MATHEMATICAL MODEL OF TUBERCULOSIS (TB) TRANSMISSION DYNAMICS INCORPORATING TREATMENT, ISOLATION AND VACCINATION

BY

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ABSTRACT

In this thesis, we developed and analysed a mathematical model of Tuberculosis (TB) transmission dynamics incorporating treatment, isolation and vaccination. The total size of the population was partitioned into seven compartments. The model has two equilibria; the Diseases-Free Equilibrium (D.F.E) and Endemic Equilibrium (E.E). The equilibrium states were obtained for their stability relatively to the effective reproduction number. The result shows that, the disease-free equilibrium state was stable and the criteria for stability of the endemic equilibrium state are established. This thesis was able to show that the Tuberculosis (TB) infectious free equilibrium is locally and globally asymptotically stable if $R_0 < 1$. Using $\rho = 0.075$, $m = 0.300$, $i. = 20$ and $N(t) =$ 209, 042, 603, $S(t) = 5000$, (1850) 1700 the number of quarantine human individual decreases as the rate at which quarantine that becomes infected increases. The analytical solution was obtained using Homotopy perturbation Method (HPM) and effective reproduction number was computed in order to measure the relative impact for individual or combined intervention for effective disease control. Numerical simulations of the model show that, the combination of isolation and vaccination is the most effective way to combat the epidemiology of Tuberculosis (TB) virus.

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ABBREVIATION, GLOSSARIES AND SYMBOLS

γ	Transmission rate among the effectively treated/recovered individuals
d_1	Death rate for infected class
A	Total number of new immigrants
β	Transmission rate among the susceptible
μ	Natural per capital death rate
π	Natural per capital birth rate
d_2	Death rate for isolated class
α	Effective transmission rate from early latent class to infected class
ω	Progression rate from late latent class to infected class
ρ	Fraction of E_1 individuals with fast TB progression.
q	Fraction of immigrants (A) having latent TB.
k	Reactivation rate of the early latent individuals
m	Fast transmission rate
l	Isolation level $(0 \le l \le 1)$
n	Rate of isolation
σ	Contact level $(0 \le \sigma \le 1)$ treated individuals have with isolated individuals

$S(t)$

$E_1(t)$

$E_2(t)$

$i.(t)$

$S(t)$

$t\ (t)$

CDC

DFE

HPM

N

WHO

EE

Susceptible

early latent

late latent

non-isolated infectious

isolated infectious

treated or recovered

Centre for Disease Control

Disease-Free Equilibrium

Homotopy Perturbation Method

Total Population

World Health Organization

Endemic Equilibrium

CHAPTER ONE

1.0 INTRODUCTION

1.1 Background to the Study

Tuberculosis (TB) is a worldwide pandemic disease. According to World Health Organization (WHO), one-third of the world's population is currently infected by the TB bacillus bacteria. Being a disease of poverty, the vast majority of TB deaths are in the developing world with more than half occurring in Asia (WHO, 2010).

The estimated global incidence rate is falling very slowly from the peak of 141 cases per 100,000 population in 2002 to 128 cases per 100,000 population in 2010. The TB death rate has also fallen by 40% since 1990 and the number of deaths is also declining. Globally, the percentage of people successfully treated reached its highest level at 87% in 2009.

Tuberculosis (TB) is a chronic bacteria infectious disease caused by Mycobacterium 1tuberculosis which pose a major health, social and economic burden globally, especially in low- and middle-income countries (Delogu *et al.,* 2013). It is the second deadliest disease due to a single infectious agent only after HIV/AIDS (WHO, 2016). The surge in HIV-TB co-infection and growing emergence of multidrug-resistant TB (MDR-TB) and extensively drug resistant TB (XDR-TB) strains has further fuelled TB epidemic. TB usually affects the lungs (pulmonary TB) but it can also affect other sites as well (extra-pulmonary TB). Tuberculosis is transmitted by tiny airborne droplets which are expelled into the air when a person with active pulmonary TB coughs or talks (Issarowa *et al.,*2015. Estimate show that TB has infected one-third of the world's population with the most infections occurring in Africa and Asia (WHO, 2016). In 2015, there were an estimated 10.4 million new TB cases (incidence) in worldwide, as well as an estimated 1.4 million

1

TB-induced deaths, and an additional 0.4 million deaths resulting from TB disease among persons living with HIV. Furthermore, over 95% of these deaths occurred in low- and middle-income countries where the cost of diagnosis and treatment is high, and not readily accessible (WHO, 2016).

Diagnosis of latent TB infections (LTBI) and prompt treatment of active cases remains an important component of effective TB control (Centers for Disease Control and Prevention, 2016). On the other hand, undetected TB infection and delay in the treatment of active TB cases leads to more severe disease conditions in the infected person which could result in wider disease spread in the community (Al-Darraji *et al.,* 2016). Such delays also contribute to increased infectivity in the community (Asefa and Teshome, 2014) whereby, the infected individuals unknowingly continue to serve as a reservoir for the pathogen (M. tuberculosis). Hence, this could lead to increased risk of disease transmission in the community. In fact, the effects of diagnosis of LTBI and delay in the treatment of active TB cases on the incidence and prevalence of TB were issues considered by some presenters at the 45th World Conference on Lung Health held in 2014. Health literacy, i.e., knowledge and education related to tuberculosis, as well as socio-cultural factors such as gender roles and status in the family has been identified as having considerable influence on undetected latent TB infection and delay in the treatment of active cases (Lin *et al.,* 2015). TB knowledge includes the ability to identify causes and understand the transmission path of the disease, recognize disease symptoms, and be aware of available treatment regimens such as directly observed treatment short course (DOTS); which is the TB treatment strategy recommended by the World Health Organization (WHO) (Okuonghae & Ahile*,* 2010). On the other hand, ignorance on the part of infected individuals about TB usually leads to postponement in seeking appropriate medical attention, and in some cases such persons will rather adopt alternative approaches, such as seeking traditional healers, before consulting DOTS facility, thereby delaying diagnosis and treatment of TB. A recent study in China identified financial difficulty as well as ignoring early TB symptoms or not understanding the meaning of such symptoms on the part of actively-infected persons as being responsible for delay in seeking appropriate medical attention (Lin *et al.,* 2015). Besides, some infected individuals are scared of undergoing TB diagnosis because of fear of having to pay for a prolong TB treatment regimen (6–8 months), which ultimately could increase the possibility of developing multidrug-resistant TB strains (Cain *et al.,* 2015).

In some developing countries, the distance and additional transportation cost to and from a DOTS facility could also discourage actively-infected persons from seeking appropriate medical attention as soon as possible. In the same vain, the life style and habit of some infected individuals have been identified as being also responsible for undetected latent TB infection and delay in the treatment of active TB cases. For example, a person who smokes cigarette may continue to trivialize early TB symptoms such as cough, thereby delaying prompt diagnosis and treatment of the disease (Bam *et al.,* 2012). Stigmatization and discrimination towards individuals infected with TB is another factor that could deter persons from seeking prompt TB diagnosis and treatment since it fosters social exclusion and saddens the infected person and members of their family. And because of the social rejection and stigmatization, some patients would rather postpone seeking appropriate medical attention due to the fear of getting to find out about their positive TB status (Cattamanchi *et al.,* 2015).

Health system delay (HSD) in the diagnosis and treatment of LTBI as well as active TB case is usually connected with an infected patient's visit to an health care center, but without receiving accurate diagnosis. HSD is often caused by unavailability of upto-date diagnostic laboratory equipments, not adhering to the diagnostic procedures based on

DOTS strategy recommended by the WHO, and difficulties in identifying TB symptoms in an infected person especially if such symptoms coexist with other chronic lung diseases and/or severe cough. Infected individuals can also experience diagnostic delays as a result of low clinical suspicion of tuberculosis on the part of health-care practitioners. A possible explanation for such wrong or delayed diagnosis on the part of health-care provider is that pulmonary TB can manifest itself with symptoms that are very similar to other diseases such as community-acquired pneumonia (CAP), which is often treated with antibiotics like fluoroquinolones. It has been shown that FQs also have antimicrobial activity against M. Tuberculosis (Wang *et al.,* 2011).

1.2 Statement of the Research Problem

Tuberculosis is an infectious pandemic disease caused by mycobacterium disease. Tuberculosis is one of the major causes of ill health in humans. Research breakthroughs like vaccines, early detention and isolation are required to minimize or eradicate this deadly pandemic disease. A total of 1.4 million people died from TB in 2019 (including 208 000 people with HIV). Worldwide, TB is one of the top 10 causes of death and the leading cause from a single infectious agent (above HIV/AIDS).

In 2019, an estimated 10 million people fell ill with tuberculosis (TB) worldwide. 5.6 million men, 3.2 million women and 1.2 million children. TB is present in all countries and age groups. But TB is curable and preventable.

In 2019, 1.2 million children fell ill with TB globally. Child and adolescent TB is often overlooked by health providers and can be difficult to diagnose and treat. World Health Organization (WHO, 2020)

According to World Health Organization (WHO), the number of people falling ill with TB each year is declining (WHO, 2010). However, this downward trend is threatened by the increasing number of TB cases in immigrants especially in countries that have substantial levels of immigration from areas with a high prevalence of the disease (Jia *et al.,* 2008).

1.3 Motivation of Study

The motivation of this research work is to look for the prevention of Tuberculosis (TB) disease through Mathematical Modeling. The researcher is also inspired to make vital information available for policy makers in the fight against Tuberculosis (TB) disease in the world.

1.4 Justification of Study

The need for detailed and qualitative scholarly work on Tuberculosis (TB) bacterial justifies the study. The thesis may also aid mathematicians and research scientists to further develop suitable models to help public health professionals to make better strategies for controlling the disease.

1.5 Scope and Limitations of the Study

This work covers the formulation and analysis of a mathematical model for the transmission dynamics of tuberculosis incorporating treatment, isolation and vaccination.

1.6 Aim and Objectives of the Study

The aim of this research work is to develop and analyze a mathematical model for the transmission dynamics of tuberculosis (TB) incorporating treatment, isolation and vaccination.

The objectives are to;

ii. formulate a mathematical model of Tuberculosis (TB) transmission dynamics Incorporating treatment, isolation and vaccination.

iii. examine the epidemiological well poseness of the model.

iv. obtain the Disease-Free Equilibrium (DFE) and the Endemic Equilibrium (EE).

v. compute the basic reproduction number of the model

vi. conduct the stability analysis of DFE

vii. solve the model equations using homotopy perturbation method (HPM)

viii. to obtain the numerical simulations of the model using computer software.

1.7 Definition of Terms

Equilibrium: This is the state of rest of a body.

Infected: This is the compartment used for persons who have Tuberculosis (TB) infections.

Recovered: These are group of persons who have been treated and recovered from the Tuberculosis (TB) illness.

Stable equilibrium: This is the state of a system such that when slightly moved tends to come back to its original state of rest.

Outbreak: a sudden, violent, or spontaneous occurrence, especially of disease or Strife.

Susceptible: These are individuals who are not yet infected but can still be infected.

Infection: is the invasion of body tissues by disease-causing microorganisms, their multiplication and the reaction of body tissues to these microorganisms and the toxins that they produce.

Transmission: The act or process of transferring a disease from a person to another.

Threat: An expression of an intention to inflict pain, injury, evil, or punishment. An indication of impending danger or harm. One that is regarded as a possible danger; a menace.

Contamination: Is the term describing the state of a person or material on coming in contact with the disease pathogen.

Disease: Can be seen as a depart from the normal healthy state of the body soul and mind of a human being, which manifests itself in an abnormal development of the physical, physiological and mental state of the human being concerned.

Epidemiology: The study of disease that affect large numbers of people. Traditionally, epidemiologist have been concerned primarily with infectious diseases such as typhoid and influenza, that arise and spread rapidly among the population as epidemics.

Environment: This is the physical, chemical, and biological condition of the region in which one lives.

Disease Free Equilibrium (DFE) is globally asymptotically stable when the reproduction number is less than one.

Endemic Equilibrium (EE) is globally asymptotically stable when the reproduction number is greater than one.

Endemic is when an infection in a population is maintained in the population without the need for external inputs.

Differential Equation is a mathematical equation that relates some function with its derivatives.

Simulation is the representation of the behavior or characteristics of one system through the use of another system.

CHAPTER TWO

2.0 LITERATURE REVIEW

2.1 Overview of Tuberculosis (TB)

Tuberculosis (TB) is believed to have been present in humans for thousands of years. Skeletal remains show that prehistoric humans (4000BCE) had TB and tubercular decay has been found in the spines of Egyptian mummies dating from 3000-2400 BCE. It was not identified as a single disease until the 1820s due to the variety of its symptoms. In 1834, Johann Lukas Schoenlein gave the disease name ‘tuberculosis’ (Herzog, 1998).

Mycobacterium tuberculosis, the bacteria that caused the tuberculosis was identified by Nobel Laureate Robert Koch in March1882 and in 1900’s, Albert Calmette and Camille Guerin achieved the first genuine success in immunizing against tuberculosis using attenuated bovine-strain tuberculosis called 'BCG' (Bacillus of Calmette and Guerin) (Herzog, 1998). It was not until 1946 with the development of the antibiotic streptomycin that effective treatment and cure became possible. However, hopes of completely eliminating the disease were dashed following the rise of drug-resistant strains in the 1980s.

2.1.1 Signs and symptoms of Tuberculosis (TB)

Symptoms of TB disease depend on where in the body the TB bacteria grow. Active TB cases may be pulmonary where it affects the lungs. The early symptoms usually include fatigue or weakness unexplained weight loss, fever, chills, loss of appetite and night sweats (WHO, 2010). Since the symptoms are very much similar to a common cold people tend to treat it as one. When the infection in the lung worsens, it may cause chest pain, bad cough that last 3 weeks or longer and coughing up of sputum and/or blood.

There are also cases where the infection spreads beyond the lungs to other parts of the body such as the bones and joints, the digestive system, the bladder and reproductive system and the nervous system. This is known as extra pulmonary TB and the 4 symptoms will depend upon the organs involved. It is more common in people with weaker immune systems, particularly those with an HIV infection

2.1.2 Diagnosis of tuberculosis (TB)

One who came with the symptoms may be suspected with TB based on the patient's medical history, medical conditions and physical examinations. There are several different ways to diagnose TB such as analysis of sputum, skin test and chest X-rays. The skin test is used to identify those who may have been exposed to tuberculosis by injecting a substance called tuberculin under the skin. A positive test shows that the person may have been infected but does not necessarily mean they have active TB. Other tests are done in making a diagnosis of active tuberculosis which includes identifying the causative organism Mycobacterium tuberculosis in the sputum. Sometimes, diagnosis may also be made using the chest X-rays by looking at things such as evidence of active tuberculosis pneumonia, and scarring or hardening in the lungs.

2.1.3 How does a person get tuberculosis (TB)

Tuberculosis is spread through the air from one person to another. The bacteria get into the air when someone who has a tuberculosis lung infection coughs, sneezes, shouts, or spits (Bhunu *et al.,* 2008). People who are nearby can then possibly breathe the bacteria into their lungs and become infected. Even though the disease is airborne, it is believed that TB is not highly infectious and so, occasional contacts with infectious person rarely lead to infection (Song *et al.,* 2002). TB cannot be spread through handshakes, sitting on toilet seats or sharing dishes and utensils with someone who has TB.

2.1.4 Who gets tuberculosis (TB)

it is said that, every second, one person in the world is newly infected with TB bacilli (WHO, 2010). Anyone can catch TB, but people who are particularly at risk include;

ii. those who live in close contact with individuals who have an active TB infection e.g. family members, nurses and doctors,

iii. those with weak immune system either because of age or health problem e.g. young children or elderly people, alcoholics, intravenous drug users, patient with diabetes, certain cancers and HIV, and

iv. those who live in environments where the level of existing TB infection is higher than normal e.g. poor and crowded environment, prison inmates, homeless people.

2.1.5 Treatment of tuberculosis (TB) positive patients

Tuberculosis is treated by killing the bacteria using antibiotics. The treatment usually last at least 6 months in duration and sometimes longer up to 24 months. It involves different antibiotics to increase the effectiveness while preventing the bacteria from becoming resistant to the medicines. The most common medicines used for active tuberculosis are Isoniazid (INH), Rifampin (RIF), Ethambutol and Pyrazinamide (Bhunu *et al.,* 2008). People with latent tuberculosis are usually treated using a single antibiotic to prevent them from progressing to active TB disease later in life.

The success of tuberculosis treatment is largely dependent on the compliance of the patient. One of the main reasons that cause the failure of TB treatment is because the patient failed to take the medications as prescribed. In most cases, proper treatment with appropriate antibiotics will cure the TB. Without treatment, tuberculosis can be a lethal infection.

2.2 Mathematical Models of Tuberculosis (TB)

In many developed nations, the main countermeasure in order to reduce the risk of TB spreading is by the screening of immigrants upon arrival. Nevertheless, several reports from many developed countries with well-performing screening and treatment systems have shown in the last few years that foreign-born TB patients do not significantly contribute to M. tuberculosis transmission to the native population (Kamper *et al.,* (2012)

Jia *et al*., (2008) investigated the impact of immigration on the transmission dynamics of tuberculosis. They too incorporated the recruitment of the latent and infectious immigrants but their model regards the immigrants as a separate subpopulation from

the local population. Their theoretical analysis indicated that the disease will persist in the population if there is a prevalence of TB in immigrants. They also showed that the disease never dies out and becomes endemic in host areas. The usual threshold condition does not apply and a unique equilibrium exists for all parameter values. The study suggests that immigrants have a considerable influence on the overall transmission dynamics behaviour of tuberculosis.

The model

$$\frac{dS_M}{dt} = \pi - \beta_1 S_M I_M - \mu S_M \tag{2.1}$$

$$\frac{dE_M}{dt} = \beta_1 S_M I_M - (k_1 + \mu) E_M \tag{2.2}$$

$$\frac{dI_M}{dt} = r_1 I_M - \mu R_M \tag{2.3}$$

$$\frac{dS_L}{dt} = \Lambda - \beta_2 S_L I_L - \beta^* I_M S_L - \mu S_L \tag{2.4}$$

$$\frac{dI_L}{dt} = \beta S_2 I_L + \beta^* I_M S_L - \rho\beta^* I_M E_L + q\beta^* I_M R_L - (k_2 + \mu)E_L \tag{2.5}$$

$$\frac{dI_L}{dt} = \rho\beta^* I_M E_L + kE_{2L} - (r_2 + \mu + \mu_{1L}) I_L \tag{2.6}$$

$$\frac{dR_L}{dt} = r_2 I_L - q\beta^* I_M R_L - \mu R_L \tag{2.7}$$

Bhunu *et al.,* (2008) presented a SEIR tuberculosis model which incorporated treatment of infectious individuals and chemoprophylaxis (treatment for the latently infected). The model assumed that the latently infected individuals develop active disease as a result of endogenous re-activation, exogenous re-infection and disease relapse.

The model equations are as follows:

$$\frac{dS_T}{dt} = \Lambda - \lambda S_T - \mu S_T \tag{2.8}$$

$$\frac{dE_T}{dt} = f\lambda S_T - \delta_1 \lambda E_T - (\mu + k) E_T + \delta_2 \lambda R_T \tag{2.9}$$

$$\frac{dI_T}{dt} = (1 - f)\lambda S_T + \delta_1 \lambda E_T + kE_T - (\mu + d + \rho) I_T + qR_T \tag{2.10}$$

$$\frac{dR_T}{dt} = \rho I_T - (\mu + q) R_T - \delta_2 \lambda R_T \tag{2.11}$$

The study shows that treatment of infectious individuals is more effective in the first years of implementation as it cleared active TB immediately. As a result, chemoprophylaxis will do better in controlling the number of infectious due to reduced progression to active TB.

Andrawus *et al.,* (2020), they presented the mathematical model of a tuberculosis transmission dynamics incorporating first and second line treatment. they calculated a control reproduction number which plays a vital role in biomathematics. The model consists of two equilibrium points namely disease-free equilibrium and endemic equilibrium point, it has been shown that the disease-free equilibrium point was locally asymptotically stable if the control reproduction number is less than one and also the endemic equilibrium point was locally asymptotically stable if the control reproduction number is greater than one. Numerical simulation was carried out which supported the analytical results.

The model equations are given below:

$$\frac{dS}{dt} = \Lambda - \lambda S - \mu S \tag{2.12}$$

$$\frac{dE}{dt} = \lambda S - (\mu + \sigma) E \tag{2.13}$$

$$\frac{dI}{dt} = \sigma E - (\gamma_1 + r_1 + \mu + \delta_1) I \tag{2.14}$$

$$\frac{dR_1}{dt} = \gamma_1 I - (\gamma_2 + r_2 + \mu + \delta_2) R_1 \tag{2.15}$$

$$\frac{dI}{dt} = \gamma_2 R_1 - (r_3 + \mu + \delta_3) R_2 \tag{2.16}$$

$$\frac{dR}{dt} = r_1 I + r_2 R_1 + r_3 R_2 - \mu R \tag{2.17}$$

The studies show that when there is an immigration of infected into the population, there will be no disease-free equilibrium. Most study of the model with immigration will focused on the endemic equilibrium and its stability, and sometimes is supported by the numerical simulations.

From these studies, we can conclude that immigration does have an effect on the spread of tuberculosis in such a way that the disease persists in the host population. However, with proper treatments and intervention, the rate of infection from immigrants has little effect to the host population. Further studies are required to determine which factor plays the bigger role in the spreading of tuberculosis in order to maintain the balance and keeping the disease under control. This will be part of our current study.

