

DEVELOPMENT OF DETERMINISTIC MODELS OF
TYPHOID FEVER WITH PREVENTION AND
CONTROL STRATEGIES

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CONTROL STRATEGIES

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(04/30 GD 117)

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A THESIS SUBMITTED TO THE
DEPARTMENT OF MATHEMATICS, FACULTY OF PHYSICAL SCIENCES,
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APRIL, 2021

CERTIFICATION

This is to certify that this thesis has been read and approved as meeting the requirements of the Department of Mathematics, University of Ilorin, Ilorin, Nigeria, for the Award of Doctor of Philosophy (Ph.D.) degree in Mathematics.

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DEDICATION

This research work is dedicated to God the Author and the Finisher of my faith.

DECLARATION

I, Olumuyiwa James PETER, a Ph.D. student in the Department of Mathematics, University of Ilorin, Ilorin, hereby declare that this thesis entitled "Development of Deterministic Models of Typhoid Fever with Prevention and Control Strategies", submitted by me is based on my actual and original work. Any materials obtained from other sources or work done by any other persons or institutions have been duly acknowledged. In addition, the research has been approved by the University of Ilorin Ethical Review Committee.

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(04/30 GD 117)

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ABSTRACT

Typhoid fever is a serious bacterial infection caused by *Salmonella typhi*. Typhoid fever is usually contracted by the ingestion of water or food contaminated with urine or faeces of infected carriers and is, therefore, common in areas with poor sanitation. In developing countries, refugee camps and crowded areas, typhoid fever outbreaks are frequent. In most existing literature on typhoid fever models, the effects of human to human and environment to human transmission of typhoid fever are not properly addressed, this study therefore aimed at extending the existing typhoid fever models to address the effects of some control strategies (educational campaign and vaccination) on human to human and environment to human transmission in typhoid fever prone communities. The objectives were to (i) obtain the existence, uniqueness and positivity solution of all the models; (ii) derive the disease free and endemic equilibria that govern the spread of typhoid fever; (iii) perform a sensitivity analysis of the models; (iv) determine the optimal strategy for implementing combine control strategies. The method employed included the application of Next Generational Matrix (NGM) technique to obtain the basic reproduction number, local and global stability analyses of the models using Lyapunov function and Lasalle's invariance principle, series solutions of the models by using Differential Transform Method (DTM) and

Variational Iteration Method (VIM), optimal control analysis to establish the conditions necessary for eradication of the disease. The findings of the study were that:

- (i) the existence, uniqueness and positivity solutions of all the models established that the models were well posed;
- (ii) the disease free and endemic equilibria that govern the spread of typhoid fever were found to be stable;
- (iii) the most sensitive parameter to typhoid fever management was education; and
- (iv) control strategies become more effective when vaccination and educational campaign program are combined, prevention methods become more effective in preventing the disease transmission.

The study concluded that possible optimal control strategies become more effective in the control and elimination of typhoid fever when vaccination and educational campaign are combined. Since educational campaign was the most sensitive to typhoid fever management, it is therefore recommended that any measure directed towards achieving typhoid fever-free society should include educational campaign.

Chapter 1

INTRODUCTION

1.1 Preamble

Mathematical modelling is a process that uses mathematical concept to represent, analyse, make predictions or otherwise provide insight into real-life phenomena for a better understanding of the problem. Infectious disease modelling is a technique used to predict the processes by which diseases spread, so as to forestall the future cause of an outbreak and to evaluate disease control strategies. (Akinwande, 2006), (Daley and Gani, 2005).

Mathematical models are mostly used in science and engineering disciplines such as physics, biological sciences and electrical engineering. It is also applicable in social sciences such as economics, sociology and political sciences. Physicists, engineers, computer scientists and economists use mathematical models extensively and it has become an important scientific approach over the last two decades and a useful tool for solving problems emerging from technology, engineering, social science, industries and society at large. (Benyah, 2005).

Infectious disease models can predict the diseases progression, to show the possible outcome of an outbreak and help guide initiatives in public health. Mathematical models use some basic assumptions to determine the parameters for different infectious diseases and use these parameters to measure the effects of various intervention strategies such as programs for mass vaccination and educational campaign.

There are two types of epidemic models defined in science and engineering literature these are; stochastic model and deterministic or compartmental model. Stochastic model allows random variance in one or more inputs over time in determining probability distribution of potential outcome. We use deterministic model when dealing with large population by assigning individual in the population to different subgroup or compartment. Each compartment represent different stages of the epidemic. For example, susceptible class, career infected class, infected class, vaccinated class e.t.c. are used to represent different stages of disease epidemic.

Mathematical modelling has become a valuable method in recent years for evaluating infectious disease dynamics and for promoting the production of control strategies. Mathematical models can be used to predict how future outbreak of infectious disease, and help guide strategies in public health.

Mathematical models on infectious disease can be used to produce new hypothesis, including cross-sectional studies, clinical trials or surveillance systems, and have been advocated for use in the planning control policies on infectious diseases.

Deterministic mathematical models use simple assumptions or collected statistical data to determine the parameters for various infectious diseases and use those parameters to quantify the effects of different intervention strategies such as, mass vaccination and educational campaigns.

Typhoid fever is attributed to *Salmonella Typhi*. At the start of the 20th century, typhoid fever gained national attention with the cases of Mr. N. Milner in England and Typhoid Mary in the United States. Throughout the decades, these people have infected hundreds of people while working in the food industry and private homes. Typhoid Mary was the first individual in the United States to be confirmed as a carrier of the infection without experiencing the symptom of the disease. She worked as a cook and has infected fifty-one people throughout her career of which three cases were fatal. She was isolated twice in her career, once in 1907 and again in 1915 for quarantine purposes. She was not released for the second time and she died in solitary confinement at age sixty-nine. Typhoid fever infects twenty-one million people annually and kills two hundred thousand people around the world. Asymptomatic carriers of typhoid fever with no clinical symptoms create a considerable difficulty when planning health initiatives, this can hinder the control and eradication of typhoid fever by diagnosis and vaccination. (May and Anderson, 2006). Compartmental mathematical models are used to simulate disease transmission dynamics. Individuals in the population are allocated to different groups in the deterministic model, each compartment represents a different stage of the disease epidemic. Typhoid fever which is caused by *Salmonella Typhi* has remained a public health concern in least developed countries due to inadequate sanitation, personal hygiene standards, and the prevalence of contaminated food. For several parts of the developing world, it is endemic, the disease occurs for the duration of days around the world. (Lifshitz, 1996).

In rural communities where waste treatment is insufficient or inadequate, this triggers typhoid fever outbreaks. It is mostly common in Africa. The current estimate of global incidence of typhoid fever is 16 million cases and 600,000 annual deaths. (The 2008 World Health Report).

There are various ways to diagnose typhoid fever, the popular method is by taking the blood sample to check for the presence of *Salmonella Typhi*. This method is known as Widal test. (Wain *et al.*, 1998), (Gasem *et al.*, 1995).

The widal test method has been the hallmark of the diagnosis of typhoid fever for many years. The main disadvantage of the Widal test, is its cross-reactivity with another microorganism of the same species and its imitation of the protozoal infection that often produces false-positive results. (Aziz and Haque, 2012). The widespread identification of high protein concentrations of these enteric bacteria serotype in patients with protozoal infection has led some people to conclude that protozoal infection co-infects with enteric fever. (Alhassan, *et al* , 2012, Mushayabasa, *et al*, 2014).

The most sensitive test for *Salmonella typhi* is a bone marrow culture, which involves isolating *Salmonella typhi* from bone marrow. This procedure, however, is extremely painful and necessitates modern equipment and trained laboratory staff, both of which are unavailable in primary support facilities in developing countries. (Wain and Hosoglu 2018), (Keddy *et al.*, 2011).

Typhoid fever diagnosis is based on the antibiotic resistance of the blood culture of the patient. If the strain is sensitive, oral chloramphenicol, amoxicillin may be used. Worldwide, multi-drug resistant strains of *Salmonella Typhi* makes the disease more difficult to treat. (Kariuki, 2004). The following are some of the most common symptoms of typhoid fever, in about 75% of cases, variable degrees of high-grade fever, muscle soreness and body pain, shivers, loss of appetite, nausea, bleeds of the nose, tiredness, diarrhoea, sore throat and cough.

There are two forms of typhoid fever vaccine namely, oral vaccine and an injectable typhoid vaccine people who are at least 6 years old should be administered an oral vaccine. It is made up of four tablets that should be taken within seven days. People over the age of two should receive the injectable vaccine. Over time, typhoid vaccinations lose their efficacy. A booster shot is required every two years for injectable vaccines and every five years for oral vaccines. (WHO, 2019).

The pictures below shows typhoid infected individuals



Figure 1.1: Image of typhoid chronic symptom



Figure 1.2: Image of typhoid fever patient receiving treatment



Figure 1.3: Image of a typhoid fever patient undergoing typhoid fever diagnosis

1.2 Background to the Study

The incidence and spread of diseases have been addressed and researched for many years. Researchers may predict outbreaks, assess preventive measures and have a significant impact on the death rate of a particular outbreak. Recurrent outbreaks of typhoid fever have occurred in Nigeria, mostly in densely populated refugee camps and urban areas. Typhoid fever causes extreme mortality rates in children around the world, with at least 18 million new cases reported each year and up to 600,000 death. (Anderson and May, 1991). The incidence of typhoid fever outbreaks is growing with its accompanied magnitude suggests that there is insufficient existing knowledge of typhoid fever dynamics and recommendations for public health to control the disease. Therefore, studies must continue until the disease is eradicated for this particular cause.

1.3 Statement of the Problem

Infectious diseases such as tuberculosis, typhoid fever, COVID-19 etc. are diseases that can easily spread to human due to pathogenic microorganisms such as, viruses, bacteria and fungi. Infectious disease can spread from human to human and from environment to human. Typhoid fever is a bacteria disease caused by Salmonella Typhi bacteria in humans. (WHO, 2003), (Naresh, 2008). In order to understand infection

transmission and determine the possible effects of control programs on reducing morbidity and mortality, mathematical models are increasingly being employed. The applications include the development of optimal strategies for the management of new and emerging infections, such as SARS-CoV-2, Zika, or Ebola or HIV, and the prediction of the effect on common infections such as rubella and tuberculosis. Researchers have developed several typhoid fever models over the years to enhance our knowledge of pathogenesis and typhoid fever epidemiology and to assess the efficacy of different control intervention strategies. Nevertheless, the rise in typhoid outbreak frequency with its accompanying severity suggests that our present understanding of typhoid fever dynamics and government health rules for controlling the disease is insufficient, therefore, studies must proceed until the disease is totally eradicated.

1.4 Justification of the Study

Typhoid fever is a bloodstream disease transmitted by the *Salmonella Typhi* bacteria. It's usually linked to direct transmission from person to person as a result of poor hygiene and unsafe food/water handling. However, recent studies suggest that people in their immediate environment may be indirectly exposed to typhoid fever by contact with faecal contamination. Typhoid fever remain a major threat to humankind in developing countries, despite advances and notable achievements in medical research. As a result of this, all measures must be put in place to prevent and manage the disease. Mathematical modelling offers an outstanding guide for infectious disease, prevention and management. The suitable use of mathematical models in infectious disease management and control of infectious disease is becoming more common as epidemiological models provide data that shield light on that nature of infections by estimating significant parameters that are helpful in making predictions about the disease transmission in a human population. (Yuan, 2012). Moreover, the threat of typhoid fever epidemics is not the only leading cause of human death, but also has the potential to have significant, social and financial effect in human, so there is an urgent need for every practical and theoretical means of controlling and potentially preventing it. However, the study's justifications emanate from the frequent occurrence of typhoid fever and the fact that the disease transmission mechanism is not just human to human, but also from environment to human. Therefore it is necessary to:

- (i) Intensify thorough research on the various ways on the disease transmission ;
- (ii) Give ultimate attention to the diagnosis, treatment and prevention of typhoid fever;
- (iii) Sensitize the need to alert against the likelihood of typhoid fever outbreak in each society, particularly in less developed countries.

1.5 Aim and Objectives of the Study

The overall goal of this study is to develop three deterministic nonlinear mathematical models of typhoid fever disease by taking into account the transmission of the disease from human to human and from environment to human transmission and investigate the effect of the use of one control, two controls and combination of three control measures in reducing the transmission of typhoid fever. The specific objectives of the work are to:

- (i) verify the basic properties of the epidemiological models by using Lipschitz criteria together with Derrick and Grossman theorem;
- (ii) examine a non-linear deterministic model;
- (iii) obtain the basic reproduction number of the models;
- (iv) conduct both local and global stability analyses of model 1 using Lyapunov function and Lasalle's invariance principle;
- (v) derive the disease free and endemic equilibria that govern the spread of typhoid fever;
- (vi) perform a sensitivity analysis of the model;
- (vii) attempt the analytic series solutions of the models by using Differential Transform Method (DTM) and Variational Iteration Method (VIM); and
- (viii) determine the optimal strategy for implementing the combine controls measures

1.6 Scope of the Study

This research work is restricted to studying typhoid fever transmission, control and intervention strategies. The research examines effectiveness of a single control strategy, two control strategies, three control strategies and how best to cope with typhoid fever epidemics. The research limitations are as follows:

- (i) The study examines the transmission of typhoid fever between humans to human and the environment to human. Other means of typhoid transmission are not taken into account ;
- (ii) Prevention and control of typhoid fever are restricted to control with educational campaign, prevention /sanitation and early Treatment /Screening This study's scope goes beyond any other forms of typhoid fever control;
- (iii) The values used for numerical simulations are taken from the literature and where the values are not available, assumed values are used;
- (iv) A single method is used to derive the basic reproduction numbers and stability analysis are derived using a single approach.
- (iv) Detailed analysis including optimal control are restricted to model 1 and Model 3

1.7 Significance of the Study

Mathematical model enable scientists to derive information about the dynamics and transmission of disease outbreak, to predict the disease outbreak, most importantly, to take into account the doubt in its predictions because well organized mathematical model provides powerful insight to the disease transmission and management interventions. (Keeling & Danon, 2009). To this end, this research work will shed more light on a number of issues that cause typhoid fever and how to prevent it. The findings of this research will assist government and non-governmental organizations (NGOs) in developing and formulations of new policies and programs to efficiently combine various measures to obtain optimum outcomes. It will also assist scientists interested in this field in gaining perspectives and understanding the path to be taken to discover a better way to end the disease outbreak. Generally speaking, this research will make it simpler for society to understand the transmission and growth of infectious diseases much better. Finally, the research can promote the creation of conferences and workshops to educate individuals on the risks of typhoid fever outbreaks and the need for sanitation and personal hygiene.

1.8 Definition of Basic Terms

Equilibrium states

The equilibrium state of a differential equation, system of first-order is the point at which the rate of change is zero. The solutions obtained at this stage are called equilibrium so-

lution.

Disease

A malfunction of the body or any part of animal or plant that typically manifests signs and symptoms.

Infectious Disease

These are organism-related diseases such as bacteria, viruses, fungi or parasites or prions to humans from another human, including food and water, from other humans, animals or the environment.

Deterministic Model

A deterministic is the approach used to simplify infectious disease mathematical modelling. The population is divided into compartments, meaning that everyone in the same compartment has the same characteristics.

Parameters

This is define as the rate of movement or probability that defines an events between state variables in a model.

Initial Conditions

These are values assigned to the state variables of a model at the beginning of the simulation.

Simulation

An analysis carried out with the aid of computer programmes such as Matlab, Maple e. t. c to verify the results in order to gain a better insight or information to a problem.

1.9 Outline of the Thesis

The thesis begins with a comprehensive background of the study, which includes, meaning, mode of transmission, signs and symptoms, vaccination and treatment of typhoid fever. Chapter one also includes details explanation of typhoid fever transmission, the background of the study, the aim and objectives of the study, justification of the study, importance of the study, scope of the work and the meaning of some basic terms. In Chapter two, the review of some existing related works on typhoid fever model are discussed. Chapter three is the model formulation, qualitative and quantitative analyses are carried out. In Chapter four, the analytical results obtained are validated by means of numerical simulations and the solutions are

illustrated by graphical results. Optimal control analysis are also carried out to see the effects of each control. The model's numerical simulation show that the control and containment of typhoid fever by optimally combining the educational vaccination campaign would minimize the spread of the disease if possible optimal control strategies become more effective. Subsequently, for model 3, we implemented three controls that is, control with educational campaign, control with prevention combined sanitation and early treatment combined with screening. The results were also discussed in Chapter four. Chapter five contains the conclusion, knowledge contribution, recommendations and suggestions for further study and references.

Chapter 2

REVIEW OF RELATED

LITERATURE

2.1 Introduction

Typhoid fever is a Salmonella infectious disease. Typhoid fever is caused by Salmonella Paratyphi A, Salmonella Paratyphi B, Salmonella Paratyphi C and Salmonella Paratyphi D. (WHO, 2004). Every Salmonella can cause different infections. In addition, the serotype can co - infect a person. Infection with Salmonella is associated with weakness, sustained fever, loss of body weight, anaemia, poor appetite, severe headache, vomiting and sometimes diarrhoea (Samal and Sahu, 1991).

Typhoid fever is an rare in the developed countries. The disease continues to be a public health problem in less developed countries despite advances in health care and modern improvements in water and environmental management. More than 15 million typhoid fever and more than 500 000 deaths worldwide are reported every year (Mushayabasa, 2012). The bacteria is transmitted by consumption infected water or food. When it moves through the human body, the bacteria passes through the intestines before entering the bloodstream. The symptoms of this disease are abdominal pain, fever and general illness. When the disease gets worse, high fever and severe diarrhoea occurs. The period of incubation is usually ten to fourteen days, sometimes three days. In Central America, it is endemic. (Kariuki, 2004; Fica, 1990; Olarte, and Galindo, 1973), Indian subcontinent (Shanahan, 1998), Southeast Asia (Mirza, 1996) and some part of African countries. (Kariuki, 2000).

The disease caused illness is estimated to be 21.6 million and 216,500 deaths worldwide in the year 2000. (Merrell and Falkow, 2004). For many researchers, studies on infectious disease models and its transmission can be useful in controlling the spread of infectious disease. (LaSalle, 1976). In the past, communicable diseases research has mostly concentrated on their effect on human populations, despite the fact that infectious diseases are still present in human populations to some extent.

Infectious diseases such as tuberculosis and meningitis have had a significant effect on population patterns, changing the age systems of countries that have been heavily affected. As a result, research into emerging infectious diseases must be prioritized. (Hyman, 2006). While typhoid has virtually disappeared in the developed countries due to widespread improvement in water and sanitation, the recent global typhoid reports indicate that the disease affects between 13.5 and 26.9 million people and claims between 190 000 and 216 000 lives annually. (Mushayabasa, 2013).

The fight against the prevention and elimination of typhoid fever in developing countries can not be won by present medical efforts since the provision of health care and medical facilities in these countries is in disgraceful conditions. Strategies that can lead to behavioural changes would therefore be better off if typhoid infections were reduced to the lowest minimum. Among other things, these strategies include safe drinking water, improved sanitation and health education (WHO, 2003). Typhoid fever bacteria are spread by consumption of contaminated water or food. (WHO, 2007).

2.2 The Review

The mathematical study of typhoid fever began with (Cvjetanovic *et al.*, 1971) in a stable population. They developed an epidemic model of the dynamics of typhoid fever for the study of the spread of disease at different levels of endemicity by incorporating a number of parameters comprising the proportions of the epidemiological compartments in the population-such as susceptible, infected, immune and rate of transition between the compartments. Parameters and assigned numerical values used are based on available data which provide a realistic simulation of stable endemicity. The model was also used to predict the possible impact of sanitation changes. Whenever the transmission of the disease is decreased due to improvements in sanitation, the incidence decreases to a new level of stability. The effect of sanitation is long-lasting and better than vaccination in this respect. The concurrent implementation of mass vaccination and sanitation results in a cumulative effect that appears to be similar to the effect of sanitation alone in some situations. The model was used to estimate the likely effect of interventions against typhoid fever, such as mass vaccination and sanitation programs, on a specified population in terms of disease prevention as well as comparative costs and benefits. This provides a useful guide for the appropriate use of funds and facilities for typhoid fever control purposes.

Typhoid fever treatment is based on the use of antibiotics such as ciprofloxacin or norfloxacin, although the use of antibiotics in severe cases is limited to mild cases. Millions of people worldwide suffer from typhoid fever, where more than 20 million cases are recorded and nearly 200 000 deaths are reported every year. (Kariuki, 2004), (Nthiiri *et al.*, 2016). There are three vaccines for typhoid fever. However, the three vaccines do not offer permanent immunity to typhoid fever infections. Many models have been developed to provide insight into the dynamics of transmission of infectious diseases in humans. Most of these models are designed in terms of first-order ordinary differential equations built around some reasonable set of assumptions. Mathematical models for the spread of typhoid are formulated in most cases to assess the potential

of direct and indirect impacts of vaccination (Pitzer et al., 2014). The model developed by Pitzer *et al.* (2014) was validated against randomized vaccines trial. The model was tested on school-based immunization strategies, and it was shown that typhoid vaccination would lead to short time indirect protection together with decline in typhoid fever incidences though typhoid fever was not certain to be eradicated through vaccination alone. A mathematical model was designed to study the effect of direct and indirect impact of vaccines and the advantages of generic vaccination strategy by Cook (2010). The total human population was divided into vaccinated and unvaccinated classes. It was discovered that susceptibility to typhoid fever infection was reduced by vaccination and fewer infectious patients spread the disease to the vaccinated and unvaccinated persons.

Nthiiri *et al.* (2016) developed a mathematical model to examine the extent to which the control measures can effectively reduce the burden of the impact of carriers on the spread of typhoid in the entire community. The transmission dynamics of typhoid fever was studied by incorporating the effect of diagnosis, carriers of the disease and health education awareness on the control of typhoid fever in Kenya and the model was built on the assumption that the exposed individuals contract the typhoid bacteria as a result of exogenous re-infection and endogenous reactivation. Besides, the distribution for the latent and the infectious period was not exponential. In the model, treatment was offered to all fully infected individuals. The contact among individuals that could result in the transmission of infection was structured and the structure was non-homogeneous which was modelled in terms of a random graph whose edges represent the contacts between individuals. Numerical results of their study showed that government of Kenya could achieve typhoid free state by 2030 if typhoid carriers were reduced by 9.5%. The study then concluded that prevention through vaccination as well as the provision of potable water and improvement in environmental sanitation could help government achieved the aim. Also, a mathematical model for typhoid fever and malaria co-infection was proposed and analyzed by Mushayabasa et al. (2014). The model was shown to exhibit backward bifurcation phenomenon. Besides, it was also shown that the outbreak of typhoid in a malaria endemic population could result in higher cases of dually-infected patients showing clinical symptoms of the two infections than singly-infected patients showing clinical symptoms of either infection.

Edward & Nyerere (2016), developed a compartmental model to access the effects of vaccination, treatment and educational campaign on the control of typhoid fever transmission in a community. The authors derived both the basic and the effective reproduction numbers of the model and stability of the model was derived in terms of the basic reproduction number. They found that typhoid fever free equilibrium of the proposed model was globally stable provided that the value of the basic reproduction number is less than one. The results from the effective reproduction number show that, each treatment, vaccination, treatment of infected individuals and awareness will reduce typhoid fever transmission in the community. Also, the results from the sensitivity analysis show that, recovery rate, awareness and vaccination rate are all sensitive to the dynamics of typhoid fever and this could have impact on the transmission rate. Both the numerical and the analytical outcome of the study showed

that multiple control strategies achieved a better result than a single intervention strategy.

Also, Edward (2017) concluded that the transmission mechanisms of typhoid fever were poorly understood, and as a result, he formulated a model with a new approach that captured the effect of human-to-human and environment-to-human interactions on typhoid fever spread. The author conducted a thorough review of the model and determined the results of various typhoid measures, such as better treatment techniques, immunization, and investments in sanitation and portable water. Besides, the researcher recommended the use of latrines, avoidance of water contamination and reduction of contact with typhoid patients as possible ways of preventing the outbreak of typhoid or managing typhoid fever outbreak. Studies on typhoid fever can also be found in Omame *et al.* (2015) and in Balaji *et al.* (2018).

Prevention, they say is better than cure but when there is an outbreak of a disease, the main concern is to reduce the severity and limit the death tolls. The best way to achieve this is to offer treatment as early as possible. A person who is infected with a disease will not want to succumb to the disease but has a single prayer of getting cured of the infection.

(Nthiiri, 2015) developed a new model to assess the causes of typhoid fever disease while keeping infection control in mind. The existence of the model's stable states is calculated by measuring the basic reproduction number using a next generation matrix method. The NPSI model is based on the idea that if an individual is treated, there will be no new infection.

In another research work, (Mushayabasa, 2011) proposed a model for the effect of vaccines on the dynamics of transmission of typhoid fever in Ghana's upper east region. Analytical findings of the model show that the vaccine reproduction number R_v and the basic reproduction number R_0 provide threshold requirements for the incidence of typhoid fever in a population. The model's assumption is that, susceptible class has a constant rate of recruitment. In this work, the effect of the vaccine on the long-term typhoid fever dynamics in the Upper East region of Ghana has been thoroughly investigated by using a deterministic mathematical model approach. Study results show that vaccination is an important strategy for typhoid intervention to reduce the region's total new cases of typhoid fever. The study therefore, suggests that the government and health sector need to encourage the vaccination of vulnerable individuals in order to reduce typhoid-induced and prevalent mortality.

(Muhammad *et al.*, 2015) developed an *SEIR* nonlinear deterministic model by incorporating incidence function. The model was divided into four classes that is, (Susceptible class, Exposed class, Infected class and Removed class). The analysis of the model show that, typhoid fever can be controlled if the control measures such as , vaccination and proper hygiene are put in place. Also, the result from the analysis futher revel that, if the value of the reproduction number is less than one, there is

every possibility that typhoid fever can be put under control. This model is important to this study on how to calculate the basic reproduction number. However, the researchers intended to use a different model of the type SEIR to analyze the dynamics of typhoid fever with incidence function.

(Moffat, 2014) developed a mathematical model to effectively manage the burden of carriers effects on typhoid fever in the the community of Kisii. This model studies extensively the dynamics of typhoid fever by implementing and evaluating the effects of treatment on the management of typhoid fever carriers in Kenya. Both infected people, except those latently infected, are ordered to be treated. The population integrates a system for the form of individual contacts that can contribute to infection transmission. This interaction structure may be non-homogeneous and is modelled as a spontaneous graph whose boundaries represent the individual contacts. In other words, if the effect of carriers is not too high, treatment can be effective in reducing the number of people who are sick. On the other hand, once carriers have become prevalent, treatment is less likely to succeed.

In this scenario, mathematical models like this can help to indicate thresholds for effective therapy and should be used modestly to avoid creating further problems by aggravating the impact of carriers. They found that rising care resulted in a smaller decrease in the number of contagious people. It was also considered in this work that doubling the rate of treatment may lead to significant changes in the size of the contagious population, but this efficacy declines as we keep increasing treatment. It is possible to find a compromise so that treating a certain percentage of people will produce optimum effectiveness per shilling invested. We observed in this work that during the parameter manipulations, they do not change the rate of recovery and therefore the proportion of people surviving is diminished relative to those receiving drugs. This work would bring information to our model on how the disease-free equilibrium point (DEF) and the endemic equilibrium point (EEP) can be measured and determined.

(Moatlhodi and Gosalamang, 2016) developed and analyzed a deterministic model of typhoid fever outbreak that integrates treatment and assume a relapse of treatment leading to increase in the rate of infection. The studies showed that the absence of infection is locally asymptotically stable when the basic number of reproduction is less than one and unstable when the basic number of reproduction is greater than one. Numerical computation also shows that increased therapy in the population supports the typhoid epidemic. The findings of these studies indicate that treating infected patients early reduces the risk of disease transmission. The study recommends developing and implementing prevention and treatment strategies to control the spread of typhoid fever. Sensitivity analysis of infectious cases, primarily carriers, will be critical in decreasing the typhoid infection burden. While this study sheds light on the typhoid fever transmission, some current problems such as control strategies and multi-drug resistance were overlooked.

(Adeboye and Haruna, 2015) proposed *SIRS* compartmental model on co-infection of typhoid fever and malaria. The model integrate control measures for two-disease control as well as studies of malaria transmission and spread of typhoid and both using the three transmission components: human component, mosquitoes and bacteria. In this study, they considered the model *SIRS* which refers to a condition in which infected individuals recovered and upon treatment become susceptible again after recovery from the infections. It has been found that it is possible to control the spread and transmission of malaria and typhoid co-infection by keeping the simple reproductive numbers R_1 and R_2 below one. The found out that some of the parameters used in the model affect the two-disease control. The control measure introduced is typhoid vaccination to monitor and prevent the spread of the bacteria to vulnerable human and malaria-infected host. The numerical findings show the minimum transmission and dissemination of typhoid if the vaccination rate of 70% or higher is introduced. The computational simulation of the model was performed by checking for optimal rates of malaria and typhoid control steps.. It was concluded that the control measures against malaria and typhoid included in the model have a significant impact on malaria and typhoid fever by managing the spread of both diseases.

(Virginia *et al.*, 2014) suggested an age-structured natural history and typhoid fever immunity model. The model was suitable for 2000-2012 data on reported cases of typhoid fever in Vellore, India, at the Christian Medical College. The model was used to measure the effects of college vaccinations using live oral, violysaccharide and viconjugate vaccines. The model was used to determine potential impact of the disease transmission. The model could replicate the occurrence of typhoid fever cases in Vellore and its age

distribution.

(Date *et al.*, 2015) suggested that vaccination against typhoid fever is one of the major way to prevent the outbreak of the disease and is recommended in both rural and urban settings for programmatic use in public health. Using current typhoid fever vaccines, they reviewed different vaccination approaches to evaluate the rationale, acceptability, efficacy, effects and lessons of implementation to inform future strategies for managing typhoid in public health. In this research , they found that all vaccination approaches were appropriate, viable and efficient in the contexts being tested, showing an impact in endemic and in the short to medium term, where available. The results showed that implementation studies should be carried out to model optimal vaccination strategies for the prevention and control of typhoid fever, with TCVs which have many anticipated benefits, such as usage potential for childhood immunization and long-term coverage programmes.

(Watson *et al.*, 2015) conducted a thorough study of typhoid fever transmission as well as a cost-benefit analysis of typhoid fever vaccination. In their work, they recommended that vaccines should be considered for the typhoid outbreak and other infectious disease. The proposed model suggests that, vaccinations can substantially reduce the burden of typhoid fever and other infectious diseases, but that indirect protection is dependent on the relative contribution of carriage to transmission in a

given environment. The study further suggested that proper hygiene and sanitation are also essential for preventing and controlling typhoid fever outbreaks.

(Jones *et al.*, 2015) studied mathematical modelling of malaria and typhoid fever coinfection dynamics. The study show that malaria and typhoid fever in developing countries are the two major diseases and have become a public health issue. In addition, due to similar signs and symptoms of malaria and typhoid co-infection and false-positive test results of the two disease, this has made it difficult to control the two diseases. This culminated in the development of mathematical models illustrating the malaria and typhoid co-infection dynamics. By the analysis of the models, distinct characteristics of the dynamics of typhoid and malaria infection and relationships associated with typhoid and malaria co-infection have been identified. The research suggests that falsified diagnosis of higher probable typhoid cases than malaria causes significant devastating social impact. The results show that both diseases need to be handled simultaneously to control co-epidemics effectively

(Adetunde, 2008) proposed a mathematical model of typhoid fever in upper-eastern Ghana's Kassena Region. The model system's equilibrium points were presented and their stability examined. The illness-free equilibrium threshold condition is presented, evaluating both the model's quantitative and qualitative results. The experimental results show that there is a permanent immunity equilibrium state and it has been confirmed to be asymptotically stable. The findings of the study show that a permanent equilibrium state exists and has been shown to be globally asymptotically stable as long as the rate of change of the infected compartment remains negative with respect to time. It was determined that the necessary condition for the basic reproduction number is less than unity, and this clearly indicates the effect of population density in deciding the pattern of infection in the population district.

The mathematical model on typhoid fever transmission proposed by (Peter *et al.*, 2019) considered the existence and singularity of the model solution, using the condition of Lipchitz, to verify the model for efficacy. The results of their studies show that the spread of typhoid fever largely depends on the contact rate of susceptible individuals with infected individuals. The stability result show that when the basic reproduction number is less than unity, and the disease will always die out.

(Awofisayo *et al.*, 2019) used the concept of differential equation to construct a compartmental model in order to determine the duration of infection and classify biological processes that may affect the duration of the incubation period. The authours used a mathematical model to predict the disease mode of transmission mechanism of Salmonella Typhi in humans. The findings demonstrate how computational models can be used to classify biological mechanisms and predict infectious disease variants. This model has also been beneficial in identifying the important characteristics of the incubation process, meaning that net delayed-phase organs and reproduction rates are key determinants of the length of the incubation period. The drawback of this studies is that no research has been conducted into other factors, such as immunization, and further work is needed in order to extend this

model with the evidence on the effect of immunization. The model was quantified, based on estimated total human and bacterial population and the calculated value of the incubation period was 9.6 days.

2.3 Appraisal of the Literature Review

We formulate three deterministic typhoid fever disease models and to complement and extend the existing ones in the literature. We extend the work of Nthiiri *et al.*, (2015) by incorporating two control variables such as vaccination and education campaign. We extend the model by incorporating carrier compartment which was not considered in the model. The second model complements the work of (Moatlhodi and Gosalamang, 2016) by incorporating educated and uneducated infected compartment. To the best of our knowledge, no work in the literature have considered educated and uneducated class. The first two models considered direct transmission of typhoid fever from person to person while the third model considered indirect transmission of typhoid by the addition of environmental bacteria concentration. That is, transmission from environment to human.

Chapter 3

MATERIALS AND METHODS

3.1 Introduction

The aim of this chapter is to study the dynamics of typhoid fever transmission by integrating certain control strategies to extend and complement existing ones in the litera-

ture.

3.2 Formulation of Model 1

In this section, we propose a deterministic mathematical model of typhoid fever transmission by incorporating control parameters. To better understand the impact of these control strategies on typhoid fever dynamics, we incorporate vaccination and educational campaigns as control parameters. The model compartments consist of the following class namely, Susceptible class $S(t)$; those in this category are the number of people vulnerable to the disease or susceptible to the disease. Infected class. Carrier class $I_c(t)$; denote individuals who show no sign of infection and are infectious. $I(t)$; Individuals in this group can spread the disease to those in the susceptible class and may recover upon treatment. Recovered class; $R(t)$; these are individuals who have been infected and recovered from the illness. Those in this category can not re-infect or transmit the infection to others.

Recruitment by immigration or birth to the susceptible population is at a rate θ . The proportion of susceptible groups is assume to migrate to carrier compartment at a rate ρ while compliment $1 - \rho$ migrates to symptomatic group. We assume that the rate of typhoid fever transmission β is higher than the rate of typhoid fever transmission rate γ for people who are symptomatically infected, because they are more likely to be ignorant of their condition and thus, continue their regular activities. Carriers individual can develop symptoms at a rate of α . Infectious individuals can be treated and recovered from the infection at a rate δ . Susceptible individuals can be vaccinated at a rate ψ to protect themselves from infection. $1 - \varphi$ is an parameter that represents educational campaign that prevent the spread of typhoid by carriers. This parameter lies between $0 \leq \varphi \leq 1$. When the educational parameter is set to zero, that is, $\varphi = 0$ this implies that there is no educational campaigns so that the entire population in the susceptible class are ignorant of the disease transmission and when educational parameter is equal to unity that is, $\varphi = 1$ in the prone class the whole population are aware of the disease transmission and how to prevent themselves from contracting typhoid fever.

Model 1 Assumptions

The following assumptions are made;

- (1) Disease transmission by carriers is higher than disease transmission by individuals with symptoms.
- (2) Susceptible individuals get infected through direct contact with infectious or carrier of the disease.

- (3) There is no reinfection after recovery from the disease.
- (4) Recruitment of the vulnerable population is either by immigration or through birth at the rate of entry θ
- (5) All parameters used are non-negative
- (6) Proportion ρ of susceptible population moved to asymptomatic class, while the complement $1 - \rho$ moved to symptomatic class
- (7) Individuals in the infectious and carrier can die naturally and also by disease-induced death.

The differential equations that governs the model is described in (3.1)

$$\left. \begin{aligned} \frac{dS}{dt} &= \theta - \mu_1 S - \lambda S(1 - \phi) - \psi S \\ \frac{dI_c}{dt} &= \rho \lambda S(1 - \phi) - \mu_2 I_c - \alpha(1 - \phi) I_c \\ \frac{dI}{dt} &= (1 - \rho) \lambda S(1 - \phi) + \alpha(1 - \phi) I_c - (\mu_3 + \delta) I \\ \frac{dR}{dt} &= \psi S + \delta I - \mu_4 R \end{aligned} \right\} \quad (3.1)$$

λ represent force of infection defined as

$$\lambda = \beta I_c + \gamma I$$

Substituting the force of infection λ into (3.1)

$$\left. \begin{aligned} \frac{dS}{dt} &= \theta - \mu_1 S - S(\beta I_c + \gamma I)(1 - \phi) - \psi S \\ \frac{dI_c}{dt} &= \rho S(\beta I_c + \gamma I)(1 - \phi) - \mu_2 I_c - \alpha(1 - \phi) I_c \\ \frac{dI}{dt} &= (1 - \rho)(1 - \phi) S(\beta I_c + \gamma I) + \alpha(1 - \phi) I_c - (\mu_3 + \delta) I \\ \frac{dR}{dt} &= \psi S + \delta I - \mu_4 R \end{aligned} \right\} \quad (3.2)$$

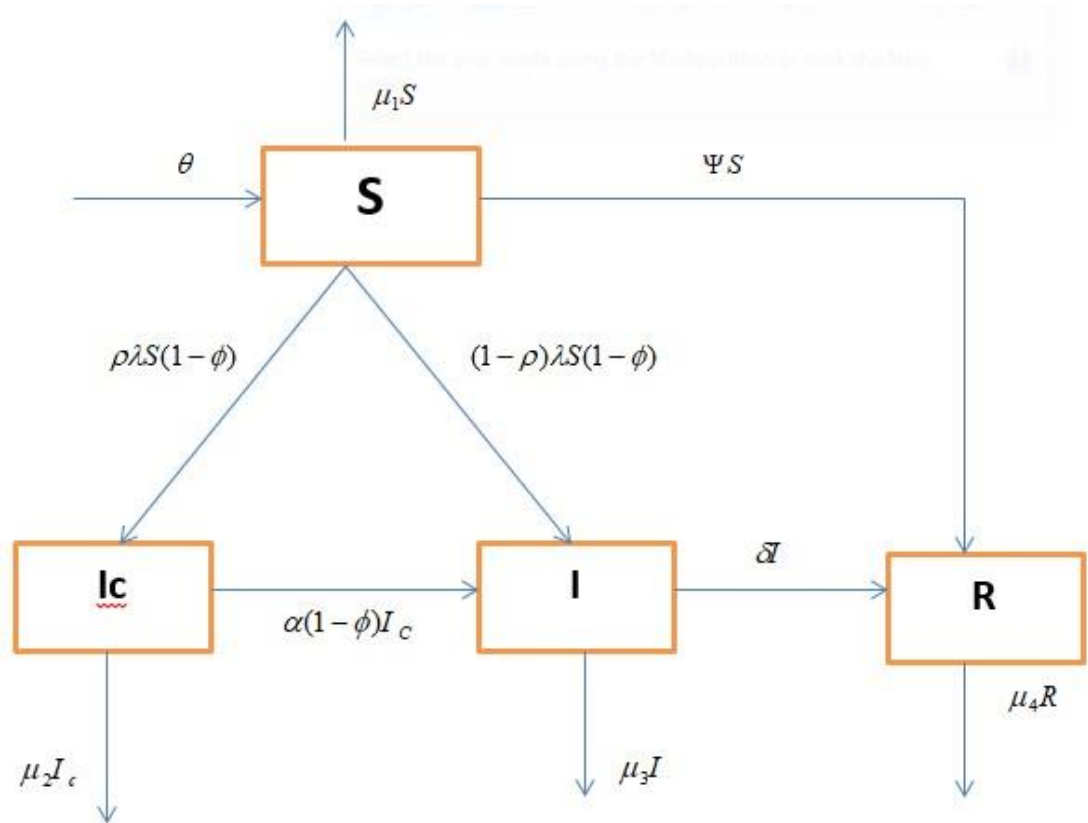


Figure 3.1: Model 1 Pictorial Representation

Table 3.1: Model 1 variables and parameters

Variables	Interpretation
$S(t)$	susceptible compartment
$I_c(t)$	asymptomatic compartment
$I(t)$	symptomatic compartment
$R(t)$	removed compartment
Parameters	Interpretation
θ	recruitment by birth or by immigration into vulnerable class
μ_1	mortality rate
μ_2	mortality rate for asymptomatic class and typhoid-induced mortality rate
μ_3	death rate for symptomatic class and typhoid fever induced death rate
μ_4	rate of natural death
α	symptoms rate developed by carrier class
φ	education parameter
ψ	rate of vaccination
ρ	the possibility that newly infected people would be asymptomatic
β	disease transmission rate for asymptomatic individuals
γ	typhoid fever transmission rate for symptomatic individuals
δ	recovery rate of individuals in infected class

3.2.1 Formulation of Model 2

In this section, we divide the human population into six classes namely; susceptible $S(t)$, protected $P(t)$, uneducated infected $Iu(t)$, educated infected $Ie(t)$, treated $T(t)$ and removed class $R(t)$. We incorporate educated infected class and uneducated infected class in this model which was not considered in any of the existing models in the literature. It is a known fact that most educated individuals are still ignorant of the cause of disease transmission and how to prevent themselves from contracting the disease. However, typhoid cases are common in slum and rural regions of developing nations where sanitation is usually not excellent and personal hygiene is poor. Ignorance on the causes of the disease as a result of lack of knowledge will result to a greater risk of contracting the infection. Recruitment into the susceptible population is at a rate Λ . It is assumed that some proportion α migrate to educated symptomatic class while $1 - \alpha$ migrate to uneducated symptomatic compartment. Vaccinations against this infection can be offered to susceptible persons at a rate τ . Since vaccine has a lifetime, immunity is lost to the vaccinated or the protected person and can then return to the susceptible class at a rate of

ω . Individuals can die naturally in each of the compartments at a rate μ . β_1 , β_2 , and β_3 be the rate of disease transmission for uneducated infected group, educated symptomatic class and treated group respectively.

Model 2 Assumptions

(1) Typhoid infections may be triggered by susceptible individuals by direct contact with educated and uneducated infected persons.

(2) All parameters used are positive.

