MATHEMATICAL MODELING OF THE TRANSMISSION DYNAMICS OF TYPHOID FEVER AND ITS CONTROL

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ABSTRACT

In this research work, a mathematical model of the transmission dynamics of typhoid fever and its control was developed using a system of ordinary differential equations. Local stability analysis on the disease-free equilibrium was done using the Jacobian matrix approach. The semi-analytical solutions of the model were obtained using the Differential Transformation method and the solutions were plotted using Maple. The result of the findings shows that the Disease Free Equilibrium State (DFE) of the model is stable if $R_0<1$. The result of the numerical simulation shows that a reduction in the contact rate with infectious individuals reduces the transmission rate of the disease. The simulation also reveals that at high treatment rates for the infected individuals, the number of recovered individuals increases. Hence, as the vaccination rate increases, the population of the exposed class decreases. However, due to Typhoid fever's connection with malaria and other febrile infections we recommend that those infections should be incorporated into the model.

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CHAPTER ONE

1.0 INTRODUCTION

1.1 Background to the Study

Typhoid fever is an infectious disease caused by a highly infectious and invasive Salmonella enteric serovar Typhi (S.Typhi) that affects humans (Nthiiri *et al.*, 2016). It is spread through contaminated food, water, or drink. The contaminated food or water that contains these bacteria causes illness upon ingestion. They travel in the human intestines and then enter the bloodstream **(**Muhammad *et al*., 2015).

It is a global health problem whose impact is difficult to estimate because the clinical representation is confused with those of many other febrile infections. The disease has a very high social and economic impact because of the hospitalization of patients with acute disease and the complications and loss of income attributed to the duration of the clinical illness (World Health Organization, 2003).

The symptoms includes prolonged fever, fatigue, headache, nausea, abdominal pain, and constipation or diarrhea (WHO, 2018). Some patients may have a rash; severe cases may lead to serious complications or even death (WHO, 2018). The symptoms are lessened with antibiotic medications, however, a great number of people treated for typhoid fever usually experience relapse, after some time with symptoms that are milder and last for a shorter period compared with the initial illness, requiring further treatment with antibiotics (Basnyat, 2017).

Typhoid fever affects millions of people worldwide each year, with an estimated 11-20 million cases and disease-induced deaths of approximately 128,000-161,000 annually (WHO, 2018). People are inoculated using vaccines, even though repeated mass vaccinations at intervals of 5

years interval are required to stymie disease incidence. However, they are not 100% efficient. If one acquires a drug-resistant strain of typhoid fever and is not treated with effective antibiotics, a serious and prolonged illness may result (Nthiiri *et al.*, 2016).

Typhoid fever is largely controlled in Europe and North America. Typhoid remains endemic in many parts of the world, notably Asia and Africa, where it is an important cause of febrile illness in crowded, low-income settings. A notable feature of typhoid is the carrier state- asymptotically infected individuals who continue to shed Salmonella typhi in their stool or urine for many years, thereby sustaining transmission (Watson & Edmunds, 2015)**.**

Despite the recommendation by the World Health Organization in 2003 that typhoid vaccination is considered for the control of endemic disease and outbreaks, in the early twentieth- century, public health officers were debating the best methods of evaluating typhoid vaccine effectiveness, and whether vaccination was a distraction from improvements in sanitation and hygiene, These remain contemporary policy issues for ministries of health and other health partners who may be considering programmatic anti-typhoid vaccination as a counterpart to other anti-typhoid measures such as improvements in income distributions, sanitation, water supplies and handwashing with soap (post-defecation and before the preparation of food in the home or sold in the street) as well as identification and management of carriers (Hardy, 2001).

1.2 Statement of the Research Problem

Typhoid fever affects millions of people worldwide each year, with an estimated 11-20 million cases and disease-induced deaths of approximately 128,000-161,000 annually (WHO, 2018). Among the factors that mitigate the control of the disease are the asymptotically carrier infected individuals who continue to shed Salmonella typhi bacteria in their stool or urine for many years,

thereby sustaining transmission and a great number of people treated for typhoid fever usually experience relapse. In 2003, WHO recommended the use of vaccines for the control of the disease. Thus, this research seeks to formulate a mathematical model that incorporates the aforementioned factors.

1.3 Aim and Objectives of the Study

This study aims to formulate and validate a mathematical model for the spread and treatment of typhoid fever using a system of first-order ordinary differential equations with seven compartments.

The objectives are to develop mathematical model that:

- Check the epidemiological well-posedness of the model.
- Obtain both the Disease-Free-Equilibrium (DFE) and the Endemic Equilibrium (EE) states of the model.
- Carry out local stability analysis on the disease-free-equilibrium
- Obtain the semi-analytical solution of the model using the Differential Transformation Method (DTM).
- Obtain the Basic Reproduction Number (R_0)

1.4 Motivation of the Study

This research was motivated by the number of Typhoid fever disease-mortalities and also because the disease is notably endemic in Africa, with Nigeria among the countries affected.

1.5 Justification for the Study

The social and economic impact of the disease due to hospitalization of patients with acute disease and the complications and loss of income attributed to the duration of the clinical illness necessitates this study. This thesis seeks to help public health practitioners make an informed decision such as strategizing ways to control the transmission of the disease. Hence, this work will be of immense value to the population at large in fighting against the threat of the disease. The compartments are susceptible class (S), Exposed Class (E), Asymptomatic infected class (C), Symptomatic infected class (I), Hospitalized or Treatment Class (T), Vaccinated class (V), and the concentration of Bacteria in the environment (B).

1.6 Scope and Limitations of the Study

The model subdivides the human population into seven mutually exclusive compartments namely, Susceptible class (S), Exposed Class (E), Asymptomatic infected class (C), Symptomatic infected class (I), Hospitalized or Treatment Class (T), Vaccinated (V). It also includes the concentration of Bacteria in the environment (B).

Some of the limitations are;

- Lack of proper documentation of data by public servants.
- The model is not age-structured

1.7 Definition of Terms

Asymptomatic: Not showing symptoms

Disease Free Equilibrium (D.F.E): is an equilibrium state that signifies the eventual absence of disease.

Endemic: the presence of a disease in a population

Endemic Equilibrium (E.E): is an equilibrium state that signifies the presence of disease in a population

Epidemiology: is the study of the spread and control of disease in a population

Equilibrium: means a state of rest of a body.

Exposed: Individuals that are infected but not yet infectious

Infected: Individuals who have Typhoid fever infection & are capable of infecting others.

A mathematical model: is the representation of a real-life phenomenon in mathematical terms.

An ordinary Differential equation: is an equation involving a dependent variable and its derivative with respect to one independent variable

Recovered: the class of individuals that have been treated and cured.

Stable Equilibrium: is the state of a system returning to its original state of rest if slightly displaced.

Susceptible: These are individuals who are prone to infection but not yet infected.

Symptomatic: showing symptoms

Treatment: Receiving medical care

Vaccinate; To inoculate against diseases.

Immunoglobulins(A,G and M): Is a medical test use to check the amount of certain antibodies.

Immunoglobulin A(lgA): The antibodies are found in areas of the body such the nose, breathing passages, digestive tract, ears, eyes, and vagina**.**

Immunoglobulin G(lgG): The antibodies found in all body fluids.

Immunoglobulin M(lgM): The antibodies are the largest antibody**.**

CHAPTER TWO

2.0 LITERATURE REVIEW

2.1 Overview of Typhoid Fever

During an acute infection, Salmonella typhi multiplies in mononuclear phagocytic cells before being released into the bloodstream. After ingestion of food or water, typhoid organisms pass through the pylorus and reach the small intestine. They rapidly penetrate the mucosal epithelium via either microfold cells or enterocytes and arrive in the lamina propria, where they rapidly elicit an influx of macrophages that ingest the bacilli but do not generally kill them. Some bacilli remain within the macrophages of the small intestinal lymphoid tissue. As a result of this silent primary bacteremia, the pathogen reaches an intracellular haven within 24 hours after ingestion throughout the organs of the reticuloendothelial system (Spleen, liver, bone marrow), where it resides during the incubation period, which usually takes 8 to 14 days. The incubation period in a particular individual depends on the number of inoculums, that is, it decreases as the number of inoculum increases, and on host factors.

This infection that grows in the intestine and blood is spread by eating/drinking food/water contaminated with the faces of an infected person. The risk factors include poor sanitation and poor hygiene. Those who travel to the developing world are also at risk and only humans can be infected (WHO, 2003)**.** Diagnosis is by either culturing the bacteria or detecting the bacterium's DNA in the blood, stool, or bone marrow, typhoid vaccine can prevent about 30% to 70% of cases during the first two years. It is recommended for those at high risk, that is people traveling to areas where the disease is common (Anwar *et al.*, 2014).

2.1.1 Symptoms of typhoid fever

The clinical presentation of typhoid fever varies from a mild illness with low-grade fever, malaise, and slight dry cough to a severe clinical picture with abdominal discomfort and multiple complications (WHO, 2003)**.** The acute non-complicated disease is characterized by prolonged fever, disturbances of bowel function, which is constipation in adults, and diarrhea in children. Cough is common in the early stage of the illness. A complicated case results in an intestinal perforation which is frequently fatal as it is accompanied by a sudden rise in pulse rate, hypertension, and subsequent abdominal rigidity (Center for Disease Control**,** 2014). Other serious complications documented with typhoid fever include haemorrhages (causing rapid death in some patients) hepatitis, myocarditis, pneumonia disseminated intravascular coagulation, etc. (WHO, 2003)**.**

2.1.2 Diagnosis of typhoid fever

Bone marrow aspirate culture is the gold standard for the diagnosis of typhoid fever**,** and it is particularly valuable for patients who have been tested to have a negative blood culture with the recommended volume of blood (Gasem *et al.,* 1995). The volume of blood cultured is one of the most important factors in the isolation of Salmonella typhi from typhoid patients. In some regions it may be impossible to collect large volumes of blood and going for alternative diagnostic methods may be necessary for cases in which blood cultures are negative, because reducing the blood volume, reduces the sensitivity of the blood culture. However, an effort should be made to draw sufficient blood if at all possible. Blood should be taken using sterile techniques of various punctures and should be inoculated immediately into a blood culture bottle with the syringe that has been used for collection. Testing can take place immediately or storage can continue for a week without affecting the antibody titre, (Wain *et al*., 2001)**.** Stools can also be collected from acute patients and they are especially useful for the diagnosis of typhoid

carriers. The isolation of Salmonella typhi from stools is suggestive of typhoid fever. Stool specimens should be collected in a sterile wide-mouthed plastic container. The likelihood of obtaining positive results increases with the number of stools collected. Specimens should preferably be processed within two hours after collection. If there is a delay, it should be stored in a refrigerator at 4^0C or in a cool box with freezer packs and should be transported to its laboratory in a cool box (Wain *et al*., 2001)**.**

In 2003, WHO presented a quick and reliable diagnostic test for typhoid fever as an alternative to the Widal test. The recent advances include the IDL tubex test marketed by a Swedish company, which reportedly can detect IgM antibodies from patients within a few minutes. Another rapid serological test is typhidot, which takes 3 hours to perform. It was developed in Malaysia for the detection of specific IgM and IgG antibodies. A newer version of the test, typhidot-M was recently developed to detect specific IgM antibodies only (Anwar *et al*, 2014).

2.1.3 Treatment of typhoid fever

Fluoroquinolones (ofloxacin, ciprofloxacin, fleroxacin, perfloxacin) are widely regarded as optimal for the treatment of typhoid fever in adults (Wain *et al*., 2001)**.** They are relatively inexpensive, well-tolerated, and more rapidly and reliably effective than the former first-line drugs; chloramphenicol, ampicillin, amoxicillin, and trimethoprim-sulfamethaxazole.

The fluoroquinolines attain excellent tissue penetration, kill S.typhi in its intracellular stationary stage in monacytes /macrophages and achieve higher active drug levels in the gall bladder than other drugs. They produce a rapid therapeutic response, that is, clearance of fever and symptoms in three to five days and very low rates of post-treatment carriage (Arnold *et al*., 1993). Treatment at home with antibiotic tablets is treated within seven to 14 days. Incubation period is usually one to two weeks, and duration of the illness is about three to four weeks. Surgery is

usually indicated in cases of intestinal perforation. Most surgeons prefer simple closure of the perforation with drainage of the peritoneum. Death occurs on 10 % to 30 % of untreated cases. (WHO, 2003).