CHAPTER THREE

3.0 MATERIALS AND METHODS

3.1 Methodology

In this Chapter, the TB transmission model is formulated. The whole population is divided into seven compartments according to their epidemiological status. The classes are the Vaccinated $(V(t))$, Susceptible $(T(t))$, Latent $(E(t))$, Mild TB $(I_m(u))$, Chronic TB $(I_c(t))$, isolated infectious $(J(t))$ and Treated $(T(t))$ groups, where t is the time variable. It is assumed that once the treatment of active TB cases is interrupted, there is no more treatment.

$$N(t) = S(t) + V(t) + E(t) + I_m(t) + I_c(t) + J(t) + T(t) \tag{3.1}$$

Basic Assumptions

The model is based on the following assumptions

1. That the population size in a compartment is differentiable with respect to time and that the epidemic process is deterministic.
2. That the population is heterogeneous. That is, the individuals that make up the population can be grouped into different compartments or groups according to their epidemiological state.
3. That a proportion of the population of newborn is immunized against TB infection through vaccination.
4. That the immunity conferred on individuals by treatment expires after some time at given rate.
5. That people in each compartment have equal natural death rate of μ

6. That there are no immigrants and emigrants. The only way of entry into the population is through new-born babies and the only way of exit is through death from natural causes or death from TB related causes.
7. That the infection does not confer immunity to the treated and recovered individuals and so they go back to the susceptible class at a given rates.
8. That all newborns are previously uninfected by TB and therefore join either the immunized compartment or the susceptible compartment depending on whether they are vaccinated or not.

3.2 The Model Formulation

When first infected with TB bacteria, a person typically goes through a latent, asymptomatic and non-infectious period during which the body's immune system fights the TB bacteria.

Using a compartmental approach, the total host population can be partitioned into seven compartments according to their epidemiological status. The groups are the Vaccinated $(V(t))$, Susceptible $(S(t))$,Latent $(E(t))$, Mild TB $(I_m(t))$, Chronic TB $(I_c(t))$, isolated infectious $(J(t))$ and Treated $(T(t))$ individual, where t is the time variable. It is assumed that once the treatment of active TB cases is interrupted, there is no more treatment. Vaccination reduces the risk of infection by a factor $\theta \in (0,1)$ and the efficacy of the vaccine is (1 –). Let a constant π stands for the number of newborn babies into the population, then $\theta\pi$ are the individuals in the vaccinated class while $(1-\theta)\pi$ are the susceptible individual. The susceptible class also increases with a waning rate of vaccine at ω, due to fact that vaccine does not confer a total immunity. We assume that μ is per capital natural death rate and d_i $(i = 1,2,3)$ is the disease induced death rate in classes $I_m(t)$

, $I_c(t)$ and $J(t)$ respectively. It is natural to assume that $d_2 \geq d_3 \geq d_1$ due to the treatment of active TB cases reducing the disease induced death rate. (= 1,2 3)

are the transmission coefficients from class $S(t)$, $E(t)$ and $T(t)$ respectively? We assume

that $\lambda_1 > \lambda_2 > \lambda_3$ because the treatment of active TB cases reduces the infectivity of active TB cases. Take $\rho(0 < \rho < 1)$ as the fraction of the latent persons who have fast TB progression. The proportion ϕ of individual in the exposed class will progress to the chronic class via endogenous us reactivation. σ is the reactivation rate from the latent persons to infected class. γ_1 is the reactivation rate of the individual in the mild TB $(I_m(t))$ to the chronic TB $(I_c(t))$. The parameters 1, 2 4 are the recovery rates

of the individual in the classes $(I_m(t))$, $(I_c(t))$ and $J(t)$ respectively. And the parameter 3 is the rate of isolation of the individuals in chronic class

$(I_c(t))$. We

combine the basic assumptions, model parameters, variables and the TB infection processes to formulate a schematic diagram for TB infection as shown in Figure 3.1

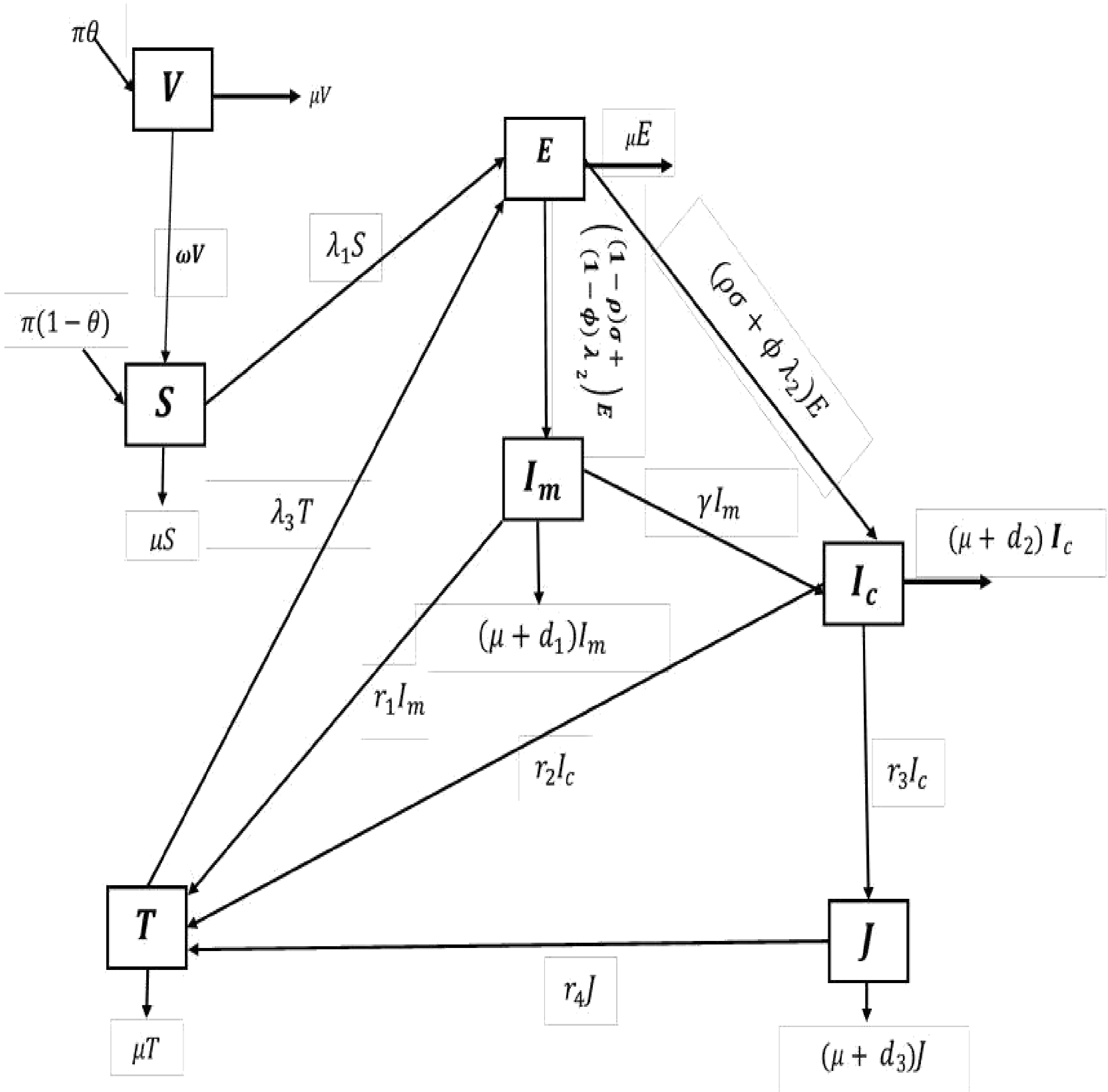

Figure 3.1: Schematic Representation of the Model

The Model Equations

The state system is the following system of seven ordinary differential equations:

$$\frac{dV}{dt} = \pi\theta - (\mu + \omega)V \tag{3.2}$$

$$\frac{dS}{dt} = \pi(1-\theta) - \lambda_1 S - \mu S + \omega V \tag{3.3}$$

$$\frac{dE}{dt} = \lambda_1 S + \lambda_3 T - \lambda_2 E - (\mu + \sigma)E \tag{3.4}$$

$$\frac{dI_m}{dt} = (1-\rho)\sigma E - (\gamma + \mu + r_1 + d_1)I_m + (1-\phi)\lambda_2 E \tag{3.5}$$

$$\frac{dI_c}{dt} = \rho\sigma E + \gamma I_m - (r_2 + r_3 + \mu + d_2)I_c + \phi\lambda_2 E \tag{3.6}$$

$$\frac{dJ}{dt} = r_3 I_c - (\mu + d_3 + r_4)J \tag{3.7}$$

$$\frac{dT}{dI} = r_4 J + r_2 I_c + r_1 I_m - (\mu + \lambda_3)T \tag{3.8}$$

where

$$\lambda_1 = \beta(I_c + \varepsilon_1 I_m + \varepsilon_2 J) \tag{3.9}$$

$$\lambda_2 = \alpha(I_c + \varepsilon_3 I_m + \varepsilon_4 J) \tag{3.10}$$

$$\lambda_3 = \gamma(I_c + \varepsilon_5 I_m + \varepsilon_6 J) \tag{3.11}$$

Table 3.1 Notation and definition of variables and parameter

Symbol	Description
$V(t)$	Vaccinated
$S(t)$	Susceptible
$E(t)$	Latent
$I_m(t)$	Mild TB
$I_c(t)$	Chronic TB
$J(t)$	Isolated infectious
$T(t)$	Treated and recovered
π	Natural per capital birth rate
θ	Fraction of newly recruited individual
ω	vaccinated Waning rate of vaccine
r_1	Treatment rate of individuals in mild class
r_2	The treatment rate for those is I_c class
r_3	The progression rate from classes I_c to J
r_4	The treatment rate for those in isolated class
β	Transmission rate among the susceptible
γ	Transmission rate among individuals from mild to chronic
μ	TB Natural per capital death rate
d_1	Death rate for mild TB individual
d_2	Death rate for chronic TB individuals
d_3	Death rate for isolated class

α	Effective transmission rate from latent class to infected class
ϕ	Progression rate from latent class to chronic class via endogenous reactivation.
ρ	Fraction of individuals with fast TB progression.
σ	Contact level ($0 \le \sigma \le 1$) from late latent class to infected class
ε_1	Relative infectiousness of humans with mild TB compared to humans in the chronic class
ε_2	Relative infectiousness of humans with TB in the isolated class compared to humans in the chronic class
ε_3	Relative infectiousness of humans with mild TB due to endogenous reactivation compared to humans in the chronic class.
ε_4	Relative infectiousness of humans on isolation after endogenous reactivation compared to humans in the chronic class
ε_5	Relative infectiousness of humans with mild TB due to exogenous re-infection compared to humans in the chronic class
ε_6	Relative infectiousness of humans on isolation after exogenous re-infection compared to humans in the chronic class

3.3 The Positive Invariant Region

The entire population size N can be determined from Equations (3.2) to (3.8)

The total population size is

$$N(t) = S(t) + V(t) + E(t) + I_m(t) + I_c(t) + J(t) + T(t) \tag{3.12}$$

Adding Equations (3.2), (3.3), (3.4), (3.5), (3.6),(3.7) and (3.8) become Equation (3.13)

$$\frac{dN}{dt} = \frac{dS}{dt} + \frac{dV}{dt} + \frac{dE}{dt} + \frac{dI_m}{dt} + \frac{dI_c}{dt} + \frac{dJ}{dt} + \frac{dT}{dt} \tag{3.13}$$

$$\frac{dN}{dt} = \pi - \mu N(t) - d_1 N - d_2 N - d_3 N \tag{3.14}$$

In the absence of the disease $\left(d_1 = d_2 = d_3 = 0 \right)$ then (3.14) gives

$$\frac{dN}{dt} = \pi - \mu N \tag{3.15}$$

Theorem 3.1

The system (3.2) to (3.8) has solution which are contained in the feasible region.

$\Omega = \Omega$ for al $t > 0$

Proof

Let $\Omega = \left(S, \mathrm{V}, E, I_m \, \mathrm{I}_c, J, T \right) \in R^7$ be any solution of the system (3.2) to (3.8) with non-negative initial condition

Using theorem on differential inequality, Birkhoff and Rota, (1982) on (3.15) gives

$$\frac{dN}{dt} \le \pi - \mu N \tag{3.16}$$

$$0 \le N \le \frac{\pi}{\mu} \tag{3.17}$$

Hence

$$\pi - \mu N \ge ke^{-\mu t} \tag{3.18}$$

where k is constant

Thus, the feasible set of the model is given by

$$\Omega = \left\{ (S, V, I_m, I_c, J, T) \in R^7 : S, V, I_m, I_c, J, T \geq 0, N \leq \frac{\pi}{\mu} \right\} \tag{3.19}$$

Which is positive invariant (i.e., solution remain positive for all time t) and the model is epidemiologically meaningful and mathematically well pose.

3.4 Positivity of Solutions

Since Equations (3.2) - (3.8) represent the population in each compartment and all model parameters are all positive, then it lies in a region **Ω** defined by

$$\Omega = \left\{ (S, V, I_m, I_c, J, T) \in R^7 : S, V, I_m, I_c, J, T \geq 0, N \leq \frac{\pi}{\mu} \right\} \tag{3.20}$$

Theorem 3.2 Let the initial data for the model Equation be given as

$$\left\{ \left(S(0), V(0), I_m(0), I_c(0), J(0), T(0) \right) \right\} \in n \tag{3.21}$$

Then the solution set

$\left\{ S(t), V(t), I_m(t), I_c(t), J(t), T(t) \right\}$ of the system (3.2) to (3.8) is positive for all $t > 0$

Proof

From equation (3.3)

$$\frac{dS}{dt} = \pi(1-\theta) + \omega V - (\lambda_1 + \mu)S \tag{3.22}$$

$$\frac{dS}{dt} \geq -(\lambda_1 + \mu)S \tag{3.23}$$

$$\frac{dS}{S} \geq -(\lambda_1 + \mu)dt \tag{3.24}$$

Integrating (3.24) gives

$$\int \frac{dS}{S} \geq - \int (\lambda_1 + \mu)dt \tag{3.25}$$

$$S(t) \geq S(0)e^{-(\lambda_1 + \mu)t} \tag{3.26}$$

From equation (3.2)

$$\frac{dV}{dt} = \theta\pi - (\mu + \omega)V \tag{3.27}$$

$$\frac{dV}{dt} \geq -(\mu + \omega)V \tag{3.28}$$

$$\frac{dV}{V} \geq -(\mu + \omega)dt \tag{3.29}$$

Integrating (3.29) gives

$$\int \frac{dV}{V} \geq - \int (\mu + \omega)dt \tag{3.30}$$

$$V(t) \geq V(0)e^{-(\mu + \omega)t} \tag{3.31}$$

From equation (3.4)

$$\frac{dE}{dt} = \lambda_1 S + \lambda_3 T - (\sigma + \mu + \lambda_2)E \tag{3.32}$$

$$\frac{dE}{dt} \geq -(\sigma + \mu + \lambda_2)E \tag{3.33}$$

$$\frac{dE}{E} \geq -\left(\sigma + \mu + \lambda_2\right)dt \tag{3.34}$$

Integrating (3.34) gives

$$\int \frac{dE}{E} \geq -\int \left(\sigma + \mu + \lambda_2\right)dt \tag{3.35}$$

$$E(t) \geq E(0)e^{-(\sigma+\mu+\lambda_2)t} \tag{3.36}$$

From equation (3.5)

$$\frac{dI_m}{dt} = (1-\rho)\sigma E + (1-\phi)\lambda_2 E - (\gamma + \mu + r_1 + d_1)I_m \tag{3.37}$$

$$\frac{dI_m}{dt} \geq -(\gamma + \mu + r_1 + d_1)I_m \tag{3.38}$$

$$\frac{dI_m}{I_m} \geq -(\gamma + \mu + r_1 + d_1)dt \tag{3.39}$$

Integrating both sides of (3.39)

$$\int \frac{dI_m}{I_m} \geq -\int (\gamma + \mu + r_1 + d_1)dt \tag{3.40}$$

$$I_m(t) \geq I_m(0)e^{-(\gamma+\mu+r_1+d_1)t} \tag{3.41}$$

From equation (3.6)

$$\frac{dI_c}{dt} = \rho\sigma E + \gamma I_m + \phi\lambda_2 E - (r_2 + r_3 + \mu + d_3)I_c \tag{3.42}$$

$$\text{—} \tag{3.43}$$

$$\frac{dI_c}{I_c} \geq -\left(r_2 + r_3 + \mu + d_3\right)dt \tag{3.44}$$

Integrating (3.44) gives

$$\int \frac{dI_c}{I_c} \geq -\int \left(r_2 + r_3 + \mu + d_3\right)dt \tag{3.45}$$

$$I_c(t) \geq I_c(0)e^{-\left(r_2 + r_3 + \mu + d_3\right)t} \tag{3.46}$$

From equation (3.7)

$$\frac{dJ}{dt} = nI_c - \left(\mu + d_3 + r_4\right)J \tag{3.47}$$

$$\frac{dJ}{dt} \geq -\left(\mu + d_3 + r_3\right)J \tag{3.48}$$

$$\frac{dJ}{J} \geq -\left(\mu + d_3 + r_3\right)dt \tag{3.49}$$

Integrating (3.49) gives

$$\int \frac{dJ}{J} \geq -\int \left(\mu + d_3 + r_3\right)dt \tag{3.50}$$

$$J(t) \geq J(0)e^{-\left(\mu + d_3 + r_3\right)t} \tag{3.51}$$

From equation (3.8)

$$\frac{dT}{dI} = r_4 J + r_2 I_c + r_1 I_m - \left(\mu + \lambda_3\right)T \tag{3.52}$$

$$\frac{dT}{dI} \geq -\left(\mu + \lambda_3\right)T \tag{3.53}$$

$$\frac{dT}{T} \geq -(\mu + \lambda_3)dt \tag{3.54}$$

Integrating (3.54) gives

$$\int \frac{dT}{T} \geq -\int (\mu + \lambda_3)dt \tag{3.55}$$

$$T(t) \geq T(0)e^{-(\mu+\lambda_3)t} \tag{3.56}$$

Therefore, all the solution of equations of system (3.2) to (3.8) are positive for all $t > 0$

3.5 The Existence and Uniqueness of Solution

The validity and implementation of any mathematical model depend on whether the given system of equations has a solution, and if it has there is need to check if the solution is unique (Ayoade *et al.,* 2019).

Theorem 3.3

Let Ω denotes the region $\pi \in \Re^{+}$. Then the model system (3.2) to (3.8) has a unique solution if it is established that $\frac{\partial m_i}{\partial m_i}$, i =1, 2, 3, 4, 5, 6, 7 are continuous and bounded in Ω.

Proof:

Let equations (3.2) to (3.8) be represented by m_1 , m_2 , m_3 , m_4 , m_5 , m_6 and m_7 respectively

From equation (3.1), the following partial derivatives are obtained

$$\left.\begin{array}{l}\left|\frac{\partial m_1}{\partial S}\right| = \left|-\beta\left(I_c+\varepsilon_1 I_m+\varepsilon_2 J\right)\right| < \infty; \left|\frac{\partial m_1}{\partial V}\right| = 0 < \infty; \quad \left|\frac{\partial m_1}{\partial E}\right| = 0 < \infty; \\ \left|\frac{\partial m_1}{\partial I_m}\right| = \left|-\beta\varepsilon_1 S\right| < \infty; \quad \left|\frac{\partial m_1}{\partial I_c}\right| = \left|-\beta S\right| < \infty; \quad \left|\frac{\partial m_1}{\partial J}\right| = \left|-\beta\varepsilon_2 S\right| < \infty; \quad \left|\frac{\partial m_1}{\partial S}\right| = 0 < \infty\end{array}\right\} \quad (3.57)$$

The above partial derivatives exist, continuous and are bounded

From equation (3.3) we obtained the following partial derivatives

$$\left.\begin{array}{l}\left|\frac{\partial m_2}{\partial S}\right| = 0 < \infty; \left|\frac{\partial m_2}{\partial V}\right| = \left|-(\mu+\omega)\right| < \infty; \left|\frac{\partial m_2}{\partial E}\right| = 0 < \infty; \left|\frac{\partial m_2}{\partial I_m}\right| = 0 < \infty; \quad \left|\frac{\partial m_2}{\partial I_c}\right| = 0 < \infty; \\ \left|\frac{\partial m_2}{\partial J}\right| = 0 < \infty; \left|\frac{\partial m_2}{\partial T}\right| = 0 < \infty;\end{array}\right\} \quad (3.58)$$

The above partial derivatives exist, continuous and are bounded

From equation (3.4) we obtained the following partial derivatives

$$\left.\begin{array}{l}\left|\frac{\partial m_3}{\partial S}\right| = \left|\beta\left(I_c+\varepsilon_1 I_m+\varepsilon_2 J\right)\right| < \infty; \left|\frac{\partial m_3}{\partial V}\right| = 0 < \infty; \left|\frac{\partial m_3}{\partial E}\right| = \left|-\beta\left(I_c+\varepsilon_1 I_m+\varepsilon_2 J\right)-(\mu+\sigma)\right| < \infty; \\ \left|\frac{\partial m_3}{\partial I_m}\right| = \left|\beta\varepsilon_1 S-\beta\varepsilon_1 E\right| 0 < \infty; \left|\frac{\partial m_3}{\partial I_c}\right| = \left|\beta S-\beta E\right| < \infty; \left|\frac{\partial m_3}{\partial J}\right| = \left|\beta\varepsilon_2 S-\beta\varepsilon_2 E\right| < \infty; \left|\frac{\partial m_3}{\partial T}\right| = 0 < \infty;\end{array}\right\} \quad (3.59)$$

The above partial derivatives exist, continuous and are bounded.