(3) Treated individuals may recovered from infection

$$\left. \begin{aligned} \frac{dP}{dt} &= \tau S - (\mu + \omega)P \\ \frac{dS}{dt} &= \Lambda - \lambda S + \omega P - (\tau + \mu)S \\ \frac{dIu}{dt} &= (1 - \alpha)\lambda S - (\mu + \delta_1 + \phi_1 + \gamma)Iu \\ \frac{dIe}{dt} &= \alpha\lambda S - (\mu + \delta_2 + \phi_2)Ie + \gamma Iu \\ \frac{dT}{dt} &= \phi_1 Iu + \phi_2 Ie - (\mu + \delta_3 + \epsilon)T \\ \frac{dR}{dt} &= \epsilon T - \mu R \end{aligned} \right\} \quad (3.3)$$

The force of infection λ is defined as:

$$\lambda = \beta_1 I_u + \beta_2 I_e + \beta_3 T \quad (3.4)$$

Substituting (3.4) into (3.3)

$$\left. \begin{aligned} \frac{dP}{dt} &= \tau S - (\mu + \omega)P \\ \frac{dS}{dt} &= \Lambda - \beta_1 I_u - \beta_2 I_e - \beta_3 T)S + \omega P - (\tau + \mu)S \\ \frac{dI_u}{dt} &= (1 - \alpha)\lambda S - (\mu + \delta_1 + \phi_1 + \gamma)I_u \\ \frac{dI_e}{dt} &= \alpha\lambda S - (\mu + \delta_2 + \phi_2)I_e + \gamma I_u \\ \frac{dT}{dt} &= \phi_1 I_u + \phi_2 I_e - (\mu + \delta_3 + \epsilon)T \\ \frac{dR}{dt} &= \epsilon T - \mu R \end{aligned} \right\} \quad (3.5)$$

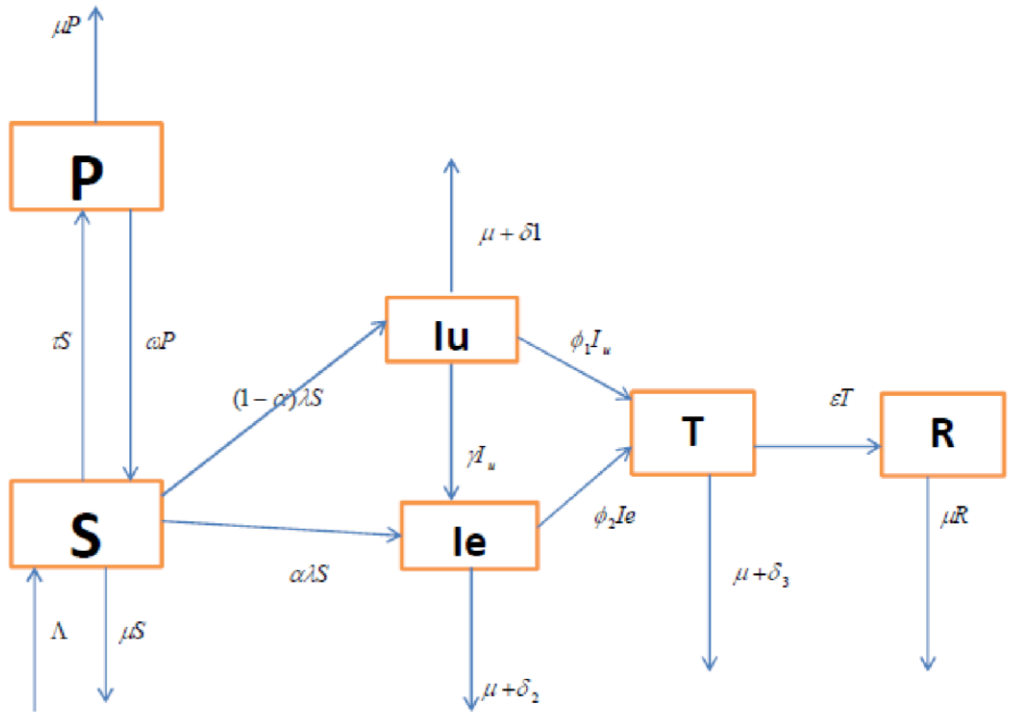


Figure 3.2: Pictorial Representation of Model 2

Table 3.2: Model 2 variables and parameters are defined

Variables	Interpretation
$P(t)$	vaccinated compartment
$S(t)$	susceptible compartment
I_u	uneducated symptomatic compartment
I_e	educated symptomatic compartment
T	treated compartment
$R(t)$	removed compartment
Parameters	Interpretation
Λ	rate of recruitment of susceptible individuals
μ	natural death rate
δ_1	typhoid fever-induced mortality rate for uneducated infected class
δ_2	typhoid fever -induced mortality rate for uneducated infectious class
δ_3	typhoid fever-induced mortality rate for treated class
φ_1	rate treatment for uneducated infected class
φ_2	treatment rate for educated infected class
ω	vaccine waning rate
	recovery rate from treatment
γ	educating or counselling uneducated symptomatic group
τ	rate at which individuals in the protected class are vaccinated
β_1	rate of transmission between susceptible and uneducated infected class
β_2	rate of transmission between susceptible and educated infected class
β_3	rate of transmission between susceptible and treated class

3.2.2 Formulation of Model 3

The model under consideration in this section divides the human population into four groups: susceptible $S(t)$, symptomatic class $I(t)$, asymptomatic class $I_c(t)$ and removed class $R(t)$. The first two models assume that typhoid is transmitted directly to vulnerable persons from infected human to human. However, typhoid fever can also be contracted by contaminated water or food and drink from environmental bacteria to humans, and can also be transmitted by exchanging contaminated food substance and beverages by direct person to person. We consider the another compartment $W(t)$, which denotes Salmonella Typhi in the environment. To incorporate this real biological phenomenon, individuals in the vulnerable group are considered to be diagnosed with the disease at a proportional rate to the vulnerable class. Individuals in the symptomatic class can recover from typhoid fever at a rate δ . Both the asymptomatic symptomatic individuals excrete bacteria into the environment. Also, the excretion rate α_2 of symptomatic group is lower than that of asymptomatic group α_1 because the asymptomatic individuals show no signs of typhoid fever. θ represents influx rate into the vulnerable class, humans can die naturally at a rate μ . Many mathematical models on typhoid fever transmission dynamics have been developed to describe the dynamics of typhoid fever, but none included combination of human to human transmission and environmental bacteria concentration to human transmission. We consider indirect transmission of typhoid by incorporating environmental bacteria concentration.

Model 3 Assumptions

- (1) There is no recruitment rate for Salmonella Typhi bacteria.
- (2) The excretion rate of bacteria to the environment by symptomatic class is higher than that of asymptomatic class, because asymptomatic individuals does not show any signs of infection.
- (3) All parameters used are non-negative.
- (4) There is natural death rate for human and bacteria
- (5) There is no death rate of bacteria caused by disease.
- (6) Bacteria are indirectly transmitted to susceptible people from the environment.
- (7) There is natural death rate for bacteria

The following systems of differential equations governs the model

$$\left. \begin{aligned} \frac{dS}{dt} &= \theta - \mu_1 S - \lambda S \\ \frac{dI_c}{dt} &= \rho \lambda S - (\mu_2 + \epsilon_1) I_c \\ \frac{dI}{dt} &= (1 - \rho) \lambda S - (\mu_3 + \delta + \epsilon_2) I \\ \frac{dR}{dt} &= \delta I - \mu_4 R \\ \frac{dW}{dt} &= \epsilon_1 I_c + \epsilon_2 I - \mu_b W \\ \lambda &= \beta_1 I_c + \beta_2 I + \beta_3 W \end{aligned} \right\} \quad (3.6)$$

By substituting λ into (3.6)

$$\left. \begin{aligned} \frac{dS}{dt} &= \theta - \mu_1 S - S(\beta_1 I_c + \beta_2 I + \beta_3 W) \\ \frac{dI_c}{dt} &= \rho S(\beta_1 I_c + \beta_2 I + \beta_3 W) - (\mu_2 + \epsilon_1) I_c \\ \frac{dI}{dt} &= (1 - \rho) S(\beta_1 I_c + \beta_2 I + \beta_3 W) - (\mu_3 + \delta + \epsilon_2) I \\ \frac{dR}{dt} &= \delta I - \mu_4 R \\ \frac{dW}{dt} &= \epsilon_1 I_c + \epsilon_2 I - \mu_b W \end{aligned} \right\} \quad (3.7)$$

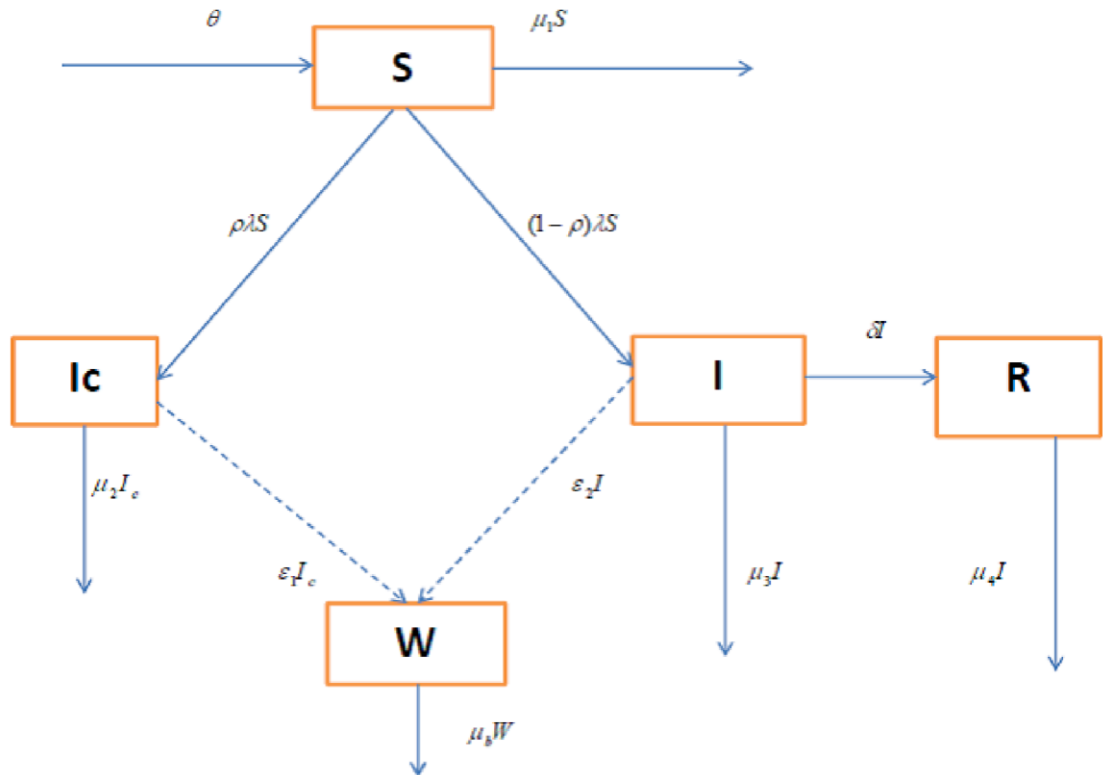


Figure 3.3: Pictorial Representation of Model 3

Table 3.3: Description of Model 3 variable and parameter			
Variables	Interpretation		
$S(t)$	susceptible compartment		
$I_c(t)$	asymptomatic compartment		
$I(t)$	symptomatic compartment		
$R(t)$	removed compartment		
$W(t)$	environmental	bacteria	concentration
	compartment		
Parameters	Meaning		
θ	recruitment rate of susceptible individuals		
μ_1	rate of natural death		
μ_2	rate of natural death for asymptomatic class and death due to typhoid fever		
μ_3	rate of natural death rate for symptomatic class and death due to typhoid fever		
μ_4	natural mortality rate		
ϵ_1	bacteria shedding rate for asymptomatic class		
ϵ_2	bacteria shedding rate for symptomatic class		
ρ	probability that newly infected individuals are carrier of infection		
β_1	rate of typhoid fever transmission between vulnerable and asymptomatic class		
β_2	rate of typhoid fever transmission between vulnerable and symptomatic class		
β_3			
δ	rate of recovery for infectious compartment		
λ	force of infection		

3.2.3 Basic Features of the Models

In order to test for the accuracy of any mathematical model, this depends on whether the model has a solution. Thus, if there exists a solution and it is unique, we proceed by using the Lipschitz criterion to test for the existence and uniqueness of the solution of the proposed models. Hence, we first consider the equations (3.2).

Recall from the system of the model equations in (3.2)

$$\begin{aligned} C_1 &= \rho S \theta - (\beta I \mu_1 S + \gamma I S) (1 - \beta I_c - \alpha \varphi \gamma I) - (1 - \mu_2 - I_c \varphi) - (1 - \psi S - \alpha \varphi) I_c \\ C_2 &= \rho S \theta - (\beta I \mu_1 S + \gamma I S) (1 - \beta I_c - \alpha \varphi \gamma I) - (1 - \mu_2 - I_c \varphi) - (1 - \psi S - \alpha \varphi) I_c \\ C_3 &= (1 - \rho)(1 - \varphi)S(\beta I_c + \gamma I) + \alpha(1 - \varphi)I_c - (\mu_3 + \delta)I \\ C_4 &= \psi S + \delta I - \mu_4 R \end{aligned} \quad (3.8)$$

Theorem 1. (Groosman and Derrick, 1976)

We let D to represent the region

$$|p - p_0| \leq a, \|q - q_0\| \leq 1, q = (q_1, q_2, \dots, q_n), q_0 = (q_{10}, q_{20}, \dots, q_{n0})$$

Suppose that $f(p, q)$ obeys the Lipschitz condition

$$\|c(p, q_1) - c(p, q_2)\| \leq k \|q_1 - q_2\|$$

whenever the pairs (p, q_1) and $(p, q_2) \in D$ and k is the Lipschitz constant, there is a non-negative constant $\delta \geq 0$. Also, a unique continuous vector solution of $q(p)$ of the system in the interval $t - t_0 \leq \delta$ exists. This criteria is established by following the condition

that $\frac{\partial c_i}{\partial q_j}$, $i, j = 1, 2, \dots$, be continuous in D and bounded in D . We are interested in

the region $0 \leq \alpha \leq R$. Next, we check for the solution that is bounded in the region and the partial derivatives obeys $c \leq \alpha \leq 0$. α and δ are non-negative constants.

Theorem 2

Let D represent the region $0 < \alpha < R$, therefore, the solution of equation (3.2) is unique if it is established that

$$\frac{\partial c_i}{\partial q_j}, \quad i, j = 1..4$$

Are bounded in D and continuous in D

For C_1

$$\begin{aligned} \left| \frac{\partial c_1}{\partial S} \right| &= | -\mu_1 - \beta (I_c + \gamma I)(1 - \phi) - \psi | < \infty, \\ \left| \frac{\partial c_1}{\partial I_c} \right| &= | -\beta (1 - \phi) | < \infty, \\ \left| \frac{\partial c_1}{\partial I} \right| &= | -S\gamma(1 - \phi) | < \infty \\ \left| \frac{\partial c_1}{\partial R} \right| &= 0 < \infty \end{aligned}$$

For C_2

$$\begin{aligned} \left| \frac{\partial c_2}{\partial S} \right| &= | \rho \beta (I_c + \gamma I)(1 - \phi) | < \infty, \\ \left| \frac{\partial c_2}{\partial I_c} \right| &= | \rho \beta (1 - \phi) - \mu_2 - \alpha(1 - \phi) | < \infty \\ \left| \frac{\partial c_2}{\partial I} \right| &= | \rho S\gamma(1 - \phi) | < \infty, \\ \left| \frac{\partial c_2}{\partial R} \right| &= 0 < \infty \end{aligned}$$

For C_3

$$\begin{aligned} \left| \frac{\partial c_3}{\partial S} \right| &= | (1 - \rho)(1 - \phi) \beta (I_c + \gamma I) | < \infty, \\ \left| \frac{\partial c_3}{\partial I_c} \right| &= | (1 - \rho)(1 - \phi) S\gamma + \alpha(1 - \phi) | < \infty, \\ \left| \frac{\partial c_3}{\partial I} \right| &= | (1 - \rho)(1 - \phi) S\gamma - (\mu_3 + \delta) | < \infty, \\ \left| \frac{\partial c_3}{\partial R} \right| &= 0 < \infty \end{aligned}$$

For C_4

$$\begin{aligned}\left|\frac{\partial c_4}{\partial S}\right| &= |\psi| < \infty, \\ \left|\frac{\partial c_4}{\partial I_c}\right| &= 0 < \infty, \\ \left|\frac{\partial c_4}{\partial I}\right| &= |\delta| < \infty, \\ \left|\frac{\partial c_4}{\partial R}\right| &= |-\mu_4| < \infty\end{aligned}$$

These partial derivatives exist, are continuous and bounded, going by theorem 2, we conclude that the solution of (3.2) is unique

Model 2 Uniqueness of Solution and Existence

Let (3.5) be represented as follows

$$\begin{aligned}F_1 &= \tau S - (\mu + \omega)P \\ F_2 &= \Lambda - \beta_1 I_u - \beta_2 I_e - \beta_3 T)S + \omega P - (\tau + \mu)S \\ F_3 &= (1 - \alpha)(\beta_1 I_u + \beta_2 I_e + \beta_3 T)S - (\mu + \delta_1 + \phi_1 + \gamma)I_u \\ F_4 &= \alpha S(\beta_1 I_u + \beta_2 I_e + \beta_3 T) - (\mu + \delta_2 + \phi_2)I_e + \gamma I_u \\ F_5 &= \phi_1 I_u + \phi_2 I_e - (\mu + \delta_3 + \epsilon)T \\ F_6 &= \epsilon T - \mu R\end{aligned}\tag{3.9}$$

Following the same procedure from model 1

$$\begin{aligned}\left|\frac{\partial f_1}{\partial P}\right| &= |-(\mu + \omega)| < \infty, \\ \left|\frac{\partial f_1}{\partial S}\right| &= |\tau| < \infty, \\ \left|\frac{\partial f_1}{\partial I_u}\right| &= 0 < \infty, \\ \left|\frac{\partial f_1}{\partial I_e}\right| &= 0 < \infty, \\ \left|\frac{\partial f_1}{\partial T}\right| &= 0 < \infty, \\ \left|\frac{\partial f_1}{\partial R}\right| &= 0 < \infty\end{aligned}$$

For F_2 ,

$$\begin{aligned} \left| \frac{\partial f_2}{\partial P} \right| &= |\omega| < \infty, \\ \left| \frac{\partial f_2}{\partial S} \right| &= |-\beta_1 I_u + \beta_2 I_e + \beta_3 I_T - (\tau + \mu)| < \infty, \\ \left| \frac{\partial f_2}{\partial I_u} \right| &= |\beta_1 S| < \infty, \\ \left| \frac{\partial f_2}{\partial I_e} \right| &= |\beta_2 S| < \infty, \\ \left| \frac{\partial f_2}{\partial T} \right| &= |\beta_3 S| < \infty, \\ \left| \frac{\partial f_2}{\partial R} \right| &= 0 < \infty, \end{aligned}$$

For F_3 ,

$$\begin{aligned} \left| \frac{\partial f_3}{\partial P} \right| &= 0 < \infty, \\ \left| \frac{\partial f_3}{\partial S} \right| &= |(1 - \alpha)\beta_1 I_u + \beta_2 I_e + \beta_3 T| < \infty, \\ \left| \frac{\partial f_3}{\partial I_e} \right| &= |(1 - \alpha)\beta_2 S| < \infty, \\ \left| \frac{\partial f_3}{\partial I_u} \right| &= |(1 - \alpha)\beta_1 S - (\mu + \delta_1 + \phi_1 + \gamma)| < \infty, \\ \left| \frac{\partial f_3}{\partial T} \right| &= |(1 - \alpha)\beta_3 S| < \infty, \\ \left| \frac{\partial f_3}{\partial R} \right| &= 0 < \infty \end{aligned}$$

We obtain the same results for F_4 through to F_6 .

Model 3 Uniqueness of Solution and Existence

Let the system (3.7) be represented as follows

$$\begin{aligned} F_1 &= \theta - \mu_1 S - S(\beta_1 I_c + \beta_2 I + \beta_3 W) \\ F_2 &= \rho S(\beta_1 I_c + \beta_2 I + \beta_3 W) - (\mu_2 + \epsilon_1) I_c \\ F_3 &= (1 - \rho) S(\beta_1 I_c + \beta_2 I + \beta_3 W) - (\mu_3 + \delta + \epsilon_2) I \end{aligned} \quad (3.10)$$

$$F_4 = \delta I - \mu_4 R$$

$$F_5 = \epsilon_1 I_c + \epsilon_2 I - \mu_b W$$

Model 3 Existence and Uniqueness of Solution also follows the same procedure with Model 1 and Model 2. For F_1 ,

$$\begin{aligned} \left| \frac{\partial f_1}{\partial S} \right| &= |-\mu_1 - \beta_1 I + \beta_2 I_c + \beta_3 W| < \infty, \\ \left| \frac{\partial f_1}{\partial I_c} \right| &= |\rho \beta_1| < \infty, \\ \left| \frac{\partial f_1}{\partial I} \right| &= |\rho \beta_2| < \infty, \\ \left| \frac{\partial f_1}{\partial W} \right| &= |\rho \beta_3| < \infty, \\ \left| \frac{\partial f_1}{\partial R} \right| &= 0 < \infty \end{aligned}$$

For F_2

$$\begin{aligned} \left| \frac{\partial f_2}{\partial S} \right| &= |\rho(-\beta_1 I_c + \beta_2 I + \beta_3 W)| < \infty, \\ \left| \frac{\partial f_2}{\partial I_c} \right| &= |\rho \beta_1 - (\mu_2 + \epsilon_1)| < \infty, \\ \left| \frac{\partial f_2}{\partial I} \right| &= |\rho \beta_2| < \infty, \\ \left| \frac{\partial f_2}{\partial R} \right| &= 0 < \infty, \\ \left| \frac{\partial f_2}{\partial W} \right| &= |\rho \beta_3| < \infty \end{aligned}$$

We obtain the same results for F_3 through to F_5 .

Equilibrium Analysis

This represents the points at which the first derivatives are equal to zero. Consider the system

$$\frac{di}{dt} = p(i, j) \quad (3.11)$$

$$\frac{dj}{dt} = q(i, j), \quad (3.12)$$

the equilibrium states are the solutions to the algebraic equations

$$p(i, j) = 0 \quad (3.13)$$

$$q(i, j) = 0, \quad (3.14)$$

(Okyere, 2012).

The two equilibrium states that are often studied in mathematical biology are Disease Free and Endemic equilibrium states. These two equilibrium states correspond to a typhoid free region and typhoid prone region in any given population respectively.

3.2.4 Equilibrium States of the Models

Typhoid Fever Free Equilibrium State: This is a situation where there is no typhoid fever infection. Thus, we obtain the typhoid fever free equilibrium for (3.2), (3.5) and (3.7) respectively in (3.15), (3.16) and (3.17).

$$(S, I_c, I) = \left[\frac{\theta}{\psi + \mu_1}, 0, 0 \right] \quad (3.15)$$

in the same vein, the Typhoid Fever Free Equilibrium State of system (3.5) is given as

$$(P, S, I_u, I_e, T, R) = \left[\frac{\Lambda\tau}{k_1k_2 - \omega\tau}, \frac{\Lambda k_1}{k_1k_2 - \omega\tau}, 0, 0, 0, 0 \right] \quad (3.16)$$

Similarly, the Typhoid Fever Free Equilibrium State of system (3.7) is given as

$$(S, I_c, I, R, W) = \left[\frac{\theta}{\mu_1}, 0, 0, 0, 0 \right] \quad (3.17)$$

$$I_e^* = \frac{(\alpha k_4 + \gamma k_3)(\Lambda \beta_{2k_1k_4k_6} + \beta_{3k_1k_4\phi_2} + \beta_{1k_1k_3k_5k_6} + \beta_{2\gamma k_1k_3k_6} + \beta_{3\gamma k_1k_3\phi_2} + \beta_{3k_1k_3k_5\phi_1} - k_1k_2k_4k_5k_6 + k_4k_5k_6\omega\tau}{(k_5k_4k_1)(\beta_{2k_4k_6} + \beta_{3k_4\phi_2} + \beta_{1k_3k_5k_6} + \beta_{2\gamma k_3k_6} + \beta_{3\gamma k_3\phi_2} + \beta_{3k_3k_5\phi_1})} \quad (3.24)$$

$$T^* = \frac{\Lambda \beta_{2k_1k_4k_6} + \Lambda \beta_{3k_1k_4\phi_2} + \beta_{1k_1k_3k_5k_6} + \beta_{2\gamma k_1k_3k_6} + \beta_{3\gamma k_1k_3\phi_2} + \beta_{3k_1k_3k_5\phi_1} - k_1k_2k_4k_5k_6 + k_4k_5k_6\omega\tau(\alpha k_4\phi_2 + \gamma k_3\phi_2 + \gamma k_3k_5\phi_1)}{(k_6k_5k_4k_1)(\beta_{2k_4k_6} + \beta_{3k_4\phi_2} + \beta_{1k_3k_5k_6} + \beta_{2\gamma k_3k_6} + \beta_{3\gamma k_3\phi_2} + \beta_{3k_3k_5\phi_1})} \quad (3.25)$$

$$R^* = \frac{\epsilon(\Lambda \beta_{2k_1k_4k_6} + \Lambda \beta_{3k_1k_4\phi_2} + \beta_{1k_1k_3k_5k_6} + \beta_{2\gamma k_1k_3k_6} + \beta_{3\gamma k_1k_3\phi_2} + \beta_{3k_1k_3k_5\phi_1} - k_1k_2k_4k_5k_6 + k_4k_5k_6\omega\tau)(\alpha k_4\phi_2 + \gamma k_3\phi_2 + \gamma k_3k_5\phi_1)}{(k_6k_5k_4k_1)(\beta_{2k_4k_6} + \beta_{3k_4\phi_2} + \beta_{1k_3k_5k_6} + \beta_{2\gamma k_3k_6} + \beta_{3\gamma k_3\phi_2} + \beta_{3k_3k_5\phi_1})} \quad (3.26)$$

where $k_1 = (\mu + \omega)$, $k_2 = (\tau + \mu)$, $k_3 = (1 - \alpha)$, $k_4 = (\mu + \delta_1 + \phi_1 + \gamma)$, $k_5 = (\mu + \delta_2 + \phi_2)$, $k_6 = (\mu + \delta_3 + \epsilon)$

The Endemic Equilibrium states of model in (3.7) is given as

$$S^* = \frac{(k_2 + \epsilon_2)\mu_b k_3}{\mu_b_{1k_1k_3} + \mu_b_{2k_2\rho} + \mu_b_{2\rho\epsilon_2} + \mu_b_{3k_1k_3\epsilon_2} + \beta_{3k_2\rho\epsilon_1} + \beta_{3\rho\epsilon_1\epsilon_2}} \quad (3.27)$$

$$I_c^* = \frac{(\mu_b_{1k_1k_3\theta} + \mu_b_{2k_2\rho\theta} + \mu_b_{2\rho\theta\epsilon_2} + \beta_{3k_1k_3\theta\epsilon_2} + \beta_{3k_2\rho\theta\epsilon_1} + \beta_{3\rho\theta\epsilon_1\epsilon_2} - \mu_b k_2 k_3 \mu_1 - \mu_b k_3 \mu_1 \epsilon_2)\rho}{k_3(\mu_b_{1k_1k_3} + \mu_b_{2k_2\rho} + \mu_b_{2\rho\epsilon_2} + \beta_{3k_1k_3\epsilon_2} + \beta_{3k_2\rho\epsilon_1} + \beta_{3\rho\epsilon_1\epsilon_2})} \quad (3.28)$$

$$I^* = \frac{(\mu_b_{1k_1k_3\theta} + \mu_b_{2k_2\rho\theta} + \mu_b_{2\rho\theta\epsilon_2} + \beta_{3k_1k_3\theta\epsilon_2} + \beta_{3k_2\rho\theta\epsilon_1} + \beta_{3\rho\theta\epsilon_1\epsilon_2} - \mu_b k_2 k_3 \mu_1 - \mu_b k_3 \mu_1 \epsilon_2)k_1}{\mu_b_{1k_1k_2k_3} + \mu_b_{1k_1k_3\epsilon_2} + \mu_b_{2k_2\rho} + 2\mu_b_{2k_2\rho\epsilon_2} + \mu_b_{2\rho\epsilon_2^2} + \beta_{3k_1k_2k_3\epsilon_2} + \beta_{3k_1k_3\epsilon_2^2} + \beta_{3k_2\rho\epsilon_1} + \beta_{3k_2\rho\epsilon_1\epsilon_2} + \beta_{3\rho\epsilon_1\epsilon_2^2})} \quad (3.29)$$

$$R^* = \frac{\delta k_1(\mu_b_{1k_1k_3\theta} + \mu_b_{2k_2\rho\theta} + \mu_b_{2\rho\theta\epsilon_2} + \beta_{3k_1k_3\theta\epsilon_2} + \beta_{3k_2\rho\theta\epsilon_1} + \beta_{3\rho\theta\epsilon_1\epsilon_2} - \mu_b k_2 k_3 \mu_1 - \mu_b k_3 \mu_1 \epsilon_2)k_1}{\mu_b_{1k_1k_2k_3} + \mu_b_{1k_1k_3\epsilon_2} + \mu_b_{2k_2\rho} + 2\mu_b_{2k_2\rho\epsilon_2} + \mu_b_{2\rho\epsilon_2^2} + \beta_{3k_1k_2k_3\epsilon_2} + \beta_{3k_1k_3\epsilon_2^2} + \beta_{3k_2\rho\epsilon_1} + \beta_{3k_2\rho\epsilon_1\epsilon_2} + \beta_{3\rho\epsilon_1\epsilon_2^2})\mu_4} \quad (3.30)$$

$$W^* = \frac{(k_1 k_3 \epsilon_2 + k_2 \rho \epsilon_1 \epsilon_2)(\mu_3 \quad_1 k_1 k_3 \theta + \mu_3 \quad_2 k_2 \rho \theta + \mu_3 \quad_2 \rho \theta \epsilon_2 + \beta \quad_3 k_1 k_3 \theta \epsilon_2 + \beta \quad_3 k_2 \rho \theta \epsilon_1 + \beta \quad_3 k_2^2 \rho \epsilon_1 \epsilon_2 - \mu_b k_2 k_3 \mu_1 - \mu_b k_3 \mu_1 \epsilon_2) k_1}{\mu_3 \quad_1 k_1 k_2 k_3 + \mu_3 \quad_1 k_1 k_3 \epsilon_2 + \mu_3 \quad_2 k_2^2 \rho + 2 \mu_3 \quad_2 k_2 \rho \epsilon_2 + \mu_3 \quad_2 \rho \epsilon_2^2 + \beta \quad_3 k_1 k_3 \epsilon_2^2 + \beta \quad_3 k_1 k_2 k_3 \epsilon_2 + \beta \quad_3 k_2^2 \rho \epsilon_1 + \beta \quad_3 k_2^2 \rho \epsilon_1 \epsilon_2 + \beta \quad_3 \rho \epsilon_1 \epsilon_2^2) k_3 \mu_b (k_2 + \epsilon_2)} \quad (3.31)$$

where $k_1 = (1 - \phi)$, $k_2 = (\mu_3 + \delta + \epsilon_2)$ $k_3 = (\mu_2 + \epsilon_1)$

3.3 Invariant Region

The invariant region establishes the feasible region for the solution of the model that is, the bound or range for the solution of the model. Any solution outside this bound is not biologically meaningful and epidemiologically well-posed. From equation (3.2), in the absence of infection, we have that,

$$\frac{dS}{dt} \leq \theta - (\psi + \mu_1)S, \text{ thus, } \limsup_{t \rightarrow \infty} S(t) \leq \frac{\theta}{\psi + \mu_1} \text{ along each solution}$$

$$\text{Also from (3.2)} \frac{dN}{dt} \leq \theta - c_1S - c_2I_c - c_3I - c_4R \leq \theta - \bar{c}N,$$

$$\text{Where } \bar{c} = \min\{c_1, c_2, c_3, c_4\}. \text{ Therefore, } \limsup_{t \rightarrow \infty} N(t) \leq \frac{\theta}{\bar{c}}$$

R does not appear in (3.15), therefore, R is omitted in our analysis. Thus, for the first model in (3.2), this can be examined in the feasible region below

$$\Gamma = \left\{ (S, I_c, I) \in \mathbb{R}_+^3 : S \leq \frac{\theta}{\psi + \mu_1}, S + I_c + I \leq \frac{\theta}{\bar{c}} \right\}$$

The feasible solutions for the human population in the system (3.7) exist in the region

$$\varsigma = \left\{ (S, I_c, I, R) \in \mathbb{R}_+^4, N(t) \leq \frac{\theta}{\mu_1} \right\} \quad (3.32)$$

Also, the population of the pathogen at time t in the system (3.7) is given by

$$\frac{dW}{dt} = \epsilon_1 I + \epsilon_2 I - \mu_b W \quad (3.33)$$

But I is a subset of the human population which has been obtained as $\frac{\theta}{\mu_1}$. Hence,

substituting I in the above, equation (3.34) becomes

$$\frac{dW}{dt} \leq \frac{\theta(\epsilon_1 + \epsilon_2)}{\mu_1} - (\mu_b W) \quad (3.34)$$

Integrating (3.34)

$$W(t) \leq \frac{\theta(\epsilon_1 + \epsilon_2)}{\mu_1 - (\mu_b W)} [1 - ce^{-(\delta + \omega)t}] \quad (3.35)$$

As t tends to infinity then

$$W(t) \leq \frac{\theta(\epsilon_1 + \epsilon_2)}{\mu_1 - (\mu_b W)} \quad (3.36)$$

Hence, the feasible solutions for the dynamics of bacteria population exist in the region

$$\zeta = \left\{ W \in \mathbb{R}^+, W(t) \leq \frac{\theta(\epsilon_1 + \epsilon_2)}{\mu_1 - (\mu_b W)} \right\} \quad (3.37)$$

Therefore, the set of all feasible solutions for the model system (3.7) exist in the region

$$\Phi = \left\{ (S, I_c, I, R, W) \in \mathbb{R}_+^5; S, I_c, I, R, W \geq 0; N(t) \leq \frac{\theta}{\mu_1}; W(t) \leq \frac{\theta(\epsilon_1 + \epsilon_2)}{\mu_1 - (\mu_b W)} \right\} \quad (3.38)$$

3.4 Positivity of Solutions

We establish the positivity of the model in (3.2) under consideration.

Theorem 3

Let the initial conditions under consideration be given as

$$\{S_0, I_{c0}, I_0, R_0\} \in \Omega,$$

Hence, each of the solution of $S(t)$, $I_c(t)$, $I(t)$ and $R(t)$ of (3.2) are nonnegative for all $t > 0$

Proof :

From the first equation of the system (3.2)

$$\frac{dS}{dt} = \theta - \mu_1 S - \lambda S(1 - \phi) - \psi S$$

then,

$$\frac{dS}{dt} \geq -\{(\mu_1 + \psi) + (1 - \phi)\lambda\}S \quad (3.39)$$

By separating the variables in (3.39) and then integrate

$$\int \frac{dS}{S} \geq - \int ((\mu_1 + \psi) + (1 - \phi)\lambda) dt \quad (3.40)$$

$$\ln S \geq -\{(\mu_1 + \psi) + (1 - \phi)\lambda\}t + c$$

$$S(t) \geq Ke^{-\{(\mu_1 + \psi) + (1 - \phi)\lambda\}t} \quad (3.41)$$

$$(3.42)$$

where $K = e^c$. At the initial time, $t = 0$, on substituting into inequality in (3.42),

$$K = S(0)$$

Thus, inequality (3.42) becomes

$$S(t) \geq S(0)e^{-\{(\mu_1 + \psi) + (1 - \phi)\lambda\}t} \geq 0 \quad (3.43)$$

By repeating the same process for the second, third and fourth equations respectively in the system (3.2),

$$I_c(t) \geq I_c(0)e^{-(\mu_2 + \alpha(1 - \phi))t} \geq 0 \quad (3.44)$$

$$I(t) \geq I(0)e^{-(\mu_3 + \delta)t} \geq 0 \quad (3.45)$$

$$R(t) \geq R(0)e^{-\mu_4 \delta t} \geq 0 \quad (3.46)$$

Since $t > 0$, hence, the solutions $\{S(t), I_c(t), I(t), R(t)\}$ of the model are non-negative for all $t > 0$.

3.5 The Basic Reproduction Number, R_0 .

The basic reproduction number, which is denoted by R_0 as defined by (Diekmann, *et al*, 1990) is the expected number of secondary cases which one case would produce in a population where all individuals are vulnerable to the disease. R_0 is an essential tool in mathematical biology, since this tool sets the threshold for understanding disease dynamics, both in predicting epidemics and in evaluating disease control. Thus, the value of the basic reproduction number determines whether typhoid fever becomes endemic or dies in a population. The basic reproduction number R_0 can also be used to analyse the stability of equilibria of epidemic models.

If $R_0 < 1$ this ensures that each infectious organism, on average, produces less than one secondary infection and that any disease outbreak in the population is controlled. But if $R_0 > 1$, this means that each infectious person has more than one secondary infection on average and that the outbreak of the disease can evade the entire population. A larger value for R_0 may indicate the possibility of a major epidemic (Edward *et al.*, 2014).

The Next Generation Matrix

The size of the basic reproduction number R_0 can be computed by using the popular technique known as the next generation matrix approach. This approach, which was formulated by Diekmann *et al.* (1990) but modified by Driessche & Watmough (2002) by constructing $n \times n$ matrix from the model equations and considering only the infective classes. The procedure are given below.

Define A_s as the set of all DFE states, i.e

$$A_s = \{a \geq 0 | a_i = 0, i = 1, 2, 3, \dots\}$$

In order to compute the basic reproduction number R_0 , it is necessary to differentiate new infections from each of the compartment

Let $F_i(a)$ represent the appearance of new typhoid fever infection in compartment i , V_i^+ denotes the movement of individuals to the group i by other mode of disease transmission

V_i^- represents movement rate of people out of the compartment i

The transmission model consists of positive initial conditions together with the following system of equations

$$a'_i = f_i(a) = F_i(a) - V_i(a), i = 1, 2, 3, \dots, n \quad (3.47)$$

where $V_i(x) = V_i^- - V_i^+$ and the functions satisfy the following conditions:

- (a) If $a \geq 0$, then $F_i(a), V_i^-(a), V_i^+(a) \geq 0$ for $i = 1, 2, 3, \dots, n$. That is, if the compartment is zero, there will be no movement of people out of the compartment by death, infections and by any other means.
- (b) If $a_i = 0$, then $V_i^-(a) = 0$ (that is, nobody leaves the compartment). However, if $a \in A_s$, then $V_i^- = 0$ for $i = 1, 2, 3, 4, \dots, m$
- (c) $F_i = 0$, for $i > m$ (m is the number of infective classes)

(d) If $x \in A_s$, then $F_i = 0$ and $V_i^- = 0$ for all $i = 1, 2, 3, \dots, m$

(e) If $F_i(a)$ is set equal zero, all the eigenvalues of $DF(a_0)$ have negative real parts.

Using Diekmann *et al.* (1990) approach, if a_0 is the DFE of the model, then $f_i(a)$ must satisfies conditions (a)–(e), then the derivatives of $DF(a_0)$ and $DV(a_0)$ are partitioned

as

$$DF(a_0) = \begin{pmatrix} f_{11} & \dots & f_{1m} \\ \vdots & \ddots & \vdots \\ f_{m1} & \dots & f_{mm} \end{pmatrix} \quad (3.48)$$

$$DV(a_0) = \begin{pmatrix} v_{11} & \dots & v_{1m} \\ \vdots & \ddots & \vdots \\ v_{m1} & \dots & v_{mm} \end{pmatrix} \quad (3.49)$$

F and V represents $n \times n$ matrix defined by:

$$F = \frac{\partial F(a_0)}{\partial a_j} \text{ and } V = \frac{\partial V(a_0)}{\partial a_j} \quad (3.50)$$

Following the approach of Diekmann *et al.* (1990), the product of the matrix FV^{-1} is called the next generation matrix for the model and the reproduction number (R_0) shall be set to the spectral radius $\rho(FV^{-1})$ i.e., $(R_0) = \rho(FV^{-1})$. However, the largest eigenvalue denotes the next generation matrix.

We shall apply procedure to (3.2) to get the basic reproduction number. It has been mentioned that only the infective compartments are needed in the computation of the reproduction number hence, $m = 2$ and according to Diekmann *et al.* (1990), F_i and V_i are obtained by finding the partial derivatives of the above matrices as defined in (3.52) and (3.53) with respect to the infective compartments.

$$F_i = \left\{ \begin{bmatrix} \beta & (1-\phi)S & \rho\gamma(1-\phi)S \\ (1-\rho)\beta & (1-\phi)S & (1-\rho)\gamma(1-\phi)S \end{bmatrix} \right\} \quad (3.51)$$

$$V_i = \left\{ \begin{bmatrix} \alpha k + \mu_2 & 0 \\ -\alpha k & \mu_3 + \delta \end{bmatrix} \right\} \quad (3.52)$$

The inverse of the matrix V is obtained

as:

$$\begin{bmatrix} (\alpha k + \mu_2)^{-1} & 0 \\ \frac{\alpha k}{(\alpha k + \mu_2)(\mu_3 + \delta)} & (\mu_3 + \delta)^{-1} \end{bmatrix} \quad (3.53)$$

FV^{-1} is the product of matrices F and V^{-1} . Therefore, $FV^{-1} =$

$$\begin{bmatrix} \beta kS & \rho\gamma kS \\ (1-\rho)\beta kS & (1-\rho)\gamma kS \end{bmatrix} \begin{bmatrix} (\alpha k + \mu_2)^{-1} & 0 \\ \frac{\alpha k}{(\alpha k + \mu_2)(\mu_3 + \delta)} & (\mu_3 + \delta)^{-1} \end{bmatrix} \quad (3.54)$$

the basic reproduction number which is the highest eigenvector for system (3.2) is given as

$$R_o = \frac{kS(\alpha k\gamma\beta - \delta\rho\beta - \rho\mu_3 - \rho\gamma\mu_2 + \gamma\mu_2)}{\alpha\delta k + \alpha k\mu_3 + \delta\mu_2 + \mu_2\mu_3} \quad (3.55)$$

This can be rewritten as

$$R_0 = \frac{k\theta}{\mu_1 + \psi} \left[\frac{\alpha\gamma k\beta - \rho(\mu_3 + \delta) + \gamma\mu_2(1-\rho)}{(\mu_3 + \delta)(\mu_2 + \alpha k)} \right] \quad (3.56)$$

Using the same approach we obtain R_0 for the system (3.5) is given as

$$R_0 = \frac{\mu_1^2 + A\mu + (\delta_3 + \epsilon)(\delta_2 + \phi_2)\beta_1 - \beta_3(\gamma + \phi_1)\phi_2 - \beta_3\delta_2\phi_1 - \beta_2\gamma(\delta_3 + \epsilon))\Lambda}{(k_1k_2 - \omega\tau)(\mu + \delta_3 + \epsilon)(\mu + \delta_2 + \phi_2)(\mu + \delta_1 + \phi_1 + \gamma)} \quad (3.57)$$

Also, the basic reproduction number for model 3 in (3.7) is

$$R_0 = \frac{\beta_3(\beta_1\epsilon_2 - \beta_2\epsilon_1)S\rho + \beta_2\mu_b - \beta_3\epsilon_2(\mu_2 + \epsilon_1))S(1-\rho) + S\rho(\mu_3 + \delta + \epsilon_2)\beta_1\mu_b - \beta_3\epsilon_1}{(\beta_3S\rho + \mu_b(\mu_2 + \epsilon_1))(\mu_3 + \delta + \epsilon_2)} \quad (3.58)$$

(3.57) can be written as

$$R_0 = \frac{k\theta}{\mu_1 + \psi} \left[\frac{\alpha\gamma k}{(\mu_3 + \delta)(\mu_2 + \alpha k)} + \frac{\beta \rho}{(\mu_2 + \alpha k)} + \frac{\gamma\mu_2(1 - \rho)}{(\mu_3 + \delta)(\mu_2 + \alpha k)} \right] \quad (3.59)$$

3.6 Local Stability of the Typhoid Free Equilibrium

To determine the local stability of the typhoid fever free equilibrium that is, in the absence of typhoid fever disease D_0 , we evaluate the Jacobian matrix at

$$D_0 = \begin{bmatrix} \frac{\theta}{\psi + \mu_1}, 0, 0 \end{bmatrix} \quad (3.60)$$

$$J(D_0) = \begin{bmatrix} -(\mu_1 + \psi) & \beta(1 - \phi) \left(\frac{\theta}{\mu_1 + \psi} \right) & -\gamma(1 - \phi) \left(\frac{\theta}{\mu_1 + \psi} \right) \\ 0 & \beta(1 - \phi) \left(\frac{\theta}{\mu_1 + \psi} \right) - (\mu_2 + \alpha(1 - \phi)) & \rho\gamma(1 - \phi) \left(\frac{\theta}{\mu_1 + \psi} \right) \\ & -\rho(1 - \phi) \gamma \left(\frac{\theta}{\mu_1 + \psi} \right) & A - (\mu_3 + \delta) \end{bmatrix} \quad (3.61)$$

where $A = (1 - \rho)(1 - \phi)\gamma \left(\frac{\theta}{\mu_1 + \psi} \right)$.

Proposition 1. D_0 is locally asymptotically stable if the basic reproduction number is less than unity otherwise, unstable.

Proof

One of the eigenvalue of $J(D_0)$ is given as $\lambda_1 = -(\mu_1 + \psi) < 0$. The remaining eigenvalues λ_2, λ_3 are 2×2 matrix given as

$$J(D_0) = \begin{bmatrix} \beta(1 - \phi) \left(\frac{\theta}{\mu_1 + \psi} \right) - (\mu_2 + \alpha(1 - \phi)) & \rho\gamma(1 - \phi) \left(\frac{\theta}{\mu_1 + \psi} \right) \\ (1 - \rho)(1 - \phi) \gamma \left(\frac{\theta}{\mu_1 + \psi} \right) + \alpha(1 - \phi) & (1 - \rho)(1 - \phi) \gamma \left(\frac{\theta}{\mu_1 + \psi} \right) - (\mu_3 + \delta) \end{bmatrix}$$

Next, we show that when the basic reproduction number R_0 is less than unity, the Routh-Hurwitz conditions hold, namely, $\text{tr}(A) < 0$ and $\det(A) > 0$

$$\text{tra}(A) = (\mu_2 + \alpha(1 - \phi)) \left[\frac{\beta(1 - \phi) \left(\frac{\theta}{\mu_1 + \psi} \right)}{\mu_2 + \alpha(1 - \phi)} - 1 \right] + (\mu_3 + \delta) \left[\frac{(1 - \rho)(1 - \phi) \gamma \left(\frac{\theta}{\mu_1 + \psi} \right)}{(\mu_3 + \delta)} - 1 \right]$$

Using the assumption that

$$R_0 = \frac{k\theta}{\mu_1 + \psi} \left[\frac{\alpha\gamma k}{(\mu_3 + \delta)(\mu_2 + \alpha k)} + \frac{\beta \rho}{(\mu_2 + \alpha k)} + \frac{\gamma\mu_2(1 - \rho)}{(\mu_3 + \delta)(\mu_2 + \alpha k)} \right] < 1$$

$$\frac{\beta (1 - \phi) \left(\frac{\theta}{\mu_1 + \psi} \right)}{\mu_2 + \alpha(1 - \phi)} < 1$$

and

$$\frac{(1 - \rho(1 - \phi)\gamma) \left(\frac{\theta}{\mu_1 + \psi} \right)}{(\mu_3 + \delta)} < 1$$

Therefore

$$\begin{aligned} \frac{\beta (1 - \phi) \left(\frac{\theta}{\mu_1 + \psi} \right)}{\mu_2 + \alpha(1 - \phi)} - 1 &< 0 \\ \text{and } \frac{(1 - \rho(1 - \phi)\gamma) \left(\frac{\theta}{\mu_1 + \psi} \right)}{(\mu_3 + \delta)} - 1 &< 0 \end{aligned}$$

This shows that $\text{tr}(A) < 0$ and the $\det(A) > 0$ provided that, $R_0 < 1$.

3.7 Global Stability of the Typhoid Fever Free Equilibrium

Theorem 1. D_0 is globally asymptotically stable in the feasible region Γ if $R_0 \leq 1$.