2.1.4 Prevention from typhoid fever

The major routes of transmission of typhoid fever are through drinking water or eating food contaminated with Salmonella typhi. Prevention is based on ensuring access to safe water and by promoting safe food handling practices, health education is paramount to raising public awareness and inducing bahaviour change (WHO, 2003)**.**

Safe Water

Typhoid fever is waterborne disease and the main preventive measure is to ensure access to safe water. The water needs to be of good quality and must be sufficient to supply all the community with enough drinking water as well as for all domestic purposes.

During outbreaks, the following control measures are of particular interest:

(a) In urban areas control and treatment of the water supply systems must be strengthened from catchment to consumer.

(b) In rural areas, well must be checked for pathogens and treated if necessary.

(c) At home, particular attention must be paid to the disinfection and the storage of the water however safe its source. Drinking water can be made safe by boiling for one minute or by chlorination. Narrow-mouthed pots with covers for storing water help reduce the secondary transmission of typhoid fever.

(d) In some situations, such as poor rural areas in developing countries or refugee camps, fuel for boiling water and storage containers may have to be supplied. (WHO, 2003)

Food Safety

Contaminated food is another important vehicle for typhoid transmission. Appropriate food handling and processing are paramount and the following basic hygiene measures must be implemented during epidemics.

(a) Washing hands with soap before preparing or eating food

(b) Avoiding raw food, shellfish, ice;

(c) Eating only cooked and still hot food or reheating it.

During, outbreaks, food safety inspections must be reinforced in restaurants and for street food vendors' activities.

Typhoid can be transmitted by chronic carriers who do not apply satisfactory food-related hygiene practices. These carriers should be excluded from any activities involving food preparation and serving. They should not resume their duties until they have had three negative cultures at least one month apart.

Sanitation

Proper sanitation contributes to reducing the risk of transmission of all diarrhoeal pathogens including Salmonella typhi.

(a) Appropriate facilities for waste disposal must be available for all community

(b) Collection and treatment of sewage especially during the rainy season must be implemented

(c) In areas where typhoid fever is known to be present the use of human excreta as fertilizer must be discouraged.

Health Education (Enlightenment Campaign)

Health education is paramount to raising public awareness of all the above-mentioned preventive measures. Health education messages for vulnerable communities need to be adapted to local conditions and translated into local languages. In order to reach communities, all possible means of communication (e.g. Media, Schools, Women groups, religious groups) must be applied. Community involvement is the cornerstone of behavior change with regard to hygiene and for setting up maintenance of the needed infrastructures. In health facilities, all staff members must be repeatedly educated about the need for:

(a) Excellent personal hygiene at work

(b) Isolation measures for patient

(c) Disinfection measure.

This campaign reduces the rate of transmission because those who are properly informed will reduce their exposure to infection whenever they meet any infectious opportunity.

2.1.5 Vaccination against typhoid fever

Vaccine is a medical product that helps in stimulating the body's immune system in order to prevent or control infection. It trains the body's immune system to fight off a particular microorganism so that it cannot establish a serious infection. Two safe and effective vaccines are now licensed and available. One is based on defined subunit antigens and the other on whole-cell live attenuated bacterial. The first of these vaccines contain Vi capsular polysaccharide(vicps) which is given in a single dose while the other is the live oral vaccine called purified capsular polysaccharide derived from Ty2la which is to be taken in three doses for two days apart on an empty stomach (Black *et al*., 1990). The occurrence of S.typhi strains that are resistant to fluoroquinolones emphasizes the need to use safe and effective vaccines to prevent typhoid fever. WHO recommends vaccination for people traveling to high-risk areas where the disease is

endemic. People living in such areas, are people in refugee camps, sewage workers, and children should be the target groups for vaccination.

Mathematical models have played a key role in the formulation of Typhoid fever control strategies and the establishment of interim goals for the intervention programmes. A model was developed by Cvjetanović *et al.* (1971), where the number of newly infected persons was expressed as a function of the infectious and susceptible people in a community within a given time. The age structures of the population are established, which enabled a more complicated detailed simulation of the effect of various interventions and strategies to control the disease in different age groups. The study indicated that once the incidence of the infection has fallen below the threshold, it cannot be maintained in a community due to the loss of the main source of infection chronic carriers, as they die out naturally.

2.2 Mathematical Models of Typhoid Fever

Khan *et al.* (2015) presented a mathematical analysis of the Typhoid model with saturated incidence. They formulated a mathematical model of the type SEIR (Susceptible, Exposed, Infected, and Removed) to understand the transmission dynamics of the disease. Local and global stability analysis was carried out on the equilibrium state. The Runge-Kutta method was used to obtain the numerical solution of the model. Their result shows that the endemic equilibrium was both locally and globally stable. Their model was given as follows; Khan *et al.* (2015)

(2.1)

Where =Growth rate of the population

= Disease contact rate

d = Natural mortality rate

=Rate of flow from class E to class S

=Rate of flow from class I to class S

=Disease-induced death rate at class E

=The rate at which latent individuals are infected.

= Disease-induced death rate at class I

=Rate of recovery from infection

q =Proportion of individuals joining the class E

k=Educational adjustment.

Adetunde (2008) formulated a mathematical model for the dynamics of typhoid fever in the Kassena-Nankana District of the upper East Region of Ghana. The equilibrium states of the model were obtained and their stability was also investigated. The threshold condition for the disease-free equilibrium to be stable was presented. The results showed that the disease-free equilibrium was globally asymptotically stable. The formulated model was given as Adetunde (2008)

(2.2)

Where S(t) = Susceptible class, I(t)= Infected class, C(t)= Carriers,

R(t)= Recovered class.

= the per capital natural mortality rate

= the rate of disease-induced death for infectious class

= the rate of infection

= Rate of which the infected become carriers

= Rate of recovery for the carrier-class

= the rate of disease-induced death for a career class

b= Rate of recovery for the infected class

Kalajdzievska and Li (2011) developed a mathematical model of the effects of carriers on the transmission dynamics of infectious diseases. They investigated that infections could be transmitted through carriers, infected individuals who are contagious but do not show any disease systems. It was assumed that the disease carriage state is infectious while those in the latent period are not. Their model incorporated demography and disease-induced death and it allows carriers to become symptomatic over time. They carried out local stability on the disease-free equilibrium. Their result showed that a greater probability to develop carriage will increase the basic reproduction number which makes the infection persist. Testing and Diagnosis of carriers were seen as an effective control measures in a country where infectious diseases persist. Their model equations were given as Kalajdzievska and Li (2011)

(2.3)

Where S= Susceptible class, = carrier-class, I= symptomatically infectious or infectious class,

R= Recovered class, = transmission coefficient for the carrier compartment.

= transmission coefficient for the symptomatically infected compartment.

= Rate of recovery

P= Probability of a newly Infected Individual,= Vaccination rate,

= Diagnosis rate, b = Rate of recruitment into susceptible class

d_1, d_4: Natural death rates for the susceptible and recovered classes

d_2, d_3: Death rates for and I compartments respectively.

Liao and Yang (2013) extended the classical SIR framework by incorporating a compartment (W) that tracked pathogen concentration in the water. Susceptible individuals are infected with multiple transmission pathways in their model titled “The Dynamics of a vaccination model with multiple transmission ways of water-borne diseases”. The control reproduction number, stability analysis of both the disease-free and endemic equilibrium were carried out. Bifurcation theory was applied to explore a variety of dynamics of their model. Their model is given as follows; Liao and Yang (2013).

(2.4)

Where S= susceptible population, I=Infected class, R= Recovered Class, W= Pathogen concentration. = transmission rate for the environment to human,= transmission rate for human

to human, = natural human/death rate, = shedding rate, = Bacteria death rate and = Recovery rate.

Rihan *et al.* (2014) formulated a fractional SIRC model with Salmonella Bacterial Infection. The solution for the fractional-order model at any time t* continuously depends on all the previous states at t<t*. The Authors stated that fractional-order dynamical models are more suitable to model biological systems with memory than their integer orders. The presence of a fractional differential order into a corresponding differential equation leads to a notable increase in the complexity of the observed behavior and enlarges the stability region of the solutions. Numerical solutions of their model were obtained using Caputo's derivative and using an unconditionally stable implicit scheme. The disease-free and endemic states equilibrium was confirmed to be asymptotically stable under some conditions. The basic reproduction number was calculated using the next-generation matrix method, in terms of contact rate recovery rate, and other parameters in their model.

Their model was given as Rihan *et al.* (2014)

(2.5)

Where S(t) = Susceptible class, I(t)= Infected class, C(t)= Cross immune individuals, R(t)= Recovered class.

= Cross immune period, = Is the fraction of the exposed cross immune individuals.= Infectious period, = Contact rate, = Rate of recovery for the carrier stage, = Total immune period, = Disease induced mortality rate and = Mortality rate.

The fractional-order of their SIRC Epidemic model was given as:

(2.6)

Mutua *et al.* (2015) developed a mathematical model for malaria and typhoid fever co-infection dynamics. They first developed a model for only typhoid fever, their model subdivides the human population of interest into four compartments susceptible humans(S), infected human (I), carrier humans(C), and recovered human (R). They later considered the incorporation of an additional compartment B, which represents bacteria in the Environment. Typhoid is largely contracted from water and food, thus transmission of typhoid through direct person-to-person contact was neglected by them. They presented that people in tropical communities are living at risk to contact both diseases (either concurrently or an acute infection superimposed on a chronic one). Through mathematical analysis, they identify distinct features of typhoid and malaria infection dynamics as well as the associated relationships. Their result shows that the global dynamics of typhoid infection can be determined by a single threshold Ro. The typhoid basic reproduction number <1 (>1) provided conditions for the global eradication (uniform persistence of the typhoid infection). Their model was given as follows; Mutua *et al.* (2015).

(2.7)

Where = contact rate, = rate at which the infected individuals either progress to carrier-class.

= recovery rate for the infected individuals.

= rate at which individuals in the carrier-class recover from typhoid.

= rate at which the infectious group excretes bacteria.

= rate at which the carrier group excretes bacteria.

They assumed that the growth rate of the bacteria in the environment logistic and becomes non-infectious at a rate, r and k represent per capita growth and carrying capacity respectively and denotes typhoid induced mortality in humans. The constant recruitment into the susceptible human is represented by while the natural death rate of a human is represented by.

Kgosimore and Kelatlhegile (2016) considered the disease typhoid as a major public health concern in tropical developing countries, especially in areas where access to clean water and other sanitation measures are limited. Typhoid has complex pathogenesis and manifests as an acute febrile disease, with a relatively long incubation period that involves the transmigration of the microorganism through the Peyer's patch, localized multiplication in the mesenteric lymph nodes, and subsequent spread to the liver and spleen prior to showing clinical symptoms. It is a serious life-threatening infection characterized by false diagnosis due to similar signs and symptoms with malaria which leads to improper control and management of the disease. They carried out a mathematical analysis of Typhoid infection with treatment where a deterministic model of Typhoid which accounts for relapse of treatment was considered. Mathematical analysis and numerical simulations were carried out to determine the transmission dynamics of typhoid in a community. They established that the disease-free equilibrium is locally asymptotically stable if <1 and unstable if >1. The endemic equilibrium exists and is stable if >1. Numerical Simulations suggested that increasing treatment sustains the typhoid epidemic in the

population. Implications of their result point to an added effect from carriers evolving from treatment relapse. The dependence of modification on transmission parameters on treated populations provides insight into the role of treatment in the transmission dynamics of the disease. Their model was given as Kgosimore and Kelatlhegile (2016)

(2.8)

Where;

S= the susceptible class, I= Infective,= Carrier Infective, T=treated Infective, R= Recovered class, = Recovery rate, = Natural death rate, = Relapse rate, B= Contact rate, = Rate at which the carriers develop symptoms, = Recruitment rate of susceptible class, , = disease-induced death rates, P= rate at which a proportion of newly infected individuals become carriers.

