,type="l",xlab="Time",ylab="Reproductive number",col="red")
plot(alpha,Ro,type="l",xlab="Time",ylab="Reproductive number",col="red")
```

Appendix 1c: R codes for numerical simulation

```
#FOR SIR EPIDEMIC MODEL
R0_estimate<-function(alpha,beta,mu){
Ro=alpha/(mu+beta))
    return(Ro)
}
# Simulating truncated beta (0.881, 2.262)
set.seed(1)
alpha=urbeta(n=1000, shape1=0.881, shape2=2.262)

#Calculating R0 for each simulated alpha value
R0=numeric(1000)
for(i in 1:1000){
    R0[i]=R0_estimate(alpha[i],beta=0.5, mu=0.007)
}
print(paste("Mean value of R0 is:",round(mean(R0),4)))
lowerlimit=mean(R0)-1.96*(sd(R0)/sqrt(1000))
upperlimit=mean(R0)+1.96*(sd(R0)/sqrt(1000))


#FOR SEIR EPIDEMIC MODEL
R0_estimate<-function(alpha,epsilon,beta,mu){
Ro=(alpha*epsilon)/((mu+epsilon)*(mu+beta))
    return(Ro)
}
# Simulating truncated beta (0.881, 2.262)
set.seed(1)
alpha=urbeta(n=1000, shape1=0.881, shape2=2.262)