Proof: To prove the global asymptotic stability of typhoid fever free equilibrium, we use the method of Lyapunov functions. Define

$$L = XI_c + YI$$

$$\text{Where } X = \frac{\beta}{(\mu_2 + \alpha k)} + \frac{\gamma\mu_2(1 - \rho)}{(\mu_3 + \delta)(\mu_2 + \alpha k)}, \text{ and } Y = \frac{\alpha\gamma k}{(\mu_3 + \delta)(\mu_2 + \alpha k)}$$

$$\frac{dL}{dt} = X \frac{dI_c}{dt} + Y \frac{dI}{dt}$$

Substituting the values of X and Y above and simplify we shall get

Using the condition $0 < S^* < \frac{\theta}{\mu_1 + \psi}$ we have

$$\frac{dL}{dt} \leq (R_0 S - 1)(I_c + \gamma I) \leq 0$$

Therefore, $\frac{dL}{dt} \leq 0$ if $R_0 \leq 1$

Furthermore, $\frac{dL}{dt} = 0$ if $I_c = I = 0$. Hence, the largest invariant set in the closure Γ , where $\frac{dL}{dt} = 0$ is the singleton $\{J_0\}$

Hence, by LaSalle's principle, J_0 is globally asymptotically stable in the feasible region Γ

3.8 Global Stability of Endemic Equilibrium (EE)

If $R_0 \geq 1$, then the system has a unique Endemic Equilibrium point J_0^* which is Globally Asymptotically Stable (GAS)

Proof

To study the global stability in the presence of typhoid fever, we consider a Lyapunov function L of the form

$$L(S, I_c, I) = c_1(S - S^* \ln S) + c_2(I_c - I_c^* \ln I_c) + c_3(I - I^* \ln I)$$

$c_1, c_2, c_3 > 0$ are constants

L is said to be at global minimum points at $T^* = (S^*, I_c^*, I^*)$ and $L(S, I_c, I) - L(T^*)$

is non-negative definite. We prove that the constant c_1, c_2, c_3 such that the Lyapunov derivatives of L is non positive definite with respect to T^*

Differentiating each state variables with respect to time and by direct calculation and applying the identity $\theta = \mu_1 S^* + \psi S^* - I_c^* S^* (1 - \phi) + \gamma I S^* (1 - \phi)$ leads to

$$\frac{dV}{dt} = c_1(S' - \frac{S^*}{S}S') + c_2(I'_c - \frac{I_c^*}{I_c}I'_c) + c_3(I' - \frac{I^*}{I}I')$$

Substituting the values of S', I'_c, I'

$$\begin{aligned} \frac{dV}{dt} &= c_1[\theta - (\mu_1 + \psi)S + \beta(I_c + \gamma I)(1 - \phi)S - \theta \frac{S^*}{S} + (\mu_1 + \psi)S^* + \beta(I_c + \gamma I)(1 - \phi)S^*] \\ &\quad + c_2[(1 - \rho)\beta(I_c + \gamma I)(1 - \phi)S - (\mu_2 + \alpha(1 - \phi))I_c - (1 - \rho)\beta I_c \frac{SI_c^*(1 - \phi)}{I_c} \\ &\quad - (1 - \rho) \frac{\gamma I S I^*(1 - \phi)}{I_c} + (\mu_2 + \alpha(1 - \phi))I_c^*] + c_3[\beta(I_c + \gamma I)(1 - \phi)S \\ &\quad - \alpha(1 - \phi)I_c - (\mu_3 + \delta)I - \beta I_c \frac{SI_c^*(1 - \phi)}{I} - \frac{\rho \gamma I S I^*(1 - \phi)}{I} \\ &\quad - \frac{\alpha I_c I^*(1 - \phi)}{I} - \frac{\alpha(1 - \phi)I_c I^*}{I} + (\mu_3 + \delta)I^*] \\ &= [c_1(\mu_1 + \psi)S^*(2 - \frac{S^*}{S} - \frac{S}{S^*})] + [c_1\beta(I_c^* + \gamma I^*)(1 - \phi)S + c_2(\mu_2 + \alpha(1 - \phi))I_c^* \\ &\quad + c_3(\mu_3 + \delta)I^* - [c_1 \frac{\beta(I_c^* + \gamma I^*)(1 - \phi)S^2}{S} \\ &\quad + c_2(1 - \rho)\beta SI_c^*(1 - \phi) + c_2(1 - \rho) \frac{\gamma I S I_c^*(1 - \phi)}{I_c} \\ &\quad + c_3 \rho \frac{\beta I_c S I^*(1 - \phi)}{I} + c_3 \rho \gamma S I^* - c_3 \frac{\alpha I_c I^*}{I}] \end{aligned}$$

We choose positive constant c_1, c_2, c_3 as

$$c_1 = 1, c_2 = \frac{(\mu_3 + \delta)S^* + \gamma S^*}{(\mu_2 + \alpha)(\mu_3 + \delta)}, c_3 = \frac{\gamma S^*}{(\mu_3 + \delta)}$$

It can be shown that it satisfy the relations

$$\begin{aligned} -c_1 + c_2(1 - \rho) + c_3\rho &= 0 \quad c_1\gamma S^* \\ -c_3(\mu_3 + \delta) &= 0 \quad c_1\beta S^* - c_2(\mu_2 + \alpha) + c_3\alpha = 0 \end{aligned}$$

Re-grouping the terms in $\frac{dV}{dt}$ such that

$$\frac{dV}{dt} = V_1 + V_2 + V_3$$

$$V_1 = (\mu_1 + \psi)S^*(2 - \frac{S^*}{S} - \frac{S}{S^*})$$

$$V_2 = c_1(\beta S^* I_c^* + \gamma I S^*)(1 - \phi) + c_2(\mu_2 + \alpha(1 - \phi)I_c^*$$

$$V_3 = -c_1 \frac{\beta I_c^* S^* + \gamma I^* S^*)(1 - \phi)}{S} + c_2(1 - \rho) \beta S I_c^*(1 - \phi) - c_2(1 - \rho) \frac{\gamma I S I_c^*(1 - \phi)}{I_c}$$

$$+ c_3 \rho \frac{\beta I_c S I^*(1 - \phi)}{I} + c_3 \rho \gamma S I^* - c_3 \frac{\alpha I_c I^*}{I}]$$

Thus, $V_1 \leq 0$, from the inequality $c = \frac{1}{c} \geq 2$ for all $c > 0$

And that $V_1=0$ if and only if $S = S^*$

Now we want to show that $V_1 + V_3 \leq 0 = 0$. Using the values for c_1, c_2, c_3 and the equilibrium relation,

$$(\rho\mu_2 + \alpha(1 - \phi))I_c = (1 - \rho)(\mu_3 + \delta)I^*$$

It follows that $V_2 + V_3 = 0$ and we can show that $\frac{dV}{dt} = 0$ if $(S^*, I_c^*, I^*) = (S^*, I_c^*, I^*)$ and thus $\frac{dV}{dt}$ is negative definite with respect to J^* which follows from the global stability theorem of Lyapunov.

3.8.1 Sensitivity Analysis

Sensitivity analysis is a mathematical biology concept that explains the relevance of each parameter in a disease model to disease spread and propagation. It's also used to see how sensitive a disease model is to changes in the different model parameters' values, as well as changes in the disease model's overall structure. (Numfor, 2010). Sensitivity analysis allows us to identify the parameters which are important in establishing the imprecision of the model predictions. (Blower & Dowlatabadi, 1994). The results obtained from sensitivity analysis are important not only for the design of the experiment but also for the simulation of the data and reduction in the complexity of the nonlinear nature of the model. Sensitivity analysis plays crucial roles in establishing the authenticity of model predictions to model parameter values since data collection and the values assigned to the parameters always involve errors. Apart from this, sensitivity analysis is used to determine the parameters which have a major impact on the reproductive ratio in order that it is targeted by the control strategies. Some of the reasons why epidemiologists conduct sensitivity analysis as summarized by Chan, Saltelli & Tarantola (1997) include the need to determine: (a) the parameters that enhance the highest degree of output variability in order to adjust the model with a view to reducing output uncertainty; (b) the parameters that are less relevant with a

view to eliminating them from the final model; (c) the parameters that interact with one another; (d) the region of optimality within the space of parameters for use in the calibration of the subsequent study.

Recently, sensitivity analysis has become a major aspect of epidemiological study and has received a considerable amount of attention. Numerous mathematical models have been designed to evaluate the sensitivity indices of the major factors that are promoting the spread and propagation of various infectious diseases (Neilan *et al.*, 2010; Abdulrahman *et al.*, 2013). Kadaleka (2011) formulated a mathematical model to study the impacts of treatment and nutrition on the transmission dynamics of cholera with reference to Malawi. The author conducted a sensitivity analysis of the crucial parameters influencing the disease transmission by using Contour Map illustration. The numerical outcome of the study revealed that the cholera transmission can be limited if both interventions, treatment and nutrition, are implemented.

Mushayabasa (2012) developed a simple model to study typhoid by considering effects of treatment on infected individuals. Mushayabasa conducted sensitivity analysis by evaluating the correlation between the model parameters and the model reproductive ratio. The author discovered that the reproduction number is most sensitivity to the education adjustment parameter. Besides, the magnitude is influenced greatly by the treatment of infectious individuals. Mushayabasa therefore suggested that the management and control of typhoid fever is based on the effective educational campaign of above 40% and the prompt treatment of both the latently infected and infectious people in the particular community.

Mondal & Kar (2013) designed a water-borne epidemic model amenable to typhoid dynamics incorporating two transmission pathways namely, person-to-person and waterto-person. The researchers studied the sensitivity of the system in relation to some major parameters and found that the proportion of the infected individuals together with the concentration of Salmonella is proportional to both transmission pathways. They also discovered that if the human-to-human transmission is not considered, then typhoid may explode from a contaminated reservoir and within a short period of time, the disease may transmit into the entire population.

Rodrigues et al. (2013) designed SIR and ASI epidemiological models that capture essential dynamics of dengue disease. They computed the reproductive number, and estimated the sensitivity indices of the reproductive number, with a view to investigating the relative relevance of the model parameters to the disease spread and transmission. They discovered that dengue epidemic could be averted if the environments were not conducive for mosquitoes and eliminated if parameters and were directly targeted by

intervention strategies.

Mushayabasa, Bhunu & Gwasira (2013) Ayo devised a statistical model to examine the impact of direct and indirect typhoid transmission. They calculated the reproduction

ratio and looked into the model's overall stability. The authors analysed a sensitivity study of the model parameters using the basic reproduction ratio and discovered that indirect transmission caused more typhoid prevalence than direct transmission.

Edward and Nyerere (2015) suggested a model that included some basic cholera transmission dynamics, as well as vaccination, sanitation, public health educational campaigns, and treatment as control techniques for cholera transmission. They performed a sensitivity study on the basic reproductive number for all of the intervention strategies and discovered that the clinical care, educational campaign, successful interaction between infected and susceptible individuals, and recruitment rate into susceptibility are the most sensitive parameters. They came to the conclusion that any effort to eradicate cholera should take into account these factors.

Tilahun, Makinde & Malonza (2017) formulated a mathematical model to assess the optimal control of typhoid fever disease with cost-effective strategies. The researchers performed sensitivity analysis on the model parameters and discovered that ingestion rate of *Salmonella* and the concentration of *Salmonella* have great impact on increasing the typhoid spread and propagation. The basic reproductive ratio rises as the values of both ingestion rate and the concentration of *Salmonella* increase which increases the average number of secondary cases of typhoid in the community. The researchers therefore concluded that efforts should be directed to the prevention of ingestion of *Salmonella* if the outbreak of typhoid is to be averted.

A compartmental mathematical model for examining the impacts of vaccination, education campaigns and treatment on the control of transmission dynamics of typhoid in a community is developed by Edward (2017). The disease free equilibrium of the model is proved to be locally asymptotically stable when the basic reproductive ratio of the model is less than unity while the endemic equilibrium is proved to be globally asymptotically stable when the reproductive ratio is greater than unity. Edward also performed the sensitivity analysis on the key parameters of the models and discovered that the typhoid outbreak tended to decrease as control parameters increase.

Adewale *et al.* (2017) studied sensitivity analysis in relation to a cholera model with a view to determining the impact and significance of each of the parameters on the reproductive number in the transmission dynamics of cholera. They found that the fraction of people with low immunity and the effective contact rate are most sensitive to the reproductive ratio. The researchers therefore urged policymakers and medical practitioners to aim those factors in an attempt to limit the transmission of cholera in various communities and possibly to establish cholera free societies.

Peter *et al* (2018) conducted a study to investigate the dynamics of cholera spread in cholera prone communities. The researcher built a model that incorporated basic prevention and control strategies and conducted sensitivity analysis on the model parameters with respect to the effective reproduction number of the model. The result obtained from the study showed that the educational parameter had the highest sensitivity index in relation to the effective reproductive ratio followed by the

recruitment rate into susceptibility then the contact rate between the infected and the susceptible individuals. Peter et al, 2018, therefore concluded that for the effective management of cholera transmission, medical attention should be promptly given to cholera infected individuals to accelerate recovery and to limit cholera mortality. Peter et al also made a case for cholera education and advocated for its emphasis in the rural communities to reduce cholera spread through avoidance of contact with dirty water and the wastes of the cholera patients.

A nonlinear deterministic compartmental mathematical model was formulated by Akanni & Adediipo (2018) to examine the effects of some control on Lassa fever. The population under consideration was divided into two, human and host. They conducted sensitivity analysis to determine the degree of sensitivity for each parameters of the model with respect to the basic reproduction number. They therefore concluded that in other to effectively control Lassa fever, government must incorporate vital parameters for the disease transmission and control.

Sensitivity indices enable researchers to examine the relative change in the variables when the parameters change. There are more than a dozen methods for conducting sensitivity analysis like the Monte Carlo method and the Partial Rank Correlation Coefficients method (PRCCs) but, the present analysis shall adopt the Normalised Forward Sensitivity Index method to perform the sensitivity analysis (Okosun & Smith, 2017 ; Peter et al, 2018; Akanni & Adediipo, 2018).

The normalised forward sensitivity index of model's compartment and the associated parameters of variables with respect to parameters are the ratios that provides the sensitivity index. The sensitivity indices of variables can also be defined in terms of partial derivative if the variables are differentiable functions of the parameters. For example, the normalised forward sensitivity index with respect to a parameter m , is defined by

$$\gamma_m^{R_o} = \frac{\partial R_o}{\partial m} \times \frac{m}{R_o} \quad (3.62)$$

m represent all the basic parameters. Going by the above formula, the sensitivity index of each of the intervention parameters are computed by determining the partial derivatives of the reproductive ratio in relation to the individual intervention parameter. By doing this, we obtained the sensitivity index in the table below

Table 3.4: Sensitivity indices of R_e to model parameters

Parameters	Sensitivity index
φ	0.3906
γ	-0.24
θ	-1.3993
ρ	-1.2517
μ_2	-1.0993
μ_3	0.757

3.8.2 The Differential Transform Method (DTM)

The Differential Transform Method (DTM) is a numerical technique for solving differential equations. The idea of the differential transform was first proposed by Zhou in 1986. DTM was implemented as a method to find solutions for electrical circuits in the field of engineering. DTM generates approximations based on an iterative process resulting from the expansion of the Taylor series. This technique is very efficient and effective in solving nonlinear and linear differential equations. Many scientists have proven that DTM is an excellent method for solving differential equations. The DTM is an iterative technique to get the analytical Taylor series results of the differential equations. The basic concept of DTM is discussed in details and some well-known properties are written in wider forms. DTM is a semi-analytical technique popularly used as approximations of the exact solution for solving nonlinear differential equations. (Hassan, 2008).

In a time interval series, we use the DTM to solve the differential equations, method that describes the models and approximates the solutions. (Benhammouda *et al*, 2014). The main advantages of DTM and VIM over other approaches are that they offers a remarkable convergence rate for the requisite accuracy and reliability of the series solution, needs less computational work in size and provides high accuracy (Mirzaee,2011; Keskin *et al*, 2011).

The Basic Properties of Differential Transform Method

With reference to Benhammouda *et al*. (2014), Moon *et al* ,(2014), Akinboro *et al* (2014), Peter *et al* (2018) and (Peter and Ibrahim, 2017). The following are procedures involved in DTM: Given any arbitrary function of a , $l(a)$ is a non-linear function of a , and $y(a)$ which can be expressed in Taylor series about a point $a=0$ as

$$l(a) = \sum_{q=0}^{\infty} a^q \frac{1}{q!} \left[\frac{d^q}{dx^q} l(a) \right]_{a=0} \quad (3.63)$$

Transforming $l(a)$ gives,

$$L(a) = \frac{1}{q!} \left[\frac{d^q}{da^q} l(a) \right]_{a=0} \quad (3.64)$$

we express the inverse of the DTM as

$$l(a) = \sum_{q=0}^{\infty} L(q) a^q \quad (3.65)$$

The table (3.5) gives the fundamental features of the DTM. Let $C(a)$ and $D(a)$ be the arbitrary functions of a , then, $C(a)$ and $D(a)$ represent the differential transformed of $c(a)$ and $d(a)$ respectively.

Table 3.5: Some fundamental principles of the DTM

S/No	Initial Function	Transformation of the Function
2		$L(q) = \alpha C(q)$, α is a constant
1	$l(a) = c(a) \pm d(a)$	$L(q) = C(q) \pm D(q)$ $L(q) = (q+1)C(q+1)$
3	$l(a) = \frac{dr(a)}{da}$	$L(q) = (q+1)(q+2)C(q+2)$
4	$l(a) = \frac{d^2r(x)}{dx^2}$	$L(q) = (q+1)(q+2)\cdots(q+n)C(q+n)$
5	$l(a) = \frac{d^n r(a)}{da^n}$	
6	$l(a) = 1$	$L(q) = \delta(q)$ is the Kronecker delta
	$l(a) = ar(a)$	
7	$l(a) = x$	$Y(q) = \delta(q-1), \delta$
8	$l(a) = e^{(\lambda a)}$	$L(q) = \frac{\lambda^q}{q!}$

Solution of Model 1 by DTM

In this section, we solve model 1 by applying DTM by applying the steps involved in DTM. Recalled from equation (3.2) ,

$$\begin{aligned}\frac{dS}{dt} &= \theta - \mu_1 S - S(\beta(I + \gamma I_c)(1 - \phi) - \psi) \\ \frac{dI_c}{dt} &= \rho S(\beta(I + \gamma I_c)(1 - \phi) - \mu_2 I_c - \alpha(1 - \phi)I_c) \\ \frac{dI}{dt} &= (1 - \rho)(1 - \phi)S(\beta(I + \gamma I_c) + \alpha(1 - \phi)I_c) - (\mu_3 + \delta)I \\ \frac{dR}{dt} &= \psi S + \delta I - \mu_4 R\end{aligned}\tag{3.66}$$

where

$$K_2 = \alpha(1 - \phi), K_1 = K_2 + \mu_2, K_3 = \mu_3 + \delta\tag{3.67}$$

Applying the DTM properties in table 3.5 and applying them to (3.66), from the first equation,

$$\frac{dS}{dt} = \theta - \mu_1 S - S(\beta(I + \gamma I_c)(1 - \phi) - \psi)$$

this transformed to,

$$(q+1)S(q+1) = \left[\theta b(q, 0) - (1 - \phi) \sum_{l=0}^q S(l)(\beta(I_c(q-l) + \gamma I(q-l)) - (\mu_1 + \psi) S(q)) \right]$$

Dividing through by (q+1) so as to make S(q+1) the subject of the expression, we have

$$S(q+1) = \frac{1}{q+1} \left[\theta b(q, 0) - (1 - \phi) \sum_{l=0}^q S(l)(\beta(I_c(q-l) + \gamma I(q-l)) - (\mu_1 + \psi) S(q)) \right]$$

Taking the second equation of system (3.66) and applying the DTM properties (1), (2) and (5) ,

$$(q+1)I_c(q+1) = \frac{1}{q+1} \left[\rho(1 - \phi) \sum_{l=0}^q S(l)(\beta(I_c(q-l) + \gamma I(q-l)) - K_1 I_c(q)) \right]$$

Dividing through by (q+1) so as to make S(q+1) the subject of the expression

$$I_c(q+1) = \frac{1}{q+1} \left[\rho(1 - \phi) \sum_{l=0}^k S(l)(\beta(I_c(q-l) + \gamma I(q-l)) - K_1 I_c(q)) \right]$$

Similarly, the third equation transformed into

$$(k+1)I(q+1) = \left[(1-\rho)(1-\phi) \sum_{l=0}^q S(l) \beta (I_c(q-l) + \gamma I(q-l)) + K_2 I_c(q) - K_3 I(q) \right]$$

$$\Rightarrow I(q+1) = \frac{1}{q+1} \left[(1-\rho)(1-\phi) \sum_{l=0}^k S(l) \beta (I_c(q-l) + \gamma I(k-l)) + K_2 I_c(q) - K_3 I(q) \right]$$

In the same vein, the fourth equation of the system becomes

$$(q+1)R(q+1) = \left[\psi S(q) + \delta I(q) - \mu_4 R(q) \right]$$

$$\Rightarrow R(q+1) = \frac{1}{q+1} \left[\psi S(q) + \delta I(q) - \mu_4 R(q) \right]$$

Hence, transforming the system of equations governing the model in (3.66) using DTM gives

$$S(q+1) = \frac{1}{q+1} \left[\theta b(q, 0) - (1-\phi) \sum_{l=0}^q S(l) \beta (I_c(q-l) + \gamma I(q-l)) - (\mu_1 + \psi) S(q) \right]$$

$$I_c(q+1) = \frac{1}{q+1} \left[\rho(1-\phi) \sum_{l=0}^q S(l) \beta (I_c(q-l) + \gamma I(q-l)) - K_1 I_c(q) \right]$$

$$I(k+1) = \frac{1}{q+1} \left[(1-\rho)(1-\phi) \sum_{l=0}^q S(l) \beta (I_c(q-l) + \gamma I(q-l)) + K_2 I_c(q) - K_3 M(q) \right]$$

$$R(q+1) = \frac{1}{q+1} \left[\psi S(q) + \delta I(q) - \mu_4 R(q) \right]$$

Hence, by solving the proposed model upto order 5, we obtain the solution for each of the variables.

$$S(t) = \sum_{q=0}^n S(q)t^q = 60.00 + 9.99931480 \times 10^5 t - 5.7096499 \times 10^5 t^2 + 98122.20010 t^3$$

$$- 9.186204735 \times 10^8 t^4 - 3.626130222 \times 10^8 t^5 + \dots$$

$$I_c(t) = \sum_{q=0}^n I_c(q)t^q = 40 + 4.60t + 1.749891240 \times 10^5 t^2 - 30915.19266 t^3$$

$$\begin{aligned}
& + 4.593079842 \times 10^8 t^4 - 3.626130222 \times 10^8 t^5 + \dots \\
I(t) &= \sum_{q=0}^k I(q) t^q = 20 + 10.4000t + 1.749856100 \times 10^5 t^2 - 50162.88353 t^3 \\
& + 4.593079842 \times 10^8 t^4 - 3.626130222 \times 10^8 t^5 + \dots \\
R(t) &= \sum_{q=0}^n R(q) t^q = 10.00 + 31.580t + 1.499913798 t^2 - 20449.68858 t^3 \\
& - 1320.411710 t^4 + 1.378007502 \times 10^8 t^5 + \dots
\end{aligned}$$

Model 2 Solution by Differential Transform Method

Applying the operational properties in table (3.5) to the model equations in (3.5) by transforming the equations into its differential transform equivalent we have

$$K_2 = \mu + \tau, \quad K_1 = \omega + \mu, \quad K_3 = \mu + \delta_1 + \phi_1 + \gamma, \quad K_4 = \mu + \delta_2 + \phi_2, \quad K_5 = \mu + \delta_3 + \epsilon \quad (3.68)$$

$$P(q+1) = \frac{1}{q+1} \left[\tau S(q) - K_1 P(q) \right]$$

$$S(q+1) = \frac{1}{q+1} \left[\Lambda b(q, 0) + \omega P(q) - \sum_{l=0}^q S(l) \beta_{1I_u}(q-l) \beta_{2I_e}(q-l) \beta_{3T}(q-l) - K_2 S \right]$$

$$I_u(q+1) = \frac{1}{q+1} \left[(1 - \alpha) \sum_{l=0}^q S(l) \beta_{1I_u}(q-l) \beta_{2I_e}(q-l) \beta_{3T}(q-l) - K_3 I_u(q) \right]$$

$$I_e(q+1) = \frac{1}{q+1} \left[\alpha \sum_{l=0}^q S(l) \beta_{1I_u}(q-l) \beta_{2I_e}(q-l) \beta_{3T}(q-l) + \gamma I_u(q) - K_4 I_e(q) \right]$$

$$T(q+1) = \frac{1}{q+1} \left[\phi_1 I_u(q) + \phi_2 I_e(q) - K_5 T(q) \right]$$

$$R(q+1) = \frac{1}{q+1} \left[\epsilon T(q) - \mu R(q) \right]$$

$$P(1) = -44.200, P(2) = -2175.731800, P(3) = -56687.74153,$$

$$P(4) = -2.278939978 \times 10^7, P(5) = 1.467445243 \times 10^9 \dots$$

$$S(1) = -43798.400, S(2) = -1.714600444 \times 10^6, S(3) = 9.112120560 \times 10^8,$$

$$S(4) = 7.351857008 \times 10^{10}, S(5) = -2.180288358 \times 10^{13} \dots$$

$$Iu(1) = 43573.7200 \times 10^{10}, Iu(2) = 1.690468474 \times 10^6, Iu(3) = -9.049550227 \times 10^8,$$

$$Iu(4) = -7.2867056 \times 10^{10}, Iu(5) = 2.165376880 \times 10^{13} \dots$$

$$Ie(1) = 338.7600, Ie(2) = 25367.74734, Ie(3) = -6.226011593 \times 10^6,$$

$$Ie(4) = -6.646692210 \times 10^8, Ie(5) = 1.482798385 \times 10^{11} \dots$$

$$T(1) = -7.760, T(2) = 924.6823600, T(3) = 24886.17805,$$

$$T(4) = -9.520339790 \times 10^6, T(5) = -6.216417920 \times 10^8 \dots$$

$$R(1) = 23.480, R(2) = -3.219080000, R(3) = 123.4433511,$$

$$R(4) = 2484.235566, R(5) = 7.616977354 \times 10^5 \dots$$

The solution when $q = 5$ is given as

$$P(t) = \sum_{q=0}^n P(q)t^q = 100 - 44.200t - 2175.731800t^2 - 56687.74153t^3 \\ - 2.278939978 \times 10^7t^4 + 1.467445243 \times 10^9t^5 + \dots$$

$$S(t) = \sum_{q=0}^n S(q)t^q = 200 - 43798.400t - 1.714600444 \times 10^6t^2 + 9.112120560 \times 10^8t^3 \\ + 7.351857008 \times 10^{10}t^4 - 2.180288358 \times 10^{13}t^5 + \dots$$

$$Iu(t) = \sum_{q=0}^n Iu(q)t^q = 140 + 43573.7200t + 1.690468474 \times 10^6t^2 - 9.049550227 \times 10^8t^3 \\ - 7.2867056 \times 10^{10}t^4 + 2.165376880 \times 10^{13}t^5 + \dots$$

$$Ie(t) = \sum_{q=0}^n Ie(q)t^q = 120 + 338.7600t + 25367.74734t^2 - 6.226011593 \times 10^6t^3 \\ - 6.646692210 \times 10^8t^4 + 1.482798385 \times 10^5t^5 + \dots$$

$$T(t) = \sum_{q=0}^n T(q)t^q = 80 - 7.760t - 924.6823600t^2 + 24886.17805t^3$$

$$- 9.520339790 \times 10^6 t^4 - 6.216417920 \times 10^8 t^5 + \dots$$

$$R(t) = \sum_{q=0}^n R(k)t^k = 60 + 23.480t - 3.21908000t^2 + 123.4433511t^3$$

$$2484.235566t^4 - 7.616977354 \times 10^5 t^5 + \dots$$

Model 3 Solution by Differential Transform Method

Applying the operational properties in Table (3.5) to the differential equations in (3.7) we transform the equations into its differential transform equivalent as follows

$$K_2 = \mu_3 + \delta, K_1 = \alpha + \mu_2, K_3 = \mu_3 + \delta \quad (3.69)$$

$$\begin{aligned} S(q+1) &= \frac{1}{q+1} \left[\theta H(q, 0) - \sum_{l=0}^q S(l) \beta_1 I_c(q-l) + \beta_2 I(q-l) + \beta_3 W(q-l) - \mu_1 S(q) \right] \\ I_c(q+1) &= \frac{1}{q+1} \left[\rho \sum_{l=0}^q S(l) \beta_1 I_c(q-l) + \beta_2 I(q-l) + \beta_3 W(q-l) - K_1 I_c(q) \right] \\ I(q+1) &= \frac{1}{q+1} \left[(1-\rho) \sum_{l=0}^q S(l) \beta_1 I_c(q-l) + \beta_2 I(q-l) \right. \\ &\quad \left. + \beta_3 W(q-l) + \alpha I_c(k) - K_2 I(q) \right] \quad (3.70) \end{aligned}$$

$$R(q+1) = \frac{1}{q+1} \left[\delta I(q) - \mu_4 R(q) \right]$$

$$W(q+1) = \frac{1}{q+1} \left[\epsilon_1 I_c(q) + \epsilon_2 I(q) - \mu_b W(q) \right]$$

$$S(1) = 9.99811480 \times 10^{10}, S(2) = -1.570777935 \times 10^6, S(3) = 3.720184350 \times 10^5,$$

$$S(4) = -5.622311122 \times 10^9, S(5) = 1.085598330 \times 10^{10} \dots$$

$$I_c(1) = 70.0, I_c(2) = 7.498781600 \times 10^5, I_c(3) = -2.738138330 \times 10^5,$$

$$I_c(4) = 2.811183185 \times 10^9, I_c(5) = -5.629273150 \times 10^9 \dots I(1) =$$

$$83.00, I(2) = 7.498667350 \times 10^5, I(3) = -3.113041231 \times 10^5,$$

$$I(4) = 2.811202358 \times 10^9, I(5) = -5.713612288 \times 10^9 \dots$$

$$R(1) = 13.580, R(2) = 30.16082000, R(3) = 1.874652561 \times 10^5,$$

$$R(4) = -65024.53968, R(5) = 4.216822002 \times 10^8 \dots$$

$$W(1) = -24.00, W(2) = 34.63000000 \times 10^5, W(3) = 2.249614284 \times 10^5,$$

$$W(4) = -66856.80228, W(5) = 5.060150244 \times 10^8 \dots$$

Hence, when $q = 5$ the solution to the system (3.7) in closed form is obtained as

$$S(t) = \sum_{q=0}^n S(q)t^q = 60 + 9.99811480 \times 10^{10}t - 1.570777935 \times 10^6t^2 + 3.720184350 \times 10^5t^3 \\ - 5.622311122 \times 10^9t^4 + 1.085598330 \times 10^{10}t^5 + \dots$$

$$Ic(t) = \sum_{q=0}^n Ic(q)t^q = 40 + 70t + 7.498781600t^2 - 2.738138330t^3 \\ 2.8111202358 \times 10^9t^4 - 5.713612288 \times 10^9t^5 + \dots$$

$$I(t) = \sum_{q=0}^n I(q)t^q = 20 + 83t + 7.498667350 \times 10^5t^2 - 3.113041231 \times 10^5t^3 \\ - 2.811202358 \times 10^9t^4 - 5.71361228 \times 10^9t^5 + \dots$$

$$R(t) = \sum_{q=0}^n R(q)t^q = 10 + 13.580t + 30.16082000t^2 + 1.874652561 \times 10^5t^3 \\ - 65024.53968t^4 + 4.216822002 \times 10^8t^5 + \dots$$

$$W(t) = \sum_{q=0}^n W(q)t^q = 200 - 24t + 34.63000000t^2 + 2.249614284 \times 10^5t^3 \\ - 66856.80228t^4 - 5.060150244 \times 10^8t^5 + \dots$$

Graphical Illustration and Numerical Simulation of Model 1

We presents the numerical simulation of the study results in model 1 using DTM. This is accomplished by using a collection of values for parameters in table 3.6, which are primarily based on literature and assumptions. The following initial conditions are used for all our analysis and the simulation of model 1. $S(0) = 60$, $Ic(0) = 40$, $I(0) = 20$,

$R(0) = 10$. For model 2, $P(0) = 100$, $S(0) = 200$, $Iu(0) = 140$, $Ie(0) = 120$, $T(0) =$

80 and $R(0) = 20$ and for model 3, $S(0) = 60$, $I_c(0) = 40$, $I(0) = 20$, $R(0) = 10$ and $W(t) = 200$.

The DTM is demonstrated against the fourth-order Runge-Kutta procedure for the solution of model 1. Figures 3.4 to 3.7 shows the combined plots of solutions of $S(t)$, $I_c(t)$ and $R(t)$ by DTM and RK4.

Table 3.6: Model 1 parameter value

Parameters	Values	Source
μ_2	0.2	Assumed
ψ	0.3	Estimated
μ_1	0.142	Mushayabasa, (2011)
μ_3	0.2	Assumed
μ_4	0.142	Mushayabasa, (2011)
α	0.3	Isere <i>et al.</i> , (2014)
ρ	0.5	Van den Driessche <i>et al.</i> , (2002)
β	0.02	Assumed
γ	0.01	Mushayabasa, (2011)
δ	0.75	Mushayabasa, (2017)
φ	0.3	Estimated
θ	1000000	Lauria <i>et al.</i> , (2009)

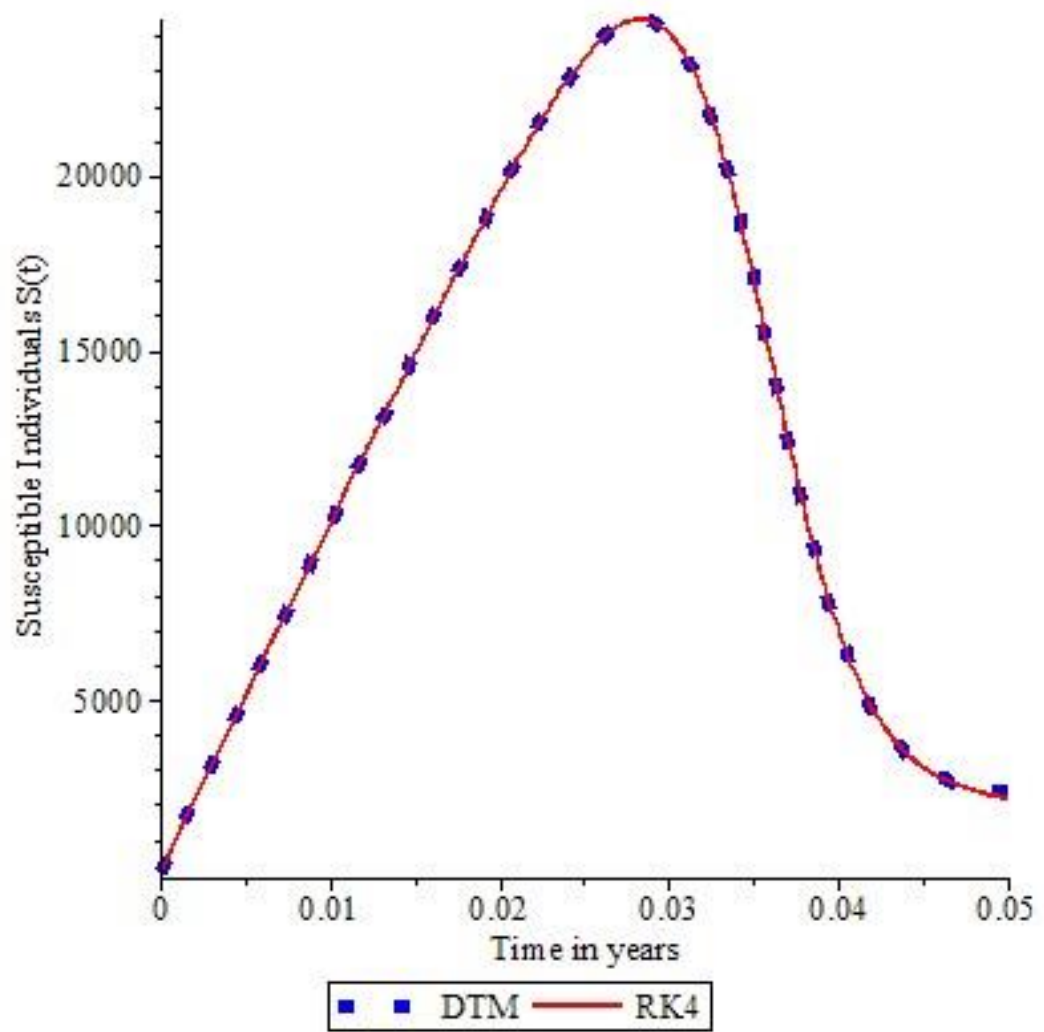


Figure 3.4: Graphical Illustration of DTM and RK4 Solution for Susceptible Class

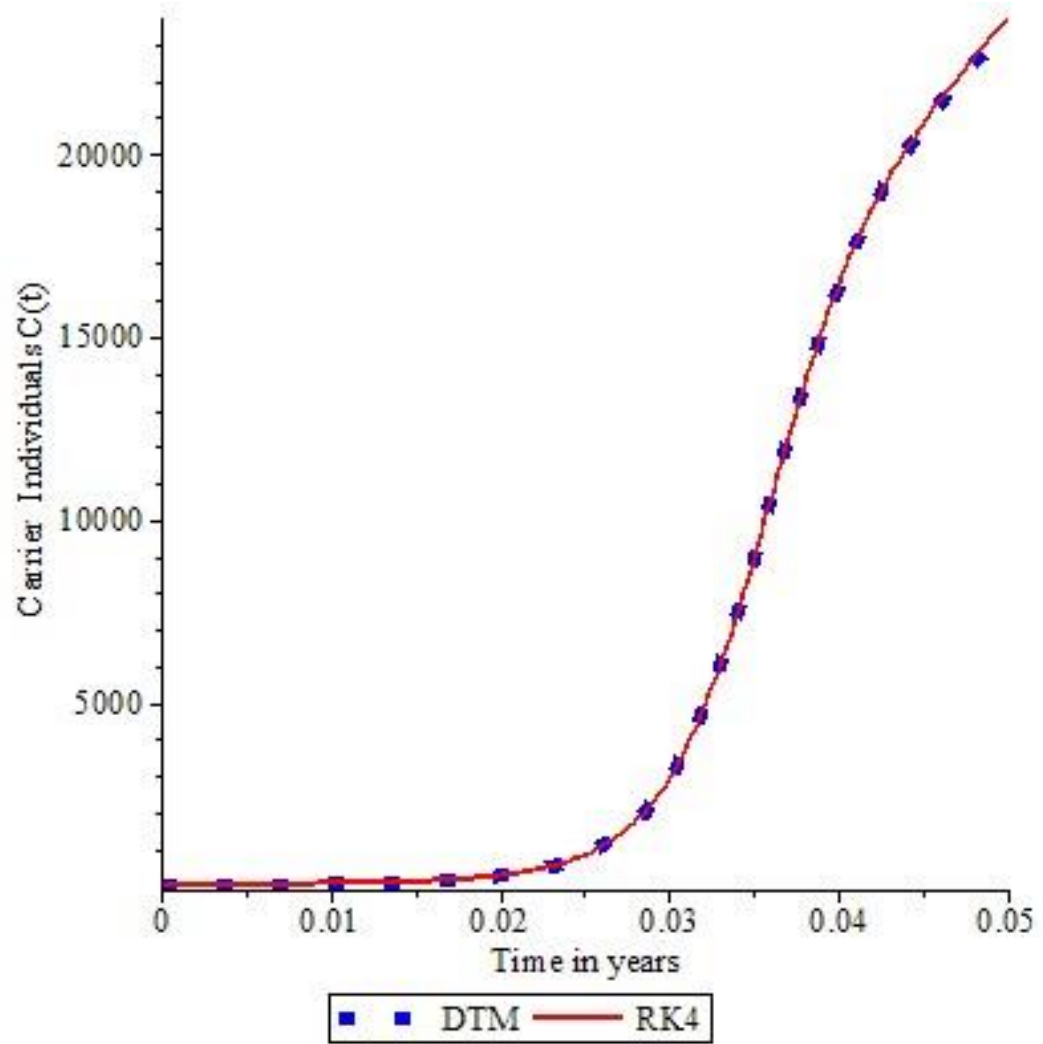


Figure 3.5: Graphical Illustration of DTM and RK4 Solution of Carrier Class

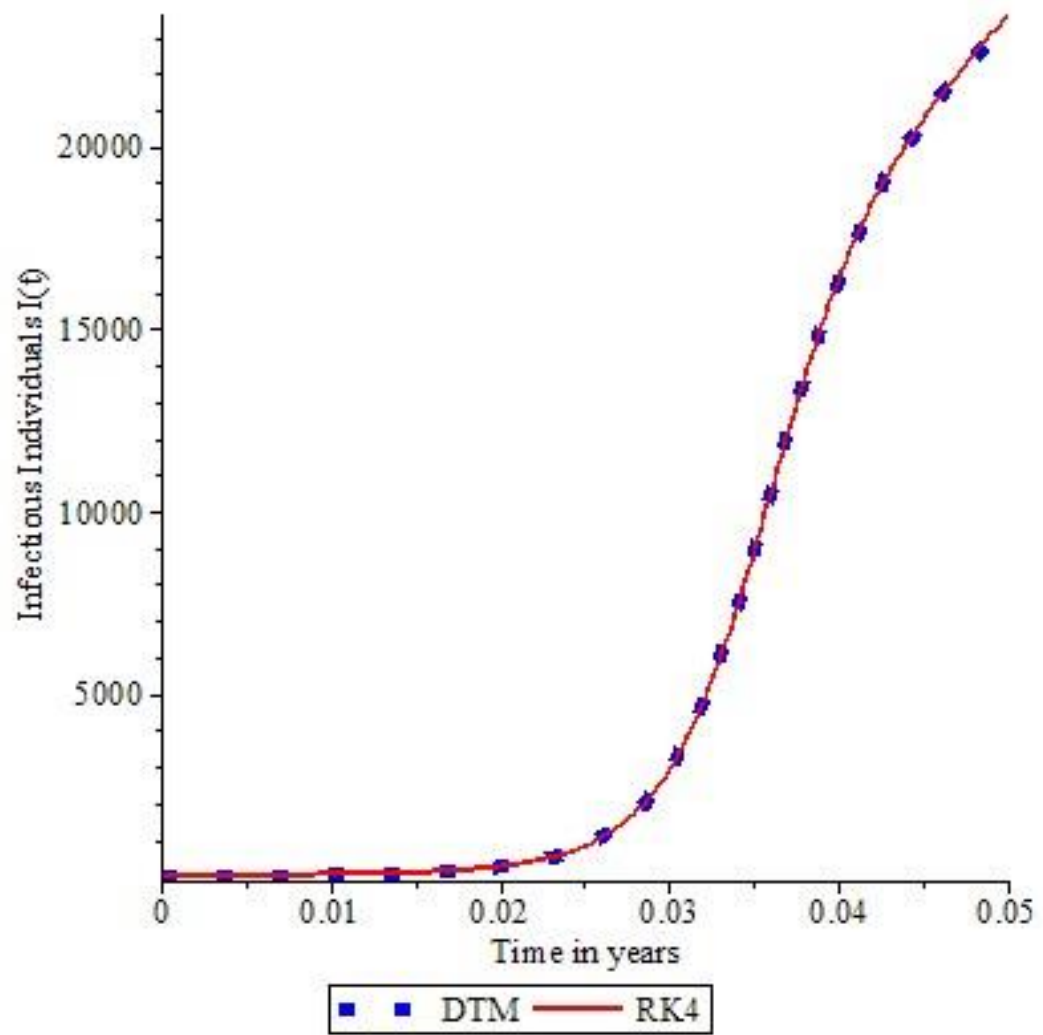


Figure 3.6: Graphical Illustration of DTM and RK4 Solution of Infected Class

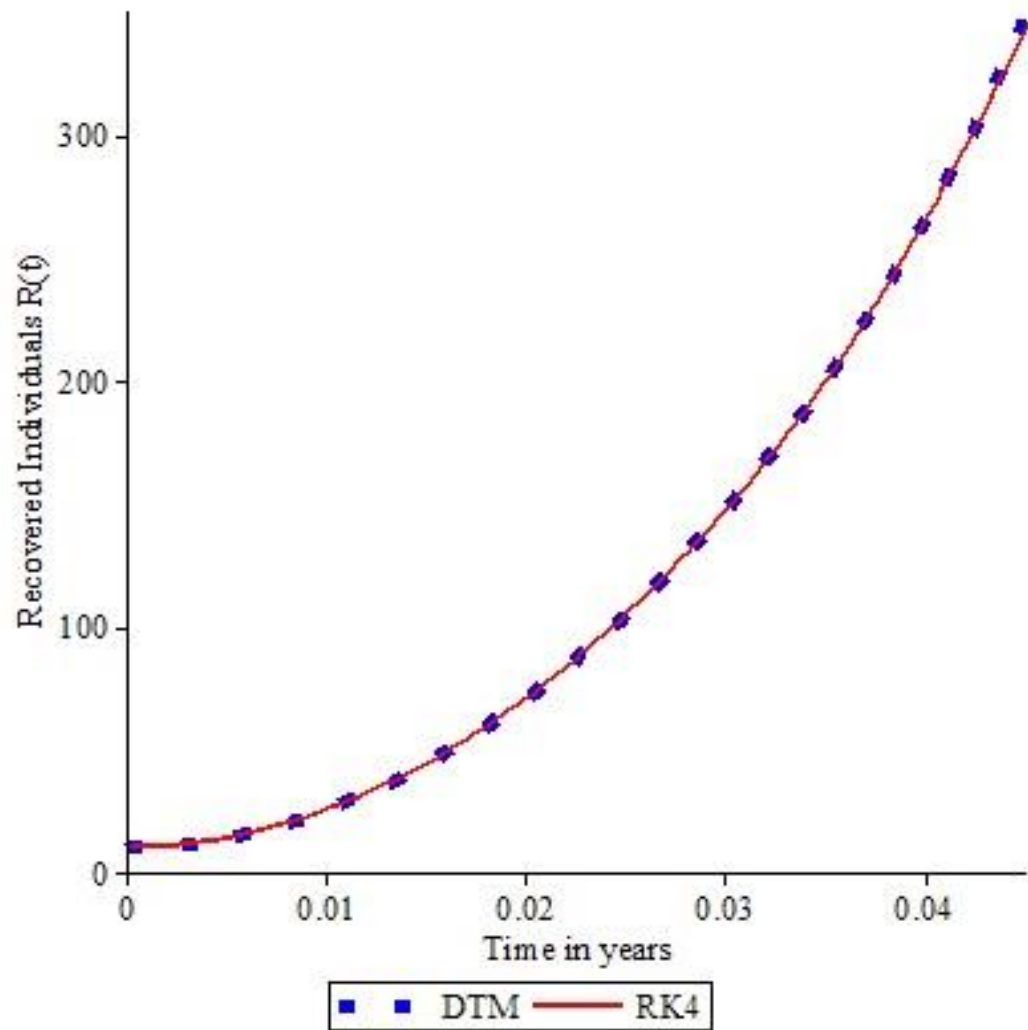


Figure 3.7: Graphical Illustration of DTM and RK4 Solution of Recovered Class Graphical Illustration of Model 2 and Numerical Simulation

Figure (3.8) to (3.13) shows the combined plots of solutions of each of the compartments for model 2.