(1-p) = Rate at which newly infected individuals became symptomatic.

Nthiiri *et al.* (2016) developed a mathematical model of Typhoid Fever Disease Incorporating protection against infection. They assumed that the bacteria are transmitted through food and water contaminated with faeces and urine of an infected patient or a carrier. Sign and symptoms include sustained fever, poor appetite, vomiting, severe headache, and fatigue. The treatment is based on antibiotic susceptibility of the patient blood culture. The Authors presented that the chronic carrier state may be eradicated using oral therapy (Ciprofloxacin or norfloxacin). The basic reproduction number of the model formulated was computed using the next generation matrix approach. Stability analysis of the model was carried out to determine the conditions that

favour the spread of the disease in a given population. Results from numerical simulation of their model showed that an increase in protection leads to low disease prevalence in a population.

Their model equations were given as Nthiiri *et al.* (2016)

(2.9)

Where p= Protected class, S= susceptible class, I= Infected class, and T= Treated class.

= Is the recruitment rate in the susceptible class, =the mortality rate, = is the disease-induced mortality rate, is the rate of treatment, and = the rate at which protection is lost by the protected class. Their model captures the transmission dynamics of Typhoid fever and its control using an extension of the standard SEIR model under some assumptions by adding some compartments like the I_T (Infected but on Treatment class), V (Vaccinated Class), and the Bacteria class (B). Three control measures considered are treatment, vaccination, and enlightenment campaign.

Peter *et al*. (2017) formulated a mathematical model that incorporated vaccination and treatment classes. They obtained the equilibrium states of the model. They carry out stability analysis on the disease-free equilibrium. Their model is as follows; Peter *et al.* (2017).

(2.10)

Tilahun *et al.* (2018) developed a mathematical model that examined the co-infection of Pneumonia and Typhoid fever. They obtained the equilibria of the model and also analyzed them for stability. They also obtained the basic reproduction number. Their optimal control analysis showed that prevention of Pneumonia and Typhoid fever cost less. Their model is as follows; Tilahun *et al.*, (2018)

(2.11)

Abboubakar and Racke (2019) developed a mathematical model for the spread and control of Typhoid fever. Their model was in two phases, a model without control and a model with control. They obtained the equilibrium states of the model, analyzed the disease-free equilibrium for both local and global stability using Lyapunov's theory. Their model equation is as follows; Abboubakar and Racke (2019)

(2.12)

Peter *et al.* (2021) formulated a model that took into account both direct and indirect transmission. They used an optimal control strategy to obtain the optimal path using Pontryagin's maximum principle. Their model equation is as follows; Peter *et al.* (2021)

(2.13)

CHAPTER THREE

3.0 MATERIALS AND METHODS

3.1 Model Formulation

Formulation of the model is the combination and the extension of the model reviewed in chapter two. The model considers the salient transmission properties. The model subdivides the human population into seven (7) mutually exclusive compartments, which are; Susceptible humans (**S),** Exposed humans (**E),** Asymptomatic infected humans (**C**), Symptomatic infected humans (**I),**

humans who are receiving Treatments (**T**), and Vaccinated humans (**V**), And one compartment for the environmental Bacterial of the reservoir (**B**).

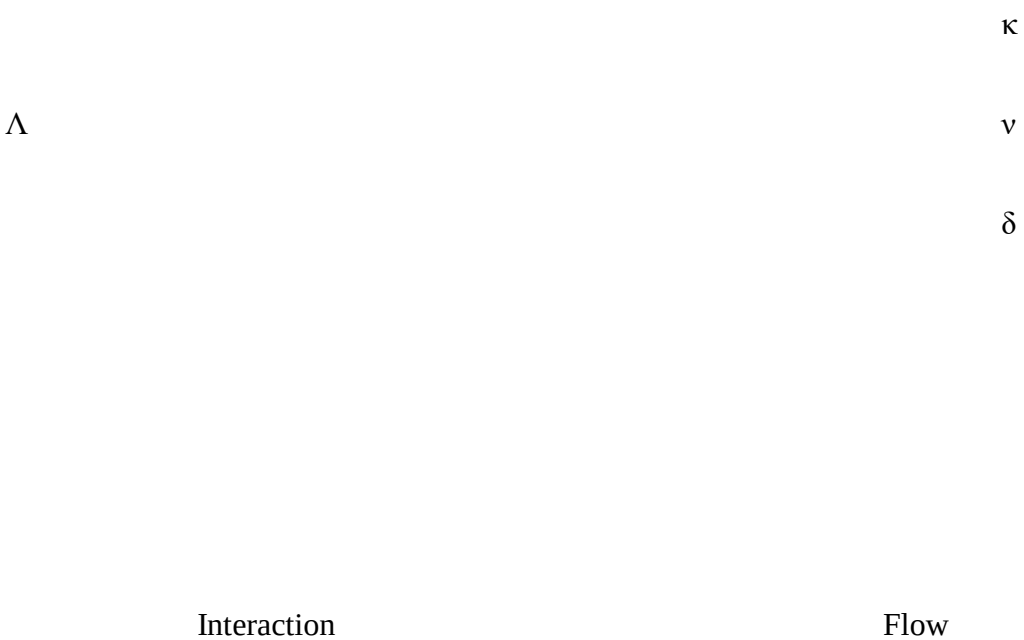

Figure 3.1: Schematic Diagram of the Model

3.1.1 Model assumptions

The population of the susceptible humans increases through constant recruitment of individuals into the population by birth or immigration, also due to relapse at the rate where , and also due to the rate at which vaccinated humans lose immunity at . It decreases as susceptible humans move to the Exposed compartment (E) through interaction with the contaminated environment at the rate, and further decreases through natural death at the rate μ and vaccination at the rate ; The

population of the exposed human compartment decreases due to natural death at the rate and also due to movement to infected classes after the incubation period at the rate. A Proportion of α move to the symptomatic infected compartment at the rate, while the remainder of the proportion move to the asymptomatic carrier infected compartment at the rate, where. The population of the asymptomatic infected carrier compartment increases due to relapse at the rate and decreases due to movement to symptomatic infectious class at the rate, , and also due to natural death at the rate, . The population of the symptomatic infected compartment decreases due to treatment at the rate, also due to disease-induced death, , and natural death at the rate.

The population of the treatment compartment decreases due to relapse at the rate, also due to disease-induced death , and also due to natural death at the rate ().

The population of the vaccinated class increases at the vaccination rate and decreases due to waning of immunity at the rate and also due to natural death at the rate. The concentration of the bacteria is proportional to contamination from asymptomatic carrier, symptomatic carrier, and hospitalized classes at the rate, respectively. And, it decreases at the decontamination rate .

From the diagram and the assumption, we have the following system of coupled nonlinear ordinary differential equations;

(3.1)

(3.2)

(3.3)

(3.4)

(3.5)

(3.6)

(3.7)

3.1.2 Description of variables and parameters

Variable/Parameter	Description
	Susceptible Humans
	Exposed Humans
	Asymptomatic Carrier humans
	Symptomatic infected
	Treated humans
	Vaccinated Humans
	Bacteria Concentration
	Recruitment rate for the Human Population
	Relapse rate
	Proportion of that move to asymptomatic carrier Class
	Proportion that move to symptomatic infected Class
	Infectious rate

Natural Death Rate for humans

Rate of Loss of Immunity

Progression rate from Exposed to infected classes

Proportion of that move to Symptomatic Infected class

Proportion of that move to Asymptomatic Carrier class

Progression rate from asymptomatic carrier toSymptomatic

Infected class

Treatment Rate for Symptomatic infected class

Disease-induced death rate

Rate of environmental contamination by asymptomatic

Carrier class

Rate of environmental contamination by symptomatic

Infected class

Rate of environmental contamination by hospitalized class

Environmental Decontamination Rate

3.2 The Positive Invariant Region

The total human population is (3.8)

Where,

(3.9)

Adding equation (3.1) to (3.7), yield for (3.10)

(3.10)

Theorem 3.1

The solutions of the system of equations (3.1) through (3.7) are feasible for if they enter the invariant region D.

Proof

Let

(3.11)

Be any solution of the system of equations (3.1) to (3.8) with positive initial conditions.

Suppose there are no disease-induced deaths, equation (3.10) becomes

(3.12)

That is,

(3.13)

Multiplying both sides of equation (3.130 by its integrating factor gives

(3.14)

(3.15)

Integrating both sides gives

(3.16)

(3.17)

Applying the initial condition, $t=0$, $N(0)=N_0$ in (3.17) gives

(3.18)

(3.19)

Substituting (3.19) into (3.17) gives

(3.20)

Similarly,

(3.21)

Separating variables gives

(3.22)

Integrating both sides gives

(3.23)

Applying the initial condition $B(0)=B_0$ gives

(3.24)

As , the human population N approaches ,where K is the carrying capacity of the human population.

Similarly at , the concentration of Bacterial B approaches B_0.

Hence all feasible solution set of the human population and the concentration of contaminant of the model (3.1) to (3.8) enter the region,

(3.25)

Therefore, region D is positively-invariant (A region is positively-invariant if the solution that starts in it remains in it). That is, if then and if then . Hence, region D is positively invariant and equations (3.1) through (3.7) are epidemiologically meaningful and mathematically well-posed in the domain D. Therefore, in this region it is appropriate to consider the dynamics of flow generated by the model (3.1) through (3.7). In addition, the usual existence, uniqueness, and continuation of the results hold for the system.

3.3 Positivity of Solutions

Let the initial condition be , Then the solution set of the system of equations (3.1) through (3.7) is positive for all

Proof

From equation (3.1), we have

(3.26)

(3.27)

Where, (3.28)

From equation (3.27), separating variables, we have

(3.29)

Integrating both sides gives

(3.30)

Taking exponents of both sides gives

(3.31)

Where (3.32)

Applying the initial condition $S(0)=S_0$ in (3.31), we have

(3.33)

Therefore,

(3.34)

Similarly, from equation (3.2), we have

(3.35)

Separating variables, we have

(3.36)

Integrating both sides gives

(3.37)

Taking exponents of both sides gives

(3.38)

Where (3.39)

Applying the initial condition $E(0)=E_0$ in (3.38) gives

$E_0=k$ (3.40)

Hence,

(3.41)

Similarly, it can be verified that the rest of the equations are positive for all $t>0$ since $e^r>0$

3.4 Equilibrium States of the Model

At equilibrium, (3.42)

This implies,

(3.43)

(3.44)

(3.45)

(3.46)

(3.47)

(3.48)

(3.49)

Let (3.50)

Substituting equation (3.50) into equations (3.43) through (3.49) gives

(3.51)

(3.52)

(3.53)

(3.54)

(3.55)

(3.56)

(3.57)

From equation (3.54), we have,

(3.58)

From equation (3.55), we have

(3.59)

Substituting equation (3.58) into (3.59) gives

(3.60)

Substituting (3.60) into (3.53) gives

(3.61)

(3.62)

(3.63)

Substituting (3.63) into (3.58) gives

(3.64)

Substituting equation (3.64) into (3.59) gives

(3.65)

Let (3.66)

And (3.67)

Substituting equations (3.66) and (3.67) into equations (3.63), (3.64) and (3.65) gives

(3.68)

(3.69)

(3.70)

Substituting equations (3.68), (3.69), (3.70) into equation (3.57) gives

(3.71)

(3.72)

From equation (3.52), we have

(3.73)

From equation (3.56), we have

(3.74)

Substituting equations (3.70), (3.73) and (3.74) into (3.51) gives

(3.75)

(3.76)

(3.77)

Substituting equations (3.72), (3.77) into equation (3.520 gives

(3.78)

This implies

Either

(3.79)

Or

(3.80)

(3.81)

This implies,

(3.82)

Substituting equations (3.79) into equations (3.63), (3.64), (3.65) and (3.72) gives

$C=I=T=B=0$ (3.83)

Substituting (3.79) into (3.77) gives

(3.84)

Substituting equation (3.840) into (3.74) gives

(3.85)

3.4.1 Disease-free equilibrium state (DFE)

Equations (3.79), (3.83), (3.84), (3.85) give the disease-free equilibrium state.