From equation (3.5) we obtained the following partial derivatives

$$\left.\begin{array}{l}\left|\frac{\partial m_4}{\partial S}\right| = 0 < \infty; \quad \left|\frac{\partial m_4}{\partial V}\right| = 0 < \infty; \quad \left|\frac{\partial m_4}{\partial E}\right| = \left|(1-\rho)\sigma-(1-\phi)\alpha\left(I_c+\varepsilon_1 I_m+\varepsilon_2 J\right)\right| < \infty; \\ \left|\frac{\partial m_4}{\partial I_m}\right| = \left|-\left(\gamma+r_1+d_1+\mu\right)+(1-\phi)\alpha\varepsilon_3 E\right| 0 < \infty; \left|\frac{\partial m_4}{\partial I_c}\right| = \left|(1-\phi)\alpha E\right| < \infty; \\ \left|\frac{\partial m_4}{\partial J}\right| = \left|(1-\phi)\alpha\varepsilon_4 E\right| < \infty; \left|\frac{\partial m_4}{\partial T}\right| = 0 < \infty;\end{array}\right\} \quad (3.60)$$

The above partial derivatives exist, continuous and are bounded

From equation (3.6) we obtained the following partial derivatives

$$\left.\begin{array}{l}\left|\frac{\partial m_5}{\partial S}\right| = 0 < \infty; \left|\frac{\partial m_5}{\partial V}\right| = 0 < \infty; \left|\frac{\partial m_5}{\partial E}\right| = \left|\rho\sigma + \phi\alpha\left(I_c + \varepsilon_1 I_m + \varepsilon_2 J\right)\right| < \infty; \\ \left|\frac{\partial m_5}{\partial I_m}\right| = \left|\gamma + \phi\alpha\varepsilon_3 E\right| < \infty; \left|\frac{\partial m_5}{\partial I_c}\right| = \left|-\left(r_2 + r_3 + \mu + d_2\right) + \phi\alpha E\right| < \infty; \\ \left|\frac{\partial m_5}{\partial J}\right| = \left|\phi\alpha\varepsilon_4 E\right| < \infty; \quad \left|\frac{\partial m_5}{\partial T}\right| = 0 < \infty;\end{array}\right\} \tag{3.61}$$

The above partial derivatives exist, continuous and are bounded

From equation (3.7) we obtained the following partial derivatives

$$\left.\begin{array}{l}\left|\frac{\partial m_6}{\partial S}\right| = 0 < \infty; \left|\frac{\partial m_6}{\partial V}\right| = 0 < \infty; \left|\frac{\partial m_6}{\partial E}\right| = 0 < \infty; \left|\frac{\partial m_6}{\partial I_m}\right| = 0 < \infty; \left|\frac{\partial m_6}{\partial I_c}\right| = |r_3| < \infty; \\ \left|\frac{\partial m_6}{\partial J}\right| = \left|-\left(\mu + d_3 + r_4\right)\right| < \infty; \left|\frac{\partial m_6}{\partial T}\right| = 0 < \infty;\end{array}\right\} \tag{3.62}$$

The above partial derivatives exist, continuous and are bounded

From equation (3.8) we obtained the following partial derivatives

$$\left.\begin{array}{l}\left|\frac{\partial m_7}{\partial S}\right| = 0 < \infty; \left|\frac{\partial m_7}{\partial V}\right| = 0 < \infty; \left|\frac{\partial m_7}{\partial E}\right| = 0 < \infty; \left|\frac{\partial m_7}{\partial I_m}\right| = \left|r_1 - \gamma\varepsilon_5 T\right| < \infty; \left|\frac{\partial m_7}{\partial I_c}\right| = \left|r_2 - \gamma T\right| < \infty; \\ \left|\frac{\partial m_7}{\partial J}\right| = \left|r_4 - \gamma\varepsilon_6 T\right| < \infty; \left|\frac{\partial m_7}{\partial T}\right| = \left|-\left(\mu + \gamma\left(I_c + \varepsilon_5 I_m + \varepsilon_6 J\right)\right)\right| < \infty;\end{array}\right\} \tag{3.63}$$

Since all the partial derivatives exist, bounded and defined, then system of equations (3.2) -(3.8) exists and has solution in $\Re_7$

3.6 Equilibrium Points of the Model

The equilibrium state is the point in which there is zero disturbance on the system under consideration. That is, the rate of change of the model variables with time is zero. Thus, at equilibrium,

$$\frac{dS}{dt} = \frac{dV}{dt} = \frac{dE}{dt} = \frac{dI_m}{dt} = \frac{dI_c}{dt} = \frac{dJ}{dt} = \frac{dT}{dt} = 0 \tag{3.64}$$

Let

$$E^* = \left(V,S,E,I_m,I_c,J,T\right) = \left(V^*,S^*,E^*,I_m^*,I_c^*,J^*,T^*\right) \tag{3.65}$$

be arbitrarily equilibrium point

Substituting equations (3.64) into equations (3.2) - (3.8) gives

$$\pi\theta - (\mu+\omega)V = 0 \tag{3.66}$$

$$\pi(1-\theta) - \lambda_1 S - \mu S + \omega V = 0 \tag{3.67}$$

$$\lambda_1 S + \lambda_3 T - \lambda_2 E - (\mu+\sigma)E = 0 \tag{3.68}$$

$$(1-\rho)\sigma E - (\gamma+\mu+r_1+d_1)I_m + (1-\phi)\lambda_2 E = 0 \tag{3.69}$$

$$\rho\sigma E + \gamma I_m - (r_2+r_3+\mu+d_2)I_c + \phi\lambda_2 E = 0 \tag{3.70}$$

$$r_3 I_c - (\mu+d_3+r_4)J = 0 \tag{3.71}$$

$$r_4 J + r_2 I_c + r_1 I_m - (\mu+\lambda_3)T = 0 \tag{3.72}$$

From equation (3.66) we have

$$V = \frac{\pi\theta}{(\mu+\omega)} \tag{3.73}$$

Substitute equation (3.73) into equation (3.67) we have

$$\pi(1-\theta)-(\lambda_1+\mu)S+\frac{\omega\theta\pi}{\mu+\omega}=0 \tag{3.74}$$

$$\frac{1}{\lambda_1+\mu}\left(\pi(1-\theta)+\frac{\omega\pi\theta}{\mu+\omega}\right)=S \tag{3.75}$$

From equation (3.71)

$$J=\frac{r_3 I_c}{r_4+\mu+d_3} \tag{3.76}$$

$$J=K_1 I_c \tag{3.77}$$

Where

$$K_1=\frac{r_3}{r_4+\mu+d_3} \tag{3.78}$$

From (3.69)

$$\left[(1-\rho)\sigma+(1-\phi)\lambda_2\right]E=\left[r_2+r_3+\mu+d_2\right]I_m \tag{3.79}$$

$\Rightarrow$

$$E=\frac{\left[r_2+r_3+\mu+d_2\right]}{\left[(1-\rho)\sigma+(1-\phi)\lambda_2\right]}I_m \tag{3.80}$$

$$E=K_2 I_m \tag{3.81}$$

Where

$$K_2=\frac{r_2+r_3+\mu+d_3}{(1-\rho)\sigma+(1-\phi)\lambda_2} \tag{3.82}$$

From equation (3.71)

$$\left(r_2 + r_3 + \mu + d_2\right) I_c = \rho\sigma E + \phi\lambda_2 E + \gamma I_m \tag{3.83}$$

Substituting equation (3.81) into equation (3.83) gives

$$I_c = \frac{\left[\left(\rho\sigma + \phi\lambda_2\right) K_2 + \gamma\right]}{r_2 + r_3 + \mu + d_2} I_m \tag{3.84}$$

$$I_c = K_3 I_m \tag{3.85}$$

Where

$$K_3 = \frac{\left(\rho\sigma + \phi\lambda_2\right) K_2 + \gamma}{r_2 + r_3 + \mu + d_2} \tag{3.86}$$

Substituting equation (3.85) into equation (3.77) gives

$$J = K_1 K_3 I_m \tag{3.87}$$

From equation (3.72)

$$T = \frac{r_4 J + r_2 I_c + r_1 I_m}{\mu + \lambda_3} \tag{3.88}$$

Substituting (3.81), (3.85) and (3.87) into equation (3.88) gives

$$T = \frac{\left(r_4 K_1 K_3 + r_2 K_3 + r_1\right) I_m}{\mu + \lambda_3} \tag{3.89}$$

$$T = K_4 I_m \tag{3.90}$$

Where

$$K_4 = \frac{\left(r_4 K_1 K_3 + r_2 K_3 + r_1\right)}{\mu + \lambda_3} \tag{3.91}$$

Recall

$$\left.\begin{aligned} \lambda_1 &= \beta\left(I_c + \varepsilon_1 I_m + \varepsilon_2 J\right) \\ \lambda_2 &= \alpha\left(I_c + \varepsilon_3 I_m + \varepsilon_4 J\right) \\ \lambda_3 &= \gamma_1\left(I_c + \varepsilon_5 I_m + \varepsilon_6 J\right) \end{aligned}\right\} \tag{3.92}$$

and

$$\left.\begin{aligned} J &= K_1 K_3 I_m \\ I_c &= K_3 I_m \end{aligned}\right\} \tag{3.93}$$

Substituting (3.93) into (3.92) gives

$$\left.\begin{aligned} \lambda_1 &= \beta I_m\left(K_3 + \varepsilon_2 K_1 K_3 + \varepsilon_1\right) \\ \lambda_2 &= \alpha I_m\left(K_3 + \varepsilon_4 K_1 K_3 + \varepsilon_3\right) \\ \lambda_3 &= \gamma_1 I_m\left(K_3 + \varepsilon_6 K_1 K_3 + \varepsilon_5\right) \end{aligned}\right\} \tag{3.94}$$

Substitute (3.81), (3.85), (3.87) and (3.90) into equation (3.68)

$$\beta I_m K_5 S + \gamma_1 I_m K_7 - \alpha I_m K_6 K_4 I_m - (\mu + \sigma) K_2 I_m = 0 \tag{3.95}$$

$$\left[\beta K_5 S + \gamma_1 K_7 - \alpha K_4 K_6 I_m - (\mu + \sigma) K_2\right] I_m = 0 \tag{3.96}$$

Therefore,

$$I_m = 0 \tag{3.97}$$

or

$$\beta K_5 S + \gamma_1 K_7 - \alpha K_6 K_4 I_m - (\mu + \sigma) K_2 = 0 \qquad (3.98)$$

Where

$$\left.\begin{aligned} K_5 &= K_3 + \varepsilon_1 + \varepsilon_2 K_1 K_3 \\ K_6 &= K_3 + \varepsilon_3 + \varepsilon_4 K_1 K_3 \\ K_7 &= K_3 + \varepsilon_5 + \varepsilon_6 K_1 K_3 \end{aligned}\right\} \qquad (3.99)$$

Substitute equation (3.100) into equation (3.95)

$$\left.\begin{aligned} \lambda_1 &= \beta K_5 I_m \\ \lambda_2 &= \alpha K_6 I_m \\ \lambda_3 &= \gamma_1 K_7 I_m \end{aligned}\right\} \qquad (3.100)$$

3.6.1 Disease free equilibrium (D.F.E)

The equilibrium state is the point at which there exist no infection in the given population.

At Disease Free Equilibrium, we let

$$\left(V, S, E, I_m, I_c, J, T\right) = E^* = \left(V^*, S^*, E, I_m^*, I_c^*, J^*, T^*\right) \qquad (3.101)$$

Lemma: The D.F.E of the model exists and is given by

$$E^0 = \left(V^*, S^*, E^*, I_m^*, I_c^*, J^*, T^*\right) = \left(\frac{\pi\theta}{(\mu+\omega)}, \frac{\pi(\mu+\omega-\mu\theta)}{\mu(\mu+\omega)}, 0,0,0,0,0\right) \qquad (3.102)$$

Proof:

Suppose

$$I_m = 0 \tag{3.103}$$

Substituting (3.103) into (3.100) gives

$$\left.\begin{aligned} \lambda_1 &= 0 \\ \lambda_2 &= 0 \\ \lambda_3 &= 0 \end{aligned}\right\} \tag{3.104}$$

Substituting equation (3.104) into equations (3.81) ,(3.85), (3.87) and (3.90), we have

$$\left.\begin{aligned} J^* &= 0 \\ E^* &= 0 \\ I_c^* &= 0 \\ T^* &= 0 \end{aligned}\right\} \tag{3.105}$$

Substitute equation (3.105) into equation (3.75)

$$S^* = \frac{\pi(\mu+\omega-\mu\theta)}{\mu(\mu+\omega)} \tag{3.106}$$

Thus, the lemma is proved.

$$\begin{pmatrix} V^* \\ S^* \\ E^* \\ I_m^* \\ I_c^* \\ J^* \\ T^* \end{pmatrix} = \begin{pmatrix} \dfrac{\pi\theta}{(\mu+\omega)} \\ \dfrac{\pi(\mu+\omega-\mu\theta)}{\mu(\mu+\omega)} \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \end{pmatrix} \tag{3.107}$$

Equation (3.107) is the Disease-Free Equilibrium

3.6.2 The endemic equilibrium

Let

$$E^{**} = (S, E_1, E_2, I, J, T) = (S^{**}, E_1^{**}, E_2^{**}, I^{**}, J^{**}, T^{**}) \tag{3.108}$$

be the Endemic Equilibrium point,

Suppose from equation (3.97)

$$I_m \neq 0 \tag{3.109}$$

then

$$\beta K_5 S + \gamma_1 K_7 - \alpha K_6 K_4 I_m - (\mu + \sigma) K_2 = 0 \tag{3.110}$$

From equation (3.110)

$$S^{**} = \frac{\alpha K_6 K_4 I_m + (\mu + \sigma) K_2 - \gamma_1 K_7}{\beta K_5} \tag{3.111}$$

$$S^{**} = K_8 I_m + K_9 \tag{3.112}$$

Where

$$\left.\begin{aligned} K_8 &= \frac{\alpha K_6 K_4}{\beta K_5} \\ K_9 &= \frac{(\mu + \sigma) K_2 - \gamma_1 K_7}{\beta K_5} \end{aligned}\right\} \tag{3.113}$$

Substitute equations (3.112) into equation (3.74)

$$\pi (1 - \theta) - (\lambda_1 + \mu)(K_8 I_m + K_9) + \frac{\omega \theta \pi}{\mu + \omega} = 0 \tag{3.114}$$

Substitute (3.100) into (3.67), we have

$$\pi(1-\theta)-(\beta K_5 I_m + \mu)(K_8 I_m + K_9)+\frac{\omega\theta\pi}{\mu+\omega}=0 \tag{3.115}$$

$$\beta K_5 K_8 I_m^2+(\beta K_5 K_9 + \mu K_8)I_m + \mu K_9 + \frac{\omega\theta\pi}{\mu+\omega} - \pi(1-\theta)=0 \tag{3.116}$$

$$K_{10} I_m^2 + K_{11} I_m + K_{12} = 0 \tag{3.117}$$

Where

$$\begin{aligned} K_{10} &= \beta K_5 K_8 \\ K_{11} &= \beta K_5 K_9 + \mu K_8 \\ K_{12} &= \mu K_9 + \frac{\omega\theta\pi}{\mu+\omega} - \pi(1-\theta) \end{aligned} \tag{3.118}$$

Now, solve (3.117) using quadratic formular

$$I_m^{**} = \frac{-K_{11} \pm K_{13}}{2K_{10}} \tag{3.119}$$

Where

$$\begin{aligned} K_{13} &= \sqrt{K_{11}^2 - 4K_{10} K_{12}} \\ K_{13} &\geq K_{11} \\ K_{11} &\geq 0 \end{aligned} \tag{3.120}$$

Since

$$I_m^{**} \geq 0 \tag{3.121}$$

Then

$$I_m^{**} = \frac{-K_{11} + K_{13}}{2K_{10}} \tag{3.122}$$

Substitute equations (3.111) and (3.118) into (3.22)

$$I_m^{**} = \frac{\gamma_1 \beta K_5 K_7 - (\mu + \sigma)\beta K_5 K_2 - \mu\alpha K_6 K_4 + \beta K_5 K_{13}}{2\alpha\beta K_5 K_6 K_4} \tag{3.123}$$

Substitute equation (3.123) into (3.81), we have

$$E^{**} = K_2 \left[\frac{\gamma_1 \beta K_5 K_7 - (\mu + \sigma)\beta K_5 K_2 - \mu\alpha K_6 K_4 + \beta K_5 K_{13}}{2\alpha\beta K_5 K_6 K_4} \right] \tag{3.124}$$

Substitute (3.123) into (3.85), we have

$$I_C^{**} = K_3 \left[\frac{\gamma_1 \beta K_5 K_7 - (\mu + \sigma)\beta K_5 K_2 - \mu\alpha K_6 K_4 + \beta K_5 K_{13}}{2\alpha\beta K_5 K_6 K_4} \right] \tag{3.125}$$

Substitute (3.123) into (3.87), we have

$$J^{**} = K_1 K_3 \left[\frac{\gamma_1 \beta K_5 K_7 - (\mu + \sigma)\beta K_5 K_2 - \mu\alpha K_6 K_4 + \beta K_5 K_{13}}{2\alpha\beta K_5 K_6 K_4} \right] \tag{3.126}$$

Substitute equation (3.123) into equation (3.90), we have

$$T^{**} = K_4 \left[\frac{\gamma_1 \beta K_5 K_7 - (\mu + \sigma)\beta K_5 K_2 - \mu\alpha K_6 K_4 + \beta K_5 K_{13}}{2\alpha\beta K_5 K_6 K_4} \right] \tag{3.127}$$

$$
\begin{bmatrix} V^{**} \\ S^{**} \\ E^{**} \\ I_m^{**} \\ I_c^{**} \\ J^{**} \\ T^{**} \end{bmatrix}
=
\begin{bmatrix}
\dfrac{\pi\theta}{(\mu+\omega)} \\[2ex]
\dfrac{K_8\left[\gamma_1 \beta K_5 K_7 - (\mu+\sigma)\beta K_5 K_2 - \mu\alpha K_6 K_4 + \beta K_5 K_{13}\right]}{2\alpha\beta K_5 K_6 K_4} + \dfrac{(\mu+\sigma)K_2 - \gamma K_7}{\beta K_5} \\[2ex]
K_2\left[\dfrac{\gamma_1 \beta K_5 K_7 - (\mu+\sigma)\beta K_5 K_2 - \mu\alpha K_6 K_4 + \beta K_5 K_{13}}{2\alpha\beta K_5 K_6 K_4}\right] \\[2ex]
\dfrac{\gamma_1 \beta K_5 K_7 - (\mu+\sigma)\beta K_5 K_2 - \mu\alpha K_6 K_4 + \beta K_5 K_{13}}{2\alpha\beta K_5 K_6 K_4} \\[2ex]
K_3\left[\dfrac{\gamma_1 \beta K_5 K_7 - (\mu+\sigma)\beta K_5 K_2 - \mu\alpha K_6 K_4 + \beta K_5 K_{13}}{2\alpha\beta K_5 K_6 K_4}\right] \\[2ex]
K_1 K_3\left[\dfrac{\gamma_1 \beta K_5 K_7 - (\mu+\sigma)\beta K_5 K_2 - \mu\alpha K_6 K_4 + \beta K_5 K_{13}}{2\alpha\beta K_5 K_6 K_4}\right] \\[2ex]
K_4\left[\dfrac{\gamma_1 \beta K_5 K_7 - (\mu+\sigma)\beta K_5 K_2 - \mu\alpha K_6 K_4 + \beta K_5 K_{13}}{2\alpha\beta K_5 K_6 K_4}\right]
\end{bmatrix}
\tag{3.128}
$$

3.7 Effective Reproduction Number

In biomathematics, the basic reproduction number (R_0) is the average number of infected contacts per infected individual. It is one of the fundamental concepts to determine the future of an epidemics in a population

When

$R_0 < 1$ The infection will die out in the long run, but if

$R_0 > 1$ The infection will be able to spread in a population

In this model, the spectral radius of the equation is given as largest Eigenvalue given as

$$R_0 = \rho f v^{-1} \tag{3.129}$$

From Equation (3.2) to Equation (3.8), we have

$$F_i = \begin{pmatrix} \lambda_1 S + \lambda_3 T \\ \left((1-\phi)\lambda_2\right) E \\ (\phi\lambda_2) E \\ 0 \end{pmatrix} \tag{3.130}$$

$$V_i = \begin{pmatrix} (\mu+\sigma)E \\ (\gamma_1 + r_1 + d_1 + \mu) I_m - (1-\rho)\sigma E \\ (r_2 + r_3 + d_2 + \mu) I_c - \gamma_1 I_m - \rho\sigma E \\ (\mu + d_3 + r_4) J - r_3 I_C \end{pmatrix} \tag{3.131}$$

$$F(DFE) = \begin{pmatrix} 0 & \dfrac{\beta\varepsilon_1\pi(\mu+\omega-\mu\theta)}{\mu(\mu+\omega)} & \dfrac{\beta\pi(\mu+\omega-\mu\theta)}{\mu(\mu+\omega)} & \dfrac{\beta\varepsilon_2\pi(\mu+\omega-\mu\theta)}{\mu(\mu+\omega)} \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix} \tag{3.132}$$

$$V = \begin{pmatrix} (\mu+\sigma) & 0 & 0 & 0 \\ -(1-\rho)\sigma & (\gamma_1 + \mu + r_1 + d_1) & 0 & 0 \\ -\rho\sigma & -\gamma_1 & (r_2 + r_3 + d_2 + \mu) & 0 \\ 0 & 0 & -r_3 & (\mu + r_4 + d_3) \end{pmatrix} \tag{3.133}$$