Table 3.7: Model 2 parameter value

Parameter	Initial Value	Source
		Assumed
		Mushayabasa, (2011)
		Kariuki, C. (2004)
γ		Assumed
ω		Assumed
Λ	200	Estimated
μ	0.142	Assumed
ϵ	0.4	Kalajdziewska, D. (2011) ,
	0.6	
	0.5	
	0.1	Assumed
α	0.0072	Assumed
β_1	1.5	Lawi, (2011)
β_2	0.05	
β_3	0.05	Estimated
$\delta_1, \delta_2, \delta_3$	0.075	
ϕ_1	0.04	
ϕ_2	0.3	
τ		

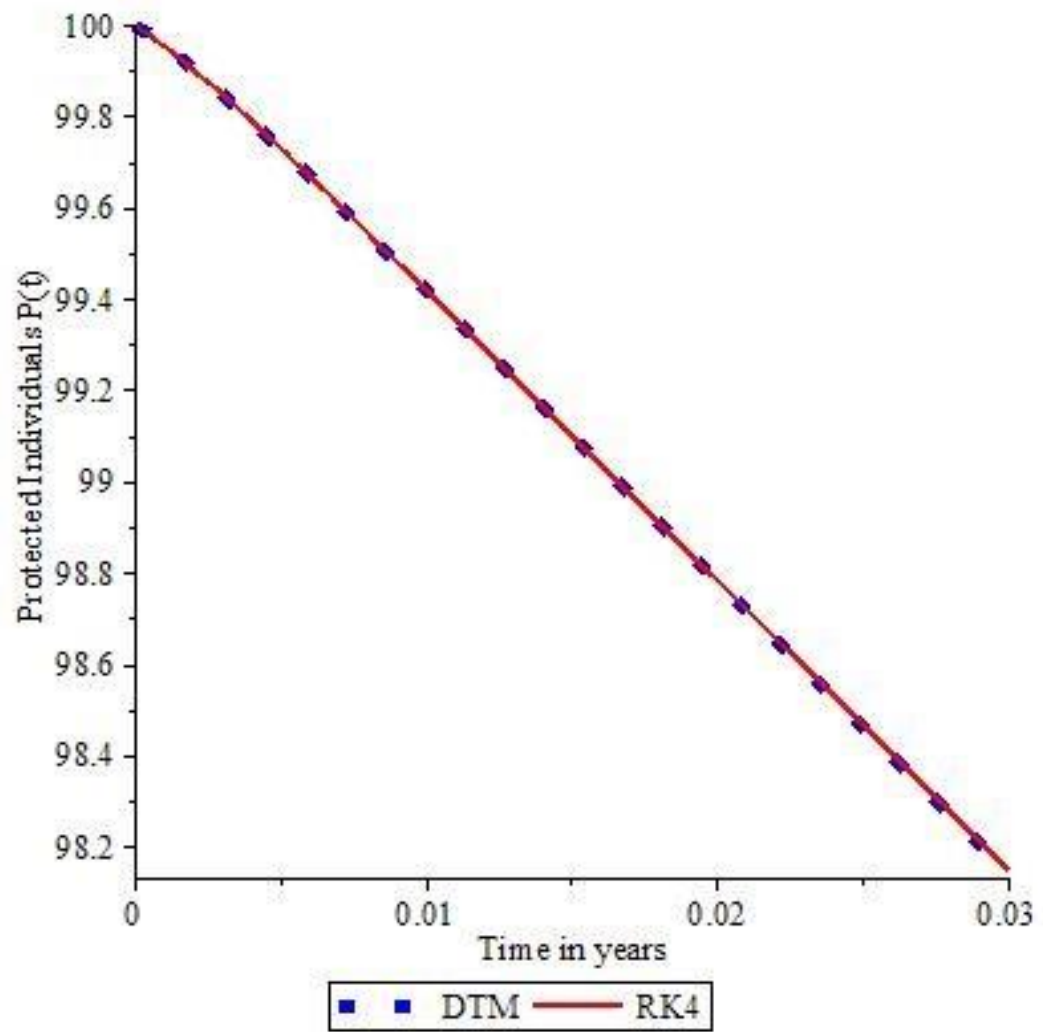


Figure 3.8: Graphical Illustration DTM and RK4 Solution of Protected Population

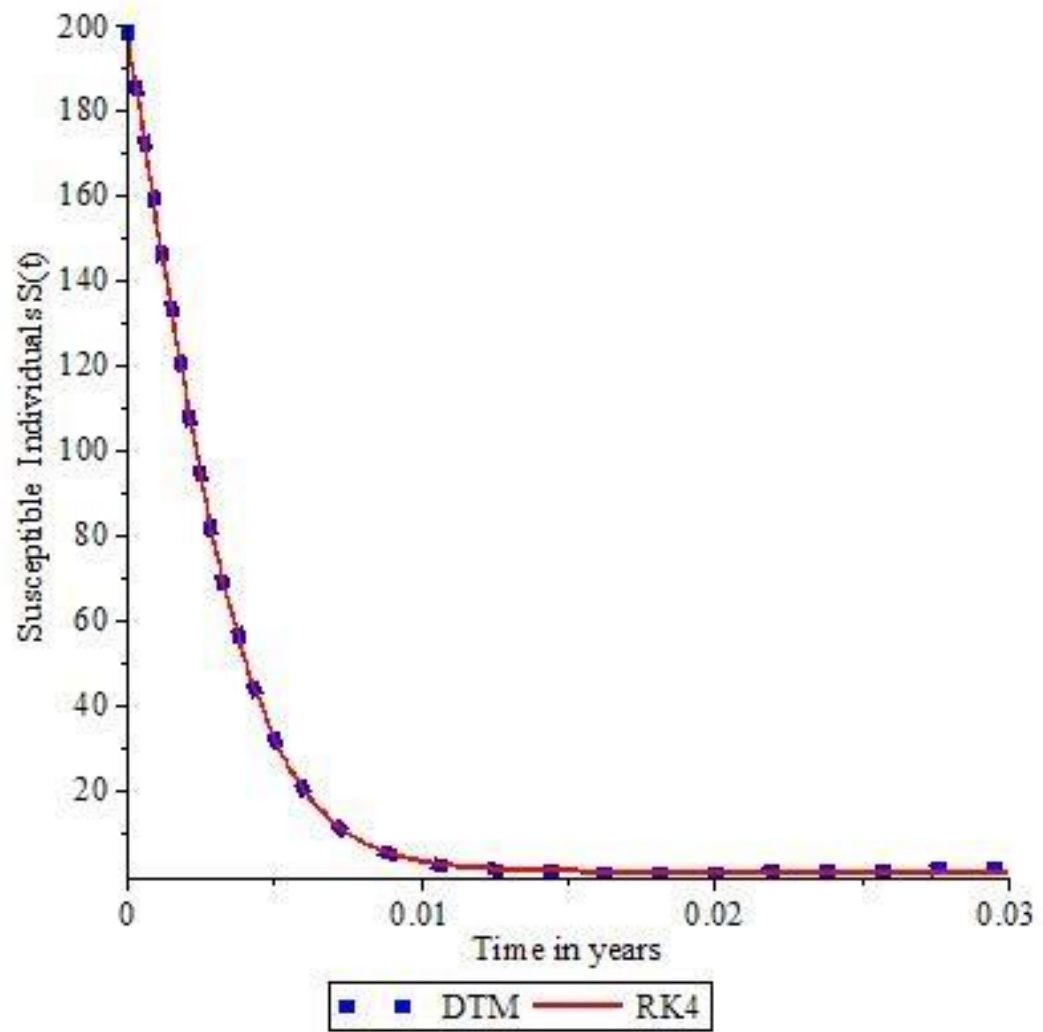


Figure 3.9: Graphical Illustration of DTM and RK4 Solution of Susceptible Population

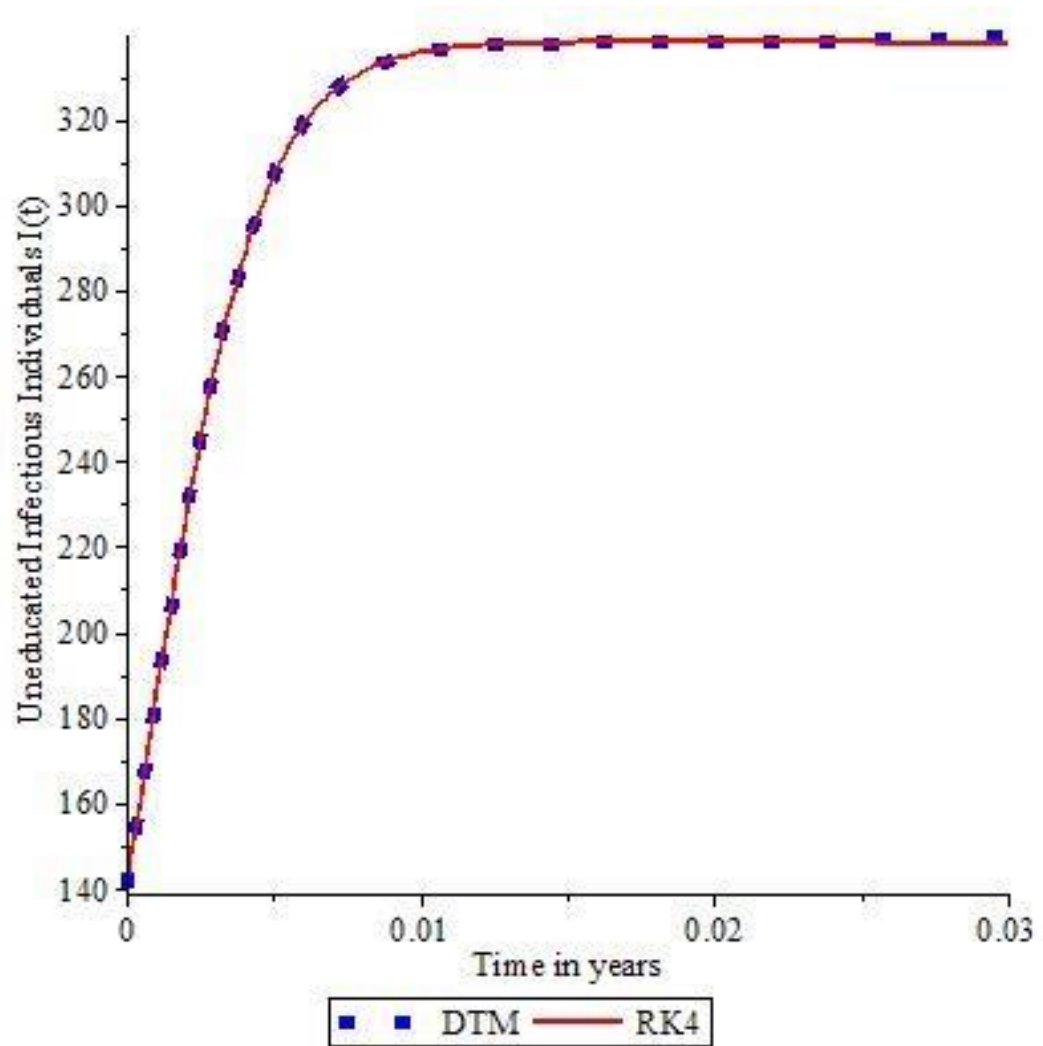


Figure 3.10: Graphical Illustration DTM and RK4 Solution of Uneducated Infectious Population

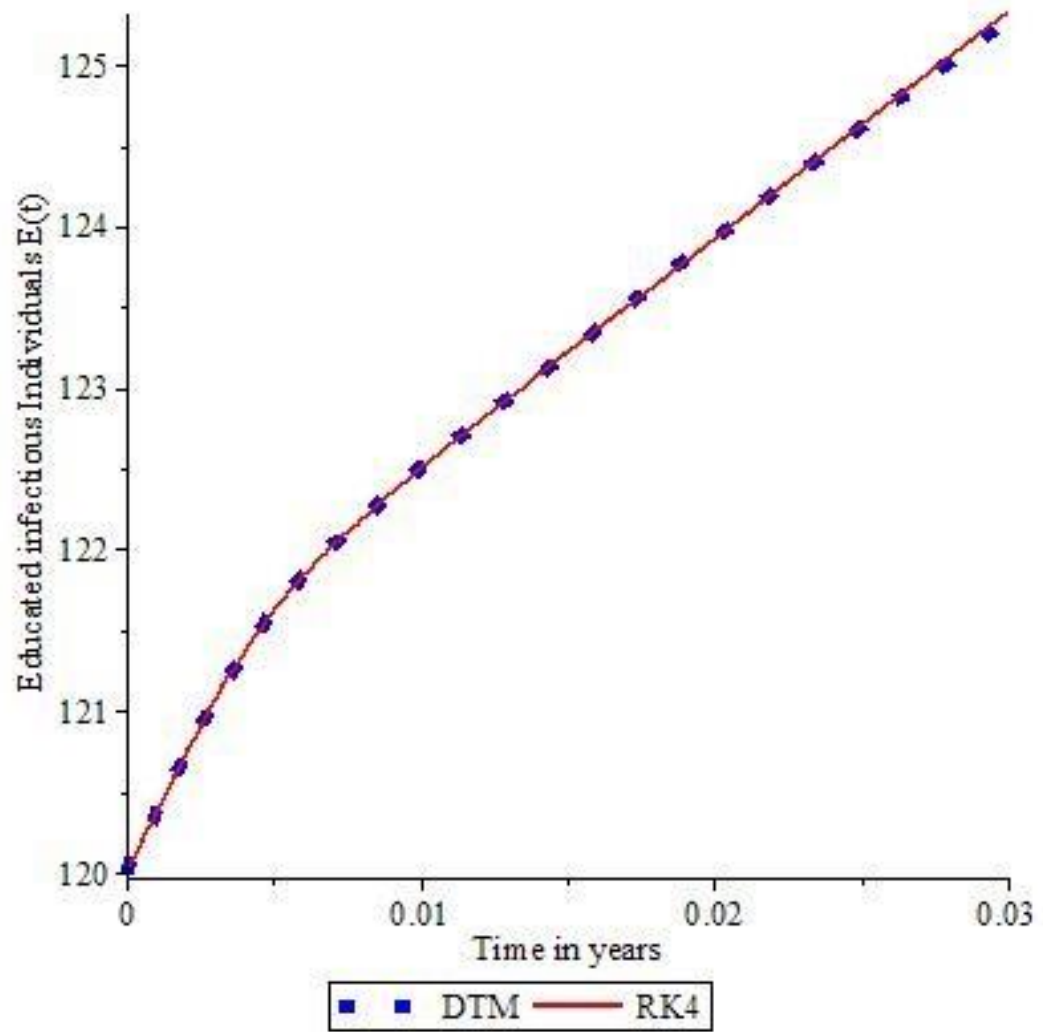


Figure 3.11: Graphical Illustration of DTM and RK4 Solution of Educated Infectious Population

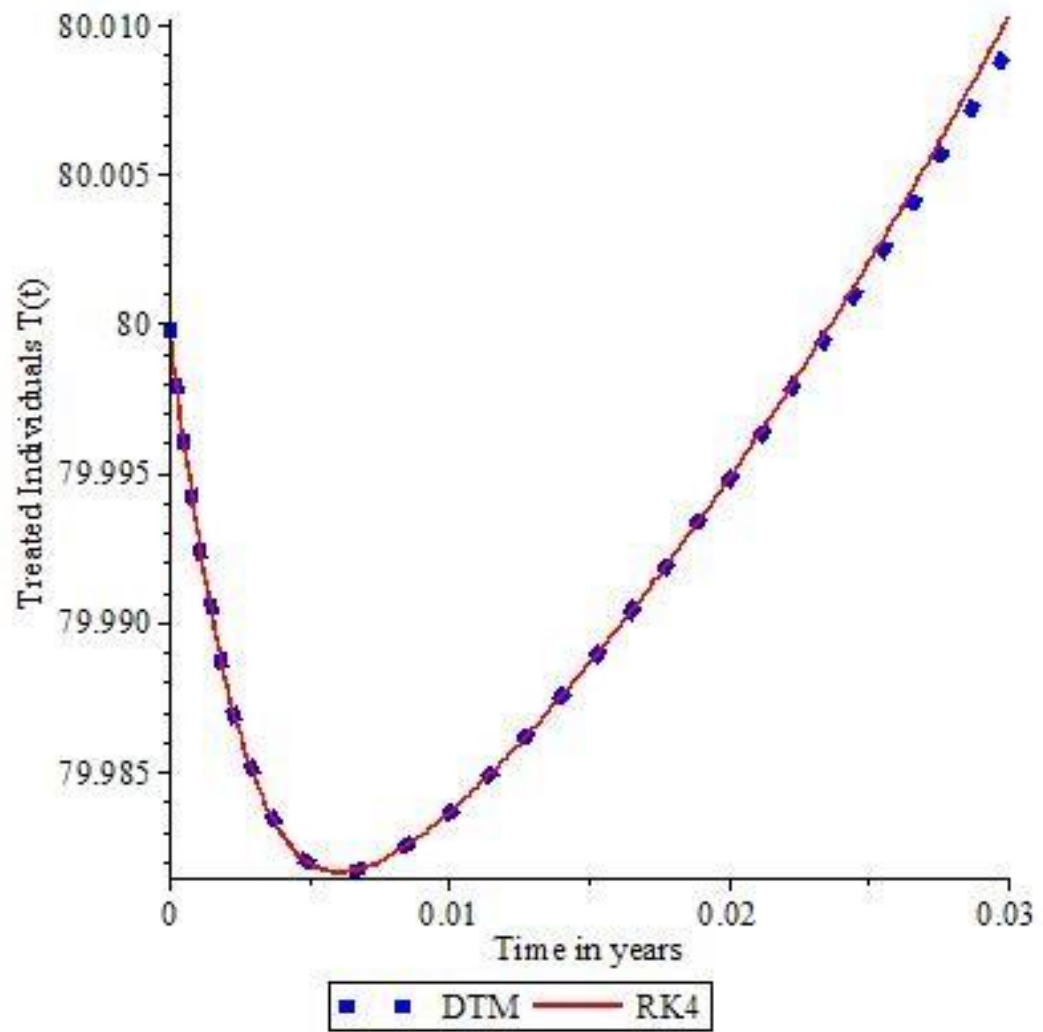


Figure 3.12: Graphical Illustration of DTM and RK4 Solution of Treated Population

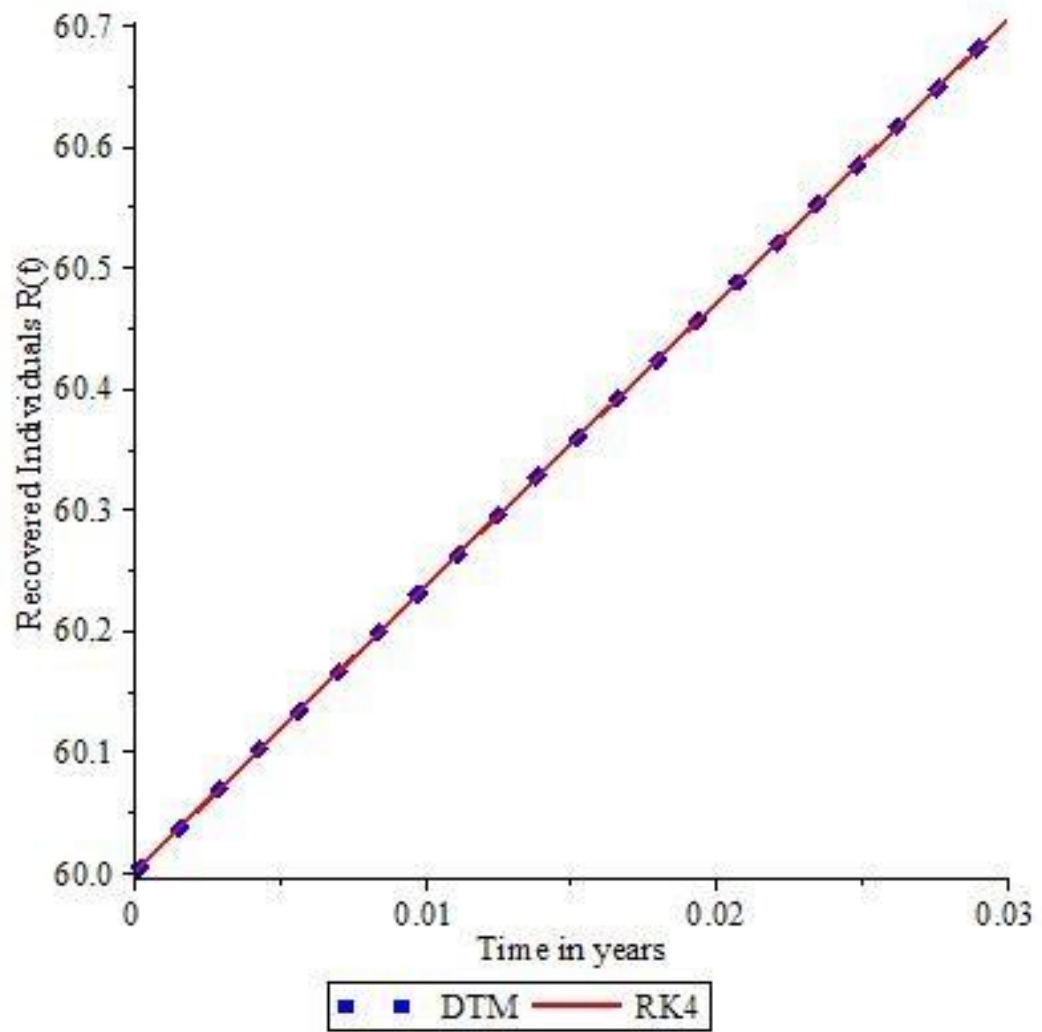


Figure 3.13: Graphical Illustration DTM and RK4 Solution of Recovered Population Graphical Illustration of Model 3 and Numerical Simulation

Figure (3.14) to (3.18) shows the combined plots of solutions of each of the compartments for model 2.

Table 3.8: Parameter value for model 3

Parameter	Value	Source
μ_2	0.2	Assumed
μ_1	0.142	Mushayabasa, (2011)
μ_3	0.2	Assumed
μ_4	0.142	Mushayabasa, (2011)
ρ	0.5	Assumed
β_1	0.02	Assumed
β_2	0.01	Assumed
β_3	0.01	Assumed
δ	0.75	Assumed
θ	1000000	Lauria <i>et al.</i> ,(2009)
ϵ_1	0.4	Estimated
ϵ_2		
μ_b	0.01	
	0.5	Estimated
		Mushayabasa, (2017)

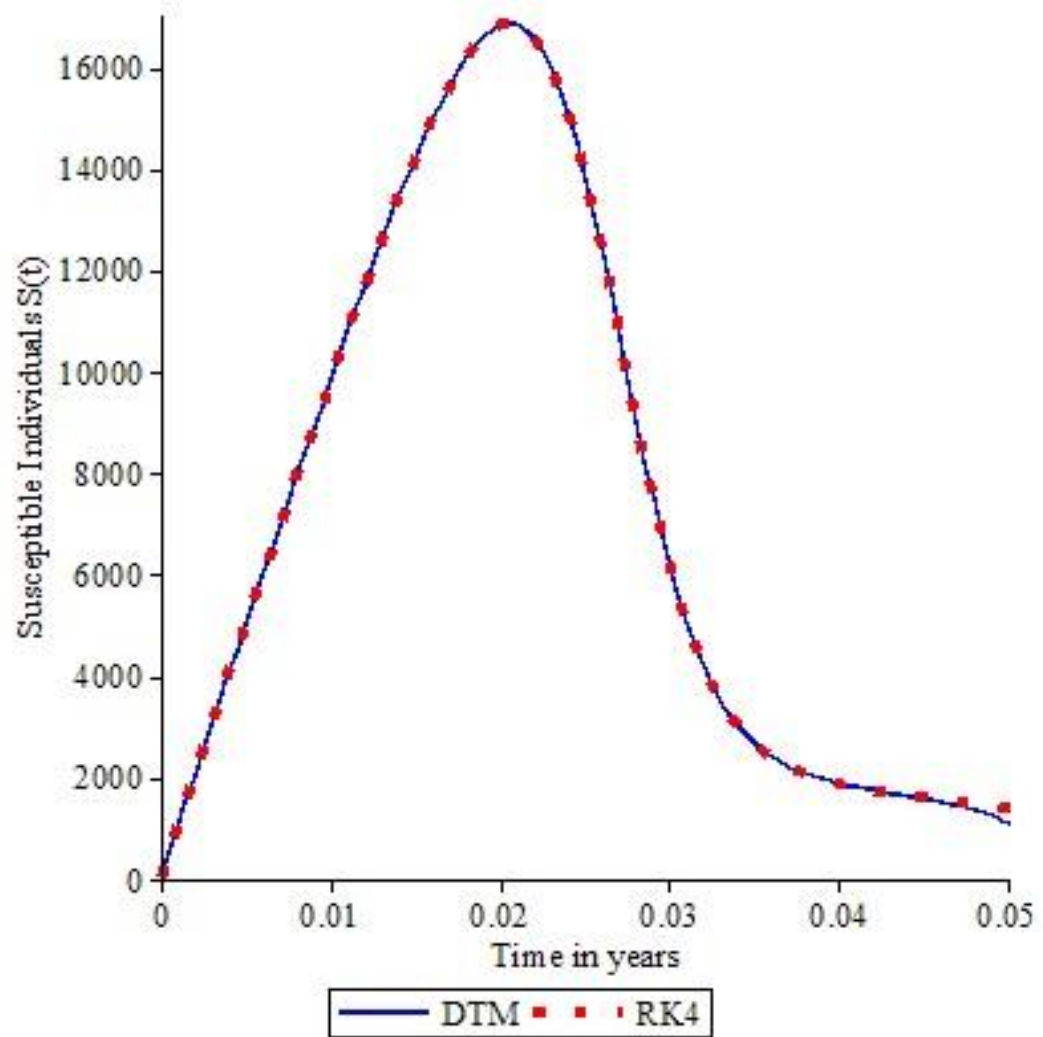


Figure 3.14: Graphical Illustration of DTM and RK4 Solution of Susceptible Population

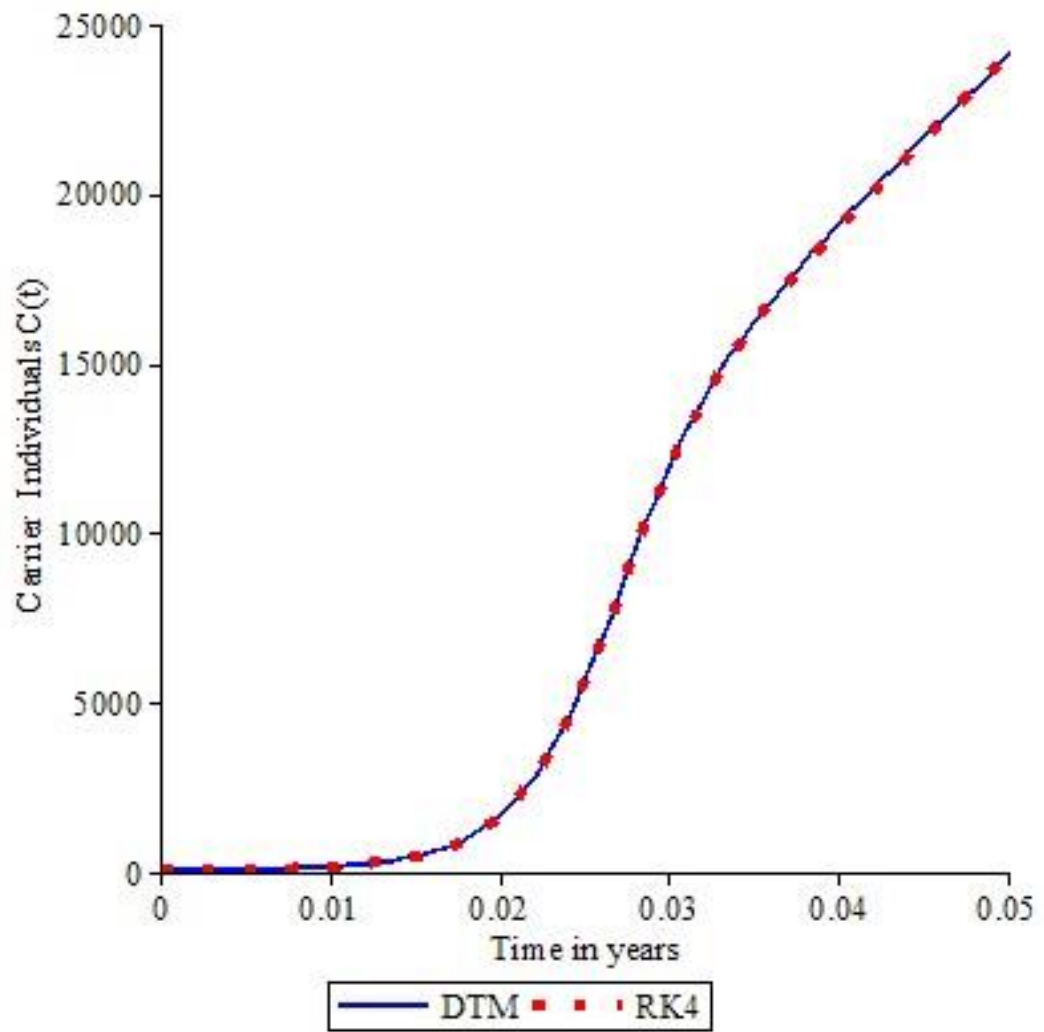


Figure 3.15: Graphical Illustration of DTM and RK4 Solution of Carrier Population

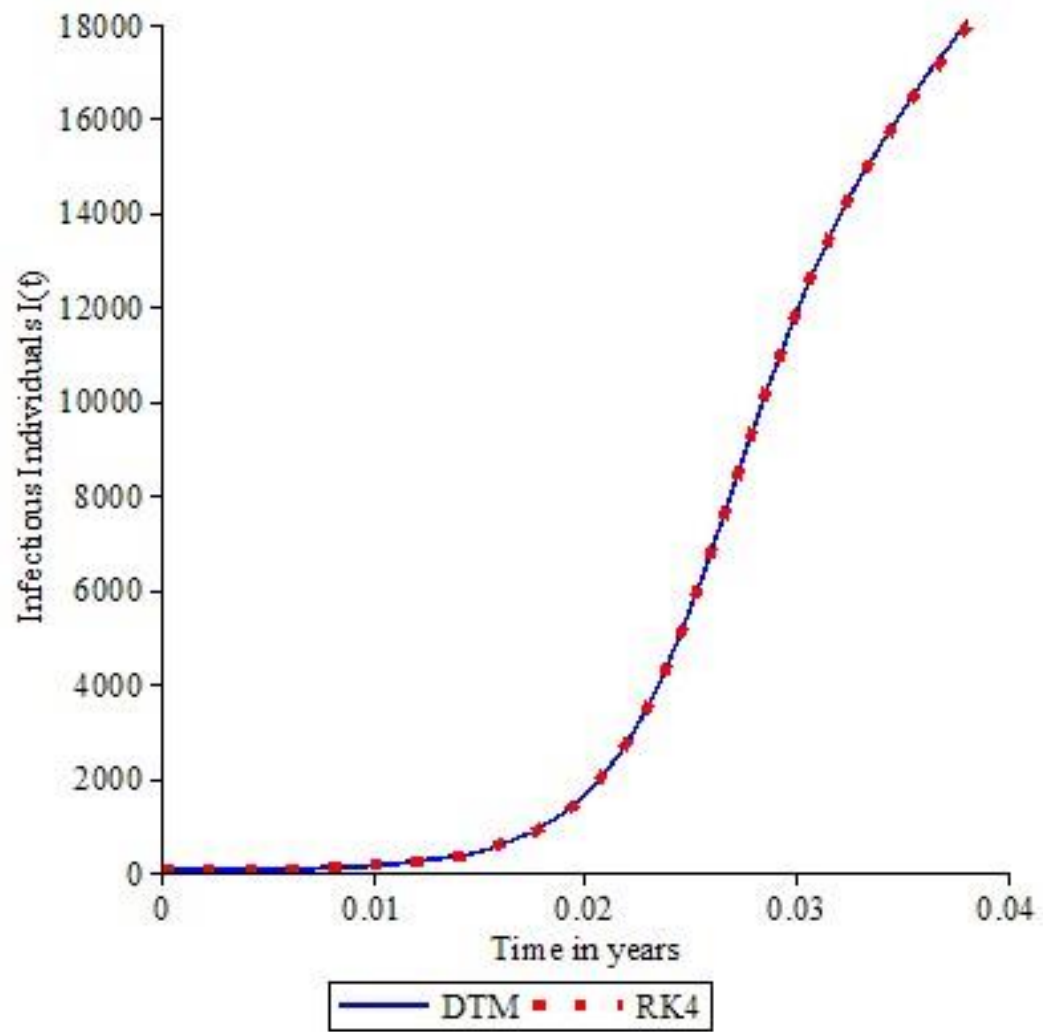


Figure 3.16: Graphical Illustration of DTM and RK4 Solution of Infected Population

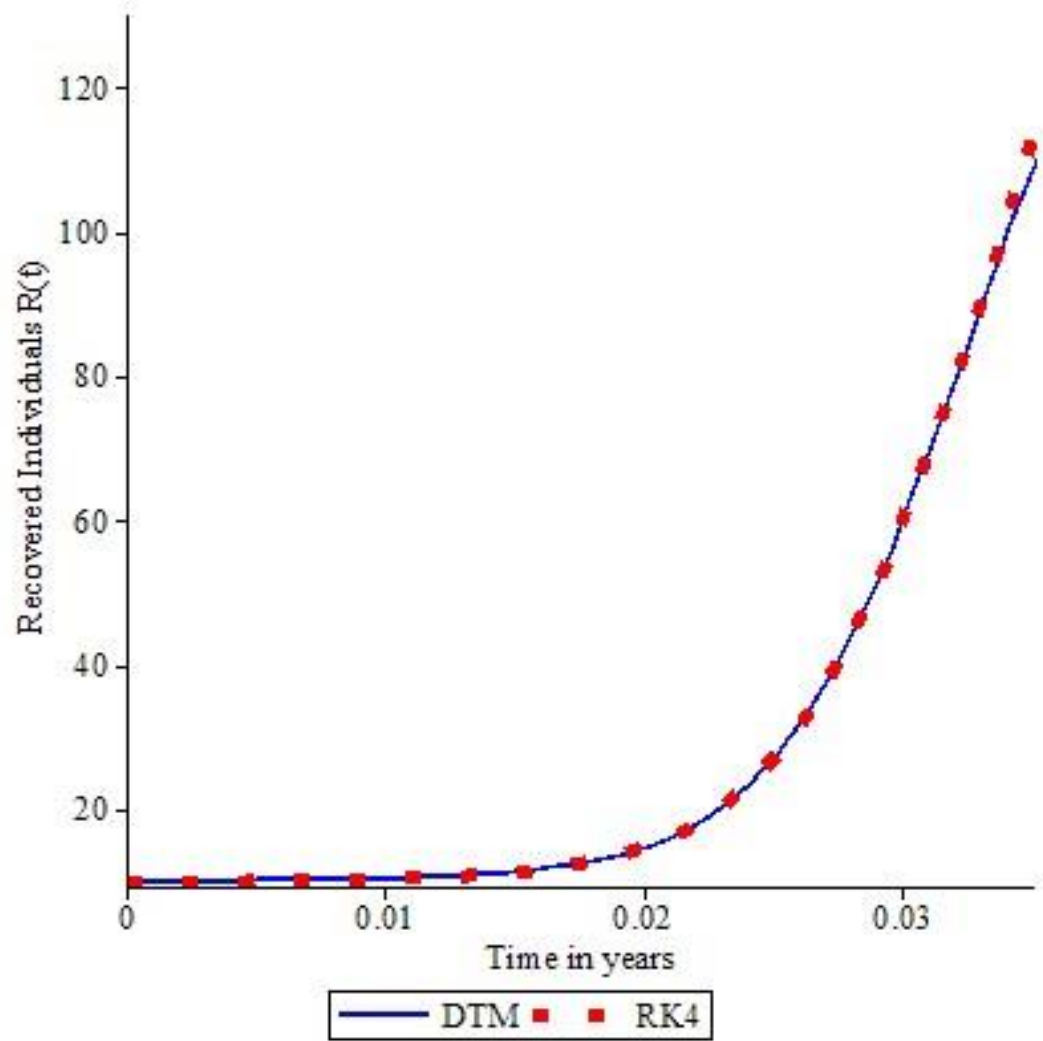


Figure 3.17: Graphical Illustration of DTM and RK4 Solution of Recovered Population

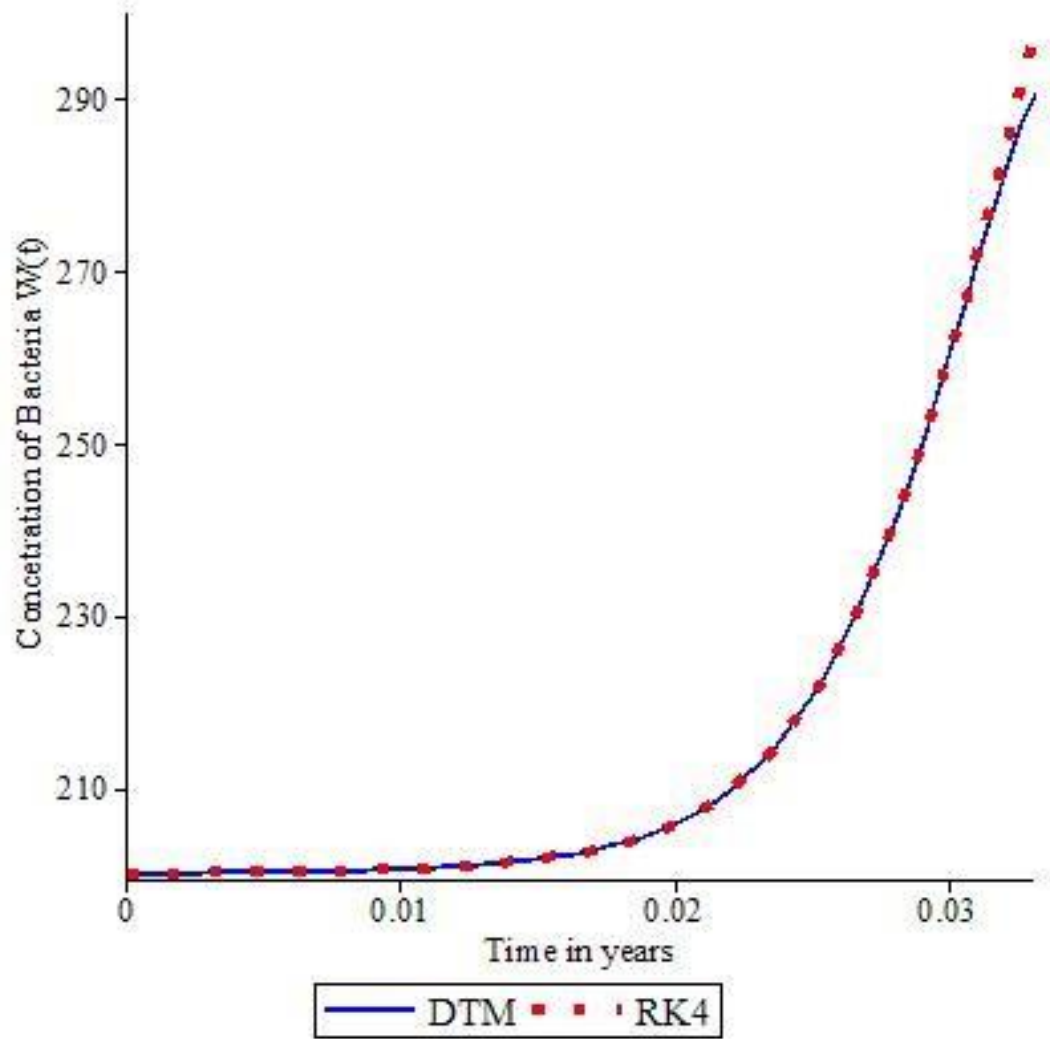


Figure 3.18: Graphical Illustration of DTM and RK4 Solution of Bacteria Population

3.8.3 Variational Iteration Method (VIM)

VIM is a semi-analytical method used for solving linear and non-linear ordinary and partial differential equations. VIM was first proposed by (He,1998). Many researchers use VIM to handle large-scale linear or nonlinear differential equations. As is often the case in applied sciences and engineering, the flexibility and adaptation provided by the method to solve non-linear equations easily and it's readily applicable in cases where the solution is unknown in advance. The VIM offers an effective algorithm for estimated theoretical solutions and numerical simulation for real-world science applications. It was successfully applied to Burgers's equation and coupled Burger's equation (Abdo and Soliman, 2005), to generalized KDV and coupled Schroedinger-KDV (Abdo and Soliman, 2005), to solve nonlinear Volterra's integro-differential equations. (Abbasbandy and Shivanian, 2009), to Helmholtz equation. (Momani and Abuasad, 2006). In this study, we use Variational Iteration Technique to solve the models and approximate the solutions in a sequence of intervals to the system of differential equations. In addition, the results obtained are compared with the fourth-order Runge-Kutta to demonstrate the precision of the VIM.

Implementation of the Method, VIM

He (1998, 1998) gave VIM's analysis as follows to explain the basic concept of the variational iteration method: we consider the differential equation (DE) of the form:

$$Ay + By = c(x) \quad (3.71)$$

A , B and $c(x)$ represents non-linear operator, linear operator and non-homogeneous term respectively. With reference to He (1998), the correctional function is defined as:

$$y_{m+1}(x) = y_m(x) + \int_0^x \lambda \{Ay_m(s) + B\tilde{y}_m(s) - c(s)\} ds \quad (3.72)$$

where λ is a Lagrangian multiplier expressed as:

$$\lambda(\eta) = \frac{(-1)^m}{(m-1)!} (\eta - t)^{m-1} \quad (3.73)$$

m represents highest power of the DE, $\tilde{y}_m$ is classified as unrestricted variation.