That is,

(3.86)

3.4.2 Endemic equilibrium state

Substituting equation (3.82) into (3.68) gives

(3.87)

Substituting equation (3.82) into equation (3.69) gives

(3.88)

Substituting equation (3.82) into (3.700) gives

(3.89)

Substituting equation (3.82) into (3.72) gives

(3.90)

Substituting equations (3.82) and (3.90) into equation (3.73) gives

(3.91)

Substituting equations (3.91) into (3.74) gives

(3.92)

Hence equations (3.87) to (3.92) gives E.E.S

3.5 Basic Reproduction Number

The basic reproduction number, R_0,is defined as the number of secondary infections that an infective individual produces throughout the infectious period in an entirely susceptible population. A basic reproduction number is a threshold number that if it is less than unity, that is if $R_0<1$ then the disease-free equilibrium (DFE) is locally asymptotically stable, and if it is greater than unity, that is if $R_0>1$ then the disease-free-equilibrium is unstable. In this study, we employ the next generation matrix approach as described by Van den Driessche and Wathmough (2002) to obtain our Basic Reproduction Number. We take the basic reproduction number as the spectral radius of the product of the two matrices,

F and V^{-1}, that is, $R_0=\rho(F\ V^{-1})$.

Our model has five infected classes; hence we have the next generation matrices F and V for new infection terms and transmission terms respectively as

(3.93)

(3.94)

Let (3.95)

Substituting equation (3.95) into (3.94) gives

(3.96)

Using Maple software,

(3.97)

(3.98)

The characteristics equation is

(3.99)

(3.100)

Hence, The Eigenvalues are

(3.101)

Therefore,

(3.102)

3.6 Local Stability Analysis of the Disease-Free Equilibrium State (DFE)

We recall from equation (3.51) through (3.57) that the system of equations of the model at equilibrium gives:

(3.103)

(3.104)

(3.105)

(3.106)

(3.107)

(3.108)

(3.109)

Where,

(3.110)

Recall from (3.86) that the disease-free equilibrium state is expressed as

(3.111)

The Jacobean matrix of the system of equations at disease-free equilibrium state gives:

(3.112)

Using Maple with elementary row operation, we transform (3.112) into upper triangular matrix as

(3.113)

From equation (3.113) we obtain the characteristics equation as

(3.114)

That is,

(3.115)

Either (or orororor

or) (3.116)

It implies that,

() (3.117)

From equation (3.117),

,

Hence, the disease-free-equilibrium state is stable

3.7 Analytical Solution of the Model

3.7.1 Differential transformation method

The differential transformation method is based on Taylor series expansion, to obtain a semi-analytical solution to both linear and nonlinear differential equations, (Ertürk, 2007).

The differential transformation of nth order derivative is given as;

(3.118)

And the inverse differential transformation method of Y(n) is

(3.119)

Using the method, finite terms of the transformation are considered. Therefore, equation (3.119) can be expressed as

(3.120)

From equations (3.118) through (3.120), the following properties are proven and established according to (Jang *et al, 2000) and* (Hassan, 2004).

- if , then
- If , then , where a is a constant

- if , then
- if , then
- if , then , where

3.7.2 Analytical solution of the model using differential transformation method

Consider our model

(3.121)

(3.122)

(3.123)

(3.124)

(3.125)

(3.126)

(3.127)

With initial conditions

(3.128)

Taking differential transformation of equations (3.121) through (3.128) gives

(3.129)

(3.130)

(3.131)

(3.132)

(3.133)

(3.134)

(3.135)

When ,

From equation (3.129) we have

(3.136)

(3.137)

From equation (3.130), we have

(3.138)

(3.139)

From equation (3.131), we have

(3.140)

(3.141)

From equation (3.132), we have

(3.142)

(3.143)

From equation (3.133), we have

(3.144)

(3.145)

From equation (3.134), we have

(3.146)

(3.147)

From equation (3.135), we have

(3.148)

(3.149)

When n=1,

From equation (3.129), we have

(3.150)

(3.151)

Substituting equations (3.128), (3.137), (3.145) and (3.149) into equation (3.151) gives

(3.152)

From equation (3.130), we have

(3.153)

(3.154)

Substituting equations (3.128),(3.137), (3.139), (3.149) into (3.154) gives

(3.155)

From equation (3.31), we hav

(3.156)

Substituting equations (3.129), (3.141), (3.145) into equation (3.156) gives

(3.157)

From Equation (3.132) we have

(3.158)

Substituting equations (3.139), (3.141), (3.143) into (3.158)

(3.159)

From equation (3.133), we have

(3.160)

Substituting equations (3.139) and (3.145) into equation (3.160)

(3.161)

From (3.134), we have

(3.162)

Substituting equations (3.137) and (3.147) into equation (3.162) gives

(3.163)

From equation (3.135), we have

(3.164)

Substituting equations (3.141), (3.143), (3.145) and (3.149) into (3.164) gives

(3.165)

From equation (3.120), the solutions to our model using differential transformation method are:

(3.166)

(3.167)

(3.168)

(3.169)

(3.170)

(3.171)

(3.172)

Substituting equations (3.128), (3.137) and (3.152) into equation (3.166) gives

(3.173)

Substituting equations (3.128), (3.139) and (3.155) into equation (3.167) gives

(3.174)

Substituting equations (3.128), (3.141) and (3.157) into equation (3.168) gives

(3.175)

Substituting equations (3.128), (3.143) and (3.159) into equation (3.169) gives

(3.176)

Substituting equation (3.128), (3.145) and (3.161) into equation (3.170) gives

(3.177)

Substituting equations (3.128), (3.147), and (3.163) into equation (3.171) gives

(3.178)

Substituting equations (3.128), (3.149) and (3.165) into equation(3.172) gives

(3.179)

Hence the analytical solutions of the model is given by (3.167) to (3.179)

CHAPTER FOUR

4.0 RESULTS AND DISCUSSION

4.1 Results

The Table 4.1 present the initial conditions and parameter values used for the simulation of the model.

Table 4.1: Initial conditions and parameter values

Parameters and State Variables	Value	Source
	10000	Nthiiri *et al.* (2016)
	3500	Nthiiri *et al.* (2016)
	1000	Nthiiri *et al.* (2016)
	1500	Mutua *et al.* (2015)
	2000	Assumed
	5000 100	Assumed Assumed
	0.0357	Nthiiri *et al.* (2016)
	0.03	Nthiiri *et al.* (2016)
	0.0002	Assumed
	0.016	Nthiiri *et al.* (2016)
	0.9	Assumed
	0.81	Nthiiri *et al.* (2016)
Σ	0.7	Nthiiri *et al.* (2016)
	0.8	Assumed
	0.9	Nthiiri*et al.* (2016)
Λ	0.005	Nthiiri *et al.* (2016)
	0.009 0.014 0.004 0.0345 0.5	Assumed Assumed Mutua *et al.* (2015) Assumed Assumed

The time *t* consider for this result simulation is in year. The Figure 4.1 – Figure 4.7 present the graphical simulation of the model

(year)

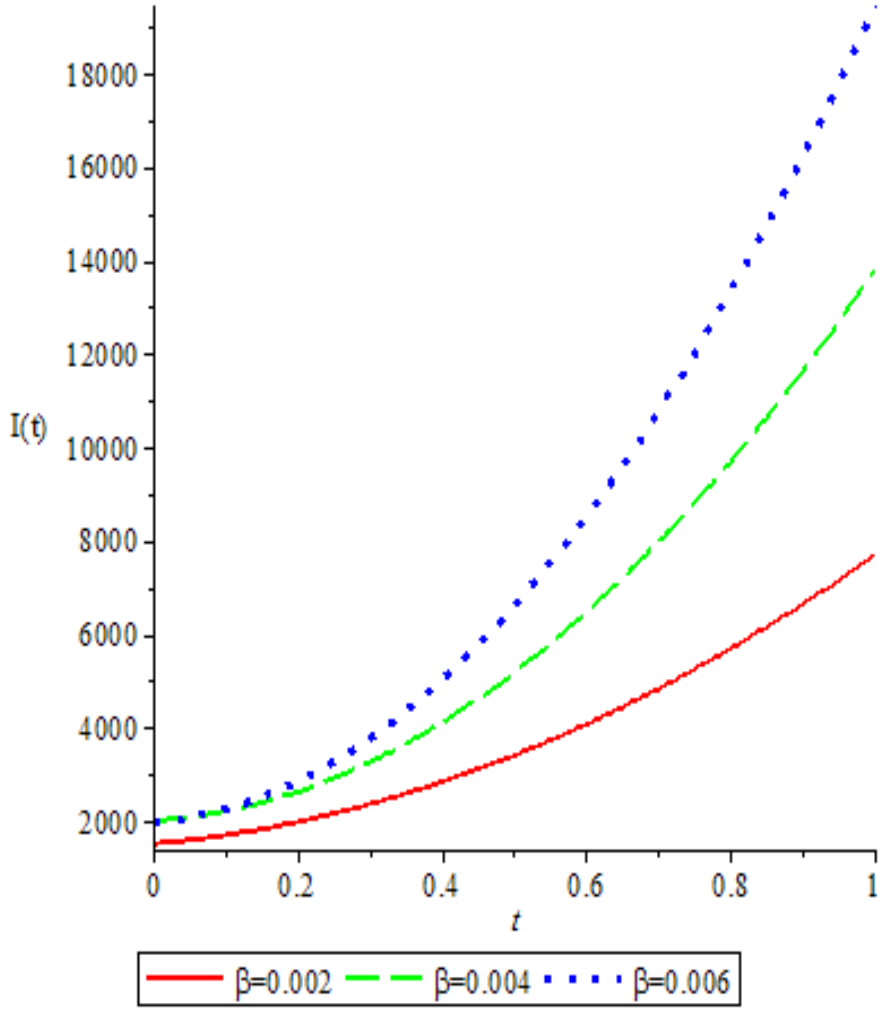

Figure 4.1: Effect of infectious rates on the infected class

From Figure 4.1, it can be seen that as the infectious increases, the population of the symptomatic infectious class also increases. The implies infectious rate, as the direct impact of the infected population. It is there by important to consider all necessary precaution needed to control the increase in infection rate of the disease.

***t* (year)**

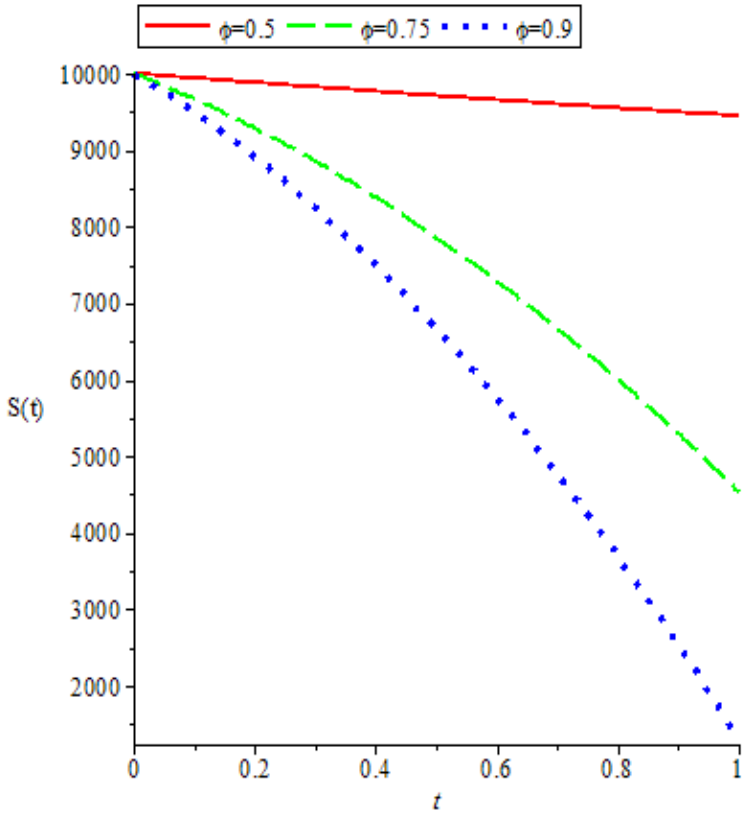

Figure 4.2: Effect of vaccination rates on the susceptible class

From the Figure 4.2, it can be seen that as the vaccination rate increases, the population of the susceptible class decreases. The susceptible population decreases and attained an equilibrium position, due to enlightenment campaign, encouraging people to go for vaccination against the disease and to avoid being exposed to contaminated water polluted food.