Let

$$V = \begin{pmatrix} Q_1 & 0 & 0 & 0 \\ -C_1 & Q_2 & 0 & 0 \\ -C_2 & -\gamma_1 & Q_3 & 0 \\ 0 & 0 & -r_3 & Q_4 \end{pmatrix} \tag{3.134}$$

where

$$
\begin{aligned}
Q_1 &= (\mu+\sigma), \\
Q_2 &= \gamma+\mu+r_1+d_1, \\
Q_3 &= r_2+r_3+d_2+\mu, \\
Q_4 &= d_3+r_4+\mu
\end{aligned}
\tag{3.135}
$$

$$
\left[V \mid I\right] = \left(\begin{array}{cccc|cccc}
Q_1 & 0 & 0 & 0 & 1 & 0 & 0 & 0 \\
-C_1 & Q_2 & 0 & 0 & 0 & 1 & 0 & 0 \\
-C_2 & -\gamma_1 & Q_3 & 0 & 0 & 0 & 1 & 0 \\
0 & 0 & -r_3 & Q_4 & 0 & 0 & 0 & 1
\end{array}\right)
\tag{3.136}
$$

Using echelon row operation on (3.136), gives

$$
= \left(\begin{array}{cccccccc}
Q_1 & 0 & 0 & 0 & 1 & 0 & 0 & 0 \\
0 & Q_1Q_2 & 0 & 0 & C_1 & Q_1 & 0 & 0 \\
0 & 0 & Q_1Q_2Q_3 & 0 & C_1\gamma_1+C_2Q_2 & Q_1\gamma_1 & Q_1Q_2 & 0 \\
0 & 0 & 0 & Q_1Q_2Q_3Q_4 & r_3(C_1\gamma_1+C_2Q_2) & r_3Q_1\gamma_1 & r_3Q_1Q_2 & Q_1Q_2Q_3
\end{array}\right)
\tag{3.137}
$$

Divide appropriately we have

$$
\left(I \mid V^{-1}\right) = \left(\begin{array}{cccccccc}
1 & 0 & 0 & 0 & \frac{1}{Q_1} & 0 & 0 & 0 \\
0 & 1 & 0 & 0 & \frac{C_1}{Q_1Q_2} & \frac{1}{Q_2} & 0 & 0 \\
0 & 0 & 1 & 0 & \frac{C_1\gamma_1+C_2Q_2}{Q_1Q_2Q_3} & \frac{\gamma_1}{Q_2Q_3} & \frac{1}{Q_3} & 0 \\
0 & 0 & 0 & 1 & \frac{r_3(C_1\gamma_1+C_2Q_2)}{Q_1Q_2Q_3Q_4} & \frac{r_3\gamma_1}{Q_2Q_3Q_4} & \frac{r_3}{Q_3Q_4} & \frac{1}{Q_4}
\end{array}\right)
\tag{3.138}
$$

Therefore

$$V^{-1}=\begin{pmatrix} \dfrac{1}{\text{[redacted]}} & 0 & 0 & 0 \\ \dfrac{(1-\rho)\sigma}{Q_1Q_2} & \dfrac{1}{Q_2} & 0 & 0 \\ \dfrac{(1-\rho)\gamma\sigma+\rho\sigma Q_2}{Q_1Q_2Q_3} & \dfrac{\gamma}{Q_2Q_3} & \dfrac{1}{Q_3} & 0 \\ \dfrac{r_3\left[(1-\rho)\gamma\sigma+\rho\sigma Q_2\right]}{Q_1Q_2Q_3Q_4} & \dfrac{r_3\gamma}{Q_2Q_3Q_4} & \dfrac{r_3}{Q_3Q_4} & \dfrac{1}{Q_4} \end{pmatrix} \tag{3.139}$$

$$FV^{-1}=\begin{pmatrix} 0 & \dfrac{\beta\varepsilon_1\pi(\mu+\omega-\mu\theta)}{\mu(\mu+\omega)} & \dfrac{\beta\pi(\mu+\omega-\mu\theta)}{\mu(\mu+\omega)} & \dfrac{\beta\varepsilon_2\pi(\mu+\omega-\mu\theta)}{\mu(\mu+\omega)} \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix}\begin{pmatrix} \dfrac{1}{(\mu+\sigma)} & 0 & 0 & 0 \\ \dfrac{(1-\rho)\sigma}{Q_1Q_2} & \dfrac{1}{Q_2} & 0 & 0 \\ \dfrac{(1-\rho)\gamma\sigma+\rho\sigma Q_2}{Q_1Q_2Q_3} & \dfrac{\gamma_1}{Q_2Q_3} & \dfrac{1}{Q_3} & 0 \\ r_3\left(\dfrac{(1-\rho)\gamma\sigma+\rho\sigma Q_2}{Q_1Q_2Q_3Q_4}\right) & \dfrac{r_3\gamma_1}{Q_2Q_3Q_4} & \dfrac{r_3}{Q_3Q_4} & \dfrac{1}{Q_4} \end{pmatrix} \tag{3.140}$$

$$FV^{-1}=\begin{pmatrix} \dfrac{\beta\varepsilon_1\sigma x(1-\rho)}{Q_1Q_2}+\dfrac{\beta x\sigma\left[(1-\rho)\gamma_1+\rho Q_2\right]}{Q_1Q_2Q_3}+\dfrac{\beta\varepsilon_2 x r_3\sigma\left[(1-\rho)\gamma_1+\rho Q_2\right]}{Q_1Q_2Q_3Q_4} & \dfrac{\beta\varepsilon_1 x}{Q_2}+\dfrac{\beta x\gamma_1}{Q_2Q_3}+\dfrac{\beta\varepsilon_2 x r_3\gamma_1}{Q_2Q_3Q_4} & \dfrac{\beta x}{Q_3}+\dfrac{\beta\varepsilon_2 x r_3}{Q_3Q_4} & \dfrac{\beta\varepsilon_2 x}{Q_4} \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix} \tag{3.141}$$

where

$$x = \frac{\pi(\mu+\omega-\mu\theta)}{\mu(\mu+\omega)}$$

From (3.141), we calculate the eigen-values to determine the basic reproduction number, R_o by taking the spectral radius (dominant eigenvalue) of the matrix FV^{-1}, This is computed by $|J-\lambda I| = 0$, hence the matrix becomes

$$|J-\lambda I| = \begin{vmatrix} T_1-\lambda_1 & T_2 & T_3 & T_4 \\ 0 & -\lambda_2 & 0 & 0 \\ 0 & 0 & -\lambda_3 & 0 \\ 0 & 0 & 0 & -\lambda_4 \end{vmatrix} = 0$$

Where

$$T_1 = \frac{\beta\varepsilon_1\sigma x(1-\rho)}{Q_1Q_2} + \frac{\beta x\sigma\left[(1-\rho)\gamma_1+\rho Q_2\right]}{Q_1Q_2Q_3} + \frac{\beta x\varepsilon_2 r_3\sigma\left[(1-\rho)\gamma_1+\rho Q_2\right]}{Q_1Q_2Q_3Q_4}$$

$$T_2 = \frac{\beta\varepsilon_1 x}{Q_2} + \frac{\beta x\gamma_1}{Q_2Q_3} + \frac{\beta\varepsilon_2 x r_3\gamma_1}{Q_2Q_3Q_4}, T_3 = \frac{\beta x}{Q_3} + \frac{\beta\varepsilon_2 x r_3}{Q_3Q_4}, T_4 = \frac{\beta\varepsilon_2 x}{Q_4}$$

and

$$x = \frac{\pi(\mu+\omega-\mu\theta)}{\mu(\mu+\omega)}$$

(3.142)

This implies that

$$\lambda_1 = T_1 = \frac{\beta\varepsilon_1\sigma x(1-\rho)}{Q_1Q_2} + \frac{\beta x\sigma\left[(1-\rho)\gamma_1+\rho Q_2\right]}{Q_1Q_2Q_3} + \frac{\beta\varepsilon_2 x r_3\sigma\left[(1-\rho)\gamma_1+\rho Q_2\right]}{Q_1Q_2Q_3Q_4} \quad (3.143)$$

$$\lambda_2 = 0, \lambda_3 = 0, \lambda_4 = 0,$$

Therefore

$$R_0 = \frac{\beta\sigma x\left[(1-\rho)(\varepsilon_1 Q_3 + \gamma_1) + \rho Q_2\right]}{Q_1 Q_2 Q_3} + \frac{\beta\varepsilon_2 x r_3 \sigma\left[(1-\rho)\gamma_1 + \rho Q_2\right]}{Q_1 Q_2 Q_3 Q_4}$$

$$= \frac{\beta\sigma\pi(\mu+\omega-\mu\theta)\left(\left[(1-\rho)(\varepsilon_1 Q_3 + \gamma_1) + \rho Q_2\right]Q_4 + \varepsilon_2 r_3\left[(1-\rho)\gamma_1 + \rho Q_2\right]\right)}{\mu(\mu+\omega)(\mu+\sigma)Q_2 Q_3 Q_4}$$

Where

$Q_2 = \gamma + \mu + r_1 + d_1$,

$Q_3 = r_2 + r_3 + d_2 + \mu$,

$Q_4 = d_3 + r_4 + \mu$

(3.144)

3.8 Local Stability of Disease-Free Equilibrium

Theorem 3.2: The Disease Equilibrium of the model system (3.2) to (3.8) is locally asymptotically Stable (LAS) if $R_0 < 1$.

Proof

Using Jacobian stability techniques, the jacobian matrix at D.F.E is given by:

$$J(E^0) = \begin{pmatrix} -(\mu+\omega) & 0 & 0 & 0 & 0 & 0 & 0 \\ \omega & -\mu & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & -(\mu+\sigma) & \frac{\beta\varepsilon_1\pi(\mu+\omega-\mu\theta)}{\mu(\mu+\omega)} & \frac{\beta\varepsilon_1\pi(\mu+\omega-\mu\theta)}{\mu(\mu+\omega)} & \frac{\beta\varepsilon_1\pi(\mu+\omega-\mu\theta)}{\mu(\mu+\omega)} & 0 \\ 0 & 0 & (1-\rho)\sigma & -(\gamma_1+\mu+d_1+r_1) & 0 & 0 & 0 \\ 0 & 0 & \rho\sigma & \gamma & -(r_2+r_3+\mu+d_3) & 0 & 0 \\ 0 & 0 & 0 & 0 & r_3 & -(\mu+d_3+r_4) & 0 \\ 0 & 0 & 0 & r_1 & r_2 & r_4 & -\mu \end{pmatrix}$$

(3.145)

Let

$$\left.\begin{aligned}
Q_1 &= (\mu+\sigma), \\
Q_2 &= (\gamma+\mu+d_1+r_1), \\
Q_3 &= -(r_2+r_3+\mu+d_3), \\
Q_4 &= (\mu+d_3+r_4), \\
Q_5 &= (\mu+\omega), \\
B_1 &= \frac{\beta\varepsilon_1\pi(\mu+\omega-\mu\theta)}{\mu(\mu+\omega)}, \\
B_2 &= \frac{\beta\pi(\mu+\omega-\mu\theta)}{\mu(\mu+\omega)}, \\
B_3 &= \frac{\beta\varepsilon_1\pi(\mu+\omega-\mu\theta)}{\mu(\mu+\omega)}, \\
C_1 &= (1-\rho)\sigma
\end{aligned}\right\} \tag{3.146}$$

$$J(E_0)=\begin{pmatrix}
-Q_5 & 0 & 0 & 0 & 0 & 0 & 0 \\
\omega & -\mu & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & -Q_1 & B_1^* & B_2 & B_3 & 0 \\
0 & 0 & C_1 & Q_2 & 0 & 0 & 0 \\
0 & 0 & \rho\sigma & \gamma & -Q_3 & 0 & 0 \\
0 & 0 & 0 & 0 & r_3 & -Q_4 & 0 \\
0 & 0 & 0 & r_1 & r_2 & r_4 & -\mu
\end{pmatrix} \tag{3.147}$$

Using Gaussian elimination row operation on (3.147), we have

$$
|J-\lambda I| = \begin{pmatrix}
-Q_5-\lambda & 0 & 0 & 0 & 0 & 0 & 0 \\
0 & -\mu Q_5-\lambda & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & -Q_1-\lambda & B_1 & B_2 & B_3 & 0 \\
0 & 0 & 0 & Q_6-\lambda & C_1B_2 & C_1B_3 & 0 \\
0 & 0 & 0 & 0 & Q_7-\lambda & Q_8 & 0 \\
0 & 0 & 0 & 0 & 0 & -Q_9-\lambda & 0 \\
0 & 0 & 0 & 0 & 0 & 0 & -Q_9Q_{10}-\lambda
\end{pmatrix} \tag{3.148}
$$

Where

$$
\begin{aligned}
Q_6 &= C_1B_1 - Q_1Q_2 \\
Q_7 &= (C_1B_1 - Q_1Q_2)(\rho\sigma B_2 - Q_1Q_3) - (\gamma Q_1 - \rho\sigma B_1)C_1B_2 \\
Q_8 &= (C_1B_1 - Q_1Q_2)\rho\sigma B_3 - (\gamma Q_1 - \rho\sigma B_1)C_1B_3 \\
Q_9 &= -\left(\left[(C_1B_1 - Q_1Q_2)(\rho\sigma B_2 - Q_1Q_3) - (\gamma Q_1 - \rho\sigma B_1)C_1B_2\right]Q_4\right) \\
&\quad + r_3\left[(C_1B_1 - Q_1Q_2)\rho\sigma B_3 - (\gamma Q_1 - \rho\sigma B_1)C_1B_3\right] \\
Q_{10} &= \mu(C_1B_1 - Q_1Q_2)\left[(C_1B_1 - Q_1Q_2)(\rho\sigma B_2 - Q_1Q_3) - (\gamma Q_1 - \rho\sigma B_1)C_1B_2\right]
\end{aligned} \tag{3.149}
$$

Where

$$
\left.\begin{aligned}
&Q_5-\lambda=0, \\
&-\mu Q_5-\lambda=0, \\
&-Q-\lambda=0, \\
&Q_6-\lambda=0, \\
&Q_9-\lambda=0, \\
&-Q_{13}Q_{15}-\lambda=0
\end{aligned}\right\} \tag{3.150}
$$

From equation (3.150)

$$
\lambda_6 = -Q_{13} \tag{3.151}
$$

$$
\lambda_6 = -\left\{\begin{aligned}
&\left[(C_1B_1 - Q_1Q_2)(\rho\sigma B_2 - Q_1Q_3) - (\gamma Q_1 - \rho\sigma B_1)C_1B_2\right]Q_4 \\
&+ r_3\left[(C_1B_1 - Q_1Q_2)\rho\sigma B_3 - (\gamma Q_1 - \rho\sigma B_1)C_1B_3\right]
\end{aligned}\right\} \tag{3.152}
$$

Substitute equation (3.146) into equation (3.152), we have

$$\left[\frac{(1-\rho)(\varepsilon Q_1+\gamma)Q_4+\rho Q_2Q_4+r\varepsilon Q_3\left((1-\rho)\gamma+\rho Q_2\right)}{\mu(\mu+\omega)Q_1Q_2Q_3Q_4}\right] \tag{3.153}$$

Therefore

$$R_0=\beta\delta\pi(\mu+\omega-\mu\theta)\left[\frac{(1-\rho)(\varepsilon Q_1+\gamma)Q_4+\rho Q_2Q_4+r\varepsilon Q_3\left((1-\rho)\gamma+\rho Q_2\right)}{\mu(\mu+\omega)Q_1Q_2Q_3Q_4}\right] \tag{3.154}$$

The DFE will be locally asymptotically stable

Following Descartes's rule of sign, all the eigenvalues of (3.154) are negatives for

$R_0<1$, since $a_1>0$ for all $i=1,2,3$. Hence the proof is established.

3.9 Global Stability Analysis of Disease-Free Equilibrium

Theorem 3.7.1. The disease-free equilibrium of equations (3.2) to (3.8) is globally asymptotically stable provided $R_0<1$ and unstable $R_0>1$

Referring to Castillo-Chavez, C., and Feng, Z. (1997). the system of equations (3.2) to (3.8) can be written as,

$$\left.\begin{aligned}\frac{dx(t)}{dt}&=F(x,y),\\ \frac{dy(t)}{dt}&=G(x,y)\end{aligned}\right\} \tag{3.155}$$

Where

$x=(S,V,T)\in\Re^3$, denote the different compartment of uninfected,

$y=(E,I_m,I_c,J)\in\Re^4$, denote the different compartment of infected

The disease-free equilibrium (DFE)= $(x_0,0)$ where

$$x_n = \left(\frac{\pi(\mu+\omega-\mu\theta)}{\mu(\mu+\omega)}, \frac{\pi\theta}{(\mu+\omega)}, 0 \right) \tag{3.156}$$

We are required to proof that

$\frac{dx(t)}{dt} = F(x, 0)$, x_n is globally asymptotically stable and

$$G(x,y) = Cy - G(x,y), G(x,y) \geq 0 \text{ for } (x,y) \in n \tag{3.157}$$

Case 1: consider the uninfected subsystem

$$\frac{dx(t)}{dt} = F(x,0) = \begin{vmatrix} \pi\theta - (\mu+\omega)V \\ \pi(1-\theta) - \lambda_1 S - \mu S + \omega V \\ r_3 I_c - (\mu + d_3 + r_4)T \end{vmatrix} \tag{3.158}$$

Where $y = 0$ that is $E = I_m = I_c = J = 0$

Then equation (3.158) becomes

$$F(x,0) = \begin{vmatrix} \pi\theta - (\mu+\omega)V \\ \pi(1-\theta) - \mu S + \omega V \\ 0 \end{vmatrix} \tag{3.159}$$

Solving equation (3.158)

For V

$$\frac{dV(t)}{dt} = \pi\theta - (\mu+\omega)V \tag{3.160}$$

$$\frac{dV(t)}{dt} + (\mu+\omega)V = \pi\theta \tag{3.161}$$

Multiplying equation (3.161) by its integrating factor $e^{(\mu+\omega)t}$ gives

$$e^{(\mu+\omega)t}\frac{dV(t)}{dt} + (\mu+\omega) V e^{(\mu+\omega)t} = (\pi\theta) e^{(\mu+\omega)t} \tag{3.162}$$

$$\frac{d}{dt}\left[V e^{(\mu+\omega)t}\right] = (\pi\theta) e^{(\mu+\omega)t} \tag{3.163}$$

Integrating equation (3.163) gives

$$\int \frac{d}{dt}\left[V e^{(\mu+\omega)t}\right] = \int (\pi\theta) e^{(\mu+\omega)t} \tag{3.164}$$

$$V e^{(\mu+\omega)t} = \left(\frac{\pi\theta}{(\mu+\omega)}\right) e^{(\mu+\omega)t} + c \tag{3.165}$$

Divide equation (3.165) by exp $(\mu+\omega)t$

$$V(t) = \left(\frac{\pi\theta}{[redacted]}\right) + c\, e^{-(\mu+\omega)t} \tag{3.166}$$

When $t = 0$ equation (3.166) become

$$c = V(0) - \left(\frac{\pi\theta}{\mu+\omega}\right) \tag{3.167}$$

Substitute equation (3.167) into equation (3.166)

$$V(t) = \left(\frac{\pi\theta}{(\mu+\omega)}\right) - \left(\frac{\pi\theta}{(\mu+\omega)}\right) e^{-(\mu+\omega)t} + V(0) e^{-(\mu+\omega)t} \tag{3.168}$$

For S

$$\frac{dS(t)}{dt} = \pi(1-\theta) - \mu S + \omega V \tag{3.169}$$

$$\frac{dS(t)}{dt} + \mu S = \pi(1-\theta) + \omega V \tag{3.170}$$

Multiply equation (3.169) by its integrating factor $\exp(\mu)t$

$$\frac{dS(t)}{dt} + e^{(\mu)t} + \mu S e^{(\mu)t} = (\pi(1-\theta) + \omega V) e^{(\mu)t} \tag{3.171}$$

$$\frac{d}{dt}\left[S e^{(\mu)t} \right] = (\pi(1-\theta) + \omega V) e^{(\mu)t} \tag{3.172}$$

Integrate equation (3.172)

$$\int \frac{d}{dt}\left[S e^{(\mu)t} \right] = \int (\pi(1-\theta) + \omega V) e^{(\mu)t} \tag{3.173}$$

$$S e^{(\mu)t} = \left(\frac{\pi(1-\theta) + \omega V}{\mu} \right) e^{(\mu)t} + c \tag{3.174}$$

Divide equation (3.174) by e $^{(\mu)t}$

$$S(t) = \left(\frac{\pi(1-\theta) + \omega V}{\mu} \right) + c\, e^{-(\mu)t} \tag{3.175}$$

When $t = 0$ equation (3.175) gives

$$c = S(0) - \left(\frac{\pi(1-\theta) + \omega V}{\mu} \right) \tag{3.176}$$

Substitute equation (3.176) into equation (3.175)

$$S(t) = \left(\frac{\pi(1-\theta) + \omega V}{\mu} \right) - \left(\frac{\pi(1-\theta) + \omega V}{\mu} \right) \exp - (\mu)t + S(0)\exp - (\mu)t \tag{3.177}$$