Application of VIM to Model 1

Using the approach of (Rao, 2012) and (Peter and Ibrahim, 2019), we presents the model's numerical approximation using variational iteration method as follows: consider the equations governing model 1 in (3.2)

$$\begin{aligned} \frac{dS}{dt} &= \theta - \mu_1 S - S(I + \gamma I_c)(1 - \phi) - \psi S \\ \frac{dI_c}{dt} &= \rho S(I + \gamma I_c)(1 - \phi) - \mu_2 I_c - \alpha(1 - \phi)I_c \\ \frac{dI}{dt} &= (1 - \rho)(1 - \phi)S(I + \gamma I_c) + \alpha(1 - \phi)I_c - (\mu_3 + \delta)I \\ \frac{dR}{dt} &= \psi S + \delta I - \mu_4 R \end{aligned} \quad (3.74)$$

Hence, transforming each equations in (3.74)

$$\begin{aligned}
S_{m+1}(t) &= S_m(t) + \int_0^t \lambda_1(y) \left\{ \frac{dS_m(y)}{dy} - \theta + (\mu_1 + \psi) \tilde{S}_m(y) + \tilde{S}_m(x) \tilde{I}_{mc}(y) + \gamma \tilde{I}_m(y) \right\} (1 - \phi) dy \\
I_{c_{m+1}}(t) &= I_{c_m}(t) + \int_0^t \lambda_2(y) \left\{ \frac{dI_{c_m}(y)}{dy} - \rho \tilde{S}_m(y) \right\} I_{c_m}(x) + \gamma \tilde{I}_m(y) (1 - \phi) + (\mu_2 + \alpha(1 - \phi)) \tilde{I}_c, \\
I_{m+1}(t) &= I_m(t) + \int_0^t \lambda_3(y) \left\{ \frac{dI_m(y)}{dy} - (1 - \rho) S_m(y) \right\} I_{c_n}(y) + \gamma \tilde{I}_m(y) (1 - \phi) \\
&\quad - \alpha(1 - \phi) \tilde{I}_{c_n}(y) + (\mu_3 + \delta) \tilde{I}_m(y) \} dy \\
R_{m+1}(t) &= R_m(t) + \int_0^t \lambda_4(y) \left\{ \frac{dR_m(y)}{dy} - \psi \tilde{S}_m(y) - \delta \tilde{I}_m(y) + \mu_4 \tilde{R}_m(y) \right\} dy
\end{aligned} \tag{3.75}$$

Where

$\lambda_i; i = 1, 2, 3, 4$ are presented in (3.73) and is defined as

$$\lambda_i(s) = \frac{(-1)^m}{(m-1)!} (s-t)^{m-1} \tag{3.76}$$

Using $m = 1$ in (3.76)

$$\lambda_i(s) = -1 \tag{3.77}$$

The correctional function is given as,

$$\begin{aligned}
S_{m+1}(t) &= S_m(t) + \int_0^t \lambda_1(y) \left\{ \frac{dS_m(y)}{dy} - \theta + (\mu_1 + \psi) \tilde{S}_m(y) + \tilde{S}_m(x) \tilde{I}_{mc}(y) + \gamma \tilde{I}_m(y) \right\} (1 - \phi) dy \\
I_{c_{m+1}}(t) &= I_{c_m}(t) + \int_0^t \lambda_2(y) \left\{ \frac{dI_{c_m}(y)}{dy} - \rho \tilde{S}_m(y) \right\} I_{c_m}(x) + \gamma \tilde{I}_m(y) (1 - \phi) + (\mu_2 + \alpha(1 - \phi)) \tilde{I}_c, \\
I_{m+1}(t) &= I_m(t) + \int_0^t \lambda_3(y) \left\{ \frac{dI_m(y)}{dy} - (1 - \rho) S_m(y) \right\} I_{c_n}(y) + \gamma \tilde{I}_m(y) (1 - \phi) \\
&\quad - \alpha(1 - \phi) \tilde{I}_{c_n}(y) + (\mu_3 + \delta) \tilde{I}_m(y) \} dy \\
R_{m+1}(t) &= R_m(t) + \int_0^t \lambda_4(y) \left\{ \frac{dR_m(y)}{dy} - \psi \tilde{S}_m(y) - \delta \tilde{I}_m(y) + \mu_4 \tilde{R}_m(y) \right\} dy
\end{aligned} \tag{3.78}$$

Using the initial conditions for model 1, we compute the iterated values below with the help of Maple 18 and values of parameters in table 3.6

$$\begin{aligned}
S(t) &= 60 + 9.999314800E5t - 5.709649913E5t^2 + 98122.20018t^3 - 9.186204736E8t^4 \\
&\quad + 6.7044721041E8t^5 - 1.607576737E12t^6 + 1.754334627E12t^7 - 5.027472145E11t^8 + \dots \\
I_c(t) &= 40 + 4.600000000t + 1.749891240E5t^2 - 30915.19268t^3 + 4.593078842E8t^4 \\
&\quad - 3.322965522E8t^5 + 8.037875054E11t^6 - 8.771674817E11t^7 + 2.513736010E11t^8 + \dots
\end{aligned}$$

$$I(t) = 20 + 10.4000000t + 1.749856100E5t^2 - 50162.88357t^3 + 4.593151063E8t^4 \\ - 3.626099520E8t^5 + 8.037964045E11t^6 - 8.771657444E11t^7 + 2.513736657E11t^8 + \dots$$

$$R(t) = 10 + 31.58000000t + 1.499913798E5t^2 - 20449.68861t^3 - 1320.411713t^4 + \\ 1.378007502E7t^5 - 1.212873460E7t^6 + 1.722497954E10t^7 - 1.644672601E10t^8 + \dots$$

Solution of Model 2 Using Variational Iteration Method

We present the analysis of model 2 using variation iteration method. We obtain the correctional function according to the same approach in (3.75) and (3.78), this is obtain

as,

$$P_{n+1}(t) = P_n(t) - \int_0^t \left\{ \frac{dP_m(y)}{dy} - \tau \tilde{S}_n(y) + (\mu + \omega) \tilde{P}_n(y) \right\} dy \\ S_{n+1}(t) = S_n(t) - \int_0^t \left\{ \frac{dS_m(y)}{dy} - \Lambda + \tilde{S}_n(y) \beta_1 \tilde{I}u_n(y) + \beta_2 \tilde{I}e_n(y) \right. \\ \left. + \beta_3 \tilde{T}_n(y) \right\} - \omega \tilde{P}_n(x) + (\tau + \mu) \tilde{S}_n(y) \} dy \\ Iu_{n+1}(t) = P_n(t) - \int_0^t \left\{ \frac{dIu_m(y)}{dy} - (1 - \alpha) \tilde{S}_n(y) \beta_1 \tilde{I}u_n(y) + \beta_2 \tilde{I}e_n(y) + \beta_3 \tilde{T}_n(y) \right. \\ \left. + (\mu + \delta_1 + \phi_1 + \gamma) \tilde{I}u_n(y) \right\} dy \\ Ie_{n+1}(t) = Ie_n(t) - \int_0^t \left\{ \frac{dIe_m(y)}{dy} - \alpha \tilde{S}_n(y) \beta_1 \tilde{I}u_n(x) + \beta_2 \tilde{I}e_n(y) + \beta_3 \tilde{T}_n(y) \right. \\ \left. + (\mu + \delta_2 + \phi_2) \tilde{I}e_n(y) - \gamma \tilde{I}u_n(y) \right\} dy \\ T_{n+1}(t) = T_n(t) - \int_0^t \left\{ \frac{dT_m(y)}{dy} - \phi_1 \tilde{I}u_n(y) - \phi_2 \tilde{I}e_n(y) + (\mu + \delta_3 + \phi_2 + \epsilon) \tilde{T}_n(y) \right\} dy \\ R_{n+1}(t) = R_n(t) - \int_0^t \left\{ \frac{dR_m(y)}{dy} - \epsilon \tilde{T}_n(y) + \mu \tilde{R}_n(y) \right\} dy \quad (3.79)$$

Using the initial conditions for model 2, we compute the iterated values below with the help of Maple 18 and values of parameters in table 3.7

$$P(t) = 100 - 44.2000000t - 2175.7310000t^2 - 56687.51841t^3 - 2.27568225098E6t^4 \\ + 1.46744524364E7t^5 + 1.527193960E11t^6 + 1.598091572E13t^7 - 2.953722158E15t^8$$

$$S(t) = 200 - 43798.40000t - 1.698452544E6t^2 + 9.108991502E8t^3 + 7.267992427E10t^4 \\ - 2.180764807E13t^5 - 2.666053569E15t^6 + 5.625407064E17t^7 + 5.477821969E19t^8$$

$$\begin{aligned}
I_u(t) = & 140 + 43468.72000t + 1.658170076E6t^2 - 9.050512703E8t^3 - 7.186470388E10t^4 \\
& + 2.166934658E13t^5 + 2.641735902E15t^6 - 5.586361152E17t^7 - 5.435293503E19t^8 \\
I_e(t) = & 120 + 257.7600000t + 25153.87584t^2 - 6.235846742E10E6t^3 - 6.575916293E8t^4 \\
& + 1.484376144E11t^5 + 2.155059323E13t^6 - 3.983302966E15t^7 - 4.086017314E17t^8 \\
T(t) = & 80 - 7.7600000t + 924.6823600t^2 + 24887.07634t^3 - 9.521970628E6t^4 \\
& - 6.196543924E8t^5 + 1.6746293363E11t^6 + 4.763620483E12t^7 - \\
& 1.00964891710E15t^8 \\
R(t) = & 60 + 23.48000000t - 3.219080000t^2 + 121.543311t^3 + 2439.392484t^4 - \\
& 7.618269290E5t^5 \\
& - 4.129142252E7t^6 + 9.569310646E9t^7 + 2.381810241E11t^8
\end{aligned}$$

Model 3 Solution Using Variational Iteration Method

By using the same approach in (3.75) and (3.78), the correctional function is obtained

as:

$$\begin{aligned}
S_{m+1}(t) = & S_m(t) - \int_0^t \left\{ \frac{dS_m(y)}{dy} - \theta + \mu_1 \tilde{S}_m(x) + \tilde{S}_n(y) \right. \\
& \left. + \beta_1 \tilde{I}_m(x) + \beta_2 \tilde{I}_m(y) \right. \\
& \left. + \beta_3 \tilde{W}_m(y) \right\} dy \\
I_{C_{m+1}}(t) = & I_{C_m}(t) - \int_0^t \left\{ \frac{dI_{C_m}(y)}{dy} - \rho S_m(x) \right. \\
& \left. + (\mu_2 + \epsilon_1) \tilde{I}_{C_n}(y) \right\} dy \\
I_{m+1}(t) = & I_m(t) - \int_0^t \left\{ \frac{dI_m(y)}{dy} - (1 - \rho) \tilde{S}_m(x) \right. \\
& \left. + (\mu_3 + \delta + \epsilon_2) \tilde{I}_n(y) \right\} dy \\
R_{m+1}(t) = & R_m(t) - \int_0^t \left\{ \frac{dR_m(y)}{dy} - \delta \tilde{I}_n(y) + \mu_4 \tilde{R}_m(y) \right\} dy \\
W_{m+1}(t) = & W_m(t) - \int_0^t \left\{ \frac{dW_m(y)}{dy} - \epsilon_1 \tilde{I}_{C_m}(y) - \epsilon_2 \tilde{I}_n(y) + \mu_b \tilde{W}_m(y) \right\} dy
\end{aligned} \tag{3.80}$$

Using the initial conditions for model 3, we compute the iterated values below with the help of Maple 18 and values of parameters in table 3.8

$$S(t) = 60 + 9.9981148001E5t - 1.570768935E6t^2 - 3.720184350E5t^3 - 5.622348246E9t^4$$

$$\begin{aligned}
& + 1.165524202E10t^5 - 1.405574263E13t^6 + 4.748083674E13t^7 - 3.003632145E13t^8 \\
I_c(t) = & 40 + 69t + 7.498713600E5t^2 - 3.117984559E5t^3 - 2.811218064E9t^4 \\
& - 6.085091149E9t^5 + 7.028058272E12t^6 - 2.374023676E12t^7 + 1.501819281E13t^8 \\
I(t) = & 20 + 81t + 7.498469350E5t^2 - 3.11612502025E5t^3 - 2.811369197E9t^4 \\
& - 6.562908640E9t^5 + 7.028405241E12t^6 - 2.373989970E13t^7 + 1.501825235E13t^8 \\
R(t) = & 10 + 13.58000000t + 21.91082000t^2 + 1.874606966E5t^3 - 1.118892677E5t^4 \\
& + 4.216098798E8t^5 - 3.061495037E8t^6 - 2.973999923E8t^7 - 5.253487415E7t^8 \\
W(t) = & 200 - 24t + 34.33000000t^2 + 2.249572427E5t^3 - 1.055985140E5t^4 \\
& + 5.059401508E8t^5 - 3.673794045E8t^6 - 3.568799909E8t^7 - 6.304184899E7t^8
\end{aligned}$$

Graphical Illustration of Model 1 and Numerical Simulation

Figures 3.19 to 3.22 shows the combined plots of the solutions of $S(t), I_c(t), I(t)$ and $R(t)$ by VIM and RK4

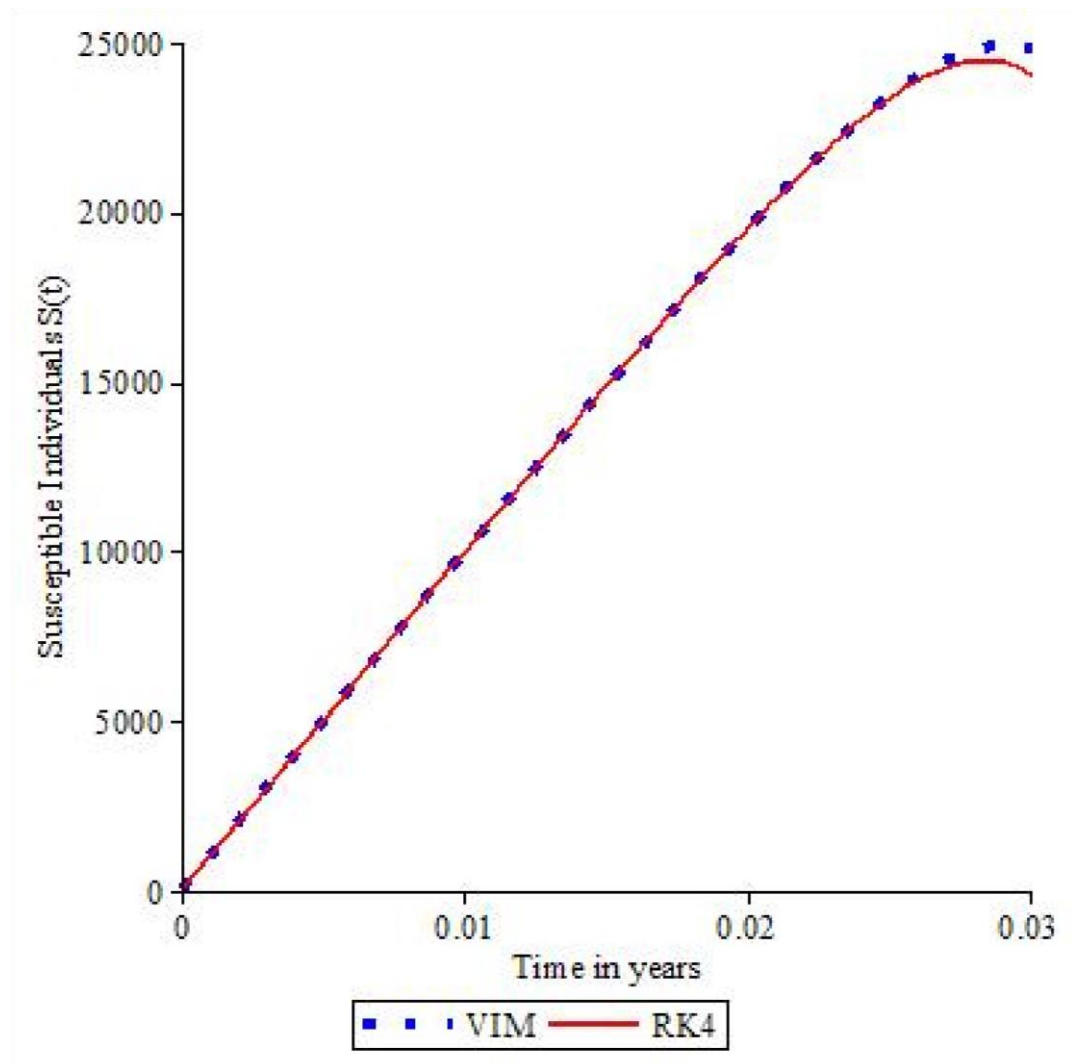


Figure 3.19: Graphical Illustration of VIM and RK4 Solution of Susceptible Class

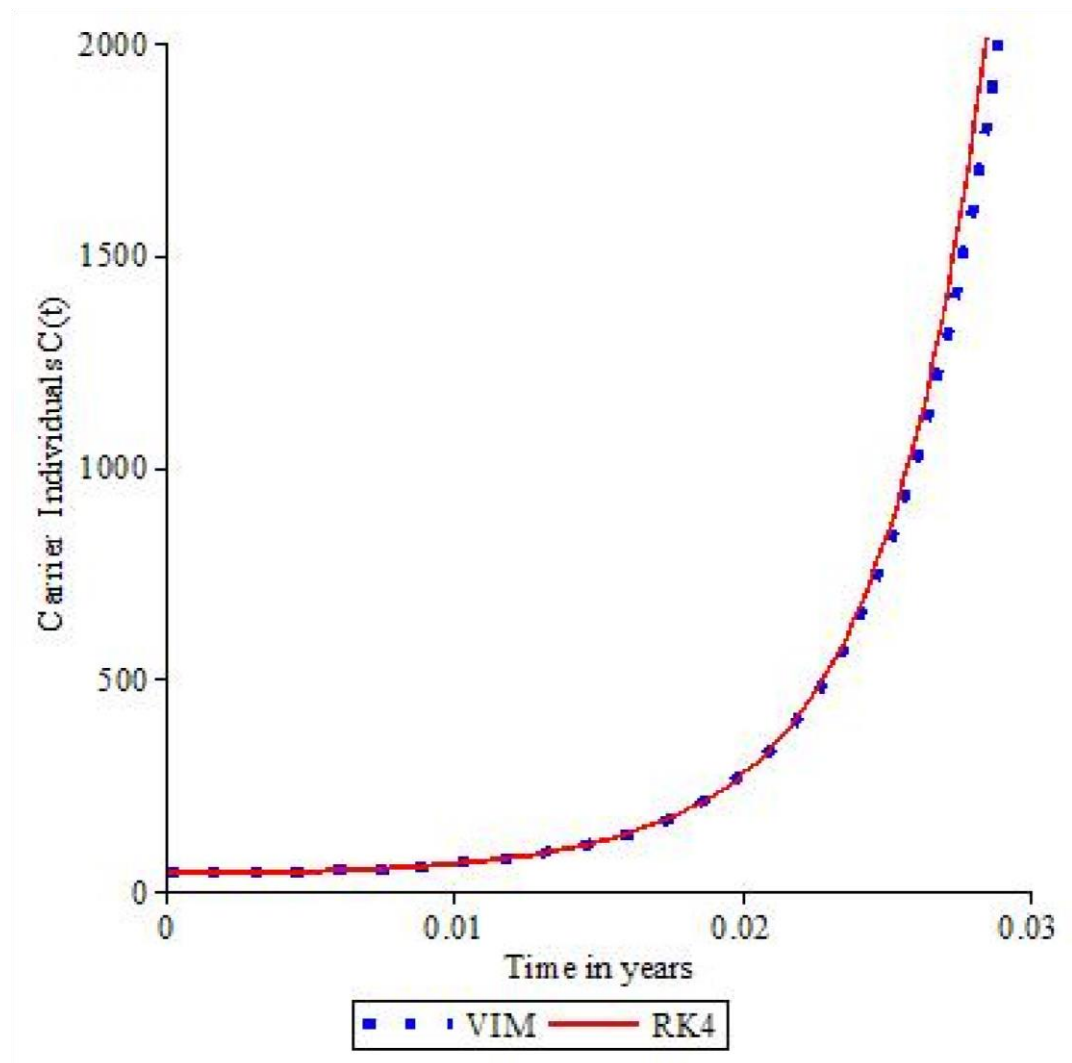


Figure 3.20: Graphical Illustration of VIM and RK4 Solution of Carrier Class

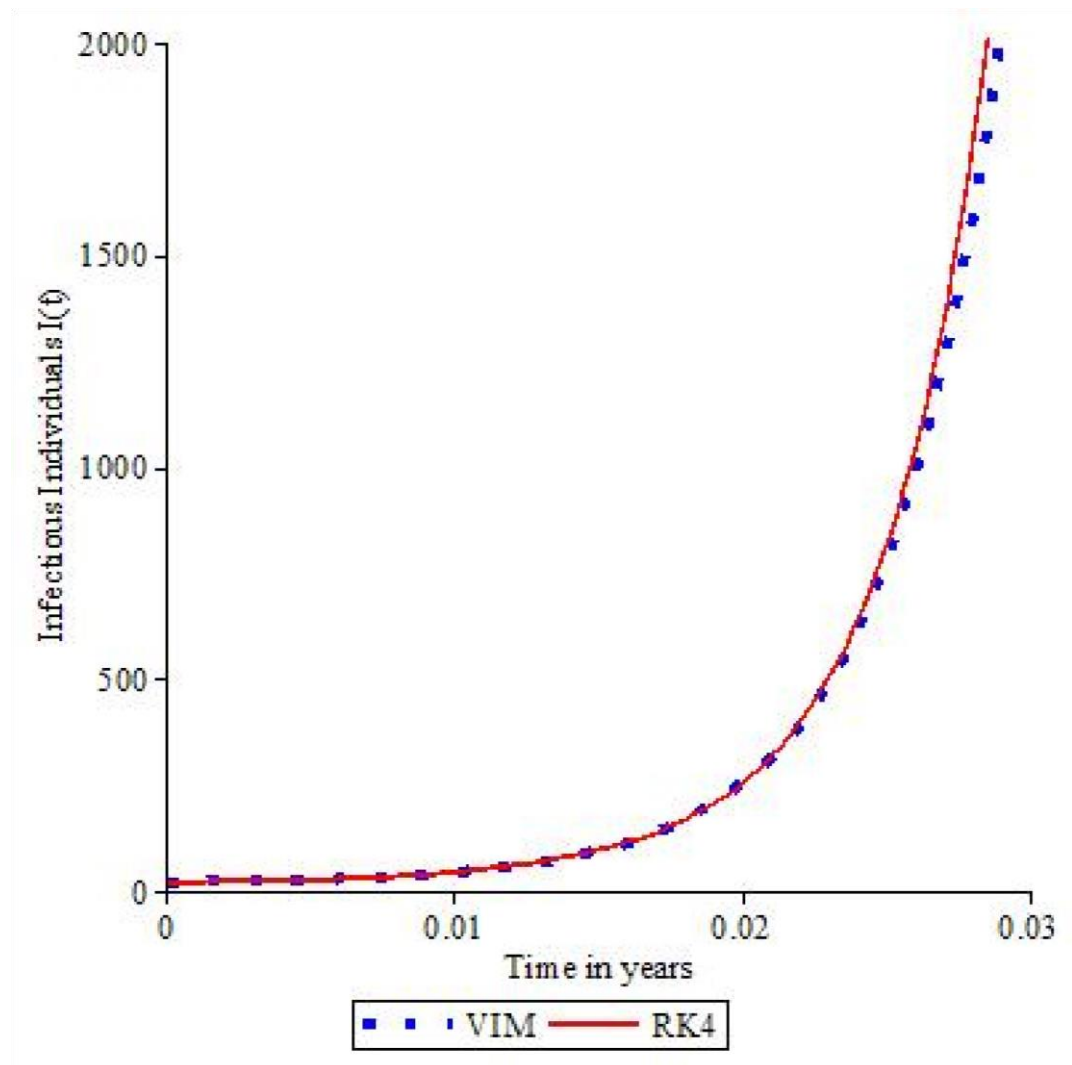


Figure 3.21: Graphical Illustration of VIM and RK4 Solution of Asymptomatic Class

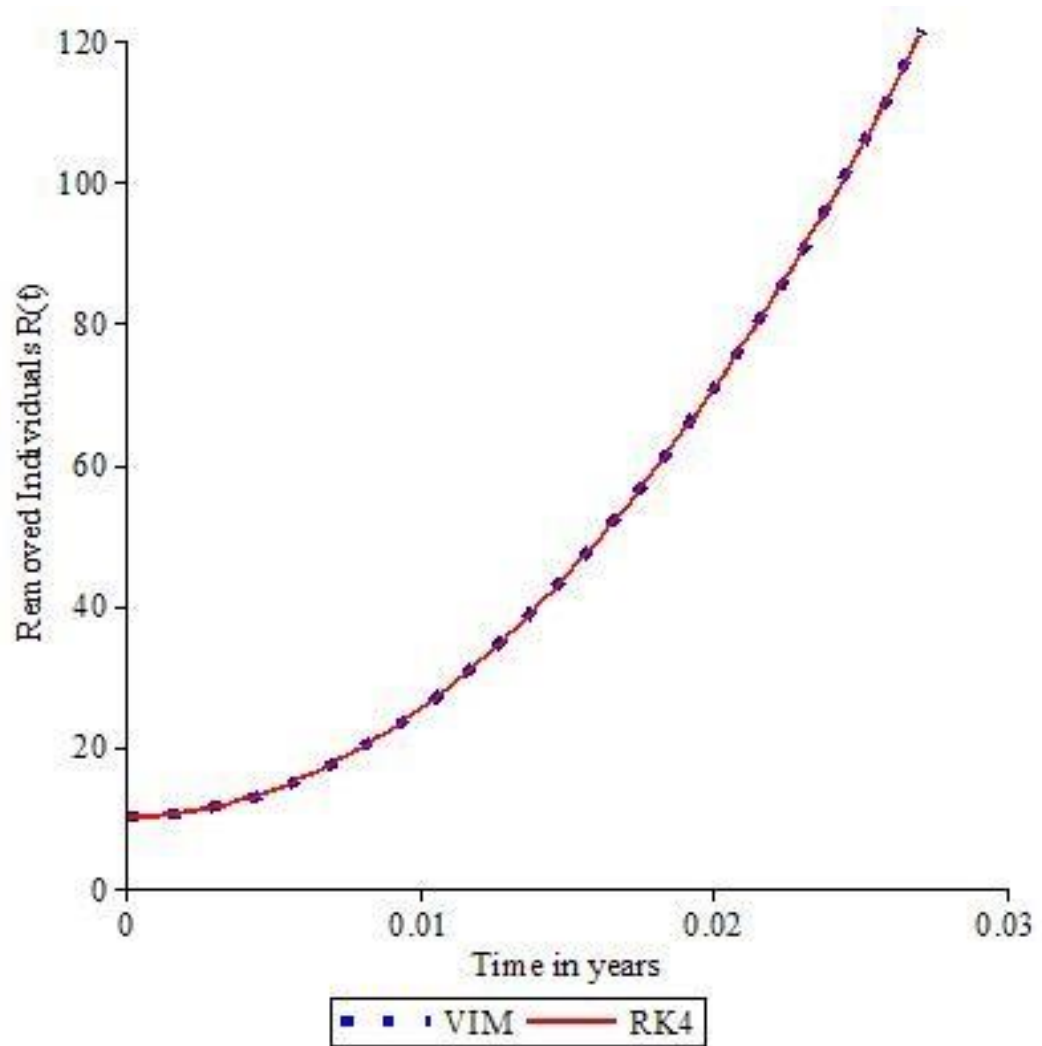


Figure 3.22: Graphical Illustration of VIM and RK4 Solution of Removed Class Graphical Illustration of Model 2 and Numerical Simulation

Figure (3.23) to (3.28) shows the combined plots of solutions of each of the compartments for model 2.

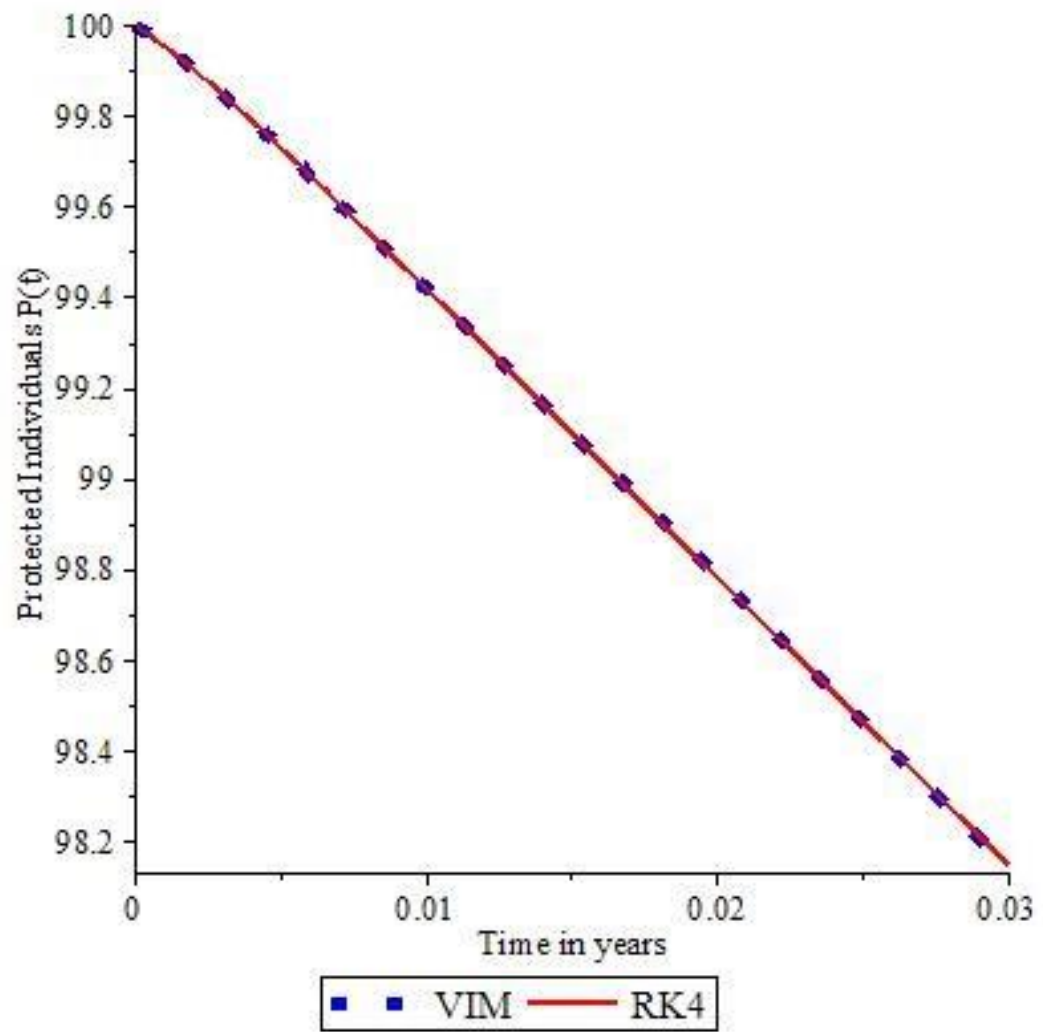


Figure 3.23: Graphical Illustration of VIM and RK4 Solution of Protected Class

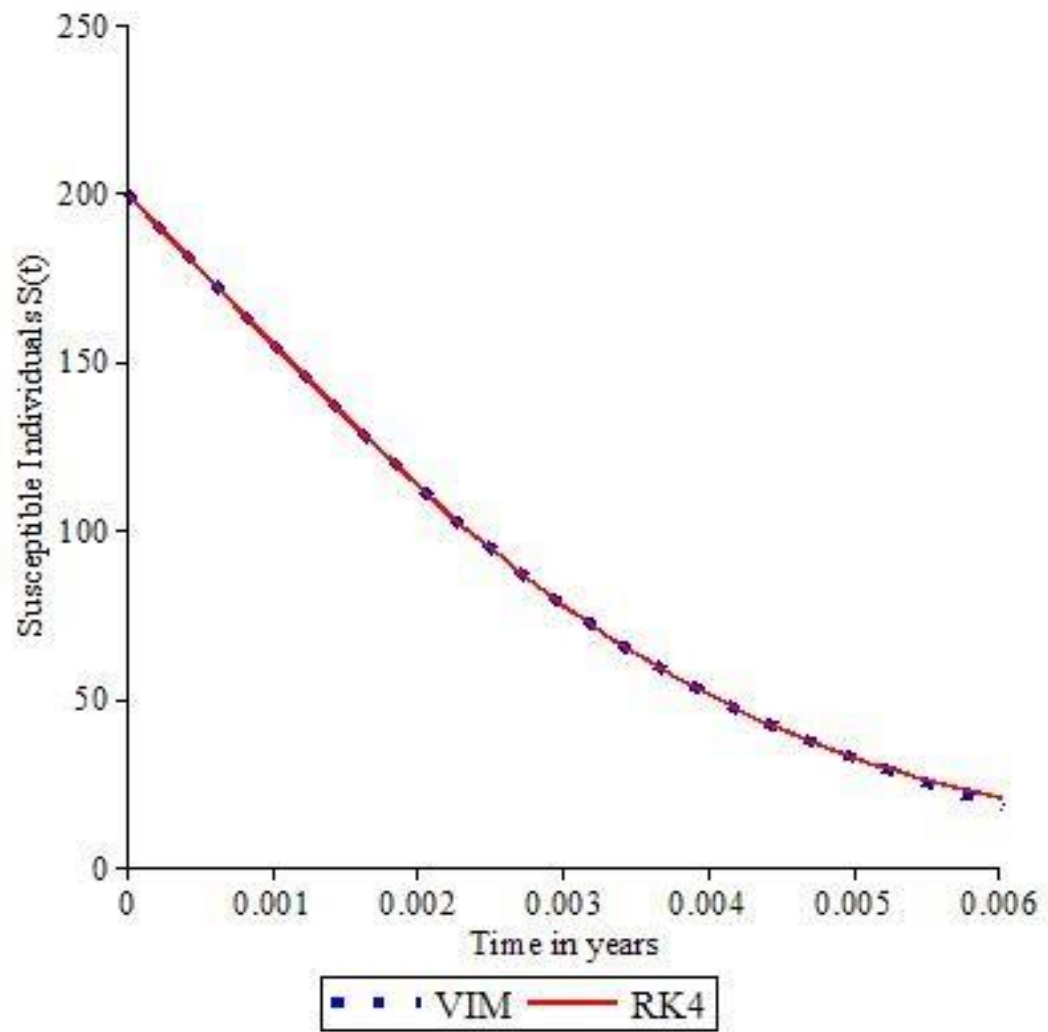


Figure 3.24: Graphical Illustration of VIM and RK4 Solution of Susceptible Class

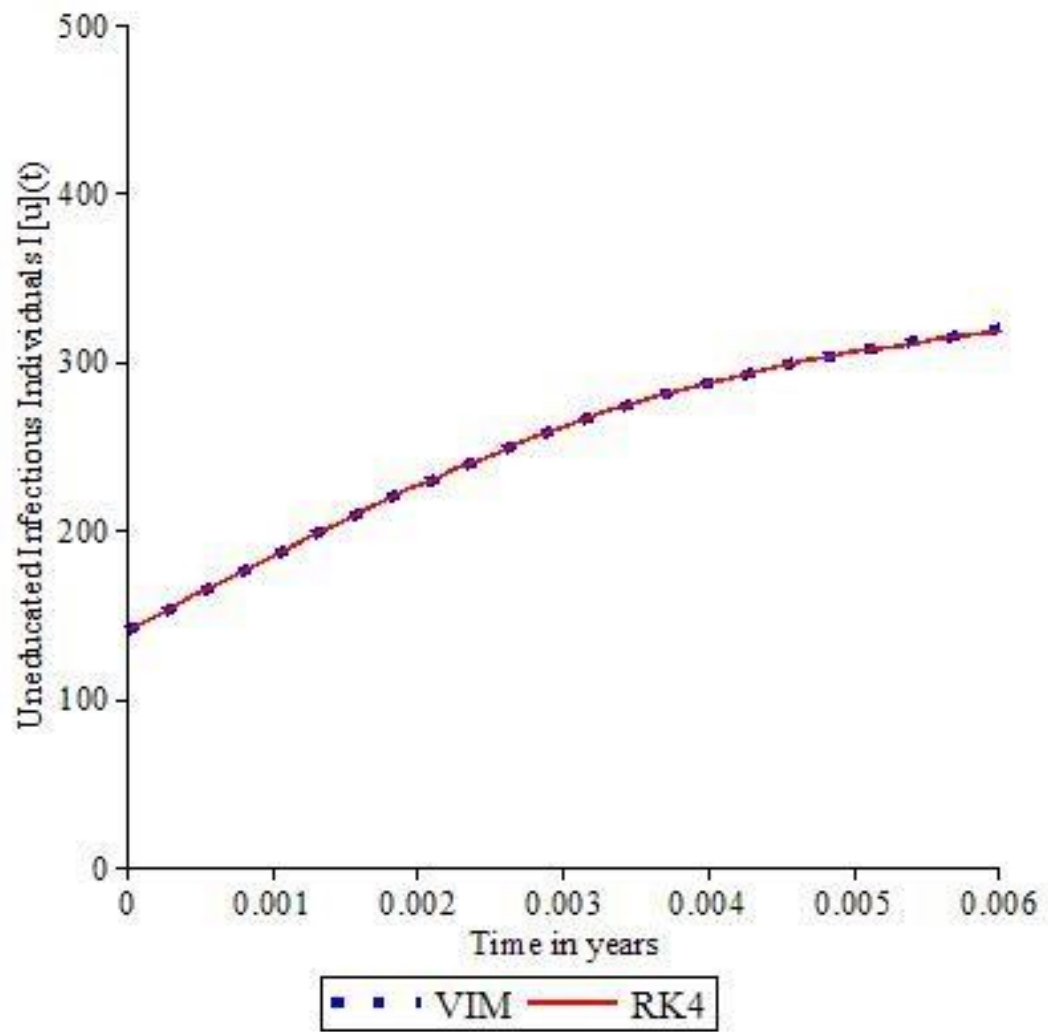


Figure 3.25: Graphical Illustration of VIM and RK4 Solution of Uneducated Infectious Class

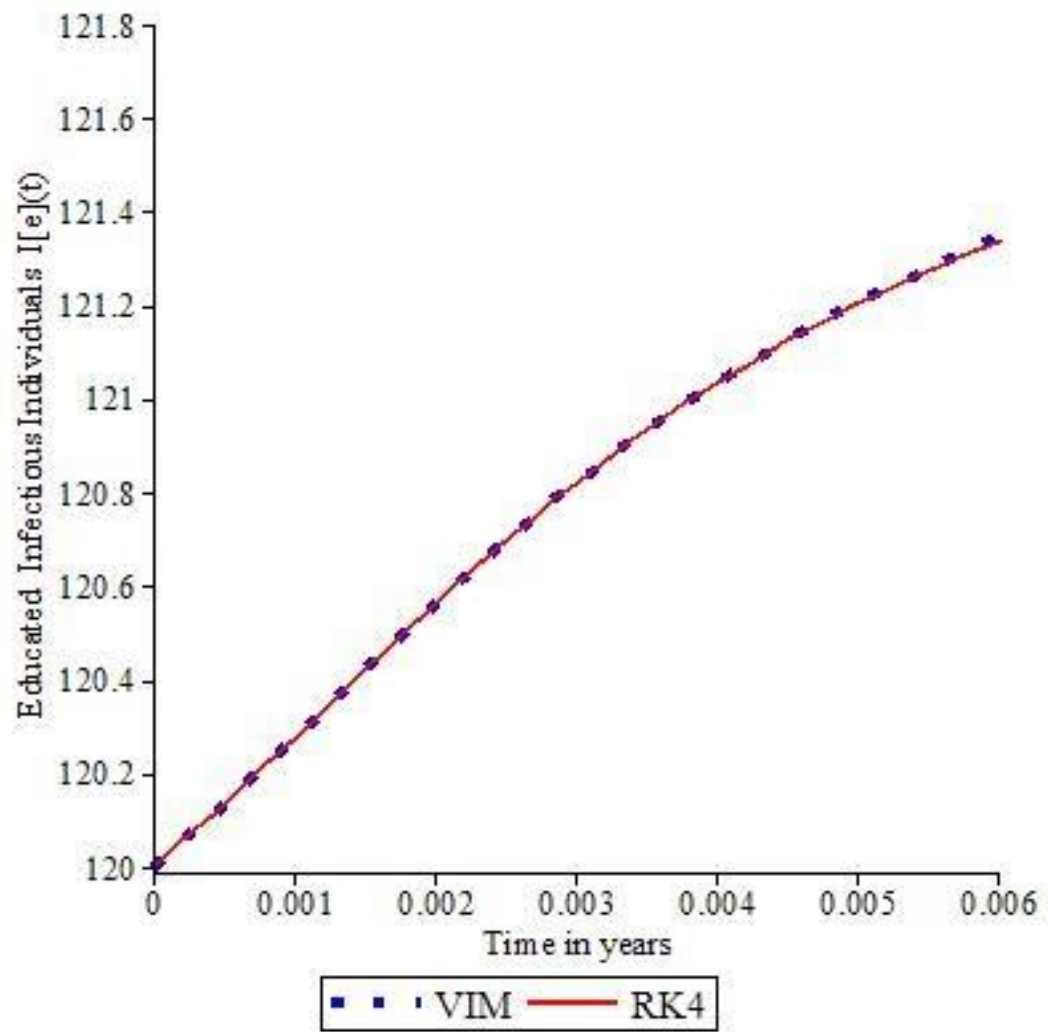


Figure 3.26: Graphical Illustration of VIM and RK4 Solution of Educated Infectious Class

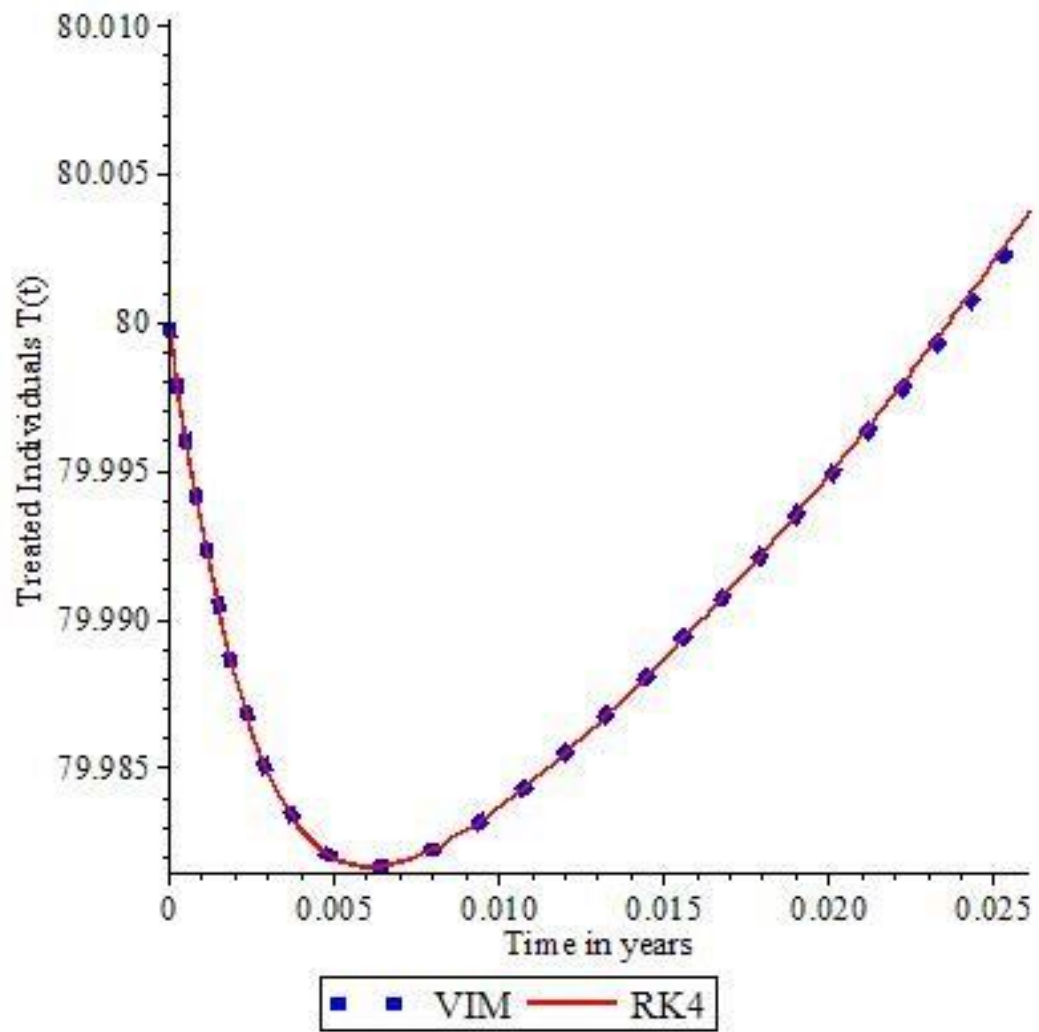


Figure 3.27: Graphical Illustration and Solution of VIM and RK4 for Treated Class

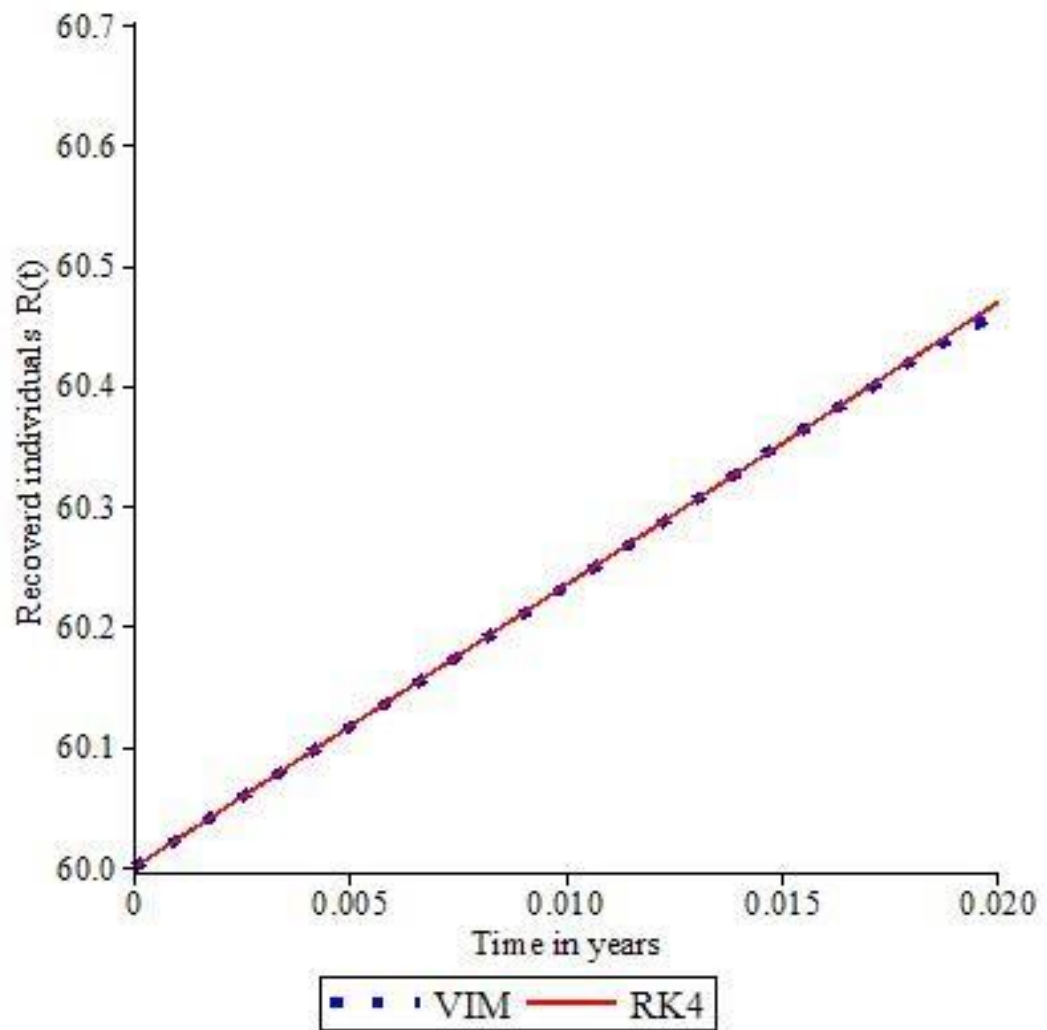


Figure 3.28: Graphical Illustration and Solution of VIM and RK4 for Removed Class

Numerical Simulation and Graphical Illustration of Model 3

Figure (3.29) to (3.33) shows the combined plots of solutions of each of the compartments for model 2.