#Calculating R0 for each simulated alpha value
R0=numeric(1000)
for(i in 1:1000){
    R0[i]=R0_estimate(alpha[i],beta=0.5,epsilon=0.1667,mu=0.007)
}
 }
print(paste("Mean value of R0 is:",round(mean(R0),4)))
lowerlimit=mean(R0)-1.96*(sd(R0)/sqrt(1000))
upperlimit=mean(R0)+1.96*(sd(R0)/sqrt(1000))
```

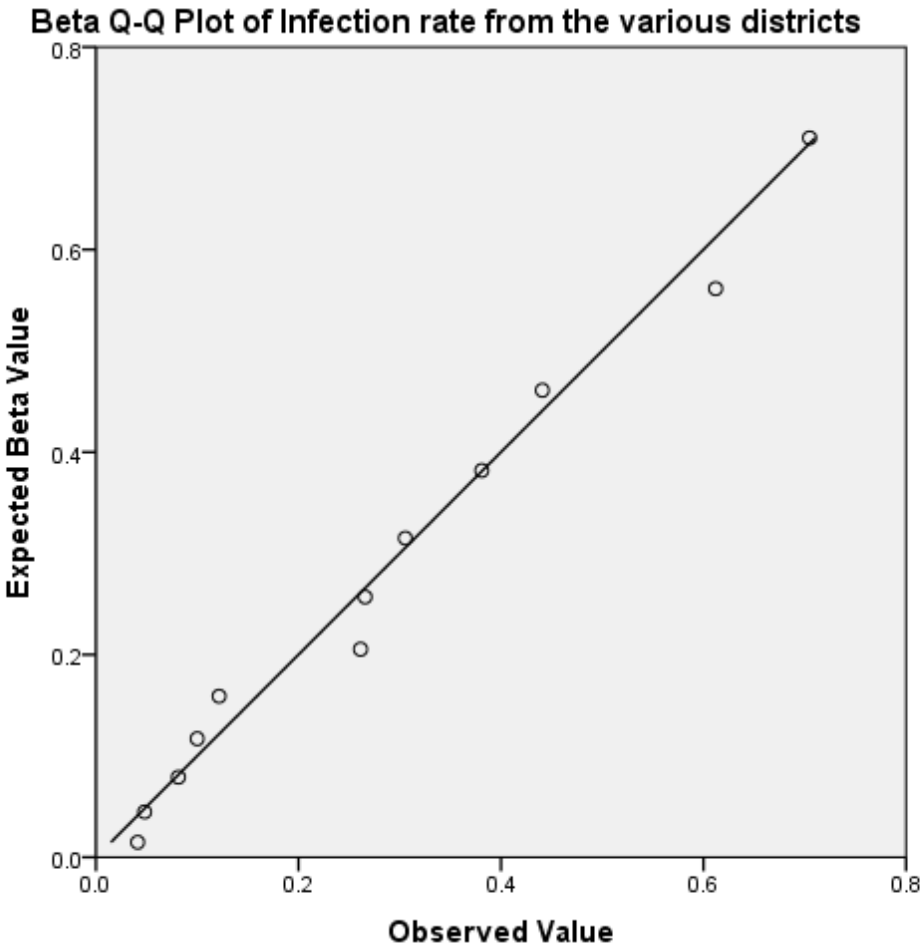
Appendix 2

Fitting beta distribution for the infection rate from the various districts

Estimated Distribution Parameters

		Infection rate from the various districts
Beta Distribution	Shape1	.881
	Shape2	2.262

.



Sample of R_0 computed for the various infection rates generated with the SIR model for the entire region

[1] 0.42878018 0.56832627 0.83105620 1.26999347 0.34523891 1.25714279

[7] 1.31772487 0.94616453 0.90469444 0.16213288 0.35085745 0.31235318

[13] 0.98048986 0.58400637 1.08888909 0.73268879 1.02053578 1.37954415

[19] 0.57868115 1.09884152 1.30467533 0.35893053 0.93422231 0.24559835

[25] 0.43102098 0.58663770 0.09878861 0.58176065 1.21957958 0.52673687

[31] 0.71224530 0.86601949 0.72724657 0.32499803 1.16419119 0.95620222

[37] 1.12082361 0.22254712 1.02851003 0.61956945 1.15577902 0.92818372

[43] 1.10602403 0.80511814 0.77459943 1.11443155 0.11179997 0.70589718

[49] 1.03977001 0.98796186 0.70640706 1.20847852 0.65467700 0.40167154

[55] 0.17377242 0.21145117 0.49522269 0.76009013 0.94774471 0.61375249

[61] 1.27610348 0.46555266 0.68212232 0.51632565 0.93317089 0.41897423

[67] 0.70761859 1.08426777 0.19153107 1.22694918 0.52506667 1.17998544

[73] 0.53502794 0.51813224 0.70474692 1.24903908 1.21257529 0.59171018

[79] 1.09867853 1.33859192 0.65017758 1.01385550 0.60480525 0.50710787

[85] 1.07219533 0.34656130 1.01203164 0.24054193 0.40257629 0.26882995

[91] 0.39490746 0.15840010 0.92193785 1.22818984 1.10076485 1.12484051

[97] 0.67716001 0.61801143 1.14259072 0.87304484 0.93821459 0.54355367

[103] 0.43499928 1.38056241 0.91042629 0.36032528 0.25059466 0.70705942

[109] 1.29076098 0.86496603 1.35894847 1.03908779 0.54817353 0.64600777

[115] 0.27525284 0.09837925 1.01784939 0.21631767 0.66539308 0.91907506

[121] 1.37945583 0.72993274 0.71521567 0.30827679 1.06922915 0.67535512

[127] 0.75032006 0.35291309 0.38054742 0.86097531 0.83369860 0.18213003

[133] 0.12778053 0.92260175 1.29670423 0.86409099 0.81541171 0.76976725

[139] 1.37062957 0.74570239 0.97494708 0.86860503 0.39391174 0.41916945

[145] 1.03583800 0.67362131 0.31048151 1.05859758 0.21867810 1.21284424

Sample of R_0 computed for the various infection rates generated with the SEIR model for the entire region

[1] 0.41150061 0.54542308 0.79756516 1.21881354 0.33132600 1.20648073

[7] 1.26462139 0.90803470 0.86823582 0.15559903 0.33671812 0.29976554

[13] 0.94097674 0.56047128 1.04500754 0.70316190 0.97940884 1.32394940

[19] 0.55536067 1.05455890 1.25209774 0.34446585 0.89657374 0.23570089

[25] 0.41365111 0.56299657 0.09480749 0.55831606 1.17043129 0.50550971

[31] 0.68354226 0.83111945 0.69793899 0.31190081 1.11727502 0.91766788

[37] 1.07565513 0.21357861 0.98706172 0.59460119 1.10920185 0.89077850

[43] 1.06145196 0.77267239 0.74338357 1.06952066 0.10729450 0.67744997

[49] 0.99786794 0.94814762 0.67793931 1.15977760 0.62829393 0.38548444

[55] 0.16676950 0.20292982 0.47526553 0.72945898 0.90955120 0.58901865

[61] 1.22467732 0.44679118 0.65463322 0.49551806 0.89556470 0.40208984

[67] 0.67910201 1.04057247 0.18381249 1.17750391 0.50390682 1.13243277

[73] 0.51346665 0.49725184 0.67634606 1.19870360 1.16370927 0.56786463

[79] 1.05440248 1.28464751 0.62397584 0.97299777 0.58043198 0.48667174

[85] 1.02898654 0.33259510 0.97124741 0.23084824 0.38635272 0.25799628

[91] 0.37899293 0.15201668 0.88478434 1.17869457 1.05640473 1.07951015

[97] 0.64987089 0.59310596 1.09654503 0.83786168 0.90040514 0.52164880

[103] 0.41746908 1.32492662 0.87373669 0.34580440 0.24049585 0.67856538

[109] 1.23874413 0.83010845 1.30418371 0.99721321 0.52608248 0.61997407

[115] 0.26416033 0.09441463 0.97683071 0.20760021 0.63857816 0.88203691

[121] 1.32386464 0.70051691 0.68639293 0.29585343 1.02613989 0.64813874

[127] 0.72008263 0.33869092 0.36521160 0.82627855 0.80010108 0.17479030

[133] 0.12263106 0.88542149 1.24444787 0.82926867 0.78255113 0.73874612

[139] 1.31539406 0.71565106 0.93565733 0.83360080 0.37803735 0.40227718

[145] 0.99409438 0.64647480 0.29796930 1.01593677 0.20986551 1.16396738

Screening report on tuberculosis infection for Ashanti region of Ghana in 2017

District	Infection Rate(α)	susceptible	Infected	Recovered/Death
Adansi south	0.1216	390	54	0
Asanti Akim North Municipal	0.4409	1202	948	0
Amansie West	0.7048	98	234	0
Mampong Municipal	0.0481	752	38	0
Atwima Nwabiagye	0.2613	325	115	0
Bekwai Municipal	0.3055	316	139	3
Bosomtwe	0.1	513	57	5
Ejusu – Juaben Municipal	0.0814	711	63	1
Obuasi Municipal	0.612	71	112	0
Offinso Municipal	0.381	13	8	0
Kumasi Metropolitan	0.2658	2387	864	1
Sekyere South	0.0412	233	10	0
Region	**0.2735**	**9663**	**2643**	**10**

	recovery/removal rate β =	exposed rate Ɛ=
Birth (λ)=Death(μ)=0.007	0.5	0.1667