(year)

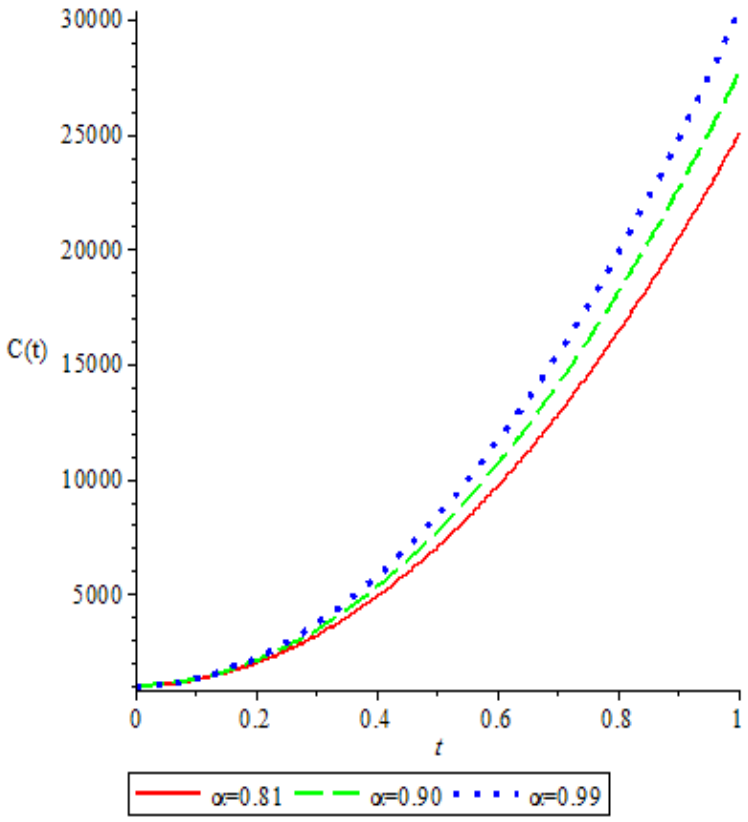

Figure 4.3: Effect of incubation rate on the asymptomatic carrier-class

From the Figure 4.3, it can be seen that as the incubation rate increases, the population of the asymptomatic carrier-class increases. This implies that incubation rate influence the population of the asymptomatic carrier of typhoid diseases. In order to manage the infection rate, there is need to consider incubation rate.

***t* (year)**

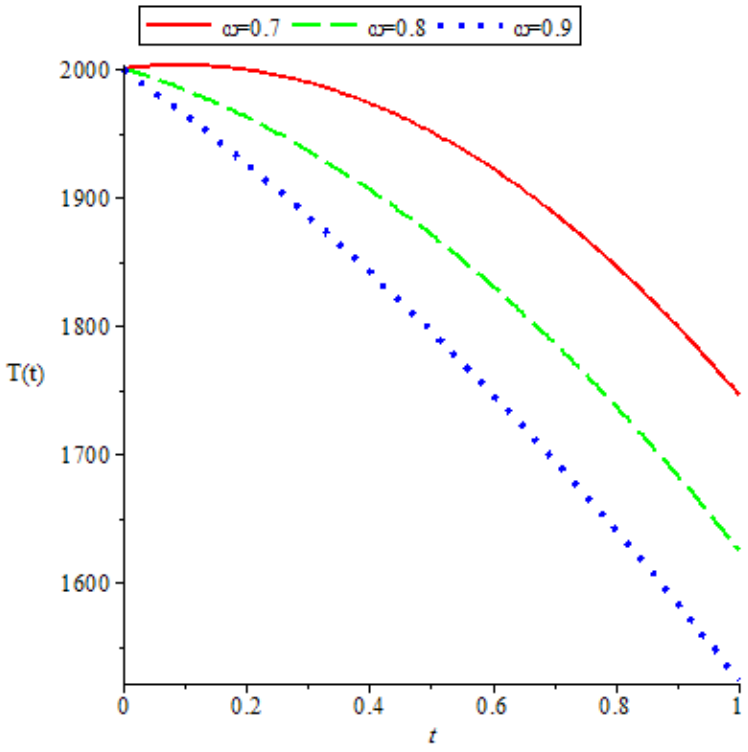

Figure 4.4: Effect of recovery rate on the treatment class

From Figure 4.4, it can be seen that as the recovery rate increases, the population of the hospitalized class decreases. This means as people recover from typhoid fever, they will be no need to still be on treatment, the population will decrease due to relapse and many also decrease due to disease induce death, due to negligent from the health practitioner, when wrong treatment is being administered.

***t* (year)**

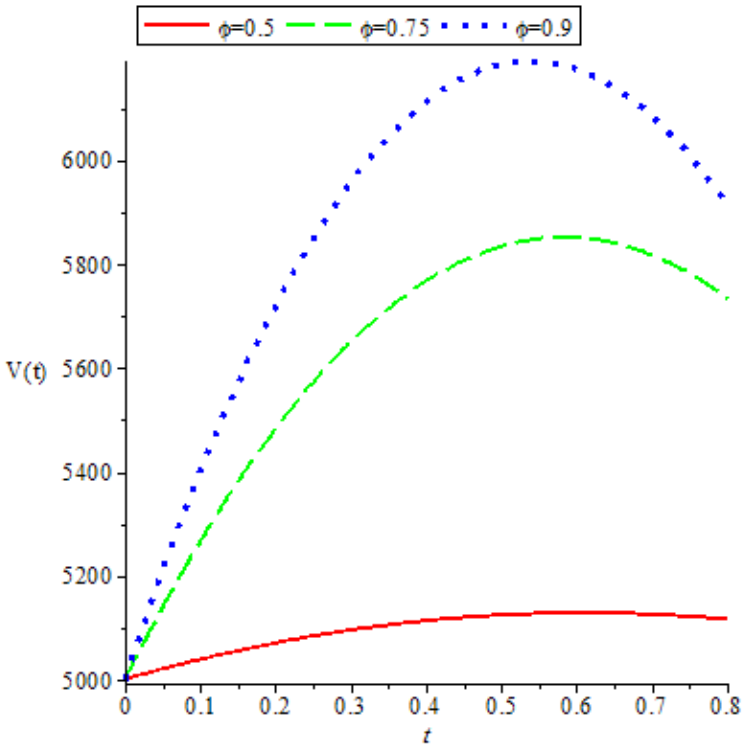

Figure 4.5: Effect of Vaccination Rate on the Vaccination Class

From Figure 4.5, it can be seen that as the vaccination rate increases, the population of the vaccination class also increases. This implies that when there is awareness on collection of vaccination, more individual will be found in the vaccination centre and this help to control the spread of the diasease among infected and susceptible individuals.

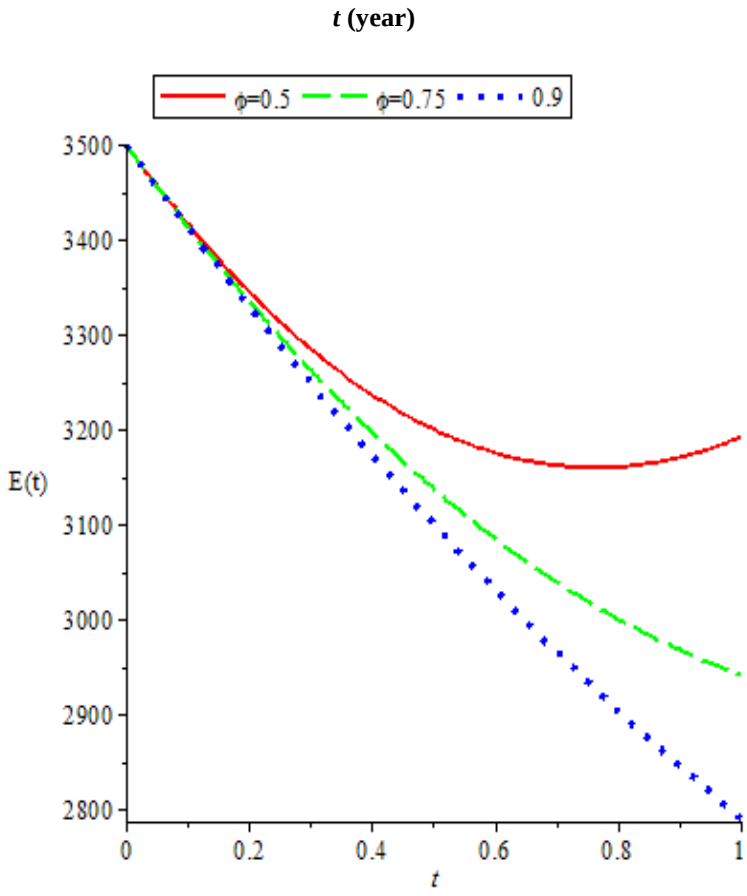

Figure 4.6: Effect of Vaccination Rate on the Exposed Class

From Figure 4.6, it can be seen that as the vaccination rates increases, the population of the exposed class decreases. More so if there is no interaction with the contaminated environment, their will be reduction in the exposed individuals, and this might in turn control infection rate.

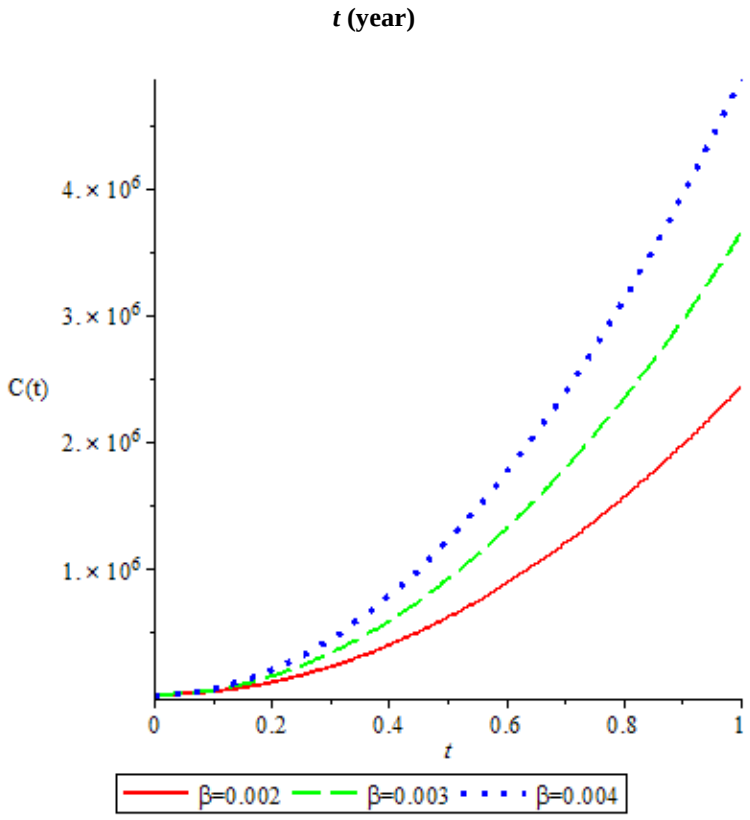

Figure 4.7: Effect of Infectious Rate on the Asymptomatic Carrier Class

From the Figure, 4.7, it can be seen that as the infectious rate increases, the population of the asymptomatic carrier increases. This depict that the infection rate has direct effect on asymptomatic carrier individuals. Hence there is no need to consider coreponding treatment given to infectious individual to asymptomatic carriers.