For T

$$\frac{dT(t)}{dt} = -\mu T \tag{3.178}$$

$$\frac{dT(t)}{dt} + \mu T = 0 \tag{3.179}$$

Equation (3.179) becomes

$$\frac{dT(t)}{dt} = -\mu T \tag{3.180}$$

Integrate equation (3.180) gives

$$lnT(t) = -\mu t + c \tag{3.181}$$

$$T(t) = e^{-\mu t + c} \tag{3.182}$$

$$T(t) = c\, e^{-\mu t} \tag{3.183}$$

Where $c\, e^{-0} = c$ when $t = 0$, equation (3.183) becomes

$$c = T(0) \tag{3.184}$$

Substitute equation (3.184) into equation (3.183)

$$T(t) = T(0)e^{-\mu t} \tag{3.185}$$

$$\text{As } t \to \infty,\ V \to \left(\frac{\pi\theta}{\mu+\mu}\right),\ S \to \left(\frac{\pi(1-\theta)+\omega V}{\mu}\right),\ T \to 0 \tag{3.186}$$

Therefore

$$x_0 = \left(\frac{\pi}{\mu(\mu+\omega)} \left(\mu + \omega - \theta(\mu+\omega) + \omega\theta \right), \quad \frac{\pi\theta}{(\mu+\omega)}, 0 \right)$$ is globally asymptotically stable

Case 2: consider the infected subsystem

$$y' = G(x, y) = \begin{bmatrix} \beta(I_c + \varepsilon_1 I_m + \varepsilon_2 J)S + \gamma(I_c + \varepsilon_5 I_m + \varepsilon_6 J)T - \alpha(I_c + \varepsilon_3 I_m + \varepsilon_4 J)E - (\mu+\sigma)E \\ (1-\rho)\sigma E - (\gamma + \mu + r_1 + d_1) I_m + (1-\phi)\alpha(I_c + \varepsilon_3 I_m + \varepsilon_4 J)E \\ \rho\sigma E + \gamma I_m - (r_2 + r_3 + \mu + d_2) I_c + \phi\alpha(I_c + \varepsilon_3 I_m + \varepsilon_4 J)E \\ r_3 I_c - (\mu + d_3 + r_4) J \end{bmatrix} \tag{3.187}$$

Given that

$$\dot{G}(x, y) = cy - G(x, y) \tag{3.188}$$

Then

$$\dot{G}(x, y) = cy - G(x, y) \tag{3.189}$$

where

$$c = dG(x, y) \tag{3.190}$$

$$c = \begin{pmatrix} -(\mu+\sigma) & \beta\varepsilon_1 S^* & \beta S^* & \beta\varepsilon_2 S^* \\ (1-\rho)\sigma & -(\gamma+\mu+r_1+d_1) & 0 & 0 \\ \rho\sigma & \gamma & -(\mu+d_2+r_2+r_3) & 0 \\ 0 & 0 & r_3 & -(\mu+d_2+r_4) \end{pmatrix} \tag{3.191}$$

$$cy = \begin{pmatrix} -(\mu+\sigma) & \beta\varepsilon_1 S^* & \beta S^* & \beta\varepsilon_2 S^* \\ (1-\rho)\sigma & -(\gamma+\mu+r_1+d_1) & 0 & 0 \\ \rho\sigma & \gamma & -(\mu+d_2+r_2+r_3) & 0 \\ 0 & 0 & r_3 & -(\mu+d_2+r_4) \end{pmatrix} \begin{pmatrix} E \\ I_m \\ I_c \\ J \end{pmatrix} \tag{3.192}$$

Evaluating equation (3.193) we have

$$cy = \begin{pmatrix} -(\mu+\sigma)E & \beta\varepsilon_1 S^* I_m & \beta S^* I_c & \beta\varepsilon_2 S^* J \\ (1-\rho)\sigma E & -(\gamma+\mu+r_1+d_1)I_m & 0 & 0 \\ \rho\sigma E & \gamma I_m & -(\mu+d_2+r_2+r_3)I_c & 0 \\ 0 & 0 & r_3 I_c & -(\mu+d_2+r_4)J \end{pmatrix} \tag{3.193}$$

Substitute equation (3.192) and equation (1.88) into equation (3.194)

$$G(x,y) = \begin{pmatrix} -(\mu+\sigma)E & \beta\varepsilon_1 S^* I_m & \beta S^* I_c & \beta\varepsilon_2 S^* J \\ (1-\rho)\sigma E & -(\gamma+\mu+r_1+d_1)I_m & 0 & 0 \\ \rho\sigma E & \gamma I_m & -(\mu+d_2+r_2+r_3)I_c & 0 \\ 0 & 0 & r_3 I_c & -(\mu+d_2+r_4)J \end{pmatrix} - \begin{bmatrix} \beta(I_c+\varepsilon_1 I_m+\varepsilon_2 J)S+\gamma(I_c+\varepsilon_5 I_m+\varepsilon_6 J)T-\alpha(I_c+\varepsilon_3 I_m+\varepsilon_4 J)E-(\;+\sigma)E \\ (1-\rho)\sigma E-(\gamma\,\mu+\mu+r_1+d_1)I_m+(1-\phi)\alpha(I_c+\varepsilon_3 I_m+\varepsilon_4 J)E \\ \rho\sigma E+\gamma I_m-(r_2+r_3+\mu+d_2)I_c+\phi\alpha(I_c+\varepsilon_3 I_m+\varepsilon_4 J)E \\ -(\mu+\;+\;)r_4 r_{3c3} I\,Jd \end{bmatrix} \tag{3.194}$$

$$\dot{G}(x,y) = \begin{pmatrix} G_1(x,y) \\ G_2(x,y) \\ G_3(x,y) \\ G_4(x,y) \end{pmatrix} = \begin{pmatrix} 0 \\ 0 \\ 0 \\ 0 \end{pmatrix} \tag{3.195}$$

Then

$$G_1(x,y) = 0 \tag{3.196}$$

Therefore, the disease-free equilibrium point is globally asymptotically stable when

$R_0 < 1$

3.10 Analytical Solution of the Model

3.10.1 Semi- analytical solution of the model using homotopy perturbation method.

The fundamental of Homotopy Perturbation Method (HPM) was first proposed by He (1998). The Homotopy Perturbation Method (HPM), which provides analytical approximate solution, is applied to various linear and non-linear equations. Abubakar *et al.,* (2013) used homotopy perturbation method to solve a SIR model of infectious diseases. The homotopy perturbation method (HPM) is a series expansion method used in the solution of nonlinear partial differential equations (Jiya, 2010).

To show the simple concepts of this method, he considered the following non-linear differential equation given as Equation (3.197) to Equation (3.198) Somma *et al,* (2017)

$$A_3(U)-f(r)=0,\ r\in\Omega \tag{3.197}$$

Subject to the boundary condition

$$B_3\left(U,\frac{\partial U}{\partial n}\right)=0,\quad r\in\Gamma \tag{3.198}$$

Where A_3 is a general differential operator, B_3 a boundary operator, $f(r)$ is a known analytical function and Γ is the boundary of the domain Ω. The operator A_3 can be divided into two parts L and N, where L is the linear part, and N is the nonlinear part. Equation (3.120) can be written as:

$$L(U)+N(U)-f(r)=0,\ r\in\Omega \tag{3.199}$$

The Homotopy Perturbation structure is shown as follows

$$H(V,h)=(1-h)[L(V)-L(U_0)]+h[A(V)-f(r)]=0 \tag{3.200}$$

Where $V(r,P):\Omega\in[0,1]\rightarrow R$

(3.201)

In Equation (3.117) $P \in [0,1]$ is an embedding parameter and U_0 is the approximation that satisfies the boundary condition. It can be assumed that the solution of the equation (3.201) can be written as power series in h given as Equation (3.202) to Equation (3.203):

$$V = V_0 + hV_1 + h^2 V_2 + \ldots \tag{3.202}$$

And the best approximation for the solution is:

$$U = \lim_{h \to 1} v = v_0 + hv_1 + h^2 v_2 + \ldots \tag{3.203}$$

The series (3.203) is convergent for most cases. However, the convergent rate depends on the nonlinear operator A (V)

3.10.2 Solution of the model equations

From differential equations (3.2) to (3.8)

$$\frac{dS}{dt} + (\mu + \lambda_1) S - \omega V - \pi (1 - \theta) = 0 \tag{3.204}$$

$$\frac{dV}{dt} + (\mu + \omega) V - \theta\pi = 0 \tag{3.205}$$

$$\frac{dE}{dt} + (\sigma + \lambda_2 + \mu) E - \lambda_3 T - \lambda_1 S = 0 \tag{3.206}$$

$$\frac{dI_m}{dt} + (\gamma + \mu + r_1 + d_1) I_m - (1 - \rho) \sigma E - (1 - \phi) \lambda_2 E = \tag{3.207}$$

$$0 \frac{dI_c}{dt} + (\mu + d_2 + r_3 + r_2) I_c - \rho\sigma E - \gamma I_m - \phi\lambda_2 E = 0 \tag{3.208}$$

$$\frac{dJ}{dt} + (\mu + d_3 + r_4) J - r_3 I_c = 0 \tag{3.209}$$

$$\frac{dT}{dI}+(\mu+\lambda_3)T-r_4J-r_{2c}I-r_{1m}I=0 \quad (3.210)$$

With the initial condition given as

$$S(0)=S_0,\ V(0)=V_0,\ E(0)=E_0,\ I_m(0)=I_{m0},\ I_c(0)=I_{c0},\ J(0)=J_0,\ T(0)=T_0 \quad (3.211)$$

Let

$$S=s_0+hs_1+h^2s_2+... \quad (3.212)$$

$$V=u_0+hu_1+h^2u_2+... \quad (3.213)$$

$$E=v_0+hv_1+h^2v_2+... \quad (3.214)$$

$$I_m=w_0+hw_1+h^2w_2+... \quad (3.215)$$

$$I_c=x_0+hx_1+h^2x_2+... \quad (3.216)$$

$$J=y_0+hy_1+h^2y_2+... \quad (3.217)$$

$$T=z_0+hz_1+h^2z_2+... \quad (3.218)$$

Applying HPM into equation (3.204)

$$(1-h)\frac{dS}{dt}+h\left[\frac{dS}{dt}+(\mu+\lambda_1)S-\omega V-\pi(1-\theta)\right]=0 \quad (3.219)$$

Substitute equation (3.212) and (3.213) into (3.219)

$$(s_0^1+hs_1^1+h^2s_2^1+...)+h\left[\begin{array}{l}(\mu+\lambda_1)(s_0+hs_1+h^2s_2+...)-\omega\\ (u_0+hu_1+h^2u_2+...)-\pi(1-\theta)\end{array}\right]=0 \quad (3.220)$$

Collecting the coefficient of power of h, we have

$$h^0 : s^1_0 = 0 \tag{3.221}$$

$$h_1 : s^1_1 + (\mu + \lambda)s_1 - \omega u_0 - \pi(1-\theta) = 0 \tag{3.222}$$

$$h_2 : s^1_2 + (\mu + \lambda)s_1 - \omega u_1 = 0 \tag{3.223}$$

Applying HPM to equation (3.205)

$$(1-h)\frac{dV}{dt} + h\left[\frac{dV}{dt} + (\mu + \omega)V - \pi\theta\right] = 0 \tag{3.224}$$

Substitute equation (3.213) into (3.224)

$$\left(u^1_0 + hu^1_1 + h^2 u^1_2 + \ldots\right) + h\left[(\mu + \omega)\left(u_0 + hu_1 + h^2 u_2 + \ldots\right) - \pi\theta\right] = 0 \tag{3.225}$$

Collecting the coefficient of power of h , we have

$$h^0 : u^1_0 = 0 \tag{3.226}$$

$$h_1 : u^1_1 + (\mu + \omega)u_0 - \pi\theta = 0 \tag{3.227}$$

$$h^2 : u^1_2 + (\mu + \omega)u_1 = 0 \tag{3.228}$$

Applying HPM to equation (3.206)

$$(1-h)\frac{dE}{dt} + h\left[\frac{dE}{dt} + (\lambda_2 + \mu + \sigma)E - \lambda_3 T - \lambda_1 S\right] = 0 \tag{3.229}$$

Substitute equation (3.214) (3.212) and (3.218) into (3.229)

$$\left(v_0^1 + hv_1^1 + h^2 v^1_2 + \ldots\right) + h\left[\begin{array}{l}(\lambda_2 + \mu + \sigma)\left(v_0 + hv_1 + h^2 v_2 + \ldots\right) - \lambda_3\left(z_0 + hz_1 + h^2 z_2 + \ldots\right) - \\ \lambda_1\left(t_0 + ht_1 + h t_2 + \ldots\right)\end{array}\right] = 0 \tag{3.230}$$

Collecting the coefficient of power of h, we have

$$h^0 : v^1_0 = 0 \tag{3.231}$$

$$h_1 : v^1_1 + (\lambda_2 + \mu + \sigma) v_0 - \lambda_3 z_0 - \lambda_1 t_0 = 0 \tag{3.232}$$

$$h_1 : v^1_2 + (\lambda_2 + \mu + \sigma) v_1 - \lambda_3 z_1 - \lambda_1 t_1 = 0 \tag{3.233}$$

Applying HPM to equation (3.207)

$$(1-h)\frac{dI_m}{dt} + h\left[\frac{dI_m}{dt} + (\gamma_1 + \mu + r_1 + d) I_m - (1-\rho)\sigma E - (1-\theta)\lambda_2 E\right] = 0 \tag{3.234}$$

Substitute equation (3.215) and (3.214) into (3.234)

$$(w^1_0 + h w^1_1 + h^2 w^1_2 + \ldots) + h\left[\begin{array}{l}(\gamma_1 + \mu + r_1 + d)(w_0 + h w_1 + h^2 w_2 + \ldots) - (1-\rho\sigma)\\ (v_0 + h v_1 + h^2 v_2 + \ldots) - (1-\theta)\lambda_2 (v_0 + h v_1 + h^2 v_2 + \ldots)\end{array}\right] = 0 \tag{3.235}$$

Collecting the coefficient of power of h, we have

$$h^0 : w^1_0 = 0 \tag{3.236}$$

$$h_1 : w^1_1 + (\gamma_1 + r_1 + d + \mu) w_0 - (1-\rho)\sigma v_0 - (1-\theta) v_0 = 0 \tag{3.237}$$

$$h_2 : w^1_2 + (\gamma_1 + r_1 + d + \mu) w_1 - (1-\rho)\sigma v_1 - (1-\theta) v_1 = 0 \tag{3.238}$$

Applying HPM to equation (3.208)

$$(1-h)\frac{dI_c}{dt} + h\left[\frac{dI_c}{dt} + (\mu + d_2 + r_2 + r_3) I_c - \rho\sigma E - \gamma I_m - \phi\lambda_2 E\right] = 0 \tag{3.239}$$

Substitute equation (3.216), (3.214) and (3.215) into (3.239)

$$\left(x_0^{1} + hx_1^{1} + h^2x_2^{1} + \dots\right) + h\left[\begin{array}{l}(\mu+d_2+r_2+r_3)\left(x_0 + hx_1 + h^2x_2 + \dots\right) - \rho\sigma\left(v_0 + hv_1 + h^2v_2 + \dots\right) - \gamma\left(w_0 + hw_1 + h^2w_2 + \dots\right) \\ -\theta\lambda_2\left(v_0 + hv_1 + h^2v_2 + \dots\right)\end{array}\right] = 0 \tag{3.240}$$

Collecting the coefficient of power of h, we have

$$h^0 : x_0^1 = 0 \tag{3.241}$$

$$h_1 : x_1^1 + (\mu+d_2+r_2+r_3)x_0 - \rho\sigma v_0 - \gamma w_0 - \phi\lambda_2 v_0 = 0 \tag{3.242}$$

$$h_2 : x_2^1 + (\mu+d_2+r_2+r_3)x_1 - \rho\sigma v_1 - \gamma w_1 - \phi\lambda_2 v_1 = 0 \tag{3.243}$$

Applying HPM to equation (3.209)

$$\left(1-h\right)\frac{dJ}{dt} + h\left[\frac{dJ}{dt} + \left(\mu+d_3+r_4\right)J - r_3 I_m\right] = 0 \tag{3.244}$$

Substitute equation (3.136) and (3.137) into (3.158)

$$\left(y_0^1 + hy_1^1 + h^2y_2^1 + \dots\right) + h\left[\left(\mu+d_3+r_3\right)\left(y_0 + hy_1 + h^2y_2 + \dots\right) - r_3\left(x_0 + hx_1 + h^2x_2 + \dots\right)\right] = 0 \tag{3.245}$$

Collecting the coefficient of power of h, we have

$$h^0 : y_0^1 = 0 \tag{3.246}$$

$$h_1 : y_1^1 + \left(\mu+d_3+r_4\right)y_0 - r_3x_0 = 0 \tag{3.247}$$

$$h_2 : y_2^1 + \left(\mu+d_3+r_4\right)y_1 - r_3x_1 = 0 \tag{3.248}$$

Applying HPM to equation (3.210)

$$\left(1-h\right)\frac{dT}{dt} + h\left[\frac{dT}{dt} + \left(\mu+\lambda_3\right)T - r_4J - r_2I_c - r_1I_m\right] = 0 \tag{3.249}$$

Substitute equations (3.218), (3.217), (3.216) and (3.215) into (3.249)

$$\left(z_0^1 + hz_1^1 + h^2 z_2^1 + \ldots\right) + h\left[\left(\mu+\lambda_3\right)\left(z_0 + hz_1 + h^2 z_2 + \ldots\right) - r_4\left(y_0 + hy_1 + h^2 y_2 + \ldots\right) - r_2\left(x_0 + hx_1 + h^2 x_2 + \ldots\right) - r_1\left(w_0 + hw_1 + h^2 w_2 + \ldots\right)\right] = 0 \tag{3.250}$$

Collecting the coefficient of power of h, we have

$$h^0 : z_0^1 = 0 \tag{3.251}$$

$$h_1 : z_1^1 + \left(\mu+\lambda_3\right)z_0 - r_4 y_0 - r_2 x_0 - r_1 w_0 = 0 \tag{3.252}$$

$$h_2 : z_2^1 + \left(\mu+\lambda_3\right)z_1 - r_4 y_1 - r_2 x_1 - r_1 w_1 = 0 \tag{3.253}$$

From equation (3.221)

$$s_0^1 = 0 \tag{3.254}$$

Integrate both side

$$s_0 = D_1 \tag{3.255}$$

Applying initial condition

$$s_0\left(0\right) = S_0 = s_0 \tag{3.256}$$

$$D_1 = S_0 \tag{3.257}$$

$$s_0 = S_0 \tag{3.258}$$

From equation (3.226)

$$u_0^1 = 0 \tag{3.259}$$

Integrate both side

$$u_0 = D_2 \tag{3.260}$$

Applying initial condition

$$u_0\left(0\right) = V_0 = u_0 \tag{3.261}$$

$$D_2 = V_0 \tag{3.262}$$

$$u_0 = V_0 \tag{3.263}$$

From equation (3.231)

$$v_0^1 = 0 \tag{3.264}$$

Integrate both side

$$v_0 = D_3 \tag{3.265}$$

Applying initial condition

$$v_0\left(0\right) = E_0 = v_0 \tag{3.266}$$

$$D_3 = E_0 \tag{3.267}$$

$$v_0 = E_0 \tag{3.268}$$

From equation (3.236)

$$w_0^1 = 0 \tag{3.269}$$

Integrate both side

$$w_0 = D_4 \tag{3.270}$$

Applying initial condition

$$w_0(0) = I_{m0} = w_0 \tag{3.271}$$

$$D_4 = I_{m0} \tag{3.272}$$

$$w_0 = I_{m0} \tag{3.273}$$

From equation (3.241)

$$x_0^1 = 0 \tag{3.274}$$

Integrate both side

$$x_0 = D_5 \tag{3.275}$$

Applying initial condition

$$x_0(0) = I_{c0} = x_0 \tag{3.276}$$

$$D_5 = I_{c0} \tag{3.277}$$

$$x_0 = I_{c0} \tag{3.278}$$

From equation (3.246)

$$y_0^1 = 0 \tag{3.279}$$

Integrate both side

$$y_0 = D_6 \tag{3.280}$$

Applying initial condition

$$y_0(0)=J_0=y_0 \tag{3.281}$$

$$D_6=y_0 \tag{3.282}$$

$$y_0=J_0 \tag{3.283}$$

From equation (3.251)

$$z^1{}_0=0 \tag{3.284}$$

Integrate both side

$$z_0=D_7 \tag{3.285}$$

Applying initial condition

$$D_7=T_0 \tag{3.286}$$

$$z_0=T_0 \tag{3.287}$$

From equation (3.221)

$$s_1^1=\pi(1-\theta)+\omega v_0-(\mu+\lambda_1)s_0 \tag{3.288}$$

Integrate both sides

$$\int ds^1{}_1=\int\left(\pi(1-\theta)+\omega v_0-(\mu+\lambda_1)s_0\right)dt \tag{3.289}$$

$$s_1(t)=\left(\pi(1-\theta)+\omega v_0-(\mu+\lambda_1)s_0\right)t+D_8 \tag{3.290}$$

Applying the initial condition

$$D_8 = 0 \qquad s_1(t) = \left(\pi\left(1-\theta\right) + \omega v_0 - \left(\mu + \lambda_1\right) s_0\right) t \tag{3.291}$$