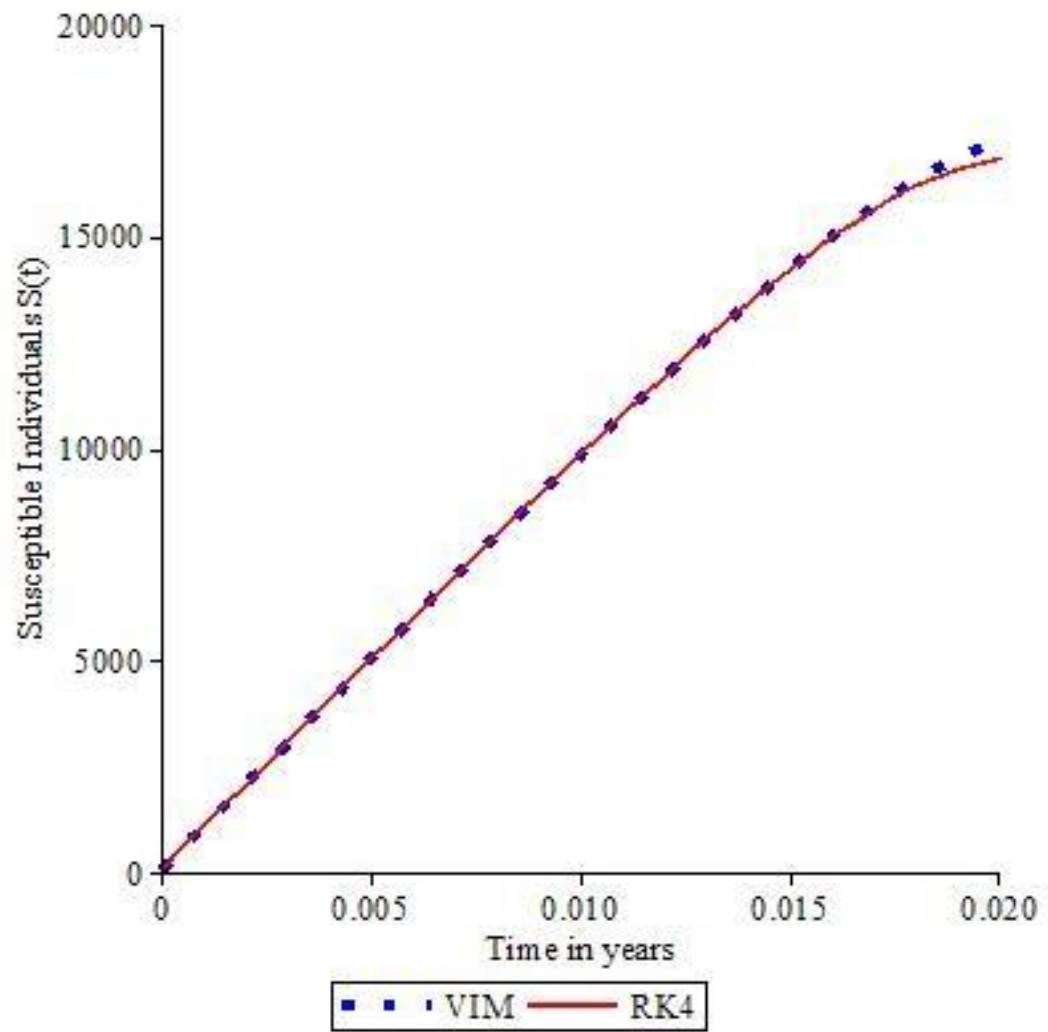


Figure 3.29: Graphical Illustration of VIM and RK4 Solution of Susceptible Class

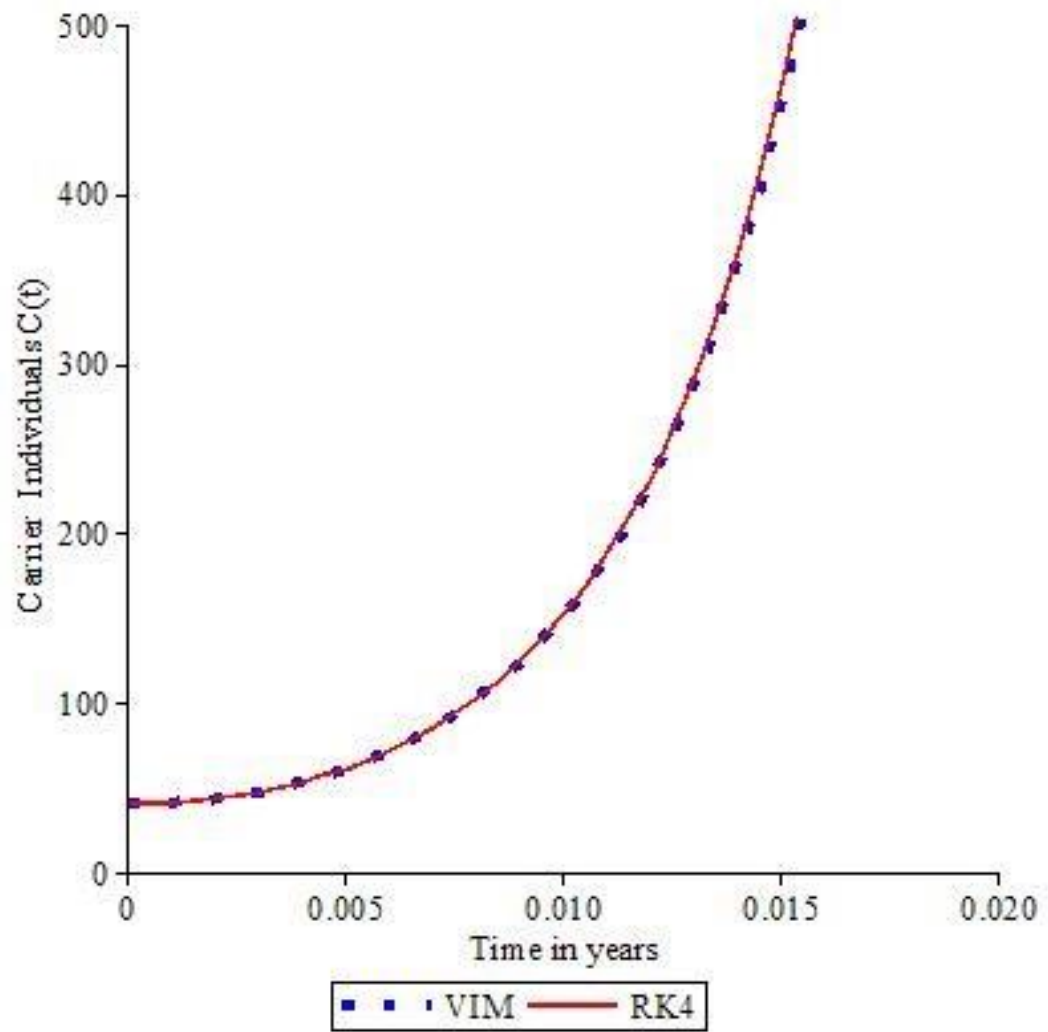


Figure 3.30: Graphical Illustration of VIM and RK4 Solution of Carrier Class

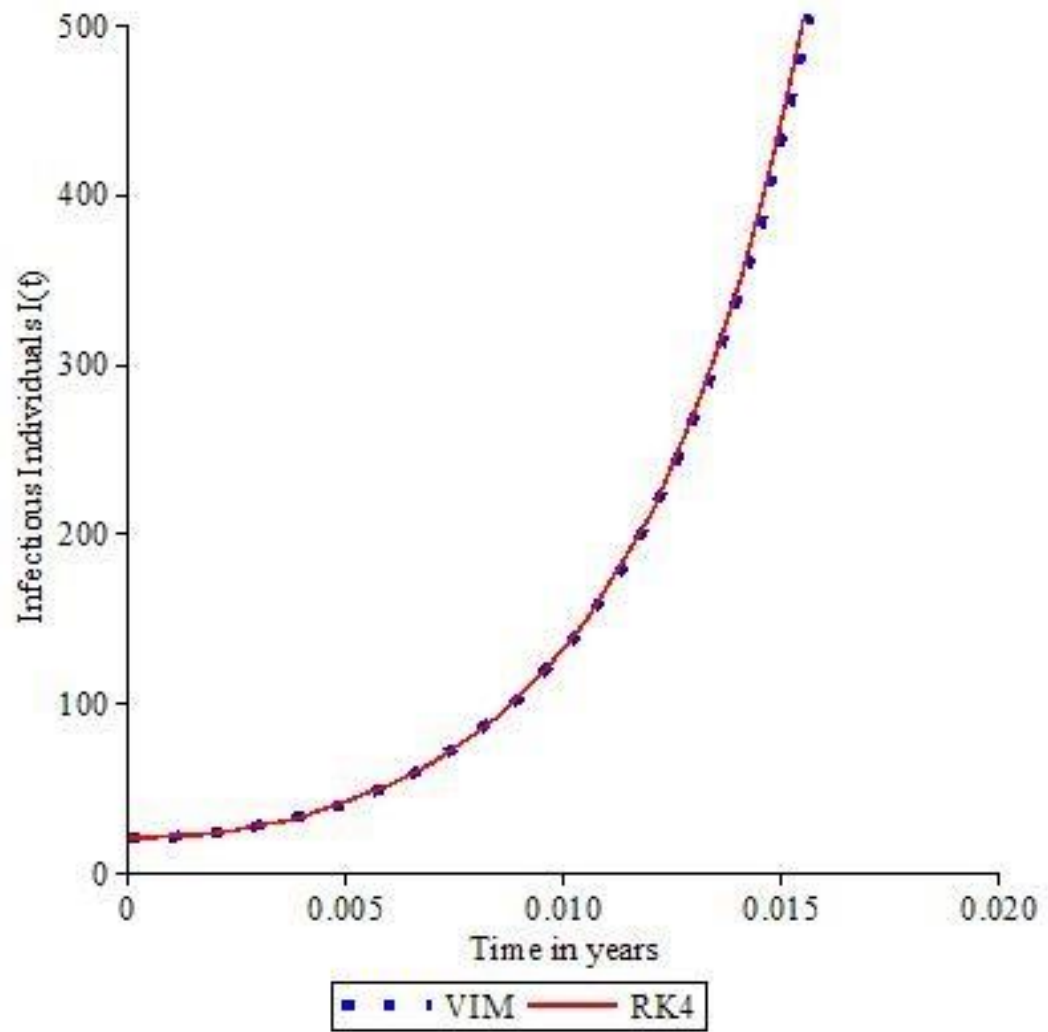


Figure 3.31: Graphical Illustration of VIM and RK4 Solution of Infected Class

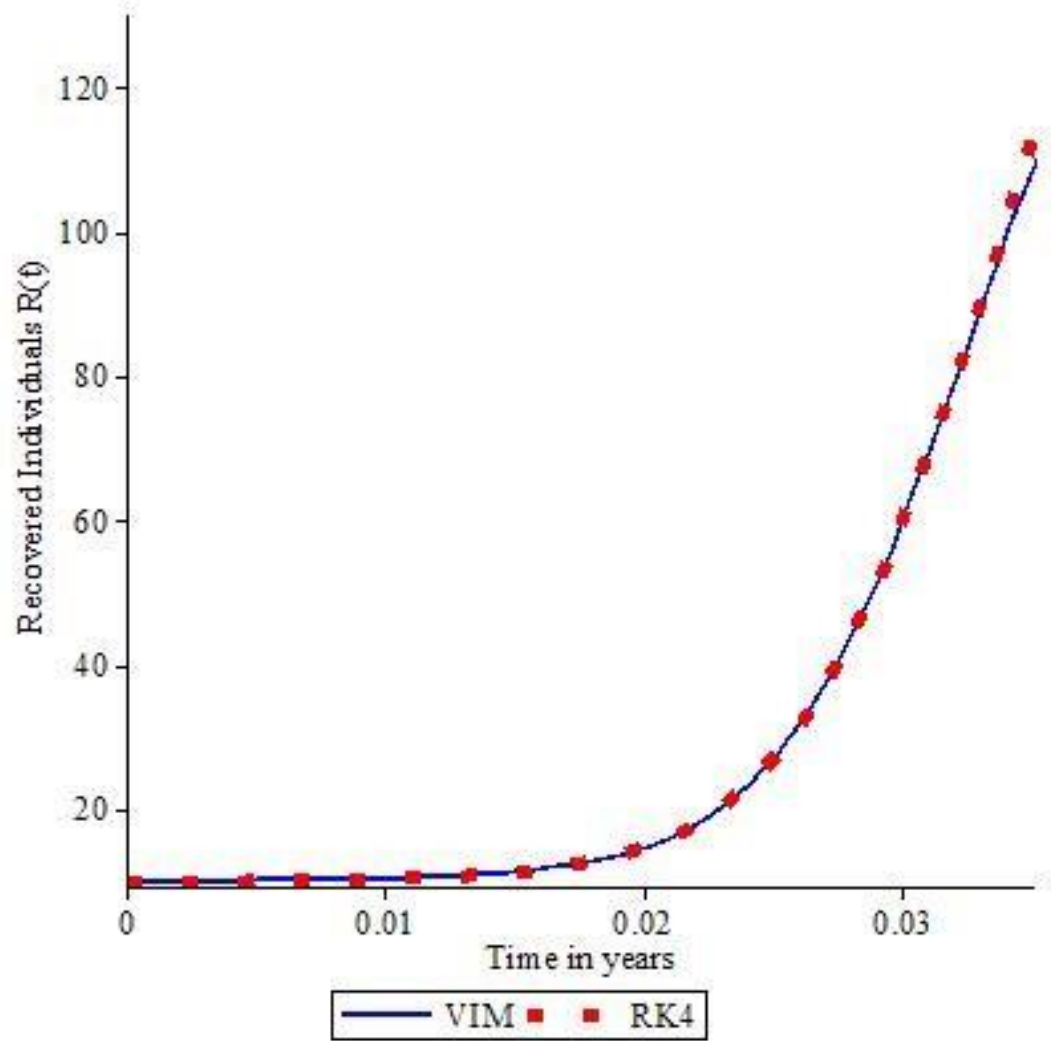


Figure 3.32: Graphical Illustration of VIM and RK4 Solution of Recovered Class

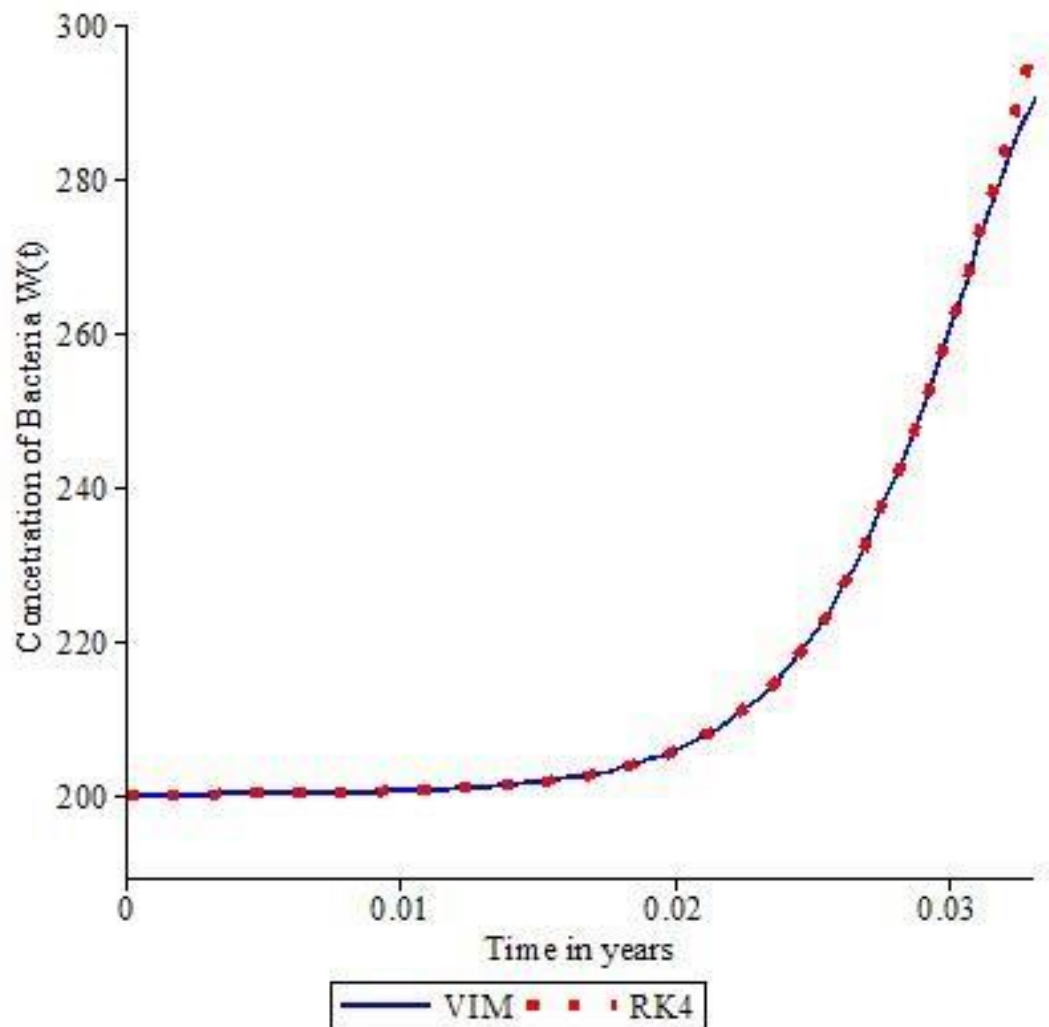


Figure 3.33: Graphical Illustration of VIM and RK4 Solution of Bacteria Class

3.8.4 Optimal Control Analysis

The study of optimal control is an aspect of mathematics that is commonly used to manage infectious disease spread. In the late 1950s, it is an effective computational method and has been used effectively to make decisions concerning complex biological problems. e.g. sending a fuel-efficient rocket into the moon or what percentage of the population can be vaccinated as time progresses in a given disease model, to minimize the number of infected people and the cost of implementing the vaccine strategy (Lenhart and Workman, 2007). In recent years, the concept of optimal control have been used in various fields such as Biomathematics, Ecological modelling, Engineering and Economics.

Research works in optimal control is known to be seen as a source of many useful and flexible tools, such as we have optimal therapies in medicine, and we use the word optimal control in economics, sciences and engineering. Optimal control methods are derived from multiple aspects of mathematical results and hypotheses, while control problems offer a rich source of profound mathematical problems. For a particular

mathematical model, there are different methods of calculating and analyzing optimal control. We have the maximum principle of the Pontryagin which is useful for calculating the optimal control for ordinary differential equation model system under certain constraints (Castillo, 2006).

Optimal control methods are derived from several aspects of mathematical results and theories, while control issues provide a rich source of deep mathematical issues. It was derived from Pontryagin's Maximum Principle for systems of mathematical models formed by Partial Differential Equations and Difference Equations. When applied to mathematical models of different systems, these techniques are very effective and can provide insights into the best path.

Processes in medicine and biology cannot be explicitly defined in terms of mathematical models based on natural or physical principles as in the case of chemistry and physics, because medicine and biology concentrate on living organisms particularly human beings. However, the principles of mathematics and physical sciences can be employed to model some biomedical processes. Recent studies focus on fusion or convergence of engineering, biology and medicine as efforts are geared towards developing devices and processes for the well-being of human beings through effective treatment.

Since the human structure is highly robust and nonlinear physiological control system, there exists a close relationship between biology and control theory (Linkens *et al.*, 2017 ; Mak & Distefano, 2007). Biological or physical optimisation of the dynamical system is a suitable article (Fister & Panetta, 2003; Ledzewicz & Schattler, 2016). Although biomedical engineering has been benefiting from the application of optimal control since the 1980s (Noldus, 2006; Fister *et al.*, 2010). currently, there is a rekindle and a deep interest in this field (Naidu *et al.*, 2008; Clemens, 2009).

The optimal control strategy is embarked upon to minimise disease transmission, and in most cases, to avoid the appearance of drug resistance. One of the major rationales for studying epidemic diseases is to enhance control and ultimately to eliminate the infection from the hosts. Models can be influential in this regards, enabling us to optimise the application of scarce resources to target control strategies in disease management. Different forms of control strategies are available; all operate to limit the average number of transmission between susceptible and infectious individuals. The control measure (or combination of measures) to be applied is a function of the hosts, the disease and the magnitude of the epidemic (Bakare *et al.*, 2014).

The use of optimal control theory in biomedical sciences is numerous, for example blood glucose management in diabetes (Swan, 2008; Swan, 2009), management of thyroid

(Mak & Distefano, 2007), anesthesia (Linkens *et al.*, 2017), circulatory system (Noldus, 2006), administration of drugs (Ollerton, 2009), Prosthetics (Fischer & Toe, 2011), cancer therapy (Fister & Panetta, 2003; Ledzewicz & Schattler, 2016), predator-prey (Parker *et al.*, 2001), Human Immunodeficiency Virus (Fister, Lenhart & McNally, 2010),

and epidemic problem (Parker *et al.*, 2001). Gaff & Schaefer (2009) employed optimal control principle to some epidemiological models in their bid to assess the best effective control method to reduce the population of individuals who are infected in the course of an outbreak by applying both vaccination and treatment as control strategies. Zaman *et al.*, (2008) embarked on a similar study to the one considered by Gaff & Schaefer (2009) but focused on a SIR deterministic model and applied only vaccination as the control measure.

Typhoid and cholera are the commonest water-borne infectious diseases. While the study of optimal control of Cholera is exhaustive in the literature (Njagarah & Nyabadza, 2015; Fister *et al.*, 2016; Lemos-Paiao *et al.*, 2017; Ainea *et al.*, 2018; Namaweje *et al.*, 2018; Ayoade *et al.*, 2019), studies on optimal control of typhoid are rare. With the exception of the work of Tilahun, Makinde & Malonza (2017) where the optimal control theory was applied to investigate the combination of the control strategies with the least cost for the transmission dynamics of typhoid fever and the work of Awoke (2019) where optimal control method was used to determine the optimal combination of three interventions (screening and treatment of carriers, vaccination and treatment of infections) with the minimum cost of the combined interventions in limiting the number of carriers and infective in the population, researches on the optimal control of Typhoid fever are limited.

The present study is motivated by the incidence and mortality of typhoid as well as the limited studies on the optimal control of the disease. A deterministic mathematical model is developed to study the transmission dynamics of Typhoid with the optimal control method as well as the cost-effectiveness of implementing the control strategies.

Extension of model 1 to optimal control system

In this section, by integrating two control measures, the basic model of typhoid fever is generalized. The controls are educational campaign and vaccination. u_1 and u_2 respectively

$$\left. \begin{aligned} \frac{dS}{dt} &= \theta - \mu_1 S - \beta(I_c + \gamma I)(1 - \phi) - \psi S - u_1 S(t) \\ \frac{dI_c}{dt} &= \rho \beta(I_c + \gamma I)(1 - \phi) - \mu_2 I_c - \alpha(1 - \phi) I_c \\ \frac{dI}{dt} &= (1 - \rho)(1 - \phi) \beta(I_c + \gamma I) + \alpha(1 - \phi) I_c - (\mu_3 + \delta) I - u_2 I(t) \\ \frac{dR}{dt} &= \psi S + \delta I - \mu_4 R + u_1 S(t) + u_2 I(t) \end{aligned} \right\} \quad (3.81)$$

With the initial conditions

$$S \geq 0, I_c \geq 0, I \geq 0, R \geq 0 \quad (3.82)$$

The objective functional is defined as

$$C(u_1, u_2) = \int_0^{t_f} (C_1 I_c + C_2 I + C_3 \frac{u_1^2}{2} + C_4 \frac{u_2^2}{2}) dt$$

The aim here is to reduce the total number of carriers and infected persons and the costs associated with the use of awareness and vaccination on $[0, t_f]$

$$C(u_1, u_2) = \min_{\{u_1, u_2\}} \int_0^{t_f} (C_1 I_c + C_2 I + C_3 \frac{u_1^2}{2} + C_4 \frac{u_2^2}{2}) dt$$

In formulating the optimal, we consider,

$$0 \leq u_1^*(t) \leq 1 \text{ and } 0 \leq u_2^*(t) \leq 1 \text{ such that } t \in [0, t_f]$$

To minimize

$$C(u_1, u_2) = \int_0^{t_f} (C_1 I_c + C_2 I + C_3 \frac{u_1^2}{2} + C_4 \frac{u_2^2}{2}) dt$$

Subject to the system in (3.2) where $u_1(t)$ and $u_2(t)$ are measurable function such that the control constraint is given by $U = \{(u_1(t), u_2(t)) | 0 \leq u_1(t) \leq 1, 0 \leq u_2(t) \leq 1, t \in [0, t_f]\}$

The main objective here is to reduce the total number of people infected and the cost of using education and vaccination for the entire people with the initial population of all classes to a minimum. $S(0)$, $I_c(0)$, $I(0)$ and $R(0)$. The first term $C_1 I_c$ from the objective function represents the total number of individuals who are infected but do not show any sign of infection and are infectious and is taken as a measure of death associated with epidemic. $C_2 I$ represents the total number of individuals who have been infected and is taken as a function of death associated with the outbreak. $C_3 \frac{u_1^2}{2}$ represent the cost associated with educational campaign and $C_4 \frac{u_2^2}{2}$ represents the cost associated with

vaccination.

Existence and Uniqueness of the Control System

Theorem 1

Suppose the objective function $C(u_1, u_2) = \min \{C(u_1, u_2) = \int_0^{t_f} (C_1 I_c + C_2 I + C_3 \frac{u_1^2}{2} +$

$$C_4 \frac{u_2^2}{2})\}dt$$

where

$$\{u_1, u_2 : 0 \leq u_1(t) \leq 1, 0 \leq u_2(t) \leq 1, t \in [0, t_f] \in R^+\}$$

there exist an optimal control

$$u^* = (u_1^*, u_2^*)$$

Such that,

$$\min_{u_1, u_2 \in u} C(u_1, u_2) = C(u_1^*, u_2^*) \text{ subject to the control system in (3.2)}$$

Proof

We use the findings in [Fleming and Rishel (1975)] to illustrate the existence of an optimal control pair. The controls and the state variables are positive. There exists constants $b_1, b_2 > 0$ and $\beta > 1$ such that the integrand of the objective functional J is

convex and satisfies $J(u_1, u_2) \geq b_1 \left(\left| \frac{u_1^2}{2} \right|^2 + \left| \frac{u_2^2}{2} \right|^2 \right)^{\frac{\beta}{2}} - b_2$ Based on prior boundedness

and the model's state variables, hence,

$$u_1^* = \begin{cases} 0 & \text{if } \frac{\lambda_S - \lambda_R}{C_3} \leq 0 \\ \frac{\lambda_S - \lambda_R}{C_3} & \text{if } 0 < \frac{\lambda_S - \lambda_R}{C_3} < 1 \\ 1 & \text{if } \frac{\lambda_S - \lambda_R}{C_3} \geq 1 \end{cases}$$

(3.83)

$$u_2^* = \begin{cases} 0 & \text{if } \frac{\lambda_I - \lambda_R}{C_4} \leq 0 \\ \frac{\lambda_I - \lambda_R}{C_4} & \text{if } 0 < \frac{\lambda_I - \lambda_R}{C_4} < 1 \\ 1 & \text{if } \frac{\lambda_I - \lambda_R}{C_4} \geq 1 \end{cases}$$

Necessary Conditions of the Control

By using Pontryagin's Maximum Principle (Pontryagin's *et.al*, 1982)

We give the minimized point-wise Hamiltonian as follows which converts system (3.2) objective functional into problem, minimizing point-wise Hamiltonian H with respect to u_1 and u_2

Theorem 2

There exist an optimal control u_1^* and u_2^* corresponding solution $S(t)$, $I_c(t)$, $I(t)$ and $R(t)$ which minimizes $C(u_1, u_2)$ over U . Furthermore, there exist adjoint variables $\lambda_i, i=1, 2, 3, 4$ satisfying

$$\begin{aligned} H(S, I_c, I, R) = & (C_1 I_c + C_2 I + C_3 \frac{u_1^2}{2} + C_4 \frac{u_2^2}{2}) + \lambda_1 (\theta - \mu_1 S - \beta I_c + \gamma I) \\ & (1 - \phi) - \psi S - u_1 S) + \lambda_2 (\rho \beta I_c + \gamma I) (1 - \phi) - \mu_2 I_c \\ & - \alpha (1 - \phi) I_c) + \lambda_3 ((1 - \rho)(1 - \phi) \beta I_c + \gamma I) + \alpha (1 - \phi) I_c \\ & - (\mu_3 + \delta) I - u_2 I(t)) + \lambda_4 (\psi S + \delta I - \mu_4 R + u_1 S(t) + u_2 I(t)) \end{aligned} \quad (3.84)$$

By differentiating the Hamiltonian in (3.84) with respect to each state variables

$$\begin{aligned} \frac{d\lambda_1}{dt} = -\frac{dH}{dS} = & -\lambda_1 (-\mu_1 - \beta I_c + \gamma I) (1 - \phi) - \psi - u_1) \\ & - \lambda_2 [\rho \beta I_c + \gamma I] (1 - \phi) - \lambda_3 [(1 - \rho)(1 - \phi) \beta I_c + \gamma I] - \lambda_4 (\psi + u_1) \\ \frac{d\lambda_2}{dt} = -\frac{dH}{dI_c} = & -\lambda_1 [-\beta (1 - \phi)] - \lambda_2 [\rho \beta (1 - \phi) - \mu_2 - \alpha (1 - \phi)] \\ & - \lambda_3 [(1 - \rho)(1 - \phi) \beta + \alpha (1 - \phi)] - C_1 \\ \frac{d\lambda_3}{dt} = -\frac{dH}{dI} = & -\lambda_1 [-S \gamma (1 - \phi)] - \lambda_2 [\rho S \gamma (1 - \phi)] - \lambda_3 [(1 - \rho)(1 - \phi) \\ & S \gamma - (u_2 + \mu_3 + \delta)] - \lambda_4 (\delta + u_2) - C_2 \\ \frac{d\lambda_4}{dt} = -\frac{dH}{dR} = & \lambda_4 \mu_4 \end{aligned} \quad (3.85)$$

With final initial conditions

$$\lambda_S(t_f) = \lambda_{I_c}(t_f) = \lambda_I(t_f) = \lambda_R(t_f) = 0 \quad (3.86)$$

To find the optimal u_1^* and u_2^* , we use the following partial differential equations

$$\frac{\partial H}{\partial u_i} = 0$$

$$\frac{\partial H(S, I_c, I, R)}{\partial u_1} = C_3 u_1 + \lambda_1 (-S) + \lambda_4 (S) = 0$$

$$\begin{aligned}\Rightarrow u_1^* &= \frac{(\lambda_1 - \lambda_4)S}{C_3} \\ \frac{\partial H(S, I_c, I, R)}{\partial u_2} &= C_4 u_2 + \lambda_3(-I) + \lambda_4(I) = 0 \\ \Rightarrow u_2^* &= \frac{(\lambda_3 - \lambda_4)I}{C_4}\end{aligned}$$

$\lambda_S, \lambda_{I_c}, \lambda_I$ and λ_R are equivalent to $\lambda_1, \lambda_2, \lambda_3$ and λ_4
Therefore,

$$\begin{aligned}u_1^* &= \max \left\{ 0, \min \left(1, \frac{(\lambda_1 - \lambda_4)S}{C_3} \right) \right\} \\ u_2^* &= \max \left\{ 0, \min \left(1, \frac{(\lambda_3 - \lambda_4)I}{C_4} \right) \right\}\end{aligned} \quad (3.87)$$

3.8.5 Numerical Simulations of the Optimal Control and the Optimality System

The optimality system consist of the model in (3.2) with control variables. Here, the optimal control set in (3.86), adjoint system in (3.85) and the initial conditions in (3.82).(3.87) gives the optimality of the system. We provide some numerical simulations of the model in (3.2) which describes the theoretical results and predict the evolution of typhoid fever in the population and the dynamical behaviour of the model is studied. We use the forward-backwards sweep method and solve the optimality system numerically. The simulation was carried out by using the values in the table 1. We used the following values for the coefficients of the states and controls $C_1=1, C_2=1.5, C_3=1.5, C_4=0.02$

$$\begin{aligned}\frac{dS}{dt} &= \theta - \mu_1 S - S \left[I_c + \gamma I \right] (1 - \phi) - \psi S - \\ &\quad \left[\max \left\{ 0, \min \left(1, \frac{(\lambda_S - \lambda_R)S}{C_3} \right) \right\} \right] S(t) \\ \frac{dI_c}{dt} &= \rho S \left[I_c + \gamma I \right] (1 - \phi) - \mu_2 I_c - \alpha (1 - \phi) I_c \\ \frac{dI}{dt} &= (1 - \rho)(1 - \phi) S \left[I_c + \gamma I \right] + \alpha (1 - \phi) I_c - (\mu_3 + \delta) I - \\ &\quad \left[\max \left\{ 0, \min \left(1, \frac{(\lambda_I - \lambda_R)I}{C_4} \right) \right\} \right] I(t) \\ \frac{dR}{dt} &= \psi S + \delta I - \mu_4 R + \left[\max \left\{ 0, \min \left(1, \frac{(\lambda_S - \lambda_R)S}{C_3} \right) \right\} \right] S(t) + \\ &\quad \left[\max \left\{ 0, \min \left(1, \frac{(\lambda_I - \lambda_R)I}{C_4} \right) \right\} \right] I(t)\end{aligned}$$

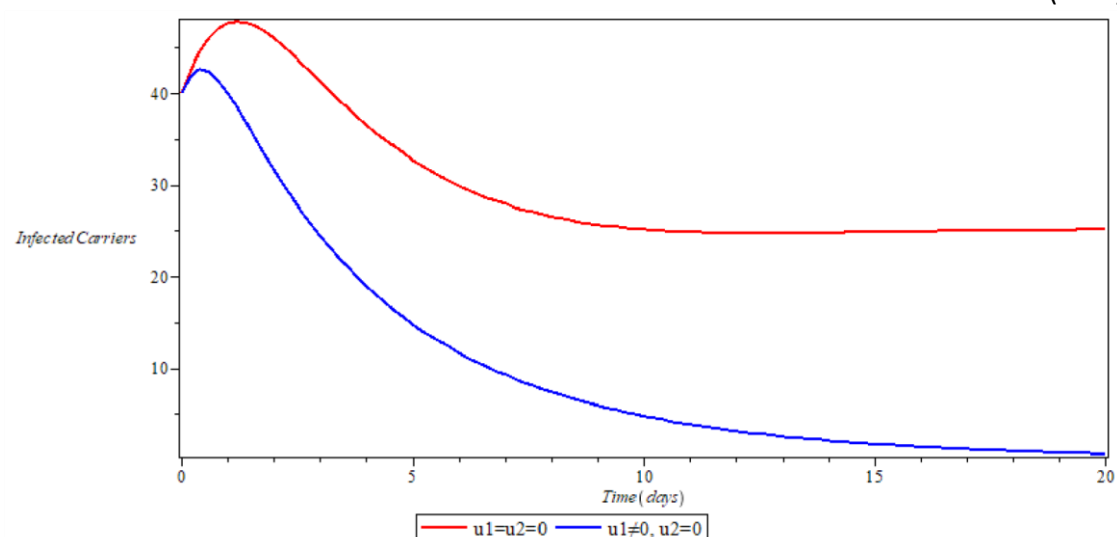


Figure 3.34: Simulation Result Showing Effect of Using Optimal Vaccination as the Only Control Strategies on Carriers Population

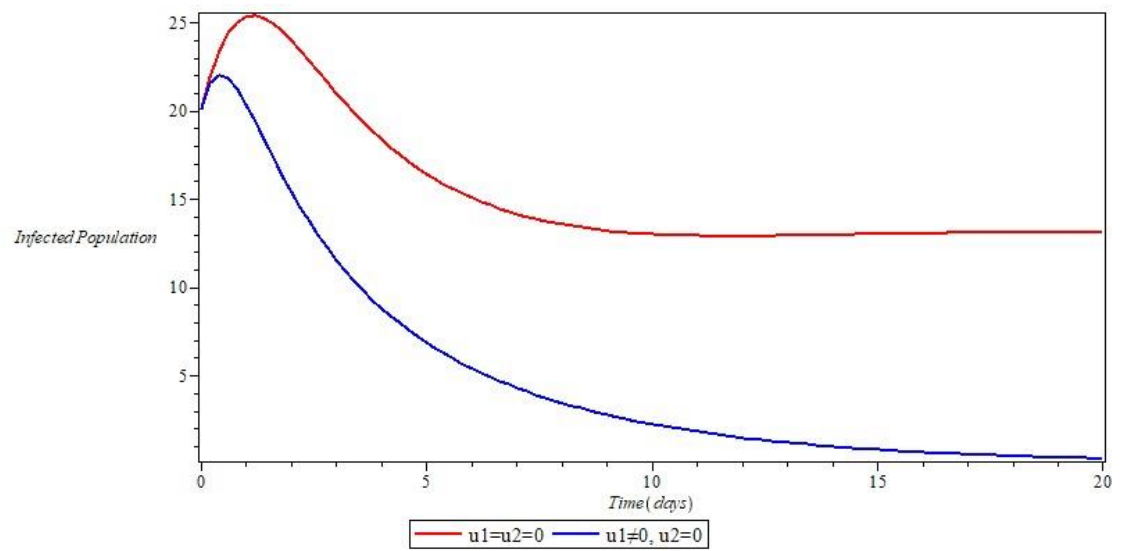


Figure 3.35: Simulation Result Showing Effect of Using Optimal Vaccination as the Only Control Strategies on Infectious Population

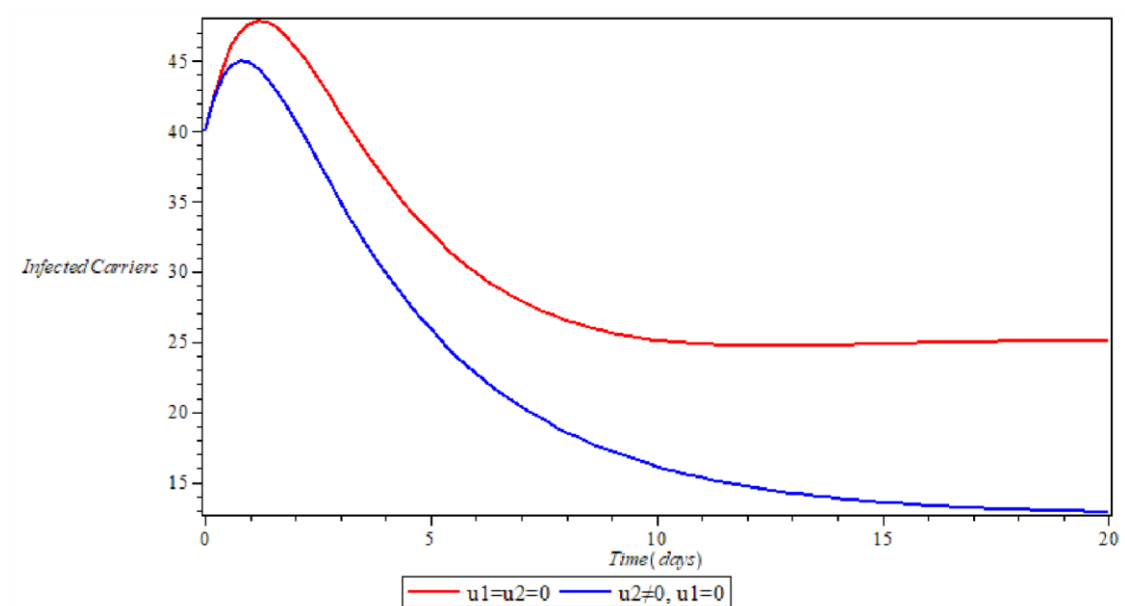


Figure 3.36: Simulation Result Showing Effect of Using Optimal Educational Campaign as the Only Control Strategies on Carriers Population

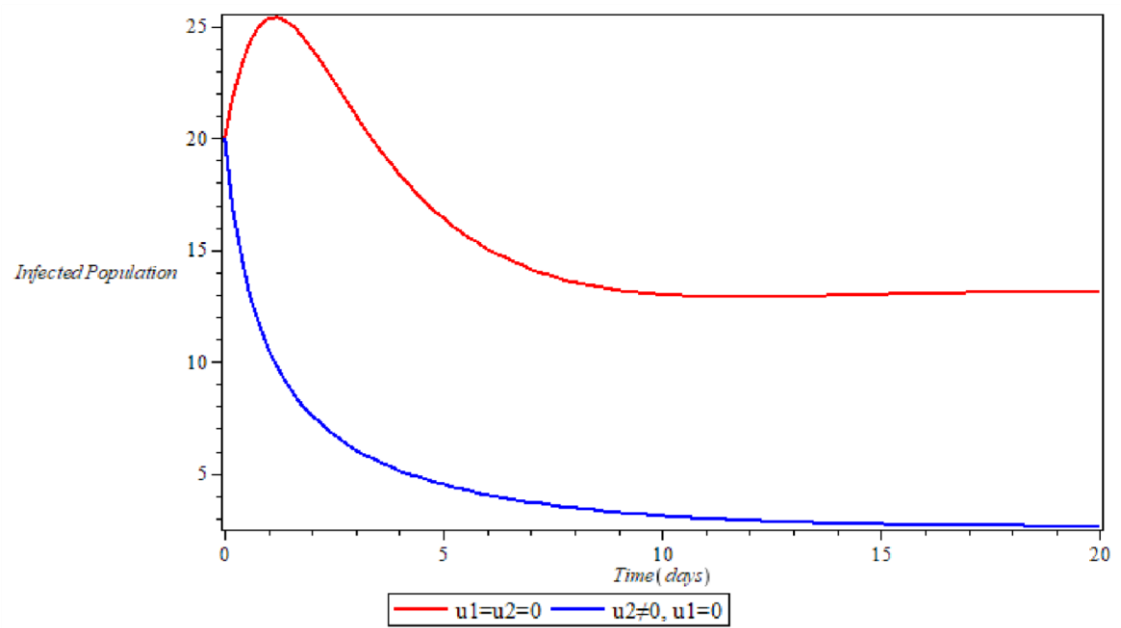


Figure 3.37: Simulation Result Showing Effect of Using Optimal Educational Campaign as the Only Control Strategies on Infected Population

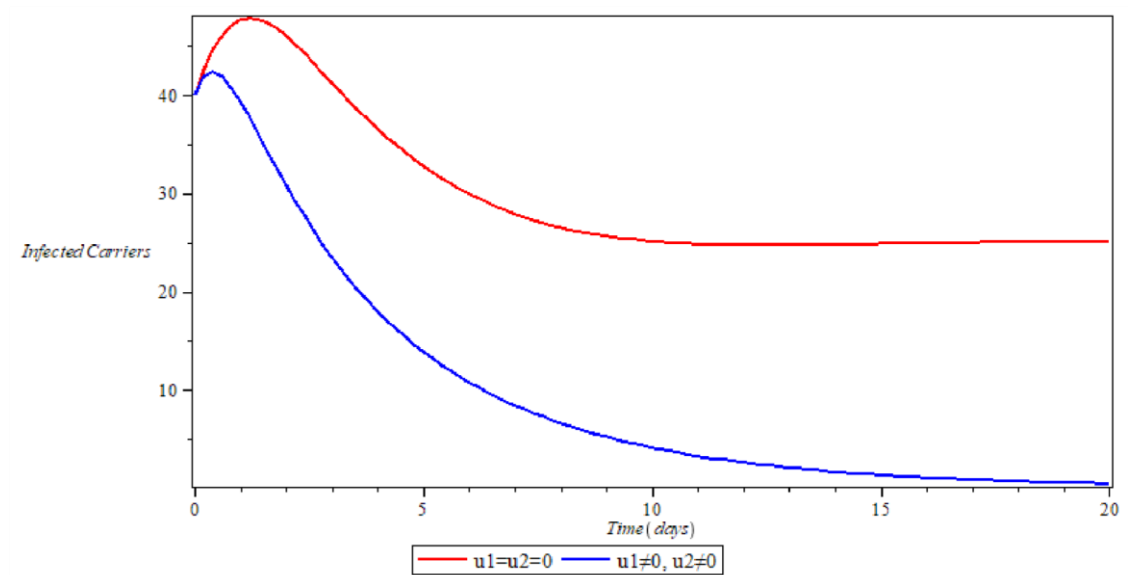


Figure 3.38: Simulation Result Showing Effect of Using Optimal Vaccination and Educational Campaign on Carriers Population