4.2 Discussion of Results

The objective of this study was to develop and authenticate a mathematical model for the transmission and management of typhoid fever, employing a system of first-order ordinary

differential equations comprising seven distinct compartments. The different compartments within the system under study include the susceptible class (S), exposed class (E), asymptomatic infected class (C), symptomatic infected class (I), hospitalised or treatment class (T), vaccinated class (V), and the concentration of bacteria in the environment (B).

this study on typhoid fever has taken different dimensions compared to existing models, as so many mathematical models in the past have assumed that susceptible individuals recovered with immunity against the disease, that is, there is no re-infection once an individual has recovered from the infection (Adetunde, 2008; Mutua *et al.*, 2015; Nthiiri *et al.*, 2016). This assumption is not realistic as fully recovered individuals still stand the risk of re-infection if they are exposed to the bacteria again which is the main target of the present study.

The findings indicate that there is a positive correlation between the infection rate and the size of the symptomatic infectious class. Furthermore, as the rate of vaccination increases, the size of the susceptible population decreases. This finding corroborated the claims made by Nthiiri *et al.* (2016) and Mutua *et al.* (2015).

This study's findings also revealed a positive correlation between the incubation rate and population growth. As the rate of recovery increases, there is a corresponding decrease in the population of individuals who are hospitalised. The findings indicate a positive correlation between vaccination rates and the size of the vaccinated population, as well as a negative correlation between vaccination rates and the size of the exposed population. This finding corroborated the claim made by Nthiiri *et al.* (2016).

CHAPTER FIVE

5.0 CONCLUSION AND RECOMMENDATIONS

5.1 Conclusion

In this work, a mathematical model for the spread and control of Typhoid fever by incorporating vaccination, treatment, waning rate, relapse rate was formulated. The equilibrium states of the model were obtained and analyzed. Local stability analysis was carried out on the disease-free equilibrium using the Jacobian matrix approach. According to the findings of this work, it can be deduced that the Disease Free Equilibrium State (DFE) of the model is stable if $R_0<1$. We obtained the semi-analytical solutions of the model using the Differential Transformation method and the solutions were plotted using Maple.

The result of the numerical simulation showed that reduction in the contact rate with infectious individuals reduces the transmission rate of the disease. Also, the findings of the study revealed that at high treatment rates for the infected individuals, the number of recovered individuals increases thereby leading to eventual dying out of the disease. It can also be concluded that as the vaccination rates increases, the population of the exposed class decreases.

5.2 Recommendations

- Policymakers and health practitioners are greatly advised to sensitize the people on the need to be vaccinated. Since, the model shows that the transmission of Typhoid fever infection rests greatly on the contact with the bacteria present in the environment

- Infected and treated individuals should be retested after recovery to avoid relapse.
- Health workers are greatly advised to uphold prevention and control measures when treating infectious individuals.
- One of the constraints of this study is the unavailability of records of Typhoid fever cases; therefore, we recommend that health workers should keep proper records to make data available for researchers.
- Due to Typhoid fever's connection with malaria and other febrile infections, co-infection of Typhoid fever and those infections can be incorporated into the model

5.3 Contribution to Knowledge

(i) We formulated and validated a mathematical model for the transmission and control of Typhoid fever by incorporating vaccination, treatment, waning rate, relapse rate.

(ii) The work has shown that the disease-free equilibrium is stable.

(iii) The work has also shown that infected individuals recovered when the treatment rates and their efficacy are high.

REFERENCES

Abboubakar, H., & Racke, R. (2019). Mathematical modelling and optimal control of typhoid fever. *Konstanzer Online-Publikation-System (KOPS),* 4(2), 56 – 71.

Adetunde I. A. (2008). Mathematical models for the dynamics of Tyhoid fever in Kassena Nankana District of upper East Region of Chana. *Journal of modern Mathematics and Statistics*, 2(2), 45-49.

Anwar, E., Goldberg, E., Fraser, A., Acosta, C. J., Paul, M., & Leibovici, L. (2014). Vaccines for preventing typhoid fever. *Cochrane Database of Systematic Reviews*, 1(1), 34 - 57.

Arnold, K., Hong, C. S., Nelwan, R., Zavala-Trujillo, I., Kadio, A., de Oliverira Barros, M. A., & de Garis, S. (1993). Randomized comparative study of fleroxacin and chloramphenicol in typhoid fever. *The American Journal of Medicine*, 94(3), 195S-200S.

Black, R. E., Levine, M. M., Ferreccio, C., Clements, M. L., Lanata, C., Rooney, J., & Chilean Typhoid Committee. (1990). Efficacy of one or two doses of Ty21a Salmonella typhi vaccine in enteric-coated capsules in a controlled field trial. *Vaccine*, *8*(1), 81-84.

Centers for Disease Control and Prevention. (2014). National center for emerging and zoonotic infectious diseases. *Internet address: http://www. cdc. gov/nczved/divisions/ dfbmd/diseases/campylobacter/technical. ht ml. Accessed Jan*, 2022.

Cvjetanović, B., Grab, B., & Uemura, K. (1971). 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.

Ertürk, V. S. (2007). Differential transformation method for solving differential equations of Lane-Emden type. *Mathematical and computational Applications*, 12(3), 135-139.

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*(4), 164-167.

Hardy, A. (2001). Methods of outbreak investigation in the "era of bacteriology" 1880–1920. *Sozial-und Präventivmedizin*, *46*, 355-360.

Hassan, I. A. H. (2004). Differential transformation technique for solving higher-order initial value problems. *Applied Mathematics and Computation*, *154*(2), 299-311.

Jang, M. J., Chen, C. L., & Liy, Y. C. (2000). On solving the initial-value problems using the differential transformation method. *Applied Mathematics and Computation*, *115*(2-3), 145-160.

Kalajdzievska, D., & Li, M. Y. (2011). Modeling the effects of carriers on transmission dynamics of infectious diseases. *Mathematical Bioscience Engineering*, *8*(3), 711-722.

Kgosimore, M., & Kelatlhegile, G. (2016). Mathematical analysis of typhoid infection with treatment. *Journal of Mathematical Sciences Advances & Applications*, 40, 75-91.

Khan, M. A., Parvez, M., Islam, S., Khan, I., Shafie, S., & Gul, T. (2015). Mathematical analysis of typhoid model with saturated incidence rate. *Advanced Studies in Biology*, *7*(2), 65-78.

Liao, S., & Yang, W. (2013). On the dynamics of a vaccination model with multiple transmission ways. *International Journal of Applied Mathematics and Computer Science*, *23*(4), 761-772.

Mutua, J. M., Wang, F. B., & Vaidya, N. K. (2015). Modeling malaria and typhoid fever co-infection dynamics. *Mathematical Biosciences*, *264*, 128-144.

Nthiiri T. K., Lawi G. O., Akinyi C. O., Oganga D. O., Muruiki W. C., Musyoka M. J., Otieno P. O., & Koech L. (2016). Mathematical modeling of typhoid fever disease incorporating protection against infection. *British Journal of Mathematics & Computer Science,* 14(1), 1-10.

Peter O. J., Ibrahim M. O., Akinduko O. B., & Rabiu, M. (2017). Mathematical Model for the Control of Typhoid Fever. *IOSR Journal of Mathematics*, 13(4), 60-66.

Peter, O. J., Ibrahim, M. O., Edogbanya, H. O., Oguntolu, F. A., Oshinubi, K., Ibrahim, A. A., & Lawal, J. O. (2021). Direct and indirect transmission of typhoid fever model with optimal control. *Results in Physics*, 27, 104463.

Rihan, F. A., Baleanu, D., Lakshmanan, S., & Rakkiyappan, R. (2014). On fractional SIRC model with salmonella bacterial infection. *Abstract and Applied Analysis*, 5(7), 487 – 499.

Tilahun, G. T., Makinde, O. D., & Malonza, D. (2018). Co-dynamics of pneumonia and typhoid fever diseases with cost effective optimal control analysis. *Applied Mathematics and Computation*, *316*, 438-459.

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.

Wain, J., Bay, P. V. B., Vinh, H. A., Duong, N. M., Diep, T. S., Walsh, A. L., ... & Day, N. P. (2001). Quantitation of bacteria in bone marrow from patients with typhoid fever: relationship between counts and clinical features. *Journal of Clinical Microbiology*, *39*(4), 1571-1576.

Watson, C. H., & Edmunds, W. J. (2015). A review of typhoid fever transmission dynamic models and economic evaluations of vaccination. *Vaccine*, *33*, C42-C54.

World Health Organization (WHO) (2003). Background document; the diagnosis, treatment and prevention of typhoid fever. World Health Organization 2003, 1-26.

World Health Organization (WHO) (2018). Typhoid Fever Fact Sheet. Retrieved from https://www. who.int/news- room/fact-sheets/detail/typhoid

Appendix A

Maple code For computation of R_0

$V := Matrix([[f, 0, 0, 0, 0], [-(1-\sigma)\cdot\alpha, g, 0, -\rho\cdot\omega, 0], [-\sigma\cdot\alpha, -\Pi, h, 0, 0], [0, 0, -\eta, p, 0], [0, -\kappa, -\delta, -\nu, \theta]])$

$$\begin{bmatrix} f & 0 & 0 & 0 & 0 \\ -(1-\sigma)\,\alpha & g & 0 & -\rho\,\omega & 0 \\ -\sigma\,\alpha & -\Pi & h & 0 & 0 \\ 0 & 0 & -\eta & p & 0 \\ 0 & -\kappa & -\delta & -\nu & \theta \end{bmatrix}$$

$V^{(-1)}$

$$\left[\left[\frac{1}{f}, 0, 0, 0, 0\right],\right.$$
$$\left[-\frac{\alpha\,(\eta\,\rho\,\omega\,\sigma - h\,p\,\sigma + h\,p)}{f\,(\Pi\,\eta\,\rho\,\omega - g\,h\,p)}, -\frac{p\,h}{\Pi\,\eta\,\rho\,\omega - g\,h\,p}, -\frac{\rho\,\omega\,\eta}{\Pi\,\eta\,\rho\,\omega - g\,h\,p},\right.$$
$$\left.-\frac{\rho\,\omega\,h}{\Pi\,\eta\,\rho\,\omega - g\,h\,p}, 0\right],$$
$$\left[\frac{\alpha\,(\Pi\,\sigma - g\,\sigma - \Pi)\,p}{(\Pi\,\eta\,\rho\,\omega - g\,h\,p)\,f}, -\frac{\Pi\,p}{\Pi\,\eta\,\rho\,\omega - g\,h\,p}, -\frac{p\,g}{\Pi\,\eta\,\rho\,\omega - g\,h\,p}, -\frac{\Pi\,\rho\,\omega}{\Pi\,\eta\,\rho\,\omega - g\,h\,p}, 0\right],$$
$$\left[\frac{\eta\,\alpha\,(\Pi\,\sigma - g\,\sigma - \Pi)}{f\,(\Pi\,\eta\,\rho\,\omega - g\,h\,p)}, -\frac{\eta\,\Pi}{\Pi\,\eta\,\rho\,\omega - g\,h\,p}, -\frac{\eta\,g}{\Pi\,\eta\,\rho\,\omega - g\,h\,p}, -\frac{h\,g}{\Pi\,\eta\,\rho\,\omega - g\,h\,p}, 0\right],$$
$$\left[\frac{1}{(\Pi\,\eta\,\rho\,\omega - g\,h\,p)\,f\,\theta}(\alpha\,(h\,p\,\kappa\,\sigma - h\,p\,\kappa + \Pi\,p\,\delta\,\sigma - g\,p\,\delta\,\sigma - \Pi\,p\,\delta - \eta\,\rho\,\kappa\,\omega\,\sigma\right.$$
$$\left.+\eta\,\Pi\,\nu\,\sigma - \eta\,g\,\nu\,\sigma - \Pi\,\eta\,\nu)), -\frac{\Pi\,\eta\,\nu + \Pi\,p\,\delta + h\,p\,\kappa}{(\Pi\,\eta\,\rho\,\omega - g\,h\,p)\,\theta}, -\frac{\eta\,\rho\,\kappa\,\omega + \eta\,g\,\nu + g\,p\,\delta}{(\Pi\,\eta\,\rho\,\omega - g\,h\,p)\,\theta},$$
$$\left.-\frac{\Pi\,\rho\,\delta\,\omega + h\,\rho\,\kappa\,\omega + g\,h\,\nu}{(\Pi\,\eta\,\rho\,\omega - g\,h\,p)\,\theta}, \frac{1}{\theta}\right]\Bigg]$$