Substitute equations (3.214) and (3.213) into (3.292)

$$s_1(t) = \left(\pi\left(1-\theta\right) + \omega E_0 - \left(\mu + \lambda_1\right) S_0\right) t \tag{3.292}$$

From equation (3.227)

$$u_1^1 = \pi\theta - \left(\mu + \omega\right) u_0 \tag{3.293}$$

Integrate both sides

$$\int du_1^1 = \int \left(\pi\theta - \left(\mu + \omega\right) u^0\right) dt \tag{3.294}$$

$$u_1(t) = \left(\pi\theta - \left(\mu + \omega\right) u_0\right) t + D_9 \tag{3.295}$$

Applying the initial condition

$$D_9 = 0 \tag{3.296}$$

$$u_1(t) = \left(\pi\theta - \left(\mu + \omega\right) u_0\right) t \tag{3.297}$$

Substitute equation (3.213) into (3.297)

$$u_1(t) = \left(\pi\theta - \left(\mu + \omega\right) V_0\right) t \tag{3.298}$$

From equation (3.232)

$$v_1^1 + \left(\sigma + \lambda_2 + \mu\right) v_0 - \lambda_2 z_0 - \lambda_{10} t = 0 \tag{3.299}$$

(3.300)

Integrating both sides

$$\int \;{}_{1}^{1} = \int\Big(\;{}_{2}\;{}_{0}\;\;\;{}_{1}{}_{0} - (\;\;\;{}_{2}\;\;\;) \;{}_{0}\Big)\, dt \tag{3.301}$$

$$v_1(t) = \big(\lambda_2 z_0 + \lambda_1 t_0 - (\sigma + \lambda_2 + \mu) v_0 \big) t + D_{10} \tag{3.302}$$

Applying the initial condition

$$D_{10} = 0 \tag{3.303}$$

$$v_1(t) = \big(\lambda_2 z_0 + \lambda_1 t_0 - (\sigma + \lambda_2 + \mu) v_0 \big) t \tag{3.304}$$

Substitute equation (3.183), (3.167), (3.193) and (3.173) into (3.205)

$$v_1(t) = \big(\lambda_2 T_0 + \lambda_1 S_0 - (\sigma + \lambda_2 + \mu) E_0 \big) t \tag{3.305}$$

From equation (3.237)

$$w_1^1 + (\gamma + \mu + r_1 + d_1) w_0 - (1-\rho)\sigma v_0 - (1-\phi)\lambda_2 v_0 = 0 \tag{3.306}$$

$$w_1^1 = (1-\rho)\sigma v_0 + (1-\phi)\lambda_2 v_0 - (\gamma + \mu + r_1 + d_1) w_0 \tag{3.307}$$

Integrating both sides

$$\int \;{}_{1}^{1} = \int\Big((\;\;\;) \;{}_{0}\; (\;\;\;){}_{2}{}_{0}\; (\;\;\;{}_{1}\;{}_{1}) \;{}_{0}\Big) \tag{3.308}$$

$$w_1(t) = \big((1-\rho)\sigma v_0 + (1-\phi)\lambda_2 v_0 - (\gamma + \mu + r_1 + d_1) w_0 \big) t + D_{11} \tag{3.309}$$

Applying the initial condition

$$D_{11} = 0 \tag{3.310}$$

$$w_1(t) = \big((1-\rho)\sigma v_0 + (1-\phi)\lambda_2 v_0 - (\gamma + \mu + r_1 + d_1) w_0 \big) t \tag{3.311}$$

Substitute equation (3.214) and (3.215) into (3.311)

$$w_1(t) = \left(\left(1-\rho\right)\sigma E_0 + \left(1-\phi\right)\lambda_2 E_0 - \left(\gamma+\mu+r_1+d_1\right) I_{m0}\right) t \tag{3.312}$$

From equation (3.242)

$$x_1^1 + (\mu + d_2 + r_2 + r_3)\,\mathrm{x}_0 - \rho\sigma v_0 - \gamma w_0 - \phi\lambda_2 v_0 = 0 \tag{3.313}$$

$$x_1^1 = \phi\lambda_2 v_0 + \rho\sigma v_0 + \gamma w_0 - (\mu + d_2 + r_2 + r_3)\,\mathrm{x}_0 \tag{3.314}$$

Integrating both sides

$$\int dx_1^1 = \int \left(\phi\lambda_2 v_0 + \rho\sigma v_0 + \gamma w_0 - (\mu + d_2 + r_2 + r_3)\,\mathrm{x}_0\right) dt \tag{3.315}$$

$$x_1(t) = \left(\phi\lambda_2 v_0 + \rho\sigma v_0 + \gamma w_0 - (\mu + d_2 + r_2 + r_3)\,\mathrm{x}_0\right) t + D_{12} \tag{3.316}$$

Applying the initial condition

$$D_{12} = 0 \tag{3.317}$$

$$x(t) = \left(\phi\lambda_2 v_0 + \rho\sigma v_0 + \gamma w_0 - (\mu + d_2 + r_2 + r_3)\,\mathrm{x}_0\right) t \tag{3.318}$$

Substitute equation (3.214), (3.215) and (3.216) into (3.318)

$$x_1(t) = \left(\phi\lambda_2 E_0 + \rho\sigma E_0 + \gamma I_{m0} - (\mu + d_2 + r_2 + r_3)\,\mathrm{xI}_{c0}\right) t \tag{3.319}$$

From equation (3.247)

$$y_1^1 + (\mu + d_3 + r_4)\, y_0 - r_3 x_0 = 0 \tag{3.320}$$

$$y_1^1 = r_3 x_0 - (\mu + d_3 + r_4)\, y_0 \tag{3.321}$$

Integrating both sides

$$\int dy_1 = \int \left(r_3 x_0 - \left(\mu + d_3 + r_4 \right) y_0 \right) dt \tag{3.322}$$

$$y_1(t) = \left(r_3 x_0 - \left(\mu + d_3 + r_4 \right) y_0 \right) t + D_{13} \tag{3.323}$$

Applying the initial condition

$$D_{13} = 0 \tag{3.324}$$

$$y_1(t) = \left(r_3 x_0 - \left(\mu + d_3 + r_4 \right) y_0 \right) t \tag{3.325}$$

Substitute equation (3.216) and (3.217) into (3.325)

$$y_1(t) = \left(r_3 I_{c0} - \left(\mu + d_3 + r_4 \right) J_0 \right) t \tag{3.326}$$

From equation (3.252)

$$z_1^1 + \left(\mu + \lambda_3 \right) z_0 - r_4 y_0 - r_2 x_0 - r_1 w_0 = 0 \tag{3.327}$$

$$z_1^1 = r_4 y_0 + r_2 x_0 + r_1 w_0 - \left(\mu + \lambda_3 \right) z_0 \tag{3.328}$$

Integrating both sides

$$\int dz_1^1 = \int \left(r_4 y_0 + r_2 x_0 + r_1 w_0 - \left(\mu + \lambda_3 \right) z_0 \right) dt \tag{3.329}$$

$$z_1(t) = \left(r_4 y_0 + r_2 x_0 + r_1 w_0 - \left(\mu + \lambda_3 \right) z_0 \right) t + D_{14} \tag{3.330}$$

Applying the initial condition

$$D_{14} = 0 \tag{3.331}$$

$$z_1(t) = \left(r_4 y_0 + r_2 x_0 + r_1 w_0 - \left(\mu + \lambda_3 \right) z_0 \right) t \tag{3.332}$$

Substitute equation (3.217), (3.216), (3.217) and (3.218) into (3.232)

$$z_1(t) = \left(rJ_{40} + rI_{2c0} + rI_{1m0} - (\mu+\lambda_3)T_0 \right)t \tag{3.333}$$

From equation (3.223)

$$s^1{}_2 + (\mu + \lambda_1)s_1 - \omega u_1 = 0 \tag{3.334}$$

$$s^1{}_2 = \omega u_1 - (\mu + \lambda_1)s_1 \tag{3.335}$$

Substitute equation (3.230) and (3.292) into (3.335)

$$S_2{}^1 = \omega\left(\pi\theta - (\mu+\omega)V_0\right)t - (\mu+\lambda_1)\left(\pi(1-\theta) + \omega E_0 - (\mu+\lambda_1)S_0\right)t \tag{3.336}$$

$$s_2^1 = \left(\omega\left(\pi\theta - (\mu+\omega)V_0\right) - (\mu+\lambda_1)\left(\pi(1-\theta) + \omega E_0 - (\mu+\lambda_1)S_0\right)\right)t \tag{3.337}$$

Integrating both sides

$$\int s_2^1 = \int \left(\omega\left(\pi\theta - (\mu+\omega)V_0\right) - (\mu+\lambda_1)\left(\pi(1-\theta) + \omega E_0 - (\mu+\lambda_1)S_0\right)\right) t\,dt \tag{3.338}$$

$$s_2(t) = \left(\omega\left(\pi\theta - (\mu+\omega)V_0\right) - (\mu+\lambda_1)\left(\pi(1-\theta) + \omega E_0 - (\mu+\lambda_1)S_0\right)\right)\frac{t^2}{2} + D_{15} \tag{3.339}$$

Applying the initial condition

$$D_{15} = 0 \tag{3.340}$$

$$s_2(t) = \left(\omega\left(\pi\theta - (\mu+\omega)V_0\right) - (\mu+\lambda_1)\left(\pi(1-\theta) + \omega E_0 - (\mu+\lambda_1)S_0\right)\right)\frac{t^2}{2} \tag{3.341}$$

Substitute equation (3.258), (3.292) and (3.341) into (3.212)

$$S(t) = s_0 + hs_1 + h^2 s_2 + \ldots \tag{3.342}$$

$$S(t) = \lim_{h\to 1}\left(s_0 + hs_1 + h^2 s_2 + \ldots\right) \tag{3.343}$$

$$S(t) = s_0 + s_1 + s_2 + \ldots \tag{3.344}$$

Hence

$$S(t) = S_0 + \left(\pi(1-\theta) + \omega E_0 - (\mu+\lambda_1)S_0\right)t + \left(\omega(\pi\theta-(\mu+\omega)V_0) - (\mu+\lambda_1)\left(\pi(1-\theta) + \omega E_0 - (\mu+\lambda_1)S_0\right)\right)\frac{t^2}{2} \tag{3.345}$$

From equation (3.228)

$$u_{\frac{1}{2}} + (\mu+\omega)u_1 = 0 \tag{3.346}$$

$$u_{\frac{1}{2}} = (\mu+\omega)u_1 \tag{3.347}$$

Substitute equation (3.230) into (3.347)

$$u_{\frac{1}{2}} = (\mu+\omega)(\pi\theta-(\mu+\omega)V_0)t \tag{3.348}$$

$$u_{\frac{1}{2}} = (\mu+\omega)(\pi\theta-(\mu+\omega)V_0)t \tag{3.349}$$

Integrating both sides

$$\int du_1^2 = \int(\mu+\omega)(\pi\theta-(\mu+\omega)V_0)\,tdt \tag{3.350}$$

$$u_2(t) = (\mu+\omega)(\pi\theta-(\mu+\omega)V_0)\frac{t^2}{2} + D_{16} \tag{3.351}$$

Applying the initial condition

$$D_{16} = 0 \tag{3.352}$$

$$u_2(t) = (\mu+\omega)(\pi\theta-(\overline{\mu}+\omega)V_0)\frac{t^2}{2} \tag{3.353}$$

Substitute equation (3.263), (3.298) and (3.353) into (3.213)

$$V(t) = u_0 + hu_1 + h^2 u_2 + \ldots \tag{3.354}$$

$$V(t) = \lim_{h \to 1} \left(u_0 + hu_1 + h^2 u_2 + \ldots \right) \tag{3.355}$$

$$V(t) = u_0 + u_1 + u_2 + \ldots \tag{3.356}$$

Hence

$$V(t) = V_0 + \left(\pi\theta - (\mu+\omega)V_0\right)t + \left((\mu+\omega)\left(\pi\theta - (\mu+\omega)V_0\right)\right)\frac{t^2}{2} \tag{3.357}$$

From equation (3.233)

$$v_{\frac{1}{2}} + (\lambda_2 + \mu + \sigma)v_1 - \lambda_3 z_1 - \lambda_1 s_1 = 0 \tag{3.358}$$

$$v_{\frac{1}{2}} = \lambda_3 z_1 + \lambda_1 s_1 - (\lambda_2 + \mu + \sigma)v_1 \tag{3.359}$$

Substitute equation (3.333), (3.305) and (3.292) into (3.359)

$$v_{\frac{1}{2}} = \lambda_3(r_4 J_0 + r_{2c} I_{c0} + r_1 I_{m0} - (\mu + \lambda_3) T_0)t + \lambda_1(\pi(1-\theta) + \omega E_0 - (\mu + \lambda_1) S_0)t - (\lambda_2 + \mu + \sigma)(\lambda_2 T_0 + \lambda_1 S_0 - (\sigma + \lambda_2 + \mu)E_0)t \tag{3.360}$$

$$v_{\frac{1}{2}} = \begin{pmatrix} \lambda_3\left(r_4 J_0 + r_{2c} I_{c0} + r_1 I_{m0} - (\mu+\lambda_3) T_0\right) + \lambda_1\left(\pi(1-\theta) + \omega E_0 - (\mu+\lambda_1) S_0\right) \\ -(\lambda_2+\mu+\sigma)\left(\lambda_2 T_0 + \lambda_1 S_0 - (\sigma+\lambda_2+\mu)E_0\right) \end{pmatrix} t \tag{3.361}$$

Integrating both sides

$$\int dv_{\frac{1}{2}} = \int \begin{pmatrix} \lambda_3\left(r_4 J_0 + r_{2c} I_{c0} + r_1 I_{m0} - (\mu+\lambda_3) T_0\right) + \lambda_1\left(\pi(1-\theta) + \omega E_0 - (\mu+\lambda_1) S_0\right) \\ -(\lambda_2+\mu+\sigma)\left(\lambda_2 T_0 + \lambda_1 S_0 - (\sigma+\lambda_2+\mu)E_0\right) \end{pmatrix} t\,dt$$

(3.362)

$$v_2(t)=\left(\begin{array}{l}\lambda_3\left(rJ_4{}_0+rI_{2c0}+rI_{1m0}-(\mu+\lambda_3)T_0\right)+\lambda_1\left(\pi(1-\theta)+\omega E_0-(\mu+\lambda_1)S^0\right)\\-(\lambda_2+\mu+\sigma)(\lambda T_{20}+\lambda S_{10}-(\sigma+\lambda_2+\mu)E_0)\end{array}\right)\frac{t^2}{2}+D_{17} \tag{3.363}$$

Applying the initial condition

$$D_{17}=0 \tag{3.364}$$

$$v_2(t)=\left(\begin{array}{l}\lambda_3\left(rJ_4{}_0+rI_{2c0}+rI_{1m0}-(\mu+\lambda_3)T_0\right)+\lambda_1\left(\pi(1-\theta)+\omega E_0-(\mu+\lambda_1)S_0\right)\\-(\lambda_2+\mu+\sigma)(\lambda T_{20}+\lambda S_{10}-(\sigma+\lambda_2+\mu)E_0)\end{array}\right)\frac{t^2}{2} \tag{3.365}$$

Substitute equation (3.268), (3.305) and (3.365) into (3.214)

$$E(t)=v_0+hv_1+h^2v_2+\dots \tag{3.366}$$

$$E(t)=\lim_{h\to 1}\left(v_0+hv_1+h^2v_2+\dots\right) \tag{3.367}$$

$$E(t)=v_0+v_1+v_2+\dots \tag{3.368}$$

Hence

$$E(t)=E_0+\left(\begin{array}{l}\lambda T_{20}+\lambda S_{10}-\\(\sigma+\lambda_2+\mu)E_0\end{array}\right)t+\left(\begin{array}{l}\lambda_2\left(rJ_{40}+rI_{2c0}+rI_{1m0}-(\mu+\lambda_3)T_0\right)+\lambda_1\\(\pi(1-\theta)+\omega E_0-(\mu+\lambda_1)S_0)\\-(\lambda_2+\mu+\sigma)(\lambda T_{20}+\lambda S_{10}-(\sigma+\lambda_2+\mu)E_0)\end{array}\right)\frac{t^2}{2} \tag{3.369}$$

From equation (3.238)

$$w^1{}_2+(\gamma+r_1+d_1+\mu)w_1-((1-\rho)\sigma+(1-\theta)\lambda_2)v_1= \tag{3.370}$$

$$0\; w^1{}_2=((1-\rho)\sigma+(1-\theta)\lambda_2)v_1-(\gamma+r_1+d_1+\mu)w_1 \tag{3.371}$$

Substitute equation (3.305) and (3.312) into (3.371)

$$w_2 = \left(\left((1-\rho)\sigma+(1-\theta)\right)\left(\lambda_2 T_0+\lambda_1 S_0-(\sigma+\lambda_2+\mu)E_0\right)t-(\gamma+r_1+d_1+\mu)\right. \left.\left(\left((1-\rho)\sigma+(1-\phi)\lambda_2\right)E_0-(\gamma+\mu+r_1+d_1)I_{m0}\right)t\right) \tag{3.372}$$

$$w_2 = \begin{pmatrix} \left((1-\rho)\sigma+(1-\theta)\right)\left(\lambda_2 T_0+\lambda_1 S_0-(\sigma+\lambda_2+\mu)E_0\right)-(\gamma+r_1+d_1+\mu) \\ \left(\left((1-\rho)\sigma+(1-\phi)\lambda_2\right)E_0-(\gamma+\mu+r_1+d_1)I_{m0}\right) \end{pmatrix} t \tag{3.373}$$

Integrating both sides

$$\int dw_2 = \int \begin{pmatrix} \left((1-\rho)\sigma+(1-\theta)\right)\left(\lambda_2 T_0+\lambda_1 S_0-(\sigma+\lambda_2+\mu)E_0\right)-(\gamma+r_1+d_1+\mu) \\ \left(\left((1-\rho)\sigma+(1-\phi)\lambda_2\right)E_0-(\gamma+\mu+r_1+d_1)I_{m0}\right) \end{pmatrix} t\,dt \tag{3.374}$$

$$w_2(t) = \begin{pmatrix} \left((1-\rho)\sigma+(1-\theta)\right)\left(\lambda_2 T_0+\lambda_1 S_0-(\sigma+\lambda_2+\mu)E_0\right)-(\gamma+r_1+d_1+\mu) \\ \left(\left((1-\rho)\sigma+(1-\phi)\lambda_2\right)E_0-(\gamma+\mu+r_1+d_1)I_{m0}\right) \end{pmatrix} \frac{t^2}{2} + D \tag{3.375}$$

Applying the initial condition

$$D_{18} = 0 \tag{3.376}$$

$$w_2(t) = \begin{pmatrix} \left((1-\rho)\sigma+(1-\theta)\right)\left(\lambda_2 T_0+\lambda_1 S_0-(\sigma+\lambda_2+\mu)E_0\right)-(\gamma+r_1+d_1+\mu) \\ \left(\left((1-\rho)\sigma+(1-\phi)\lambda_2\right)E_0-(\gamma+\mu+r_1+d_1)I_{m0}\right) \end{pmatrix} \frac{t^2}{2} \tag{3.377}$$

Substitute equation (3.273), (3.312) and (3.377) into (3.215)

$$I_m(t) = w_0 + hw_1 + h^2 w_2 + \dots \tag{3.378}$$

$$I_m(t) = \lim_{h\to 1}\left(w_0 + hw_1 + h^2 w_2 + \dots\right) \tag{3.379}$$

$$I_m(t) = w_0 + w_1 + w_2 + \dots \tag{3.380}$$

Hence

$$I_m(t) = I_{m0} + \Big((1-\rho)\sigma E_0 + (1-\phi)\lambda_2 E_0 - (\gamma+\mu+r_1+d_1)I_{m0}\Big)t + \left(\begin{array}{l} ((1-\rho)\sigma + (1-\theta))(\lambda_2 T_0 + \lambda_1 S_0 - (\sigma+\lambda_2+\mu)E_0) - (\gamma+r_1+d_1+\mu) \\ ((1-\rho)\sigma + (1-\phi)\lambda_2 E_0 - (\gamma+\mu+r_1+d_1)I_{m0}) \end{array}\right)\frac{t^2}{2} \quad (3.381)$$

From equation (3.243)

$$x_2' + (\mu + d_2 + r_2 + r_3)\,\mathrm{x}_1 - \rho\sigma v_1 - \gamma w_1 - \phi\lambda_2 v_1 = 0 \quad (3.382)$$

$$x_2' = (\rho\sigma + \phi\lambda_2)v_1 + \gamma w_1 - (\mu + d_2 + r_2 + r_3)\,\mathrm{x}_1 \quad (3.383)$$

Substitute equation (3.306), (3.312) and (3.319) into (3.386)

$$\begin{aligned} x_2' &= (\rho\sigma+\phi\lambda_2)\big(\lambda_2 T_0 + \lambda_1 S_0 - (\sigma+\lambda_2+\mu)E_0\big)t + \\ &\gamma\big((1-\rho)\sigma E_0 + (1-\phi)\lambda_2 E_0 - (\gamma+\mu+r_1+d_1)I_{m0}\big)t - \\ &(\mu+d_2+r_2+r_3)\big(\phi\lambda_2 E_0 + \rho\sigma E_0 + \gamma I_{m0} - (\mu+d_2+r_2+r_3)\,\mathrm{xI}_{c0}\big)t \end{aligned} \quad (3.384)$$

$$x_2' = \left(\begin{array}{l} (\rho\sigma+\phi\lambda_2)\big(\lambda_2 T_0 + \lambda_1 S_0 - (\sigma+\lambda_2+\mu)E_0\big) + \\ \gamma\big((1-\rho)\sigma E_0 + (1-\phi)\lambda_2 E_0 - (\gamma+\mu+r_1+d_1)I_{m0}\big) - \\ (\mu+d_2+r_2+r_3)\big(\phi\lambda_2 E_0 + \rho\sigma E_0 + \gamma I_{m0} - (\mu+d_2+r_2+r_3)\,\mathrm{xI}_{c0}\big) \end{array}\right)t \quad (3.385)$$