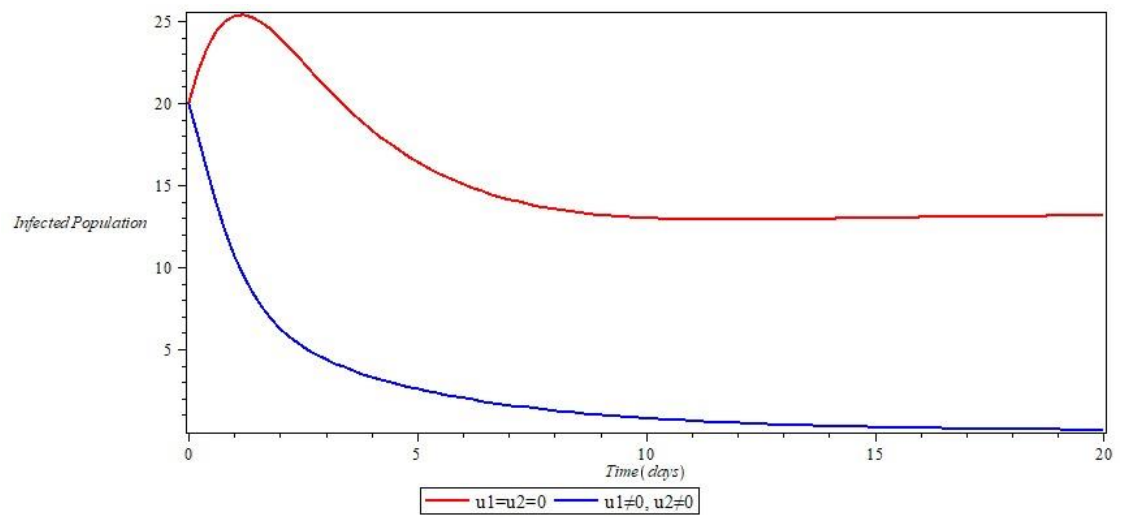


Figure 3.39: Simulation Result Showing Effect of Using Optimal Vaccination and Educational Campaign on Infectious Population

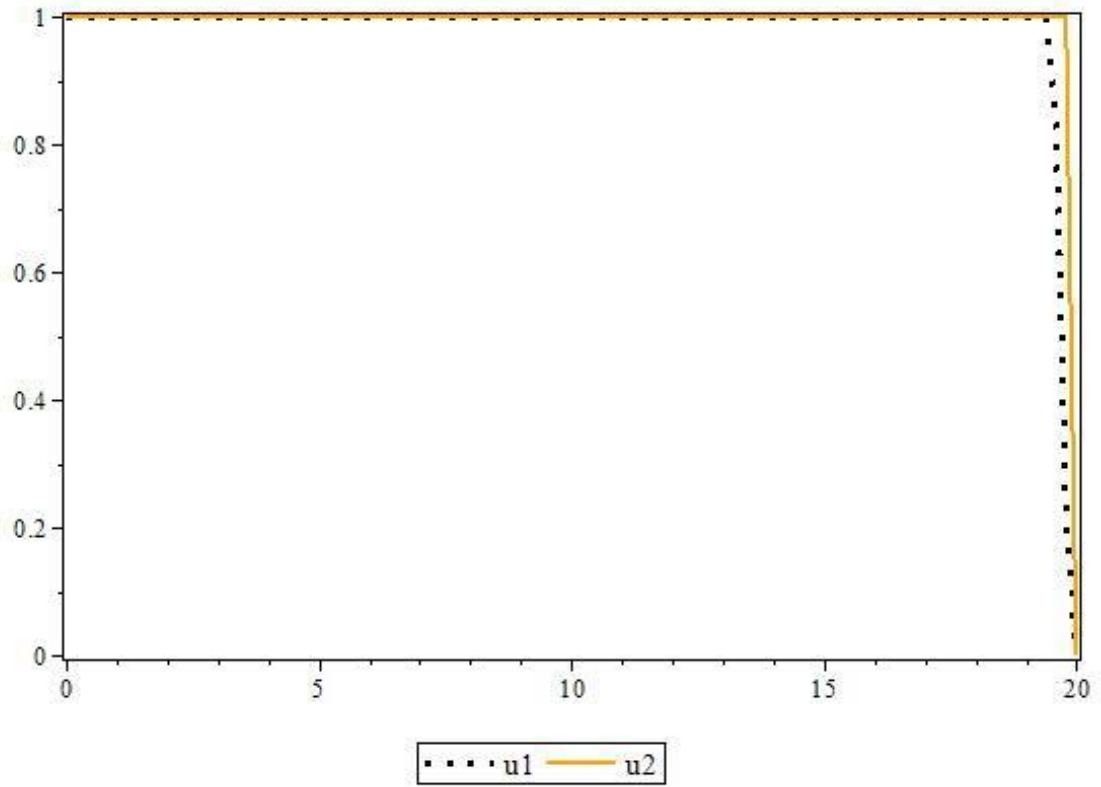


Figure 3.40: Simulation Result Showing Control Profile of u1 and u2

3.9 Extension of Model 3 into Optimal Control

In this section, we extend the basic model in (3.7) which comprises both direct and indirect transmission of typhoid fever by incorporating three control strategies: namely, educational campaign, prevention and sanitation and early treatment and screening. We also incorporate a parameter φ which denote progression rate from infected carriers to infected individuals. Therefore the model equations with controls is given as

$$\left. \begin{aligned}
 \frac{dS}{dt} &= \theta - \mu_1 S - S(\beta_1 I_c + \beta_2 I + \beta_3 W)(1 - u_1^*) \\
 \frac{dI_c}{dt} &= \rho S(1 - u_1^*)(\beta_1 I_c + \beta_2 I + \beta_3 W) - (\mu_2 + \epsilon_1)I_c - (\phi + u_2^*)I_c \\
 \frac{dI}{dt} &= (1 - \rho)(1 - u_1^*)(\beta_1 I_c + \beta_2 I + \beta_3 W) + (1 - u_2^*)\phi I_c - (u_3^* + \delta)I - (\epsilon_2 + \mu_3)I \\
 \frac{dR}{dt} &= (u_3^* + \delta)I - \mu_4 R \\
 \frac{dW}{dt} &= \epsilon_1 I_c + \epsilon_2 I - \mu_b W
 \end{aligned} \right\} \quad (3.89)$$

$$S \geq 0, I_c \geq 0, I \geq 0, R \geq 0, W \geq 0 \quad (3.90)$$

The objective function is used to minimized the total number of carrier infected as well as the infected individuals with typhoid fever and the cost associated with the control variables u_1, u_2 and u_3 .

The objective function is defined as

$$J(u_1, u_2, u_3) = \int_0^{t_f} (A_1 I_c + A_2 I + K_1 \frac{u_1^2}{2} + K_2 \frac{u_2^2}{2} + K_3 \frac{u_3^2}{2}) dt \quad (3.91)$$

Subject to the state equations in (3.7) where A_1 and A_2 are non negative weight constant of infected carriers and infected individuals. K_1, K_2 and K_3 are cost associated with educational campaign, prevention with sanitation and early treatment with screening. Our

main target is to find the optimal control function $(u_1^*), (u_2^*), (u_3^*)$ such that,

$$J(u_1^*, u_2^*, u_3^*) = \min \{ J(u_1, u_2, u_3) \mid (u_1, u_2, u_3) \in \Omega \}$$

where

$$\Omega = \{ u = ((u_1, u_2, u_3)) : u_i(t) \text{ is Lebesgue Measurable on } [0, t_f], 0 \leq u_i \leq 1, i = 1, 2, 3 \}$$

3.9.1 Existence of the Optimal Control

The essential conditions is derived from Potryagin's Maximum Principle to be fulfilled by the controls and the corresponding state. (Pontryagins's et. al., 1986). Using the differentials equations of the state variables in (3.89), the Halmitonian H is defined as

$$H = \frac{dJ}{dt} + \lambda_1 \frac{dS}{dt} + \lambda_2 \frac{dI_c}{dt} + \lambda_3 \frac{dI}{dt} + \lambda_4 \frac{dR}{dt} + \lambda_5 \frac{dW}{dt}$$

that is,

$$\begin{aligned}
H(S, I_c, I, R, W) = & \left(A_1 I_c + A_2 I + K_1 \frac{u_1^2}{2} + K_2 \frac{u_2^2}{2} + K_3 \frac{u_3^2}{2} \right) \\
& + \lambda_1 (\theta - \mu_1 S - (1 - u_1) \beta_1 I_c + \beta_2 I + \beta_3 W) S \\
& + \lambda_2 ((1 - u_1) \beta_1 I_c + \beta_2 I + \beta_3 W) \rho S - (\mu_2 + \epsilon_1) I_c - (\phi + u_2) I_c \\
& + \lambda_3 ((1 - \rho)(1 - u_1) \beta_1 I_c + \beta_2 I + \beta_3 W) S \\
& + (1 - u_2) \phi I_c - (u_3 + \delta) I - (\mu_3 + \epsilon_2) I \\
& + \lambda_4 ((u_3 + \delta) I - \mu_4 R) \\
& + \lambda_5 (\epsilon_1 I_c + \epsilon_2 I + u_b W) \quad (3.92)
\end{aligned}$$

where $\lambda_1, \lambda_2, \lambda_3, \lambda_4$ and λ_5 are the adjoint variable functions.

Theorem 1

There exists an optimal control with the corresponding solution (S, I_c, I, R, W) corresponding to the state equations in (3.89) and the adjoint variables $\lambda_1(t), \lambda_2(t), \lambda_3(t), \lambda_4(t), \lambda_5(t)$ such that

$$\begin{aligned}
\lambda_1' = & -\lambda_1 (-\mu - (1 - u_1) \beta_1 I_c + \beta_2 I + \beta_3 W) \\
& - \lambda_2 (\rho(1 - u_1) \beta_1 I_c + \beta_2 I + \beta_3 W) \\
& - \lambda_3 ((1 - \rho)(1 - u_1) \beta_1 I_c + \beta_2 I + \beta_3 W) \\
\lambda_2' = & -\lambda_1 (-(1 - u_1) \beta_1 S) \\
& - \lambda_2 ((1 - u_1) \beta_1 S - (\mu_2 + \epsilon_1) - (\phi + u_2)) - A_1 \\
& - \lambda_3 ((1 - \rho)(1 - u_1) \beta_1 S + (1 - u_2) \phi) - \lambda_5 \epsilon_1 \\
\lambda_3' = & -\lambda_1 (-(1 - u_1) \beta_2 S) - \lambda_2 (1 - u_1) \beta_2 S \\
& - \lambda_3 ((1 - \rho)(1 - u_1) \beta_2 S - (\mu_3 + \epsilon_2) - (u_3 + \delta)) - A_2 \\
& - \lambda_4 (u_3 + \delta) - \lambda_5 \epsilon_2 \\
\lambda_4^0 = & -\lambda_4 (-\mu_4) \quad \lambda_5^0 = -\lambda_5 u_b - \\
& \lambda_1 ((1 - u_1) \beta_3 S).
\end{aligned}$$

with boundary conditions $\lambda_1(t_f) = \lambda_2(t_f) = \lambda_3(t_f) = \lambda_4(t_f) = \lambda_5(t_f) = 0$ furthermore, the optimal control u_1^*, u_2^* and u_3^* are given by

$$u_1^* = \max \left\{ 0, \min \left(1, \frac{S_1 I_c + \beta_2 I + \beta_3 W}{K_1} (\lambda_3(1 - \rho) + \rho \lambda_2 - \lambda) \right) \right\}$$

$$u_2^* = \max \left\{ 0, \min \left(1, \frac{(\lambda_2 + \lambda_3 \phi) I_c}{K_2} \right) \right\}$$

$$u_3^* = \max \left\{ 0, \min \left(1, \frac{(\lambda_3 - \lambda_4) I}{K_3} \right) \right\}$$

Proof

Using the results of (Fleming and Rishel, 1975) accordingly to obtain the adjoint variables, we differentiate the Hamiltonian H in (3.92) with respect to each variables that is, $S(t)$, I_c , $I(t)$, $R(t)$, and $W(t)$

$$\begin{aligned} \frac{d\lambda_1}{dt} &= -\frac{\partial H}{\partial S} = -\lambda_1(-\mu - (1 - u_1)\beta_1 I_c + \beta_2 I + \beta_3 W) \\ &\quad - \lambda_2(\rho(1 - u_1)\beta_1 I_c + \beta_2 I + \beta_3 W) \\ &\quad - \lambda_3((1 - \rho)(1 - u_1)\beta_1 I_c + \beta_2 I + \beta_3 W) \\ \frac{d\lambda_2}{dt} &= -\frac{\partial H}{\partial I_c} = -\lambda_1(-(1 - u_1)\beta_1 S) \\ &\quad - \lambda_2((1 - u_1)\beta_1 S - (\mu_2 + \epsilon_1) - (\phi + u_2)) - A_1 \\ &\quad - \lambda_3((1 - \rho)(1 - u_1)\beta_1 S + (1 - u_2)\phi) - \lambda_5 \epsilon_1 \\ \frac{d\lambda_3}{dt} &= -\frac{\partial H}{\partial I} = -\lambda_1(-(1 - u_1)\beta_2 S) - \lambda_2(1 - u_1)\beta_2 S \\ &\quad - \lambda_3((1 - \rho)(1 - u_1)\beta_2 S - (\mu_3 + \epsilon_2) - (u_3 + \delta)) - A_2 \\ &\quad - \lambda_4(u_3 + \delta) - \lambda_5 \epsilon_2 \\ \frac{d\lambda_4}{dt} &= -\frac{\partial H}{\partial R} = -\lambda_4(-\mu_4) \\ \frac{d\lambda_5}{dt} &= -\frac{\partial H}{\partial W} = -\lambda_5 u_b - \lambda_1((1 - u_1)\beta_3 S). \end{aligned}$$

Also, to find the optimal control of the control variables set u_1^*, u_2^* and u_3^* using the partial differential equation

$$\frac{\partial H}{\partial u_i} = 0 : i = 1, 2, 3$$

for u_1^*

$$\frac{\partial H(S, I_c, I, R, W)}{\partial u_1} = 0$$

therefore,

$$u_1^* = \frac{S(I_1 I_c + \beta_2 I + \beta_3 W)(\lambda_3(1 - \rho) + \rho\lambda_2 - \lambda_1)}{K_1}$$

for u^*2

$$\frac{\partial H(S, I_c, I, R, W)}{\partial u_1} = 0$$

$$u_2^* = \frac{(\lambda_2 + \lambda_3\phi)I_c}{K_2}$$

for u^*3

$$\frac{\partial H(S, I_c, I, R, W)}{\partial u_1} = 0$$

$$u_3^* = \frac{(\lambda_3 - \lambda_4)I}{K_3}$$

Therefore,

$$u_1^* = \max \left\{ 0, \min \left(1, \frac{S(I_1 I_c + \beta_2 I + \beta_3 W)(\lambda_3(1 - \rho) + \rho\lambda_2 - \lambda_1)}{k_1} \right) \right\}$$

$$u_2^* = \max \left\{ 0, \min \left(1, \frac{(\lambda_2 + \lambda_3\phi)I_c}{K_2} \right) \right\}$$

$$u_3^* = \max \left\{ 0, \min \left(1, \frac{(\lambda_3 - \lambda_4)I}{K_3} \right) \right\}$$

Based on the Prior boundedness of the state and adjoint variables, the uniqueness of the optimal control has been established. By standard control arguments which involve the bounds on the controls, we can say that

$$u_1^* = \begin{cases} 0 & \text{if } \frac{S(I_1 I_c + \beta_2 I + \beta_3 W)(\lambda_3(1 - e) + \rho\lambda_2 - \lambda_1)}{K_1} < 0 \\ (0, 1) & \text{if } \frac{S(I_1 I_c + \beta_2 I + \beta_3 W)(\lambda_3(1 - e) + \rho\lambda_2 - \lambda_1)}{K_1} \leq 1 \\ 1 & \text{if } \frac{S(I_1 I_c + \beta_2 I + \beta_3 W)(\lambda_3(1 - e) + \rho\lambda_2 - \lambda_1)}{K_1} > 1 \end{cases}$$

(3.93)

$$u_2^* = \begin{cases} 0 & \text{if } \frac{(\lambda_2 - \lambda_3\phi)I_c}{K_2} < 0 \\ (0, 1) & \text{if } \frac{(\lambda_2 - \lambda_3\phi)I_c}{K_2} \leq 1 \\ 1 & \text{if } \frac{(\lambda_2 - \lambda_3\phi)I_c}{K_2} > 1 \end{cases} \quad (3.94)$$

$$u_3^* = \begin{cases} 0 & \text{if } \frac{(\lambda_3 - \lambda_4)I}{K_3} < 0 \\ (0, 1) & \text{if } \frac{(\lambda_3 - \lambda_4)I}{K_3} \leq 1 \\ 1 & \text{if } \frac{(\lambda_3 - \lambda_4\phi)I}{K_3} > 1 \end{cases} \quad (3.95)$$

Numerical Simulation of the Optimal Control for Model 3

We carried out the numerical simulations by using the values in table (3.8). We also incorporate progression from carrier class to infected class to model 3 as additional parameter. We solved the optimality system which consists of the state and adjoint equations. We use the forward-backwards sweep method and solve the optimality system numerically. The simulation was carried out by using the values in table 1. We use assumed value of 10 for the recruitment rate θ . The following values for the coefficients for the states and controls $A_1=1, A_2=1.5, K_1=1.5, K_2=0.02, K_3=0.15$ are used

To examine the effect of the control intervention, we considered the following strategies

- (1) Applying educational campaign as the only control intervention u_1
- (2) Applying prevention and sanitation as the only control intervention u_2
- (3) Applying screening with early treatment as the only control intervention u_3
- (4) Applying educational campaign and prevention with sanitation as control intervention u_1 and u_2
- (5) Applying educational campaign and screening with early treatment as control intervention u_1 and u_3
- (6) Applying prevention with sanitation and screening with early treatment as control intervention u_2 and u_3
- (7) Applying educational campaign, prevention with sanitation and screening with early treatment as control intervention u_1, u_2 and u_3 respectively

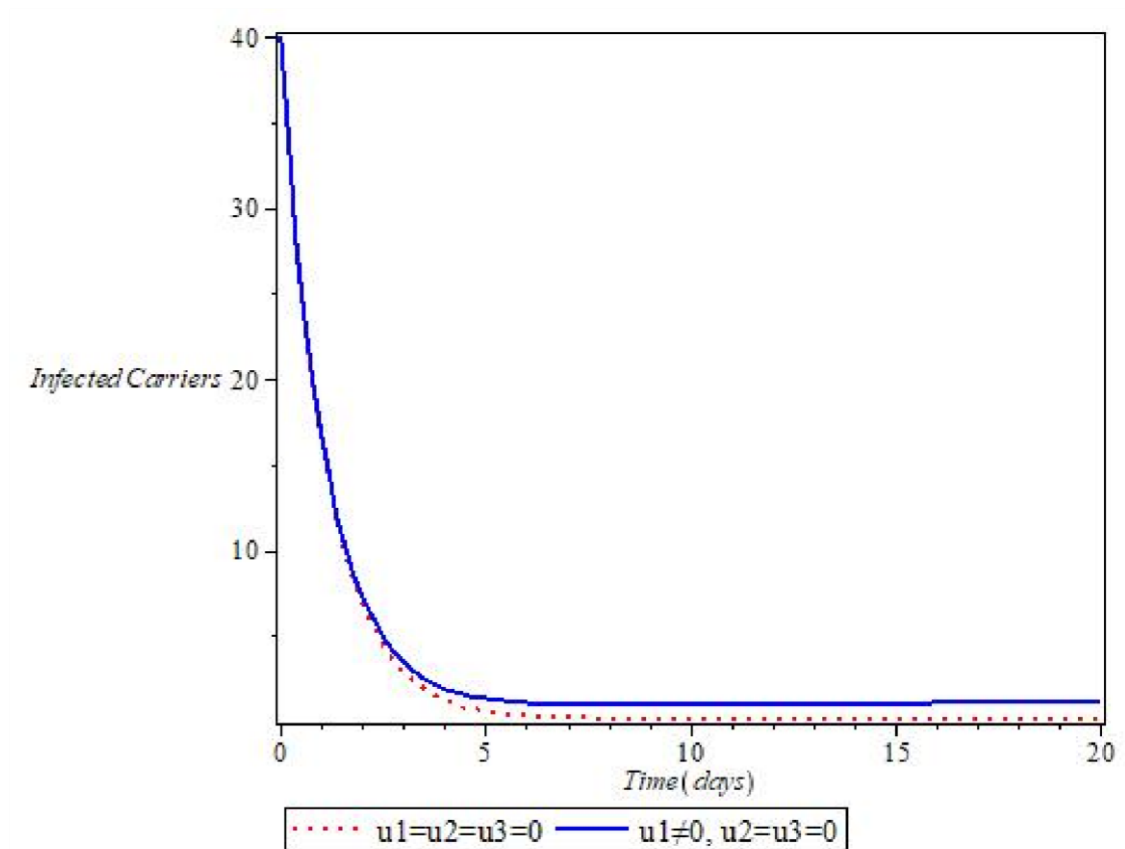


Figure 3.41: Simulation Result Showing Effect of Using Optimal Educational Campaign as the Only Control Strategies on Carriers Population

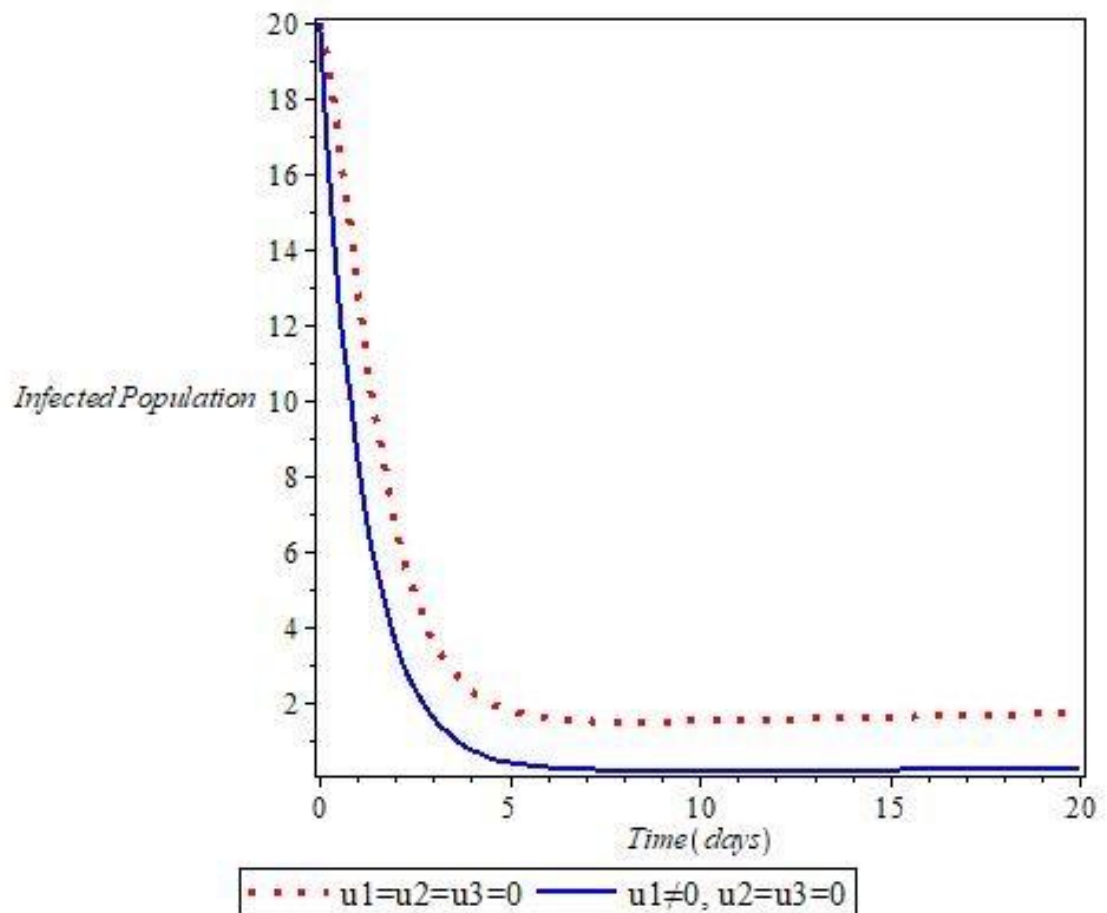


Figure 3.42: Simulation Result Showing Effect of Using Optimal Educational Campaign as the Only Control Strategies on Infected Population

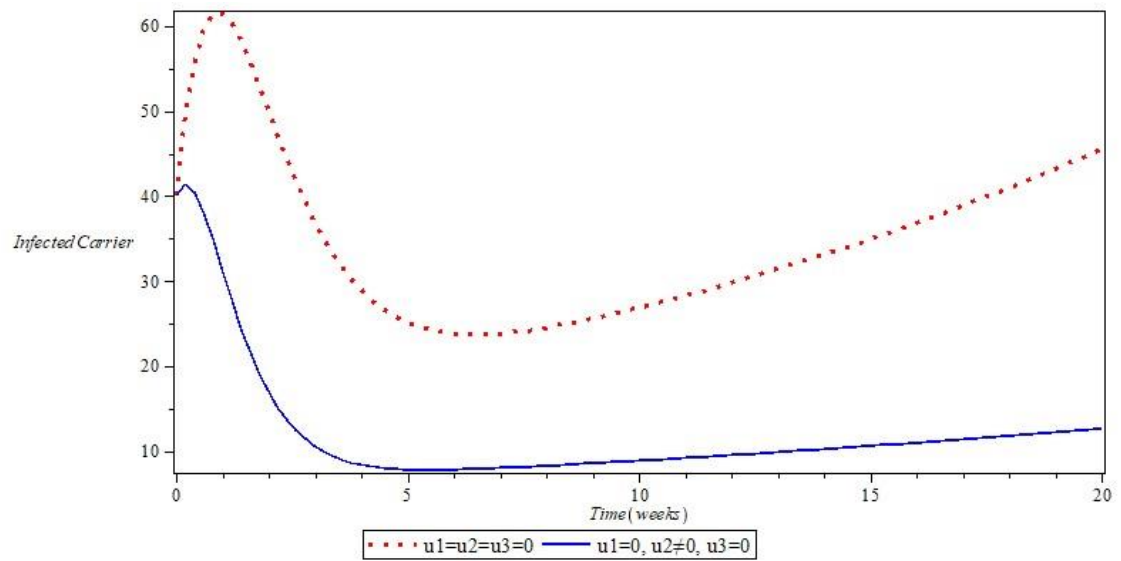


Figure 3.43: Simulation Result Showing Effect of Using Prevention and Sanitation as the Only Control Strategies on Carriers Population

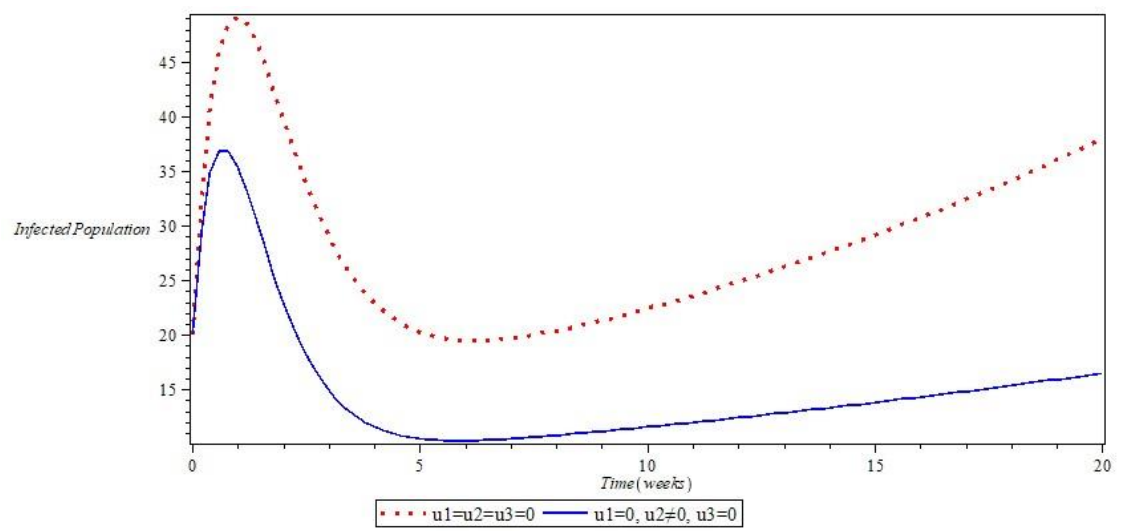


Figure 3.44: Simulation Result Showing Effect of Using Prevention with Sanitation as the Only Control Strategies on Infected Population

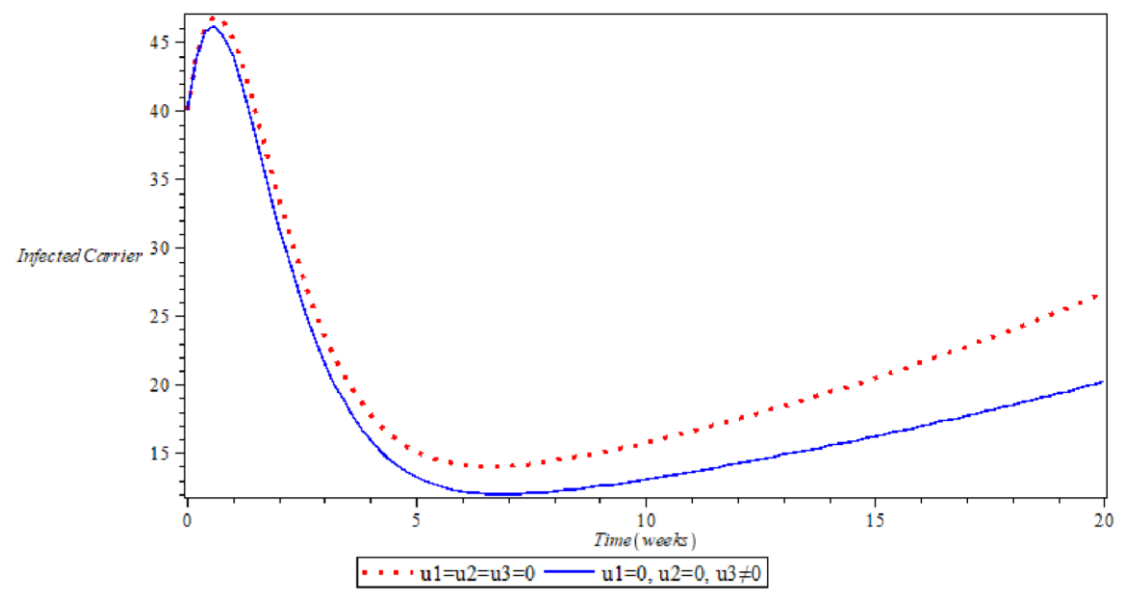


Figure 3.45: Simulation Result Showing Effect of Using Optimal Screening with early treatment as the only Control Strategies on Carriers Population

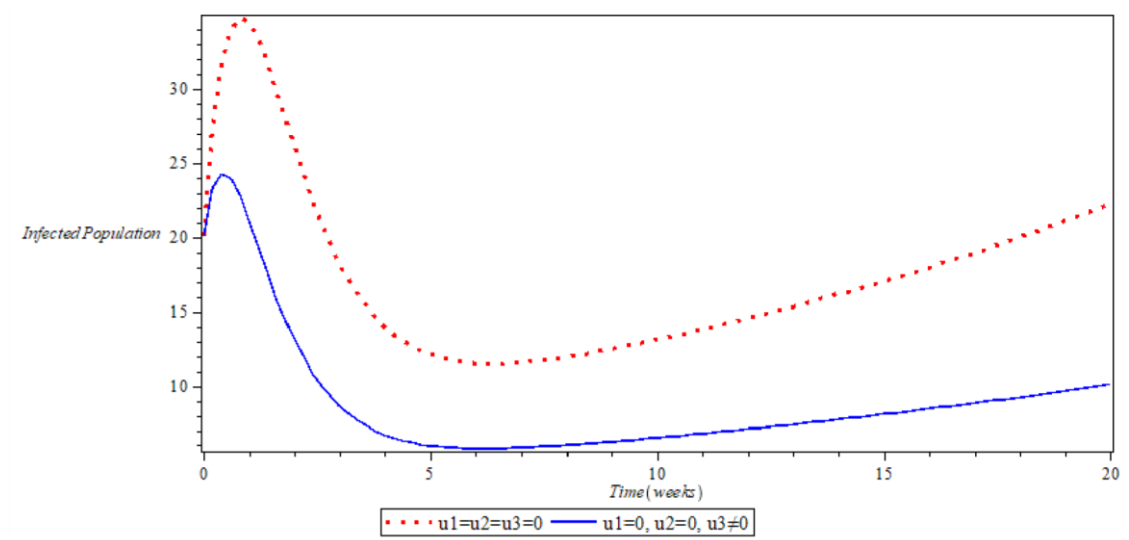


Figure 3.46: Simulation Result Showing Effect of Using Optimal Screening with Early Treatment as the only Control Strategies on Infected Population

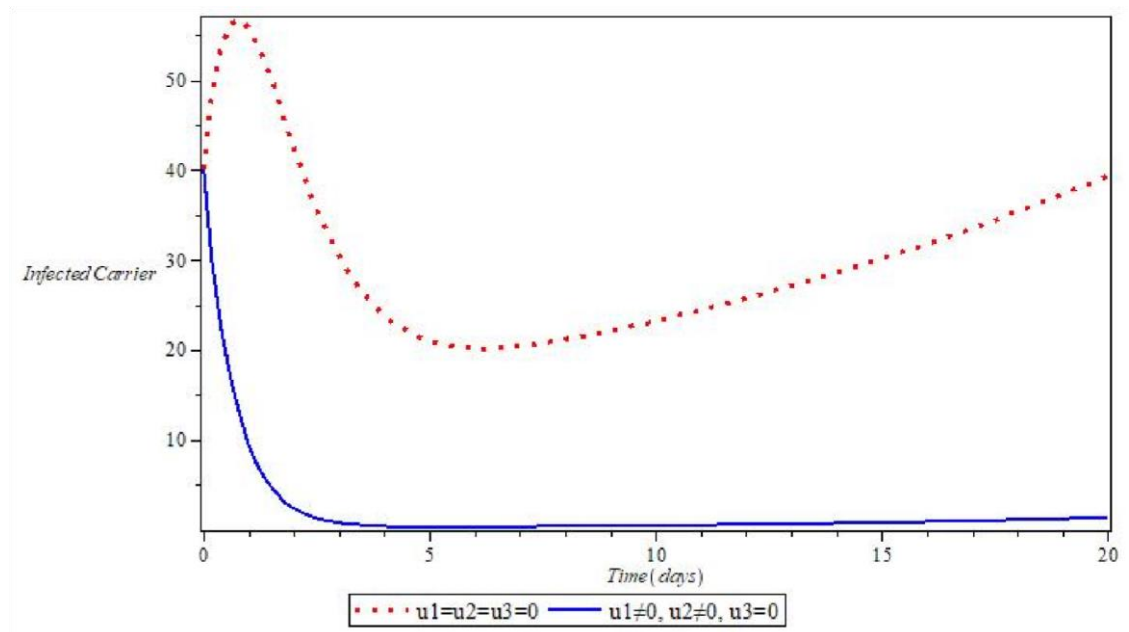


Figure 3.47: Simulation Result Showing Effect of Using Optimal Educational Campaign and Prevention with Sanitation as Control Strategies on Carriers Population

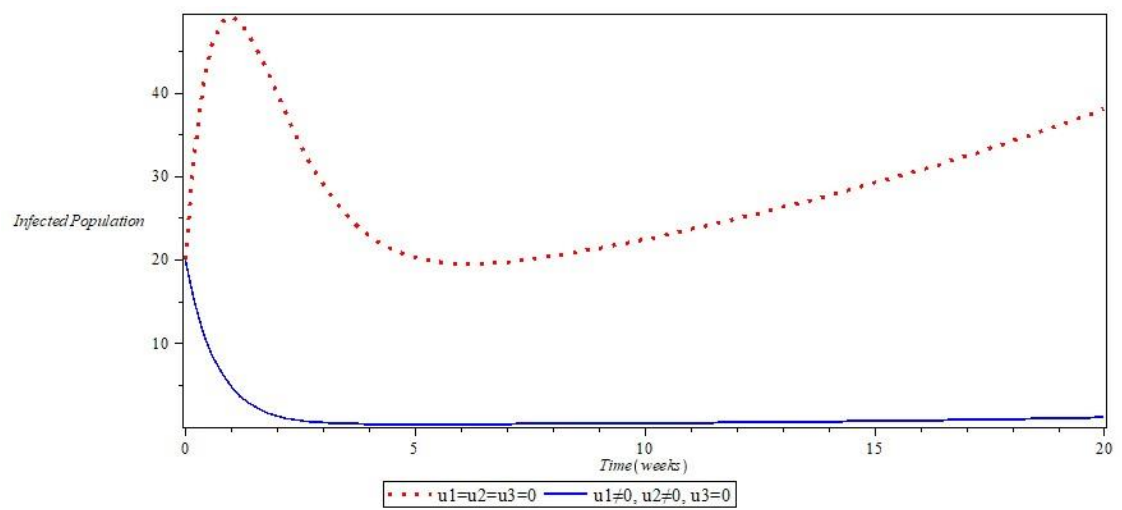


Figure 3.48: Simulation Result Showing Effect of Using Optimal Educational Campaign and Prevention with Sanitation as Control Strategies on Infected Population

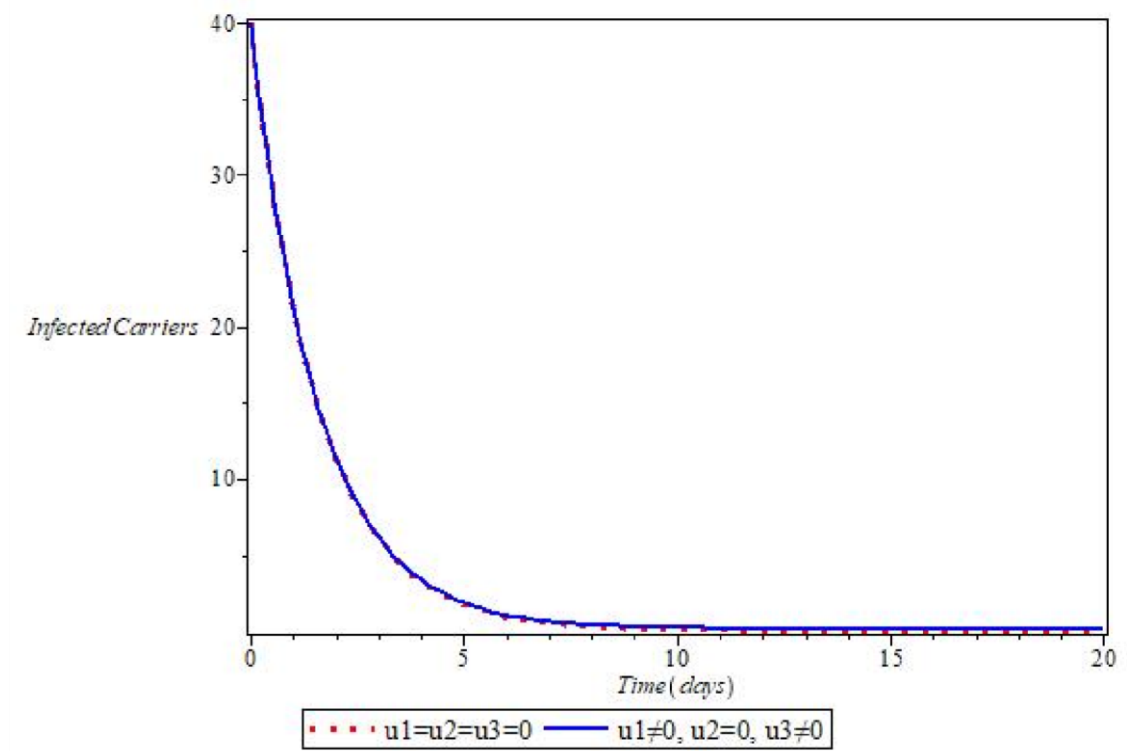


Figure 3.49: Simulation Result Showing Effect of Using Optimal Educational Campaign and screening with Early Treatment as Control Strategies on Carriers Population

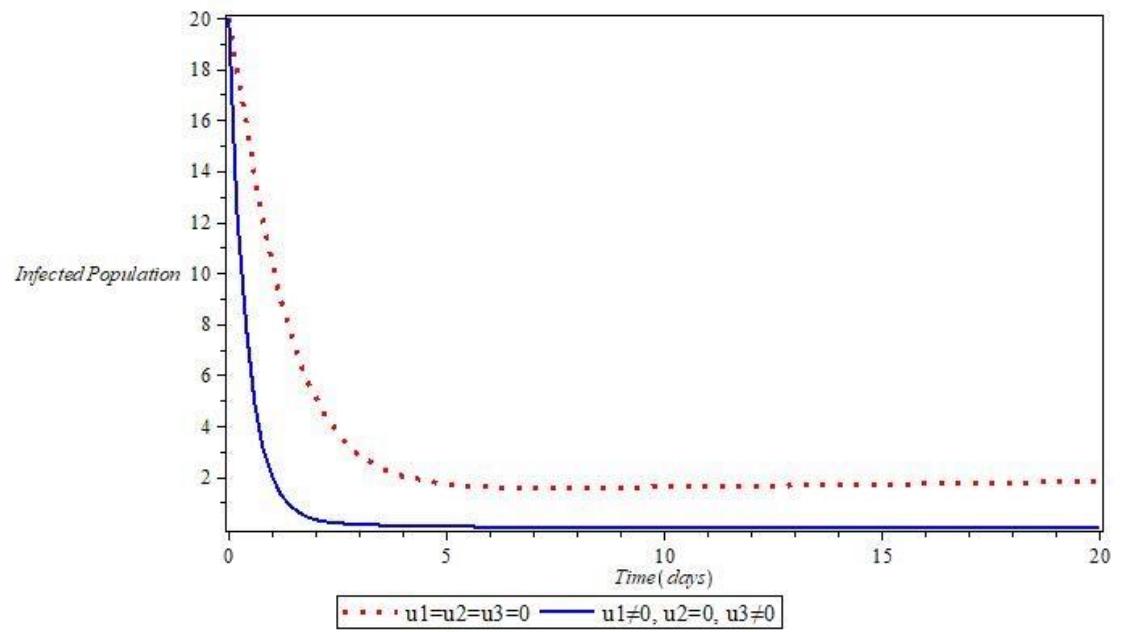


Figure 3.50: Simulation Result Showing Effect of Using Optimal Educational Campaign and screening with Early Treatment as Control Strategies on Infected Population

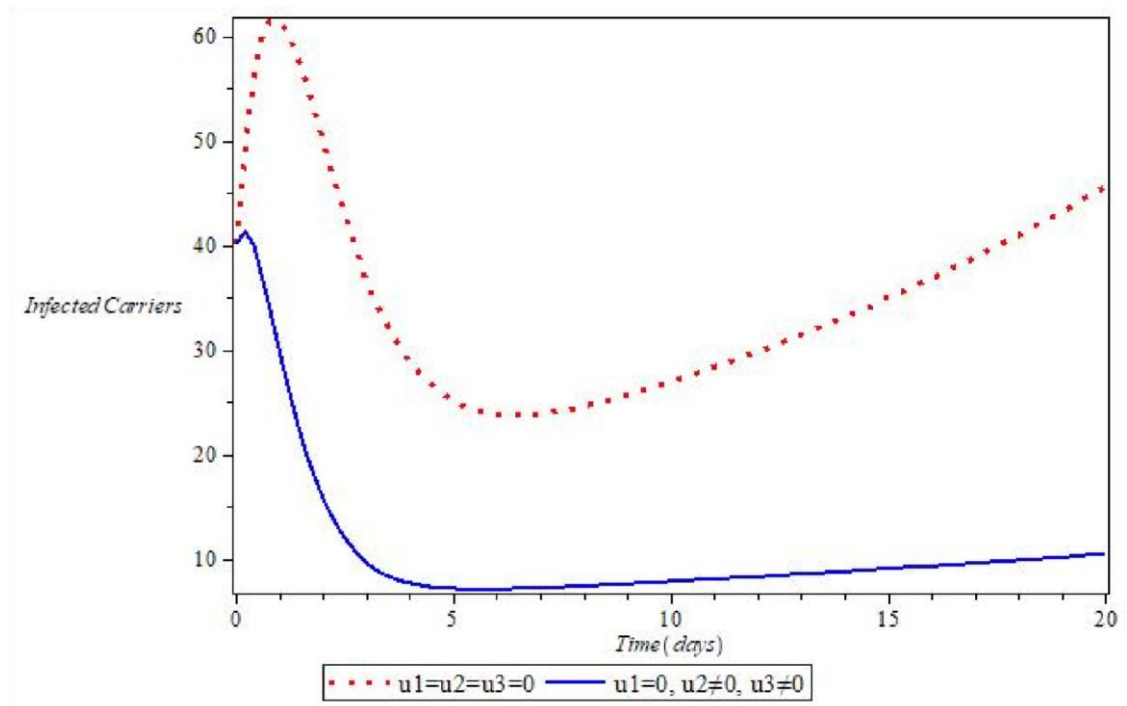


Figure 3.51: Simulation Result Showing Effect of Using Optimal Prevention with Sanitation and Early Treatment with Screening as Control Strategies on Carriers Population