$factor((2))$

$$F := Matrix\left(\left[\left[0, 0, 0, 0, \frac{\beta \cdot \Lambda}{az - \phi\psi}\right], [0, 0, 0, 0, 0], [0, 0, 0, 0, 0], [0, 0, 0, 0, 0], [0, 0, 0, 0, 0]\right]\right)$$

$$\begin{bmatrix} 0 & 0 & 0 & 0 & \frac{\beta \Lambda}{az - \phi\psi} \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{bmatrix}$$

$$F.V^{(-1)}$$

$$\left[\left[\frac{1}{(az - \phi\psi)\,(\Pi\,\eta\,\rho\,\omega - g\,h\,p)\,f\,\theta}(\beta\,\Lambda\,\alpha\,(h\,p\,\kappa\,\sigma - h\,p\,\kappa + \Pi\,p\,\delta\,\sigma - g\,p\,\delta\,\sigma - \Pi\,p\,\delta \right.\right.$$
$$\left. - \eta\,\rho\,\kappa\,\omega\,\sigma + \eta\,\Pi\,\nu\,\sigma - \eta\,g\,\nu\,\sigma - \Pi\,\eta\,\nu)), -\frac{\beta\,\Lambda\,(\Pi\,\eta\,\nu + \Pi\,p\,\delta + h\,p\,\kappa)}{(az - \phi\psi)\,(\Pi\,\eta\,\rho\,\omega - g\,h\,p)\,\theta},$$
$$-\frac{\beta\,\Lambda\,(\eta\,\rho\,\kappa\,\omega + \eta\,g\,\nu + g\,p\,\delta)}{(az - \phi\psi)\,(\Pi\,\eta\,\rho\,\omega - g\,h\,p)\,\theta}, -\frac{\beta\,\Lambda\,(\Pi\,\rho\,\delta\,\omega + h\,\rho\,\kappa\,\omega + g\,h\,\nu)}{(az - \phi\psi)\,(\Pi\,\eta\,\rho\,\omega - g\,h\,p)\,\theta}, \left.\frac{\beta\,\Lambda}{(az - \phi\psi)\,\theta}\right],$$
$$[0, 0, 0, 0, 0],$$
$$[0, 0, 0, 0, 0],$$
$$[0, 0, 0, 0, 0],$$
$$\left.[0, 0, 0, 0, 0]\right]$$

Appendix B

Maple code For Figure 4.1

```
> i := t→i[0] + (σ·α·E[0] + χ·C[0] − (η + λ + μ)·i[0])·t + 1/2·(σ·α·(β·B[0]·S[0]
      − (α + μ)·E[0]) + χ·((1 − σ)·α·E[0] + ρ·ω·T[0] − (χ + μ)·C[0]) − (η + λ
      + μ)·(σ·α·E[0] + χ·C[0] − (η + χ + μ)·i[0]))·t^2
```

$$i := t \to i_0 + \left(\sigma\,\alpha\,E_0 + \chi\,C_0 - (\eta + \lambda + \mu)\,i_0\right) t + \left(\frac{1}{2}\,\sigma\,\alpha\left(\beta\,B_0\,S_0 - (\alpha + \mu)\,E_0\right) + \frac{1}{2}\,\chi\left((1 - \sigma)\,\alpha\,E_0 + \rho\,\omega\,T_0 - (\chi + \mu)\,C_0\right) - \frac{1}{2}\,(\eta + \lambda + \mu)\left(\sigma\,\alpha\,E_0 + \chi\,C_0 - (\eta + \chi + \mu)\,i_0\right)\right) t^2$$

```
> B1 := eval(i(t), {S[0] = 10000, E[0] = 3500, C[0] = 1000, i[0] = 1500, T[0] = 2000, V[0]
      = 5000, B[0] = 1000, Λ = 500, ω = 0.7, ρ = 0.03, β = 0.002, μ = 0.016, ψ = 0.9, α = 0.81, σ
      = 0.7, χ = 0.8, η = 0.9, λ = 0.005, κ = 0.009, δ = 0.014, ν = 0.004, θ = 0.0345, ϕ = 0.5})
```

$$B1 := 1500 + 1403.000\,t + 4784.066250\,t^2$$

```
> B2 := eval(i(t), {S[0] = 10000, E[0] = 3500, C[0] = 1000, i[0] = 2000, T[0] = 2000, V[0]
      = 5000, B[0] = 1000, Λ = 500, ω = 0.7, ρ = 0.03, β = 0.004, μ = 0.016, ψ = 0.9, α = 0.81, σ
      = 0.7, χ = 0.8, η = 0.9, λ = 0.005, κ = 0.009, δ = 0.014, ν = 0.004, θ = 0.0345, ϕ = 0.7})
```

$$B2 := 2000 + 942.500\,t + 10849.17525\,t^2$$

```
> B3 := eval(i(t), {S[0] = 10000, E[0] = 3500, C[0] = 1000, i[0] = 2000, T[0] = 2000, V[0]
      = 5000, B[0] = 1000, Λ = 500, ω = 0.7, ρ = 0.03, β = 0.006, μ = 0.016, ψ = 0.9, α = 0.81, σ
      = 0.7, χ = 0.8, η = 0.9, λ = 0.005, κ = 0.009, δ = 0.014, ν = 0.004, θ = 0.0345, ϕ = 0.9})
```

$$B3 := 2000 + 942.500\,t + 16519.17525\,t^2$$

```
> plot([B1, B2, B3], t = 0..1, thickness = [1, 2, 3], color = [red, green, blue], linestyle = [solid,
      dash, dot])
```

Appendix C

Maple Code for Figure 4.2

```
> S := t→S[0] + (Λ − β·S[0]·B[0] − (ϕ + μ)·S[0] + (1 − ρ)·ω·T[0] + ψ·V[0])·t + 1/2
  ·(β·(B[0]·(Λ − β·S[0]·B[0] − (ϕ + μ)·S[0] + (1 − ρ)·ω·T[0] + ψ·V[0]) + S[0]
  ·(κ·C[0] + δ·i[0] + ν·T[0] − θ·B[0])) + (ϕ + μ)·(Λ − β·S[0]·B[0] − (ϕ + μ)·S[0
  + (1 − ρ)·ω·T[0] + ψ·V[0]) − (1 − ρ)·ω·(η·i[0] − (ω + λ + μ)·T[0]) − ψ·(ϕ
  ·S[0] − (ψ + μ)·V[0]))·t^2
```

$$S := t \to S_0 + \left(\Lambda - \beta S_0 B_0 - (\phi + \mu) S_0 + (1 - \rho)\,\omega T_0 + \psi V_0\right) t + \left(\frac{1}{2}\beta\left(B_0\left(\Lambda - \beta S_0 B_0 - (\phi + \mu) S_0 + (1 - \rho)\,\omega T_0 + \psi V_0\right) + S_0\left(\nu T_0 + \delta i_0 + \kappa C_0 - \theta B_0\right)\right) + \frac{1}{2}(\phi + \mu)\left(\Lambda - \beta S_0 B_0 - (\phi + \mu) S_0 + (1 - \rho)\,\omega T_0 + \psi V_0\right) - \frac{1}{2}(1 - \rho)\,\omega\left(\eta i_0 - (\omega + \lambda + \mu) T_0\right) - \frac{1}{2}\psi\left(\phi S_0 - (\psi + \mu) V_0\right)\right) t^2$$

```
> B1 := eval(S(t), {S[0] = 10000, E[0] = 3500, C[0] = 1000, i[0] = 1500, T[0] = 2000, V[0]
  = 5000, B[0] = 100, Λ = 500, ω = 0.8, ρ = 0.03, β = 0.002, μ = 0.016, ψ = 0.9, α = 0.81, σ
  = 0.7, χ = 0.8, η = 0.9, λ = 0.005, κ = 0.009, δ = 0.014, ν = 0.004, θ = 0.0345, ϕ = 0.5})
```

$$B1 := 10000 - 608.000\,t + 52.1320000\,t^2$$

```
> B2 := eval(S(t), {S[0] = 10000, E[0] = 3500, C[0] = 1000, i[0] = 1500, T[0] = 2000, V[0]
  = 5000, B[0] = 100, Λ = 500, ω = 0.8, ρ = 0.03, β = 0.002, μ = 0.016, ψ = 0.9, α = 0.81, σ
  = 0.7, χ = 0.8, η = 0.9, λ = 0.005, κ = 0.009, δ = 0.014, ν = 0.004, θ = 0.0345, ϕ = 0.75})
```

$$B2 := 10000 - 3108.000\,t - 2356.368000\,t^2$$

```
> B3 := eval(S(t), {S[0] = 10000, E[0] = 3500, C[0] = 1000, i[0] = 1500, T[0] = 2000, V[0]
  = 5000, B[0] = 100, Λ = 500, ω = 0.8, ρ = 0.03, β = 0.002, μ = 0.016, ψ = 0.9, α = 0.81, σ
  = 0.7, χ = 0.8, η = 0.9, λ = 0.005, κ = 0.009, δ = 0.014, ν = 0.004, θ = 0.0345, ϕ = 0.9})
```

$$B3 := 10000 - 4608.000\,t - 4101.468000\,t^2$$

```
> plot([B1, B2, B3], t = 0..1, thickness = [1, 2, 3], color = [red, green, blue], linestyle = [solid, dash, dot])
```

Appendix D

Maple code for Figure 4.3

```
> C := t→C[0] + ((1 − σ)·α·E[0] + ρ·ω·T[0] − (χ + μ)·C[0])·t + 1/2((1 − σ)·α·(β·B[0]·S[0] − (α + μ)·E[0]) + ρ·ω(η·I[0] − (ω + χ + μ)·T[0]) − (χ + μ)·((1 − σ)·α·E[0] + ρ·ω·T[0] − (χ + μ)C[0]))·t^2
```

$$C := t \to C_0 + \left((1-\sigma)\,\alpha E_0 + \rho\,\omega\,T_0 - (\chi+\mu)\,C_0\right) t + \left(\frac{1}{2}(1-\sigma)\,\alpha\left(\beta B_0 S_0 - (\alpha + \mu) E_0\right) + \frac{1}{2}\rho\,\omega\left(\mathrm{I}\eta[0] - (\omega+\chi+\mu)\,T_0\right) - \frac{1}{2}(\chi+\mu)\left((1-\sigma)\,\alpha E_0 + \rho\,\omega\,T_0 - (\chi+\mu)\,C_0\right)\right) t^2$$

```
> B1 := eval(C(t), {S[0] = 10000, E[0] = 3500, C[0] = 1000, T[0] = 2000, V[0] = 5000, B[0] = 10000, Λ = 500, ω = 0.8, ρ = 0.03, β = 0.002, μ = 0.016, ψ = 0.9, α = 0.81, σ = 0.7, χ = 0.8, η = 0.9, λ = 0.005, κ = 0.009, δ = 0.014, ν = 0.004, θ = 0.0345, ϕ = 0.5})
```

$$B1 := 1000 + 82.500\,t + 23915.09550\,t^2$$

```
> B2 := eval(C(t), {S[0] = 10000, E[0] = 3500, C[0] = 1000, T[0] = 2000, V[0] = 5000, B[0] = 10000, Λ = 500, ω = 0.8, ρ = 0.03, β = 0.002, μ = 0.016, ψ = 0.9, α = 0.90, σ = 0.7, χ = 0.8, η = 0.9, λ = 0.005, κ = 0.009, δ = 0.014, ν = 0.004, θ = 0.0345, ϕ = 0.5})
```

$$B2 := 1000 + 177.000\,t + 26494.98600\,t^2$$

```
> B3 := eval(C(t), {S[0] = 10000, E[0] = 3500, C[0] = 1000, T[0] = 2000, V[0] = 5000, B[0] = 10000, Λ = 500, ω = 0.8, ρ = 0.03, β = 0.002, μ = 0.016, ψ = 0.9, α = 0.99, σ = 0.7, χ = 0.8, η = 0.9, λ = 0.005, κ = 0.009, δ = 0.014, ν = 0.004, θ = 0.0345, ϕ = 0.5})
```

$$B3 := 1000 + 271.500\,t + 29066.37150\,t^2$$

```
> plot([B1, B2, B3], t = 0..1, thickness = [1, 2, 3], color = [red, green, blue], linestyle = [solid, dash, dot])
```