Integrating both sides

$$\int dx_2' = \int \left(\begin{array}{l} (\rho\sigma+\phi\lambda_2)\big(\lambda_2 T_0 + \lambda_1 S_0 - (\sigma+\lambda_2+\mu)E_0\big) + \\ \gamma\big((1-\rho)\sigma E_0 + (1-\phi)\lambda_2 E_0 - (\gamma+\mu+r_1+d_1)I_{m0}\big) - \\ (\mu+d_2+r_2+r_3)\big(\phi\lambda_2 E_0 + \rho\sigma E_0 + \gamma I_{m0} - (\mu+d_2+r_2+r_3)\,\mathrm{xI}_{c0}\big) \end{array}\right)t\,dt \quad (3.386)$$

$$x_2(t) = \left(\begin{array}{l} (\rho\sigma+\phi\lambda_2)\big(\lambda_2 T_0 + \lambda_1 S_0 - (\sigma+\lambda_2+\mu)E_0\big) + \\ \gamma\big((1-\rho)\sigma E_0 + (1-\phi)\lambda_2 E_0 - (\gamma+\mu+r_1+d_1)I_{m0}\big) - \\ (\mu+d_2+r_2+r_3)\big(\phi\lambda_2 E_0 + \rho\sigma E_0 + \gamma I_{m0} - (\mu+d_2+r_2+r_3)\,\mathrm{xI}_{c0}\big) \end{array}\right)\frac{t^2}{2} + D_{19} \quad (3.387)$$

Applying the initial condition

$$D_{19} = 0 \tag{3.388}$$

$$x_2(t) = \begin{pmatrix} (\rho\sigma+\phi\lambda_2)(\lambda T_{20}+\lambda S_{10}-(\sigma+\lambda+\mu)E_{20})+ \\ \gamma((1-\rho)\sigma E_0+(1-\phi)\lambda E_{20}-(\gamma+\mu+r_1+d_1)I_{m0})- \\ (\mu+d_2+r_2+r_3)(\phi\lambda E_{20}+\rho\sigma E_0+\gamma I_{m0}-(\mu+d_2+r_2+r_3)\mathrm{xI}_{c0}) \end{pmatrix}\frac{t^2}{2} \tag{3.389}$$

Substitute equation (3.278), (3.319) and (3.388) into (3.216)

$$I_c(t) = x_0 + hx_1 + h^2x_2 + \ldots \tag{3.390}$$

$$I_c(t) = \lim_{h\to 1}(x_0 + hx_1 + h^2x_2 + \ldots) \tag{3.391}$$

$$I_c(t) = x_0 + x_1 + x_2 + \ldots \tag{3.392}$$

Hence

$$I_c(t) = I_{c0} + (\phi\lambda_2 E_0+\rho\sigma E_0+\gamma I_{m0}-(\mu+d_2+r_2+r_3)\mathrm{xI}_{c0})t + \begin{pmatrix} (\rho\sigma+\phi\lambda_2)(\lambda T_{20}+\lambda S_{10}-(\sigma+\lambda+\mu)E_{20})+ \\ \gamma((1-\rho)\sigma E_0+(1-\phi)\lambda E_{20}-(\gamma+\mu+r_1+d_1)I_{m0})- \\ (\mu+d_2+r_2+r_3)(\phi\lambda E_{20}+\rho\sigma E_0+\gamma I_{m0}-(\mu+d_2+r_2+r_3)\mathrm{xI}_{c0}) \end{pmatrix}\frac{t^2}{2} \tag{3.393}$$

From equation (3.248)

$$y_2^1 + (\mu+d_3+r_4)y_1 - r_3x_1 = 0 \tag{3.394}$$

$$y^1{}_2 = r_3 x_1 - (\mu + d_3 + r_4) y_1 \text{ b} \tag{3.395}$$

Substitute equation (3.321) and (3.326) into (3.395)

$$y^1{}_2 = r_3(\phi\lambda_2 E_0 + \rho\sigma E_0 + \gamma I_{m0} - (\mu + d_2 + r_2 + r_3)\mathrm{xI}_{c0})t - (\mu + d_3 + r_4)(r_3 I_{c0} - (\mu + d_3 + r_4) J_0)t \tag{3.396}$$

$$\frac{dy_2}{dt} = \begin{pmatrix} r_3\left(\phi\lambda_2 E_0 + \rho\sigma E_0 + \gamma I_{m0} - (\mu + d_2 + r_2 + r_3)\,\mathrm{x}I_{c0}\right) - (\mu + d_3 + r_4) \\ \left(r_3 I_{c0} - (\mu + d_3 + r_4) J_0\right) \end{pmatrix} t \tag{3.397}$$

Integrating both sides

$$\int dy_2 = \int \begin{pmatrix} r_3\left(\phi\lambda_2 E_0 + \rho\sigma E_0 + \gamma I_{m0} - (\mu + d_2 + r_2 + r_3)\,\mathrm{x}I_{c0}\right) - (\mu + d_3 + r_4) \\ \left(r_3 I_{c0} - (\mu + d_3 + r_4) J_0\right) \end{pmatrix} t\,dt \tag{3.398}$$

$$y_2(t) = \begin{pmatrix} r_3\left(\phi\lambda_2 E_0 + \rho\sigma E_0 + \gamma I_{m0} - (\mu + d_2 + r_2 + r_3)\,\mathrm{x}I_{c0}\right) - (\mu + d_3 + r_4) \\ \left(r_3 I_{c0} - (\mu + d_3 + r_4) J_0\right) \end{pmatrix} \frac{t^2}{2} + D_{20} \tag{3.399}$$

Applying the initial condition

$$D_{20} = 0 \tag{3.400}$$

$$y_2(t) = \begin{pmatrix} r_3\left(\phi\lambda_2 E_0 + \rho\sigma E_0 + \gamma I_{m0} - (\mu + d_2 + r_2 + r_3)\,\mathrm{x}I_{c0}\right) - (\mu + d_3 + r_4) \\ \left(r_3 I_{c0} - (\mu + d_3 + r_4) J_0\right) \end{pmatrix} \frac{t^2}{2} \tag{3.401}$$

Substitute equation (3.284), (3.326) and (3.401) into (3.197)

$$J(t) = y_0 + hy_1 + h^2 y_2 + \ldots \tag{3.402}$$

$$J(t) = \lim_{h \to 1}\left(y_0 + hy_1 + h^2 y_2 + \ldots\right) \tag{3.403}$$

$$J(t) = \left(y_0 + y_1 + y_2 + \ldots\right) \tag{3.404}$$

Hence

$$J(t) = J_0 + \begin{pmatrix} r_3 I_{c0} - (\mu + d_3 + r_4) \\ J_0 \end{pmatrix} t + \begin{pmatrix} r_3\left(\phi\lambda_2 E_0 + \rho\sigma E_0 + \gamma I_{m0} - (\mu + d_2 + r_2 + r_3)\,\mathrm{x}I_{c0}\right) - \\ (\mu + d_3 + r_4)\left(r_3 I_{c0} - (\mu + d_3 + r_4) J_0\right) \end{pmatrix} \frac{t^2}{2} \tag{3.405}$$

From equation (3.253)

$$z_2^1 + (\mu+\lambda_3)z_1 - r_4 y_1 - r_2 x_1 - r_1 w_1 = 0 \tag{3.406}$$

$$z_2^1 = r_4 y_1 + r_2 x_1 + r_1 w_1 - (\mu+\lambda_3) z_1 \text{b} \tag{3.407}$$

Substitute equation (3.326), (3.319), (3.312) and (3.332) into (3.407)

$$z_2^1 = r_4\left(r_3 I_{c0} - (\mu+d_3+r_4)J_0\right)t + r_2\left(\phi\lambda_2 E_0 + \rho\sigma E_0 + \gamma I_{m0} - (\mu+d_2+r_2+r_3)\text{xI}_{c0}\right)t + r_1\left(\left((1-\rho)\sigma E_0 + (1-\phi)\lambda_2 E_0\right) - (\gamma+\mu+r_1+d_1) I_{m0}\right)t - (\mu+\lambda_3)\left(\begin{matrix} r_4 J_0 + r_2 I_{c0} + r_1 I_{m0} \\ -(\mu+\lambda_3)T_0 \end{matrix}\right)t \tag{3.408}$$

$$z_2^1 = \left(\begin{matrix} r_4\left(r_3 I_{c0} - (\mu+d_3+r_4)J_0\right) + r_2\left(\phi\lambda_2 E_0 + \rho\sigma E_0 + \gamma I_{m0} - (\mu+d_2+r_2+r_3)\text{xI}_{c0}\right) \\ + r_1\left(\left((1-\rho)\sigma E_0 + (1-\phi)\lambda_2 E_0\right) - (\gamma+\mu+r_1+d_1) I_{m0}\right) - (\mu+\lambda_3)\left(\begin{matrix} r_4 J_0 + r_2 I_{c0} + r_1 I_{m0} \\ -(\mu+\lambda_3)T_0 \end{matrix}\right)\end{matrix}\right)t \tag{3.409}$$

Integrating both sides

$$\int dz_2^1 = \int\left(\begin{matrix} r_4\left(r_3 I_{c0} - (\mu+d_3+r_4)J_0\right) + r_2\left(\phi\lambda_2 E_0 + \rho\sigma E_0 + \gamma I_{m0} - (\mu+d_2+r_2+r_3)\text{xI}_{c0}\right) \\ + r_1\left(\left((1-\rho)\sigma E + (1-\phi)\lambda_2 E_0\right) - (\gamma+\mu+r_1+d_1) I_{m0}\right) - (\mu+\lambda_3)\left(\begin{matrix} r_4 J_0 + r_2 I_{c0} + r_1 I_{m0} \\ -(\mu+\lambda_3)T_0 \end{matrix}\right)\end{matrix}\right)tdt \tag{3.410}$$

$$z_2(t) = \left(\begin{matrix} r_4\left(r_3 I_{c0} - (\mu+d_3+r_4)J_0\right) + r_2\left(\phi\lambda_2 E_0 + \rho\sigma E_0 + \gamma I_{m0} - (\mu+d_2+r_2+r_3)\text{xI}_{c0}\right) \\ + r_1\left(\left((1-\rho)\sigma E + (1-\phi)\lambda_2 E_0\right) - (\gamma+\mu+r_1+d_1) I_{m0}\right) - (\mu+\lambda_3)\left(\begin{matrix} r_4 J_0 + r_2 I_{c0} + r_1 I_{m0} \\ -(\mu+\lambda_3)T_0 \end{matrix}\right)\end{matrix}\right)\frac{t^2}{2} + D_{22} \tag{3.411}$$

Applying the initial condition

$$D_{22} = 0 \tag{3.412}$$

$$z_2(t) = \left(\begin{matrix} r_4\left(r_3 I_{c0} - (\mu+d_3+r_4)J_0\right) + r_2\left(\phi\lambda_2 E_0 + \rho\sigma E_0 + \gamma I_{m0} - (\mu+d_2+r_2+r_3)\text{xI}_{c0}\right) \\ + r_1\left(\left((1-\rho)\sigma E + (1-\phi)\lambda_2 E_0\right) - (\gamma+\mu+r_1+d_1) I_{m0}\right) - (\mu+\lambda_3)\left(\begin{matrix} r_4 J_0 + r_2 I_{c0} + r_1 I_{m0} \\ -(\mu+\lambda_3)T_0 \end{matrix}\right)\end{matrix}\right)\frac{t^2}{2} \tag{3.413}$$

Substitute equation (3.287), (3.335) and (3.417) into (3.218)

$$T(t) = z_0 + hz_1 + h^2 z_2 + \ldots \tag{3.414}$$

$$T(t) = \lim_{h \to 1} \left(z_0 + hz_1 + h^2 z_2 + \ldots \right) \tag{3.415}$$

$$T(t) = z_0 + z_1 + z_2 + \ldots v \tag{3.416}$$

Hence

$$T(t) = T_0 + \left(r_4 J_0 + r_2 I_{c0} + r_1 I_{m0} - (\mu + \lambda_3) T_0 \right) t + \left(\begin{array}{l} r_4 \left(r_3 I_{c0} - (\mu + d_3 + r_4) J_0 \right) + \\ r_2 \left(\begin{array}{l} \phi\lambda_2 E_0 + \rho\sigma E_0 + \gamma I_{m0} - \\ (\mu + d_2 + r_2 + r_3)\, \mathrm{x} I_{c0} \end{array} \right) + \\ r_1 \left(\left((1-\rho)\sigma E_0 + (1-\phi)\lambda_2 E_0 - \right) I_{m0} \right) \\ - (\mu + \lambda_3) \left(\begin{array}{l} r_4 J_0 + r_2 I_{c0} + r_1 I_{m0} \\ - (\mu + \lambda_3) T_0 \end{array} \right) \end{array} \right) \frac{t^2}{2} \tag{3.417}$$

CHAPTER FOUR

4.0 RESULTS AND DISCUSSION

4. 1 Numerical Simulations

The graphical representations are the analytical solution of the model equations. They are plotted using Maple Software.

Table 4.1 shows the initial conditions for each parameter and variable's values.

Parameters and State Variables	Value	Source
$S(t)$	160,840,589	Assumed
$E(t)$	1,700,000	Assumed
$I_m(t)$	90,000	Assumed
$I_c(t)$	10,400,000	WHO (2020)
$J(t)$	1,000,000	Assumed
$T(t)$	1,109,000	NMOHR (2019)
	8,000,000	Assumed
$V(t)$	23,000,000	WHO (2020)
π	2,895,131	Calculated
μ	0.018	UNICEF (2020)
d_1	0.0365	Assumed
d_2	0.68	WHO (2020)
d_3	0.02	Assumed
r_1	0.02	Assumed

r_2	0.02	Assumed
r_3	0.02	Assumed
	(0-1)	Varies
r_4	(0-1)	Varies
θ	0.020	Assumed
ω	(0-1)	Varies
ρ	0.075	Assumed
ϕ	0.3	Assumed
λ_1	(0-1)	Varies
λ_2	0.2	Assumed
λ_3	0.2	Assumed
γ	(0-1)	Varies
σ	0.01	Assumed

$N = S(t) + E(t) + I_m(t) + I_c(t) + J(t) + T(t) + V(t) =$ 206,139, 589 (NBS 2020).

4.2 Graphical Representation of Solutions of the Model Equation

The graphical representations are from the analytical solutions of the model equations. They are plotted using MAPLE software.

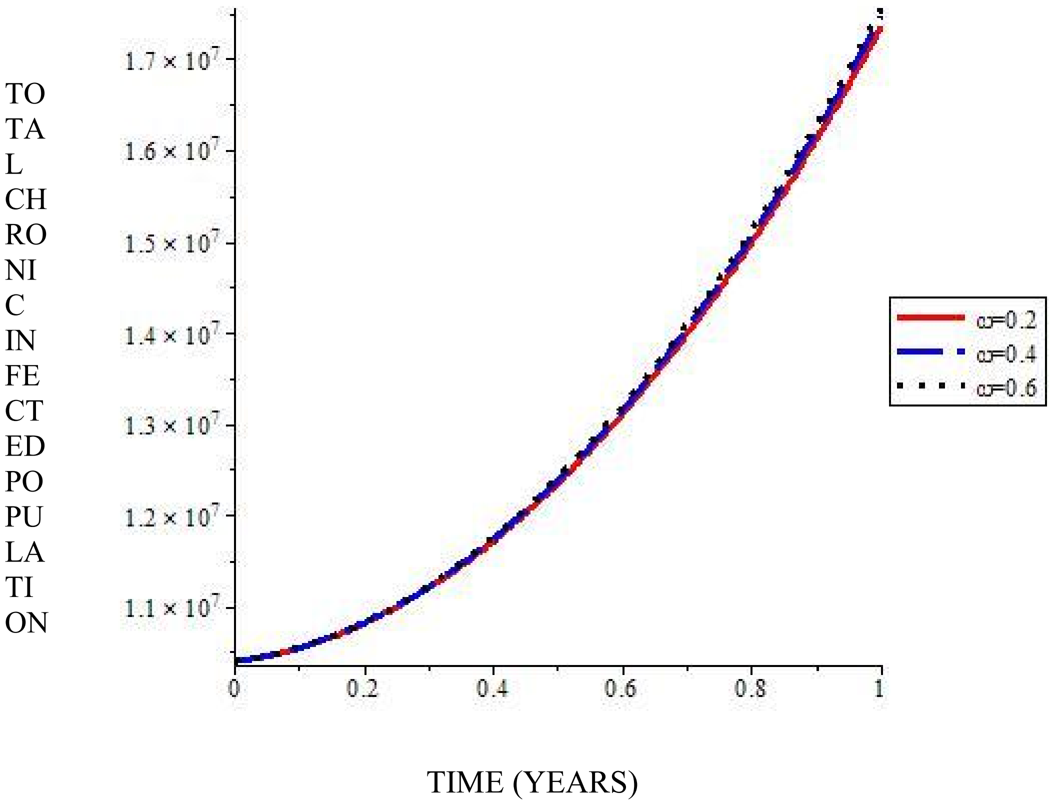

Figure 4.1 Effect of waning rate of vaccine on the Chronic class

Figure 4.1 is the graph of Chronic Infected Individuals against time for different values of waning rate of vaccine. We carried out simulations by varying waning rate of vaccine as 0.2, 0.4 and 0.6. It could be observed that different level of waning rate does not have effect on the infected population. For different level of waning rate, the TB infection continues to persist in the given population.

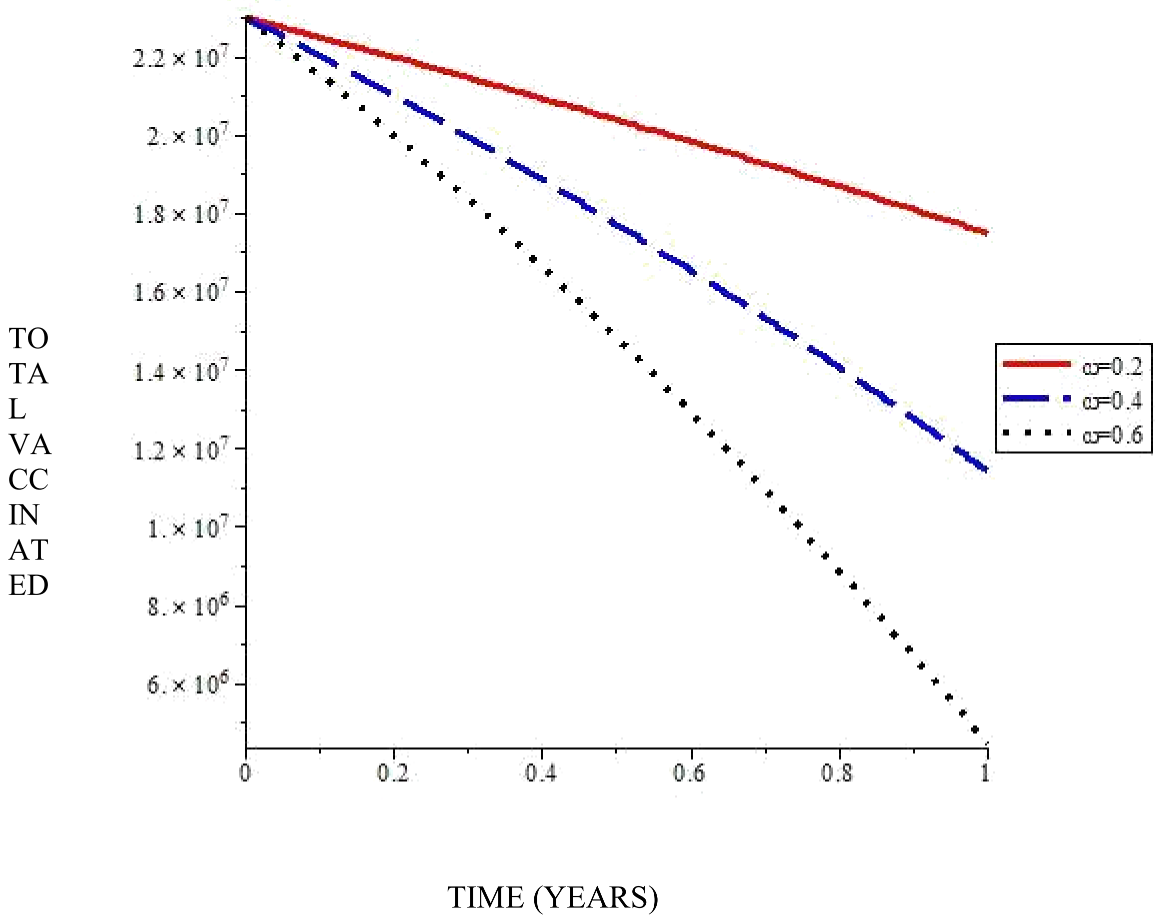

Figure 4.2 Effect of waning rate of vaccine on Vaccinated Class

Figure 4.2 is the graph of Vaccinated Individuals against time for different values of waning] rate of vaccine. It was observed that the vaccinated population decreases with increase in the vaccination rate. Therefore, high waning rate of vaccine reduces the vaccinated population and thus puts them at the risk of contracting the disease.