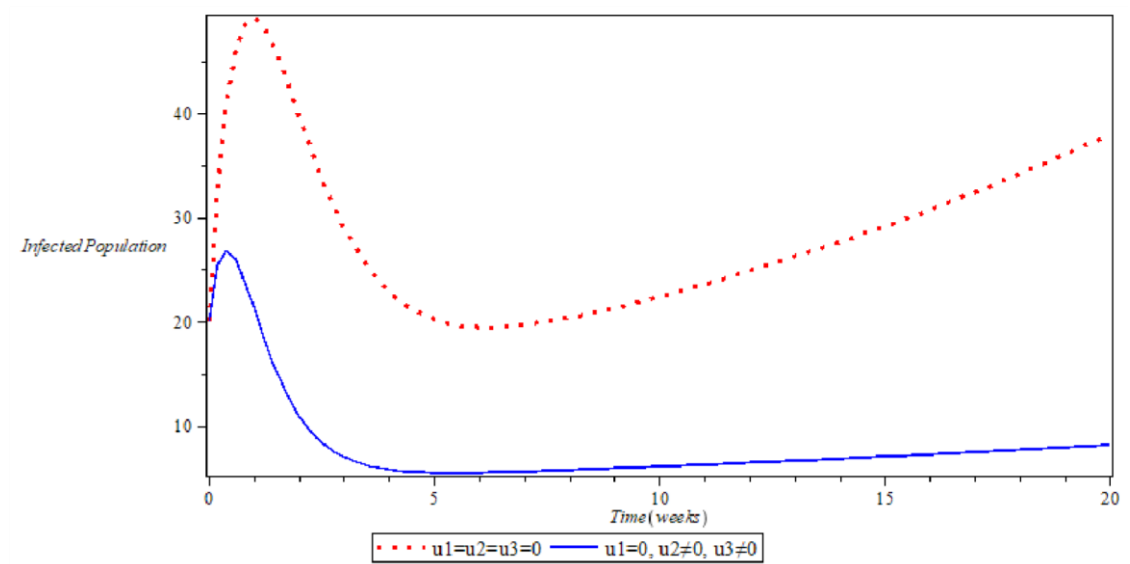


Figure 3.52: Simulation Result Showing Effect of Using Optimal Prevention with Sanitation and Screening with Early Treatment as Control Strategies on Infected Population

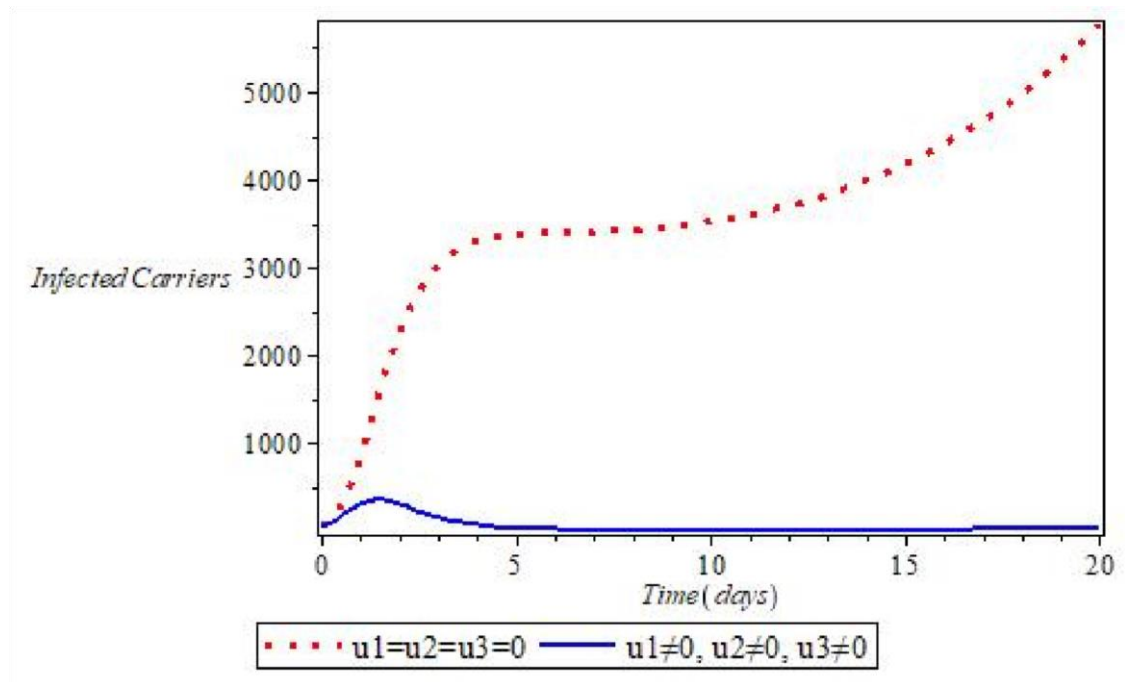


Figure 3.53: Simulation Result Showing Effect of Using Optimal Educational Campaign, Prevention and Sanitation and Screening with Early Treatment as Control Strategies on Carriers Population

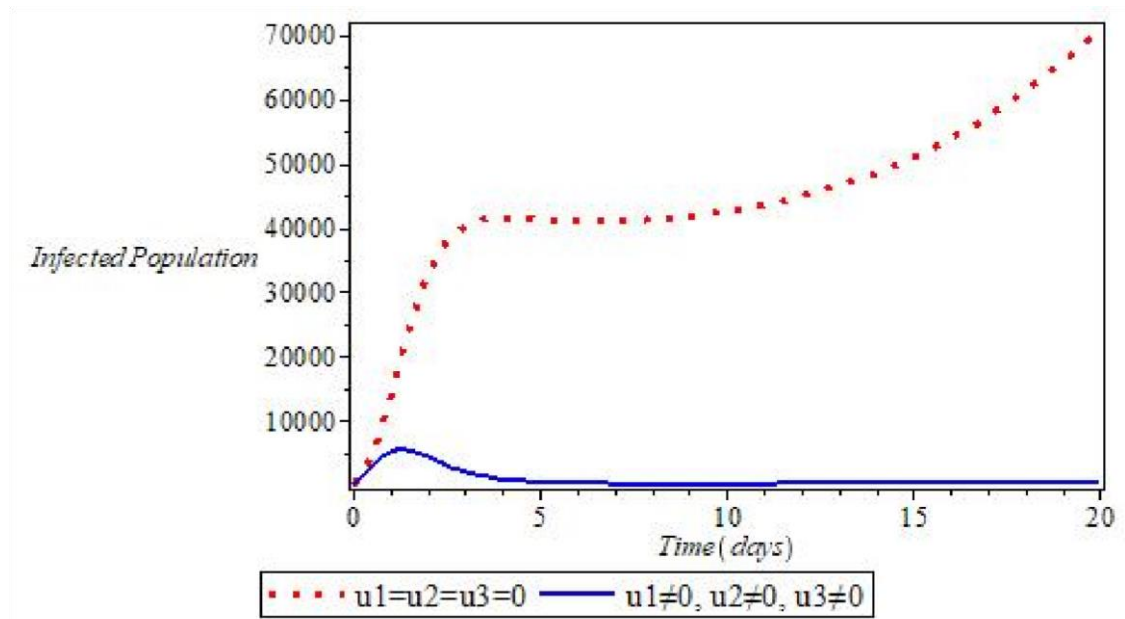


Figure 3.54: Simulation Result Showing Effect of Using Optimal Educational Campaign, Prevention and Sanitation and Screening with Early Treatment and Screening as Control Strategies on Infected Population

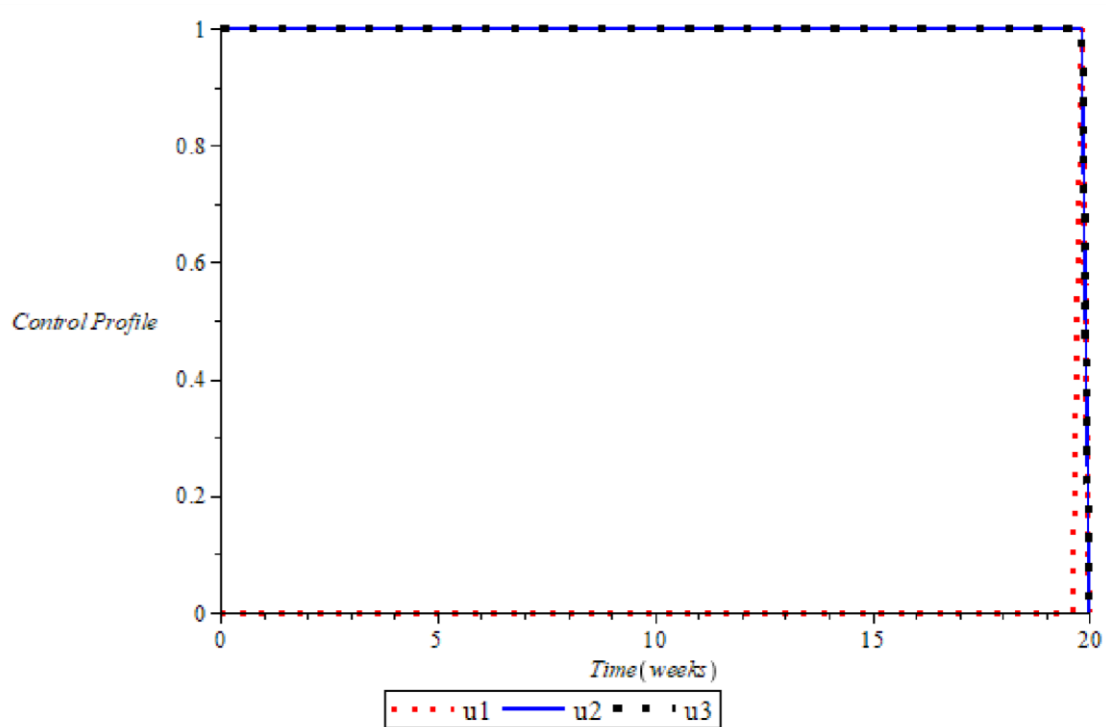


Figure 3.55: Simulation Result Showing Control Profile u_1, u_2 and u_3

Chapter 4

NUMERICAL SIMULATION AND DISCUSSION OF RESULTS

4.1 Introduction

To validate the analytical results obtained for proposed models, numerical simulations shall be conducted. Discussion of results shall also be made for equilibrium analysis, stability analyses, reproduction numbers, sensitivity analysis and numerical methods. Initial values for the parameters of the models are drawn from the literature to ensure the reliability and compliance of the results of the simulations with the biological framework of the models and where they are not available, assumed values are adopted.

4.2 Discussion of Results for Equilibrium Analysis

For the proposed models, there exists a disease-free equilibrium and endemic equilibrium. The interpretation of these equilibrium states is that it is possible to have a community that is free from typhoid fever if proper controls are put in place and also a communities that is prone to typhoid fever due to certain prevailing conditions that can be found in a population. Privileged communities in a country are likely to be typhoid-free, while communities with less privilege may be prone to typhoid fever.

4.3 Discussion of Results for Stability Analysis

The disease - free equilibrium and the endemic equilibrium of models 1 are shown to be locally and globally stable, while conditions for the disease-free equilibrium state and the endemic equilibrium state of model 1 are established as stable locally and globally. The epidemiological and biological interpretation of the local stability of the diseasefree equilibrium is that the outbreak of typhoid is condemned to a rapid failure, even if the person with the bacteria is introduced into the typhoid-free population, since the infected person would cause less than one secondary infection on average, while the local instability of the disease-free equilibrium implies that the condition that sustains the typhoid free population have been relaxed and the . The community is no longer free from typhoid but is prone to typhoid.

4.4 Discussion of Results for Basic Reproduction Numbers

For model 1, 2 and 3, if we substitute the values of the parameters in tables 3.6 and 3.7 and 3.8, each of the basic reproduction number will be less than one, this shows that the disease can be controlled if adequate preventive measures are put in place and if the basic reproduction number is greater than one it means the disease may evade the entire population and the entire population is at risk.

4.5 Discussion of Results for Sensitivity Analysis

With reference to table 3.4, the parameter with the highest sensitivity index with respect to the basic reproduction number R'_0 is the education campaign denoted by φ followed by the recruitment rate π . The signs of φ and θ agreed with our expectation. There is a saying that ignorance is a disease, it is therefore important to enlighten people on how to prevent themselves from acquiring typhoid fever. Also, educational campaign in terms of sensitization and enlightenment programmes by government and non-governmental organization must be on the ground because as more and more people are educated about the dangers of getting infected with typhoid fever, adequate prevention and control will be put in place and there will be fewer people to be infected. As for θ , R'_e is expected to be an increasing function of θ because an increase in θ brings about an increase in the number of susceptible

4.6 Discussion of Results for Numerical Methods

As for the differential transform method (*DTM*) and Variational Iteration Method (*VIM*) figure 3.4 to 3.18 and figure 3.19 to 3.33 respectively show that the solutions obtained by using the *DTM* and (*VIM*) compared favorably and are in good agreement with 4th-Order Runge-Kutta Method .

Discussion of Results for Optimal Control Model 1

In figure 3.34 and 3.35 when a single intervention strategy is implemented i.e vaccination, there is a decrease in the population of the infected carrier and the infected individuals. Also when vaccination is intensified to bring the disease under

control there is a noticeable decrease in the population of the infected individuals and the infected carrier individuals. The implication of this, is that, vaccination timing, efficacy and coverage must be high enough before it can have desirable impact on typhoid propagation and

eradication.

In figure 3.36 and 3.37 when education campaign is implemented as a single intervention the population of infected carrier individuals and infected individuals fall continuously. The implication of this is that education campaign as a control strategy has more influence in reducing the population of both the infected individuals and the infected carrier individuals

In figure 3.38 and 3.39 when both interventions, vaccination and education campaign are implemented at an optimum level the population of the susceptible individuals, infected individuals and infected carrier individuals falls rapidly while the population of recovered individuals rises continuously until after the third month when it begins to fall. The population of susceptible individuals falls from 60 to 15 before it is steady while the population of infected individuals and infected carrier individuals approach extinction after the fourth month.

In all, each of the interventions is capable of influencing typhoid outbreak but the combination of the two strategies that is , vaccination and educational campaign are more efficient in limiting the spread and propagation of the disease and should be implemented in every typhoid prone communities.

Discussion of Results for Optimal Control Model 3

Control with Educational Campaign u_1

In figure (3.41) and (3.42) we applied educational campaign $u_1 \neq 0$ as the only control on the infected carrier and infected population while we set other controls u_2 and u_3 to zero. We observed that this strategy has a positive effect on the infected carrier and infected population by decreasing the population of both classes. Thus, there should be a need for public awareness mostly in typhoid fever prone communities

Control with Prevention and Sanitation u_2

We incorporate prevention and sanitation as the only intervention that is, $u_2 \neq 0$, while we set other controls to zero that is $u_1, u_3=0$. Figure (3.43) and (3.44) shows the rapid decrease in the population of the infected carrier and infected population. We conclude that, when prevention is combined with sanitation, this will reduce typhoid fever infec-

tion.

Control with Screening with Early Treatment u_3

We applied early treatment and screening in this strategy to control the spread of typhoid fever. Figure (3.45) and (3.46) show optimized Early Treatment combined with Screening. Screening helps the asymptomatic carrier and the symptomatic infected individuals to know their status and when this is done and early treatment is implemented, this will drastically reduce the population of the asymptomatic carrier and the symptomatic infected population as shown in figure (3.45) and (3.46).

Control with Educational Campaign and Prevention with Sanitation u_1 and u_2 respectively

In these strategies, we applied educational campaign and prevention combined with sanitation. Figure (3.47) and (3.48) shows the effect of these controls. Public awareness is a vital tool in controlling the spread of infectious disease. When this is combined with sanitation as in the case of typhoid fever, this will have a positive impact in controlling the spread of typhoid fever.

Control with Educational Campaign and Screening with Early Treatment u_1 and u_3 respectively

Figure (3.49) and (3.50) show the effect of educating carrier infected and infected individual and how an individual could prevent themselves from contracting typhoid fever together with screening of asymptomatic carrier of typhoid and early treatment of infected individual will reduce the spread of typhoid fever.

Control with Prevention /Sanitation and Early Treatment /Screening u_2 and u_3 respectively

Figure (3.51) and (3.52) show the effect of applying prevention /sanitation and early treatment /screening. In this case we set $u_2, u_3 \neq 0$ as control intervention. We conclude that by applying Prevention /Sanitation and screening of asymptomatic individual will reduce the infected carrier population. Also, When early treatment is implemented, on the infected individual, this will reduce the infected population

Control with Educational Campaign, Prevention /Sanitation and Early Treatment /Screening u_1 , u_2 and u_3 respectively

Here, we implemented all the three controls that is, control with educational campaign, control with prevention combined sanitation and early treatment combined with screening u_1 , u_2 and u_3 as an intervention to control typhoid fever. Figure (3.53) and (3.54) shows that after the implementation of the control, the population of the

infected carrier and infected individuals reduced drastically. We, therefore, conclude that by applying the combination of the three strategies is more effective in the control and containment of typhoid fever in typhoid fever prone community in a specific period

Chapter 5

SUMMARY, CONCLUSIONS AND

RECOMMENDATIONS

5.1 Introduction

Mathematical modelling has been revealed as a powerful tool for analyzing the epidemiology of infectious diseases, understanding their behavior, predicting their social impact and finding out how external factors influence their impact (Benyah, 2005).

5.2 Summary

We showed that the models are mathematically and epidemiologically well positioned in a biologically feasible region in human populations. We also carried out a detailed analysis to determine the equilibrium states of the models and the basic reproduction number R_0 necessary for the diseases control. It was established that the disease free equilibrium states is locally asymptotically stable when $R_0 < 1$ and globally asymptotically stable whenever $R_0 \leq 1$. We analyzed the existence and the stability of endemic equilibrium point $R_0 > 1$. We also carried out the global asymptotic stability of the endemic equilibrium point for model 1 and found out whether the endemic equilibrium of the model equations is globally asymptotically stable whenever $R_0 > 1$ using the LaSalle's principles. The optimal control strategies were used to minimize the

infected carriers and infected individuals and the adverse side effects of one or more of the control strategies.

The Sensitivity Index was used to assess the most sensitive parameter for controlling typhoid fever in order to achieve disease control. To attempt the series solution of the models, DTM and VIM were employed, to compare the results obtained by DTM and VIM with the 4th order Runge-Kutta Method, which confirms the accuracy of the two methods

5.3 Conclusion

We formulated a control problem for model 1 and 3 and we derived the conditions for optimal control for the models using Pontryagin's Maximum Principle and it was shown that an optimal control exists for our proposed model. The study concluded that each of the measures was capable of managing typhoid fever disease but the combination of measures was more effective. For model one, we conclude that, educational campaign was most sensitive to typhoid management, it was therefore recommended that any measure directed towards achieving typhoid free society should include educational campaign and treatment. The optimality system was solved numerically; the corresponding uncertain problem was solved by proposing new techniques. Numerical simulations were carried out to illustrate the analytical results. The numerical simulation of the model shows that a possible optimal control strategies become more effective in the control and containment of typhoid when all the controls are combined optimally would reduce the spread of the disease.

5.4 Recommendations

Given the results of this study, the best measure to eradicate the incidence of typhoid fever is to implement mixed preventive measures such as vaccination and educational campaigns. All intervention strategies depend on each other for better performance, but when vaccination, educational campaigns are combined, the best result is achieved. It is also suggested that all obstacles to vaccination introduction be removed as an instrument for managing typhoid. Removing the obstacles to vaccination becomes essential because vaccination comes after education down to typhoid management.

Lastly, Differential Transform Method and Variational Iteration Method are recommended to attempt the series solutions of typhoid fever models. Reliable results are obtained with these numerical methods of solution.

5.5 Contribution to Knowledge

The extension and modification of the typhoid model with prevention and control measures and the possibility of the transmission of diseases from person to person leads to the following contributions to existing knowledge:

- (i) Development of a deterministic model involving direct and indirect transmission dynamics of typhoid fever.
- (ii) Confirmation of the basic properties of the epidemiological models
- (iii) Derivation of the basic reproduction number
- (iv) Discovery that typhoid outbreaks in a population can fail even if some percentage of typhoid - infected individuals find their way into the community.
- (v) Typhoid outbreak may evade the entire population if adequate control measures are not implemented.
- (vi) The control strategies become more effective when vaccination and educational campaign are combined optimally
- (vii) The most sensitive parameter to typhoid fever management is an educational campaign.

5.6 Suggestions for Further Studies

Finally, it is suggested that the constraints of this research be extended for further research. It is suggested that researchers interested in this research area consider it:

- (i) other form of typhoid controls apart from those examined in this study;
- (ii) typhoid fever models with more control parameters;
- (iii) other techniques apart from the ones used in this research to obtain the basic reproduction numbers and conduct the stability analysis for the purpose of comparison; and

(iv) other numerical methods of solutions (e.g. Parameter Expansion Method, Linear Multi-step Method, Adomian Decomposition Method, Multi-step Differential Transform Method, etc.) to solve other typhoid models and confirm their degree of accuracy.

(v) prediction of typhoid fever epidemic using machine learning

REFERENCES

- Abbasbandy, E. & Shivanian, E. (2009). Application of the variational iteration method for system of nonlinear Volterra's integro-differential equations. *Mathematical and Computer Applications*, 4(2), 147–158.
- Abdou, M. A. & Soliman, A. A. (2005). New application of Variational iteration method. *Physica D: Nonlinear Phenomena*, 211(1-2), 1 – 8.
- Abdou, M. A. & Soliman, A. A. (2005). Variational iteration method for solving Burger's and coupled Burger's equation. *Journal of Computational and Applied Mathematics*, 181(2), 245–251.
- Abdulrahman, S., Akinwande, N. I., Awojoyogbe, O. M. & Abubakar, U. Y. (2013). Sensitivity analysis of the parameters of a mathematical model of hepatitis B virus transmission. *Universal Journal of Applied Mathematics*, 1(4), 230–241.
- Adeboye, K. R. & Haruna, M. (2015). A mathematical model for the transmission and control of malaria and typhoid co-infection using SIRS approach. *Research Journal's Journal of Mathematics*, 2(2), 1–24.
- Adetunde, I. A. (2008). Mathematical model for the dynamics of typhoid fever in kassena-nankana district of upper east region of Ghana. *Journal of Modern Mathematics and Statistics*, 2, 45–49.
- Adewale, S. O., Adeniran, G. A., Olapade, I. A., Ajao, S. O. & Mohammed, I. T. (2017). Mathematical and sensitivity analysis of the dynamical spread of cholera. *International Journal of Innovation and Applied Studies*, 19(1), 46–54.
- Ainea, N., Matofali, A. X. & Mkwizu, M. (2018). Optimal control analysis of a cholera disease transmission model in Tanzania. *International Journal of Scientific Research in Science, Engineering and Technology*, 4(4), 865–872.
- Akanni J. O. & Adedipo. A. D. (2018). Sensitivity analysis of the dynamical transmission and control of lassa fever virus. *Asian Research Journal of Mathematics*, 9(3), 1–11.
- Akinboro, F. S., Alao, S. & Akinpelu, F. O. (2014). Numerical solution of SIR model using differential transformation method and variational iteration method. *General Mathematics Notes*, 22(2), 82–92.

- Akinwande, N. I. (2006). A mathematical model of yellow fever epidemics. *Afrika Matematika*, 6(9), 56–58.
- Alhassan, H. M., Shidali, N. N., Manga, S. B., Abdullahi, K. & Hamid, K. M. (2012). Co-infection profile of Salmonella typhi and Malaria parasite in Sokoto-Nigeria. *Global Journal of Science, Engineering and Technology*, 2201(2), 13–20.
- Anderson, R. M. & May, R. M. (1991). Infectious diseases of humans: Dynamics and control. *Jama the Journal of the American Medical Association*, 268(23), 33–81.
- Awofisayo, O. A., Pratt, A., McCarthy, N. & Hall, I. (2019). Within-host mathematical modelling of the incubation period of Salmonella Typhi. *Royal Society Open Science*, 6, 182143. doi:10.1098/rsos.182143
- Awoke, T. D. (2019). Optimal control strategies for the transmission dynamics of typhoid fever. *American Journal of Applied Mathematics*, 7(2), 37–48.
- Ayoade, A. A., Peter, O. J., Ayoola, T. A., Oguntolu, F. A., Amadiogwu, S. & Abioye, A. I. (2019). Optimal intervention strategies for transmission dynamics of cholera disease. *Malaysian Journal of Applied Sciences*, 4(1), 26–37.
- Aziz, T. & Haque, S. (2012). Role of widal test in the diagnosis of typhoid fever in context to other test. *American Journal of Biochemistry*, 2(1), 16–18.
- Bakare, E. A., Nwagwo, A. & Danso-Addo, E. (2014). Optimal control analysis of an SIR epidemic model with constant recruitment. *International Journal of Applied Mathematics Research*, 3(3), 273–285.
- Balaji, V., Kapil, A., Shastri, J., Pragasam, A. K., Gole, G. & John, J. (2018). Longitudinal typhoid fever trends in India from 2000 to 2015. *American Journal of Tropical Medicine and Hygiene*, 99(3), 1 – 7.
- Benhammouda, B., Leal, H. V. & Martinez, H. L. (2014). Modified differential transform method for solving the model of pollution for a system of lakes. *Discrete Dynamics and Society*. Article ID645726.
- Benyah, F. (2005). *Introduction to mathematical modeling*. A paper presented at the 7th Regional Conference on modeling, simulation and optimization, Cape Coast, Ghana.
- Blower, B. & Dowlatabadi, H. (1994). Sensitivity analysis of complex models of disease transmission: an HIV model as an example. *International Statistical Review*, 62(2), 229–243.
- Castillo, C. (2006). Optimal control of an epidemic through educational campaigns. *Electronic Journal of Differential Equations*, 125, 1–11.
- Chan, K., Saltelli, A. & Tarantola, S. (1997). Sensitivity analysis of model output: Varianced-based methods make the difference. Proceedings of the 1997 Winter Simulation Conference. European Commission Joint Research Centre, Ispra, Italy.

- Clemens, A. (2009). A feedback control dynamics for glucose controlled insulin infusion system. *Medical Progress through Technology*, 6, 91–98.
- Cook, J. H. (2010). Are cholera and typhoid vaccines a good investment for slum in Kolkata, India?. *Infectious Disease Journal*, 9(5), 485–496.
- Cvjetanovic, B., Grab, B. & Uemura, K. (2014). Epidemiological model of typhoid fever and its use in the planning and evaluation of antityphoid immunization and sanitation programmes. *Bulletin of the World Health Organization*, 45(1), 53–75.
- Daley, D. J. & Gani, J. (2005). *Epidemic Modeling: An Introduction*. New York: Cambridge University Press.
- Date, K. A., Bentsi-Enchill, A., Marks, F. & Fox, K. (2015). Typhoid fever vaccination strategies, *Vaccine*, 33, 55–61.
- Derrick, N. R. & Grossman, S. L. (1976). *Differential Equation with Application*. Philippines: Addison Wesley Publishing Company, Inc. .
- Diekmann, O., Heesterbeek, J. A. P. & Metz, J. A. J. (1990). On the definition and computation of the basic reproduction ratio R_0 in models for infectious diseases in heterogeneous populations. *Journal of Mathematical Biology*, 28, 365–382.
- Driessche, P. V and Watmough, J.(2002). Reproduction numbers and sub-threshold endemic equilibria for compartmental models of disease transmission. *Mathematical Biosciences*. 180(1-2),29-48.
- Edward, S. (2017). A deterministic mathematical model for direct and indirect transmission dynamics of typhoid fever. *Open Access Library Journal*, 4, e3493. <http://doi.org/10.4236/oalib.1103493>
- Edward, S. & Nyerere, N. (2009). Modeling typhoid fever with education, vaccination and treatment. *Engineering Mathematics*, 1(1), 44–52.
- Edward, S. & Nyerere, N. (2015). A mathematical model for the dynamics of cholera with control measures. *Applied and Computational Mathematics*, 4(2), 53–63.
- Edward, S., Kuznestsov, D. & Mirau, S. (2014). Modeling the impact of immunization on epidemiology of varicella zoster virus. *Mathematical Theory and Modeling*, 4(8), 16–25.
- Fica, A. (1990). Epidemic typhoid in Chile: Analysis by molecular and conventional methods of Salmonella typhi strain diversity in epidemic and non epidemic. *Journal of Clinical Microbiology*, 34, 1701–1707.
- Fischer, M. & Toe, K. (2011). Optimal insulin infusion resulting from a mathematical model of blood glucose dynamics. *Transactions in Biomedical Engineering*, 36 , 479–486.
- Fister, R. K., Gaff, H., Lenhart, S., Numfor, E., Schaefer, E. & Wang, J. (2016). Optimal control of vaccination in an age-structure cholera model. *Mathematical and*

Statistical Modeling for Emerging and Re-emerging Infectious Diseases, 15, 221 – 248.

Fister, K., Lenhart, S. & McNally, J. S. (2010). Optimising chemotherapy in an HIV model. *Electronic Journal of Differential Equations*, 32, 1–12.

Fister, K. & Panetta, C. (2003). Optimal control applied to competing chemotherapeutic cell-kill strategies. *SIAM Journal on Applied Mathematics*, 63(6), 1954–1971.

Fleming, W. H. & Rishel, R. W. (1975). *Deterministic and Stochastic Optimal Control*, I. New York: Springer.

Gasem, M. H., Dolmans, W. M., Isbandrio, B. B., Wahyono, H., Keuter, M. & Djokomoeljanto, R. (1995). Culture of *Salmonella typhi* and *Salmonella paratyphi* from blood and bone marrow in suspected typhoid fever. *Tropical and Geographical Medicine*, 47, 164–167.

Gaff, H. & Schaefer, E. (2009). Optimal control applied to vaccination and treatment strategies for various epidemiological models. *Mathematical Biosciences and Engineering*, 6, 469–492.

Getachew, T. T., Oluwale D. M. & David, M. (2017). Modeling and optimal control of typhoid fever disease with cost-effective strategies. *Computational and Mathematical Methods in Medicine*, Article ID 2324518. doi:10.1155/2017/2324518

Grimsha, R. (1990). *Nonlinear Ordinary Differential Equations*. Oxford, London: Blackwell Scientific Publications.

Hassan, I. H. (2008). Application of Differential Transform Method for solving systems of Differential Equations. *Applied Mathematical Modelling*, 32, 2552–2559.

He, J. H. (1998). A variational approach to nonlinear problems and its application. *Mechanics Applications*, 20(1) 30–31.

He, J. H. (1999). Variational iteration method a kind of nonlinear analytical technique: Some examples. *International Journal of Nonlinear Mechanics*, 34, 669–708.

Hyman, J. M. (2006). Differential susceptibility and infective epidemic models, *Mathematical Biosciences and Engineering*, 3, 88–100.

Ikere, A. O. & Osemwenkhae, J. E. (2010). Vibrio cholera in Nigeria: A logistic investigation of its stability in its habitat. *Journal of Nigerian Annals of Nature Science*, 10(1), 71–76.

Jones M. M., Feng-B, W. & Naveen, K. V. (2015). Modeling malaria and typhoid fever co-infection dynamics. *Mathematical Biosciences*, 264, 128–144.

Kalajdzievska, D. (2011). Modeling the effects of carriers on the transmission dynamics of infectious diseases, *Mathematical Biosciences and Engineering*, 8(3), 711–722.

- Kariuki, S., Gilks, C., Revathi, G. & Hart, C. A. (2000). Genotypic analysis of multidrug-resistant *Salmonella enterica* Serovar Typhi Kenya. *Emerging Infectious Diseases*, 6, 649–651.
- Kariuki, C. (2004). Characterization of multidrug-resistant typhoid outbreaks in Kenya. *Journal of Clinical Microbiology*, 42(4), 1477–1482.
- Kadaleka, S. (2011). Assessing the Effect of Nutrition and Treatment in Cholera Dynamics: The case of Malawi. Unpublished M. Sc. Dissertation. Department of Mathematical Sciences. University of Der es Salaam.
- Keddy, K. H., Sooka, A., Letsoalo, M. E., Hoyland, G., Chaignat, C. L., Morrissey, A. B. & Crump, J. A. (2011). Sensitivity and specificity of typhoid fever rapid antibody tests for laboratory diagnosis at two sub-Saharan African sites. *Bulletin of the World Health Organization*, 89, 640–647.
- Keeling, M. J. & Danon, L. (2009). Mathematical modeling of infectious diseases. *British Medical Bulletin*, 92(1), 33–42. doi:10.1093/bomb/dp038
- Keskin Y., Servi, S. & Oturane, G. (2011). Reduced differential transform method for solving Klein Gordorm equations. *Proceeding of World Congress on Engineering*, London 11, 22–29.
- LaSalle, J. P. (1976). The Stability of dynamical systems. Regional Conference Series in Applied Mathematics, SIAM, Philadelphia.
- Lauria, D. T., Maskery, B., Poulos, C. & Whittington, D. (2009). An optimization model for reducing typhoid cases in developing countries without increasing public spending. *Vaccine*, 27(10), 1609–1621.
- Lawi, G. O., Mugisha, J. Y. T. & Ongati, N. O. (2011). Mathematical model for malaria and meningitis co-infection among children. *Applied Mathematical Sciences*, 5(47), 2337–2359.
- Ledzewicz, U. & Schattler, H. (2016). Drug resistance in cancer chemotherapy as an optimal control problem. *Discrete and continuous Dynamical System, Series B*, 6(1), 129–150.
- Lemos-Paiao, A. P., Silva, C. J. & Torres, D. F. M. (2017). An epidemic model for cholera with optimal control treatment. *Journal of Computational and Applied Mathematics*, 318, 168–180.
- Lenhart, S. & Workman, J. T. (2007). *Optimal Control Applied to Biological Models*. New York: Chapman and Hall.
- Lifshitz, E. I. (1996). Travel trouble: Typhoid fever - a case presentation and review. *J.A. College Health*. 45(3), 99–105.

- Linkens, D., Abbod, M. & Backory, J. (2017). Closed-loop control of depth of anaesthesia: A simulation study using auditory evoked resources. *Control Engineering Practice*, 5(12), 1717–1726.
- Mak, P. & Distefano, J. (2007). Optimal control policies for the prescription of thyroid hormones. *Mathematical Biosciences*, 42, 159–186.
- Merrell, D., Falkow, S. (2004). Frontal and stealth attack strategies in microbial pathogenesis. *Nature*, 430, 250–256.
- Mirza, S. H. (1996). Multidrug resistant typhoid: A global problem. *Journal of Medical Microbiology*, 44, 317–319.
- Mirzaee, F. (2011). Differential transform method for solving linear and nonlinear systems of ordinary differential equations. *Applied Mathematical Sciences*, 5(70), 3465–3472.
- Moatlhodl, K. & Gosaamang, R. K. (2016). Mathematical analysis of typhoid infection with treatment. *Journal of Mathematical Sciences: Advances and Applications*, 40(1), 75–91.
- Moffact, N. (2014). Mathematical model and simulation of the effects of carriers on the transmission dynamics of typhoid fever. *Transactions on Computer Science Engineering and its Applications*, 2(3), 14–20.
- Mondal, P. K. & Kar, J. K. (2013). Global dynamics of water–borne disease model with multiple transmission pathways. *Applications and Applied Mathematics*, 8(1), 75–98.
- Moon, S. D., Bhosale, A. B., Gajbhiye, P. P. & Lonare, G. G. (2014). Solution of nonlinear differential equation by using differential transform method. *International Journal of Mathematics and Statistical Invention*, 2(3), 78 – 82
- Muhammad, A. K., Muhammad, P., Saeed I., Ilyas, K., Sharidan S. & Taza, G. (2015). Mathematical analysis of typhoid model with saturated incidence rate. *Advanced Studies in Biology*, 7(2), 65–78.
- Mushayabasa, S. (2011). Impact of vaccines on controlling typhoid. *Journal of Modern Mathematics and Statistics*, 5(2), 54–59.
- Mushayabasa, S., Bhunu, C. P. & Gwasira, E. T. N. (2013). Assessing the impact of drug resistance on the transmission dynamics of typhoid fever. *Computational Biology Journal*, Article ID303645. doi:10.1155/2013/303645
- Mushayabasa, S., Bhunu, C. P. & Mhlana, N. A. (2014). Modeling the transmission dynamics of typhoid in malaria endemic setting. *International Journal of Application and Applied Mathematics*, 9(1), 121–140.

- Mushayabasa, S. (2017). A simple epidemiological model for typhoid with saturated incidence rate and treatment effect. *International Journal of Sciences: Basic and Applied Research*, 32(1), 151–168.
- Naidu, D., Chen, C. H., Perez, A. & Schoen, M. (2008). Control strategies for smart prosthetic hand technology: An overview. Proceeding of the 30th Annual International IEEE Conference, Vancouver, British Columbia, Canada, 4314-4317.
- Namawejje, H., Obuya, E. & Lubbohi, L. (2018). Modelling optimal control of cholera disease under the interventions of vaccination, treatment and education awareness. *Journal of Mathematics Research*, 7(8), 58–69.
- Naresh, R., Pandey, S. & Misra, A. K. (2008). Analysis of a Vaccination Model for Carrier Dependent Infectious Diseases with Environmental Effects. *Nonlinear Analysis: Modelling and Control*, 13, 331–350.
- Neilan, R. L. M., Schaefer, E., Ga, H., Fister, K. R. & Lenhart, S. (2010). Modeling optimal intervention strategies for cholera. *Bulletin of the Mathematical Biology*, 72, 2004–2018. doi:10.1007/s11538-010-9521-8
- Njagarah, J. B. H. & Nyabadza, F. (2015). Modelling optimal control of cholera in communities linked by migration. *Computation and Mathematical Methods in Medicine*. Article ID 898264, doi:10.1155/215/898264
- Noldus, E. (2006). Optimal control aspects of left ventricular ejection dynamics. *Journal of Theoretical Biology*, 63, 275–309.
- Nthiiri, J. K. (2016). Mathematical modelling of typhoid fever disease incorporating protection against infection. *British Journal of Mathematics and Computer Science*, 14(1), 1–10.
- Numfor, E. S. (2014). Mathematical modeling, simulation, and time series analysis of seasonal epidemics. Unpublished Master's thesis. Department of Mathematical Sciences. East Tennessee State University.
- Okosun, K. O. & Smith, R. (2017). Optimal control analysis of malaria-schistosomiasis co-infection dynamics. *Mathematical Biosciences and Engineering*, 14(2), 337 – 405.
- Okyere, S. (2012). Epidemiological Model of Influenza A (H1N1) Transmission in Ashanti Region Ghana. Unpublished Master of Philosophy thesis. Department of Mathematical Sciences, Kwame Nkrumah University of Science and Technology, Ghana.
- Olarte, J. & Galindo, E. (1973). Salmonella typhi resistant to chloramphenicol, ampicillin and other antimicrobial agents: Strains isolated during an extensive typhoid fever epidemic in Mexico. *Antimicrob Agents Chemother*, 4, 597–601.
- Ollerton, R. (2009). Application of optimal control theory to diabetes mellitus. *International Journal of Control*, 50, 2503–2522.

- Omame, A., Umana, R. A., Iheonu, N. O. & Inyama, S. C. (2015). On the existence of a stochastic model of typhoid fever. *Mathematical Theory and Modeling*, 5(8) , 104–113.
- Parker, R., Doyle, F. & Peppas, N. (2001). The intravenous route to blood glucose control. *IEEE Engineering in Medicine and Biology Magazine*, 20, 67–73.
- Peter, O. J., Ibrahim, M. O., Akinduko, O. B. & Rabi, M. (2017). Mathematical Model for the Control of typhoid fever. *IOSR Journal of Mathematics*, 13(4) 60–66.
- Peter, O. J., Akinduko, O. B., Ishola C. Y. and Afolabi, O. A.(2018). Series Solution of Typhoid Fever Model using Differential Transform Method. *Malaysian Journal of Computing*, 3(1), 67-80.
- Peter O. J. and Mohammed O. I, "Application of Variational Iteration Method in Solving Typhoid Fever Model," (2019). *Big Data, Knowledge and Control Systems Engineering (BdKCSE)*, Sofia, Bulgaria, pp. 1-5. doi: 10.1109 /BdKCSE 48644.2019.9010598
- Peter, O. J & Ibrahim, M. O.(2017). Application of differential transform method in solving a typhoid fever model. *International Journal of Mathematical analysis and Optimization: Theory and Applications*. 1(1),250-260.
- Peter, O. J., Ayode, A. A., Abioye, A. I., Victor, A. A. & Akpan, C. E. (2018). Sensitivity analysis of the parameters of a cholera model. *Journal of Applied Sciences and Environmental. Management*, 22(4), 477—481. doi:10.4314/jasem.v22i4.6
- Rodrigues, H. S., Monteiro, M. T. T. & Torres, D. F. M. (2013). Sensitivity analysis in a dengue epidemiology model. Assessed on 13/04/2016 from <http://dx.doi.org/10.1155/2013/721406>
- Roumagnac, P., Weill F. X., Dolecek, C., Baker, S., Brises S., Chinh, N. T., Le TA, Acosta, C. J., Farrar, J., Dougan, G. & Achtman, M., (2006). Evolutionary history of *Salmonella typhi*. *Science*, 314, 1301–1304.
- Samal, K. K. & Sahu, C. S. (1991). Malaria and widal reaction. *Journal of Association of Physicians India*, 10, 745–747.
- Shanahan, P. M. (1998). Molecular analysis of and identification of antibiotic resistance genes in clinical isolates of *Salmonella typhi* from India. *Journal of Clinical Microbiology*, 36, 1595–1600.
- Swan, G. (2008). Optimal control application in biomedical engineering – a survey. *Applications and Methods*, 2, 311–334.
- Swan, G. (2009). An optimal control model of diabetes mellitus. *Bulletin of the Mathematical Biology*, 44, 793–808.
- Tilahun, G. T., Makinde, O. D. & Malonza, D. (2017). Modelling and optimal control of typhoid fever disease with cost-effective strategies. *Computational and Mathematical Methods in Medicine*, doi:10.1155/2017/2324518

- Van den Driessche, P. & Watmough, J. (2002). Reproduction numbers and sub-threshold endemic equilibria for compartmental models of disease transmission. *Mathematical Biosciences*, 180(1-2), 29–48.
- Virginia, E. P., Cayley, C., Bowles, C., Stephen B., Gagandeep, K., Veeraraghavan, B, Jeremy, J., Farrar, B. T. & Grenfell, G. (2014). Predicting the impact of vaccination on the transmission dynamics of typhoid in South Asia. A Mathematical Modeling Study. *PLoS Neglected Tropical Disease*, 8(1), 26–42. doi:10.1371/journal.pntd.0002642
- Wain, J., Diep, T. S., Ho, V. A., Walsh, A. M., Hoa, T. T. N., Parry, C. M. & White, N. J. (1998). Quantitation of bacteria in blood of typhoid fever patients and relationship between counts and clinical features, transmissibility, and antibiotic resistance. *Journal of Clinical Microbiology*, 36, 1683–1687.
- Wain, J. & Hosoglu, S. (2008). The laboratory diagnosis of enteric fever. *Journal Infect Developing Countries*, 2, 421–425.
- Watson, C. H. & Edmunds, W. J. A. (2015). Review of typhoid fever transmission dynamic models and economic evaluations of vaccination. *Vaccine*, 33, 42–54. doi:10.1016/j.vaccine.2015.04.013
- World Health Organization (WHO/V and B/03.7). (2003). Background document: The diagnosis, treatment and prevention of Typhoid fever. Assessed on 20/11/2016 from <http://www.who.int/iris/typhoid/media/world-typhoid-report-2016/en/>
- WHO/CDC (2003). Manual for laboratory identification and antimicrobial susceptibility testing of bacteria pathogens of public health importance in developing world. Assessed on 05/07/2017. 103–115.
- WHO (2004). Background document: The diagnosis, treatment and prevention of typhoid fever. Assessed on 05/07/2017 from <http://archives.who.int/hq/2003/WHO V%26B 03.07 .pdf>
- WHO (2007). Background paper on vaccination against typhoid fever using new generation vaccines- presented at the SAGE.
- World Health Organization (2008). Background document: The diagnosis, treatment and prevention of typhoid fever Assessed on 05/07/2017 from <http://www.who.int/iris/typhoid/media/world-typhoid-epidemic disease-2015/en/>
- World Health Organization (2019). Immunization, Vaccines and Biologicals. Assessed on 05/07/2017 from <https://www.who.int/immunization/diseases/typhoid/en/>
- Yuan, Y. (2012). The collision regions between two epidemic models: SIRVS Unpublished Senior Project. Bard College, New York.
- Zaman, G., Kang, Y., & Jung, I. (2008). Stability analysis and optimal vaccination of an sir epidemic model. *Biosystems*, 93, 240–249.

Zhou, J. K. (1986). Differential Transformation and Its Applications for Electrical Circuits. Wuhan: Huazhong University Press.