Appendix E

Maple Code for Figure 4.4

```
> T := t→T[0] + (η·i[0] − (ω + λ + μ)·T[0])·t + 1/2·(η·(σ·α·E[0] + χ·C[0] − (η + χ + μ)·i[0]) − (ω + λ + μ)·(η·i[0] − (ω + λ + μ)·T[0]))·t^2
```

$$T := t \to T_0 + \left(\eta\, i_0 - (\omega + \lambda + \mu)\, T_0\right) t + \left(\frac{1}{2}\,\eta\left(\sigma\,\alpha\, E_0 + \chi\, C_0 - (\eta + \chi + \mu)\, i_0\right) - \frac{1}{2}\,(\omega + \lambda + \mu)\left(\eta\, i_0 - (\omega + \lambda + \mu)\, T_0\right)\right) t^2$$

```
> B1 := eval(T(t), {S[0] = 10000, E[0] = 3500, C[0] = 1000, i[0] = 3000, T[0] = 2000, V[0] = 5000, B[0] = 1000000, Λ = 500, ω = 0.7, ρ = 0.03, β = 0.002, μ = 0.016, ψ = 0.9, α = 0.81, σ = 0.7, χ = 0.8, η = 0.5, λ = 0.005, κ = 0.009, δ = 0.014, ν = 0.004, θ = 0.0345, ϕ = 0.5})
```

$$B1 := 2000 + 58.000\, t - 311.7840000\, t^2$$

```
> B2 := eval(T(t), {S[0] = 10000, E[0] = 3500, C[0] = 1000, i[0] = 3000, T[0] = 2000, V[0] = 5000, B[0] = 1000000, Λ = 500, ω = 0.8, ρ = 0.03, β = 0.002, μ = 0.016, ψ = 0.9, α = 0.81, σ = 0.7, χ = 0.8, η = 0.5, λ = 0.005, κ = 0.009, δ = 0.014, ν = 0.004, θ = 0.0345, ϕ = 0.5})
```

$$B2 := 2000 - 142.000\, t - 232.5840000\, t^2$$

```
> B3 := eval(T(t), {S[0] = 10000, E[0] = 3500, C[0] = 1000, i[0] = 3000, T[0] = 2000, V[0] = 500, B[0] = 1000000, Λ = 500, ω = 0.9, ρ = 0.03, β = 0.002, μ = 0.016, ψ = 0.9, α = 0.81, σ = 0.7, χ = 0.8, η = 0.5, λ = 0.005, κ = 0.009, δ = 0.014, ν = 0.004, θ = 0.0345, ϕ = 0.5})
```

$$B3 := 2000 - 342.000\, t - 133.3840000\, t^2$$

```
> plot([B1, B2, B3], t = 0..1, thickness = [1, 2, 3], color = [red, green, blue], linestyle = [solid,
      dash, dot])
```

Appendix F

Maple code for Figure 4.5

```
> V := t→V[0] + (ϕ·S[0] − (ψ + μ)·V[0])·t + 1/2·(ϕ·(Λ − β·B[0]·S[0] − (ϕ + μ)·S[0]
      + (1 − ρ)·ω·T[0] + ψ·V[0]) − (ψ + μ)·(ϕ·S[0] − (ψ + μ)·V[0]))·t^2
```

$$V := t \to V_0 + \left(\phi S_0 - (\psi + \mu)\, V_0\right) t + \left(\frac{1}{2}\,\phi\left(\Lambda - \beta B_0 S_0 - (\phi + \mu) S_0 + (1 - \rho)\,\omega T_0 + \psi V_0\right) - \frac{1}{2}\,(\psi + \mu)\left(\phi S_0 - (\psi + \mu) V_0\right)\right) t^2$$

```
> B1 := eval(V(t), {S[0] = 10000, E[0] = 3500, C[0] = 1000, T[0] = 2000, V[0] = 5000, B[0]
      = 100, Λ = 500, ω = 0.8, ρ = 0.03, β = 0.002, μ = 0.016, ψ = 0.9, α = 0.81, σ = 0.7, χ = 0.8,
      η = 0.9, λ = 0.005, κ = 0.009, δ = 0.014, ν = 0.004, θ = 0.0345, ϕ = 0.5})
```

$$B1 := 5000 + 420.000\, t - 344.3600000\, t^2$$

```
> B2 := eval(V(t), {S[0] = 10000, E[0] = 3500, C[0] = 1000, T[0] = 2000, V[0] = 5000, B[0]
      = 100, Λ = 500, ω = 0.8, ρ = 0.03, β = 0.002, μ = 0.016, ψ = 0.9, α = 0.81, σ = 0.7, χ = 0.8,
      η = 0.9, λ = 0.005, κ = 0.009, δ = 0.014, ν = 0.004, θ = 0.0345, ϕ = 0.75})
```

$$B2 := 5000 + 2920.000\, t - 2502.860000\, t^2$$

```
> B3 := eval(V(t), {S[0] = 10000, E[0] = 3500, C[0] = 1000, T[0] = 2000, V[0] = 5000, B[0]
      = 100, Λ = 500, ω = 0.8, ρ = 0.03, β = 0.002, μ = 0.016, ψ = 0.9, α = 0.81, σ = 0.7, χ = 0.8,
      η = 0.9, λ = 0.005, κ = 0.009, δ = 0.014, ν = 0.004, θ = 0.0345, ϕ = 0.9})
```

$$B3 := 5000 + 4420.000\,t - 4097.960000\,t^2$$

```
> plot([B1, B2, B3], t = 0..0.8, thickness = [1, 2, 3], color = [red, green, blue], linestyle = [solid,
      dash, dot])
```

Appendix G

Maple code for Figure 4.6

```
> E := t→E[0] + (β·B[0]·S[0] - (α + μ)·E[0])·t + 1/2·(β·(B[0]·(Λ - β·B[0]·S[0] - (ϕ
      + μ)·S[0] + (1 - ρ)·ω·T[0] + ψ·V[0]) + S[0]·(κ·C[0] + δ·i[0] + ν·T[0] - θ
      ·B[0])) - (α + μ)·(β·S[0]·B[0] - (α + μ)·E[0]))·t^2
```

$$E := t \to E_0 + \left(\beta B_0 S_0 - (\alpha + \mu) E_0\right) t + \left(\frac{1}{2}\beta\left(B_0\left(\Lambda - \beta B_0 S_0 - (\phi + \mu) S_0 + (1 - \rho)\,\omega T_0 + \psi V_0\right) + S_0\left(\nu T_0 + \delta i_0 + \kappa C_0 - \theta B_0\right)\right) - \frac{1}{2}(\alpha + \mu)\left(\beta B_0 S_0 - (\alpha + \mu) E_0\right)\right) t^2$$

```
> B1 := eval(E(t), {S[0] = 10000, E[0] = 3500, C[0] = 1000, i[0] = 1000, T[0] = 2000, V[0]
      = 5000, B[0] = 100, Λ = 500, ω = 0.8, ρ = 0.03, β = 0.002, μ = 0.016, ψ = 0.9, α = 0.81, σ
      = 0.7, χ = 0.8, η = 0.9, λ = 0.005, κ = 0.009, δ = 0.014, ν = 0.004, θ = 0.0345, ϕ = 0.5})
```

$$B1 := 3500 - 891.000\,t + 582.6830000\,t^2$$

```
> B2 := eval(E(t), {S[0] = 10000, E[0] = 3500, C[0] = 1000, i[0] = 1000, T[0] = 2000, V[0]
      = 5000, B[0] = 100, Λ = 500, ω = 0.8, ρ = 0.03, β = 0.002, μ = 0.016, ψ = 0.9, α = 0.81, σ
      = 0.7, χ = 0.8, η = 0.9, λ = 0.005, κ = 0.009, δ = 0.014, ν = 0.004, θ = 0.0345, ϕ = 0.75})
```

$$B2 := 3500 - 891.000\,t + 332.6830000\,t^2$$

```
B3 := eval(E(t), {S[0] = 10000, E[0] = 3500, C[0] = 1000, i[0] = 1000, T[0] = 2000, V[0]
      = 5000, B[0] = 100, Λ = 500, ω = 0.8, ρ = 0.03, β = 0.002, μ = 0.016, ψ = 0.9, α = 0.81, σ
      = 0.7, χ = 0.8, η = 0.9, λ = 0.005, κ = 0.009, δ = 0.014, ν = 0.004, θ = 0.0345, ϕ = 0.9})
>
```

$$B3 := 3500 - 891.000\,t + 182.6830000\,t^2$$

```
plot([B1, B2, B3], t = 0..1, thickness = [1, 2, 3], color = [red, green, blue], linestyle = [solid,
      dash, dot])
>
```

Appendix H

Maple Code for Figure 4.7

```
C := t→C[0] + ((1 − σ)·α·E[0] + ρ·ω·T[0] − (χ + μ)·C[0])·t + 1/2((1 − σ)·α·(β
      ·B[0]·S[0] − (α + μ)·E[0]) + ρ·ω(η·I[0] − (ω + χ + μ)·T[0]) − (χ + μ)·((1
      − σ)·α·E[0] + ρ·ω·T[0] − (χ + μ)C[0]))·t^2
>
```

$$C := t \to C_0 + \left((1-\sigma)\,\alpha\,E_0 + \rho\,\omega\,T_0 - (\chi+\mu)\,C_0\right)t + \left(\frac{1}{2}(1-\sigma)\,\alpha\left(\beta\,B_0\,S_0 - (\alpha + \mu)\,E_0\right) + \frac{1}{2}\rho\,\omega\left(\mathrm{I}\eta[0] - (\omega+\chi+\mu)\,T_0\right) - \frac{1}{2}(\chi+\mu)\left((1-\sigma)\,\alpha\,E_0 + \rho\,\omega\,T_0 - (\chi+\mu)\,C_0\right)\right)t^2$$

```
B1 := eval(C(t), {S[0] = 10000, E[0] = 3500, C[0] = 1000, T[0] = 2000, V[0] = 5000, B[0]
      = 1000000, Λ = 500, ω = 0.0357, ρ = 0.03, β = 0.002, μ = 0.016, ψ = 0.9, α = 0.81, σ = 0.7,
      χ = 0.8, η = 0.9, λ = 0.005, κ = 0.009, δ = 0.014, ν = 0.004, θ = 0.0345, ϕ = 0.5})
>
```

$$B1 := 1000 + 36.642000\,t + 2.429633795\,10^6\,t^2$$

```
B2 := eval(C(t), {S[0] = 10000, E[0] = 3500, C[0] = 1000, T[0] = 2000, V[0] = 5000, B[0]
      = 1000000, Λ = 500, ω = 0.0357, ρ = 0.03, β = 0.003, μ = 0.016, ψ = 0.9, α = 0.81, σ = 0.7,
      χ = 0.8, η = 0.9, λ = 0.005, κ = 0.009, δ = 0.014, ν = 0.004, θ = 0.0345, ϕ = 0.5})
>
```

$$B2 := 1000 + 36.642000\,t + 3.644633795\,10^{6}\,t^{2}$$

```
B3 := eval(C(t), {S[0] = 10000, E[0] = 3500, C[0] = 1000, T[0] = 2000, V[0] = 5000, B[0]
      = 1000000, Λ = 500, ω = 0.0357, ρ = 0.03, β = 0.004, μ = 0.016, ψ = 0.9, α = 0.81, σ = 0.7,
      χ = 0.8, η = 0.9, λ = 0.005, κ = 0.009, δ = 0.014, ν = 0.004, θ = 0.0345, ϕ = 0.5})
>
```

$$B3 := 1000 + 36.642000\,t + 4.859633795\,10^{6}\,t^{2}$$

```
plot([B1, B2, B3], t = 0 ..1, thickness = [1, 2, 3], color = [red, green, blue], linestyle = [solid,
      dash, dot])
>
```