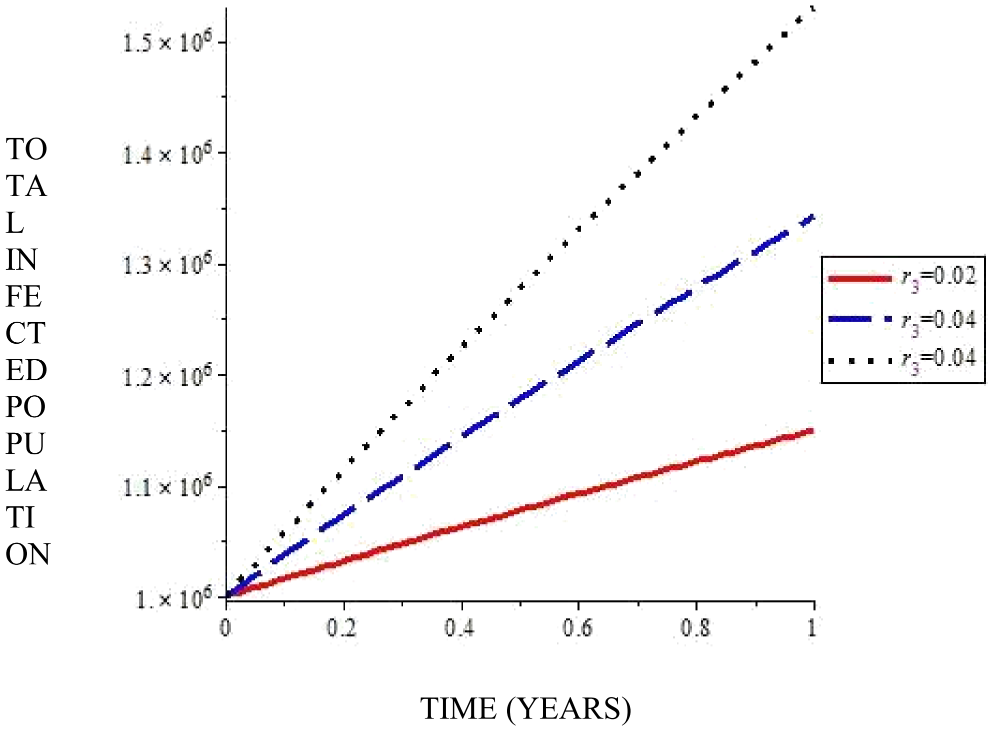

Figure 4.3 Effect of isolation rate on the Isolated Compartment

Figure 4.3 is the graph of isolated infectious individuals against time at different values of Progression rate from chronic TB class to isolated infected class. It was observed that the number of isolated Individuals increases as Progression rate from chronic TB class to isolated infected class Increases.

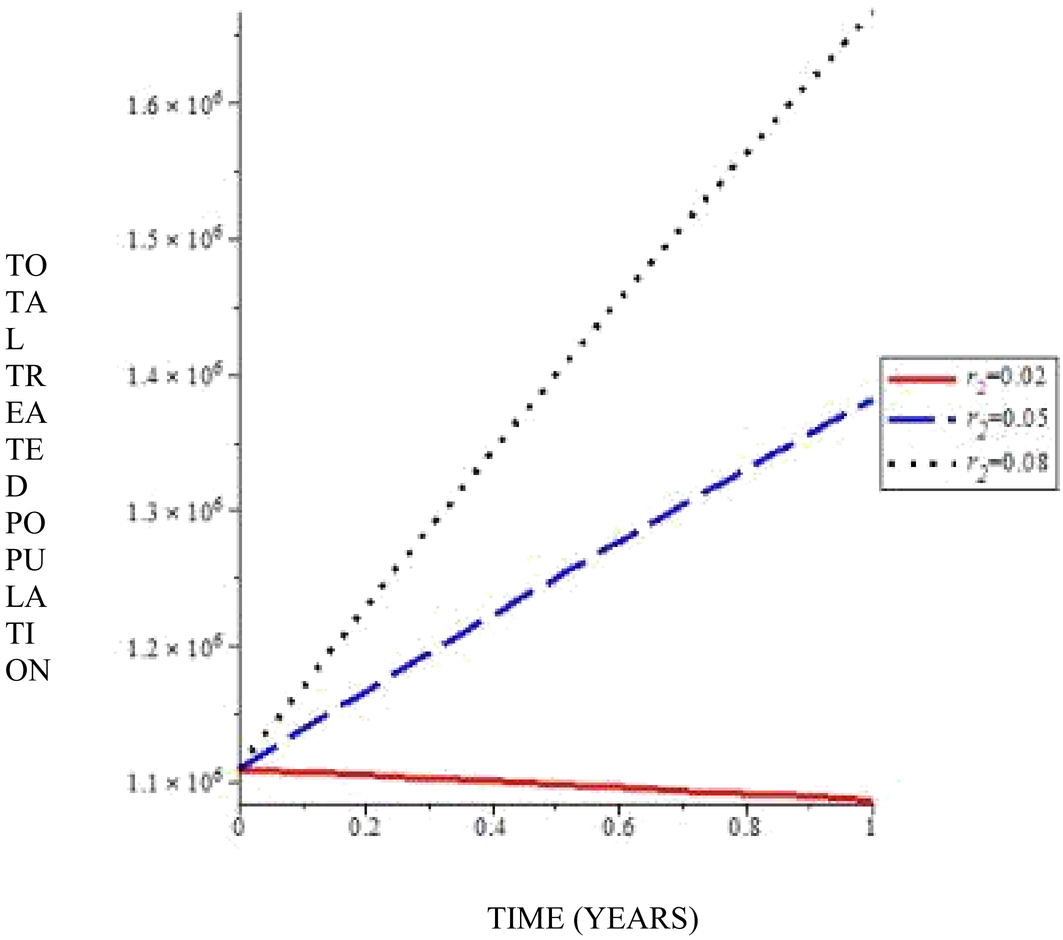

Figure 4.4 Graph of Treated individual against time for different values of recovery rate for Chronic Class.

Figure 4.4 is the graph of treated TB individuals against time. It was observed that the number of treated TB individual increases as the recovery rate among the chronic TB individual increases. This implies that increase in the progression rate will lead to increase in number of individuals with chronic TB disease.

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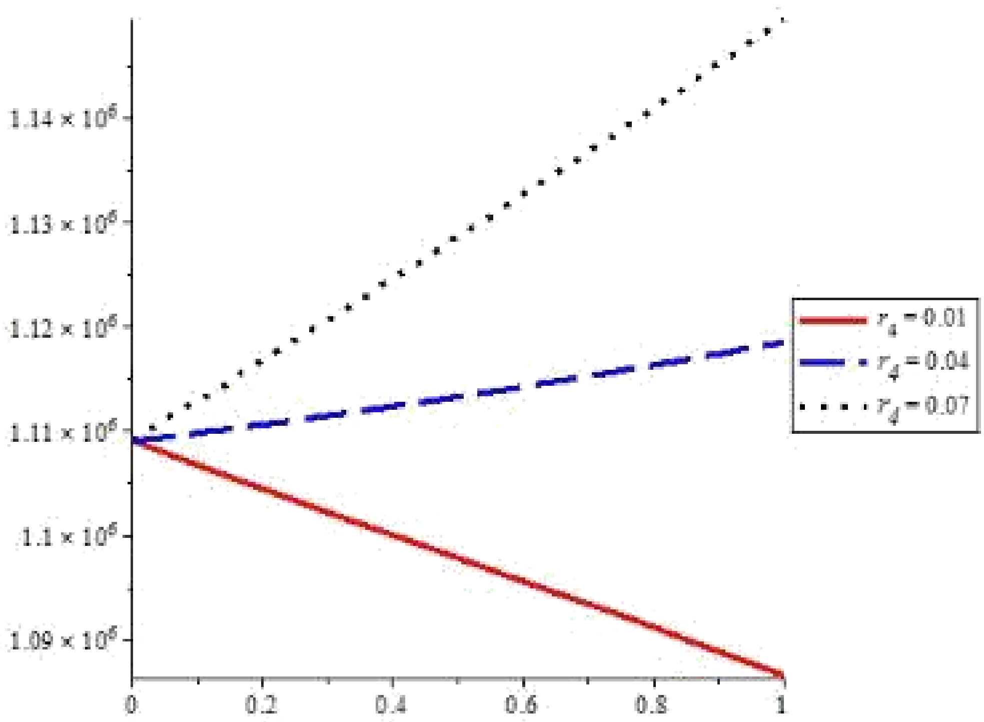

TIME (YEARS)

Figure 4.5 Effect of recovery rate for those in isolated class

Figure 4.5 is the graph of recovered individual against time. The lower the treated rate the lower the number of recovered individuals. The lowest percentage almost decrease to zero.

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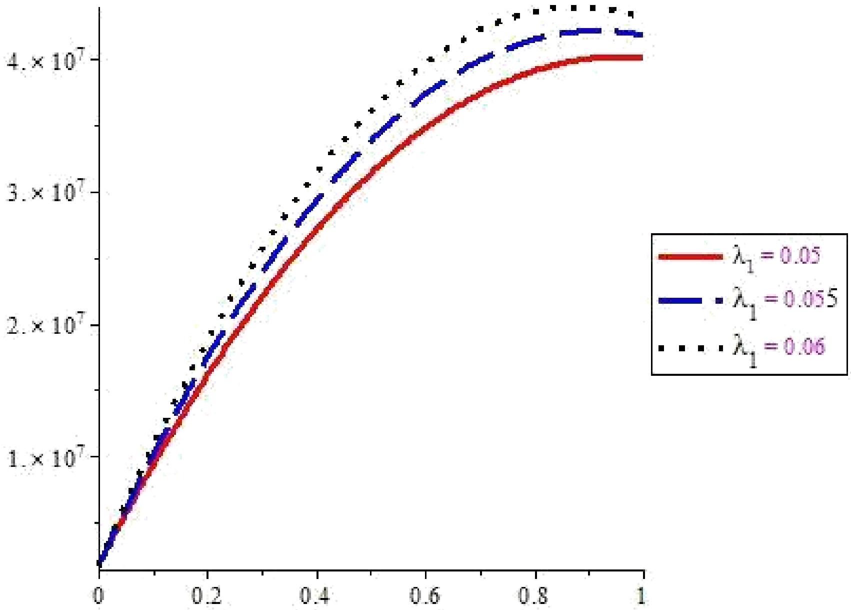

TIME (YEARS)

Figure 4.6 Impact of effective interaction between susceptible and Infected classes.

Figure 4.6 is the graph of exposed individual against time for different values of contact rate 1. We can observe that infected individuals increase as contact rate increases. The figure illustrates the great influence of effective contact rate on the exposed population.

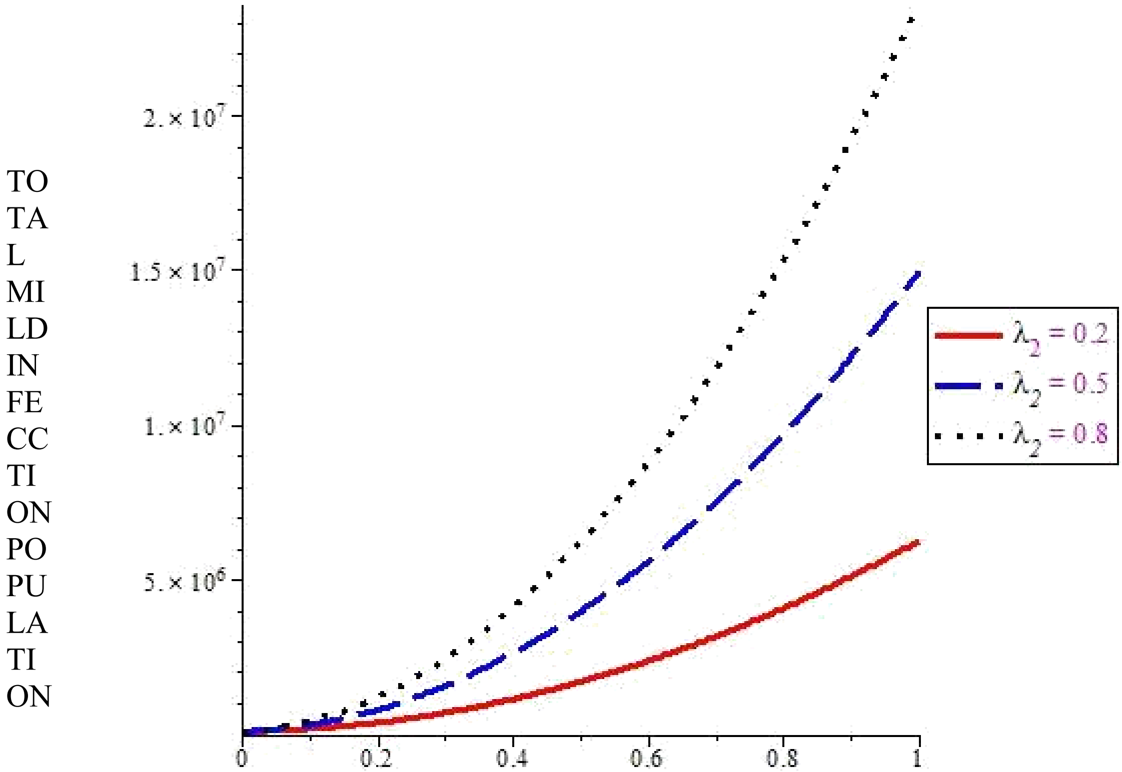

Figure 4.7: Graph of mild TB individual against time for different values of Transmission rate.

Figure 4.7 is the graph of mild TB individual against time. It was observed that the number of mild TB individual increases as the transmission rate from the exposed to the chronic individuals increases.

CHAPTER FIVE

5.0 CONCLUSION AND RECOMMENDATIONS

5.1 Conclusion

In this study, a mathematical model of Tuberculosis (TB) transmission dynamics incorporating treatment, isolation and vaccination using the system of first order ordinary differential equations was developed and analyzed. It was discovered that the model has two equilibria. The equilibrium states were obtained and analyzed for their stability relatively to the effective reproduction number. The result shows that, the disease-free equilibrium was stable. We are able to show that the Tuberculosis (TB) infectious free equilibrium is locally and globally asymptotically stable if $R_0 < 1$. The analytical solution was obtained using Homotopy Perturbation Method (HPM) and effective reproduction number was computed in order to measure the relative impact for individual or combined intervention for effective disease control.

The graphs illustrate the impact of a combined effect of contact rate, waning rate of vaccine and rate of isolation. One can observe that this combine effects reduce the size of infected compartments. Thus, the simultaneous increase of effectiveness of vaccination rate, isolation rate and treatment rate are effective control measures against TB infection.

5.2 Contribution to Knowledge

i. Developed and validated a mathematical model of Tuberculosis (TB) transmission dynamics incorporating treatment, isolation and vaccination.
ii. The system of seven ordinary differential equation was solved using Homotopy Perturbation Method (HPM)

iii. The model incorporates the mathematical model for transmission dynamics treatments and vaccination.

iv. The work has also shown that infected populations will be reduced when the isolation and treatment rates and their effectiveness are more than 60%.

5.3 Recommendations

i. The model shows that the spread of tuberculosis (TB) infection depends largely on the contact rate, hence the ministry of health and other health workers should emphasize on the improvement in early detection of tuberculosis (TB) infection cases, so that transmission can be minimized.

ii. Infected individuals should be isolated and treated immediately.

iii. Individuals infected with tuberculosis (TB) should be given antiretroviral drugs immediately.

iv. Optimal control strategy can be incorporated into the model for greater insight into the dynamics.

REFERENCE

Abubakar, S., Akinwande, N. I., Jimoh, O. R., Oguntolu, F. A. & Ogwumu, O. D. (2013). Approximate solution of sir infectious disease model using homotopy perturbation method (HPM). *Pacific Journal of Science and Technology,* 14(2), 163-169

Al-Darraji, H. A. A., Altice, F. L. & Kamarulzaman, A. (2016). Undiagnosed pulmonary tuberculosis among prisoners in Malaysia: an overlooked risk for tuberculosis in the community. *Tropical Medicine and International Health,* 4(4), 401 -871.

Andrawus, J., Eguda, F., Usman, I., Maiwa, S., Dibal, I., Urum, T. & Anka, G. (2020). A mathematical model of a tuberculosis transmission dynamics incorporating first and second line treatment. *Journal Applied Science Environment Management*, 24 (5), 917-922.

Asefa, A. & Teshome, W. (2014). Total delay in treatment among smear positive pulmonary tuberculosis patients in five primary health centers, southern Ethiopia: a cross sectional study. *PLoS One*, 9(7), 102- 117.

Ayoade, A. A., Ibrahim, M. O., Peter, O. J. & Amadiegwu, S. (2019). On validation of an epidemiological model. *Journal of Fundamental and Applied Sciences,* 11(2), 578- 586.

Bam, T. S., Enarson, D. A. & Hinderaker, S. G. (2012) Longer delay in accessing treatment among current smokers with new sputum smear-positive tuberculosis in Nepal. Union. *Journal of Tuberculosis Lung Dis*eases, 16(6), 822–827.

Bhunu,C. P., Garira, W., Mukandavire, Z. & Zimba, M. (2008). Tuberculosis transmission model with chemoprophylaxis and treatment. *Bulletin of Mathematical Biology,* 7(2), 1163-1191.

Birkhoff, G. & Rota, G. C. (1982). Ordinary Differential Equations, Ginn, Boston.

Cain, K. P., Marano, N. & Kamene, M. (2015). The movement of multidrug-resistant tuberculosis across borders in East Africa needs a regional and global solution. *PLoS Med*, 2(3), 101- 791

Castillo-Chavez, C. & Feng, Z. (1997). To treat or not to treat: the case of tuberculosis. *Journal of Mathematical Biology*, 35 (7), 629–659.

Cattamanchi, A., Miller, C. R. & Tapley, A. (2015). Health worker perspectives on barriers to delivery of routine tuberculosis diagnostic evaluation services in Uganda: a qualitative study to guide clinic-based interventions. *BMC Health Serv. Res*., 1(5), 10 -91.

Centers for Disease Control and Prevention (CDC) (2016) Testing for TB infection. http://www.cdc. gov/tb/topic/testing/.

Delogu, G., Sali, M. & Fadda, G. (2013). The biology of mycobacterium tuberculosis infection. *Mediterrean Journal Hematology of Infectious Diseases*, 4(2), 45 - 98.

Herzog, B. (1998). History of tuberculosis. *Respiration*, 65 (1), 5-15

Issarowa, C. M., Muldera, N. & Wood, R. (2015). Modelling the risk of airborne infectious disease using exhaled air. *Journal Theoretical. Biology*, 37(2), 100–106.

He, J. H. (1999). Homotopy perturbation technique. *Computer Methods in Applied Mechanics and Engineering*. 1(7), 257-262

Jia, Z. W., Tang, G.Y., Zhen, J., Dye, C., Vlas, S. J. & Li, X. W. (2008). Modeling the impact of immigration on the epidemiology of tuberculosis. *Theoretical Population Biology*, 7(3), 437–448.

Jiya, M. (2010). Application of homotopy perturbation method (HPM) for the solution of some non-linear differential equations. *Pacific Journal of Science and Technology,* 11(2), 268-272.

Kamper-Jorgensen, Z., Andersen, A. B. & Kok-Jensen, A. (2012). Migrant tuberculosis: the extent of transmission in a low burden country. *BMC Infectious Disease*, 1(2), 60 - 87.

Lin, Y., Enarson, D. A. & Chiang, C. Y. (2015). Patient delay in the diagnosis and treatment of tuberculosis in China: findings of case detection projects. *Union Public Health Action*, 5(1), 65–69.

National Bureau of Statistics (NBS) (2020). Data on Spread of Tuberculosis Infections. National Bureau of Statistics Abuja.

National Ministry of Huanan Resources (NMOHR) (2019). Tuberculosis Transmission Rate. National Ministry of Huanan Resources Centre, Nigeria .

Okuonghae, D. & Aihie, V. (2010). Optimal control measures for tuberculosis mathematical models including immigration and isolation of infective. *Journal. Biology System,* 18(1), 17–54.

Somma, A., Akinwande, N. I. & Ashezua, T. T. (2017). Homotopy Perturbation Method (HPM) For Solving System of First Order Ordinary Differential Equations. Workshop On Mathematical Modelling, Department of Mathematics, University of Nigeria, Nsukka.

Song, B., Castillo-Chavez, C. & Aparicio, J. P. (2002). Tuberculosis models with fast and slow dynamics: the role of close and casual contacts. *Math. Biosciences*, 1(8), 29-48.

United Nations Children's Fund (UNICEF) (2020). Spread Rate of Tuberculosis. UNICEF, Nigeria.

Wang, M., FitzGerald, J. M. & Richardson, K. (2011). Is the delay in diagnosis of pulmonary tuberculosis related to exposure to fluoroquinolones or any antibiotic? *International Journal of Tuberculosis Lung Dis*eases, 15(8), 1062–1068.

World Health Organization (WHO) (2010). Tuberculosis Fact sheet N°104. Retrieved 25 August 2019 from http://www.who.int/ mediacentre/f actsheets/fs104/en/ index.html

World Health Organization (WHO) (2016). Global tuberculosis report. WHO report

World Health Organization (WHO) (2019). Tuberculosis (TB)Disease, WHO, Geneva, 2019.

World Health Organization (WHO) (2020). Concern on Tuberculosis (TB)Disease, WHO, Geneva, 2020.